2.7.4 臨床的安全性

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略語及び定義一覧

略語又は用語	省略していない表現又は説明 (英語)	省略していない表現又は説明 (日本語)
AD	atopic dermatitis	アトピー性皮膚炎
ADA	adalimumab	アダリムマブ
ALT	alanine aminotransferase	アラニンアミノトランスフェラーゼ
AS	ankylosing spondylitis	強直性脊椎炎
AST	aspartate aminotransferase	アスパラギン酸アミノトランスフェラーゼ
AUC	area under the plasma concentration-time curve	血漿中濃度－時間曲線下面積
AUC_{inf}	area under the plasma concentration-time curve from time zero to infinity	0 時間から無限大時間までの血漿中濃度－時間曲線下面積
bDMARD	biologic disease-modifying anti-rheumatic drug	生物学的疾患修飾性抗リウマチ薬
bDMARD-IR	biologic disease modifying anti-rheumatic drug inadequate response	生物学的疾患修飾性抗リウマチ薬で効果不十分又は忍容性のない被験者
BID	twice daily	1 日 2 回
BMI	body mass index	体格指数
CAC	Cardiovascular Adjudication Committee	心血管イベント判定委員会
CD	Crohn's disease	クローン病
CI	confidence interval	信頼区間
C_{max}	maximum plasma concentration	最高血漿中濃度
CMQ	company MedDRA query	--
CPK	creatine phosphokinase	クレアチンホスホキナーゼ
CSR	clinical study report	治験総括報告書
CTCAE	common terminology criteria for adverse events	有害事象共通用語規準
CV	cardiovascular	心血管系
DMARD	disease-modifying anti-rheumatic drug	疾患修飾性抗リウマチ薬
DNA	deoxyribonucleic acid	デオキシリボ核酸
eDISH	evaluation of drug-induced serious hepatotoxicity	重篤な薬物肝毒性の評価
eGFR	estimated glomerular filtration rate	推算糸球体濾過率
EOW	every other week	隔週
HBc Ab	hepatitis B core antibody	B 型肝炎ウイルスコア抗体
HBV	hepatitis B virus	B 型肝炎ウイルス
HDL-C	high-density lipoprotein cholesterol	高比重リポ蛋白コレステロール
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use	医薬品規制調和国際会議
INR	international normalized ratio	国際標準化比
ISS	Integrated Summary of Safety	--

略語又は用語	省略していない表現又は説明 (英語)	省略していない表現又は説明 (日本語)
IUD	intrauterine device	子宮内避妊器具
JAK	janus kinase	ヤヌスキナーゼ
J-ISS	Japan Integrated Summary of Safety	--
JSA	Japan population sub-group analysis	--
LDL-C	low-density lipoprotein cholesterol	低比重リポ蛋白コレステロール
MACE	major adverse cardiovascular event	主要心血管イベント
Max	maximum	最大値
MedDRA	Medical Dictionary for Regulatory Activities	ICH 国際医薬用語集
Min	minimum	最小値
MTX	methotrexate	メトトレキサート
NCI	National Cancer Institute	(米) 国立がん研究所
NMSC	non-melanoma skin cancer	非黒色腫皮膚癌
non-bDMARD	non-biologic disease-modifying anti-rheumatic drug	非生物学的疾患修飾性抗リウマチ薬
non-bDMARD-IR	non-biologic disease modifying anti-rheumatic drug inadequate response	非生物学的疾患修飾性抗リウマチ薬で効果不十分又は忍容性のない被験者
NSAIDs	non-steroidal anti-inflammatory drugs	非ステロイド性抗炎症薬
PBO	Placebo	プラセボ
PCR	polymerase chain reaction	ポリメラーゼ連鎖反応
PPD	purified protein derivative	精製ツベルクリンたん白
PsA	psoriatic arthritis	乾癬性関節炎
PT	preferred term	基本語
PY	patient-year	人年
Q	quartile	四分位数
QD	once daily	1 日 1 回
RA	rheumatoid arthritis	関節リウマチ
SD	standard deviation	標準偏差
SIR	standard incidence ratios	標準化罹患比
SMQ	standard MedDRA query	MedDRA 標準検索式
SOC	system organ class	器官別大分類
SSA	study size adjusted	--
TBL	total bilirubin	総ビリルビン
TNF	tumor necrosis factor	腫瘍壊死因子
UC	ulcerative colitis	潰瘍性大腸炎
ULN	upper limit of normal	基準値上限
UPA	upadacitinib	ウパダシチニブ

略語又は用語	省略していない表現又は説明 (英語)	省略していない表現又は説明 (日本語)
vs	versus	対
VTE	venous thromboembolic events	静脈血栓塞栓症
W	week	週 (間)

2.7.4.1 医薬品への曝露

2.7.4.1.1 総括的安全性評価計画及び安全性試験の記述

2.7.4.1.1.1 安全性の評価に用いた臨床試験

ウパダシチニブの安全性は，臨床データパッケージのうち，主に乾癬性関節炎を対象とした 2 つの第 III 相試験について評価した。安全性評価に用いた臨床試験の一覧を表 2.7.4-1 に示す（詳細は表 2.7.3-1 参照）。

2 つの第 III 相試験はいずれも評価資料であり，日本人を含む国際共同試験の M15-572 試験（5.3.5.1-1 項）及び M15-554 試験（5.3.5.1-2 項）であった。試験対象は，M15-572 試験が 1 種類以上の非生物学的疾患修飾性抗リウマチ薬（以下「non-bDMARD」）で効果不十分又は忍容性のない中等症から重症の活動性乾癬性関節炎であり，M15-554 試験が 1 種類以上の生物学的疾患修飾性抗リウマチ薬（以下「bDMARD」）で効果不十分又は忍容性のない中等症から重症の活動性乾癬性関節炎であった。いずれの試験も実施中である。各試験の 24 週間（以下「W24」）の治験総括報告書（以下「CSR」）のデータカットオフ日は，M15-572 試験が 20[redacted] 年 [redacted] 月 [redacted] 日，M15-554 試験が 20[redacted] 年 [redacted] 月 [redacted] 日であり，56 週間（以下「W56」）の CSR のデータカットオフ日は，M15-572 試験が 20[redacted] 年 [redacted] 月 [redacted] 日，M15-554 試験が 20[redacted] 年 [redacted] 月 [redacted] 日であった。本臨床的安全性の評価は，投与 56 週時データカットオフまでの結果に基づき行った。なお，ウパダシチニブ市販予定製剤のバイオアベイラビリティを第 III 相試験で使用した製剤と比較した第 I 相試験（M20-017 試験，参考資料）の安全性の結果は，2.7.6 項及び M20-017 試験 CSR（5.3.1.2-1 項）に示し，本項では重篤な有害事象の結果のみを示した。

表 2.7.4-1. 安全性評価に用いた臨床試験の一覧

評価 / 参考資料	試験番号 資料番号	国内 / 海外試験	対象患者	試験の相	比較 / 非盲検試験	試験の進行状況 報告書の種類
評価資料	M15-572 5.3.5.1-1 (24 週間) 5.3.5.1-1-2 (56 週間)	日本人を含む国際共同試験	乾癬性関節炎	第 III 相	比較試験	継続中 24 週間治験総括報告書 (データカットオフ日：20[redacted] 年 [redacted] 月 [redacted] 日) 56 週間治験総括報告書 (データカットオフ日：20[redacted] 年 [redacted] 月 [redacted] 日)
評価資料	M15-554 5.3.5.1-2 (24 週間) 5.3.5.1-2-2 (56 週間)	日本人を含む国際共同試験	乾癬性関節炎	第 III 相	比較試験	継続中 24 週間治験総括報告書 (データカットオフ日：20[redacted] 年 [redacted] 月 [redacted] 日) 56 週間治験総括報告書 (データカットオフ日：20[redacted] 年 [redacted] 月 [redacted] 日)
参考資料	M20-017 5.3.1.2-1	多施設共同試験	おおむね健康な被験者	第 I 相	非盲検試験	終了 治験総括報告書

2.7.4.1.1.2 安全性に関する評価方法

2.7.4.1.1.2.1 解析対象集団

2.7.4.1.1.2.1.1 併合解析の解析対象集団

ウパダシチニブの安全性の評価では，個々の試験に加え，併合解析対象集団を設定した。安全性併合解析の統計解析計画及び解析結果は，申請時データカットオフを Integrated Summary of Safety（以下「ISS」：5.3.5.3-2 項），更新時データカットオフを ISS update（5.3.5.3-2-2 項）に示した。

安全性併合解析には，2 つの第 III 相試験（M15-572 試験及び M15-554 試験）を用いた。ISS での申請時データカットオフ日は，各試験の CSR W24 のデータカットオフ日と同じ日とした。また，更新時データカットオフ日は 20[redacted] 年 [redacted] 月 [redacted] 日とした（ISS を構成する各試験のデータカットオフ日は，M15-572 試験は 20[redacted] 年 [redacted] 月 [redacted] 日，M15-554 試験は CSR W56 と同じ日［20[redacted] 年 [redacted] 月 [redacted] 日］であった）。

ISS の安全性併合解析対象集団の構成及び定義を表 2.7.4-2 に示す。なお，アダリムマブは M15-572 試験でのみ投与されたことから，アダリムマブの詳細データは原則として安全性併合解析には含めなかったが，有害事象の概要及び特に注目すべき有害事象の概要にはアダリムマブ群も記載した。

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また，各併合解析対象集団では，日本人部分集団を解析対象とした部分集団解析も実施した。日本人部分集団の結果は，申請時データカットオフを Japan Integrated Summary of Safety（以下「J-ISS」：5.3.5.3-3 項），更新時データカットオフを J-ISS update（5.3.5.3-3-2 項）に示した。

表 2.7.4-2. ISS の安全性併合解析対象集団の構成及び定義

解析対象集団	定義及び目的 [b]	解析	併合した試験	投与群
プラセボ対照併合解析集団 (PBO-controlled Analysis Set)	ウパダシチニブ 15 mg 及び 30 mg の短期安全性をプラセボと比較し評価する。 ウパダシチニブ 15 mg 群及び 30 mg 群，並びにプラセボ群の投与 24 週時までのデータを併合した。	短期 (24 週)	M15-572 M15-554	ウパダシチニブ 15 mg 併合群 (UPA 15 mg QD) ウパダシチニブ 30 mg 併合群 (UPA 30 mg QD) プラセボ併合群 (Placebo)
全ウパダシチニブ併合解析集団 [a] (Any Upadacitinib Analysis Set)	ウパダシチニブの長期安全性を評価する。 ウパダシチニブ 15 mg 又は 30 mg を投与された被験者のデータを併合した。	長期 (全曝露)	M15-572 M15-554	ウパダシチニブ 15 mg 併合群 (プラセボからの切り替えを含まない)[c] (UPA 15 mg QD [No Cross-Over from Placebo]) ウパダシチニブ 30 mg 併合群 (プラセボからの切り替えを含まない)[c] (UPA 30 mg QD [No Cross-Over from Placebo]) 全ウパダシチニブ 15 mg 併合群 [d] (Any UPA 15 mg QD) 全ウパダシチニブ 30 mg 併合群 [d] (Any UPA 30 mg QD)

PBO = プラセボ，QD = 1 日 1 回，UPA = ウパダシチニブ

a. ウパダシチニブを投与されたすべての被験者

b. 投与群の比較は，有害事象の概要，特に注目すべき有害事象の概要及び臨床的に意義があると判断した臨床検査値について行った。

c. ランダム化時にウパダシチニブ 15 mg / 30 mg の投与を開始した被験者

d. ランダム化時にウパダシチニブ 15 mg / 30 mg の投与を開始した被験者及びプラセボからウパダシチニブ 15 mg / 30 mg に切り替えた被験者

相互参照：ISS Statistical Analysis Plan Table 2

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2.7.4.1.1.2.1.2 個々の試験の解析対象集団

M15-572 試験及び M15-554 試験とも，安全性の解析は，治験薬を投与されたすべての被験者を安全性解析対象集団として実施した。被験者はランダム化された投与群にかかわらず，実際に投与された治験薬に基づいて投与群に割り振られた。

M15-572 試験及び M15-554 試験の安全性解析の概要を表 2.7.4-3 に示す。

表 2.7.4-3. M15-572 試験及び M15-554 試験の安全性解析の概要

解析	説明	投与群
投与 24 週時までの安全性解析	投与 24 週時までのプラセボ対照期間のデータを用いた。投与 24 週時までは，治験実施計画書で規定した治験薬の切り替えは発生しない。	ウパダシチニブ 15 mg 群 (UPA 15 mg QD) ウパダシチニブ 30 mg 群 (UPA 30 mg QD) プラセボ群 (Placebo) アダリムマブ群 (ADA 40 mg EOW，M15-572 試験のみ)
長期安全性解析	データカットオフまでのデータを用いた。ウパダシチニブ各群には，試験開始時にウパダシチニブ 15 mg / 30 mg の投与を開始した被験者及び投与 24 週時にウパダシチニブ 15 mg / 30 mg に切り替えた被験者を含めた。	全ウパダシチニブ 15 mg 群 (プラセボからの切り替えを含む) (UPA 15 mg QD) 全ウパダシチニブ 30 mg 群 (プラセボからの切り替えを含む) (UPA 30 mg QD) アダリムマブ群 (ADA 40 mg EOW，M15-572 試験のみ)

ADA = アダリムマブ，EOW = 隔週，QD = 1 日 1 回，UPA = ウパダシチニブ

相互参照：M15-572 試験 Statistical Analysis Plan，M15-554 試験 Statistical Analysis Plan

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2.7.4.1.1.2.1.3 日本人部分集団

M15-572 試験及び M15-554 試験は，日本人を含む国際共同第 III 相比較試験であり，日本人のデータのみを抽出した日本人部分集団を解析対象として部分集団解析を行った。投与 24 週時データカットオフは，M15-572 試験 Japan population sub-group analysis（以下「JSA」）：5.3.5.4-1 項及び M15-554 試験 JSA：5.3.5.4-2 項，投与 56 週時データカットオフは，M15-572 試験 JSA W56：5.3.5.4-1-2 項及び M15-554 試験 JSA W56：5.3.5.4-2-2 項に示す。

2.7.4.1.1.2.2 有害事象

2.7.4.1.1.2.2.1 安全性併合解析の有害事象

治験薬投与後に発現した有害事象は，治験薬投与開始日から投与終了後 30 日まで（アダリムマブは 70 日まで）に発現した又は重症度が悪化した有害事象と定義し，本項では特に記載のない限り，治験薬投与後に発現した有害事象を示した。

有害事象コーディング辞書として ICH 国際医薬用語集（以下「MedDRA」）version 22.0（有害事象和訳辞書は MedDRA/J）を用い，器官別大分類（以下「SOC」）別及び基本語（以下「PT」）別の有害事象を投与群別に集計した。

有害事象の集計では，発現割合，100 人年あたりの発現件数及び 100 人年あたりの発現被験者数を算出した。発現割合の算出では，分母は全被験者数，分子は有害事象の発現被験者数とした。100 人年あたりの発現件数の算出では，分母は総曝露期間，分子は有害事象の発現件数とし，同一被験者が同一の有害事象を複数回発現した場合，それぞれの発現をカウントした。100 人年あたりの発現被験者数の算出では，分母は最初の有害事象が発現するまでの総曝露期間，分子は有害事象の発現被験者数とした。また，有害事象の集計に加え，治験薬と関連ありの有害事象，高度（Grade 3 以上又は重症度不明）の有害事象（以下「Grade 3 以上の有害事象」），死亡に至った有害事象，重篤な有害事象，治験薬の投与中止に至った有害事象及び特に注目すべき有害事象も集計した。

更に，試験の被験者数（試験サイズ）の違いを考慮するため，試験サイズで調整した発現割合及び 100 人年あたりの発現件数 / 発現被験者数も示した。短期解析では，各併合群の発現割合及びウパダシチニブ各併合群とプラセボ併合群の差の 95%信頼区間を試験サイズで調整した推定法[1]を用いて算出した。長期解析では，各併合群の発現割合及び全ウパダシチニブ 15 mg 併合群と 30 mg 併合群の差の 95%信頼区間を試験サイズで調整した推定法を用いて算出した。ウパダシチニブ 15 mg 併合群と 30 mg 併合群の比較は，ランダム化時ウパダシチニブ併合群における比較と全ウパダシチニブ併合群における比較の 2 種類で行った。100 人年あたりの発現件数 / 発現被験者数も同様に算出した。

特に注目すべき有害事象の定義を表 2.7.4-4 に示す。

表 2.7.4-4. 特に注目すべき有害事象の定義

特に注目すべき有害事象	MedDRA 検索式	検索基準
重篤な感染症	CMQ	CMQ「Infections (感染症)」のうち，重篤な事象
日和見感染 (結核及び帯状疱疹を除く)	CMQ	CMQ「Opportunistic Infection Excluding Tuberculosis and Herpes Zoster (日和見感染から結核及び帯状疱疹を除いた事象) 」
悪性腫瘍 (可能性を含む)	SMQ (狭域)	「悪性疾患」
悪性腫瘍	SMQ	「悪性腫瘍」
非黒色腫皮膚癌 (NMSC)	SMQ (狭域)	SMQ「悪性皮膚腫瘍」(狭域) から CMQ 「Melanoma (黒色腫) 」を除いた事象
悪性腫瘍 (NMSC を除く)	－	SMQ「悪性腫瘍」から NMSC を除いた事象
リンパ腫	SMQ	「悪性リンパ腫」
薬物性肝障害	SMQ (狭域)	「薬剤に関連する肝障害－包括的検索」
消化管穿孔	SMQ「消化管の穿孔」(狭域) で特定し，メディカルレビューで判定された事象	－
貧血	CMQ	「Non-Hemolytic and Non-Aplastic Anemias (非溶血性及び非再生不良性貧血) 」
好中球減少症	CMQ	「Hematological Toxicity – Neutropenia (血液学的毒性－好中球減少症) 」
リンパ球減少症	CMQ	「Hematological Toxicity – Lymphopenia (血液学的毒性－リンパ球減少症) 」
帯状疱疹	CMQ	「Herpes Zoster (帯状疱疹) 」
CPK 増加	PT	「血中クレアチンホスホキナーゼ増加」
腎機能障害	SMQ (狭域)	「急性腎不全」
活動性結核	CMQ	「Active Tuberculosis (活動性結核) 」
委員会判定された心血管イベント	CAC で判定された事象	－
主要心血管イベント (MACE)[a]	(同上)	－
心血管イベントによる死亡	(同上)	－
非致死性心筋梗塞	(同上)	－

特に注目すべき有害事象	MedDRA 検索式	検索基準
非致死性脳卒中	(同上)	－
その他の委員会判定された心血管イベント	(同上)	－
死亡 (原因未特定 / 不明)	(同上)	－
血栓症	CAC で判定された事象	－
静脈血栓塞栓症 [b]	(同上)	－
深部静脈血栓症	(同上)	－
肺塞栓症	(同上)	－
その他の静脈血栓症	(同上)	－
動脈血栓塞栓症 (非心臓性，非神経性)	(同上)	－

CAC = 心血管イベント判定委員会，CMQ = company MedDRA query，CPK = クレアチンホスホキナーゼ，MedDRA = ICH 国際医薬用語集，NMSC = 非黒色腫皮膚癌，PT = 基本語，SMQ = MedDRA 標準検索式

a. 主要心血管イベントは，心血管イベントによる死亡，非致死性心筋梗塞及び非致死性脳卒中と定義した。

b. 静脈血栓塞栓症は，深部静脈血栓症及び肺塞栓症（致死性及び非致死性）と定義した。

相互参照：ISS Statistical Analysis Plan Table 5

重要な有害事象の初回発現の時間的傾向を検討するため，重篤な有害事象，重篤な感染症，日和見感染（結核及び帯状疱疹を除く），帯状疱疹，悪性腫瘍（非黒色腫皮膚癌［以下「NMSC」］を除く），NMSC，主要心血管イベント（以下「MACE」）及び判定された静脈血栓塞栓症について，3 ヵ月，6 ヵ月，12 ヵ月，18 ヵ月，24 ヵ月，30 ヵ月及び 36 ヵ月時点の Kaplan-Meier 推定値を算出してプロットを作成した。本解析では，試験を層別因子として用いた。また，重篤な薬物肝毒性の評価（以下「eDISH」）のプロットを含め，必要なデータの図を作成した。

2.7.4.1.1.2.2.2 個々の試験の有害事象

治験薬投与後に発現した有害事象の定義

M15-572 試験及び M15-554 試験とも，治験薬投与後に発現した有害事象は，治験薬投与開始日から投与終了後 30 日まで（皮下投与する治験薬［アダリムマブ］は 70 日まで）に発現した又は重症度が悪化した有害事象と定義し，本項では特に記載のない限り，治験薬投与後に発現した有害事象を示した。

有害事象の収集期間

M15-572 試験では，すべての有害事象の収集期間は，治験薬の投与開始日から皮下投与する治験薬の投与終了後 70 日まで，及び経口投与する治験薬の投与終了後 30 日までとし，調査結果か，被験者の自発報告であるかにかかわらず収集した。治験薬の投与を中止したが，試験に参

加している被験者は，治験薬の投与を中止した後も，試験に参加している間は継続して重篤な有害事象及び非重篤な有害事象を収集した。また，重篤な有害事象及び治験実施計画書の手順と関連した非重篤な有害事象（試験の手順により発現した有害事象）は，被験者の同意を文書で取得した時点から収集した。なお，アダリムマブを投与した被験者では，治験薬の最終投与から 70 日を超えて発現した有害事象，ウパダシチニブ又はプラセボを投与した被験者では，治験薬の最終投与から 30 日を超えて発現した有害事象は，治験薬投与後に発現した有害事象の要約に含めなかった。

M15-554 試験では，すべての有害事象の収集期間は，治験薬投与開始日から投与終了後 30 日までとし，調査結果か，被験者の自発報告であるかにかかわらず収集した。治験薬の投与を中止したが，試験に参加している被験者は，治験薬の投与を中止した後も，試験に参加している間は継続して重篤な有害事象及び非重篤な有害事象を収集した。また，重篤な有害事象及び治験実施計画書の手順と関連した非重篤な有害事象（試験の手順により発現した有害事象）は，被験者の同意を文書で取得した時点から収集した。なお，治験薬の最終投与から 30 日を超えて発現した有害事象は，治験薬投与後に発現した有害事象の要約に含めなかった。

<u>重症度の定義</u>

M15-572 試験及び M15-554 試験とも，（米）国立がん研究所（NCI）有害事象共通用語規準（以下「CTCAE」）version 5.0 に基準がある場合，この基準に従って有害事象の重症度を評価した。特定の事象に対するガイダンスがない場合，以下のとおり重症度を評価した。

- 軽度（Grade 1）：無症状又は軽度の症状，臨床所見又は診断所見のみ，治療介入不要
- 中等度（Grade 2）：最低限の局所的又は非侵襲的な治療介入を要する，年齢に応じた手段的日常生活動作に制限が生じる（手段的日常生活動作とは，食事の準備，食料品や衣類の買い物，電話の使用，金銭の管理などを指す）
- 高度（Grade 3–5）：
  - Grade 3：重症又は医学的に重大であるが直ちに生命を脅かすわけではない，入院又は入院期間の延長を要する，障害に至る，自立日常生活動作に制限が生じる（自立日常生活動作とは，入浴，着替え，食事，トイレ，薬の服用，及び寝たきりではない状態を指す）
  - Grade 4：生命を脅かす結果に至る。緊急の治療介入を要する
  - Grade 5：有害事象に関連する死亡

<u>因果関係の定義</u>

M15-572 試験及び M15-554 試験とも，治験責任医師は，以下の定義に従って，有害事象の治験薬との因果関係を評価した。

- 関連あり（Reasonable possibility）：イベントの発現時期，生物学的妥当性，臨床的判断，潜在的代替的要因を含む要因を考慮した上で，因果関係を示唆する十分な証拠（情報）がある。
- 関連なし（No reasonable possibility）：イベントの発現時期，生物学的妥当性，臨床的判断，潜在的な代替原因などの要因を考慮した上で，因果関係を示唆する証拠（情報）は不十分である。

治験薬との因果関係の評価に関しては，治験薬との合理的な因果関係があると考えられる場合を「関連あり」，治験薬との合理的な因果関係がないと考えられる場合を「関連なし」と評価した。因果関係が報告されなかった有害事象又は評価不能と判定された有害事象は，治験薬との因果関係「関連あり」として取り扱った。

なお，治験責任医師が重篤な有害事象を「関連なし」と評価する場合は，治験責任医師はその他の原因を示すこととした。

<u>重篤な有害事象の定義</u>

M15-572 試験及び M15-554 試験とも，有害事象が以下の基準に該当した場合，重篤な有害事象とした。

- 死亡：被験者が死亡した事象
- 生命を脅かすもの：適切な処置をしなければ患者を死の危険にさらしていたと判断される事象。その事象がもっと重症なものであった場合，死に至ったかもしれないという仮定的な意味ではない。
- 入院又は入院期間の延長：期間の長短にかかわらず，被験者を入院又は入院中についてはその期間延長に至らしめた事象。救急救命室や外来措置となった事象はこれに該当しない。
- 先天性の異常：出産時又は出産後に認められた奇形，あるいは胎児死亡に至った事象。
- 永続的又は顕著な障害 / 機能不全：被験者の日常生活の活動に支障をきたす永続的又は顕著な障害 / 機能不全。医学的重要性が比較的低い事象，例えば頭痛，嘔気，嘔吐，下痢，インフルエンザ又は足首の捻挫などの突発的な外傷などは該当しない。
- 重篤な転帰を防ぐために内科的又は外科的処置を必要とする医学的に重要な事象：直ちに生命を脅かす，あるいは死に至る又は入院が必要とはならない場合でも，医学的判断から被験者を臨床上好ましくない状態に至らしめる事象，あるいは上記の転帰（死亡，生命を脅かすもの，入院又は入院期間の延長，先天性の異常，永続的又は顕著な障害 / 機能不全）に至らないように医学的又は外科的処置を必要とする事象。更に，自然流産，人工流産，死産はすべて医学的に重要な事象とする。これには救急救命室又は自宅にて集中治療を必要とするアレルギー性気管支痙攣，入院には至らない悪液質又は痙攣，あるいは薬物依存又は薬物乱用が該当する。

有害事象の解析

M15-572 試験及び M15-554 試験では，有害事象コーディング辞書として MedDRA version 22.0（有害事象和訳辞書は MedDRA/J）を用い，SOC 別及び PT 別の有害事象を投与群別に集計した。また，長期での有害事象発現状況を評価するため，有害事象の 100 人年あたりの発現件数も算出した。有害事象の集計に加え，治験薬と関連ありの有害事象，重篤な有害事象，高度（Grade 3 以上又は重症度不明）の有害事象（以下「Grade 3 以上の有害事象」），死亡に至った有害事象，治験薬の投与中止に至った有害事象及び特に注目すべき有害事象も集計した。

2.7.4.1.1.2.3 臨床検査

M15-572 試験及び M15-554 試験の臨床検査測定項目は，各試験の治験実施計画書に示した。血液学的検査，血液生化学検査及び尿検査パラメータについては，測定時点ごと及び投与群別に要約統計量を示した。ヘモグロビン，血小板，リンパ球，好中球，白血球（ISS のみ），クレアチニン，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（以下「CPK」），低比重リポ蛋白コレステロール（以下「LDL-C」），高比重リポ蛋白コレステロール（以下「HDL-C」），総コレステロール / HDL-C 比，LDL-C / HDL-C 比及び総コレステロールでは，ベースラインからの変化量について治療を因子とした分散分析（M15-572 試験及び M15-554 試験）又は共分散分析（ISS）モデルを用いて投与群間比較した。プラセボ群（両試験）又はアダリムマブ群（M15-572 試験のみ）との平均値の差及び 95%信頼区間を示した。

臨床的に意義があると判断した臨床検査値の基準に該当した被験者数及びその割合を投与群別に要約した。臨床的に意義があると判断した臨床検査値の基準は，CTCAE で Grade がベースラインと比較して悪化し，Grade 2，Grade 3，Grade 4，又は Grade 3 以上に該当した場合とした。CTCAE は version 4.03 を用いた。

2.7.4.1.1.2.4 バイタルサイン及び心電図

M15-572 試験及び M15-554 試験とも，収縮期血圧，拡張期血圧，脈拍数，呼吸数，体重，体温及び 12 誘導心電図を測定した。バイタルサイン（収縮期血圧，拡張期血圧，脈拍数及び体重）については，測定時点ごと及び投与群別に要約統計量を示した。また，臨床的に意義があると判断したバイタルサインの基準（表 2.7.4-5）に該当した被験者数及びその割合を投与群別に要約した。

表 2.7.4-5. 臨床的に意義があると判断したバイタルサインの基準

バイタルサイン	カテゴリー	基準
収縮期血圧	低値	≤ 90 mmHg かつベースラインから≥ 20 mmHg 低下
	高値	≥ 160 mmHg かつベースラインから≥ 20 mmHg 上昇
拡張期血圧	低値	≤ 50 mmHg かつベースラインから≥ 10 mmHg 低下
	高値	≥ 100 mmHg かつベースラインから≥ 10 mmHg 上昇
脈拍数	低値	≤ 50 bpm かつベースラインから≥ 15 bpm 低下
	高値	≥ 120 bpm かつベースラインから≥ 15 bpm 上昇
体重	低値	ベースラインから> 7%減少
	高値	ベースラインから> 7%増加

2.7.4.1.2 全般的な曝露状況

2.7.4.1.2.1 被験者の内訳

本項では，安全性併合解析集団の被験者の内訳を示す。個々の試験のデータは 2.7.3.3.1.1 項に示した。

2.7.4.1.2.1.1 プラセボ対照併合解析

プラセボ対照併合解析集団（投与 24 週時）では，ウパダシチニブ 15 mg 併合群 640 名，ウパダシチニブ 30 mg 併合群 641 名及びプラセボ併合群 635 名に治験薬を投与した（ISS Table 2.1__1.1）。プラセボ対照期間に治験薬の投与を中止した被験者の割合は，ウパダシチニブ 15 mg 併合群で 8.8%（56/640 名），ウパダシチニブ 30 mg 併合群で 9.8%（63/641 名），プラセボ併合群で 13.7%（87/635 名）であった。最も多かった中止理由は，ウパダシチニブ併合群では有害事象（15 mg 併合群：3.9%［25/640 名］，30 mg 併合群：5.5%［35/641 名］），プラセボ併合群では同意撤回（5.0%［32/635 名］）であった。効果不十分により治験薬の投与を中止した被験者の割合は，ウパダシチニブ 15 mg 併合群で 0.9%（6/640 名），ウパダシチニブ 30 mg 併合群で 0.3%（2/641 名），プラセボ併合群で 3.3%（21/635 名）であった。

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団では，ウパダシチニブ 15 mg 併合群 17 名，ウパダシチニブ 30 mg 併合群 18 名及びプラセボ併合群 15 名に治験薬を投与した（J-ISS Table 2.2__1.1.1_J）。

2.7.4.1.2.1.2 全ウパダシチニブ併合解析

申請時データカットオフ

全ウパダシチニブ併合解析集団（長期）では，申請時データカットオフ時点で全ウパダシチニブ 15 mg 併合群 907 名，30 mg 併合群 920 名，合計 1827 名のデータが得られた。全ウパダシ

チニブ 15 mg 併合群で 757 名（83.5%），全ウパダシチニブ 30 mg 併合群で 752 名（81.7%）が治験薬の投与を継続しており（ISS Table 2.1__1.2），全ウパダシチニブ 15 mg 併合群で 150 名（16.5%），全ウパダシチニブ 30 mg 併合群で 168 名（18.3%）が治験薬の投与を中止した。最も多かった中止理由は，いずれの投与群でも有害事象であった（全ウパダシチニブ 15 mg 併合群：5.2%［47/907 名］，全ウパダシチニブ 30 mg 併合群：6.4%［59/920 名］）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，申請時データカットオフ時点で全ウパダシチニブ 15 mg 併合群 23 名，30 mg 併合群 26 名のデータが得られた（J-ISS Table 2.2__1.2.1_J）。

20[redacted]年[redacted]月[redacted]日データカットオフ

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，全ウパダシチニブ 15 mg 併合群 907 名，30 mg 併合群 921 名，合計 1828 名のデータが得られた。全ウパダシチニブ 15 mg 併合群で 697 名（76.8%），全ウパダシチニブ 30 mg 併合群で 708 名（76.9%）が治験薬の投与を継続しており（ISS update Table 2.1__1），全ウパダシチニブ 15 mg 併合群で 199 名（21.9%），全ウパダシチニブ 30 mg 併合群で 207 名（22.5%）が治験薬の投与を中止した。最も多かった中止理由は，いずれの投与群でも有害事象であった（全ウパダシチニブ 15 mg 併合群：6.7%［61/907 名］，全ウパダシチニブ 30 mg 併合群：8.3%［76/921 名］）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，全ウパダシチニブ 15 mg 併合群 23 名，30 mg 併合群 26 名のデータが得られた（J-ISS update Table 2.3__1.2.1_J）。

2.7.4.1.2.2 曝露状況

2.7.4.1.2.2.1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 24 週時）の曝露状況を表 2.7.4-6（期間の要約）及び表 2.7.4-7（期間別の被験者数）に示す。

プラセボ対照併合解析集団（投与 24 週時）では，合計 1281 名がウパダシチニブを投与され，曝露期間の平均値はウパダシチニブ 15 mg 併合群で 160.9 日，ウパダシチニブ 30 mg 併合群で 160.2 日であった。5 ヵ月以上治験薬を投与された被験者は，ウパダシチニブ 15 mg 併合群で 590 名（92.2%），ウパダシチニブ 30 mg 併合群で 585 名（91.3%）であった。

表 ラセボ 照併 析集団 投 の曝露状 の 約

P				168.0	1.0	167.0	168.0	183.0
Upadacitinib 15 mg QD	640	160.9	28.75	168.0	1.0	167.0	169.0	190.0
Upadacitinib 30 mg QD	641	160.2	29.17	168.0	1.0	167.0	169.0	184.0

Note: Duration of treatment = last dose date by Week 24 - first dose date + 1.

相互参照：ISS Table 2.3__1.1.1

表 2.7.4-7. プラセボ対照併合解析集団（投与 24 週時）の曝露状況（期間別の被験者数）

		Upadacitinib	
Duration	Placebo (N = 635) n (%)	15 mg QD (N = 640) n (%)	30 mg QD (N = 641) n (%)
>= 2 weeks	623 (98.1)	636 (99.4)	637 (99.4)
>= 1 month	612 (96.4)	628 (98.1)	633 (98.8)
>= 2 months	593 (93.4)	619 (96.7)	615 (95.9)
>= 3 months	571 (89.9)	605 (94.5)	603 (94.1)
>= 4 months	560 (88.2)	595 (93.0)	593 (92.5)
>= 5 months	552 (86.9)	590 (92.2)	585 (91.3)
>= 6 months	2 (0.3)	3 (0.5)	2 (0.3)

Note: Duration of treatment = last dose date by Week 24 - first dose date + 1.

相互参照：ISS Table 2.3__1.1.2

日本人部分集団

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の曝露状況を表 2.7.4-8（期間の要約）及び表 2.7.4-9（期間別の被験者数）に示す。

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団では，合計 35 名がウパダシチニブを投与され，曝露期間の平均値はウパダシチニブ 15 mg 併合群で 156.3 日，ウパダシチニブ 30 mg 併合群で 154.1 日であった。5 ヵ月以上治験薬を投与された被験者は，ウパダシチニブ 15 mg 併合群で 15 名（88.2%），ウパダシチニブ 30 mg 併合群で 15 名（83.3%）であった。

表 2.7.4-8. プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の曝露状況（期間［日数］の要約）

Treatment	N	Mean	SD	Median	Min	Q1	Q3	Max
Placebo	15	158.9	32.40	168.0	42.0	167.0	168.0	168.0
Upadacitinib 15 mg QD	17	156.3	35.88	168.0	28.0	168.0	169.0	170.0
Upadacitinib 30 mg QD	18	154.1	35.53	168.0	35.0	167.0	168.0	171.0

Note: Duration of treatment = last dose date by Week 24 - first dose date + 1.

相互参照：J-ISS Table 2.3__1.1.1_J

表 2.7.4-9. プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の曝露状況（期間別の被験者数）

		Upadacitinib	
Duration	Placebo (N = 15) n (%)	15 mg QD (N = 17) n (%)	30 mg QD (N = 18) n (%)
>= 2 weeks	15 (100)	17 (100)	18 (100)
>= 1 month	15 (100)	16 (94.1)	18 (100)
>= 2 months	14 (93.3)	16 (94.1)	17 (94.4)
>= 3 months	14 (93.3)	16 (94.1)	17 (94.4)
>= 4 months	14 (93.3)	15 (88.2)	15 (83.3)
>= 5 months	14 (93.3)	15 (88.2)	15 (83.3)
>= 6 months	0	0	0

Note: Duration of treatment = last dose date by Week 24 - first dose date + 1.

相互参照：J-ISS Table 2.3__1.1.2_J

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2.7.4.1.2.2.2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

全ウパダシチニブ併合解析集団（長期）の曝露状況を表 2.7.4-10（期間の要約）及び表 2.7.4-11（期間別の被験者数）に示す。

全ウパダシチニブ併合解析集団（長期）では，合計 1827 名がウパダシチニブを投与され，曝露期間の平均値は，全ウパダシチニブ 15 mg 併合群で 329.0 日，全ウパダシチニブ 30 mg 併合群で 326.4 日であった。12 ヵ月以上投与された被験者は，全ウパダシチニブ 15 mg 併合群で 359 名（39.6%），全ウパダシチニブ 30 mg 併合群で 363 名（39.5%）であった。

表 2.7.4-10. 全ウパダシチニブ併合解析集団（長期）の曝露状況（期間［日数］の要約）

Treatment	N	Mean	SD	Median	Min	Q1	Q3	Max
Upadacitinib 15 mg QD (No Cross-Over from Placebo)	640	372.0	189.15	342.5	1.0	222.0	497.0	889.0
Upadacitinib 30 mg QD (No Cross-Over from Placebo)	641	368.7	189.41	346.0	1.0	217.0	506.0	849.0
Any Upadacitinib 15 mg QD	907	329.0	196.30	297.0	1.0	191.0	458.0	889.0
Any Upadacitinib 30 mg QD	920	326.4	195.80	291.5	1.0	187.0	460.5	849.0

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：ISS Table 2.3__1.2.1

			Any 15 mg QD (N = 907) n (%)	Any 30 mg QD (N = 920) n (%)
>= 2 weeks	636 (99.4)	637 (99.4)	897 (98.9)	909 (98.8)
>= 1 month	628 (98.1)	633 (98.8)	866 (95.5)	882 (95.9)
>= 3 months	605 (94.5)	603 (94.1)	796 (87.8)	800 (87.0)
>= 6 months	564 (88.1)	553 (86.3)	701 (77.3)	701 (76.2)
>= 9 months	401 (62.7)	397 (61.9)	490 (54.0)	491 (53.4)
>= 12 months	303 (47.3)	299 (46.6)	359 (39.6)	363 (39.5)
>= 18 months	128 (20.0)	128 (20.0)	142 (15.7)	143 (15.5)
>= 2 years	28 (4.4)	28 (4.4)	29 (3.2)	28 (3.0)
>= 2.5 years	0	0	0	0

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：ISS Table 2.3__1.2.2

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団の曝露状況を表 2.7.4-12（期間の要約）及び表 2.7.4-13（期間別の被験者数）に示す。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，合計 49 名がウパダシチニブを投与され，曝露期間の平均値は，全ウパダシチニブ 15 mg 併合群で 365.8 日，全ウパダシチニブ 30 mg 併合群で 395.0 日であった。12 ヵ月以上投与された被験者は，全ウパダシチニブ 15 mg 併合群で 12 名（52.2%），全ウパダシチニブ 30 mg 併合群で 15 名（57.7%）であった。

		390.9	199.00	408.0	28.0	252.0	538.0	696.0
Upadacitinib 30 mg QD (No Cross-Over from Placebo)	18	423.6	196.51	477.0	35.0	308.0	573.0	708.0
Any Upadacitinib 15 mg QD	23	365.8	185.64	372.0	28.0	199.0	482.0	696.0
Any Upadacitinib 30 mg QD	26	395.0	188.21	437.5	35.0	253.0	547.0	708.0

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：J-ISS Table 2.3__1.2.1_J

表 2 7 4- 3　　全ウパダシチニブ併合解析集団（長期）の日本人部分集団の曝露状況（期間別の被験者数）

	Upadacitinib			
Duration	15 mg QD No Cross-Over from Placebo) N = 17) n %)	30 mg QD No Cross-Over from Placebo) N = 18) n %)	Any 15 mg QD N = 23) n %)	Any 30 mg QD N = 26) n (%)
>= 2 weeks	17 100)	18 100)	23 100)	26 100)
>= 1 month	16 94.1)	18 100)	22 95.7)	100)
>= 3 months	16 (94.1)	17 (94.4)	22 (95.7)	24 (92.3)
>= 6 months	15 (88.2)	15 (83.3)	20 (87.0)	22 (84.6)
>= 9 months	11 (64.7)	14 (77.8)	14 (60.9)	19 (73.1)
>= 12 months	10 (58.8)	11 (61.1)	12 (52.2)	15 (57.7)
>= 18 months	4 (23.5)	6 (33.3)	4 (17.4)	6 (23.1)
>= 2 years	0	0	0	0
>= 2.5 years	0	0	0	0

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：J-ISS Table 2.3__1.2.2_J

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20[redacted]年[redacted]月[redacted]日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の曝露状況を表 2.7.4-14（期間の要約）及び表 2.7.4-15（期間別の被験者数）に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，合計 1828 名がウパダシチニブを投与され，曝露期間の平均値は，全ウパダシチニブ 15 mg 併合群で 502.2 日，全ウパダシチニブ 30 mg 併合群で 498.6 日であった。12 ヵ月以上投与された被験者は，全ウパダシチニブ 15 mg 併合群で 663 名（73.1%），全ウパダシチニブ 30 mg 併合群で 664 名（72.1%）であった。

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表 2 7 4- 4　　全ウパダシチニブ併合解析集団（2 [redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の曝露状況（期間［日数］の要約）

Treatment	N	Mean	SD	Median	Min	Q1	Q3	Max
Upadacitinib 15 mg QD No Cross-Over from Placebo)	640	543.0	242.67	533.0	1.0	398.0	716.0	1083.0
Upadacitinib 30 mg QD No Cross-Over from Placebo)	641	538.7	245.95	534.0	1.0	394.0	714.0	1077.0
Any Upadacitinib 15 mg QD	907	502.2	239.75	482.0	1.0	336.0	663.0	1083.0
Any Upadacitinib 30 mg QD	921	498.6	242.01	482.0	1.0	326.0	667.0	1077.0

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：ISS update Table 2.3__1.1

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表 2 7 4- 5　　全ウパダシチニブ併合解析集団（2 ■ 年 ■ 月 ■ 日データカットオフ）の曝露状況（期間別の被験者数）

	Upadacitinib			
Duration	15 mg QD No Cross-Over from Placebo) N = 640) n %)	30 mg QD No Cross-Over from Placebo) 641) n (%)	Any 15 mg QD (N = 907) n (%)	Any 30 mg QD (N = 921) n (%)
>= 2 weeks	636 (99.4)	637 (99.4)	903 (99.6)	915 (99.3)
>= 1 month	628 (98.1)	633 (98.8)	894 (98.6)	909 (98.7)
>= 3 months	605 (94.5)	603 (94.1)	858 (94.6)	862 (93.6)
>= 6 months	581 (90.8)	571 (89.1)	821 (90.5)	822 (89.3)
>= 9 months	549 (85.8)	540 (84.2)	744 (82.0)	742 (80.6)
>= 12 months	527 (82.3)	521 (81.3)	663 (73.1)	664 (72.1)
>= 18 months	306 (47.8)	312 (48.7)	366 (40.4)	381 (41.4)
>= 2 years	147 (23.0)	149 (23.2)	171 (18.9)	172 (18.7)
>= 2.5 years	46 (7.2)	43 (6.7)	46 (5.1)	43 (4.7)

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：ISS update Table 2.3__1.2

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日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団の曝露状況を表 2.7.4-16（期間の要約）及び表 2.7.4-17（期間別の被験者数）に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，合計 49 名がウパダシチニブを投与され，曝露期間の平均値は，全ウパダシチニブ 15 mg 併合群で 559.3 日，全ウパダシチニブ 30 mg 併合群で 563.8 日であった。12 ヵ月以上投与された被験者は，全ウパダシチニブ 15 mg 併合群で 19 名（82.6%），全ウパダシチニブ 30 mg 併合群で 20 名（76.9%）であった。

表２７４- ６　　全ウパダシチニブ併合解析集団（2 [redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団の曝露状況（期間［日数］の要約）

Treatment	N	Mean	SD	Median	Min	Q1	Q3	Max
Upadacitinib 15 mg QD No Cross-Over from Placebo)	17	574.3	269.67	645.0	28.0	399.0	747.0	961.0
Upadacitinib 30 mg QD No Cross-Over from Placebo)	18	593.6	297.91	709.5	35.0	308.0	812.0	973.0
Any Upadacitinib 15 mg QD	23	559.3	245.37	581.0	28.0	387.0	728.0	961.0
Any Upadacitinib 30 mg QD	26	563.8	271.72	653.0	35.0	400.0	777.0	973.0

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
5 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：J-ISS update Table 2.3__1.2.1_J

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表 2 7 4- 7　　全ウパダシチニブ併合解析集団（2 [redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団の曝露状況（期間別の被験者数）

	Upadacitinib			
Duration	15 mg QD No Cross-Over from Placebo) N = 17) n %)	30 mg QD No Cross-Over from Placebo) N = 18) n %)	Any 15 mg QD N = 23) n %)	Any 30 mg QD N = 26) n (%)
>= 2 weeks	17 100)	18 100)	23 100)	26 100)
>= 1 month	16 94.1)	18 100)	22 95.7)	26 100)
>= 3 months	16 94.1)	17 94.4)	22 95.7)	24 92.3)
>= 6 months	15 88.2)	15 83.3)	21 91.3)	22 84.6)
>= 9 months	14 82.4)	14 77.8)	20 87.0)	21 80.8)
>= 12 months	14 82.4)	13 72.2)	19 82.6)	20 76.9)
>= 18 months	10 58.8)	12 66.7)	13 56.5)	16 61.5)
>= 2 years	5 29.4)	8 44.4)	5 21.7)	8 30.8)
>= 2.5 years	2 11.8)	1 5.6)	2 8.7)	1 3.8)

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Patients could be included in more than one treatment group.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照：J-ISS update Table 2.3__1.2.2_J

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2.7.4.1.2.2.3 M15-572 試験

投与 24 週時

M15-572 試験の投与 24 週時までの曝露状況を表 2.7.4-18 に示す。

投与 24 週時までの曝露期間の平均値は，ウパダシチニブ各用量群（15 mg 群：161.7 日，30 mg 群：161.1 日）とアダリムマブ群（161.4 日）で同様であった。

M15-572 試験の投与 24 週時データカットオフまでの曝露状況を表 2.7.4-19 に示す。

投与 24 週時データカットオフまでの曝露期間の平均値は，全ウパダシチニブ 15 mg 群（310.3 日）と 30 mg 群（313.9 日）では同様であり，アダリムマブ群では 335.8 日であった。ただし，投与 24 週時までプラセボを投与した被験者も，全ウパダシチニブ各用量群に含まれている。

表 2 7 4- 8 投与 24 週時までの曝露状況（安全性解析対象集団）：M 5 572 試験

	Placebo to UPA 15 mg QD N = 211)	Placebo to UPA 30 mg QD N = 212)	All Placebo N = 423)	ADA 40 mg EOW (N = 429)	UPA 15 mg QD N = 429)	UPA 30 mg QD N = 423)
Duration day)						
N	211	212	423	429	429	423
Mean SD)	159.4 (28.64)	157.6 35.47)	158.5 32.22)	161.4 28.24)	161.7 28.57)	161.1 28.05)
Median	168.0	168.0	168.0	168.0	168.0	168.0
Min, Max	10, 183	1, 183	1, 183	14, 186	1, 190	1, 183
Duration Interval - n %)						
>= 2 weeks	210 99.5)	208 98.1)	418 98.8)	429 100)	425 99.1)	419 99.1)
>= 1 month	209 99.1)	205 96.7)	414 97.9)	420 (97.9)	420 97.9)	417 98.6)
>= 2 months	205 97.2)	200 94.3)	405 95.7)	412 (96.0)	415 96.7)	409 96.7)
>= 3 months	198 93.8)	195 92.0)	393 92.9)	410 (95.6)	407 94.9)	400 94.6)
>= 4 months	192 91.0)	193 91.0)	385 91.0)	404 (94.2)	404 94.2)	395 93.4)
>= 5 months	190 90.0)	191 90.1)	381 90.1)	393 (91.6)	403 93.9)	391 92.4)
>= 6 months	1 0.5)	1 (0.5)	2 0.5)	2 0.5)	(0.5)	1 (0.2)

Note: Duration of treatment = last dose date by Week 24 - overall-study first dose date + 1.
Duration of ADA 40 mg = last dose date by Week 24 - overall-study first dose date + 14.

相互参照：M15-572 試験 CSR W24 Table 14.1__8.1

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表 2 7 4- 9　　投与 24 週時データカットオフまでの曝露状況（安全性解析対象集団）：M 5 572 試験

	ADA 40 mg EOW N = 429)	UPA 15 mg QD N = 617)	UPA 30 mg QD N = 612)	Total N = 1658)
Duration day)				
n	429	617	612	1658
Mean SD)	335.8 162.27)	310.3 183.65)	313.9 187.50)	318.2 (180.03)
Median	308.0	281.0	278.0	289.0
Min, Max	14, 826	1, 859	1, 821	1, 859
Duration Interval - n %)				
>= 2 weeks	429 100)	607 98.4)	602 98.4)	1638 98.8)
>= 1 month	420 97.9)	586 95.0)	585 95.6)	1591 96.0)
>= 3 months	410 95.6)	538 87.2)	532 86.9)	1480 89.3)
>= 6 months	362 84.4)	473 76.7)	466 76.1)	1301 78.5)
>= 9 months	237 55.2)	314 50.9)	313 51.1)	864 (52.1)
>= 12 months	171 39.9)	226 36.6)	228 37.3)	625 (37.7)
>= 18 months	52 12.1)	74 (12.0)	82 13.4)	208 (12.5)
>= 2 years	10 2.3)	12 1.9)	14 2.3)	36 (2.2)
>= 2.5 years	0	0	0	0

Note: Duration of exposure to study drug in this analysis is period 1 and period 2 combined exposure. Exposure is presented by treatment actually received.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.
Exposure to ADA 40 mg = date of last study medication of ADA 40 mg - date of first study medication of ADA 40 mg + 14

相互参照　M15-57　試験 CSR W24 Tab e 14 1　8 2

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの曝露状況を表 2.7.4-20 に示す。

投与 56 週時データカットオフまでの曝露期間の平均値は，全ウパダシチニブ 15 mg 群（496.7 日），30 mg 群（502.2 日）及びアダリムマブ群（537.6 日）で同様であった。

表 2 7 4-20 投与 56 週時データカットオフまでの曝露状況（安全性解析対象集団）：M 5 572 試験

	ADA 40 mg EOW N = 429)	UPA 15 mg QD N = 617)	UPA 30 mg QD N = 613)	Total N = 1659)
Duration day)				
N	429	617	613	1659
Mean SD)	537.6 221.71)	496.7 216.32)	502.2 222.24)	509.3 (220.43)
Median	542.0	486.0	486.0	501.0
Min, Max	14, 1122	1, 1083	1, 1045	1, 1122
Duration Interval - n %)				
>= 2 weeks	429 100)	613 99.4)	608 99.2)	1650 99.5)
>= 1 month	420 97.9)	608 98.5)	606 98.9)	1634 98.5)
>= 3 months	410 95.6)	585 94.8)	582 94.9)	1577 95.1)
>= 6 months	393 91.6)	569 92.2)	563 91.8)	1525 91.9)
>= 9 months	365 85.1)	515 83.5)	515 84.0)	1395 84.1)
>= 12 months	355 82.8)	463 75.0)	455 74.2)	1273 76.7)
>= 18 months	212 49.4)	243 39.4)	243 39.6)	698 (42.1)
>= 2 years	73 17.0)	92 (14.9)	99 16.2)	264 (15.9)
>= 2.5 years	15 3.5)	17 2.8)	20 3.3)	52 (3.1)

Note: Duration of exposure to study drug in this analysis is period 1 and period 2 combined exposure. Exposure is presented by treatment actually received.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.
Exposure to ADA 40 mg = date of last study medication of ADA 40 mg - date of first study medication of ADA 40 mg + 14.

相互参照 M15-57 試験 CSR W56 Tab e 14 1__3

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2.7.4.1.2.2.4 M15-554 試験

投与 24 週時

M15-554 試験の投与 24 週時までの曝露状況を表 2.7.4-21 に示す。

投与 24 週時までの曝露期間の平均値は，ウパダシチニブ 15 mg 群（159.1 日）と 30 mg 群（158.6 日）で同様であった。

表 2 7 4-2 投与 24 週時までの曝露状況（安全性解析対象集団）：M 5 554 試験

	Placebo to UPA 15 mg QD N = 106)	Placebo to UPA 30 mg QD N = 106)	All Placebo N = 212)	UPA 15 mg QD N = 211)	UPA 30 mg QD N = 218)
Duration day)					
N	106	106	212	211	218
Mean SD)	139.9 54.95)	153.4 39.55)	146.7 48.24)	159.1 29.10)	158.6 31.22)
Median	168.0	168.0	168.0	168.0	168.0
Min, Max	1, 182	5, 180	1, 182	22, 184	16, 184
Duration Interval - n %)					
>= 2 weeks	101 95.3)	104 98.1)	205 96.7)	211 100)	218 100)
>= 1 month	96 90.6)	102 96.2)	198 93.4)	208 98.6)	216 99.1)
>= 2 months	90 84.9)	98 92.5)	188 88.7)	204 96.7)	206 94.5)
>= 3 months	84 79.2)	94 88.7)	178 84.0)	198 93.8)	203 93.1)
>= 4 months	83 78.3)	92 86.8)	175 82.5)	191 90.5)	198 90.8)
>= 5 months	80 75.5)	91 85.8)	171 80.7)	187 88.6)	194 89.0)
>= 6 months	0	0	0	1 0.5)	1 0.5)

Note: Duration of treatment = last dose date by Week 24 - overall-study first dose date + 1.

相互参照 M15-55 試験 CSR W24 Tab e 14 1 8 1

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投与 56 週時

M15-554 試験の投与 56 週時データカットオフまでの曝露状況を表 2.7.4-22 に示す。

投与 56 週時データカットオフまでの曝露期間の平均値は，全ウパダシチニブ 15 mg 群（528.3 日）と 30 mg 群（502.2 日）で同様であった。

表 2 7 4-22 投与 56 週時データカットオフまでの曝露状況（安全性解析対象集団）：M 5 554 試験

	UPA		
	15 mg QD N = 290)	30 mg QD N = 308)	Total N = 598)
Duration day)			
N	290	308	598
Mean SD)	528.3 273.17)	502.2 269.64)	514.9 (271.44)
Median	512.0	497.0	500.5
Min, Max	16, 1083	12, 1058	12, 1083
Duration Interval - n %)			
>= 2 weeks	290 100)	307 99.7)	597 (99.8)
>= 1 month	286 98.6)	303 98.4)	589 (98.5)
>= 3 months	271 93.4)	280 90.9)	551 (92.1)
>= 6 months	252 86.9)	259 84.1)	511 (85.5)
>= 9 months	228 78.6)	232 75.3)	460 (76.9)
>= 12 months	201 69.3)	209 67.9)	410 (68.6)
>= 18 months	135 46.6)	137 44.5)	272 (45.5)
>= 2 years	76 26.2)	75 24.4)	151 (25.3)
>= 2.5 years	26 9.0)	20 6.5)	46 (7.7)

Note: Duration of exposure to study drug in this analysis is Period 1 and Period 2 combined exposure. Exposure is presented by treatment actually received.
Exposure to UPA 15 mg = date of last study medication of UPA 15 mg - date of first study medication of UPA 15 mg + 1.
Exposure to UPA 30 mg = date of last study medication of UPA 30 mg - date of first study medication of UPA 30 mg + 1.

相互参照 M15-55 試験 CSR W56 Tab e 14 1__3

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2.7.4.1.3 人口統計学的特性及びその他の基準値の特性

本項では，安全性併合解析集団の人口統計学的特性及びその他の基準値の特性を示す。個々の試験のデータは 2.7.3.3.1.2 項に示した。

2.7.4.1.3.1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 24 週時）の人口統計学的特性を表 2.7.4-23 及び表 2.7.4-24 に示す。

プラセボ対照併合解析集団（投与 24 週時）の人口統計学的特性は，ウパダシチニブ各用量群とプラセボ併合群でおおむね同様であった。各群の女性の割合は 52.1%–54.8%，白人の割合は 88.7%–89.4%であり，各群の年齢の平均値は 50.9–52.0 歳，体格指数（以下「BMI」）の平均値は 30.4–30.8 kg/m^2 であった。地理的地域は，北米が 32.4%–32.9%，東欧が 34.0%–36.6%であった。

表 2.7.4-23. プラセボ対照併合解析集団（投与 24 週時）の人口統計学的特性（カテゴリカルデータ）

Variable	Placebo (N = 635) n (%)	Upadacitinib 15 mg QD (N = 640) n (%)	Upadacitinib 30 mg QD (N = 641) n (%)
Sex			
Male	304 (47.9)	289 (45.2)	290 (45.2)
Female	331 (52.1)	351 (54.8)	351 (54.8)
Age (year)			
<40	118 (18.6)	105 (16.4)	128 (20.0)
>=40 and <65	419 (66.0)	436 (68.1)	416 (64.9)
>=65 and <75	89 (14.0)	83 (13.0)	84 (13.1)
>=75	9 (1.4)	16 (2.5)	13 (2.0)
Race			
WHITE	563 (88.7)	569 (88.9)	573 (89.4)
BLACK OR AFRICAN AMERICAN	10 (1.6)	6 (0.9)	8 (1.2)
AMERICAN INDIAN OR ALASKA NATIVE	2 (0.3)	3 (0.5)	2 (0.3)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	2 (0.3)	1 (0.2)	2 (0.3)
ASIAN	54 (8.5)	56 (8.8)	50 (7.8)
MULTIPLE	4 (0.6)	5 (0.8)	6 (0.9)

Variable	Placebo N = 635) n %)	Upadacitinib 15 mg QD N = 640) n %)	Upadacitinib 30 mg QD N = 641) n %)
Geographic Region			
NORTH AMERICA	206 32.4)	208 32.5)	211 32.9)
WESTERN EUROPE AND OCEANIA	63 9.9)	76 (11.9)	72 (11.2)
EASTERN EUROPE	216 34.0)	234 36.6)	225 35.1)
LATIN-AMERICA	85 (13.4)	63 9.8)	66 (10.3)
ASIA	46 7.2)	44 6.9)	43 6.7)
OTHER	19 3.0)	15 2.3)	24 3.7)
Ethnicity			
HISPANIC OR LATINO	119 18.7)	95 (14.8)	103 16.1)
NOT HISPANIC OR LATINO	516 81.3)	545 85.2)	538 83.9)
Weight kg)			
<60	44 6.9)	55 8.6)	52 8.1)
>= 60 and < 100	421 66.3)	439 68.6)	441 68.8)
>= 100	170 26.8)	146 22.8)	148 23.1)
Body Mass Index BMI) kg/m^2)			
< 25	133 20.9)	127 19.8)	143 22.3)
>= 25	501 78.9)	513 80.2)	498 77.7)
Missing	1 (0.2)	0	0

相互参照 SS Tab e 2 2 1 1 1

表 2 7 4-24　　プラセボ対照併合解析集団（投与 24 週時）の人口統計学的特性（連続データ）

Variable	Treatment	N	Mean	SD	Median	Min	Max
Age years)	Placebo	635	51.6	12.11	52.0	20.0	83.0
	Upadacitinib 15 mg QD	640	52.0	12.15	53.0	22.0	83.0
	Upadacitinib 30 mg QD	641	50.9	12.34	52.0	19.0	82.0
Weight kg)	Placebo	635	88.3	21.94	86.0	41.0	180.3
	Upadacitinib 15 mg QD	640	86.3	20.64	83.5	46.3	188.2
	Upadacitinib 30 mg QD	641	86.0	19.86	84.1	41.9	181.8
Body Mass Index BMI) kg/m^2)	Placebo	634	30.8	7.05	30.1	15.6	61.9
	Upadacitinib 15 mg QD	640	30.6	6.76	29.5	17.5	64.9
	Upadacitinib 30 mg QD	641	30.4	6.85	29.5	16.3	61.1

相互参照　SS Tab e 2 2 _ 1 1 2

プラセボ対照併合解析集団（投与 24 週時）のベースラインのその他の基準値の特性を表 2.7.4-25 に示す。

プラセボ対照併合解析集団（投与 24 週時）のベースライン時の non-bDMARD の投与状況は，ウパダシチニブ各用量群とプラセボ併合群で同様であった。50%以上の被験者はメトトレキサート（以下「MTX」）単独投与であり（ウパダシチニブ 15 mg 併合群：55.2%，ウパダシチニブ 30 mg 併合群：53.2%，プラセボ併合群：53.9%），non-bDMARD を併用しなかった被験者は，ウパダシチニブ 15 mg 併合群で 29.5%，ウパダシチニブ 30 mg 併合群で 30.7%，プラセボ併合群で 29.6%であった。

表 2.7.4-25. プラセボ対照併合解析集団（投与 24 週時）のベースラインのその他の基準値の特性

Variable	Placebo (N = 635) n (%)	Upadacitinib 15 mg QD (N = 640) n (%)	Upadacitinib 30 mg QD (N = 641) n (%)
Concomitant Non-Biologic DMARD at Baseline			
MTX ALONE	342 (53.9)	353 (55.2)	341 (53.2)
MTX AND OTHER NON-BIOLOGIC DMARD	33 (5.2)	26 (4.1)	32 (5.0)
NON-BIOLOGIC DMARD OTHER THAN MTX	72 (11.3)	72 (11.3)	71 (11.1)
NONE	188 (29.6)	189 (29.5)	197 (30.7)
Concomitant Corticosteroid Use at Baseline			
Yes	94 (14.8)	95 (14.8)	84 (13.1)
No	541 (85.2)	545 (85.2)	557 (86.9)
Screening eGFR (mL/min/1.73 m^2)			
>= 90	323 (50.9)	304 (47.5)	294 (45.9)
>= 60 and <90	281 (44.3)	297 (46.4)	322 (50.2)
>= 40 and <60	29 (4.6)	38 (5.9)	24 (3.7)
Missing	2 (0.3)	1 (0.2)	1 (0.2)
Prior History of Herpes Zoster Vaccination			
Yes	26 (4.1)	28 (4.4)	30 (4.7)
No	549 (86.5)	567 (88.6)	564 (88.0)
Unknown	60 (9.4)	45 (7.0)	47 (7.3)
Prior History of Venous Thrombosis			
Yes	18 (2.8)	12 (1.9)	11 (1.7)
No	617 (97.2)	628 (98.1)	630 (98.3)
CV Risk Factors at Baseline			
Baseline Medical History of Hypertension			
Yes	283 (44.6)	288 (45.0)	248 (38.7)
No	352 (55.4)	352 (55.0)	393 (61.3)

Note: Prior history of venous thrombosis is defined based on "embolic and thrombotic events, venous (Narrow SMQ)" from medical history data.

Variable	Placebo (N = 635) n (%)	Upadacitinib 15 mg QD (N = 640) n (%)	Upadacitinib 30 mg QD (N = 641) n (%)
Diabetes Mellitus			
Yes	37 (5.8)	26 (4.1)	42 (6.6)
No	598 (94.2)	614 (95.9)	599 (93.4)
History of Tobacco/Nicotine Use			
CURRENT	123 (19.4)	138 (21.6)	114 (17.8)
FORMER	138 (21.7)	141 (22.0)	167 (26.1)
NEVER	374 (58.9)	361 (56.4)	360 (56.2)
Elevated LDL-C			
Yes (>= 3.36 mmol/L)	177 (27.9)	180 (28.1)	180 (28.1)
No (< 3.36 mmol/L)	446 (70.2)	441 (68.9)	445 (69.4)
Missing	12 (1.9)	19 (3.0)	16 (2.5)
Low HDL-C			
Yes (<= 1.55 mmol/L)	455 (71.7)	449 (70.2)	444 (69.3)
No (> 1.55 mmol/L)	175 (27.6)	186 (29.1)	192 (30.0)
Missing	5 (0.8)	5 (0.8)	5 (0.8)
NSAIDs Use at Baseline			
Yes	400 (63.0)	387 (60.5)	389 (60.7)
No	235 (37.0)	253 (39.5)	252 (39.3)
Statin Use at Baseline			
Yes	88 (13.9)	84 (13.1)	92 (14.4)
No	547 (86.1)	556 (86.9)	549 (85.6)

Variable	Placebo N = 635) n %)	Upadacitinib 15 mg QD N = 640) n %)	Upadacitinib 30 mg QD N = 641) n %)
Hepatitis B Core Antibody Testing at Screening			
POSITIVE	41 6.5)	50 7.8)	40 6.2)
NEGATIVE	588 92.6)	583 91.1)	600 93.6)
Missing	6 0.9)	7 1.1)	1 0.2)
TB Test Results			
POSITIVE	28 4.4)	29 4.5)	33 5.1)
NEGATIVE	607 95.6)	611 95.5)	608 94.9)

Note: TB Test: Composite endpoint of PPD skin and quantiFERON-TB gold test.

相互参照 SS Tab e 2 2__1 1 3

日本人部分集団

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の人口統計学的特性を表 2.7.4-26 及び表 2.7.4-27 に示す。

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団では，各群での女性の割合は 38.9%–46.7%であり，年齢の平均値は 47.6–53.3 歳，BMI の平均値は 26.1–27.3 kg/m^2 であった。

プラセボ対照併合解析集団（投与 24 週時）の人口統計学的特性は，日本人部分集団では全体集団と比較して，各投与群での女性の割合，体重及び BMI がやや低い傾向を示したが，その差は大きなものではなかった。

表 2.7.4-26. プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の人口統計学的特性（カテゴリカルデータ）

Variable	Placebo (N = 15) n (%)	Upadacitinib 15 mg QD (N = 17) n (%)	Upadacitinib 30 mg QD (N = 18) n (%)
Sex			
Male	8 (53.3)	10 (58.8)	11 (61.1)
Female	7 (46.7)	7 (41.2)	7 (38.9)
Age (year)			
<40	2 (13.3)	3 (17.6)	2 (11.1)
>=40 and <65	11 (73.3)	11 (64.7)	16 (88.9)
>=65 and <75	2 (13.3)	3 (17.6)	0
>=75	0	0	0
Race			
WHITE	0	0	0
BLACK OR AFRICAN AMERICAN	0	0	0
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	0	0
ASIAN	15 (100)	17 (100)	18 (100)
MULTIPLE	0	0	0

Variable	Placebo N = 15) n %)	Upadacitinib 15 mg QD N = 17) n %)	Upadacitinib 30 mg QD N = 18) n %)
Geographic Region			
NORTH AMERICA	0	0	0
WESTERN EUROPE AND OCEANIA	0	0	0
EASTERN EUROPE	0	0	0
LATIN-AMERICA	0	0	0
ASIA	15 100)	17 100)	18 100)
OTHER	0	0	0
Ethnicity			
HISPANIC OR LATINO	0	0	0
NOT HISPANIC OR LATINO	15 100)	17 100)	18 100)
Weight kg)			
<60	3 20.0)	6 35.3)	3 16.7)
>= 60 and < 100	10 (66.7)	8 47.1)	14 (77.8)
>= 100	2 13.3)	3 17.6)	1 (5.6)
Body Mass Index BMI) kg/m^2)			
< 25	5 33.3)	8 47.1)	8 44.4)
>= 25	10 (66.7)	9 52.9)	10 (55.6)

相互参照 J ISS Tab e 2 2 1 1 1 J

表 2 7 4-27　　プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の人口統計学的特性（連続データ）

Variable	Treatment	N	Mean	SD	Median	Min	Max
Age years)	Placebo	15	53.3	9.70	53.0	38.0	69.0
	Upadacitinib 15 mg QD	17	48.1	11.67	45.0	32.0	72.0
	Upadacitinib 30 mg QD	18	47.6	8.30	48.0	23.0	60.0
Weight kg)	Placebo	15	73.7	19.21	70.0	46.6	116.8
	Upadacitinib 15 mg QD	17	76.8	21.56	77.2	47.5	106.7
	Upadacitinib 30 mg QD	18	72.3	18.95	70.4	41.9	125.5
Body Mass Index BMI) kg/m^2)	Placebo	15	26.8	6.22	25.9	18.1	44.4
	Upadacitinib 15 mg QD	17	27.3	6.08	26.0	19.7	39.4
	Upadacitinib 30 mg QD	18	26.1	6.36	25.8	16.3	44.3

相互参照　J ISS

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団のベースラインのその他の基準値の特性を表 2.7.4-28 に示す。

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団でのベースライン時の non-bDMARD の投与状況は，MTX 単独投与の被験者がウパダシチニブ 15 mg 併合群で 35.3%，ウパダシチニブ 30 mg 併合群で 22.2%，プラセボ併合群で 46.7%であり，non-bDMARD を併用しなかった被験者は，ウパダシチニブ 15 mg 併合群で 35.3%，ウパダシチニブ 30 mg 併合群で 50.0%，プラセボ併合群で 33.3%であった。

プラセボ対照併合解析集団（投与 24 週時）のベースラインのその他の基準値の特性は，日本人部分集団と全体集団で大きな差はなかった。

表 2.7.4-28. プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団のベースラインのその他の基準値の特性

Variable	Placebo (N = 15) n (%)	Upadacitinib 15 mg QD (N = 17) n (%)	Upadacitinib 30 mg QD (N = 18) n (%)
Concomitant Non-Biologic DMARD at Baseline			
MTX ALONE	7 (46.7)	6 (35.3)	4 (22.2)
MTX AND OTHER NON-BIOLOGIC DMARD	3 (20.0)	4 (23.5)	1 (5.6)
NON-BIOLOGIC DMARD OTHER THAN MTX	0	1 (5.9)	4 (22.2)
NONE	5 (33.3)	6 (35.3)	9 (50.0)
Concomitant Corticosteroid Use at Baseline			
Yes	3 (20.0)	0	0
No	12 (80.0)	17 (100)	18 (100)
Screening eGFR (mL/min/1.73 m^2)			
>= 90	11 (73.3)	12 (70.6)	12 (66.7)
>= 60 and <90	4 (26.7)	5 (29.4)	6 (33.3)
>= 40 and <60	0	0	0
Prior History of Herpes Zoster Vaccination			
Yes	0	1 (5.9)	0
No	14 (93.3)	16 (94.1)	17 (94.4)
Unknown	1 (6.7)	0	1 (5.6)
Prior History of Venous Thrombosis			
Yes	0	0	0
No	15 (100)	17 (100)	18 (100)
CV Risk Factors at Baseline			
Baseline Medical History of Hypertension			
Yes	6 (40.0)	4 (23.5)	7 (38.9)
No	9 (60.0)	13 (76.5)	11 (61.1)

Note: Prior history of venous thrombosis is defined based on "embolic and thrombotic events, venous (Narrow SMQ)" from medical history data.

Variable	Placebo (N = 15) n (%)	Upadacitinib 15 mg QD (N = 17) n (%)	Upadacitinib 30 mg QD (N = 18) n (%)
Diabetes Mellitus			
Yes	0	0	0
No	15 (100)	17 (100)	18 (100)
History of Tobacco/Nicotine Use			
CURRENT	5 (33.3)	4 (23.5)	6 (33.3)
FORMER	6 (40.0)	6 (35.3)	8 (44.4)
NEVER	4 (26.7)	7 (41.2)	4 (22.2)
Elevated LDL-C			
Yes (>= 3.36 mmol/L)	5 (33.3)	5 (29.4)	6 (33.3)
No (< 3.36 mmol/L)	10 (66.7)	12 (70.6)	12 (66.7)
Low HDL-C			
Yes (<= 1.55 mmol/L)	10 (66.7)	8 (47.1)	11 (61.1)
No (> 1.55 mmol/L)	5 (33.3)	9 (52.9)	7 (38.9)
NSAIDs Use at Baseline			
Yes	14 (93.3)	15 (88.2)	13 (72.2)
No	1 (6.7)	2 (11.8)	5 (27.8)
Statin Use at Baseline			
Yes	1 (6.7)	1 (5.9)	0
No	14 (93.3)	16 (94.1)	18 (100)
Hepatitis B Core Antibody Testing at Screening			
POSITIVE	2 (13.3)	1 (5.9)	4 (22.2)
NEGATIVE	12 (80.0)	16 (94.1)	14 (77.8)
Missing	1 (6.7)	0	0

Variable	Placebo N = 15) n %)	Upadacitinib 15 mg QD N = 17) n %)	Upadacitinib 30 mg QD N = 18) n %)
TB Test Results			
POSITIVE	1 6.7)	0	1 5.6)
NEGATIVE	14 93.3)	17 100)	17 94.4)

Note: TB Test: Composite endpoint of PPD skin and quantiFERON-TB gold test.

相互参照 J ISS Tab e 2 2 1 1 3 J

2.7.4.1.3.2 全ウパダシチニブ併合解析

全体集団

全ウパダシチニブ併合解析集団（長期）の人口統計学的特性を表 2.7.4-29 及び表 2.7.4-30 に示す。

全ウパダシチニブ併合解析集団（長期）の人口統計学的特性は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で同様であった。女性の割合は 52.7%及び 54.8%（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の順で記載，以下同順），白人の割合は 88.9%及び 89.1%であり，年齢の平均値は 51.5 歳及び 51.4 歳，BMI の平均値はいずれも 30.6 kg/m^2 であった。地理的地域は，北米が 32.1%及び 31.7%，東欧が 36.5%及び 35.1%であった。

表 2.7.4-29. 全ウパダシチニブ併合解析集団（長期）の人口統計学的特性（カテゴリカルデータ）

Variable	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) n (%)	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) n (%)	Upadacitinib Any 15 mg QD (N = 907) n (%)	Upadacitinib Any 30 mg QD (N = 920) n (%)
Sex				
Male	289 (45.2)	290 (45.2)	429 (47.3)	416 (45.2)
Female	351 (54.8)	351 (54.8)	478 (52.7)	504 (54.8)
Age (year)				
<40	105 (16.4)	128 (20.0)	161 (17.8)	174 (18.9)
>=40 and <65	436 (68.1)	416 (64.9)	617 (68.0)	601 (65.3)
>=65 and <75	83 (13.0)	84 (13.1)	111 (12.2)	129 (14.0)
>=75	16 (2.5)	13 (2.0)	18 (2.0)	16 (1.7)
Race				
WHITE	569 (88.9)	573 (89.4)	806 (88.9)	820 (89.1)
BLACK OR AFRICAN AMERICAN	6 (0.9)	8 (1.2)	12 (1.3)	11 (1.2)
AMERICAN INDIAN OR ALASKA NATIVE	3 (0.5)	2 (0.3)	4 (0.4)	2 (0.2)
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	1 (0.2)	2 (0.3)	1 (0.1)	3 (0.3)
ASIAN	56 (8.8)	50 (7.8)	78 (8.6)	77 (8.4)
MULTIPLE	5 (0.8)	6 (0.9)	6 (0.7)	7 (0.8)

Note: Patients could be included in more than one treatment group.

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Variable	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) n %)	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 641) n %)	Upadacitinib Any 15 mg QD N = 907) n %)	Upadacitinib Any 30 mg QD N = 920) n %)
Geographic Region				
NORTH AMERICA	208 32.5)	211 (32.9)	291 32.1)	292 31.7)
WESTERN EUROPE AND OCEANIA	76 11.9)	72 11.2)	100 11.0)	98 10.7)
EASTERN EUROPE	234 36.6)	225 (35.1)	331 36.5)	323 35.1)
LATIN-AMERICA	63 9.8)	66 10.3)	98 (10.8)	108 11.7)
ASIA	44 6.9)	43 (6.7)	62 6.8)	66 7.2)
OTHER	15 2.3)	24 (3.7)	25 2.8)	33 3.6)
Ethnicity				
HISPANIC OR LATINO	95 14.8)	103 (16.1)	145 16.0)	156 17.0)
NOT HISPANIC OR LATINO	545 85.2)	538 (83.9)	762 84.0)	764 83.0)
Weight kg)				
<60	55 8.6)	52 (8.1)	70 7.7)	76 8.3)
>= 60 and < 100	439 68.6)	441 (68.8)	623 68.7)	621 67.5)
>= 100	146 22.8)	148 (23.1)	214 23.6)	223 24.2)
Body Mass Index BMI) kg/m^2)				
< 25	127 19.8)	143 (22.3)	192 21.2)	)
>= 25	513 (80.2)	498 (77.7)	715 (78.8)	724 (78.7)
Missing	0	0	0	1 (0.1)

Note: Patients could be included in more than one treatment group.

相互参照：ISS Table 2.2__1.2.1

表 2 7. -30. 全ウパダシチニブ併合解析集団（長期）の人口統計学的特性（連続データ）

Variable	Treatment	N	Mean	SD	Median	Min	Max
Age (year)	Upadacitinib 15 mg QD No Cross-Over from Placebo)	640	52 0	12 15	53 0	22 0	83 0
	Upadacitinib 30 mg QD No Cross-Over from Placebo)	641	50 9	12 34	52 0	19 0	82 0
	Any Upadacitinib 15 mg QD	907	51 5	12 10	52 0	20 0	83 0
	Any Upadacitinib 30 mg QD	920	51 4	12 25	52 0	19 0	83 0
Weight (kg)	Upadacitinib 15 mg QD No Cross-Over from Placebo)	640	86 3	20 64	83 5	46 3	188 2
	Upadacitinib 30 mg QD No Cross-Over from Placebo)	641	86 0	19 86	84 1	41 9	181 8
	Any Upadacitinib 15 mg QD	907	86 7	20 75	84 0	41 0	188 2
	Any Upadacitinib 30 mg QD	920	86 8	21 01	85 0	41 9	181 8
Body Mass Index (BMI) (kg/m^2)	Upadacitinib 15 mg QD No Cross-Over from Placebo)	640	30 6	6 76	29 5	17 5	64 9
	Upadacitinib 30 mg QD No Cross-Over from Placebo)	641	30 4	6 85	29 5	16 3	61 1
	Any Upadacitinib 15 mg QD	907	30 6	6 87	29 6	15 6	64 9
	Any Upadacitinib 30 mg QD	919	30 6	6 92	29 6	16 3	61 7

more than one treatment group.

相互参照：ISS Table 2.2__1.2.2

全ウパダシチニブ併合解析集団（長期）のベースラインのその他の基準値の特性を表 2.7.4-31 に示す。

全ウパダシチニブ併合解析集団（長期）のベースライン時の non-bDMARD の投与状況は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で同様であった。50%以上の被験者は MTX 単独投与であり（全ウパダシチニブ 15 mg 併合群：56.9%，全ウパダシチニブ 30 mg 併合群：52.8%），non-bDMARD を併用しなかった被験者は，全ウパダシチニブ 15 mg 併合群で 28.1%，全ウパダシチニブ 30 mg 併合群で 30.0%であった。

表 2.7.4-31. 全ウパダシチニブ併合解析集団（長期）のベースラインのその他の基準値の特性

Variable	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) n (%)	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) n (%)	Upadacitinib Any 15 mg QD (N = 907) n (%)	Upadacitinib Any 30 mg QD (N = 920) n (%)
Concomitant Non-Biologic DMARD at Baseline				
MTX ALONE	353 (55.2)	341 (53.2)	516 (56.9)	486 (52.8)
MTX AND OTHER NON-BIOLOGIC DMARD	26 (4.1)	32 (5.0)	37 (4.1)	48 (5.2)
NON-BIOLOGIC DMARD OTHER THAN MTX	72 (11.3)	71 (11.1)	99 (10.9)	110 (12.0)
NONE	189 (29.5)	197 (30.7)	255 (28.1)	276 (30.0)
Concomitant Corticosteroid Use at Baseline				
Yes	95 (14.8)	84 (13.1)	136 (15.0)	124 (13.5)
No	545 (85.2)	557 (86.9)	771 (85.0)	796 (86.5)
Screening eGFR (mL/min/1.73 m^2)				
>= 90	304 (47.5)	294 (45.9)	438 (48.3)	439 (47.7)
>= 60 and <90	297 (46.4)	322 (50.2)	418 (46.1)	441 (47.9)
>= 40 and <60	38 (5.9)	24 (3.7)	49 (5.4)	38 (4.1)
Missing	1 (0.2)	1 (0.2)	2 (0.2)	2 (0.2)
Prior History of Herpes Zoster Vaccination				
Yes	28 (4.4)	30 (4.7)	35 (3.9)	41 (4.5)
No	567 (88.6)	564 (88.0)	801 (88.3)	805 (87.5)
Unknown	45 (7.0)	47 (7.3)	71 (7.8)	74 (8.0)
Prior History of Venous Thrombosis				
Yes	12 (1.9)	11 (1.7)	23 (2.5)	15 (1.6)
No	628 (98.1)	630 (98.3)	884 (97.5)	905 (98.4)

Note: Patients could be included in more than one treatment group.
Prior history of venous thrombosis is defined based on "embolic and thrombotic events, venous (Narrow SMQ)" from medical history data.

Variable	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) n (%)	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) n (%)	Upadacitinib Any 15 mg QD (N = 907) n (%)	Upadacitinib Any 30 mg QD (N = 920) n (%)
CV Risk Factors at Baseline				
Baseline Medical History of Hypertension				
Yes	288 (45.0)	248 (38.7)	402 (44.3)	373 (40.5)
No	352 (55.0)	393 (61.3)	505 (55.7)	547 (59.5)
Diabetes Mellitus				
Yes	26 (4.1)	42 (6.6)	43 (4.7)	56 (6.1)
No	614 (95.9)	599 (93.4)	864 (95.3)	864 (93.9)
History of Tobacco/Nicotine Use				
CURRENT	138 (21.6)	114 (17.8)	186 (20.5)	165 (17.9)
FORMER	141 (22.0)	167 (26.1)	199 (21.9)	226 (24.6)
NEVER	361 (56.4)	360 (56.2)	522 (57.6)	529 (57.5)
Elevated LDL-C				
Yes (>= 3.36 mmol/L)	180 (28.1)	180 (28.1)	253 (27.9)	264 (28.7)
No (< 3.36 mmol/L)	441 (68.9)	445 (69.4)	629 (69.3)	635 (69.0)
Missing	19 (3.0)	16 (2.5)	25 (2.8)	21 (2.3)
Low HDL-C				
Yes (<= 1.55 mmol/L)	449 (70.2)	444 (69.3)	637 (70.2)	649 (70.5)
No (> 1.55 mmol/L)	186 (29.1)	192 (30.0)	262 (28.9)	264 (28.7)
Missing	5 (0.8)	5 (0.8)	8 (0.9)	7 (0.8)

Note: Patients could be included in more than one treatment group.

Variable	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) n (%)	Upadacitinib 30 mg QD No Cross-Over from Placebo) N = 641) n (%)	Upadacitinib Any 15 mg QD (N = 907) n (%)	Upadacitinib Any 30 mg QD (N = 920) n (%)
NSAIDs Use at Baseline				
Yes	387 60 5)	389 60 7)	561 61 9)	565 61 4)
No	253 39 5)	252 39 3)	346 38 1)	355 38 6)
Statin Use at Baseline				
Yes	84 (13 1)	92 (14 4)	123 13 6)	124 13 5)
No	556 86 9)	549 85 6)	784 86 4)	796 86 5)
Hepatitis B Core Antibody Testing at Screening				
POSITIVE	50 7 8)	40 6 2)	65 7 2)	60 6 5)
NEGATIVE	583 91 1)	600 93 6)	832 91 7)	858 93 3)
Missing	7 (1 1)	1 (0 2)	10 1 1)	2 0 2)
TB Test Results				
POSITIVE	29 4 5)	33 5 1)	39 4 3)	48 5 2)
NEGATIVE	611 95 5)	608 94 9)	868 95 7)	872 94 8)

Note Patients could be included in more than one treatment group
TB Test Composite endpoint of PPD skin and quantiFERON-TB gold test

相互参照：ISS Table 2.2 1.2.3

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団の人口統計学的特性を表 2.7.4-32 及び表 2.7.4-33 に示す。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，女性の割合が 39.1%及び 42.3%（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の順で記載，以下同順）であり，年齢の平均値は 49.0 歳及び 49.2 歳，BMI の平均値は 27.2 kg/m^2 及び 26.4 kg/m^2 であった。

全ウパダシチニブ併合解析集団（長期）の人口統計学的特性は，日本人部分集団では全体集団と比較して，各投与群での女性の割合，体重及び BMI がやや低い傾向を示したが，その差は大きなものではなかった。

表 2.7.4-32. 全ウパダシチニブ併合解析集団（長期）の日本人部分集団の人口統計学的特性（カテゴリカルデータ）

Variable	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 17) n (%)	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 18) n (%)	Upadacitinib Any 15 mg QD (N = 23) n (%)	Upadacitinib Any 30 mg QD (N = 26) n (%)
Sex				
Male	10 (58.8)	11 (61.1)	14 (60.9)	15 (57.7)
Female	7 (41.2)	7 (38.9)	9 (39.1)	11 (42.3)
Age (year)				
<40	3 (17.6)	2 (11.1)	3 (13.0)	4 (15.4)
>=40 and <65	11 (64.7)	16 (88.9)	17 (73.9)	21 (80.8)
>=65 and <75	3 (17.6)	0	3 (13.0)	1 (3.8)
>=75	0	0	0	0
Race				
WHITE	0	0	0	0
BLACK OR AFRICAN AMERICAN	0	0	0	0
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0	0
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	0	0	0
ASIAN	17 (100)	18 (100)	23 (100)	26 (100)
MULTIPLE	0	0	0	0

Note: Patients could be included in more than one treatment group.

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Variable	Upadacitinib 15 mg QD No Cross-Over from Placebo) (N = 17) n (%)	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 18) n (%)	Upadacitinib Any 15 mg QD (N = 23) n (%)	Upadacitinib Any 30 mg QD (N = 26) n (%)
Geographic Region				
NORTH AMERICA	0	0	0	0
WESTERN EUROPE AND OCEANIA	0	0	0	0
EASTERN EUROPE	0	0	0	0
LATIN-AMERICA	0	0	0	0
ASIA	17 100)	18 100)	23 100)	26 100)
OTHER	0	0	0	0
Ethnicity				
HISPANIC OR LATINO	0	0	0	0
NOT HISPANIC OR LATINO	17 100)	18 100)	23 100)	26 100)
Weight (kg)				
<60	6 (35 3)	3 (16 7)	7 (30 4)	4 (15 4)
>= 60 and < 100	8 (47 1)	14 (77 8)	12 52 2)	20 76 9)
>= 100	3 (17 6)	1 (5 6)	4 (17 4)	2 7 7)
Body Mass Index (BMI) (kg/m^2)				
< 25	8 (47 1)	8 (44 4)	9 (39 1)	11 42 3)
>= 25	9 (52 9)	10 (55 6)	14 60 9)	15 57 7)

Note Patients could be included in more than one treatment group

相互参照：J-ISS Table 2 2 1.2.1 J

表 2 7. -33. 全ウパダシチニブ併合解析集団（長期）の日本人部分集団の人口統計学的特性（連続データ）

Variable	Treatment	N	Mean	SD	Median	Min	Max
Age (year)	Upadacitinib 15 mg QD No Cross-Over from Placebo)	17	48 1	11 67	45 0	32 0	72 0
	Upadacitinib 30 mg QD No Cross-Over from Placebo)	18	47 6	8 30	48 0	23 0	60 0
	Any Upadacitinib 15 mg QD	23	49 0	10 56	48 0	32 0	72 0
	Any Upadacitinib 30 mg QD	26	49 2	9 26	49 0	23 0	68 0
Weight (kg)	Upadacitinib 15 mg QD No Cross-Over from Placebo)	17	76 8	21 56	77 2	47 5	106 7
	Upadacitinib 30 mg QD No Cross-Over from Placebo)	18	72 3	18 95	70 4	41 9	125 5
	Any Upadacitinib 15 mg QD	23	76 9	20 43	77 2	47 5	106 7
	Any Upadacitinib 30 mg QD	26	73 0	18 69	70 4	41 9	125 5
Body Mass Index (BMI) (kg/m^2)	Upadacitinib 15 mg QD No Cross-Over from Placebo)	17	27 3	6 08	26 0	19 7	39 4
	Upadacitinib 30 mg QD No Cross-Over from Placebo)	18	26 1	6 36	25 8	16 3	44 3
	Any Upadacitinib 15 mg QD	23	27 2	5 75	26 0	18 1	39 4
	Any Upadacitinib 30 mg QD	26	26 4	6 57	26 0	16 3	44 4

Note Patients could be included in more than one treatment group

相互参照：J-ISS Table 2 2 1.2.2 J

全ウパダシチニブ併合解析集団（長期）の日本人部分集団のベースラインのその他の基準値の特性を表 2.7.4-34 に示す。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団でのベースライン時の non-bDMARD の投与状況は，MTX 単独投与の被験者が 47.8%及び 23.1%（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の順で記載，以下同順）であり，non-bDMARD を併用しなかった被験者は 26.1%及び 50.0%であった。

全ウパダシチニブ併合解析集団（長期）のベースラインのその他の基準値の特性は，non-bDMARD の投与状況に関して，日本人部分集団では全体集団と比較して，MTX 単独投与がやや少ない傾向を示した。

表 2.7.4-34. 全ウパダシチニブ併合解析集団（長期）の日本人部分集団のベースラインのその他の基準値の特性

Variable	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 17) n (%)	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 18) n (%)	Upadacitinib Any 15 mg QD (N = 23) n (%)	Upadacitinib Any 30 mg QD (N = 26) n (%)
Concomitant Non-Biologic DMARD at Baseline				
MTX ALONE	6 (35.3)	4 (22.2)	11 (47.8)	6 (23.1)
MTX AND OTHER NON-BIOLOGIC DMARD	4 (23.5)	1 (5.6)	5 (21.7)	3 (11.5)
NON-BIOLOGIC DMARD OTHER THAN MTX	1 (5.9)	4 (22.2)	1 (4.3)	4 (15.4)
NONE	6 (35.3)	9 (50.0)	6 (26.1)	13 (50.0)
Concomitant Corticosteroid Use at Baseline				
Yes	0	0	0	3 (11.5)
No	17 (100)	18 (100)	23 (100)	23 (88.5)
Screening eGFR (mL/min/1.73 m^2)				
>= 90	12 (70.6)	12 (66.7)	15 (65.2)	19 (73.1)
>= 60 and <90	5 (29.4)	6 (33.3)	8 (34.8)	7 (26.9)
>= 40 and <60	0	0	0	0
Prior History of Herpes Zoster Vaccination				
Yes	1 (5.9)	0	1 (4.3)	0
No	16 (94.1)	17 (94.4)	22 (95.7)	24 (92.3)
Unknown	0	1 (5.6)	0	2 (7.7)
Prior History of Venous Thrombosis				
Yes	0	0	0	0
No	17 (100)	18 (100)	23 (100)	26 (100)

Note: Patients could be included in more than one treatment group.
Prior history of venous thrombosis is defined based on "embolic and thrombotic events, venous (Narrow SMQ)" from medical history data.

Variable	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 17) n (%)	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 18) n (%)	Upadacitinib Any 15 mg QD (N = 23) n (%)	Upadacitinib Any 30 mg QD (N = 26) n (%)
CV Risk Factors at Baseline				
Baseline Medical History of Hypertension				
Yes	4 (23.5)	7 (38.9)	5 (21.7)	11 (42.3)
No	13 (76.5)	11 (61.1)	18 (78.3)	15 (57.7)
Diabetes Mellitus				
Yes	0	0	0	0
No	17 (100)	18 (100)	23 (100)	26 (100)
History of Tobacco/Nicotine Use				
CURRENT	4 (23.5)	6 (33.3)	6 (26.1)	9 (34.6)
FORMER	6 (35.3)	8 (44.4)	8 (34.8)	11 (42.3)
NEVER	7 (41.2)	4 (22.2)	9 (39.1)	6 (23.1)
Elevated LDL-C				
Yes (>= 3.36 mmol/L)	5 (29.4)	6 (33.3)	8 (34.8)	8 (30.8)
No (< 3.36 mmol/L)	12 (70.6)	12 (66.7)	15 (65.2)	18 (69.2)
Low HDL-C				
Yes (<= 1.55 mmol/L)	8 (47.1)	11 (61.1)	12 (52.2)	16 (61.5)
No (> 1.55 mmol/L)	9 (52.9)	7 (38.9)	11 (47.8)	10 (38.5)
NSAIDs Use at Baseline				
Yes	15 (88.2)	13 (72.2)	21 (91.3)	21 (80.8)
No	2 (11.8)	5 (27.8)	2 (8.7)	5 (19.2)

Note: Patients could be included in more than one treatment group.

Variable	Upadacitinib 15 mg QD No Cross-Over from Placebo) (N = 17) n (%)	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 18) n (%)	Upadacitinib Any 15 mg QD (N = 23) n (%)	Upadacitinib Any 30 mg QD (N = 26) n (%)
Statin Use at Baseline				
Yes	1 (5 9)	0	1 4 3)	0
No	16 (94 1)	18 100)	22 95 7)	26 100)
Hepatitis B Core Antibody Testing at Screening				
POSITIVE	1 (5 9)	4 (22 2)	1 4 3)	5 (19 2)
NEGATIVE	16 (94 1)	14 (77 8)	21 91 3)	21 80 8)
Missing	0	0	1 4 3)	0
TB Test Results				
POSITIVE	0	1 (5 6)	0	2 7 7)
NEGATIVE	17 100)	17 (94 4)	23 100)	24 92 3)

Note Patients could be included in more than one treatment group
TB Test Composite endpoint of PPD skin and quantiFERON-TB gold test

相互参照：J-ISS Table 2 2 1.2.3 J

2.7.4.2 有害事象

2.7.4.2.1 有害事象の解析

<u>プラセボ対照併合解析</u>

<u>全体集団</u>

プラセボ対照併合解析集団（投与 24 週時）の有害事象の概要を表 2.7.4-35 及び表 2.7.4.7-1（100 人年あたりの発現状況）に示す。

プラセボ対照併合解析集団（投与 24 週時）の有害事象の発現割合は，ウパダシチニブ 15 mg 併合群（65.9%）とプラセボ併合群（61.6%）で同様であったが，ウパダシチニブ 30 mg 併合群（74.3%）で高かった。重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の発現割合（以下，同順で記載）は，プラセボ併合群（2.7%，3.8%及び 3.8%）と比較してウパダシチニブ各用量群の方が高く，ウパダシチニブ群では 15 mg 併合群（4.1%，4.4%及び 5.3%）と比較して 30 mg 併合群（6.9%，6.4%及び 6.7%）の方が高かった。死亡は，プラセボ併合群で 2 名に認められた。

表 2 7. -35. プラセボ対照併合解析集団（投与 2 週時）の有害事象の概要

	Placebo N = 635) n (%) [SSA %]	----- Upadacitinib ----- 15 mg QD (N = 640) n (%) SSA %]	30 mg QD (N = 641) n (%) SSA %]	Adalimumab 40 mg EOW (N = 429) n (%)	-Treatment Comparison 95% CI) A]- 15 mg QD - Placebo	30 mg QD - Placebo
Subjects with						
Any adverse event AE)	391 61 6) 61 6]	422 65 9) 65 9]	476 74 3) 74 2]	278 (64 8)	4 3 (-0 9, 9 6)	12 6 (7 6, 17 7)
Any serious AE	17 2 7) 2 7]	26 4 1) [4 1]	44 6 9) [6 9]	16 (3 7)	1 4 (-0 6, 3 4)	4 2 (1 9, 6 5)
Any AE leading to discontinuation of study drug	24 3 8) 3 8]	28 4 4) [4 4]	41 6 4) [6 4]	22 (5 1)	0 6 (-1 6, 2 8)	2 6 (0 2, 5 0)
Any severe AE	24 3 8) 3 8]	34 5 3) [5 3]	43 6 7) [6 7]	28 (6 5)	1 5 (-0 7, 3 8)	2 9 (0 5, 5 4)
Any AE with reasonable possibility of being related to study drug$	173 27 2) 27 2]	212 33 1) 33 1]	265 41 3) 41 4]	168 (39 2)	5 8 0 8, 10 8)	14 1 (9 0, 19 3)
Any AE leading to death	2 (0 3) 0 3]	0	0	0	-0 3 (-0 8, 0 1)	-0 3 (-0 8, 0 1)
Deaths#	2 (0 3) 0 3]	0	0	0	-0 3 (-0 8, 0 1)	-0 3 (-0 8, 0 1)

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
ng a reasonable possibility of being related to study drug.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

相互参照：ISS Table 2.4 1.1.1.1

日本人部分集団

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の有害事象の概要を表 2.7.4-36 及び表 2.7.4.7-2（100 人年あたりの発現状況）に示す。

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団での有害事象の発現割合は，ウパダシチニブ 15 mg 併合群で 82.4%，30 mg 併合群で 88.9%，プラセボ併合群で 60.0%であった。重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の発現割合（以下，同順で記載）は，ウパダシチニブ 15 mg 併合群で 5.9%，5.9%及び 5.9%，ウパダシチニブ 30 mg 併合群で 16.7%，16.7%及び 16.7%であり，プラセボ併合群ではいずれも発現しなかった。投与 24 週時までに死亡した被験者は認められなかった。

表 2 7. -36. プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団の有害事象の概要

	Placebo (N = 15) n (%) [SSA %]	----- Upadacitinib ----- 15 mg QD (N = 17) n (%) SSA %]	30 mg QD (N = 18) n (%) SSA %]	Adalimumab 40 mg EOW N = 4) n (%)	-Treatment Comparison 95% CI) A]- 15 mg QD - Placebo	30 mg QD - Placebo
Subjects with						
Any adverse event AE)	9 (60 0) 60 2]	14 (82 4) 82 0]	16 88 9) 88 9]	3 75 0)	21 8 (-8 7, 52 3)	28 7 (0 1, 57 2)
Any serious AE	0	1 (5 9) [6 0]	3 (16 7) 16 7]	1 25 0)	6 0 (-5 3, 17 3)	16 7 (-0 1, 33 5)
Any AE leading to discontinuation of study drug	0	1 (5 9) [6 0]	3 (16 7) 16 7]	1 25 0)	6 0 (-5 3, 17 3)	16 7 (-0 1, 33 5)
Any severe AE	0	1 (5 9) [6 0]	3 (16 7) 16 7]	2 50 0)	6 0 (-5 3, 17 3)	16 7 (-0 1, 33 5)
Any AE with reasonable possibility of being related to study drug$	5 (33 3) 34 2]	7 (41 2) 41 0]	12 66 7) 66 6]	2 50 0)	6 8 (-25 5, 39 2)	32 5 (1 3, 63 7)
Any AE leading to death	0	0	0	0	0 0	0 0
Deaths#	0	0	0	0	0 0	0 0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
SSA = Study size adjusted
A] Study size adjusted risk difference between treatment groups
$ As assessed by investigator
# Includes both treatment-emergent and non-treatment-emergent deaths

相互参照：J-ISS Table 2. 1.1.1.1 J

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全ウパダシチニブ併合解析（申請時データカットオフ）

全体集団

全ウパダシチニブ併合解析集団（長期）の有害事象の概要を表 2.7.4.7-3 及び表 2.7.4-37（100 人年あたりの発現状況）に示す。

全ウパダシチニブ併合解析集団（長期）の有害事象，重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の 100 人年あたりの発現件数（以下，同順で記載）は，全ウパダシチニブ 30 mg 併合群（379.4 件/100 人年，14.8 件/100 人年，9.5 件/100 人年及び 18.2 件/100 人年）と比較して，全ウパダシチニブ 15 mg 併合群（308.9 件/100 人年，10.9 件/100 人年，8.4 件/100 人年及び 12.4 件/100 人年）の方が少なかった。死亡は，ウパダシチニブを投与した被験者で 3 名に認められた。このうち 1 名（全ウパダシチニブ 30 mg 併合群）は評価期間中に死亡し，他の 2 名（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名）は，評価期間以降（治験薬の最終投与 30 日後より後）に死亡した。

表 2.7.4-37. 全ウパダシチニブ併合解析集団（長期）の有害事象の概要（100 人年あたりの発現状況）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 920)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 394.5) Events (E/100 PYs)		
Any adverse event (AE)	2111 (323.9) [323.9]	2638 (407.7) [407.6]	2523 (308.9) [308.8]	3120 (379.4) [379.5]	1294 (328.0)	83.7 (62.9, 104.5)	70.6 (52.7, 88.6)
Any serious AE	76 (11.7) [11.6]	98 (15.1) [15.1]	89 (10.9) [10.9]	122 (14.8) [14.8]	43 (10.9)	3.5 (-0.5, 7.5)	3.9 (0.5, 7.4)
Any AE leading to discontinuation of study drug	59 (9.1) [9.0]	70 (10.8) [10.8]	69 (8.4) [8.5]	78 (9.5) [9.5]	40 (10.1)	1.8 (-1.6, 5.2)	1.0 (-1.9, 3.9)
Any severe AE	88 (13.5) [13.5]	118 (18.2) [18.2]	101 (12.4) [12.4]	150 (18.2) [18.2]	51 (12.9)	4.7 (0.4, 9.1)	5.9 (2.1, 9.7)
Any AE with reasonable possibility of being related to study drug$	763 (117.1) [117.2]	1087 (168.0) [167.9]	901 (110.3) [110.2]	1256 (152.7) [152.8]	594 (150.6)	50.7 (37.7, 63.7)	42.6 (31.5, 53.7)
Any AE leading to death	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]	0	-0.2 (-0.5, 0.1)	-0.0 (-0.3, 0.3)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD N = 920)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted incidence rate	n/PYs (n/100 PYs) SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) SSA n/100 PYs]	n/PYs (n/100 PYs)		
Deaths#	1/652 0 0 2) [0 2]	1/647 2 0 2) 0 2]	1/817 1 (0 1) [0 1]	2/822 9 0 2) 0 2]	0/394 5	0 0 (-0 4, 0 4)	0 1 (-0 3, 0 5)

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups
Includes both treatment-emergent and non-treatment-emergent deaths

相互参照：ISS Table 2. 1.2.1.2

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団の有害事象の概要を表 2.7.4.7-4 及び表 2.7.4-38（100 人年あたりの発現状況）に示す。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団での有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 382.6 件/100 人年，30 mg 併合群で 565.8 件/100 人年であった。100 人年あたりの発現件数（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の順で記載，以下同順）は，重篤な有害事象が 17.4 件/100 人年及び 56.9 件/100 人年，治験薬の投与中止に至った有害事象が 4.3 件/100 人年及び 17.8 件/100 人年，Grade 3 以上の有害事象が 13.0 件/100 人年及び 67.6 件/100 人年であった。死亡は，全ウパダシチニブ 30 mg 併合群で 1 名に認められた。

表 2.7.4-38. 全ウパダシチニブ併合解析集団（長期）の日本人部分集団の有害事象の概要（100 人年あたりの発現状況）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 18.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 20.9) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 23.0) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 28.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 5.2) Events (E/100 PYs)		
Any adverse event (AE)	77 (423.1) [420.9]	110 (526.3) [535.5]	88 (382.6) [378.1]	159 (565.8) [579.1]	8 (153.8)	114.6 (-24.4, 253.6)	201.0 (79.7, 322.4)
Any serious AE	3 (16.5) [15.1]	8 (38.3) [38.9]	4 (17.4) [15.8]	16 (56.9) [59.8]	1 (19.2)	23.8 (-8.3, 55.9)	44.0 (10.8, 77.3)
Any AE leading to discontinuation of study drug	1 (5.5) [5.0]	3 (14.4) [15.6]	1 (4.3) [3.9]	5 (17.8) [19.4]	1 (19.2)	10.6 (-9.6, 30.9)	15.4 (-3.2, 34.1)
Any severe AE	2 (11.0) [10.0]	8 (38.3) [38.9]	3 (13.0) [11.8]	19 (67.6) [70.4]	3 (57.7)	28.8 (-1.7, 59.4)	58.5 (24.0, 93.0)
Any AE with reasonable possibility of being related to study drug$	21 (115.4) [119.7]	35 (167.5) [164.1]	24 (104.3) [107.6]	60 (213.5) [215.1]	2 (38.5)	44.4 (-31.5, 120.3)	107.6 (37.1, 178.0)
Any AE leading to death	0	0	0	1 (3.6) [3.9]	0	0.0	3.9 (-3.7, 11.5)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted incidence rate	n/PYs (n/100 PYs) SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) SSA n/100 PYs]	n/PYs (n/100 PYs)		
Deaths#	0/18 2	0/20 9	0/23 0	1/28 7 3 5) 3 8]	0/5 2	0 0	3 8 (-3 6, 11 2)

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups
Includes both treatment-emergent and non-treatment-emergent deaths

相互参照：J-ISS Table 2. 1.2.1.2 J

全ウパダシチニブ併合解析（20[redacted]年[redacted]月[redacted]日データカットオフ）

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の有害事象の概要を表 2.7.4.7-87 及び表 2.7.4-39（100 人年あたりの発現状況）に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の有害事象，重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の 100 人年あたりの発現件数（以下，同順で記載）は，申請時データカットオフまでの結果と同様に，全ウパダシチニブ 30 mg 併合群（321.5 件/100 人年，13.2 件/100 人年，7.8 件/100 人年及び 15.5 件/100 人年）と比較して，全ウパダシチニブ 15 mg 併合群（263.9 件/100 人年，10.3 件/100 人年，6.7 件/100 人年及び 10.7 件/100 人年）の方が少なかった。死亡は，ウパダシチニブを投与した被験者 5 名に認められた。このうち，申請時データカットオフ以降に死亡した被験者は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名であった。

表 2.7.4-39. 全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の有害事象の概要（100 人年あたりの発現状況）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 951.5) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 945.4) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 1247.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 1257.4) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 549.7) Events (E/100 PYs)		
Any adverse event (AE)	2638 (277.2) [277.3]	3263 (345.1) [345.1]	3291 (263.9) [263.9]	4043 (321.5) [321.5]	1575 (286.5)	67.8 (51.9, 83.7)	57.7 (44.3, 71.1)
COVID-19 related AE	4 (0.4) [0.4]	6 (0.6) [0.6]	6 (0.5) [0.5]	10 (0.8) [0.8]	2 (0.4)	0.2 (-0.4, 0.9)	0.3 (-0.3, 0.9)
Any serious AE	101 (10.6) [10.6]	124 (13.1) [13.1]	129 (10.3) [10.3]	166 (13.2) [13.2]	53 (9.6)	2.5 (-0.6, 5.6)	2.9 (0.2, 5.5)
Any AE leading to discontinuation of study drug	64 (6.7) [6.7]	80 (8.5) [8.5]	83 (6.7) [6.7]	98 (7.8) [7.8]	43 (7.8)	1.8 (-0.7, 4.2)	1.1 (-1.0, 3.2)
Any severe AE	104 (10.9) [10.9]	145 (15.3) [15.3]	133 (10.7) [10.7]	195 (15.5) [15.5]	69 (12.6)	4.4 (1.2, 7.7)	4.8 (2.0, 7.7)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any AE with reasonable possibility of being related to study drug$	934 (98.2) [98.3]	1303 (137.8) [137.7]	1153 (92.4) [92.4]	1589 (126.4) [126.4]	678 (123.3)	39.4 (29.6, 49.2)	34.0 (25.8, 42.2)
Any AE leading to death	2 (0.2) [0.2]	0	2 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.4)	-0.2 (-0.5, 0.1)	-0.0 (-0.3, 0.3)
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		
Deaths	2/951.6 (0.2) [0.2]	1/945.5 (0.1) [0.1]	2/1247.2 (0.2) [0.2]	3/1257.4 (0.2) [0.2]	1/549.8 (0.2)	-0.1 (-0.5, 0.3)	0.1 (-0.3, 0.4)
Treatment-emergent deaths	1/951.4 (0.1) [0.1]	0/945.4	1/1247.1 (<0.1) [<0.1]	2/1257.2 (0.2) [0.2]	1/549.8 (0.2)	-0.1 (-0.3, 0.1)	0.1 (-0.2, 0.3)
COVID-19 related	0/951.5	0/945.4	0/1247.2	1/1257.2 (<0.1) [<0.1]	0/549.7	0.0	0.1 (-0.1, 0.2)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Non-treatment-emergent deaths	1/951 7 0 1) [0 1]	1/945 5 0 1) 0 1]	1/1247 3 (<0 1) [<0 1]	1/1257 5 (<0 1) [<0 1]	0/549 7	0 0 (-0 3, 0 3)	-0 0 (-0 2, 0 2)
COVID-19 related	0/951 5	0/945 4	0/1247 2	0/1257 4	0/549 7	0 0	0 0

Note Treatment emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups

相互参照：ISS update Table 2. 1.2

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団の有害事象の概要を表 2.7.4.7-88 及び表 2.7.4-40（100 人年あたりの発現状況）に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団での有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 329.5 件/100 人年，30 mg 併合群で 488.8 件/100 人年であった。100 人年あたりの発現件数（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の順で記載，以下同順）は，重篤な有害事象が 14.2 件/100 人年及び 52.4 件/100 人年，治験薬の投与中止に至った有害事象が 2.8 件/100 人年及び 17.5 件/100 人年，Grade 3 以上の有害事象が 11.4 件/100 人年及び 67.3 件/100 人年であった。死亡が全ウパダシチニブ 30 mg 併合群の 1 名に認められたが，本事象は申請時データカットオフまでに報告されたものであった。

表 2.7.4-40. 全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団の有害事象の概要（100 人年あたりの発現状況）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 26.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 29.3) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 35.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 40.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 6.6) Events (E/100 PYs)		
Any adverse event (AE)	99 (370.8) [366.8]	130 (443.7) [452.2]	116 (329.5) [324.0]	196 (488.8) [502.7]	10 (151.5)	85.4 (-21.6, 192.4)	178.7 (86.1, 271.3)
COVID-19 related AE	0	0	0	0	0	0.0	0.0
Any serious AE	4 (15.0) [13.9]	11 (37.5) [38.7]	5 (14.2) [13.1]	21 (52.4) [55.2]	1 (15.2)	24.8 (-1.9, 51.5)	42.1 (15.8, 68.4)
Any AE leading to discontinuation of study drug	1 (3.7) [3.5]	4 (13.7) [14.7]	1 (2.8) [2.6]	7 (17.5) [18.9]	1 (15.2)	11.3 (-4.7, 27.2)	16.3 (1.4, 31.1)
Any severe AE	3 (11.2) [10.4]	12 (41.0) [42.4]	4 (11.4) [10.5]	27 (67.3) [70.6]	3 (45.5)	31.9 (5.1, 58.8)	60.2 (31.5, 88.8)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any AE with reasonable possibility of being related to study drug$	27 (101.1) [103.0]	48 (163.8) [163.1]	34 (96.6) [97.2]	82 (204.5) [208.2]	3 (45.5)	60.1 (-0.9, 121.0)	111.1 (54.8, 167.3)
Any AE leading to death	0	0	0	1 (2.5) [2.7]	0	0.0	2.7 (-2.6, 8.0)
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		
Deaths	0/26.7	0/29.3	0/35.2	1/40.2 (2.5) [2.7]	0/6.6	0.0	2.7 (-2.6, 8.0)
Treatment-emergent deaths	0/26.7	0/29.3	0/35.2	1/40.2 (2.5) [2.7]	0/6.6	0.0	2.7 (-2.6, 8.0)
COVID-19 related	0/26.7	0/29.3	0/35.2	0/40.1	0/6.6	0.0	0.0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD (No Cross-Over from Placebo) N = 17)	30 mg QD (No Cross-Over from Placebo) N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Non-treatment-emergent deaths	0/26 7	0/29 3	0/35 2	0/40 1	0/6 6	0 0	0 0
COVID-19 related	0/26 7	0/29 3	0/35 2	0/40 1	0/6 6	0 0	0 0

Note Treatment emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups

相互参照：J-ISS update T 1 2 1 2 1 2 J

M15-572 試験

投与 24 週時

M15-572 試験の投与 24 週時までの有害事象の概要を表 2.7.4-41，投与 24 週時データカットオフまでの有害事象の概要を表 2.7.4.7-5（100 人年あたりの発現状況）及び表 2.7.4.7-6 に示す。

投与 24 週時までの有害事象の発現割合は，プラセボ群（59.6%）と比較してウパダシチニブ 15 mg 群（66.9%）及びウパダシチニブ 30 mg 群（72.3%）の方が高かった。重篤な有害事象，Grade 3 以上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（以下，同順で記載）は，プラセボ群（3.1%，3.8%及び 3.1%）と比較して，ウパダシチニブ 15 mg 群（3.3%，4.9%及び 3.0%）では同様であったが，ウパダシチニブ 30 mg 群（6.1%，6.4%及び 5.0%）では高かった。

投与 24 週時までの有害事象及び重篤な有害事象の発現割合（以下，同順で記載）は，アダリムマブ群（64.8%及び 3.7%）と比較して，ウパダシチニブ 15 mg 群（66.9%及び 3.3%）では同様であったが，ウパダシチニブ 30 mg 群（72.3%及び 6.1%）では高かった。Grade 3 以上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（以下，同順で記載）は，ウパダシチニブ 15 mg 群（4.9%及び 3.0%）で最も低く，ウパダシチニブ 30 mg 群（6.4%及び 5.0%）とアダリムマブ群（6.5%及び 5.1%）で同様であった。投与 24 週時までに，死亡がプラセボ群の 1 名に認められた。

投与 24 週時データカットオフまでの有害事象及び Grade 3 以上の有害事象の 100 人年あたりの発現件数（以下，同順で記載）は，アダリムマブ群（328.0 件/100 人年及び 12.9 件/100 人年）と比較して，全ウパダシチニブ 15 mg 群（321.1 件/100 人年及び 10.5 件/100 人年）では同様であったが，全ウパダシチニブ 30 mg 群（383.1 件/100 人年及び 15.8 件/100 人年）では多かった。重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群（8.6 件/100 人年）で最も少なく，全ウパダシチニブ 30 mg 群（12.9 件/100 人年）で最も多かった。治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群（5.9 件/100 人年）で最も少なく，アダリムマブ群（10.1 件/100 人年）で最も多かった。投与 24 週時から投与 24 週時データカットオフまでに，死亡が全ウパダシチニブ 15 mg 群及び 30 mg 群で各 1 名に認められた。いずれの被験者も治験薬の最終投与 30 日後より後に死亡した。

M15-572 試験の日本人部分集団の結果は，2.7.4.5.1.1 項に示す。

表 2 7. - 1. 投与 2 週時までの有害事象の概要（安全性解析対象集団）：M15-572 試験

	Placebo N = 423) n (%)	ADA 40 mg EOW N = 429) n (%)	---- UPA ------ 15 mg QD (N = 429) n (%)	30 mg QD N = 423) n (%)	-- UPA VS Placebo (95% CI)[A] -- 15 mg QD VS Placebo	30 mg QD VS Placebo	-- UPA VS ADA 95% CI) A] -- 15 mg QD VS ADA	30 mg QD VS ADA
Subjects with								
Any adverse event AE)	252 (59 6)	278 64 8)	287 66 9)	306 (72 3)	7 3 (0 9, 13 8)	12 8 6 4, 19 1)	2 1 (-4 2, 8 4)	7 5 1 3, 13 8)
Any serious AE (SAE)	13 3 1)	16 3 7)	14 (3 3)	26 6 1)	0 2 (-2 2, 2 5)	3 1 (0 3, 5 9)	-0 5 (-2 9, 2 0)	2 4 (-0 5, 5 3)
Any AE leading to discontinuation of study drug	13 3 1)	22 5 1)	13 (3 0)	21 5 0)	-0 0 (-2 4, 2 3)	1 9 (-0 8, 4 5)	-2 1 (-4 7, 0 5)	-0 2 (-3 1, 2 8)
Any severe AE	16 3 8)	28 6 5)	21 (4 9)	27 6 4)	1 1 (-1 6, 3 8)	2 6 (-0 4, 5 6)	-1 6 (-4 7, 1 5)	-0 1 (-3 4, 3 2)
Any AE with reasonable possibility of being related to study drug$	120 (28 4)	168 39 2)	157 36 6)	186 (44 0)	8 2 (2 0, 14 5)	15 6 9 2, 22 0)	-2 6 (-9 1, 3 9)	4 8 (-1 8, 11 4)
Any AE leading to death	1 0 2)	0	0	0	-0 2 (-0 7, 0 2)	-0 2 (-0 7, 0 2)	0 0	0 0
Deaths								
Occurring <= 30 days (ADA for 70 days) after last dose	1 0 2)	0	0	0	-0 2 (-0 7, 0 2)	-0 2 (-0 7, 0 2)	0 0	0 0
Occurring > 30 days ADA for 70 days) after last dose	0	0	0	0	0 0	0 0	0 0	0 0

Note Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug

A] The point estimate and 95% CI are based on normal approximation to binomial distribution

$ As assessed by investigator

相互参照：M15-572 試験 CSR W2 T 1 1 3 1 1 1 1

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況）を表 2.7.4-42 に示す。

投与 56 週時データカットオフまでの有害事象，重篤な有害事象及び Grade 3 以上の有害事象の 100 人年あたりの発現件数（以下，同順で記載）は，全ウパダシチニブ 15 mg 群（281.1 件/100 人年，9.1 件/100 人年及び 10.5 件/100 人年）とアダリムマブ群（265.9 件/100 人年，9.3 件/100 人年及び 12.4 件/100 人年）で同様であったが，全ウパダシチニブ 30 mg 群（333.9 件/100 人年，12.3 件/100 人年及び 14.0 件/100 人年）では多かった。治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群（4.6 件/100 人年）で最も少なく，全ウパダシチニブ 30 mg 群（6.6 件/100 人年）とアダリムマブ群（7.4 件/100 人年）で同様であった。死亡は全ウパダシチニブ 15 mg 群及び 30 mg 群で各 2 名，アダリムマブ群で 1 名に認められた。このうち，投与 24 週時データカットオフ以降の死亡は，全ウパダシチニブ 15 mg 群，30 mg 群及びアダリムマブ群で各 1 名であった。この 3 名のうち 1 名（全ウパダシチニブ 15 mg 群）は，治験薬の最終投与 30 日後より後に死亡した。

M15-572 試験の日本人部分集団の結果は，2.7.4.5.1.1 項に示す。

表 2 7. - 2. 投与 56 週時データカットオフまでの有害事象の概要（安全性解析対象集団，100 人年あたりの発現状況）：M15-572 試験

	UPA 15 mg QD N = 617) PYs = 839 1)	UPA 30 mg QD N = 613) PYs = 842 8)	ADA 40 mg EOW N = 429) PYs = 631 4)	-- UPA VS ADA 95% CI) A] -- 15 mg QD VS ADA	30 mg QD VS ADA
Exposure-adjusted event rate	Events E/100 PYs)	Events E/100 PYs)	Events E/100 PYs)		
Any adverse event (AE)	2359 (281 1)	2814 (333 9)	1679 (265 9)	15 2 (-1 8, 32 3)	68 0 (50 3, 85 7)
Any serious AE SAE)	76 (9 1)	104 (12 3)	59 (9 3)	-0 3 (-3 4, 2 8)	3 0 (-0 4, 6 4)
Any AE leading to discontinuation of study drug	39 (4 6)	56 (6 6)	47 (7 4)	-2 8 (-5 4, -0 2)	-0 8 (-3 5, 1 9)
Any severe AE	88 (10 5)	118 (14 0)	78 (12 4)	-1 9 (-5 4, 1 6)	1 6 (-2 1, 5 4)
Any AE with reasonable possibility of being related to study drug$	969 (115 5)	1242 (147 4)	708 (112 1)	3 3 (-7 7, 14 4)	35 2 (23 6, 46 9)
Any AE leading to death	1 (0 1)	1 (0 1)	2 (0 3)	-0 2 (-0 7, 0 3)	-0 2 (-0 7, 0 3)
Exposure-adjusted incidence rate	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)		
All deaths	2/839 4 0 2)	2/843 0 0 2)	1/631 5 0 2)	0 1 (-0 4, 0 5)	0 1 (-0 4, 0 5)
Occurring <= 30 days (ADA for 70 days) after last dose	0/839 1	1/842 8 0 1)	1/631 5 0 2)	-0 2 (-0 5, 0 2)	-0 0 (-0 4, 0 3)
Occurring > 30 days ADA for 70 days) after last dose	2/839 4 0 2)	1/842 9 0 1)	0/631 4	0 2 (-0 1, 0 6)	0 1 (-0 1, 0 4)

after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A]: The point estimate and 95% CI are based on normal approximation to poisson distribution.
$ As assessed by investigator.

相互参照：M15-572 試験 CSR W56 Table 14.3__1.1.1

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M15-554 試験

投与 24 週時

M15-554 試験の投与 24 週時までの有害事象の概要を表 2.7.4-43，投与 24 週時データカットオフまでの有害事象の概要を表 2.7.4.7-7（100 人年あたりの発現状況）及び表 2.7.4.7-8 に示す。

投与 24 週時までの有害事象の発現割合は，プラセボ群（65.6%）及びウパダシチニブ 15 mg 群（64.0%）と比較して，ウパダシチニブ 30 mg 群（78.0%）の方が高かった。重篤な有害事象，Grade 3 以上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（以下，同順で記載）は，プラセボ群（1.9%，3.8%及び 5.2%）と比較して，ウパダシチニブ 15 mg 群（5.7%，6.2%及び 7.1%）及びウパダシチニブ 30 mg 群（8.3%，7.3%及び 9.2%）の方が高かった。投与 24 週時までに，死亡がプラセボ群の 1 名に認められた。

投与 24 週時データカットオフまでの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群（286.9 件/100 人年）と比較して，全ウパダシチニブ 30 mg 群（373.1 件/100 人年）の方が多かったが，重篤な有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数（以下，同順で記載）は，全ウパダシチニブ 15 mg 群（15.0 件/100 人年及び 13.0 件/100 人年）と全ウパダシチニブ 30 mg 群（18.2 件/100 人年及び 13.2 件/100 人年）で同様であった。投与 24 週時から投与 24 週時データカットオフまでに，死亡が全ウパダシチニブ 30 mg 群の 1 名に認められた。

M15-554 試験の日本人部分集団の結果は，2.7.4.5.1.2 項に示す。

表 2 7. - 3. 投与 2 週時までの有害事象の概要（安全性解析対象集団）：M15-55 試験

	Placebo N = 212) n (%)	------- UPA ------- 15 mg QD (N = 211) n (%)	30 mg QD N = 218) n (%)	------ UPA VS Placebo 95% CI) [A] ------- 15 mg QD VS Placebo	30 mg QD VS Placebo
Subjects with					
Any adverse event AE)	139 (65 6)	135 (64 0)	170 78 0)	-1 6 (-10 7, 7 5)	12 4 (4 0, 20 9)
Any serious AE (SAE)	4 (1 9)	12 (5 7)	18 8 3)	3 8 0 2, 7 4)	6 4 2 3, 10 5)
Any AE leading to discontinuation of study drug	11 (5 2)	15 (7 1)	20 9 2)	1 9 (-2 7, 6 5)	4 0 (-0 9, 8 8)
Any severe AE	8 (3 8)	13 (6 2)	16 7 3)	2 4 (-1 7, 6 5)	3 6 (-0 7, 7 9)
Any AE with reasonable possibility of being related to study drug$	53 (25 0)	55 26 1)	79 (36 2)	1 1 (-7 2, 9 4)	11 2 (2 6, 19 9)
Any AE leading to death	1 (0 5)	0	0	-0 5 (-1 4, 0 5)	-0 5 (-1 4, 0 5)
Deaths					
Occurring <= 30 days after last dose	1 (0 5)	0	0	-0 5 (-1 4, 0 5)	-0 5 (-1 4, 0 5)
Occurring > 30 days after last dose	0	0	0	0 0	0 0

Note Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing
Severe adverse events are defined as events with grade 3 or above based on the Common Terminology Criteria for Adverse Events CTCAE) version 5 0
$ As assessed by investigator
A] The point estimate and 95% CI are based on normal approximation to binomial distribution

相互参照：M15-55 試験 CSR W2 T 1 1 3 1111

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投与 56 週時

M15-554 試験の投与 56 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況）を表 2.7.4-44 に示す。

投与 56 週時データカットオフまでの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群（260.6 件/100 人年）と比較して，全ウパダシチニブ 30 mg 群（334.4 件/100 人年）の方が多かったが，重篤な有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数（以下，同順で記載）は，全ウパダシチニブ 15 mg 群（14.3 件/100 人年及び 10.0 件/100 人年）と全ウパダシチニブ 30 mg 群（15.8 件/100 人年及び 11.1 件/100 人年）で同様であった。死亡が全ウパダシチニブ 30 mg 群の 1 名に認められたが，本事象は投与 24 週時データカットオフまでに報告されたものであった。

M15-554 試験の日本人部分集団の結果は，2.7.4.5.1.2 項に示す。

表 2 7. - . 投与 56 週時データカットオフまでの有害事象の概要（安全性解析対象集団，100 人年あたりの発現状況）：M15-55 試験

	UPA 15 mg QD (N = 290) (PYs = 419 4)	UPA 30 mg QD (N = 308) (PYs = 423 5)
Exposure-adjusted event rate	Events (E/100 PYs)	Events (E/100 PYs)
Any adverse event (AE)	1093 260 6)	1416 334 4)
Any serious AE SAE)	60 14 3)	67 15 8)
Any AE leading to discontinuation of study drug	42 10 0)	47 11 1)
Any severe AE	54 12 9)	86 20 3)
Any AE with reasonable possibility of being related to study drug$	253 60 3)	438 103 4)
Any AE leading to death	0	1 0 2)
Exposure-adjusted incidence rate	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
All deaths	0/419 4	1/423 6 (0 2)
Occurring <= 30 days after last dose	0/419 4	1/423 6 (0 2)
Occurring > 30 days after last dose	0/419 4	0/423 5

Note Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
E/100 PYs = Events per 100 patient-years n/100 PYs = Number of subjects with at least one event per 100 patient-years
$ As assessed by investigator

相互参照：M15-55 試験 CSR W56 Table 1 .3 1 1 1

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2.7. .2.1.1 比較的よく見られる有害事象

2.7. .2.1.1.1 有害事象及び治験薬と関連ありの有害事象

2.7. .2.1.1.1.1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 2 週時）で発現割合が高かった有害事象（いずれかの投与群で発現割合 2%以上）を表 2.7. - 5 に示す。また，治験薬と関連ありの有害事象を表 2.7. .7-9 に示す。

プラセボ対照併合解析集団（投与 2 週時）で発現割合が高かった有害事象（発現割合 5%以上）は，ウパダシチニブ 15 mg 併合群では上気道感染（8.9%）及び血中クレアチンホスホキナーゼ増加（6.6%），ウパダシチニブ 30 mg 併合群では上気道感染（9.7%），血中クレアチンホスホキナーゼ増加（8.3%），上咽頭炎（7.2%）及びアラニンアミノトランスフェラーゼ増加（5.5%），プラセボ併合群では上気道感染（6.9%）及び上咽頭炎（6 0%）であった。いずれかの投与群で発現割合が 10%以上であった有害事象は認められなかった。

SOC 別で発現割合が高かった有害事象（ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現割合 10%以上。以下，同順で記載）は，感染症および寄生虫症（37.0%及び 5.1%），臨床検査（13.9%及び 19.7%），胃腸障害（15 0%及び 15.8%），筋骨格系および結合組織障害（10.3%及び 9.8%）であった（ISS Table 2. 1 1.3.1）。プラセボ併合群の SOC 別で発現割合が高かった有害事象（発現割合 10%以上）は，感染症および寄生虫症（33.1%），胃腸障害（11.7%）及び筋骨格系および結合組織障害（11.5%）であった。

プラセボ対照併合解析集団（投与 2 週時）で，治験薬と関連ありの有害事象のうち発現割合が高かった有害事象（ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現割合 2%以上。以下，同順で記載）は，リンパ球減少症（0 8%及び 2.0%），好中球減少症（0.8%及び 2.7%），口腔ヘルペス（0.8%及び 3.0%），上気道感染（ . %及び 1%），尿路感染（2.5%及び 1.9%），アラニンアミノトランスフェラーゼ増加（3.0%及び . %），アスパラギン酸アミノトランスフェラーゼ増加（2.0%及び 2.8%）及び血中クレアチンホスホキナーゼ増加（ .7%及び 6.6%）であった。

表 2.7.4-45. プラセボ対照併合解析集団（投与 24 週時）で発現割合が高かった有害事象（いずれかの投与群で発現割合 2%以上）

MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
上気道感染	44 (6.9) [6.9]	57 (8.9) [8.9]	62 (9.7) [9.7]
血中クレアチンホスホキナーゼ増加	10 (1.6) [1.6]	42 (6.6) [6.5]	53 (8.3) [8.3]
上咽頭炎	38 (6.0) [6.0]	31 (4.8) [4.8]	46 (7.2) [7.2]
アラニンアミノトランスフェラーゼ増加	13 (2.0) [2.0]	21 (3.3) [3.3]	35 (5.5) [5.5]
気管支炎	14 (2.2) [2.2]	24 (3.8) [3.8]	31 (4.8) [4.8]
尿路感染	22 (3.5) [3.5]	27 (4.2) [4.2]	26 (4.1) [4.0]
下痢	22 (3.5) [3.5]	23 (3.6) [3.6]	26 (4.1) [4.0]
頭痛	16 (2.5) [2.5]	21 (3.3) [3.3]	26 (4.1) [4.1]
悪心	15 (2.4) [2.4]	13 (2.0) [2.0]	24 (3.7) [3.7]
アスパラギン酸アミノトランスフェラーゼ増加	9 (1.4) [1.4]	14 (2.2) [2.2]	22 (3.4) [3.4]
口腔ヘルペス	6 (0.9) [0.9]	7 (1.1) [1.1]	22 (3.4) [3.4]
咳嗽	10 (1.6) [1.6]	16 (2.5) [2.5]	21 (3.3) [3.3]
貧血	4 (0.6) [0.6]	4 (0.6) [0.6]	20 (3.1) [3.1]
胃腸炎	7 (1.1) [1.1]	8 (1.3) [1.3]	19 (3.0) [3.0]
好中球減少症	2 (0.3) [0.3]	6 (0.9) [0.9]	18 (2.8) [2.8]
インフルエンザ	8 (1.3) [1.3]	19 (3.0) [3.0]	17 (2.7) [2.6]
高血圧	19 (3.0) [3.0]	20 (3.1) [3.1]	16 (2.5) [2.5]
発熱	5 (0.8) [0.8]	6 (0.9) [0.9]	16 (2.5) [2.5]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
SSA = Study size adjusted.
The 2% threshold is based on the crude proportions in any treatment group.
Events are presented by decreasing frequency of preferred terms in the upadacitinib 30 mg treatment group.

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MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
リンパ球減少症	5 (0.8) [0.8]	5 (0.8) [0.8]	15 (2.3) [2.4]
背部痛	10 (1.6) [1.6]	12 (1.9) [1.9]	14 (2.2) [2.2]
副鼻腔炎	15 (2.4) [2.4]	12 (1.9) [1.9]	13 (2.0) [2.0]
白血球減少症	4 (0.6) [0.6]	10 (1.6) [1.6]	13 (2.0) [2.0]
帯状疱疹	5 (0.8) [0.8]	7 (1.1) [1.1]	13 (2.0) [2.0]
乾癬性関節症	24 (3.8) [3.8]	16 (2.5) [2.5]	10 (1.6) [1.6]
乾癬	15 (2.4) [2.4]	4 (0.6) [0.6]	5 (0.8) [0.8]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
SSA = Study size adjusted.
The 2% threshold is based on the crude proportions in any treatment group.
Events are presented by decreasing frequency of preferred terms in the upadacitinib 30 mg treatment group.

相互参照：ISS Table 2.4__1.1.3.8

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日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団で発現割合が高かった有害事象（発現割合 10%以上）は，ウパダシチニブ 15 mg 併合群では上咽頭炎（35.3%［6/17 名］），腹部不快感，便秘，毛包炎，インフルエンザ及び血中クレアチンホスホキナーゼ増加（各 11.8%［2/17 名］），ウパダシチニブ 30 mg 併合群では上咽頭炎（22.2%［ /18 名］），血中クレアチンホスホキナーゼ増加（16.7%［3/18 名］），発熱，胃腸炎及び上気道感染（各 11.1%［2/18 名］），プラセボ併合群では上咽頭炎（20.0%［3/15 名］）であった（J-ISS Table 2. 1.1.3.1 J）。

SOC 別で発現割合が高かった有害事象（ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で 20%以上に発現。以下，同順で記載）は，感染症および寄生虫症（52.9%［9/17 名］及び 61.1%［11/18 名］），胃腸障害（29. %［5/17 名］及び 33.3%［6/18 名］）及び臨床検査（23.5%［ /17 名］及び 22.2%［ /18 名］）であった。プラセボ併合群では，SOC 別で発現割合が高かった有害事象（20%以上に発現）は，感染症および寄生虫症（33.3%［5/15 名］）及び胃腸障害（20.0%［3/15 名］）であった（J-ISS Table 2. 1.1.3.1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団で，治験薬と関連ありの有害事象のうち発現割合が高かった有害事象（ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現割合 10%以上。以下，同順で記載）は，上咽頭炎（11.8%［2/17 名］及び 0/18 名）及び血中クレアチンホスホキナーゼ増加（0/17 名及び 11.1%［2/18 名］）であった（J-ISS Table 2. 1.1.3. J）。

2.7. .2.1.1.1.2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

全ウパダシチニブ併合解析集団（長期）の有害事象を ISS Table 2. 1.2.3.1 及び表 2.7. .7-10（100 人年あたりの発現件数）に示す。また，治験薬と関連ありの有害事象を表 2.7. .7-11（100 人年あたりの発現件数）に示す。

全ウパダシチニブ併合解析集団（長期）で 100 人年あたりの発現件数が多かった有害事象（10 件/100 人年以上）は，全ウパダシチニブ 15 mg 併合群では上気道感染（15 8 件 100 人年），血中クレアチンホスホキナーゼ増加（11. 件/100 人年）及び上咽頭炎（10.2 件 100 人年），全ウパダシチニブ 30 mg 併合群では血中クレアチンホスホキナーゼ増加（17.0 件 100 人年），上気道感染（16.9 件/100 人年）及び上咽頭炎（13.1 件/100 人年）であった。

全ウパダシチニブ併合解析集団（長期）で，治験薬と関連ありの有害事象のうち 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現

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件数 2 件/100 人年以上。以下，同順で記載）は，血中クレアチンホスホキナーゼ増加（8.1 件/100 人年，13.0 件/100 人年），上気道感染（8.1 件/100 人年，8.6 件/100 人年），アラニンアミノトランスフェラーゼ増加（5. 件/100 人年，5.8 件/100 人年），尿路感染（ .5 件/100 人年， . 件/100 人年），アスパラギン酸アミノトランスフェラーゼ増加（3 6 件/100 人年， .1 件/100 人年），上咽頭炎（2.9 件/100 人年，2.9 件/100 人年），帯状疱疹（2.7 件/100 人年，5.8 件/100 人年），気管支炎（2.6 件/100 人年，3.3 件/100 人年），白血球減少症（1.8 件 100 人年，2.8 件/100 人年），リンパ球減少症（1.8 件/100 人年，2. 件/100 人年），好中球減少症（1.7 件/100 人年，3.6 件/100 人年），貧血（1.3 件/100 人年，2 2 件 100 人年），頭痛（1.3 件/100 人年，2.1 件/100 人年），口腔ヘルペス（1.2 件/100 人年，5.0 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団で 100 人年あたりの発現件数が多かった有害事象（10 件/100 人年以上）は，全ウパダシチニブ 15 mg 併合群では上咽頭炎（12 件［52 2 件/100 人年］），腹部不快感，便秘及び血中クレアチンホスホキナーゼ増加（各 件［17. 件/100 人年］），毛包炎及びインフルエンザ（各 3 件［13.0 件/100 人年］），全ウパダシチニブ 30 mg 併合群では上咽頭炎（15 件［53. 件/100 人年］），口内炎（6 件［21. 件/100 人年］），帯状疱疹及び血中クレアチンホスホキナーゼ増加（各 5 件［17.8 件 100 人年］），毛包炎，口腔ヘルペス及び薬疹（各 件［1 .2 件/100 人年］），下痢，インフルエンザ，上気道感染，白血球数減少及び不眠症（各 3 件［10.7 件/100 人年］）であった（J-ISS Table 2. 1.2.3.2 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団で，治験薬と関連ありの有害事象のうち 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で 10 件/100 人年以上。以下，同順で記載）は，帯状疱疹（2 件［8.7 件/100 人年］及び 5 件［17.8 件/100 人年］），上咽頭炎（3 件［13 0 件 100 人年］及び 3 件［10.7 件/100 人年］），血中クレアチンホスホキナーゼ増加（2 件［8.7 件/100 人年］及び 3 件［10.7 件/100 人年］），口腔ヘルペス（1 件［ 3 件/100 人年］及び 3 件［10.7 件/100 人年］），口内炎及び白血球数減少（各 0 件及び各 3 件［10.7 件/100 人年］）であった（J-ISS T 1 2 1 2 3 5 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団の有害事象を J-ISS Table 2. 1.2.3.1 J に示す。

20[redacted]年[redacted]月[redacted]日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の有害事象を ISS update Table 2. 3.1 及び表 2.7. .7-89（100 人年あたりの発現件数）に示す。また，治験薬と関連ありの有害事象を表 2.7. .7-90（100 人年あたりの発現件数）及び表 2.7. .7-91 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）で 100 人年あたりの発現件数が多かった有害事象（10 件/100 人年以上）は，全ウパダシチニブ 15 mg 併合群では上気道感染（13 5 件/100 人年），全ウパダシチニブ 30 mg 併合群では上気道感染（15.3 件/100 人年），血中クレアチンホスホキナーゼ増加（13 8 件/100 人年）及び上咽頭炎（10.8 件/100 人年）であった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）で，治験薬と関連ありの有害事象のうち 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現件数 2 件/100 人年以上。以下，同順で記載）は，上気道感染（7.1 件/100 人年，8.0 件/100 人年），血中クレアチンホスホキナーゼ増加（6. 件/100 人年，10.3 件/100 人年），アラニンアミノトランスフェラーゼ増加（ . 件 100 人年， .5 件/100 人年），尿路感染（3.8 件/100 人年，3.9 件 100 人年），帯状疱疹（3.0 件/100 人年，5.0 件/100 人年），アスパラギン酸アミノトランスフェラーゼ増加（3.0 件/100 人年，3.3 件/100 人年），気管支炎（2.8 件/100 人年，3 0 件 100 人年），上咽頭炎（2.7 件/100 人年，2.6 件/100 人年），白血球減少症（1.6 件/100 人年，2.5 件/100 人年），リンパ球減少症（1.6 件/100 人年，2 1 件 100 人年），好中球減少症（1.3 件/100 人年，2.8 件/100 人年），口腔ヘルペス（1.2 件/100 人年， 0 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団で 100 人年あたりの発現件数が多かった有害事象（10 件/100 人年以上）は，全ウパダシチニブ 15 mg 併合群では上咽頭炎（15 件［ 2 6 件/100 人年］），便秘（5 件［1 .2 件/100 人年］），腹部不快感及び血中クレアチンホスホキナーゼ増加（各 件［11. 件/100 人年］），全ウパダシチニブ 30 mg 併合群では上咽頭炎（17 件［ 2. 件/100 人年］），帯状疱疹（8 件［20 0 件/100 人年］），口内炎及び血中クレアチンホスホキナーゼ増加（各 6 件［15.0 件/100 人年］），口腔ヘルペス（5 件［12.5 件/100 人年］），毛包炎，上気道感染，白血球数減少及び薬疹（各 件［10.0 件/100 人年］）であった（J-ISS update Table 2. 1.2.3.2 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団で，治験薬と関連ありの有害事象のうち 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で 10 件 100 人年以上。以下，同順で記載）は，上咽頭

炎（ 件［11. 件/100 人年］及び 5 件［12.5 件/100 人年］），帯状疱疹（3 件［8.5 件/100 人年］及び 8 件［20.0 件/100 人年］），口腔ヘルペス（3 件［8.5 件/100 人年］及び 件［10.0 件/100 人年］），血中クレアチンホスホキナーゼ増加（2 件［5.7 件/100 人年］及び 件［10 0 件/100 人年］）及び白血球数減少（0 件及び 件［10 0 件 100 人年］）であった（J-ISS update Table 2. 1.2.3.5 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団の有害事象を J-ISS update Table 2. 1.2 3.1 J，治験薬と関連ありの有害事象を表 2.7. .7-92 に示す。

2.7. .2.1.1.1.3 M15-572 試験

投与 2 週時

M15-572 試験で投与 2 週時までの発現割合が高かった有害事象（いずれかの投与群で発現割合 2%以上）を表 2.7. - 6，投与 2 週時までのすべての有害事象，投与 2 週時データカットオフまでの有害事象（100 人年あたりの発現件数）を M15-572 試験（投与 2 週時）2.7.6 項に示す。また，投与 2 週時までの治験薬と関連ありの有害事象のうち，発現割合が高かった事象（いずれかの投与群で発現割合 2%以上）を表 2.7. - 7，投与 2 週時までのすべての治験薬と関連ありの有害事象，投与 2 週時データカットオフまでの治験薬と関連ありの有害事象（100 人年あたりの発現件数）を M15-572 試験（投与 2 週時）2.7.6 項に示す。

投与 2 週時までの発現割合が高かった有害事象（ウパダシチニブ 15 mg 群，30 mg 群，アダリムマブ群又はプラセボ群で発現割合 5%以上。以下，同順で記載）は，上気道感染（10.3%，9.2%，7.0%及び 8.0%），上咽頭炎（ 9%，6.1%，6.8%及び 5 0%），血中クレアチンホスホキナーゼ増加（8.9%，9.7%，5.6%及び 1. %），アラニンアミノトランスフェラーゼ増加（ . %，6. %，7.5%及び 2.8%）及びアスパラギン酸アミノトランスフェラーゼ増加（3.3%，3.5%，5.1%及び 1.9%）であった。これらの有害事象の発現割合は，ウパダシチニブ各用量群とアダリムマブ群でおおむね同様であったが，血中クレアチンホスホキナーゼ増加はウパダシチニブ 15 mg 群及び 30 mg 群の方が高かった。

投与 2 週時までの SOC 別で発現割合が最も高かった有害事象は，いずれの投与群でも感染症および寄生虫症であり，発現割合はウパダシチニブ 15 mg 群（38.9%［167/ 29 名］），アダリムマブ群（3 .0%［1 6/ 29 名］）及びプラセボ群（32.6%［138/ 23 名］）と比較して，ウパダシチニブ 30 mg 群（ 3 0%［182/ 23 名］）の方が高かった（M15-572 試験 CSR W2 Table 1 3 1.2 1）。感染症および寄生虫症で発現割合が高かった有害事象（いずれかの投与群で発現割合 10%以上）は上気道感染であり，プラセボ群で 8 0%，アダリムマブ群で 7.0%，ウパダシチニブ 15 mg 群で 10.3%，30 mg 群で 9.2%であった。

投与 2 週時までの治験薬と関連ありの有害事象の発現割合は，プラセボ群（28. %）と比較してウパダシチニブ 15 mg 群（36.6%）及びウパダシチニブ 30 mg 群（ .0%）の方が高く，ア

ダリムマブ群（39.2%）と比較してウパダシチニブ 15 mg 群では同様であり，ウパダシチニブ 30 mg 群ではやや高かった（M15-572 試験 CSR W2 Table 1 .3 1 6.1）。

投与 2 週時までの治験薬と関連ありの有害事象のうち，発現割合が高かった有害事象（発現割合 2%以上）は，ウパダシチニブ 15 mg 群では血中クレアチンホスホキナーゼ増加（6.5%），上気道感染（5.6%），アラニンアミノトランスフェラーゼ増加（ .2%），アスパラギン酸アミノトランスフェラーゼ増加（3.0%），白血球減少症（2.3%）及び尿路感染（2.3%），ウパダシチニブ 30 mg 群では血中クレアチンホスホキナーゼ増加（7.8%），アラニンアミノトランスフェラーゼ増加（5.0%），口腔ヘルペス（ 3%），上気道感染（ 0%），好中球減少症（3.5%），アスパラギン酸アミノトランスフェラーゼ増加（2.8%），リンパ球減少症（2.6%），気管支炎（2.1%），白血球減少症（2.1%）及び上咽頭炎（2.1%）であった。治験薬と関連ありの注射部位反応は，ウパダシチニブ 30 mg 群の 1 名を除き，アダリムマブ群のみで発現した。

表 2.7.4-46. 投与 24 週時までの発現割合が高かった有害事象（いずれかの投与群で発現割合 2%以上）（安全性解析対象集団）：M15-572 試験

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
血液およびリンパ系障害				
貧血	3 (0.7)	0	3 (0.7)	10 (2.4)
白血球減少症	4 (0.9)	5 (1.2)	10 (2.3)	11 (2.6)
リンパ球減少症	5 (1.2)	1 (0.2)	5 (1.2)	13 (3.1)
好中球減少症	1 (0.2)	8 (1.9)	4 (0.9)	16 (3.8)
胃腸障害				
下痢	10 (2.4)	9 (2.1)	18 (4.2)	14 (3.3)
悪心	8 (1.9)	10 (2.3)	9 (2.1)	13 (3.1)
一般・全身障害および投与部位の状態				
注射部位反応	0	12 (2.8)	0	2 (0.5)
発熱	5 (1.2)	2 (0.5)	3 (0.7)	12 (2.8)
感染症および寄生虫症				
気管支炎	9 (2.1)	9 (2.1)	14 (3.3)	19 (4.5)
胃腸炎	5 (1.2)	7 (1.6)	5 (1.2)	13 (3.1)
インフルエンザ	5 (1.2)	2 (0.5)	11 (2.6)	6 (1.4)
上咽頭炎	21 (5.0)	29 (6.8)	21 (4.9)	26 (6.1)
口腔ヘルペス	4 (0.9)	6 (1.4)	7 (1.6)	19 (4.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
感染症および寄生虫症 (Cont.)				
気道感染	2 (0.5)	4 (0.9)	9 (2.1)	8 (1.9)
上気道感染	34 (8.0)	30 (7.0)	44 (10.3)	39 (9.2)
尿路感染	10 (2.4)	14 (3.3)	18 (4.2)	15 (3.5)
臨床検査				
アラニンアミノトランスフェラーゼ増加	12 (2.8)	32 (7.5)	19 (4.4)	27 (6.4)
アスパラギン酸アミノトランスフェラーゼ増加	8 (1.9)	22 (5.1)	14 (3.3)	15 (3.5)
血中クレアチンホスホキナーゼ増加	6 (1.4)	24 (5.6)	38 (8.9)	41 (9.7)
トランスアミナーゼ上昇	0	10 (2.3)	2 (0.5)	7 (1.7)
代謝および栄養障害				
高コレステロール血症	1 (0.2)	2 (0.5)	2 (0.5)	10 (2.4)
筋骨格系および結合組織障害				
背部痛	7 (1.7)	8 (1.9)	6 (1.4)	9 (2.1)
乾癬性関節症	13 (3.1)	5 (1.2)	6 (1.4)	7 (1.7)
神経系障害				
頭痛	10 (2.4)	18 (4.2)	17 (4.0)	17 (4.0)
精神障害				
不眠症	2 (0.5)	2 (0.5)	10 (2.3)	4 (0.9)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

System Organ Class MedDRA 22 0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
呼吸器、胸郭および縦隔障害				
咳嗽	5 1 2)	7 (1 6)	11 2 6)	14 (3 3)
皮膚および皮下組織障害				
乾癬	7 1 7)	9 (2 1)	3 (0 7)	4 0 9)
血管障害				
高血圧	10 (2 4)	8 (1 9)	16 3 7)	12 (2 8)

Note Treatment emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total

相互参照：M15-572 試験 CSR W2 Table 1 .3 1 3 1

表 2 7. - 7. 投与 2 週時までの治験薬と関連ありの有害事象のうち発現割合が高かった事象（いずれかの投与群で発現割合 2%以上）（安全性解析対象集団）：M15-572 試験

System Organ Class MedDRA 22 0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
血液およびリンパ系障害				
白血球減少症	2 0 5)	4 (0 9)	10 2 3)	9 2 1)
リンパ球減少症	3 0 7)	1 (0 2)	5 (1 2)	11 (2 6)
好中球減少症	1 0 2)	6 (1 4)	4 (0 9)	15 (3 5)
一般・全身障害および投与部位の状態				
注射部位反応	0	10 (2 3)	0	1 0 2)
感染症および寄生虫症				
気管支炎	2 0 5)	5 (1 2)	3 (0 7)	9 2 1)
上咽頭炎	7 1 7)	19 (4 4)	7 (1 6)	9 2 1)
口腔ヘルペス	4 0 9)	5 (1 2)	5 (1 2)	18 (4 3)
上気道感染	18 (4 3)	21 (4 9)	24 5 6)	17 (4 0)
尿路感染	6 1 4)	8 (1 9)	10 2 3)	6 1 4)
臨床検査				
アラニンアミノトランスフェラーゼ増加	7 1 7)	24 (5 6)	18 4 2)	21 (5 0)
アスパラギン酸アミノトランスフェラーゼ増加	4 0 9)	18 (4 2)	13 3 0)	12 (2 8)
血中クレアチンホスホキナーゼ増加	4 0 9)	17 (4 0)	28 6 5)	33 (7 8)

Note Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug

相互参照：M15-572 試験 CSR W2 Table 1 .3 1 3 2

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの有害事象及び治験薬と関連ありの有害事象（100 人年あたりの発現件数）を M15-572 試験（投与 56 週時）2.7.6 項に示す。

投与 56 週時データカットオフまでの 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 群，30 mg 群又はアダリムマブ群で発現件数 10 件/100 人年以上。以下，同順で記載）は，上気道感染（14.8 件/100 人年，18.0 件/100 人年及び 11.6 件/100 人年），血中クレアチンホスホキナーゼ増加（11.9 件/100 人年，17.3 件/100 人年及び 7.3 件/100 人年）及び上咽頭炎（8.6 件/100 人年，10.0 件/100 人年及び 10.6 件/100 人年）であった。いずれかの投与群で 5 件/100 人年以上発現した有害事象のうち，多くの事象の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 群で最も多かった。

投与 56 週時データカットオフまでの SOC 別で 100 人年あたりの発現件数が最も多かった有害事象は，いずれの投与群でも感染症および寄生虫症（全ウパダシチニブ 15 mg 群 92.6 件/100 人年，全ウパダシチニブ 30 mg 群 112.1 件/100 人年，アダリムマブ群 70.0 件/100 人年）であった。感染症および寄生虫症で 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 群，30 mg 群又はアダリムマブ群で発現件数 5 件/100 人年以上。以下，同順で記載）は，上気道感染（14.8 件/100 人年，18.0 件/100 人年及び 11.6 件/100 人年），上咽頭炎（8.6 件/100 人年，10.0 件/100 人年及び 10.6 件/100 人年），尿路感染（6.7 件/100 人年，9.4 件/100 人年及び 3.6 件/100 人年），気管支炎（5.7 件/100 人年，6.6 件/100 人年及び 2.9 件/100 人年），帯状疱疹（3.5 件/100 人年，5.8 件/100 人年及び 0.5 件/100 人年）及び口腔ヘルペス（2.4 件/100 人年，6.8 件/100 人年及び 2.7 件/100 人年）であった。上気道感染，尿路感染，気管支炎及び帯状疱疹の 100 人年あたりの発現件数は，アダリムマブ群と比較して全ウパダシチニブ群の方が多かった。口腔ヘルペスの 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群及びアダリムマブ群と比較して，全ウパダシチニブ 30 mg 群の方が多く，上咽頭炎は投与群間で同様であった。

投与 56 週時データカットオフまでの治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 115.5 件/100 人年，全ウパダシチニブ 30 mg 群で 147.4 件/100 人年，アダリムマブ群で 112.1 件/100 人年であった。

投与 56 週時データカットオフまでの治験薬と関連ありの有害事象のうち，100 人年あたりの発現件数が多かった有害事象（発現件数 5 件/100 人年以上）は，全ウパダシチニブ 15 mg 群では血中クレアチンホスホキナーゼ増加（9.2 件/100 人年），上気道感染（8.7 件/100 人年）及びアラニンアミノトランスフェラーゼ増加（6.8 件/100 人年），全ウパダシチニブ 30 mg 群では血中クレアチンホスホキナーゼ増加（12.9 件/100 人年），上気道感染（9.8 件/100 人年），口腔ヘルペス（5.5 件/100 人年）及びアラニンアミノトランスフェラーゼ増加（5.3 件/100 人年），アダリムマブ群では上気道感染（8.2 件/100 人年），アラニンアミノトランスフェラーゼ増加（6.7 件/100 人年），上咽頭炎（5.7 件/100 人年）及び血中クレアチンホスホキナーゼ増加（5.2 件/100 人年）であった。

2.7. .2.1.1.1. M15-55 試験

投与 2 週時

M15-55 試験で投与 2 週時までの発現割合が高かった有害事象（いずれかの投与群で発現割合 2%以上）を表 2.7. - 8，投与 2 週時までのすべての有害事象，投与 2 週時データカットオフまでの有害事象（100 人年あたりの発現件数）を M15-55 試験（投与 2 週時）2.7.6 項に示す。また，投与 2 週時までの治験薬と関連ありの有害事象のうち，発現割合が高かった事象（いずれかの投与群で発現割合 2%以上）を表 2.7. - 9，投与 2 週時までのすべての治験薬と関連ありの有害事象，投与 2 週時データカットオフまでの治験薬と関連ありの有害事象（100 人年あたりの発現件数）を M15-55 試験（投与 2 週時）2.7.6 項に示す。

投与 2 週時までの発現割合が高かった有害事象（ウパダシチニブ 15 mg 群，30 mg 群又はプラセボ群で発現割合 5%以上。以下，同順で記載）は，上気道感染（6.2%，10.6%及び .7%），上咽頭炎（ .7%，9 2%及び 8.0%），尿路感染（ .3%，5 0%及び 5.7%），下痢（2. %，5.5%及び 5.7%），血中クレアチンホスホキナーゼ増加（1 9%，5.5%及び 1.9%），気管支炎（ .7%，5.5%及び 2. %），乾癬性関節症（ .7%，1. %及び 5.2%），インフルエンザ（3.8%，5 0%及び 1. %）及び悪心（1.9%，5 0%及び 3.3%）であった。これらの有害事象のうち，多くの発現割合はウパダシチニブ 15 mg 群とプラセボ群でおおむね同様であったが，上咽頭炎及び下痢の発現割合はプラセボ群の方が高く，気管支炎及びインフルエンザの発現割合はウパダシチニブ 15 mg 群の方が高かった。いずれかの投与群で発現割合が 5%以上であった有害事象のうち，乾癬性関節症を除くすべての発現割合は，ウパダシチニブ 15 mg 群と比較してウパダシチニブ 30 mg 群の方が高かった。

投与 2 週時までの SOC 別で発現割合が最も高かった有害事象は，いずれの投与群でも感染症および寄生虫症であり，発現割合はウパダシチニブ 15 mg 群（33.2%［70/211 名］）及びプラセボ群（3 .0%［72/212 名］）と比較して，ウパダシチニブ 30 mg 群（ 9 1%［107/218 名］）の方が高かった（M15-55 試験 CSR W2 T 1 1 3 1 2 1）。感染症および寄生虫症で発現割合が高かった有害事象（いずれかの投与群で発現割合 10%以上）は上気道感染であり，発現割合はウパダシチニブ 30 mg 群で最も高かった（ウパダシチニブ 15 mg 群：6 2%，30 mg 群：10.6%，プラセボ群： .7%）。

投与 2 週時までの治験薬と関連ありの有害事象の発現割合は，プラセボ群（25.0%）と比較して，ウパダシチニブ 15 mg 群（26.1%）では同様であり，ウパダシチニブ 30 mg 群（36.2%）では高かった（M15-55 試験 CSR W2 Table 1 .3 1.6.1）。

シチニブ 30 mg 群では上気道感染（4.1%），血中クレアチンホスホキナーゼ増加（4.1%），帯状疱疹（3.7%），アラニンアミノトランスフェラーゼ増加（3.2%），尿路感染（2.8%），アスパラギン酸アミノトランスフェラーゼ増加（2.8%），貧血（2.3%）及び頭痛（2.3%）であった。

表 2.7.4-48. 投与 24 週時までの発現割合が高かった有害事象（いずれかの投与群で発現割合 2%以上）（安全性解析対象集団）：M15-554 試験

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
血液およびリンパ系障害			
貧血	1 (0.5)	1 (0.5)	10 (4.6)
胃腸障害			
便秘	1 (0.5)	3 (1.4)	5 (2.3)
下痢	12 (5.7)	5 (2.4)	12 (5.5)
悪心	7 (3.3)	4 (1.9)	11 (5.0)
嘔吐	5 (2.4)	0	4 (1.8)
感染症および寄生虫症			
気管支炎	5 (2.4)	10 (4.7)	12 (5.5)
胃腸炎	2 (0.9)	3 (1.4)	6 (2.8)
帯状疱疹	2 (0.9)	3 (1.4)	8 (3.7)
インフルエンザ	3 (1.4)	8 (3.8)	11 (5.0)
上咽頭炎	17 (8.0)	10 (4.7)	20 (9.2)
副鼻腔炎	9 (4.2)	5 (2.4)	6 (2.8)
上気道感染	10 (4.7)	13 (6.2)	23 (10.6)
尿路感染	12 (5.7)	9 (4.3)	11 (5.0)

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
傷害、中毒および処置合併症			
転倒	0	1 (0.5)	5 (2.3)
臨床検査			
アラニンアミノトランスフェラーゼ増加	1 (0.5)	2 (0.9)	8 (3.7)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.5)	0	7 (3.2)
血中クレアチンホスホキナーゼ増加	4 (1.9)	4 (1.9)	12 (5.5)
好中球数減少	0	0	5 (2.3)
代謝および栄養障害			
高脂血症	1 (0.5)	5 (2.4)	1 (0.5)
筋骨格系および結合組織障害			
背部痛	3 (1.4)	6 (2.8)	5 (2.3)
乾癬性関節症	11 (5.2)	10 (4.7)	3 (1.4)
神経系障害			
浮動性めまい	2 (0.9)	4 (1.9)	6 (2.8)
頭痛	6 (2.8)	4 (1.9)	9 (4.1)
精神障害			
不安	5 (2.4)	2 (0.9)	1 (0.5)
うつ病	5 (2.4)	2 (0.9)	7 (3.2)

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

System Organ Class MedDRA 22 0 Preferred Term	Placebo N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
呼吸器、胸郭および縦隔障害			
咳嗽	5 (2 4)	5 (2 4)	7 3 2)
皮膚および皮下組織障害			
乾癬	8 (3 8)	1 (0 5)	1 0 5)
血管障害			
高血圧	9 (4 2)	4 (1 9)	4 1 8)

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

相互参照：M15-55 試験 CSR W2 Table 1 .3 1 3 1

表 2 7. - 9. 投与 2 週時までの治験薬と関連ありの有害事象のうち発現割合が高かった事象（いずれかの投与群で発現割合 2%以上）（安全性解析対象集団）：M15-55 試験

System Organ Class MedDRA 22 0 Preferred Term	Placebo N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
血液およびリンパ系障害			
貧血	0	1 (0 5)	5 2 3)
感染症および寄生虫症			
気管支炎	1 (0 5)	5 (2 4)	3 1 4)
帯状疱疹	0	3 (1 4)	8 3 7)
副鼻腔炎	7 (3 3)	3 (1 4)	2 0 9)
上気道感染	3 (1 4)	4 (1 9)	9 4 1)
尿路感染	5 (2 4)	6 (2 8)	6 2 8)
臨床検査			
アラニンアミノトランスフェラーゼ増加	1 (0 5)	1 (0 5)	7 3 2)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0 5)	0	6 2 8)
血中クレアチンホスホキナーゼ増加	4 (1 9)	2 (0 9)	9 4 1)
神経系障害			
頭痛	2 (0 9)	1 (0 5)	5 2 3)

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

相互参照：M15-55 試験 CSR W2 Table 1 .3 1 3 2

投与 56 週時

M15-554 試験の投与 56 週時データカットオフまでの有害事象及び治験薬と関連ありの有害事象（100 人年あたりの発現件数）を M15-554 試験（投与 56 週時）2.7.6 項に示す。

投与 56 週時データカットオフまでの 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 群又は 30 mg 群で発現件数 10 件/100 人年以上。以下，同順で記載）は，上咽頭炎（11.7 件/100 人年及び 12.8 件/100 人年）及び上気道感染（11.0 件/100 人年及び 11.6 件/100 人年）であった。

投与 56 週時データカットオフまでの SOC 別で 100 人年あたりの発現件数が最も多かった有害事象は，いずれの投与群でも感染症および寄生虫症（全ウパダシチニブ 15 mg 群 88.5 件/100 人年，全ウパダシチニブ 30 mg 群 110.5 件/100 人年）であった。感染症および寄生虫症で 100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 群又は 30 mg 群で発現件数 5 件/100 人年以上。以下，同順で記載）は，上咽頭炎（11.7 件/100 人年及び 12.8 件/100 人年），上気道感染（11.0 件/100 人年及び 11.6 件/100 人年），尿路感染（9.8 件/100 人年及び 8.0 件/100 人年），気管支炎（8.8 件/100 人年及び 7.6 件/100 人年），副鼻腔炎（5.5 件/100 人年及び 5.0 件/100 人年），インフルエンザ（5.2 件/100 人年及び 5.2 件/100 人年）及び帯状疱疹（3.6 件/100 人年及び 6.8 件/100 人年）であった。

投与 56 週時データカットオフまでの治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 60.3 件/100 人年，全ウパダシチニブ 30 mg 群で 103.4 件/100 人年であった。

投与 56 週時データカットオフまでの治験薬と関連ありの有害事象のうち，100 人年あたりの発現件数が多かった有害事象（発現件数 5 件/100 人年以上）は，全ウパダシチニブ 15 mg 群では尿路感染（5.0 件/100 人年），全ウパダシチニブ 30 mg 群では血中クレアチンホスホキナーゼ増加（6.8 件/100 人年），帯状疱疹（5.9 件/100 人年）及び上気道感染（5.2 件/100 人年）であった。

2.7.4.2.1.1.2 重症度別の有害事象

2.7.4.2.1.1.2.1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 24 週時）の Grade 3 以上の有害事象を表 2.7.4.7-12 に示す。

プラセボ対照併合解析集団（投与 24 週時）では，Grade 3 以上の有害事象の発現割合は，ウパダシチニブ 15 mg 併合群で 5.3%（34/640 名），ウパダシチニブ 30 mg 併合群で 6.7%（43/641 名），プラセボ併合群で 3.8%（24/635 名）であった。ウパダシチニブ 15 mg 併合群，30 mg 併合群又はプラセボ併合群で 3 名以上に発現した Grade 3 以上の有害事象（以下，同順で記載）は，

肺炎（2 名， 名，1 名），アラニンアミノトランスフェラーゼ増加（2 名，3 名，1 名）及びリンパ球減少症（3 名，2 名，1 名）であった。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 以上の有害事象の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 16.7%（3/18 名）であり，プラセボ併合群では発現しなかった。いずれかの投与群で 2 名以上に発現した Grade 3 以上の有害事象は認められなかった。各投与群で発現した Grade 3 以上の有害事象は，ウパダシチニブ 15 mg 併合群ではリンパ球数減少，ウパダシチニブ 30 mg 併合群では小腸潰瘍，肺炎，尿路感染，卵巣癌及びヘルペス後神経痛（いずれも各 1 名）であった（J-ISS T 1 2 1 1 3 3 J）。

2.7. .2.1.1.2.2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

全ウパダシチニブ併合解析集団（長期）の Grade 3 以上の有害事象（100 人年あたりの発現件数）を表 2.7. .7-13 に示す。

全ウパダシチニブ併合解析集団（長期）では，Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 12. 件/100 人年（101 件），全ウパダシチニブ 30 mg 併合群で 18.2 件/100 人年（150 件）であった。100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現件数 0.5 件/100 人年以上。以下，同順で記載）は，血中クレアチンホスホキナーゼ増加（0 5 件/100 人年，0.6 件 100 人年），リンパ球減少症（0.5 件/100 人年，0. 件/100 人年），肺炎（0. 件 100 人年，0.7 件/100 人年），帯状疱疹（0.1 件/100 人年，0.9 件/100 人年），気管支炎（0.1 件/100 人年，0.5 件/100 人年），貧血（0 件/100 人年，0.5 件/100 人年），背部痛（0 件 100 人年，0.5 件/100 人年），慢性閉塞性肺疾患（0 件/100 人年，0.5 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 13.0 件/100 人年（3 件），全ウパダシチニブ 30 mg 併合群で 67.6 件/100 人年（19 件）であった。いずれかの投与群で 5 件/100 人年以上発現した Grade 3 以上の有害事象は，帯状疱疹（全ウパダシチニブ 15 mg 併合群：0 件/100 人年，30 mg 併合群：7.1 件/100 人年）であった（J-ISS Table 2. 1.2.3. J）。

20[redacted]年[redacted]月[redacted]日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の Grade 3 以上の有害事象（100 人年あたりの発現件数）を表 2.7. .7-93 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 10.7 件/100 人年（133 件），全ウパダシチニブ 30 mg 併合群で 15.5 件 100 人年（195 件）であった。100 人年あたりの発現件数が多かった有害事象（全ウパダシチニブ 15 mg 併合群又は 30 mg 併合群で発現件数 0.5 件/100 人年以上。以下，同順で記載）は，帯状疱疹（0.3 件/100 人年，0.8 件/100 人年），血中クレアチンホスホキナーゼ増加（0.3 件/100 人年，0.5 件/100 人年）及び肺炎（0.2 件/100 人年，0.9 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 11. 件/100 人年（ 件），全ウパダシチニブ 30 mg 併合群で 67.3 件/100 人年（27 件）であった。いずれかの投与群で 5 件/100 人年以上発現した Grade 3 以上の有害事象は，帯状疱疹及び肺炎（全ウパダシチニブ 15 mg 併合群：各 0 件/100 人年，30 mg 併合群：各 5.0 件/100 人年）であった（J-ISS update Table 2. 1.2.3. J）。

2.7. .2.1.1.2.3 M15-572 試験

投与 2 週時

M15-572 試験の投与 2 週時までに発現した Grade 3 以上の有害事象を表 2.7. .7-1 に示す。

投与 2 週時までに発現した有害事象の多くは軽度又は中等度であった。Grade 3 以上の有害事象の発現割合は，プラセボ群（3.8%［16/ 23 名］）と比較してウパダシチニブ 15 mg 群（ .9%［21/ 29 名］）では同様であったが，ウパダシチニブ 30 mg 群（6. %［27/ 23 名］）では高く，アダリムマブ群（6.5%［28/ 29 名］）と比較してウパダシチニブ 30 mg 群では同様であり，ウパダシチニブ 15 mg 群では低かった。いずれかの投与群で 3 名以上に発現した Grade 3 以上の有害事象はリンパ球減少症のみであった（ウパダシチニブ 15 mg 群：3 名，30 mg 群：2 名，アダリムマブ群：0 名，プラセボ群：1 名）。

投与 2 週時までの重症度別の有害事象を，M15-572 試験 CSR W2 Table 1 .3 1.5 に示す。

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでに発現した Grade 3 以上の有害事象（100 人年あたりの発現件数）を表 2.7. .7-9 に示す。

投与 56 週時データカットオフまでの Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 10 5 件/100 人年，全ウパダシチニブ 30 mg 群で 1 .0 件/100 人年，アダリムマブ群で 12. 件/100 人年であった。Grade 3 以上の有害事象の 100 人年あたりの発現件数は，血中クレアチンホスホキナーゼ増加が全ウパダシチニブ 30 mg 群で 1.1 件/100 人年であった以外は，いずれの投与群でも 1.0 件/100 人年以下であった。各投与群で 3 件以上発現した Grade 3 以上の有害事象は，全ウパダシチニブ 15 mg 群ではアラニンアミノトランスフェラーゼ増加（6 件［0.7 件/100 人年］），帯状疱疹（5 件［0.6 件/100 人年］），リンパ球減少症，肺炎（各 件［0.5 件/100 人年］）及び血中クレアチンホスホキナーゼ増加（3 件［0. 件/100 人年］），全ウパダシチニブ 30 mg 群では血中クレアチンホスホキナーゼ増加（9 件［1.1 件/100 人年］），帯状疱疹，肺炎（各 6 件［0.7 件/100 人年］），貧血，アスパラギン酸アミノトランスフェラーゼ増加（各 件［0.5 件/100 人年］），リンパ球減少症，アラニンアミノトランスフェラーゼ増加，背部痛，変形性関節症及び肺塞栓症（各 3 件［0. 件/100 人年］），アダリムマブ群では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，血中クレアチンホスホキナーゼ増加（各 件［0.6 件/100 人年］），好中球減少症，蜂巣炎及び椎間板突出（各 3 件［0 5 件/100 人年］）であった。

2.7. .2.1.1.2. M15-55 試験

投与 2 週時

M15-55 試験の投与 2 週時までに発現した Grade 3 以上の有害事象を表 2.7. .7-15 に示す。

投与 2 週時までに発現した有害事象の多くは軽度又は中等度であった。Grade 3 以上の有害事象の発現割合は，プラセボ群（3.8%［8/212 名］）と比較してウパダシチニブ 15 mg 群（6.2%［13/211 名］）及びウパダシチニブ 30 mg 群（7.3%［16/218 名］）の方が高かった。いずれかの投与群で 2 名以上に発現した Grade 3 以上の有害事象は，肺炎のみであった（ウパダシチニブ 15 mg 群：1 名，ウパダシチニブ 30 mg 群：3 名，プラセボ群：0 名）。

投与 2 週時までの重症度別の有害事象を，M15-55 試験 CSR W2 T 1 1 3 1 5 に示す。

投与 56 週時

M15-55 試験の投与 56 週時データカットオフまでに発現した Grade 3 以上の有害事象（100 人年あたりの発現件数）を表 2.7. .7-95 に示す。

投与 56 週時データカットオフまでの Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 12 9 件/100 人年，全ウパダシチニブ 30 mg 群で 20.3 件/100 人年であった。いずれの投与群でも，Grade 3 以上の有害事象（各 PT）の 100 人年あたりの発現件数は 2 件/100 人年未満であった。各投与群で 3 件以上発現した Grade 3 以上の有害事象は，全ウパダシチニブ 15 mg 群では乾癬性関節症（3 件［0.7 件/100 人年］），全ウパダシチニブ 30 mg 群では肺炎（6 件［1. 件 100 人年］）及び帯状疱疹（5 件［1 2 件/100 人年］）であった。

2.7. .2.1.1.3 発現時期別の有害事象

申請時データカットオフ

全ウパダシチニブ併合解析集団（長期）の発現時期別（3 ヵ月間隔）の有害事象の概要（100 人年あたりの発現状況）を表 2.7. .7-16，有害事象（100 人年あたりの発現件数）を ISS-J Table 2. 3.2 J に示す。

全ウパダシチニブ併合解析集団（長期）では，発現時期別の有害事象の 100 人年あたりの発現件数（全ウパダシチニブ 15 mg 併合群，30 mg 併合群の順に記載）は，0 から 3 ヵ月未満が 38.9 件/100 人年及び 5 1.3 件 100 人年，3 ヵ月以上から 6 ヵ月未満が 36 . 件/100 人年及び 09.5 件 100 人年，6 ヵ月以上から 9 ヵ月未満が 320.2 件/100 人年及び 3 6.9 件 100 人年，9 ヵ月以上から 12 ヵ月未満が 170.3 件/100 人年及び 269.6 件/100 人年，12 ヵ月以上から 15 ヵ月未満が 173.5 件/100 人年及び 275.6 件/100 人年，15 ヵ月以上から 18 ヵ月未満が 173.2 件/100 人年及び 232.2 件 100 人年，18 ヵ月以上から 21 ヵ月未満が 71 9 件/100 人年及び 167.3 件/100 人年，21 ヵ月以上から 2 ヵ月未満が 123.1 件/100 人年及び 1 0.6 件/100 人年，2 ヵ月以上が 266.7 件/100 人年及び 138.9 件 100 人年であった。

20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の発現時期別（3 ヵ月間隔）の有害事象の概要（100 人年あたりの発現状況）を表 2.7. .7-96，有害事象（100 人年あたりの発現件数）を ISS-J update Table 2. 3.2 に示す。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，発現時期別の有害事象の 100 人年あたりの発現件数（全ウパダシチニブ 15 mg 併合群，30 mg 併合群の順に記載）は，0 から 3 ヵ月未満が .2 件/100 人年及び 538 8 件 100 人年，3 ヵ月以上から 6 ヵ月未満が 3 8.6 件/100 人年及び 397.2 件 100 人年，6 ヵ月以上から 9 ヵ月未満が 305.7 件/100 人年及び 3 6.3 件 100 人年，9 ヵ月以上から 12 ヵ月未満が 166 3 件/100 人年及び 2 3.0 件/100 人年，12 ヵ月以上から 15 ヵ月未満が 179.7 件/100 人年及び 221 3 件/100 人年，15 ヵ月以上から 18 ヵ月未満が 180.8 件/100 人年及び 22 .7 件/100 人年，18 ヵ月以上から 21 ヵ月未満が 113. 件/100 人年及び 175. 件/100 人年，21 ヵ月以上から 2 ヵ月未満が 125 5 件/100 人年及び 181.0 件/100 人年，2 ヵ月以上が 125.6 件/100 人年及び 1 0.5 件 100 人年であった。

2.7. .2.1.2 死亡

申請時データカットオフ

プラセボ対照併合解析集団（投与 2 週時）の死亡に至った有害事象を表 2.7. -50，全ウパダシチニブ併合解析集団（長期）の死亡に至った有害事象（100 人年あたりの発現件数）を表 2.7. -51 に示す。また，評価期間中の死亡の一覧表を表 2.7. -52，評価期間以降の死亡の一覧表を表 2.7. -53 に示す。

M15-572 試験及び M15-55 試験の投与 2 週時までの死亡に至った有害事象を M15-572 試験 CSR W2 Table 1 3 2.3.1 及び M15-55 試験 CSR W2 Table 1 .3 2.3.1 に示し，M15-572 試験及び M15-55 試験の死亡の詳細は 2.7.6 項に示す。

乾癬性関節炎の臨床開発プログラムでは，外部委員会である心血管イベント判定委員会（以下「CAC」）がすべての死亡について判定した。

プラセボ対照併合解析集団（投与 2 週時）では，評価期間中の死亡がプラセボ併合群の 2 名に発現した。このうち 1 名は，自動車事故に遭い，肋骨骨折及び外傷性血胸により死亡した。他の 1 名については，治験責任医師は心停止による死亡と報告したが，CAC は原因未特定 / 不明の死亡と判定した。

全ウパダシチニブ併合解析集団（長期）では，投与 2 週時から投与 2 週時データカットオフまでに，評価期間中の死亡が全ウパダシチニブ 30 mg 併合群で 1 名に認められた。治験責任医師は，死亡原因を汎血球減少症と報告したが，死亡診断書には，診断医により急性呼吸窮迫症候群及び右気胸と記載されていた。本被験者には，入院期間中に人工呼吸器の使用，胸腔鏡下肺全摘除，気胸，間質性肺疾患，脳梗塞，ニューモシスチス・イロベチイ肺炎，サイトメガロウイルス感染，播種性血管内凝固及び十二指腸潰瘍などが認められた。

また，評価期間以降（治験薬の最終投与 30 日後より後）に，死亡が全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名に認められた。死亡原因は，全ウパダシチニブ 15 mg 併合群の被験者が遠隔転移を伴う肺癌，全ウパダシチニブ 30 mg 併合群の被験者が間質性肺疾患であった。遠隔転移を伴う肺癌の有害事象としての発現日は評価期間中であり，本事象は死亡に至った有害事象として報告された。

M15-572 試験（長期）では，アダリムマブ群で死亡は認められなかった（M15-572 試験 CSR W2 Table 1 .3 1.1.1.2.2）。

死亡した被験者の詳細は，2.7.6 項に示した。

表 2 7. -50. プラセボ対照併合解析集団（投与 2 週時）の死亡に至った有害事象

System Organ Class MedDRA 22 0 Preferred Term	Placebo N = 635) n (%) SSA%]	Upadacitinib 15 mg QD N = 640) n (%) SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
Any adverse event	2 0 3) [0 3]	0	0
心臓障害	1 0 2) [0 2]	0	0
心停止	1 0 2) [0 2]	0	0
傷害、中毒および処置合併症	1 0 2) [0 2]	0	0
肋骨骨折	1 0 2) [0 2]	0	0
外傷性血胸	1 0 2) [0 2]	0	0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo
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
SSA = Study size adjusted

相互参照：ISS Table 2. 1.1.3.6

表 2 7. -51. 全ウパダシチニブ併合解析集団（長期）の死亡に至った有害事象（100 人年あたり発現件数）

System Organ Class MedDRA 22 0 Preferred Term	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) PYs = 651 8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 641) (PYs = 647 1) Events (E/100 PYs) SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816 9) Events E/100 PYs) SSA E/100 PYs]	Upadacitinib Any 30 mg QD N = 920) PYs = 822 3) Events E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	1 0 2) 0 2]	0	1 (0 1) [0 1]	1 0 1) [0 1]
血液およびリンパ系障害	0	0	0	1 0 1) [0 1]
汎血球減少症	0	0	0	1 0 1) [0 1]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 0 2) 0 2]	0	1 (0 1) [0 1]	0
遠隔転移を伴う肺癌	1 0 2) 0 2]	0	1 (0 1) [0 1]	0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo
Patients could be included in more than one treatment group
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted

相互参照：ISS Table 2. 1.2.3.7

表 2 7. -52. 評価期間中の死亡の一覧表（安全性併合解析，安全性解析対象集団）

試験番号 被験者番号 年齢 / 性別 / 人種	死亡時の治験薬	死亡日* / 最終投与からの日数	治験薬の投与順序	初回投与からの日数	死亡原因 基本語$ (判定事象名)
M15-554 [redacted] 7[redacted] / 男性 / 白人	プラセボ	16 / 2	プラセボ / ウパダシチニブ15 mg 1日1回	16	肋骨骨折 (非心血管系死亡)
	プラセボ	16 / 2	プラセボ/ ウパダシチニブ15 mg 1日1回	16	外傷性血胸 (非心血管系死亡)
M15-554 [redacted] 5[redacted] / 男性 / アジア人	ウパダシチニブ30 mg 1日 回	494 / 30	プラセボ/ ウパダシチニブ30 mg 1日1回	662	汎血球減少症 (非心血管系死亡)
M15-572 [redacted] 5[redacted] / 男性 / 白人	プラセボ	62 / 6	プラセボ/ ウパダシチニブ30 mg 1日1回	62	心停止 (原因未特定 / 不明の死亡)

* 死亡日は，治験薬の初回投与からの日数。ウパダシチニブ投与下で発現した場合，死亡日はウパダシチニブの初回投与からの日数。
$ 転帰が死亡と報告された基本語

相互参照：ISS Table 2. 1.3.1

表 2 7. -53. 評価期間以降の死亡の一覧表（安全性併合解析，安全性解析対象集団）

試験番号 被験者番号 年齢 / 性別 / 人種	死亡時の治験薬	死亡日* / 最終投与からの日数	治験薬の投与順序	初回投与からの日数	死亡原因 基本語$ (判定事象名)
M15-572 [redacted] 7[redacted] / 男性 / 白人	ウパダシチニブ15 mg 1日 回	313 / 67	ウパダシチニブ15 mg 1日1回	313	遠隔転移を伴う肺癌 (非心血管系死亡)
M15-572 [redacted] 4[redacted] / 女性 / 白人	ウパダシチニブ30 mg 1日 回	243 / 52	ウパダシチニブ30 mg 1日1回	243	間質性肺疾患 (非心血管系死亡)

* 死亡日は，治験薬の初回投与からの日数。ウパダシチニブ投与下で発現した場合，死亡日はウパダシチニブの初回投与からの日数。
$ 転帰が死亡と報告された基本語

相互参照：ISS Table 2. 1.3.2

20[redacted]年[redacted]月[redacted]日データカットオフ

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の死亡に至った有害事象（100 人年あたりの発現件数）を表 2.7. -5 に示す。また，評価期間中の死亡の一覧表を表 2.7. -55 に示す。

M15-572 試験及び M15-55 試験の投与 56 週時データカットオフまでの死亡に至った有害事象（100 人年あたりの発現件数）を M15-572 試験 CSR W56 Table 1 .3 2.3 及び M15-55 試験 CSR W56 Table 1 3 2.3 に示し，死亡の一覧表を M15-572 試験 CSR W56 Table 1 .3 2.18.3.2 及び M15-55 試験 CSR W56 Table 1 .3 2 18.3.2 に示す。M15-572 試験及び M15-55 試験の死亡の詳細は，M15-572 試験（投与 56 週時）2.7.6 項及び M15-55 試験（投与 56 週時）2.7.6 項に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，申請時データカットオフ以降に，評価期間中の死亡が全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名に認められた。死亡原因は，全ウパダシチニブ 15 mg 併合群の被験者（被験者番号 [redacted]）では事象名がコード化されておらず，全ウパダシチニブ 30 mg 併合群の被験者（被験者番号 [redacted] ではコロナウイルス感染であった。死亡原因の事象名がコード化されなかった全ウパダシチニブ 15 mg 併合群の 1 名（被験者番号 [redacted] は，重篤な有害事象である「COVID-19 疑いによる下気道感染」により死亡した。しかし，治験実施医療機関は SARS-CoV-2 感染を確認できなかったことから，20[redacted]年[redacted]月[redacted]日データカットオフ後に COVID-19 に関する事象名は削除された。その後の M15-572 試験 CSR W56 では，本被験者の死亡原因は下気道感染と報告された。

なお，全ウパダシチニブ併合解析集団の 20[redacted]年[redacted]月[redacted]日データカットオフから M15-572 試験の投与 56 週時データカットオフ（20[redacted]年[redacted]月[redacted]日）までに死亡した被験者は認められなかった。

また，申請時データカットオフ以降に新たに認められた評価期間以降（治験薬の最終投与 30 日後より後）の死亡はなかった（ISS update Table 2. 7 2）。

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）では，申請時データカットオフ以降に評価期間中の死亡がアダリムマブ群で 1 名に認められた。死亡原因は，多発性外傷及び交通事故であった。

死亡した被験者の詳細は，2 7 6 項に示した。

表 2 7. -5 . 全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の死亡に至った有害事象（100 人年あたり発現件数）

System Organ Class MedDRA 22 0 Preferred Term	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) PYs = 951 5) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 641) (PYs = 945 4) Events (E/100 PYs) SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 1247 2) Events E/100 PYs) SSA E/100 PYs]	Upadacitinib Any 30 mg QD N = 921) (PYs = 1257 4) Events E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	2 0 2) 0 2]	0	2 (0 2) [0 2]	2 0 2) [0 2]
*** Not Coded ***	1 0 1) 0 1]	0	1 (<0 1) [<0 1]	0
*** Not Coded ***	1 0 1) 0 1]	0	1 (<0 1) [<0 1]	0
血液およびリンパ系障害	0	0	0	1 (<0 1) [<0 1]
汎血球減少症	0	0	0	1 (<0 1) [<0 1]
感染症および寄生虫症	0	0	0	1 (<0 1) [<0 1]
コロナウイルス感染	0	0	0	1 (<0 1) [<0 1]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 0 1) 0 1]	0	1 (<0 1) [<0 1]	0
遠隔転移を伴う肺癌	1 0 1) 0 1]	0	1 (<0 1) [<0 1]	0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo
Patients could be included in more than one treatment group
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted

相互参照：ISS update T 1 2 3 7

1 5

表 2.7.4-55. 20[redacted] 年 [redacted] 月 [redacted] 日データカットオフまでの評価期間中の死亡の一覧表（安全性併合解析，安全性解析対象集団）

試験番号 被験者番号 年齢 / 性別 / 人種	死亡時の治験薬	死亡日* / 最終投与からの日数	治験薬の投与順序	初回投与からの日数	死亡原因 基本語$ (判定事象名)
M15-554 [redacted] 7[redacted] / 男性 / 白人	プラセボ	16 / 2	プラセボ / ウパダシチニブ15 mg 1日1回	16	肋骨骨折 (非心血管系死亡)
	プラセボ	16 / 2	プラセボ/ ウパダシチニブ15 mg 1日1回	16	外傷性血胸 (非心血管系死亡)
M15-554 [redacted] 5[redacted] / 男性 / アジア人	ウパダシチニブ30 mg 1日1回	494 / 30	プラセボ/ ウパダシチニブ30 mg 1日1回	662	汎血球減少症 (非心血管系死亡)
M15-572 [redacted] 4[redacted] / 女性 / 白人	ウパダシチニブ30 mg 1日1回	807	プラセボ/ ウパダシチニブ30 mg 1日1回	975	コロナウイルス感染
M15-572 [redacted] 5[redacted] / 男性 / 白人	プラセボ	62 / 6	プラセボ/ ウパダシチニブ30 mg 1日1回	62	心停止 (原因未特定 / 不明の死亡)
M15-572 [redacted] 5[redacted] / 男性 / 白人	ウパダシチニブ15 mg 1日1回	346	ウパダシチニブ15 mg 1日1回	346	コード化されず#
M15-572 [redacted] 4[redacted] / 男性 / 白人	アダリムマブ40 mg隔週投与	523/60	アダリムマブ40 mg隔週投与	523	多発性外傷 (非心血管系死亡)
	アダリムマブ40 mg隔週投与	523/60	アダリムマブ40 mg隔週投与	523	交通事故 (非心血管系死亡)

* 死亡日は，治験薬の初回投与からの日数。ウパダシチニブ投与下で発現した場合，死亡日はウパダシチニブの初回投与からの日数。
$ 転帰が死亡と報告された基本語
# その後のM15-572試験CSR W56では，本被験者の死亡原因は下気道感染と報告された。

相互参照：ISS update Table 2.4__7.1

2.7.4.2.1.3 その他の重篤な有害事象

2.7.4.2.1.3.1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 24 週時）の重篤な有害事象を表 2.7.4.7-17 に示す。

プラセボ対照併合解析集団（投与 24 週時）では，重篤な有害事象の発現割合は，ウパダシチニブ 15 mg 併合群で 4.1%（26/640 名），ウパダシチニブ 30 mg 併合群で 6.9%（44/641 名），プラセボ併合群で 2.7%（17/635 名）であった。多くの重篤な有害事象は，発現被験者数が各投与群で 1 名のみであり，2 名以上に発現した重篤な有害事象は，ウパダシチニブ 15 mg 併合群ではびらん性胃炎，肺炎，敗血症，乾癬性関節症及び腎結石症（各 2 名），ウパダシチニブ 30 mg 併合群では肺炎（6 名），異型肺炎及び菌血症（各 2 名），プラセボ併合群では肺炎（2 名）であった。

日本人部分集団

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の重篤な有害事象を表 2.7.4.7-18 に示す。

プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団では，重篤な有害事象の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 16.7%（3/18 名）であり，プラセボ併合群では発現しなかった。発現した重篤な有害事象は，ウパダシチニブ 15 mg 併合群では乾癬性関節症（1 名），ウパダシチニブ 30 mg 併合群では小腸潰瘍，肺炎，尿路感染及び卵巣癌（各 1 名）であった。

2.7.4.2.1.3.2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

全ウパダシチニブ併合解析集団（長期）の重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-19 に示す。

全ウパダシチニブ併合解析集団（長期）では，重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 10.9 件/100 人年（89 件），全ウパダシチニブ 30 mg 併合群で 14.8 件/100 人年（122 件）であった。100 人年あたりの発現件数が最も多かった重篤な有害事象は，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群のいずれも肺炎（0.5 件/100 人年，1.0 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団の重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-20 に示す。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 17.4 件/100 人年（4 件），全ウパダシチニブ 30 mg 併合群で 56.9 件/100 人年（16 件）であった。全ウパダシチニブ 15 mg 併合群で発現した重篤な有害事象は，いずれも 1 件であった。全ウパダシチニブ 30 mg 併合群で 2 件以上発現した有害事象は，帯状疱疹（2 件，7.1 件/100 人年）であった。

20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-97 に示す。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 10.3 件/100 人年（129 件），全ウパダシチニブ 30 mg 併合群で 13.2 件/100 人年（166 件）であった。100 人年あたりの発現件数が最も多かった重篤な有害事象は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群のいずれも肺炎（0.5 件/100 人年，1.0 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団の重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-98 に示す。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 14.2 件/100 人年（5 件），全ウパダシチニブ 30 mg 併合群で 52.4 件/100 人年（21 件）であった。各投与群で 2 件以上発現した重篤な有害事象は，全ウパダシチニブ 15 mg 併合群では乾癬性関節症（2 件［5.7 件/100 人年］），全ウパダシチニブ 30 mg 併合群では帯状疱疹及び肺炎（各 2 件［5.0 件/100 人年］）であった。

2.7.4.2.1.3.3 M15-572 試験

投与 24 週時

M15-572 試験の投与 24 週時までの重篤な有害事象を表 2.7.4.7-21，投与 24 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-22，重篤な有害事象の一覧表を表 2.7.4.7-23（投与 24 週時）及び表 2.7.4.7-24（投与 24 週時データカットオフまで）に示す。また，M15-572 試験の重篤な有害事象の詳細は M15-572 試験（投与 24 週時）2.7.6 項に示す。

投与 2 週時までの重篤な有害事象の発現割合は，ウパダシチニブ 15 mg 群（3.3%［1 / 29 名］），アダリムマブ群（3.7%［16/ 29 名］）及びプラセボ群（3 1%［13/ 23 名］）では同様であり，ウパダシチニブ 30 mg 群（6 1%［26/ 23 名］）では高かった。いずれかの投与群で 2 名以上に発現した重篤な有害事象は，肺炎（ウパダシチニブ 30 mg 群：3 名，プラセボ群：2 名），異型肺炎（ウパダシチニブ 30 mg 群：2 名）及び敗血症（ウパダシチニブ 15 mg 群：2 名）であった。

投与 2 週時までに治験薬の投与中止に至った重篤な有害事象は，ウパダシチニブ 15 mg 群で 名，ウパダシチニブ 30 mg 群で 8 名，アダリムマブ群で 6 名，プラセボ群で 名に発現した（M15-572 試験 CSR W2 Table 1 .3 2.18 1.1）。

投与 2 週時データカットオフまでの重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 8.6 件/100 人年，全ウパダシチニブ 30 mg 群で 12.9 件/100 人年，アダリムマブ群で 10.9 件/100 人年であり，全ウパダシチニブ 15 mg 群が最も少なく，全ウパダシチニブ 30 mg 群が最も多かった。いずれかの投与群で 2 件以上発現した重篤な有害事象は，肺炎（全ウパダシチニブ 30 mg 群：5 件），帯状疱疹（全ウパダシチニブ 30 mg 群： 件），虫垂炎，異型肺炎，気管支炎，骨壊死及び発熱（全ウパダシチニブ 30 mg 群：各 2 件），肺塞栓症（全ウパダシチニブ 15 mg 群及び 30 mg 群：各 2 件），敗血症及び子宮脱（全ウパダシチニブ 15 mg 群：各 2 件），蜂巣炎及び脳血管発作（アダリムマブ群：各 2 件）であった。

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7. .7-99，重篤な有害事象の一覧表を表 2.7. .7-100 に示す。また，M15-572 試験の重篤な有害事象の詳細は M15-572 試験（投与 56 週時）2.7.6 項に示す。

M15-572 試験の投与 56 週時データカットオフまでの重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 9.1 件/100 人年，全ウパダシチニブ 30 mg 群で 12.3 件/100 人年，アダリムマブ群で 9.3 件/100 人年であり，全ウパダシチニブ 15 mg 群とアダリムマブ群では同様であったが，全ウパダシチニブ 30 mg 群で多かった。いずれかの投与群で 3 件以上発現した重篤な有害事象は，肺炎（全ウパダシチニブ 15 mg 群：6 件，全ウパダシチニブ 30 mg 群：8 件），変形性関節症（全ウパダシチニブ 30 mg 群：3 件，アダリムマブ群： 件），帯状疱疹（全ウパダシチニブ 30 mg 群： 件），虫垂炎，気管支炎及び肺塞栓症（全ウパダシチニブ 30 mg 群：各 3 件）及び蜂巣炎（アダリムマブ群：3 件）であった。その他の重篤な有害事象は，いずれも各投与群で 2 件以下であった。

2.7. .2.1.3. M15-55 試験

投与 2 週時

M15-55 試験の投与 2 週時までの重篤な有害事象を表 2.7. .7-25，投与 2 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7. .7-26，重篤な有害事象の一覧表を表 2.7. .7-27（投与 2 週時）及び表 2.7. .7-28（投与 2 週時データカットオフまで）に示す。また，M15-55 試験の重篤な有害事象の詳細は M15-55 試験（投与 2 週時）2.7.6 項に示す。

投与 2 週時までの重篤な有害事象の発現割合は，プラセボ群（1.9%［ /212 名］）と比較してウパダシチニブ 15 mg 群（5.7%［12/211 名］）及びウパダシチニブ 30 mg 群（8.3%［18/218 名］）の方が高かった。いずれかの投与群で 2 名以上に発現した重篤な有害事象は，肺炎（ウパダシチニブ 30 mg 群：3 名），乾癬性関節症及び腎結石症（ウパダシチニブ 15 mg 群：各 2 名）であった。

投与 2 週時までに治験薬の投与中止に至った重篤な有害事象は，ウパダシチニブ 15 mg 群で 6 名，ウパダシチニブ 30 mg 群で 7 名，プラセボ群で 2 名に発現した（M15-55 試験 CSR W2 Table 1 3 2.18.2 1）。

投与 2 週時データカットオフまでの重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 15 0 件/100 人年，全ウパダシチニブ 30 mg 群で 18.2 件/100 人年であった。いずれかの投与群で 2 件以上発現した重篤な有害事象は，肺炎（全ウパダシチニブ 15 mg 群及び 30 mg 群：各 3 件），乾癬性関節症（全ウパダシチニブ 15 mg 群：2 件），腎結石症（全ウパダシチニブ 15 mg 群：2 件），蜂巣炎及びウイルス性胃腸炎（全ウパダシチニブ 30 mg 群：各 2 件），心房細動（全ウパダシチニブ 30 mg 群：2 件）であった。

投与 56 週時

M15-55 試験の投与 56 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7. .7-101，重篤な有害事象の一覧表を表 2.7. .7-102 に示す。また，M15-55 試験の重篤な有害事象の詳細は M15-55 試験（投与 56 週時）2.7.6 項に示す。

投与 56 週時データカットオフまでの重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 1 3 件/100 人年，全ウパダシチニブ 30 mg 群で 15.8 件/100 人年であった。各投与群で 3 件以上発現した重篤な有害事象は，全ウパダシチニブ 15 mg 群では乾癬性関節症（ 件）及び肺炎（3 件），全ウパダシチニブ 30 mg 群では肺炎（5 件）であった。その他の重篤な有害事象はいずれも各投与群で 2 件以下の発現であった。

2.7. .2.1.3.5 M20-017 試験

M20-017 試験の重篤な有害事象の一覧表を表 2.7. .7-29 に示す。

M20-017 試験では，重篤な有害事象が 1 名（ウパダシチニブ 15 mg を投与）に発現した。発現した事象は Grade の胆石症であり，治験薬と関連なしと判断された。本事象により，治験薬の投与を中止した。

2.7. .2.1. その他の重要な有害事象

本項では，治験薬の投与中止に至った有害事象について評価した。

2.7. .2.1. .1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 2 週時）の治験薬の投与中止に至った有害事象を表 2.7. .7-30 に示す。

プラセボ対照併合解析集団（投与 2 週時）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 15 mg 併合群で . %（28/6 0 名），ウパダシチニブ 30 mg 併合群で 6. %（ 1/6 1 名），プラセボ併合群で 3.8%（2 /635 名）であった。3 名以上に発現した治験薬の投与中止に至った有害事象は，ウパダシチニブ 15 mg 併合群では乾癬性関節症（5 名），ウパダシチニブ 30 mg 併合群では下痢及びアラニンアミノトランスフェラーゼ増加（各 3 名）であった。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，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 15 mg 併合群で 5 9%（1/17 名），ウパダシチニブ 30 mg 併合群で 16.7%（3/18 名）であり，プラセボ併合群では発現しなかった（J-ISS T 1 2 1 1 3 5 J）。発現した治験薬の投与中止に至った有害事象は，ウパダシチニブ 15 mg 併合群では乾癬性関節症（1 名），ウパダシチニブ 30 mg 併合群では小腸潰瘍，肺炎及び尿路感染（各 1 名）であった。

2.7. .2.1. .2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

全ウパダシチニブ併合解析集団（長期）の治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を表 2.7. .7-31 に示す。

全ウパダシチニブ併合解析集団（長期）では，治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 8. 件 100 人年（69 件），全ウパダシチニブ 30 mg 併合群で 9.5 件/100 人年（78 件）であった。100 人年あたりの発現件数が最も多

かった有害事象は，ウパダシチニブ 15 mg 併合群では乾癬性関節症（0.6 件/100 人年），ウパダシチニブ 30 mg 併合群では発熱（0.5 件/100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で .3 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 17.8 件/100 人年（5 件）であった（J-ISS Table 2. 1.2.3.6 J）。内訳は，全ウパダシチニブ 15 mg 併合群では乾癬性関節症（1 件），全ウパダシチニブ 30 mg 併合群では汎血球減少症，小腸潰瘍，肺炎，尿路感染及び気胸（各 1 件）であった。

20[redacted]年[redacted]月[redacted]日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を表 2.7. .7-103 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 6.7 件/100 人年（83 件），全ウパダシチニブ 30 mg 併合群で 7.8 件/100 人年（98 件）であった。100 人年あたりの発現件数が最も多かった有害事象は，全ウパダシチニブ 15 mg 併合群では乾癬性関節症（0.5 件/100 人年），全ウパダシチニブ 30 mg 併合群では発熱及び血中クレアチンホスホキナーゼ増加（各 0.3 件 100 人年）であった。

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.8 件 100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 17.5 件/100 人年（7 件）であった（J-ISS update Table 2. 1.2 3.6 J）。内訳は，全ウパダシチニブ 15 mg 併合群では乾癬性関節症（1 件），全ウパダシチニブ 30 mg 併合群では汎血球減少症，小腸潰瘍，薬物性肝障害，肺炎，尿路感染，喘息及び気胸（各 1 件）であった。

2.7. .2.1. .3 M15-572 試験

投与 2 週時

M15-572 試験の投与 2 週時までの治験薬の投与中止に至った有害事象を表 2.7. .7-32，投与 2 週時データカットオフまでの治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を M15-572 試験 CSR W2 Table 1 .3 2.2.2 に示す。

投与 2 週時までの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（3.1%［13/ 23 名］）と比較してウパダシチニブ 15 mg 群（3.0%［13/ 29 名］）では同様であったが，ウパダシチニブ 30 mg 群（5 0%［21/ 23 名］）では高く，アダリムマブ群（5.1%［22/ 29 名］）と比較してウパダシチニブ 30 mg 群では同様であり，ウパダシチニブ 15 mg 群では低かった。治験薬の投与中止に至った有害事象の多くは，軽度又は中等度であった（M15-572 試験 CSR W2 Table 1 .3 2.18.2.1）。

投与 2 週時までに 2 名以上に発現した治験薬の投与中止に至った有害事象は，ウパダシチニブ 15 mg 群では敗血症（0 5%［2/ 29 名］），ウパダシチニブ 30 mg 群ではリンパ球減少症及び発熱（各 0.5%［2/ 23 名］），アダリムマブ群ではアラニンアミノトランスフェラーゼ増加，脱毛症及びアスパラギン酸アミノトランスフェラーゼ増加（各 0.5%［2/ 29 名］），プラセボ群では筋痙縮（0.5%［2/ 23 名］）であった。

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を表 2.7. .7-10 に示す。

投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群（ .6 件 100 人年）で最も少なく，全ウパダシチニブ 30 mg 群（6.6 件/100 人年）とアダリムマブ群（7. 件/100 人年）では同様であった。いずれかの投与群で 3 件以上発現した治験薬の投与中止に至った有害事象は，リンパ球減少症及び発熱（全ウパダシチニブ 30 mg 群で各 3 件），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，乾癬性関節症及び乾癬（アダリムマブ群で各 3 件）であった。その他の治験薬の投与中止に至った有害事象は，いずれも各投与群で 2 件以下であった。

2.7. .2.1. . M15-55 試験

投与 2 週時

M15-55 試験の投与 2 週時までの治験薬の投与中止に至った有害事象を表 2.7. .7-33，投与 2 週時データカットオフまでの治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を M15-55 試験 CSR W2 Table 1 .3 2.2.2 に示す。

投与 2 週時までの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（5.2%［11/212 名］）と比較して，ウパダシチニブ 15 mg 群（7.1%［15/211 名］）及びウパダシチニブ 30 mg 群（9.2%［20/218 名］）の方が高かった。治験薬の投与中止に至った有害事象の多くは，軽度又は中等度であった（M15-55 試験 CSR W2 Table 1 .3 2 18.2.1）。

投与 2 週時までに 2 名以上に発現した治験薬の投与中止に至った有害事象は，ウパダシチニブ 15 mg 群では乾癬性関節症（1.9%［ 211 名］）及び白血球数減少（0.9%［2/211 名］），ウパダシチニブ 30 mg 群では下痢，帯状疱疹，肺炎，アラニンアミノトランスフェラーゼ増加，肝酵素上昇及び尿路感染（各 0.9%［2/218 名］），プラセボ群では乾癬性関節症及び乾癬（各 0.9%［2/212 名］）であった。

投与 56 週時

M15-55 試験の投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を表 2.7. .7-105 に示す。

投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 10.0 件/100 人年，全ウパダシチニブ 30 mg 群で 11.1 件/100 人年であった。各投与群で 3 件以上発現した治験薬の投与中止に至った有害事象は，全ウパダシチニブ 15 mg 群の乾癬性関節症（5 件）のみであった。

2.7. .2.1.5 器官別又は症候群別有害事象の解析

2.7. .2.1.5.1 特に注目すべき有害事象

特に注目すべき有害事象として，重篤な感染症，日和見感染（結核及び帯状疱疹を除く），帯状疱疹，活動性結核，悪性腫瘍（リンパ腫含む），薬物性肝障害，消化管穿孔，貧血，好中球減少症，リンパ球減少症，CPK 増加，腎機能障害，MACE 及びその他の委員会判定された心血管イベント並びに血栓症を評価した。これらの事象は，他のヤヌスキナーゼ（以下「JAK」）阻害薬で報告された安全性の懸念，ウパダシチニブの前臨床試験及び関節リウマチの臨床開発プログラムのデータ，新規低分子医薬品の一般的な規制上の懸念に基づき設定した。特に注目すべき有害事象の定義は表 2.7. - に示した。また，本項では安全性併合解析の結果を用いて評価した。

プラセボ対照併合解析集団（投与 2 週時）の特に注目すべき有害事象の概要を表 2.7. -56（全体集団）及び表 2.7. -57（日本人部分集団）に示す。また，申請時データカットオフまでの全ウパダシチニブ併合解析集団（長期）の特に注目すべき有害事象の概要の 100 人年あたりの発現件数又は被験者数を表 2.7. -58（全体集団）及び表 2.7. -59（日本人部分集団），100 人年あたりの発現被験者数を表 2.7. .7-3 （全体集団）及び表 2.7. .7-35（日本人部分集団）に示す。

表 2.7.4-56. プラセボ対照併合解析集団（投与 24 週時）の特に注目すべき有害事象の概要

	Placebo (N = 635) n (%) [SSA %]	----- Upadacitinib ----- 15 mg QD (N = 640) n (%) [SSA %]	30 mg QD (N = 641) n (%) [SSA %]	Adalimumab 40 mg EOW (N = 429) n (%)	-Treatment Comparison (95% CI) [A]- 15 mg QD - Placebo	30 mg QD - Placebo
Subjects with:						
Any infections	213 (33.5) [33.5]	240 (37.5) [37.5]	291 (45.4) [45.4]	146 (34.0)	3.9 (-1.3, 9.2)	11.8 (6.5, 17.1)
Any serious infections	5 (0.8) [0.8]	6 (0.9) [0.9]	17 (2.7) [2.7]	3 (0.7)	0.1 (-0.9, 1.2)	1.9 (0.4, 3.3)
Any opportunistic infection excluding tuberculosis and herpes zoster	0	1 (0.2) [0.2]	4 (0.6) [0.6]	0	0.2 (-0.1, 0.5)	0.6 (0.0, 1.2)
Any herpes zoster	5 (0.8) [0.8]	7 (1.1) [1.1]	13 (2.0) [2.0]	0	0.3 (-0.8, 1.4)	1.2 (-0.1, 2.5)
Any active tuberculosis	0	0	0	0	0.0	0.0
Any possible malignancy	2 (0.3) [0.3]	6 (0.9) [0.9]	6 (0.9) [0.9]	4 (0.9)	0.6 (-0.2, 1.5)	0.6 (-0.2, 1.5)
Any malignancy	1 (0.2) [0.2]	4 (0.6) [0.6]	6 (0.9) [0.9]	3 (0.7)	0.5 (-0.2, 1.2)	0.8 (-0.0, 1.6)
Any non-melanoma skin cancer (NMSC)	1 (0.2) [0.2]	1 (0.2) [0.2]	3 (0.5) [0.5]	0	0.0 (-0.4, 0.4)	0.3 (-0.3, 0.9)
Any malignancy other than NMSC	0	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.7)	0.5 (-0.1, 1.0)	0.5 (-0.1, 1.0)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.

	Placebo N = 635) n (%) [SSA %]	----- Upadacitinib ----- 15 mg QD (N = 640) n (%) SSA %]	30 mg QD (N = 641) n (%) SSA %]	Adalimumab 40 mg EOW (N = 429) n (%)	-Treatment Comparison 95% CI) A]- 15 mg QD - Placebo	30 mg QD - Placebo
Any lymphoma	0	1 (0 2) [0 2]	0	0	0 2 (-0 2, 0 5)	0 0
Any hepatic disorder	19 3 0) 3 0]	43 6 7) [6 7]	70 10 9) 10 9]	67 15 6)	3 7 1 4, 6 0)	8 0 5 2, 10 7)
Any adjudicated gastrointestinal perforation	0	0	0	0	0 0	0 0
Any anemia	6 (0 9) 0 9]	7 (1 1) [1 1]	34 5 3) [5 3]	1 0 2)	0 2 (-1 0, 1 3)	4 3 (2 5, 6 2)
Any neutropenia	2 (0 3) 0 3]	6 (0 9) [0 9]	27 4 2) [4 2]	10 (2 3)	0 6 (-0 2, 1 5)	3 9 (2 3, 5 5)
Any lymphopenia	5 (0 8) 0 8]	8 (1 3) [1 2]	17 2 7) [2 7]	1 0 2)	0 5 (-0 6, 1 6)	1 9 (0 5, 3 3)
Any creatine phosphokinase (CPK) elevation	10 1 6) 1 6]	42 6 6) [6 5]	53 8 3) [8 3]	24 (5 6)	5 0 2 8, 7 1)	6 7 (4 4, 9 1)
Any renal dysfunction	2 (0 3) 0 3]	0	1 0 2) [0 2]	0	-0 3 (-0 8, 0 1)	-0 2 (-0 7, 0 4)
Any adjudicated MACE*	1 (0 2) 0 2]	1 (0 2) [0 2]	0	2 0 5)	0 0 (-0 4, 0 4)	-0 2 (-0 5, 0 2)
Any adjudicated VTE**	1 (0 2) 0 2]	1 (0 2) [0 2]	1 0 2) [0 2]	2 0 5)	0 0 (-0 4, 0 4)	0 0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
SSA = Study size adjusted

roups.

* MACE: Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.
** VTE: Venous thromboembolic events, defined as deep vein thrombosis (DVT) And pulmonary embolism (PE) (fatal and non-fatal).

相互参照：ISS Table 2.4 1.1.2.1

表 2.7.4-57. プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の特に注目すべき有害事象の概要

	Placebo (N = 15) n (%) [SSA %]	----- Upadacitinib ----- 15 mg QD (N = 17) n (%) [SSA %]	30 mg QD (N = 18) n (%) [SSA %]	Adalimumab 40 mg EOW (N = 4) n (%)	-Treatment Comparison (95% CI) [A]- 15 mg QD - Placebo	30 mg QD - Placebo
Subjects with:						
Any infections	5 (33.3) [33.3]	9 (52.9) [53.0]	11 (61.1) [61.2]	1 (25.0)	19.7 (-14.0, 53.3)	27.9 (-3.7, 59.5)
Any serious infections	0	0	2 (11.1) [11.1]	0	0.0	11.1 (-3.2, 25.4)
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	0	0.0	0.0
Any herpes zoster	0	1 (5.9) [6.0]	1 (5.6) [5.6]	0	6.0 (-5.3, 17.3)	5.6 (-5.0, 16.1)
Any active tuberculosis	0	0	0	0	0.0	0.0
Any possible malignancy	0	0	1 (5.6) [5.6]	1 (25.0)	0.0	5.6 (-5.0, 16.1)
Any malignancy	0	0	1 (5.6) [5.6]	1 (25.0)	0.0	5.6 (-5.0, 16.1)
Any non-melanoma skin cancer (NMSC)	0	0	0	0	0.0	0.0
Any malignancy other than NMSC	0	0	1 (5.6) [5.6]	1 (25.0)	0.0	5.6 (-5.0, 16.1)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.

	Placebo (N = 15) n (%) [SSA %]	----- Upadacitinib ----- 15 mg QD (N = 17) n (%) SSA %]	30 mg QD (N = 18) n (%) SSA %]	Adalimumab 40 mg EOW N = 4) n (%)	-Treatment Comparison 95% CI) A]- 15 mg QD - Placebo	30 mg QD - Placebo
Any lymphoma	0	1 (5 9) [6 0]	0	0	6 0 (-5 3, 17 3)	0 0
Any hepatic disorder	0	3 (17 6) 17 0]	1 5 6) [5 6]	0	17 0 1 4, 32 6)	5 6 (-5 0, 16 1)
Any adjudicated gastrointestinal perforation	0	0	0	0	0 0	0 0
Any anemia	0	1 (5 9) [6 0]	2 (11 1) 11 1]	0	6 0 (-5 3, 17 3)	11 1 (-3 2, 25 4)
Any neutropenia	0	1 (5 9) [6 0]	1 5 6) [5 5]	0	6 0 (-5 3, 17 3)	5 5 (-3 8, 14 8)
Any lymphopenia	0	1 (5 9) [6 0]	2 (11 1) 11 1]	0	6 0 (-5 3, 17 3)	11 1 (-3 0, 25 1)
Any creatine phosphokinase (CPK) elevation	0	2 (11 8) 11 5]	3 (16 7) 16 6]	1 25 0)	11 5 (-3 2, 26 2)	16 6 (1 5, 31 6)
Any renal dysfunction	0	0	0	0	0 0	0 0
Any adjudicated MACE*	0	0	0	0	0 0	0 0
Any adjudicated VTE**	0	0	0	0	0 0	0 0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
SSA = Study size adjusted
A] Study size adjusted risk difference between treatment groups
* MACE Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke
** VTE Venous thromboembolic events, defined as deep vein thrombosis (DVT) And pulmonary embolism (PE) fatal and non-fatal)

相互参照：J-ISS T 1 2 1121 J

表 2.7.4-58. 全ウパダシチニブ併合解析集団（長期）の特に注目すべき有害事象の概要（100 人年あたりの発現件数又は被験者数）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 920)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 394.5) Events (E/100 PYs)		
Any infections	662 (101.6) [101.6]	868 (134.1) [134.1]	827 (101.2) [101.2]	1047 (127.3) [127.3]	343 (86.9)	32.5 (20.7, 44.4)	26.1 (15.8, 36.5)
Any serious infections	15 (2.3) [2.3]	39 (6.0) [6.0]	19 (2.3) [2.3]	49 (6.0) [6.0]	6 (1.5)	3.7 (1.5, 5.9)	3.6 (1.7, 5.6)
Any opportunistic infection excluding tuberculosis and herpes zoster	3 (0.5) [0.5]	7 (1.1) [1.1]	4 (0.5) [0.5]	9 (1.1) [1.1]	0	0.6 (-0.3, 1.6)	0.6 (-0.3, 1.5)
Any herpes zoster	23 (3.5) [3.5]	48 (7.4) [7.4]	29 (3.6) [3.6]	65 (7.9) [7.9]	2 (0.5)	3.9 (1.4, 6.4)	4.4 (2.0, 6.7)
Any active tuberculosis	0	0	0	0	0	0.0	0.0
Any hepatic disorder	110 (16.9) [16.9]	154 (23.8) [23.8]	133 (16.3) [16.3]	183 (22.3) [22.3]	122 (30.9)	6.9 (2.0, 11.8)	6.0 (1.7, 10.2)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 920)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any adjudicated gastrointestinal perforation	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0	0	-0.2 (-0.5, 0.1)	-0.1 (-0.4, 0.1)
Any anemia	21 (3.2) [3.2]	50 (7.7) [7.7]	23 (2.8) [2.8]	57 (6.9) [6.9]	6 (1.5)	4.5 (2.0, 7.1)	4.1 (2.0, 6.3)
Any neutropenia	15 (2.3) [2.3]	42 (6.5) [6.5]	18 (2.2) [2.2]	51 (6.2) [6.2]	23 (5.8)	4.2 (1.9, 6.5)	4.0 (2.0, 6.0)
Any lymphopenia	19 (2.9) [2.9]	26 (4.0) [4.0]	20 (2.4) [2.4]	29 (3.5) [3.5]	1 (0.3)	1.1 (-0.9, 3.1)	1.1 (-0.6, 2.8)
Any creatine phosphokinase (CPK) elevation	78 (12.0) [12.0]	121 (18.7) [18.7]	93 (11.4) [11.4]	140 (17.0) [17.0]	36 (9.1)	6.7 (2.4, 11.0)	5.7 (2.0, 9.3)
Any renal dysfunction	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]	0	-0.2 (-0.7, 0.4)	-0.1 (-0.5, 0.3)
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD N = 920)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any possible malignancy	10/647 6 (1 5) [1 5]	12/642 9 1 9) 1 9]	13/812 4 (1 6) [1 6]	13/817 9 (1 6) 1 6]	7/392 7 (1 8)	0 3 (-1 1, 1 8)	-0 0 (-1 2, 1 2)
Any malignancy	8/649 2 1 2) [1 2]	11/643 8 1 7) 1 7]	11/814 0 (1 4) [1 4]	12/818 8 (1 5) 1 5]	6/393 7 (1 5)	0 5 (-0 8, 1 8)	0 1 (-1 0, 1 3)
Any non-melanoma skin cancer (NMSC)	3/649 4 0 5) [0 5]	5/644 5 0 8) 0 8]	5/814 3 (0 6) [0 6]	5/819 6 0 6) 0 6]	2/394 2 (0 5)	0 3 (-0 5, 1 2)	-0 0 (-0 8, 0 8)
Any malignancy other than NMSC	5/651 6 0 8) [0 8]	6/646 5 0 9) 0 9]	7/816 6 (0 9) [0 9]	7/821 4 0 9) 0 9]	4/394 0 (1 0)	0 2 (-0 8, 1 2)	-0 0 (-0 9, 0 9)
Any lymphoma	1/650 0 0 2) [0 2]	0/647 1	2/815 0 (0 2) [0 2]	0/822 3	0/394 5	-0 2 (-0 5, 0 1)	-0 2 (-0 6, 0 1)
Any adjudicated MACE*	4/649 1 0 6) [0 6]	1/646 0 0 2) 0 2]	4/814 2 (0 5) [0 5]	2/821 2 0 2) 0 2]	3/394 2 (0 8)	-0 5 (-1 1, 0 2)	-0 2 (-0 8, 0 3)
Any adjudicated VTE**	4/651 1 0 6) [0 6]	2/647 1 0 3) 0 3]	4/816 2 (0 5) [0 5]	2/822 3 0 2) 0 2]	2/392 8 (0 5)	-0 3 (-1 0, 0 4)	-0 2 (-0 8, 0 3)

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups
* MACE Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke
** VTE Venous thromboembolic events, defined as deep vein thrombosis (DVT) And pulmonary embolism (PE) fatal and non-fatal)

相互参照：ISS Table 2. 1.2.2.2.1

表 2.7.4-59. 全ウパダシチニブ併合解析集団（長期）の日本人部分集団の特に注目すべき有害事象の概要（100 人年あたりの発現件数又は被験者数）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 18.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 20.9) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 23.0) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 28.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 5.2) Events (E/100 PYs)		
Any infections	26 (142.9) [142.0]	43 (205.7) [215.8]	28 (121.7) [120.8]	62 (220.6) [230.4]	1 (19.2)	73.8 (-11.5, 159.1)	109.6 (36.1, 183.2)
Any serious infections	1 (5.5) [5.0]	6 (28.7) [28.5]	1 (4.3) [3.9]	9 (32.0) [32.7]	0	23.4 (-1.6, 48.4)	28.8 (5.9, 51.6)
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	2 (7.1) [7.7]	0	0.0	7.7 (-3.0, 18.5)
Any herpes zoster	2 (11.0) [10.0]	7 (33.5) [35.1]	2 (8.7) [7.9]	7 (24.9) [26.0]	0	25.0 (-4.6, 54.7)	18.1 (-4.1, 40.4)
Any active tuberculosis	0	0	0	0	0	0.0	0.0
Any hepatic disorder	4 (22.0) [25.8]	3 (14.4) [15.6]	5 (21.7) [24.9]	4 (14.2) [15.5]	2 (38.5)	-10.1 (-41.5, 21.2)	-9.4 (-36.5, 17.8)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any adjudicated gastrointestinal perforation	0	0	0	0	0	0.0	0.0
Any anemia	1 (5.5) [5.0]	2 (9.6) [10.4]	1 (4.3) [3.9]	2 (7.1) [7.7]	0	5.4 (-12.1, 22.9)	3.8 (-9.4, 17.0)
Any neutropenia	1 (5.5) [5.0]	1 (4.8) [3.8]	1 (4.3) [3.9]	1 (3.6) [2.8]	0	-1.2 (-13.6, 11.1)	-1.2 (-10.6, 8.3)
Any lymphopenia	1 (5.5) [5.0]	2 (9.6) [9.0]	1 (4.3) [3.9]	4 (14.2) [12.3]	0	4.0 (-12.0, 20.0)	8.3 (-6.1, 22.7)
Any creatine phosphokinase (CPK) elevation	2 (11.0) [12.9]	5 (23.9) [23.2]	4 (17.4) [18.4]	5 (17.8) [17.2]	1 (19.2)	10.4 (-17.2, 37.9)	-1.1 (-25.1, 22.8)
Any renal dysfunction	0	0	0	0	0	0.0	0.0
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any possible malignancy	0/18 2	1/20 9 (4 8) 5 2]	0/23 0	1/28 2 3 5) 3 9]	1/4 8 20 8)	5 2 (-5 0, 15 4)	3 9 (-3 7, 11 4)
Any malignancy	0/18 2	1/20 9 (4 8) 5 2]	0/23 0	1/28 2 3 5) 3 9]	1/4 8 20 8)	5 2 (-5 0, 15 4)	3 9 (-3 7, 11 4)
Any non-melanoma skin cancer (NMSC)	0/18 2	0/20 9	0/23 0	0/28 1	0/5 2	0 0	0 0
Any malignancy other than NMSC	0/18 2	1/20 9 (4 8) 5 2]	0/23 0	1/28 2 3 5) 3 9]	1/4 8 20 8)	5 2 (-5 0, 15 4)	3 9 (-3 7, 11 4)
Any lymphoma	1/16 4 6 1) [5 6]	0/20 9	2/21 1 9 5) [8 7]	0/28 1	0/5 2	-5 6 (-16 6, 5 4)	-8 7 (-20 7, 3 3)
Any adjudicated MACE*	0/18 2	0/20 9	0/23 0	1/28 1 3 6) 3 9]	0/5 2	0 0	3 9 (-3 7, 11 5)
Any adjudicated VTE**	0/18 2	0/20 9	0/23 0	0/28 1	0/5 2	0 0	0 0

Note Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups
* MACE Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke
** VTE Venous thromboembolic events, defined as deep vein thrombosis (DVT) And pulmonary embolism (PE) fatal and non-fatal)

相互参照：J-ISS Table 2. 1.2.2.2.1 J

20[redacted]年[redacted]月[redacted]日データカットオフ

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の特に注目すべき有害事象の概要の 100 人年あたりの発現件数又は被験者数を表 2.7.4-60（全体集団）及び表 2.7.4-61（日本人部分集団），100 人年あたりの発現被験者数を表 2.7.4.7-106（全体集団）及び表 2.7.4.7-107（日本人部分集団）に示す。

表 2.7.4-60. 全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の特に注目すべき有害事象の概要（100 人年あたりの発現件数又は被験者数）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 951.5)	(PYs = 945.4)	(PYs = 1247.2)	(PYs = 1257.4)	(PYs = 549.7)		
	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs) [SSA E/100 PYs]	Events (E/100 PYs)		
Any infections	867 (91.1) [91.1]	1095 (115.8) [115.8]	1125 (90.2) [90.2]	1387 (110.3) [110.3]	424 (77.1)	24.7 (15.5, 33.8)	20.1 (12.3, 27.9)
Any serious infections	20 (2.1) [2.1]	46 (4.9) [4.9]	29 (2.3) [2.3]	65 (5.2) [5.2]	7 (1.3)	2.8 (1.1, 4.4)	2.8 (1.3, 4.4)
Any opportunistic infection excluding tuberculosis and herpes zoster	3 (0.3) [0.3]	7 (0.7) [0.7]	5 (0.4) [0.4]	11 (0.9) [0.9]	0	0.4 (-0.2, 1.1)	0.5 (-0.2, 1.1)
Any herpes zoster	33 (3.5) [3.5]	59 (6.2) [6.2]	48 (3.8) [3.8]	84 (6.7) [6.7]	3 (0.5)	2.8 (0.8, 4.8)	2.8 (1.0, 4.6)
Any active tuberculosis	0	0	0	0	0	0.0	0.0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

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	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any hepatic disorder	136 (14.3) [14.3]	183 (19.4) [19.3]	169 (13.6) [13.5]	234 (18.6) [18.6]	146 (26.6)	5.0 (1.3, 8.7)	5.1 (1.9, 8.2)
Any adjudicated gastrointestinal perforation	1 (0.1) [0.1]	0	1 (<0.1) [<0.1]	0	0	-0.1 (-0.3, 0.1)	-0.1 (-0.2, 0.1)
Any anemia	25 (2.6) [2.6]	55 (5.8) [5.8]	28 (2.2) [2.2]	70 (5.6) [5.6]	9 (1.6)	3.2 (1.3, 5.0)	3.3 (1.8, 4.9)
Any neutropenia	18 (1.9) [1.9]	52 (5.5) [5.5]	22 (1.8) [1.8]	64 (5.1) [5.1]	26 (4.7)	3.6 (1.9, 5.3)	3.3 (1.9, 4.8)
Any lymphopenia	26 (2.7) [2.7]	35 (3.7) [3.7]	27 (2.2) [2.2]	38 (3.0) [3.0]	1 (0.2)	1.0 (-0.7, 2.6)	0.9 (-0.4, 2.1)
Any creatine phosphokinase (CPK) elevation	93 (9.8) [9.8]	139 (14.7) [14.7]	113 (9.1) [9.1]	173 (13.8) [13.8]	41 (7.5)	4.9 (1.7, 8.0)	4.7 (2.1, 7.3)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any renal dysfunction	3 (0.3) [0.3]	3 (0.3) [0.3]	3 (0.2) [0.2]	3 (0.2) [0.2]	0	0.0 (-0.5, 0.5)	-0.0 (-0.4, 0.4)
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		
Any possible malignancy	14/943.1 (1.5) [1.5]	14/938.3 (1.5) [1.5]	19/1237.1 (1.5) [1.5]	17/1249.0 (1.4) [1.4]	7/546.8 (1.3)	0.0 (-1.1, 1.1)	-0.2 (-1.1, 0.8)
Any malignancy	12/945.5 (1.3) [1.3]	13/939.2 (1.4) [1.4]	17/1239.5 (1.4) [1.4]	16/1249.8 (1.3) [1.3]	6/548.3 (1.1)	0.1 (-0.9, 1.2)	-0.1 (-1.0, 0.8)
Any non-melanoma skin cancer (NMSC)	5/945.8 (0.5) [0.5]	6/940.6 (0.6) [0.6]	9/1239.9 (0.7) [0.7]	7/1252.0 (0.6) [0.6]	2/548.8 (0.4)	0.1 (-0.6, 0.8)	-0.2 (-0.8, 0.5)
Any malignancy other than NMSC	7/951.2 (0.7) [0.7]	8/943.1 (0.8) [0.9]	9/1246.7 (0.7) [0.7]	10/1254.4 (0.8) [0.8]	4/549.1 (0.7)	0.1 (-0.7, 0.9)	0.1 (-0.6, 0.8)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD N = 921)	Adalimumab 40 mg EOW (N = 429)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any lymphoma	1/949 0 0 1) [0 1]	0/945 4	2/1243 8 (0 2) [0 2]	0/1257 4	0/549 7	-0 1 (-0 3, 0 1)	-0 2 (-0 4, 0 1)
Any adjudicated MACE*	4/947 5 0 4) [0 4]	2/943 3 0 2) 0 2]	4/1243 2 (0 3) [0 3]	3/1255 3 (0 2) 0 2]	3/548 6 (0 5)	-0 2 (-0 7, 0 3)	-0 1 (-0 5, 0 3)
Any adjudicated VTE**	4/950 3 0 4) [0 4]	2/945 4 0 2) 0 2]	4/1245 9 (0 3) [0 3]	3/1257 4 (0 2) 0 2]	2/547 0 (0 4)	-0 2 (-0 7, 0 3)	-0 1 (-0 5, 0 3)

Note Treatment emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups
* MACE Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke
** VTE Venous thromboembolic events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) fatal and non-fatal)

相互参照：ISS update Table 2. 2.2.1

表 2.7.4-61. 全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団の特に注目すべき有害事象の概要（100 人年あたりの発現件数又は被験者数）

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Exposure-adjusted event rate:	(PYs = 26.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 29.3) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 35.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 40.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 6.6) Events (E/100 PYs)		
Any infections	34 (127.3) [125.7]	54 (184.3) [191.5]	39 (110.8) [108.9]	81 (202.0) [210.5]	1 (15.2)	65.8 (-1.0, 132.5)	101.6 (44.0, 159.2)
Any serious infections	1 (3.7) [3.5]	8 (27.3) [27.6]	1 (2.8) [2.6]	12 (29.9) [30.9]	0	24.2 (3.7, 44.6)	28.3 (10.0, 46.6)
Any opportunistic infection excluding tuberculosis and herpes zoster	0	0	0	2 (5.0) [5.4]	0	0.0	5.4 (-2.1, 12.9)
Any herpes zoster	3 (11.2) [10.4]	9 (30.7) [31.3]	3 (8.5) [7.8]	10 (24.9) [25.5]	0	20.9 (-2.8, 44.6)	17.7 (-0.5, 35.9)
Any active tuberculosis	0	0	0	0	0	0.0	0.0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any hepatic disorder	4 (15.0) [17.0]	5 (17.1) [18.4]	5 (14.2) [15.8]	7 (17.5) [18.9]	2 (30.3)	1.4 (-22.0, 24.8)	3.0 (-16.9, 22.9)
Any adjudicated gastrointestinal perforation	0	0	0	0	0	0.0	0.0
Any anemia	1 (3.7) [3.5]	2 (6.8) [7.4]	1 (2.8) [2.6]	3 (7.5) [8.1]	0	3.9 (-8.4, 16.2)	5.5 (-5.0, 16.0)
Any neutropenia	1 (3.7) [3.5]	1 (3.4) [2.8]	1 (2.8) [2.6]	1 (2.5) [2.0]	0	-0.7 (-9.4, 8.0)	-0.6 (-7.1, 5.8)
Any lymphopenia	1 (3.7) [3.5]	2 (6.8) [6.5]	1 (2.8) [2.6]	4 (10.0) [8.7]	0	3.0 (-8.3, 14.3)	6.0 (-3.9, 16.0)
Any creatine phosphokinase (CPK) elevation	2 (7.5) [8.5]	6 (20.5) [20.3]	4 (11.4) [11.8]	6 (15.0) [14.8]	1 (15.2)	11.8 (-8.5, 32.0)	2.9 (-13.9, 19.7)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) [A]--	
	15 mg QD (No Cross-Over from Placebo) (N = 17)	30 mg QD (No Cross-Over from Placebo) (N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any renal dysfunction	0	0	0	0	0	0.0	0.0
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		
Any possible malignancy	0/26.7	1/29.3 (3.4) [3.7]	0/35.2	1/40.2 (2.5) [2.7]	1/6.1 (16.4)	3.7 (-3.5, 10.9)	2.7 (-2.6, 8.0)
Any malignancy	0/26.7	1/29.3 (3.4) [3.7]	0/35.2	1/40.2 (2.5) [2.7]	1/6.1 (16.4)	3.7 (-3.5, 10.9)	2.7 (-2.6, 8.0)
Any non-melanoma skin cancer (NMSC)	0/26.7	0/29.3	0/35.2	0/40.1	0/6.6	0.0	0.0
Any malignancy other than NMSC	0/26.7	1/29.3 (3.4) [3.7]	0/35.2	1/40.2 (2.5) [2.7]	1/6.1 (16.4)	3.7 (-3.5, 10.9)	2.7 (-2.6, 8.0)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
Patients could be included in more than one treatment group.
[A] Study size adjusted risk difference between treatment groups.

	Upadacitinib					--Treatment Comparison (95% CI) A]--	
	15 mg QD (No Cross-Over from Placebo) N = 17)	30 mg QD (No Cross-Over from Placebo) N = 18)	Any 15 mg QD (N = 23)	Any 30 mg QD (N = 26)	Adalimumab 40 mg EOW (N = 4)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Any lymphoma	1/24 2 (4 1) 3 9]	0/29 3	2/31 8 6 3) [5 8]	0/40 1	0/6 6	-3 9 (-11 4, 3 7)	-5 8 (-13 9, 2 2)
Any adjudicated MACE*	0/26 7	0/29 3	0/35 2	1/40 2 2 5) 2 7]	0/6 6	0 0	2 7 (-2 6, 8 0)
Any adjudicated VTE**	0/26 7	0/29 3	0/35 2	0/40 1	0/6 6	0 0	0 0

Note Treatment emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab
E/100 PYs = Events per 100 patient-years SSA = Study size adjusted
n/100 PYs = Number of subjects with at least one event per 100 patient-years
Patients could be included in more than one treatment group
A] Study size adjusted risk difference between treatment groups
* MACE Major Adverse Cardiovascular Events, defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke
** VTE Venous thromboembolic events, defined as deep vein thrombosis (DVT) and pulmonary embolism (PE) fatal and non-fatal)

相互参照：J-ISS update Table 2. 1.2.2 2 1 J

2.7. .2.1.5.1.1 重篤な感染症

項目	全体集団 (ISS)		日本人部分集団 (J-ISS)
	Tab e	F gure	Tab e
プラセボ対照併合解析集団の発現被験者数及び発現割合			
重篤な感染症	2. 1.1. .1.2	--	2. 1 1. .1.2 J
Grade 3 以上の重篤な感染症	2. 1.1. .3.2	--	--
治験薬の投与中止に至った重篤な感染症	2. 1.1. . .2	--	--
プラセボ対照併合解析集団で重篤な感染症が発現した被験者のベースライン時の慢性閉塞性肺疾患の病歴	2. 1.1.7.2	--	2. 1 1.7.2 J
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数			
重篤な感染症	2. 1.2. .1.2 Update 2. 1 2	--	2. 1 2. .1.2 J Upda e 2. 1.2. .1 2 J
Grade 3 以上の重篤な感染症	2. 1.2. .3.2 Update 2. 3 2	--	--
治験薬の投与中止に至った重篤な感染症	2. 1.2. . .2 Update 2. . 2	--	--
全ウパダシチニブ併合解析集団の部分集団別の重篤な感染症の発現被験者数及び発現割合			
人種	2. 1.2.6.7.1	--	--
年齢	2. 1.2.6.8.1	--	2. 1 2.6.8.1 J
性別	2. 1.2.6.9.1	--	--
BMI	2. 1.2.6.10.1	--	2. 1.2.6.10.1 J
ベースライン時の non-bDMARD 併用投与	2. 1.2.6.11.1	--	2. 1.2.6.11.1 J
ウパダシチニブの単独又は併用投与	2. 1.2.6.12.1	--	2. 1.2.6.12.1 J
ベースライン時の腎機能	2. 1.2.6.13.1	--	--
ベースライン時の慢性閉塞性肺疾患の病歴	2. 1.2.6.1 .1	--	2. 1.2.6.1 .1 J
ベースライン時の糖尿病の病歴	2. 1.2.6.15.1	--	2. 1.2.6.15.1 J
ベースライン時の心血管イベントの病歴	2. 1.2.6.16.1	--	2. 1.2.6.16.1 J

項目	全体集団 (ISS)		日本人部分集団 (J-ISS)
	Tab e	F gure	Tab e
全ウパダシチニブ併合解析集団の部分集団別の重篤な感染症の 100 人年あたりの発現件数			
人種	2. 1.2.6.7.2	--	--
年齢	2. 1.2.6.8.2	--	2. 1 2.6.8.2 J
性別	2. 1.2.6.9.2	--	--
BMI	2. 1.2.6.10.2	--	2. 1.2.6.10.2 J
ベースライン時の non-bDMARD 併用投与	2. 1.2.6.11.2	--	2. 1.2.6.11.2 J
ウパダシチニブの単独又は併用投与	2. 1.2.6.12.2	--	2. 1.2.6.12.2 J
ベースライン時の腎機能	2. 1.2.6.13.2	--	--
ベースライン時の慢性閉塞性肺疾患の病歴	2. 1.2.6.1 .2	--	2. 1.2.6.1 .2 J
ベースライン時の糖尿病の病歴	2. 1.2.6.15.2	--	2. 1.2.6.15.2 J
ベースライン時の心血管イベントの病歴	2. 1.2.6.16.2	--	2. 1.2.6.16.2 J
全ウパダシチニブ併合解析集団での重篤な感染症を発現した被験者の副腎皮質ステロイド投与量の要約	2. 1.2.7.3	--	2. 1 2.7.3 J
全ウパダシチニブ併合解析集団で重篤な感染症を発現した被験者のベースライン時の慢性閉塞性肺疾患の病歴	2. 1.2.7.	--	2. 1 2.7. J
重篤な感染症の一覧表			
プラセボ対照併合解析集団	2 1 1 8 5	--	--
全ウパダシチニブ併合解析集団	2 1 2 8 5 Update 2. 6 5	--	--
重篤な感染症の Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2. 1 2 9.2 Upda e 2. 8.2	--

重篤な感染症に関する有害事象は，表 2.7. - の定義を用いて特定した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の重篤な感染症の発現状況を表 2.7. .7-36 に示す。

プラセボ対照併合解析集団（投与 2 週時）の重篤な感染症の発現割合は，ウパダシチニブ 15 mg 併合群で 0.9%（6/6 0 名），ウパダシチニブ 30 mg 併合群で 2.7%（17 6 1 名），プラセボ併合群で 0.8%（5/635 名）であった。各投与群で 2 名以上に発現した重篤な感染症は，ウパダシチニブ 15 mg 併合群では肺炎及び敗血症（各 0.3%［2 6 0 名］），ウパダシチニブ 30 mg 併合

群では肺炎（0.9%［6/6 1 名］），異型肺炎及び菌血症（各 0.3%［2/6 1 名］），プラセボ併合群では肺炎（0.3%［2/635 名］）であった。治験薬の投与中止に至った重篤な感染症は，ウパダシチニブ 15 mg 併合群で 6 0 名中 3 名（0.5%），ウパダシチニブ 30 mg 併合群で 6 1 名中 7 名（1.1%），プラセボ併合群で 635 名中 3 名（0.5%）に発現した。内訳は，ウパダシチニブ 15 mg 併合群では敗血症（0 3%［2/6 0 名］）及び肺炎（0.2%［1/6 0 名］），ウパダシチニブ 30 mg 併合群では肺炎（0.3%［2/6 1 名］），異型肺炎，菌血症，肺感染，尿路感染及び尿路性敗血症（各 0.2%［1/6 1 名］），プラセボ併合群では乳房蜂巣炎，ブドウ球菌感染性滑液包炎及び肺炎（各 0.2%［1/635 名］）であった（ISS Table 2. 1.1. . 2）。死亡に至った重篤な感染症は発現しなかった（ISS Table 2. 1.1.8.5）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，重篤な感染症の発現割合は，ウパダシチニブ 30 mg 併合群で 11.1%（2/18 名）であり，ウパダシチニブ 15 mg 併合群及びプラセボ併合群では発現しなかった。ウパダシチニブ 30 mg 併合群の内訳は，肺炎及び尿路感染（各 5.6%［1 18 名］）であった（J-ISS Table 2. 1.1. .1.2 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の重篤な感染症の発現状況（100 人年あたりの発現件数）を表 2.7. .7-37 に示す。

全ウパダシチニブ併合解析集団（長期）では，重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.3 件/100 人年（19 件），全ウパダシチニブ 30 mg 併合群で 6.0 件/100 人年（ 9 件）であった。発現件数が多かった重篤な感染症は，全ウパダシチニブ 15 mg 併合群では肺炎（ 件［0.5 件/100 人年］），全ウパダシチニブ 30 mg 併合群では肺炎（8 件［1.0 件/100 人年］）及び帯状疱疹（5 件［0.6 件/100 人年］）であった。治験薬の投与中止に至った重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.9 件/100 人年（7 件），全ウパダシチニブ 30 mg 併合群で 1.3 件/100 人年（11 件）であり，2 件以上発現した事象は，全ウパダシチニブ 15 mg 併合群では敗血症（2 件［0.2 件/100 人年］），全ウパダシチニブ 30 mg 併合群では肺炎（2 件［0 2 件/100 人年］）であった（ISS Table 2. 1.2. . .2）。全ウパダシチニブ 30 mg 併合群の 2 名にニューモシスチス・イロベチイ肺炎が発現した。

死亡原因となった感染症は認められなかったが，M15-55 試験では，ウパダシチニブ 30 mg を投与された 1 名（被験者番号 [redacted]）で，汎血球減少症による死亡に先立ってニューモシスチス・イロベチイ肺炎及びサイトメガロウイルス感染が発現した。M15-572 試験でも，ウパダシチニブ 30 mg の 1 名（被験者番号 [redacted]）で気管支炎の発現後に間質性肺疾患が発現するとともに，新たに皮膚筋炎が発現した。気管支炎の発現時に治験薬の投与は中止され，被験者は治験薬の最終投与 52 日後に間質性肺疾患により死亡した（詳細は 2.7. .2 1.2 項及び 2.7 6 項参照）。

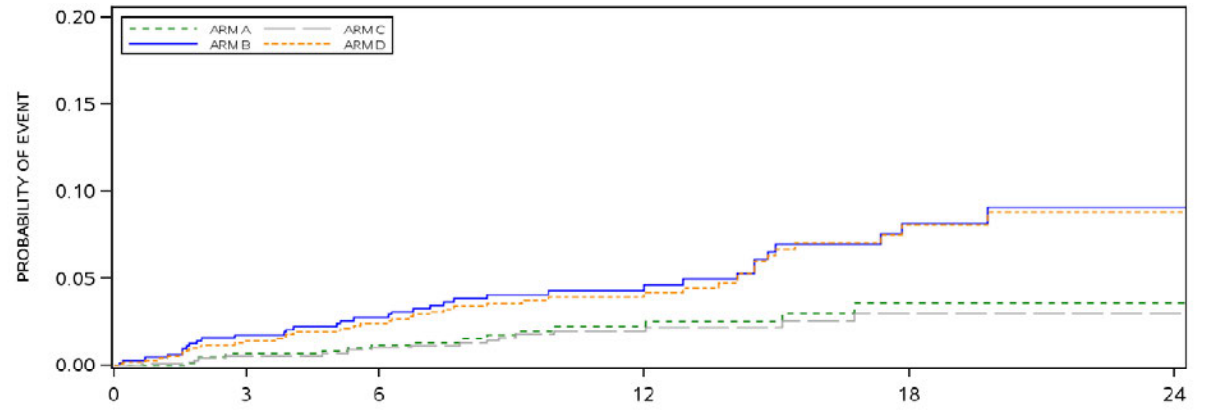
全ウパダシチニブ併合解析集団（長期）で，ベースライン時の慢性閉塞性肺疾患及び糖尿病の病歴の有無を因子とした部分集団解析を実施した結果，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群のいずれでも，重篤な感染症の 100 人年あたりの発現件数は，これらの病歴のない被験者と比較して病歴のある被験者の方が多い傾向が認められた（ISS Table 2. 1 2.6 1 .2, Table 2. 1.2.6.15.2）。この結果は，一般集団でも予測されたことであった [2] [3]。重篤な感染症を発現した被験者の副腎皮質ステロイドの投与量については，一定の傾向は認められなかったが，これは重篤な感染症発現時に副腎皮質ステロイドを使用していた被験者が少なかったことによる可能性が考えられた（ISS Table 2. 1 2.7 3）。その他の部分集団解析については，2.7. .5.2 項及び 2.7. .5.3 項に示す。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で .3 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 32.0 件/100 人年（9 件）であった。2 件以上発現した重篤な感染症は，全ウパダシチニブ 30 mg 併合群では帯状疱疹（7 1 件/100 人年［2 件］）であり，全ウパダシチニブ 15 mg 併合群では認められなかった（J-ISS Table 2. 1.2. .1 2 J）。

全ウパダシチニブ併合解析集団（長期）の重篤な感染症の Kaplan-Meier プロットを図 2.7. -1 に示す。

ウパダシチニブ 15 mg を投与された被験者では，重篤な感染症が発現するリスクの経時的な増加は認められなかった。

図 2 7. -1. 全ウパダシチニブ併合解析集団（長期）の重篤な感染症の Kaplan-Meier プロット



Subjects at Risk

ARM A	640	616	585	325	143	39
ARM B	641	609	578	321	144	39
ARM C	907	828	734	387	161	41
ARM D	920	832	735	385	168	41

		Probability of Event (95% CI)				
	Events	Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 640)	15	0.7%(0.0%, 1.3%)	1.2%(0.2%, 2.1%)	2.2%(0.8%, 3.7%)	3.6%(1.1%, 6.0%)	3.6%(1.1%, 6.0%)
ARM B (N = 641)	35	1.8%(0.6%, 2.9%)	2.8%(1.3%, 4.2%)	4.3%(2.4%, 6.2%)	8.2%(4.5%, 11.7%)	9.1%(4.9%, 13.1%)
ARM C (N = 907)	18	0.5%(<0.1%, 1.0%)	1.0%(0.3%, 1.8%)	2.0%(0.7%, 3.2%)	3.0%(1.0%, 4.9%)	3.0%(1.0%, 4.9%)
ARM D (N = 920)	44	1.4%(0.6%, 2.3%)	2.4%(1.3%, 3.6%)	3.9%(2.3%, 5.5%)	8.1%(4.8%, 11.2%)	8.8%(5.1%, 12.4%)

Note: ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.
Patients could be included in more than one treatment group.

相互参照：ISS Figure 2. 1.2.9.2

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 2.1 件/100 人年（11 件），全ウパダシチニブ 30 mg 群で 5.5 件/100 人年（29 件），アダリムマブ群で 1.5 件/100 人年（6 件）であった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2 2）。全ウパダシチニブ 30 mg 群とアダリムマブ群で発現件数の差が大きかった重篤な感染症は，肺炎（1.0 件/100 人年［5 件］及び 0.3 件/100 人年［1 件］）及び帯状疱疹（0.8 件/100 人年［ 件］及び 0 件/100 人年）であった（M15-572 試験 CSR W2 Table 1 3 2. .2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の重篤な感染症の発現状況（100 人年あたりの発現件数）を表 2.7. .7-108 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.3 件/100 人年（29 件），全ウパダシチニブ 30 mg 併合群で 5.2 件/100 人年（65 件）であった。各投与群で 5 件以上発現した重篤な感染症は，全ウパダシチニブ 15 mg 併合群では肺炎（6 件［0.5 件/100 人年］），全ウパ

ダシチニブ 30 mg 併合群では肺炎（12 件［1.0 件/100 人年］）及び帯状疱疹（5 件［0. 件/100 人年］）であった。治験薬の投与中止に至った重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.8 件/100 人年（10 件），全ウパダシチニブ 30 mg 併合群で 1.2 件/100 人年（15 件）であり，2 件以上発現した事象は，全ウパダシチニブ 15 mg 併合群では敗血症（2 件［0.2 件/100 人年］），全ウパダシチニブ 30 mg 併合群では肺炎（3 件［0.2 件/100 人年］）であった（ISS update Table 2. . .2）。

全ウパダシチニブ 30 mg 併合群の 1 名（被験者番号 [redacted] が重篤な感染症のコロナウイルス感染及び肺炎により死亡したが（ISS update Table 2. 6.5），死亡原因はコロナウイルス感染と判断された（2.7. .2 1.2 項参照）。また，全ウパダシチニブ 15 mg 併合群の 1 名（被験者番号 [redacted] が重篤な有害事象の「COVID-19 疑いによる下気道感染」により死亡した。しかし，治験実施医療機関は SARS-CoV-2 感染を確認できなかったことから，20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ後に COVID-19 に関する事象名は削除された。その後の M15-572 試験 CSR W56 では，本被験者の死亡原因は下気道感染と報告された。いずれの死亡も申請時データカットオフ以降に認められた。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.8 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 29.9 件/100 人年（12 件）であった。2 件以上発現した重篤な感染症は，全ウパダシチニブ 30 mg 併合群では帯状疱疹及び肺炎（各 5.0 件/100 人年［2 件］）であり，全ウパダシチニブ 15 mg 併合群では認められなかった（J-ISS update Table 2. 1.2. .1.2 J）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の重篤な感染症の Kaplan-Meier プロットを ISS update Figure 2. 8.2 に示す。

アダリムマブとの比較（M15-572 試験［20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ］）

M15-572 試験（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）での重篤な感染症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 2.2 件/100 人年（18 件），全ウパダシチニブ 30 mg 群で .7 件/100 人年（38 件），アダリムマブ群で 1.3 件/100 人年（7 件）であった（ISS update Table 2. 8.6）。全ウパダシチニブ 30 mg 群とアダリムマブ群で発現件数の差が大きかった重篤な感染症は，肺炎（0.9 件/100 人年［7 件］及び 0.2 件/100 人年［1 件］）及び帯状疱疹（0.5 件/100 人年［ 件］及び 0 件/100 人年）であった。

B 型肝炎の再活性化

ス（以下「HBV」）デオキシリボ核酸（以下「DNA」）定性検査

（ポリメラーゼ連鎖反応［以下「PCR」］法）の結果が陰性であれば参加可能であった。全ウパダシチニブ解析対象集団では，スクリーニング時の HBc Ab 検査が陽性であった被験者は，全ウパダシチニブ 15 mg 併合群で 907 名中 65 名（7.2%），全ウパダシチニブ 30 mg 併合群で 920 名中 60 名（6.5%）であった（ISS Table 2.2 1.2.3）。

ウパダシチニブ 15 mg を投与された被験者で，非重篤の B 型肝炎再活性化が 1 件発現した。本被験者（被験者番号 [redacted] は 5[redacted] 歳のアジア人男性であり，肝機能異常の病歴があった（20[redacted] 年 [redacted] 月及び 20[redacted] 年 [redacted] 月）。スクリーニング時では，HBc Ab 陽性，B 型肝炎ウイルス表面抗体陰性，HBV DNA 定性検査（PCR 法）陰性であった。投与 8 週時にトランスアミナーゼがベースラインから軽度に増加したが，投与 12 週時にはベースライン値付近に戻っており，HBV DNA 検査結果（PCR 法）は 82 IU/mL であった。有害事象の B 型肝炎再活性化が 85 日目に報告された。113 日目にエンテカビル 0.5 mg（1 日 1 回）の投与を開始した。HBV DNA の再検査（PCR 法）を 169 日目に実施したが，HBV DNA は検出されなかった。治験薬の投与は中断又は中止されなかった。本事象は，申請時データカットオフ時点で継続中であった（M15-572 試験 CSR W2 Appendix 16.2 .2.1，Appendix 16 2 .5，Appendix 16.2 7.1.1，Appendix 16 2 7.3，Appendix 16.2 8 2.1）。

2.7. .2.1.5.1.2 日和見感染（結核及び帯状疱疹を除く）

	全体集団 (ISS)		日本人部分集団 (J- SS)
項目	Table	F gure	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合			
日和見感染 (結核及び帯状疱疹を除く)	2. 1 1. .1.3	--	2. 1.1. 1.3 J
重篤な日和見感染 (結核及び帯状疱疹を除く)	2. 1 1. .2.1	--	--
Grade 3 以上の日和見感染 (結核及び帯状疱疹を除く)	2. 1 1. .3.3	--	--
治験薬の投与中止に至った日和見感染 (結核及び帯状疱疹を除く)	2. 1 1. . .3	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数			
日和見感染 (結核及び帯状疱疹を除く)	2 1 2 1 3 Upda e 2. .1.3	--	2 1 2 1 3 J Update 2. 1.2. .1.3 J
重篤な日和見感染 (結核及び帯状疱疹を除く)	2. 1 2. .2.1 Upda e 2 2 1	--	--
Grade 3 以上の日和見感染 (結核及び帯状疱疹を除く)	2 1 2 3 3 Upda e 2. .3.3	--	--
治験薬の投与中止に至った日和見感染 (結核及び帯状疱疹を除く)	2. 1 2. . .3 Upda e 2 3	--	--

項目	全体集団 (ISS)		日本人部分集団 (J- SS)
	Table	F gure	Table
日和見感染 結核及び帯状疱疹を除く) の一覧表			
プラセボ対照併合解析集団	2. 1 1.8.6	--	--
全ウパダシチニブ併合解析集団	2. 1 2.8.6 Update 2. 6.6	--	--
日和見感染 結核及び帯状疱疹を除く) の Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2. 1.2.9.8 Update 2. 8.8	--

日和見感染（結核及び帯状疱疹を除く）に関する有害事象は，表 2.7. - の定義を用いて特定した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の日和見感染（結核及び帯状疱疹を除く）の発現状況を表 2.7. .7-38 に示す。

プラセボ対照併合解析集団（投与 2 週時）の日和見感染の発現割合は，ウパダシチニブ 15 mg 併合群で 0.2%（1/6 0 名），ウパダシチニブ 30 mg 併合群で 0.6%（ /6 1 名）であり，プラセボ併合群では発現しなかった。発現した日和見感染は，ウパダシチニブ 15 mg 併合群ではカンジダ性尿道炎（0.2%［1/6 0 名］），ウパダシチニブ 30 mg 併合群では気管カンジダ症，サイトメガロウイルス感染，中咽頭カンジダ症及びニューモシスチス・イロベチイ肺炎（各 0.2%［1/6 1 名］）であった。重篤な日和見感染は，ウパダシチニブ 30 mg 併合群の 1 名（ニューモシスチス・イロベチイ肺炎）に発現した（ISS T 1 2 1 1 2 1）。本事象は，治験薬と関連ありと判断された（ISS Table 2. 1.1.8.6）。プラセボ対照期間では，死亡及び治験薬の投与中止に至った日和見感染は発現しなかった（ISS Table 2. 1.1. . .3，Table 2. 1 1.8 6）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，日和見感染（結核及び帯状疱疹を除く）は発現しなかった（J-ISS Table 2. 1 1. 1.3 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の日和見感染（結核及び帯状疱疹を除く）の発現状況（100 人年あたりの発現件数）を表 2.7. .7-39 に示す。

全ウパダシチニブ併合解析集団（長期）では，日和見感染の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.5 件/100 人年（ 件），全ウパダシチニブ 30 mg 併合群で 1.1 件/100 人年（9 件）であった。各投与群で 2 件以上発現した日和見感染は，全ウパダシチニブ 15 mg 併合群では認められず，全ウパダシチニブ 30 mg 併合群ではサイトメガロウイルス感

染，口腔真菌感染，中咽頭カンジダ症及びニューモシスチス・イロベチイ肺炎（各 2 件［0 2 件/100 人年］）であった。多く認められた日和見感染は，粘膜のカンジダ感染に関連する事象（全ウパダシチニブ 15 mg 併合群：食道カンジダ症及びカンジダ性尿道炎，30 mg 併合群：中咽頭カンジダ症及び口腔真菌感染）であった。重篤な日和見感染は，全ウパダシチニブ 30 mg 併合群で 3 件（ニューモシスチス・イロベチイ肺炎 2 件，サイトメガロウイルス感染 1 件）発現し，全ウパダシチニブ 15 mg 併合群では発現しなかった（ISS Table 2. 1 2. 2.1）。治験薬の投与中止に至った日和見感染は，全ウパダシチニブ 15 mg 併合群で 1 件（コクシジオイデス症）発現し，全ウパダシチニブ 30 mg 併合群では発現しなかった（ISS Table 2. 1.2. . 3）。

投与 2 週時から申請時データカットオフまでに，全ウパダシチニブ 30 mg 併合群の 1 名（被験者番号 [redacted] がニューモシスチス・イロベチイ肺炎及びサイトメガロウイルス感染を発現し，いずれも重篤で治験薬と関連ありと判断された。治験責任医師により，日和見感染が原因と判断された死亡は認められなかったが（ISS T 1 2 1 2 8 6），ニューモシスチス・イロベチイ肺炎及びサイトメガロウイルス感染を発現した被験者は，これらの事象を発現した後に死亡した。死亡原因は，汎血球減少症と報告された（表 2.7. -52）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，日和見感染（結核及び帯状疱疹を除く）の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 併合群で 7.1 件/100 人年（2 件）であり，全ウパダシチニブ 15 mg 併合群では発現しなかった。全ウパダシチニブ 30 mg 併合群で発現した日和見感染は，前述のサイトメガロウイルス感染及びニューモシスチス・イロベチイ肺炎（各 1 件［3.6 件/100 人年］）であった（J-ISS Table 2. 1.2. .1.3 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの日和見感染（結核及び帯状疱疹を除く）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 0. 件/100 人年（2 件），全ウパダシチニブ 30 mg 群で 1.0 件/100 人年（5 件）であり，アダリムマブ群では発現しなかった（M15-572 試験 CSR W2 Table 1 .3 1.1.2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日和見感染（結核及び帯状疱疹を除く）の発現状況（100 人年あたりの発現件数）を表 2.7. .7-109 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，日和見感染の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0. 件/100 人年（5 件），全ウパダシチニブ 30 mg 併合群で 0.9 件/100 人年（11 件）であった。各投与群で 2 件以上発現した日和見感染は，全ウパダシチニブ 15 mg 併合群では認められず，全ウパダシチニブ 30 mg 併合群では口腔真菌感染（ 件［0 3 件/100 人年］），サイトメガロウイルス感染，中咽頭カンジダ症及びニューモシスチス・イロベチイ肺炎（各 2 件［0.2 件/100 人年］）であった。重篤な日和見感染は，全ウパダシチニブ 30 mg 併合群で 3 件（ニューモシスチス・イロベチイ肺炎 2 件，

サイトメガロウイルス感染 1 件）発現し，全ウパダシチニブ 15 mg 併合群では発現しなかった（ISS update Table 2. .2.1）。治験薬の投与中止に至った日和見感染は，全ウパダシチニブ 15 mg 併合群で 1 件（コクシジオイデス症）発現し，全ウパダシチニブ 30 mg 併合群では発現しなかった（ISS update Table 2. .3）。申請時データカットオフ以降に新たに発現した重篤又は治験薬の投与中止に至った日和見感染は認められなかった。

死亡に至った日和見感染は発現しなかった（ISS update Table 2. 6.6）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，日和見感染（結核及び帯状疱疹を除く）の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 併合群で 5.0 件/100 人年（2 件）であり，全ウパダシチニブ 15 mg 併合群では発現せず，申請時データカットオフ以降に新たに発現した事象はなかった（J-ISS update T 1 2 1 2 1 3 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での日和見感染（結核及び帯状疱疹を除く）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 0.2 件/100 人年（2 件），全ウパダシチニブ 30 mg 群で 0.9 件/100 人年（7 件）であり，アダリムマブ群では発現しなかった（ISS update Table 2. 8.7）。

2.7. .2.1.5.1.3 帯状疱疹

	全体集団（SS）		日本人部分集団（J-ISS）
項目	Table	F gure	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合			
帯状疱疹	2. 1 1. .1.1	--	2. 1 1. .1.1 J
重篤な帯状疱疹	2 1 1 2 12	--	--
Grade 3 以上の帯状疱疹	2 1 1 3 1	--	--
治験薬の投与中止に至った帯状疱疹	2 1 1 1	--	--
プラセボ対照併合解析集団の部分集団別の帯状疱疹の発現被験者数及び発現割合			
地理的地域	2. 1 1 6.1	--	--
年齢	2. 1 1 6.2	--	2. 1.1.6 2 J
帯状疱疹ワクチンの接種歴	2. 1 1 6.3	--	2. 1.1.6 3 J
帯状疱疹の既往歴	2. 1 1 6.	--	2. 1.1.6. J
ベースライン時の non-bDMARD 併用投与	2 1 1 6 5	--	2 1 1 6 5 J

項目	全体集団（SS） Table	全体集団（SS） F gure	日本人部分集団（J-ISS） Table
ベースライン時の副腎皮質ステロイド併用投与	2. 1 1 6.6	--	2. 1.1.6 6 J
全ウパダシチニブ併合解析集団の100 人年あたりの発現件数			
帯状疱疹	2. 1 2. .1.1 Update 2. .1 1	--	2. 1 2. .1.1 J Update 2. 1.2. .1.1 J
重篤な帯状疱疹	2. 1 2. .2.12 Update 2. .2 12	--	--
Grade 3 以上の帯状疱疹	2. 1 2. .3.1 Update 2. .3 1	--	--
治験薬の投与中止に至った帯状疱疹	2. 1 2. . .1 Update 2. . 1	--	--
全ウパダシチニブ併合解析集団の部分集団別の帯状疱疹の 100 人年あたりの発現件数			
地理的地域	2. 1 2 6.1	--	--
年齢	2. 1 2 6.2	--	2. 1.2.6 2 J
帯状疱疹ワクチンの接種歴	2. 1 2 6.3	--	2. 1.2.6 3 J
帯状疱疹の既往歴	2. 1 2 6.	--	2. 1.2.6. J
ベースライン時の non-bDMARD 併用投与	2. 1 2 6.5	--	2. 1.2.6 5 J
ベースライン時の副腎皮質ステロイド併用投与	2. 1 2 6.6	--	2. 1.2.6 6 J
帯状疱疹を発現した被験者の副腎皮質ステロイド投与量の要約			
全ウパダシチニブ併合解析集団	2 1 2 7 1	--	2 1 2 7 1 J
帯状疱疹を発現した被験者の罹患範囲の要約			
プラセボ対照併合解析集団	2. 1 1.7.1	--	2. 1.1.7 1 J
全ウパダシチニブ併合解析集団	2. 1 2.7.2 Upda e 2. 5	--	2. 1.2.7 2 J
帯状疱疹の一覧表			
プラセボ対照併合解析集団	2 1 1 8 17	--	--
全ウパダシチニブ併合解析集団	2 1 2 8 17 Update 2. 6.17	--	--
帯状疱疹の Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2. 1 2 9.5 Upda e 2. 8.5	--

M15-572 試験及び M15-55 試験では，再発又は播種性帯状疱疹，若しくは播種性単純ヘルペスの既往歴を有する患者は除外した。

帯状疱疹に関する有害事象（非重篤及び重篤を含む）は，表 2.7. - の定義を用いて特定した。また，両試験では，治験責任医師は帯状疱疹の罹患範囲を症例報告書（補足）に記載することとした。この情報についても以下に要約する。

また，帯状疱疹について，ウパダシチニブを投与された被験者でリスク因子となり得る 6 つの部分集団カテゴリーを検討した。検討した部分集団は，地理的地域（北米，西欧及びオセアニア，ラテンアメリカ，東欧，アジア，その他），年齢（50 歳未満，50 歳以上 65 歳未満，65 歳以上），帯状疱疹の既往歴（あり，なし），帯状疱疹ワクチンの接種歴（あり，なし），ベースライン時の non-bDMARD 併用（MTX 単独，MTX 及び MTX 以外の non-bDMARD，MTX 以外の non-bDMARD）及びベースライン時の副腎皮質ステロイド併用（あり，なし）であった。

プラセボ対照併合解析集団（投与 2 週時）では，帯状疱疹ワクチンの接種歴を有した被験者の割合は，ウパダシチニブ 15 mg 併合群で . %（28/6 0 名），ウパダシチニブ 30 mg 併合群で .7%（30/6 1 名），プラセボ併合群で .1%（26/635 名）であった（表 2.7. -25）。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の帯状疱疹の発現状況を表 2.7. .7- 0 に示す。

プラセボ対照併合解析集団（投与 2 週時）の帯状疱疹の発現割合は，ウパダシチニブ 15 mg 併合群で 1.1%（7/6 0 名），ウパダシチニブ 30 mg 併合群で 2.0%（13/6 1 名），プラセボ併合群で 0.8%（5 635 名）であった。内訳は，いずれの投与群でもすべて PT の帯状疱疹であったが，このうちウパダシチニブ 30 mg 併合群の 3 名及びプラセボ併合群の 1 名ではヘルペス後神経痛も発現した。重篤な帯状疱疹は発現しなかった（ISS Table 2. 1.1. .2.12）。治験薬の投与中止に至った帯状疱疹は，ウパダシチニブ 15 mg 併合群で 1 名（0.2%），ウパダシチニブ 30 mg 併合群で 2 名（0.3%），プラセボ併合群で 1 名（0 2%）に発現した（ISS T 1 2 1 1 1 ）。

帯状疱疹の発現割合について部分集団解析を実施したが，各部分集団での帯状疱疹の発現被験者数が少なかったため，結論を見出せなかった（ISS Table 2. 1.1.6.1 から Table 2. 1.1.6.6）。この他の部分集団の結果は，2.7. .5.2 項及び 2.7. 5.3 項に示す。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，帯状疱疹の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 5.6%（1/18 名）であり，プラセボ併合群では発現しなかった（J-ISS Table 2. 1.1. .1.1 J）。内訳は，ウパダシチニブ 15 mg 併合群では PT の帯状疱疹（5.9%［1/17 名］），ウパダシチニブ 30 mg 併合群では PT の帯状疱疹及びヘルペス後神経痛（各 5 6%［1/18 名］）であった。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の帯状疱疹の発現状況（100 人年あたりの発現件数）を表 2.7. .7- 1 に示す。

全ウパダシチニブ併合解析集団（長期）では，帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 3.6 件/100 人年（29 件），全ウパダシチニブ 30 mg 併合群で 7.9 件/100 人年（65 件）であった。内訳は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群のいずれも，多くが PT の帯状疱疹（3.2 件/100 人年，6.9 件/100 人年）であり，次いでヘルペス後神経痛（0.2 件/100 人年，1.0 件/100 人年）であった。重篤な帯状疱疹（PT はいずれも帯状疱疹）は，全ウパダシチニブ 15 mg 併合群で 1 件（0.1 件 100 人年），全ウパダシチニブ 30 mg 併合群で 5 件（0 6 件/100 人年）発現した（ISS Table 2. 1.2. .2 12）。治験薬の投与中止に至った帯状疱疹（PT はいずれも帯状疱疹）は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 2 件（0.2 件/100 人年）発現した（ISS Table 2. 1.2. . .1 ）。

死亡に至った帯状疱疹は認められなかった（ISS Table 2. 1.2.8.17）。

帯状疱疹の多くの事象は，単一のデルマトーム（全ウパダシチニブ 15 mg 併合群：65. %，30 mg 併合群：68 5%）又は同側の 2 つのデルマトーム（全ウパダシチニブ 15 mg 併合群：23.1%，30 mg 併合群：2 1%）に分布していた。3 つ以上のデルマトームに分布していた被験者の割合は，全ウパダシチニブ 15 mg 併合群で 15. %，全ウパダシチニブ 30 mg 併合群で 9.3%であった。眼部帯状疱疹が 1 名（全ウパダシチニブ 30 mg 併合群），耳帯状疱疹（ラムゼーハント症候群）が 1 名（全ウパダシチニブ 15 mg 併合群）に認められ，中枢神経系，肺又は肝臓等に発現した事象は認められなかった（ISS Table 2. 1.2.7.2）。

帯状疱疹の 100 人年あたりの発現件数について部分集団解析を実施した。その結果，帯状疱疹の 100 人年あたりの発現件数（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の順に記載）は，地理的地域ではアジア以外の地域（0–6 0 件 100 人年及び 3 9–15.6 件/100 人年）と比較してアジア（12.1 件/100 人年及び 18.0 件/100 人年）で多く（ISS Table 2. 1.2.6 1），年齢では 50 歳未満（1.2 件/100 人年及び 6.0 件/100 人年）と比較して 50 歳以上 65 歳未満（5.7 件/100 人年及び 9 3 件/100 人年）及び 65 歳以上（ .3 件/100 人年及び 9.3 件/100 人年）で多かった（ISS Table 2. 1.2.6.2）。ベースライン時の non-bDMARD 併用の有無別では，投与あり（2.9–3.7 件/100 人年及び 5. –13.9 件/100 人年）と投与なし（3 5 件 100 人年及び 9 9 件/100 人年）でおおむね同様であったが（ISS Table 2. 1.2.6.5），ベースライン時の副腎皮質ステロイド併用の有無別では，全ウパダシチニブ 15 mg 併合群と全ウパダシチニブ 30 mg 併合群のいずれでも，帯状疱疹の発現リスクに一定の傾向は認められなかった（ISS Table 2. 1.2.6.6）。

この他の部分集団の結果は，2.7. .5.2 項及び 2.7. .5.3 項に示す。

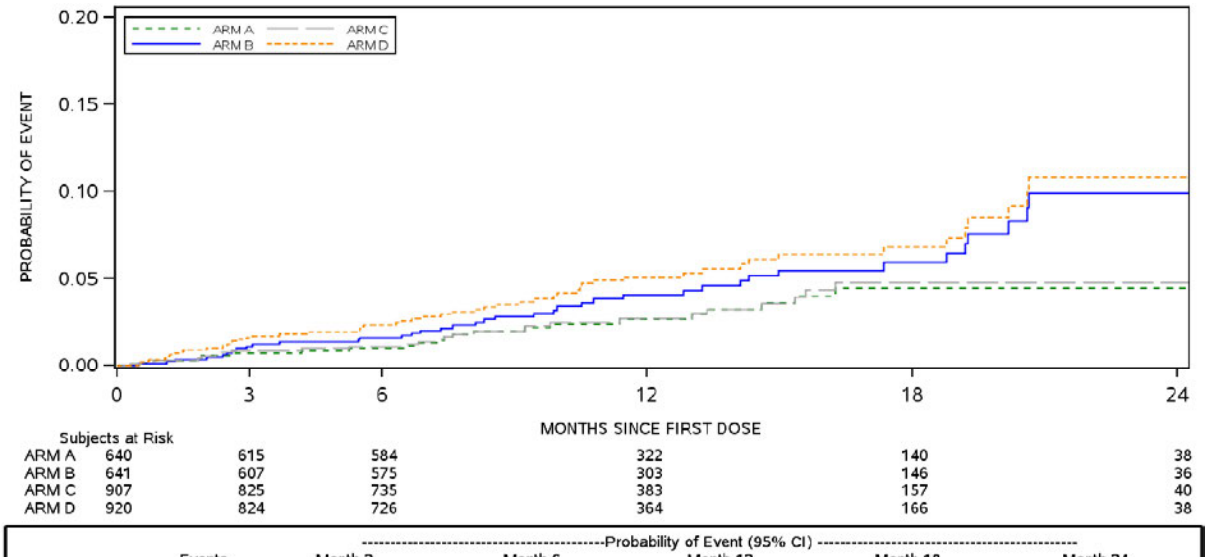
全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 8.7 件/100 人年（2 件），全ウパダシチニブ

30 mg 併合群で 2 9 件/100 人年（7 件）であった。内訳は，全ウパダシチニブ 15 mg 併合群ではいずれも PT の帯状疱疹であり，全ウパダシチニブ 30 mg 併合群ではヘルペス後神経痛 2 件を除くすべてが PT の帯状疱疹であった（J-ISS Table 2. 1.2. .1.1 J）。

全ウパダシチニブ併合解析集団（長期）の帯状疱疹の Kaplan-Meier プロットを図 2.7. -2 に示す。

ウパダシチニブ 15 mg を投与された被験者では，帯状疱疹が発現するリスクは一定で推移した。

図 2 7. -2. 全ウパダシチニブ併合解析集団（長期）の帯状疱疹の Kaplan-Meier プロット



Subjects at Risk

ARM A	640	615	584	322	140	38
ARM B	641	607	575	303	146	36
ARM C	907	825	735	383	157	40
ARM D	920	824	726	364	166	38

		Probability of Event (95% CI)				
	Events	Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 640)	21	0.7%(<0.1%, 1.4%)	1.0%(0.2%, 1.8%)	2.7%(1.0%, 4.2%)	4.4%(1.8%, 7.0%)	4.4%(1.8%, 7.0%)
ARM B (N = 641)	39	1.1%(0.3%, 1.9%)	1.6%(0.6%, 2.6%)	4.0%(2.1%, 6.0%)	5.9%(3.1%, 8.7%)	9.9%(4.8%, 14.7%)
ARM C (N = 907)	26	0.9%(0.2%, 1.5%)	1.1%(0.4%, 1.9%)	2.7%(1.3%, 4.2%)	4.8%(2.2%, 7.2%)	4.8%(2.2%, 7.2%)
ARM D (N = 920)	54	1.6%(0.8%, 2.5%)	2.4%(1.3%, 3.4%)	5.1%(3.1%, 7.1%)	6.8%(4.1%, 9.4%)	10.8%(6.1%, 15.4%)

Note: ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.
Patients could be included in more than one treatment group.

相互参照：ISS Figure 2. 1.2.9.5

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 3. 件/100 人年（18 件），全ウパダシチニブ 30 mg 群で 6.5 件/100 人年（3 件），アダリムマブ群で 0.5 件/100 人年（2 件）であった（M15-572 試験 CSR W2 Table 1 .3 1.1.2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の帯状疱疹の発現状況（100 人年あたりの発現件数）を表 2.7. .7-110 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 3 8 件/100 人年（ 8 件），全ウパダシチニブ 30 mg 併合群で 6.7 件/100 人年（8 件）であった。内訳は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群のいずれも，多くが PT の帯状疱疹（3. 件/100 人年，5.8 件/100 人年）であり，次いでヘルペス後神経痛（0 3 件/100 人年，0.7 件/100 人年）であった。重篤な帯状疱疹は，全ウパダシチニブ 15 mg 併合群で 2 件（0.2 件/100 人年），全ウパダシチニブ 30 mg 併合群で 6 件（0.5 件/100 人年）発現し，全ウパダシチニブ 30 mg 併合群の 1 件（皮膚播種性帯状疱疹）を除くすべてが PT の帯状疱疹であった（ISS update Table 2. .2.12）。治験薬の投与中止に至った帯状疱疹は，全ウパダシチニブ 15 mg 併合群で 2 件（0 2 件/100 人年），全ウパダシチニブ 30 mg 併合群で 件（0.3 件/100 人年）発現し，全ウパダシチニブ 30 mg 併合群の 1 件（皮膚播種性帯状疱疹）を除くすべてが PT の帯状疱疹であった（ISS update Table 2. . .1 ）。

死亡に至った帯状疱疹は認められなかった（ISS update Table 2. 6.17）。

帯状疱疹の多くの事象は，単一のデルマトーム（全ウパダシチニブ 15 mg 併合群：66.7%，30 mg 併合群：6 8%）又は同側の 2 つのデルマトーム（全ウパダシチニブ 15 mg 併合群：19.0%，30 mg 併合群：21 1%）に分布していた。3 つ以上のデルマトームに分布していた被験者の割合は，全ウパダシチニブ 15 mg 併合群で 11.9%，全ウパダシチニブ 30 mg 併合群で 1 .1%であった。眼部帯状疱疹が全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名，中枢神経系での発現が全ウパダシチニブ 30 mg 併合群で 1 名，耳帯状疱疹（ラムゼーハント症候群）が全ウパダシチニブ 15 mg 併合群で 1 名及び 30 mg 併合群で 2 名，皮膚以外（肺又は肝臓等）での発現が全ウパダシチニブ 30 mg 併合群で 3 名に認められた（ISS update T 1 2 5）。中枢神経系又は皮膚以外（肺又は肝臓等）での発現が認められたが，メディカルレビューに基づくと，いずれも誤分類又は誤入力であり，メディカルレビューで中枢神経系又は皮膚以外（肺又は肝臓等）での発現が認められた事象はなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 8.5 件/100 人年（3 件），全ウパダシチニブ 30 mg 併合群で 2 9 件/100 人年（10 件）であった。内訳は，全ウパダシチニブ 15 mg 併合群ではいずれも PT の帯状疱疹であり，全ウパダシチニブ 30 mg 併合群ではヘルペス後神経痛 2 件を除くすべてが PT の帯状疱疹であった（J-ISS update Table 2. 1.2. .1.1 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の帯状疱疹の Kaplan-Meier プロットを ISS update Figure 2. 8.5 に示す。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で .0 件/100 人年（32 件），全ウパダシチニブ 30 mg 群で 5.9 件/100 人年（ 8 件），アダリムマブ群で 0.5 件/100 人年（3 件）であった（ISS update Table 2. 8.18）。

2.7. .2.1.5.1. 活動性結核

項目	全体集団（SS） Tab e	日本人部分集団（J-ISS） Table
プラセボ対照併合解析集団の発現被験者数及び発現割合		
活動性結核	2. 1.1. 1 17	2. 1.1. 1 17 J
重篤な活動性結核	2. 1.1. 2 15	--
Grade 3 以上の活動性結核	2. 1.1. 3 17	--
治験薬の投与中止に至った活動性結核	2. 1.1. . 17	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数		
活動性結核	2. 1.2. 1 17 Update 2 1 17	2. 1.2. 1 17 J Update 2 1 2 1 17 J
重篤な活動性結核	2 1 2 2 15 Update 2. .2.15	--
Grade 3 以上の活動性結核	2. 1.2. 3 17 Update 2 3 17	--
治験薬の投与中止に至った活動性結核	2 1 2 17 Update 2. . .17	--
プラセボ対照併合解析集団のベースライン時の安全性に関する特性 カテゴリカルデータ)	2 2 1.1.3	--
活動性結核の一覧表		
プラセボ対照併合解析集団	2. 1.1 8 20	--
全ウパダシチニブ併合解析集団	2. 1.2 8 20 Update 2. 6.20	--

M15-572 試験及び M15-55 試験では，スクリーニング時にクォンティフェロン TB ゴールド検査を用いて結核検査を実施した。精製ツベルクリンたん白（PPD）皮膚検査は，クォンティフェロン TB ゴールド検査が実施できない場合にのみ実施した。活動性結核のエビデンスが認められた被験者は，両試験に組み入れないこととした。ただし，潜在性結核のエビデンスが認められた被験者は，治験薬初回投与の 2 週間以上前（又は当該地域のガイドラインで規定された期間のいずれか長い方）に予防療法を開始した後であれば試験に参加できることとした。

プラセボ対照併合解析集団（投与 2 週時）では，スクリーニング時のクォンティフェロン TB ゴールド検査で陽性であった被験者は，ウパダシチニブ 15 mg 併合群で .5%（29/6 0 名），ウパダシチニブ 30 mg 併合群で 5.1%（33/6 1 名），プラセボ併合群で . %（28/635 名）であった（表 2.7. -25）。

活動性結核に関する有害事象は，表 2.7. - の定義を用いて特定した。

全ウパダシチニブ併合解析集団（長期）の活動性結核の発現状況（100 人年あたりの発現件数）を表 2.7. .7- 2 に示す。

全ウパダシチニブ併合解析集団（長期）では，申請時データカットオフまでに活動性結核は発現しなかった。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の活動性結核の発現状況（100 人年あたりの発現件数）を表 2.7. .7-111 に示す。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，活動性結核は発現しなかった。

2.7. .2.1.5.1.5 悪性腫瘍（リンパ腫含む）

悪性腫瘍 (可能性を含む)	全体集団 (SS)	日本人部分集団 (J-ISS)
項目	Tab e	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合		
悪性腫瘍 (可能性を含む)	2. 1.1. .1.	2. 1.1. .1. J
重篤な悪性腫瘍 (可能性を含む)	2. 1.1. .2.2	--
Grade 3 以上の悪性腫瘍 (可能性を含む)	2. 1.1. .3.	--
治験薬の投与中止に至った悪性腫瘍 (可能性を含む)	2. 1.1. . .	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現被験者数		
悪性腫瘍 (可能性を含む)	2. 1.2. .1. Update 2. 1.	2. 1.2. .1. J Update 2. 1 2. .1. J
重篤な悪性腫瘍 (可能性を含む)	2. 1.2. .2.2 Update 2. 2.2	--
Grade 3 以上の悪性腫瘍 (可能性を含む)	2. 1.2. .3. Update 2. 3.	--
治験薬の投与中止に至った悪性腫瘍 (可能性を含む)	2. 1.2. . . Update 2. . .	--

悪性腫瘍 (可能性を含む)	全体集団 (SS)	日本人部分集団 (J-ISS)
項目	Tab e	Table
悪性腫瘍 (可能性を含む) の一覧表		
プラセボ対照併合解析集団	2. 1.1.8.7	--
全ウパダシチニブ併合解析集団	2. 1.2.8.7 Update 2 6 7	--

悪性腫瘍 (NMSC を含む)	全体集団 (SS)	日本人部分集団 (J-ISS)
項目	Tab e	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合		
悪性腫瘍	2 1 1 1 5	2 1 1 1 5 J
重篤な悪性腫瘍	2 1 1 2 3	--
Grade 3 以上の悪性腫瘍	2 1 1 3 5	--
治験薬の投与中止に至った悪性腫瘍	2. 1.1. . .5	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現被験者数		
悪性腫瘍	2. 1.2. .1.5 Update 2. 1.5	2. 1.2. .1.5 J Update 2. 1 2. .1.5 J
重篤な悪性腫瘍	2. 1.2. .2.3 Update 2. 2.3	--
Grade 3 以上の悪性腫瘍	2. 1.2. .3.5 Update 2. 3.5	--
治験薬の投与中止に至った悪性腫瘍	2. 1.2. . .5 Update 2. . .5	--
悪性腫瘍の一覧表		
プラセボ対照併合解析集団	2. 1.1.8.8	--
全ウパダシチニブ併合解析集団	2. 1.2.8.8 Update 2 6 8	--

悪性腫瘍 (NMSC を除く)	全体集団 (ISS)		日本人部分集団 (J- SS)
項目	Table	Figure	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合			
悪性腫瘍 (NMSC を除く)	2. 1 1. .1.7	--	2. 1.1. 1.7 J
重篤な悪性腫瘍 (NMSC を除く)	2. 1 1. .2.5	--	--
Grade 3 以上の悪性腫瘍 (NMSC を除く)	2. 1 1. .3.7	--	--
治験薬の投与中止に至った悪性腫瘍 (NMSC を除く)	2. 1 1. . .7	--	--

悪性腫瘍 (NMSC を除く)	全体集団 (ISS)		日本人部分集団 (J- SS)
項目	Table	Figure	Table
全ウパダシチニブ併合解析集団の 100 人年あたりの発現被験者数			
悪性腫瘍 (NMSC を除く)	2. 1 2. .1.7 Upda e 2. .1.7	--	2. 1.2. 1.7 J Update 2. 1.2. .1.7 J
重篤な悪性腫瘍 (NMSC を除く)	2. 1 2. .2.5 Upda e 2. .2.5	--	--
Grade 3 以上の悪性腫瘍 (NMSC を除く)	2. 1 2. .3.7 Upda e 2. .3.7	--	--
治験薬の投与中止に至った悪性腫瘍 (NMSC を除く)	2. 1 2. . .7 Upda e 2. . .7	--	--
悪性腫瘍 (NMSC を除く)の一覧表			
プラセボ対照併合解析集団	2. 1.1.8.10	--	--
全ウパダシチニブ併合解析集団	2. 1.2.8.10 Update 2 6 10	--	--
悪性腫瘍 (NMSC を除く) の Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2 1 2 9 3 Update 2. 8 3	--

NMSC	全体集団 (SS)		日本人部分集団 (J ISS)
項目	Table	F gure	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合			
NMSC	2. 1 1. .1.6	--	2. 1.1. 1 6 J
重篤な NMSC	2. 1 1. .2.	--	--
Grade 3 以上の NMSC	2. 1 1. .3.6	--	--
治験薬の投与中止に至った NMSC	2. 1 1. . .6	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現被験者数			
NMSC	2. 1 2. .1.6 Upda e 2 1 6	--	2. 1.2. 1 6 J Update 2 1 2 1 6 J
重篤な NMSC	2 1 2 2 Upda e 2. .2.	--	--
Grade 3 以上の NMSC	2. 1 2. .3.6 Upda e 2 3 6	--	--
治験薬の投与中止に至った NMSC	2 1 2 6 Upda e 2. . .6	--	--

NMSC	全体集団（SS）		日本人部分集団（J ISS）
項目	Table	F gure	Table
NMSC の一覧表			
プラセボ対照併合解析集団	2. 1 1 8.9	--	--
全ウパダシチニブ併合解析集団	2. 1 2 8.9 Upda e 2 6 9	--	--
NMSC の Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2. 1 2 9. Upda e 2. 8.	--

リンパ腫	全体集団（SS）	日本人部分集団（J-ISS）
項目	Tab e	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合		
リンパ腫	2. 1.1. .1.8	2. 1.1. .1.8 J
重篤なリンパ腫	2. 1.1. .2.6	--
Grade 3 以上のリンパ腫	2. 1.1. .3.8	--
治験薬の投与中止に至ったリンパ腫	2. 1.1. . .8	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現被験者数		
リンパ腫	2 1 2 1 8 Update 2. 1.8	2 1 2 1 8 J Update 2. 1 2. .1.8 J
重篤なリンパ腫	2. 1.2. .2.6 Update 2. 2.6	--
Grade 3 以上のリンパ腫	2. 1.2. .3.8 Update 2. 3.8	--
治験薬の投与中止に至ったリンパ腫	2. 1.2. . .8 Update 2. . .8	--
リンパ腫の一覧表		
プラセボ対照併合解析集団	2. 1.1 8 11	--
全ウパダシチニブ併合解析集団	2. 1.2 8 11 Update 2. 6.11	--

M15-572 試験及び M15-55 試験では，悪性腫瘍（治療に成功した NMSC 又は局所性の子宮頸部上皮内癌を除く）の既往を有する患者は除外した。

ウパダシチニブによる悪性腫瘍の発現の可能性を検討するため，悪性腫瘍に関する有害事象を検索した。悪性腫瘍に関する有害事象については，表 2.7. - の定義を用いて特定した。

全ウパダシチニブ解析対象集団での悪性腫瘍の結果は，100 人年あたりの発現被験者数で示した。

本項では，悪性腫瘍（NMSC を除く），NMSC 及びリンパ腫に分けて検討した。悪性腫瘍（NMSC を含む）のプラセボ対照併合解析集団（投与 2 週時）の発現状況は表 2.7. .7- 3，全ウパダシチニブ併合解析集団（長期）の発現状況（100 人年あたりの発現被験者数）は表 2.7. .7- に示す。また，全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の発現状況（100 人年あたりの発現被験者数）は表 2.7. .7-112 に示す。

悪性腫瘍（NMSC を除く）

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の悪性腫瘍（NMSC を除く）の発現状況を表 2.7. .7- 5 に示す。

プラセボ対照併合解析集団（投与 2 週時）の悪性腫瘍（NMSC を除く）の発現割合は，ウパダシチニブ 15 mg 併合群で 0 5%（3/6 0 名），ウパダシチニブ 30 mg 併合群で 0.5%（3/6 1 名）であり，プラセボ併合群では発現しなかった。内訳は，ウパダシチニブ 15 mg 併合群では神経内分泌癌，前立腺癌及び直腸癌（各 1 名），ウパダシチニブ 30 mg 併合群では肺腺癌及び直腸腺癌（各 1 名），子宮内膜癌及び卵巣癌（1 名が両事象を発現）であった。重篤な悪性腫瘍（NMSC を除く）は，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 3 名（0.5%）に発現した。内訳は，ウパダシチニブ 15 mg 併合群では神経内分泌癌，前立腺癌及び直腸癌（各 1 名），ウパダシチニブ 30 mg 併合群では肺腺癌，卵巣癌及び直腸腺癌（各 1 名）であった（ISS Table 2. 1.1. .2.5）。治験薬の投与中止に至った悪性腫瘍（NMSC を除く）は，ウパダシチニブ 15 mg 併合群で 3 名（0.5%），30 mg 併合群で 2 名（0.3%）に発現した。内訳は，ウパダシチニブ 15 mg 併合群では神経内分泌癌，前立腺癌及び直腸癌（各 1 名），ウパダシチニブ 30 mg 併合群では肺腺癌及び直腸腺癌（各 1 名）であった（ISS Table 2. 1.1. . .7）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，悪性腫瘍（NMSC を除く）の発現割合はウパダシチニブ 30 mg 併合群で 5.6%（1/18 名）であり，ウパダシチニブ 15 mg 併合群及びプラセボ併合群では発現しなかった。発現した悪性腫瘍（NMSC を除く）は，子宮内膜癌及び卵巣癌（1 名が両事象を発現）であった（J-ISS Table 2. 1.1. .1.7 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の悪性腫瘍（NMSC を除く）の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7- 6 に示す。

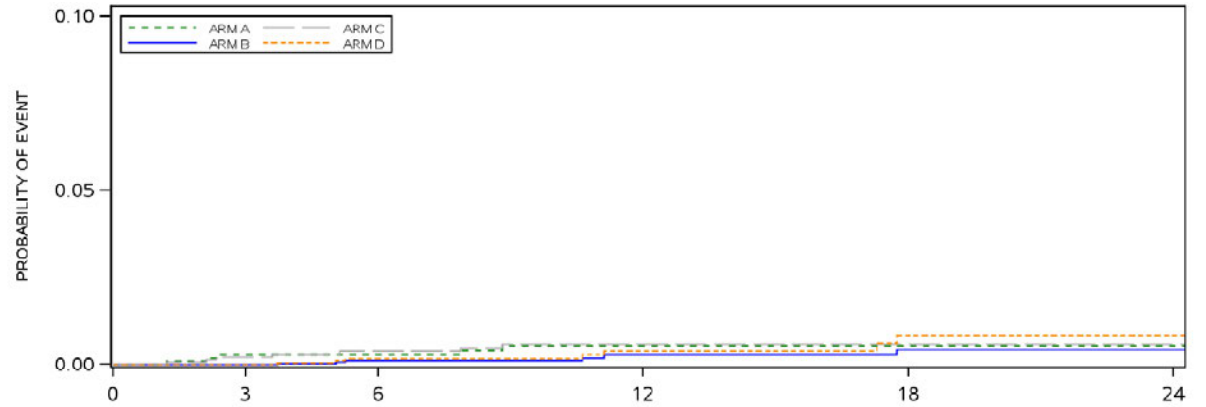
全ウパダシチニブ併合解析集団（長期）では，悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群及び全ウパダシチニブ 30 mg 併合群とも 0.9 名/100 人年（7 名）であった。全ウパダシチニブ 15 mg 併合群の前立腺癌及び全ウパダシチニブ 30 mg 併合群の扁平上皮癌の 100 人年あたりの発現被験者数は 0 2 名/100 人年であり，それ以外の事象では 0.1 名/100 人年以下であった。なお，メディカルレビューにより，全ウパダシチニブ 30 mg 併合群の扁平上皮癌 2 件及び基底扁平上皮癌 1 件は，NMSC であると判断された（NMSC

の項を参照）。重篤な悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.6 名/100 人年（5 名），全ウパダシチニブ 30 mg 併合群で 0.5 名/100 人年（ 名）であった（ISS Table 2. 1.2. .2.5）。治験薬の投与中止に至った悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.9 名/100 人年（7 名），全ウパダシチニブ 30 mg 併合群で 0. 名/100 人年（3 名）であった（ISS Table 2. 1.2. . .7）。全ウパダシチニブ 15 mg 併合群で，評価期間以降に 1 名が遠隔転移を伴う肺癌により死亡した（詳細は 2.7. .2.1.2 項を参照）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は全ウパダシチニブ 30 mg 併合群で 3.5 名/100 人年（1 名）であり，全ウパダシチニブ 15 mg 併合群では発現しなかった（J-ISS Table 2. 1.2. .1.7 J）。発現した悪性腫瘍（NMSC を除く）は，子宮内膜癌及び卵巣癌（1 名が両事象を発現）であった。

全ウパダシチニブ併合解析集団（長期）の悪性腫瘍（NMSC を除く）の Kaplan-Meier プロットを図 2.7. -3 に示す。
ウパダシチニブ 15 mg を投与された被験者では，悪性腫瘍（NMSC を除く）が発現するリスクの経時的な増加は認められなかった。

図 2 7. -3. 全ウパダシチニブ併合解析集団（長期）の悪性腫瘍（NMSC を除く）の Kaplan-Meier プロット



Subjects at Risk

ARM A	640	617	590	329	148	40
ARM B	641	615	583	324	149	40
ARM C	907	830	740	391	166	42
ARM D	920	840	744	393	172	42

Probability of Event (95% CI)

	Events	Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 640)	5	0.3%(0.0%, 0.7%)	0.3%(0.0%, 0.7%)	0.5%(0.0%, 1.3%)	0.5%(0.0%, 1.3%)	0.5%(0.0%, 1.3%)
ARM B (N = 641)	6	0	0.1%(0.0%, 0.4%)	0.3%(0.0%, 0.8%)	0.4%(0.0%, 1.3%)	0.4%(0.0%, 1.3%)
ARM C (N = 907)	7	0.2%(0.0%, 0.5%)	0.4%(0.0%, 0.8%)	0.6%(0.0%, 1.3%)	0.6%(0.0%, 1.3%)	0.6%(0.0%, 1.3%)
ARM D (N = 920)	7	0	0.2%(0.0%, 0.5%)	0.4%(0.0%, 1.0%)	0.8%(0.0%, 2.1%)	0.8%(0.0%, 2.1%)

Note: ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.
Patients could be included in more than one treatment group.

相互参照：ISS Figure 2. 1.2.9.3

一般集団を対象とした The Sur eillance Epidemiology and End Results 18 レジストリ研究データ（2000 年から 2015 年）から得られた，年齢ー性別別の悪性腫瘍データを用いて標準化罹患比（以下「SIR」）の解析を実施した結果，悪性腫瘍（NMSC を除く）の SIR 推定値は，ウパダシチニブ 15 mg 群で 1.17（95%信頼区間：0. 7–2. 2），ウパダシチニブ 30 mg 群で 1.16（95%信頼区間：0. 7–2.39）であった。いずれの投与群でも悪性腫瘍（NMSC を除く）は 7 名に認められたが，悪性腫瘍の期待罹患数は 6 名であった。この結果に基づくと，ウパダシチニブを投与した被験者での悪性腫瘍（NMSC を除く）の発現被験者数は予測値を上回らなかった。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験（長期）での悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0.6 名/100 人年（3 名），全ウパダシチニブ 30 mg 群で 0. 名/100 人年（2 名），アダリムマブ群で 1 0 名/100 人年（ 名）であった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2.2）。アダリムマブ群で発現した悪性腫瘍（NMSC を除く）の内訳は，遠隔転移を伴う結腸癌，卵巣癌，遠隔転移を伴う膵癌及び子宮癌（各 1 件）であった（M15-572 試験 CSR W2 Table 1 .3 2.6. .2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の悪性腫瘍（NMSC を除く）の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-113 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.7 名/100 人年（9 名），全ウパダシチニブ 30 mg 併合群で 0 8 名/100 人年（10 名）であった。全ウパダシチニブ 15 mg 併合群の前立腺癌の 100 人年あたりの発現被験者数は 0.2 名/100 人年であり，それ以外の事象では 0.1 名/100 人年以下であった。なお，申請時データカットオフでは，メディカルレビューにより，全ウパダシチニブ 30 mg 併合群の扁平上皮癌 2 件及び基底扁平上皮癌 1 件が NMSC であると判断されたが，20[redacted]年[redacted]月[redacted]日データカットオフでは，扁平上皮癌のうち 1 件は再コード化されず，他の 1 件は皮膚有棘細胞癌に更新され，メディカルレビューにより NMSC に再分類された。基底扁平上皮癌の 1 件は，皮膚基底有棘細胞癌に更新され，20[redacted]年[redacted]月[redacted]日データカットオフ後に NMSC に再分類された。重篤な悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群及び全ウパダシチニブ 30 mg 併合群で各 0.6 名 100 人年（7 名）であった（ISS update Table 2. .2 5）。治験薬の投与中止に至った悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.7 名/100 人年（9 名），全ウパダシチニブ 30 mg 併合群で 0.3 名/100 人年（ 名）であった（ISS update Table 2. . .7）。申請時データカットオフ以降に，悪性腫瘍（NMSC を除く）による死亡は認められなかった（ISS update Table 2. 6.10）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 30 mg 併合群で 2.5 名/100 人年（1 名）であり，全ウパダシチニブ 15 mg 併合群では発現せず，申請時データカットオフから新たに発現した事象はなかった（J-ISS update T 1 2 1 2 1 7 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の悪性腫瘍（NMSC を除く）の Kaplan-Meier プロットを ISS update Figure 2. 8.3 に示す。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0 5 名/100 人年（ 名），全ウパダシチニブ 30 mg 群で 0.6 名/100 人年（5 名），アダリムマブ群で 0.7 名/100 人年（ 名）であった（ISS update Table 2. 2 8）。アダリムマブ群では，投与 2 週時データカットオフから新たに発現した事象はなかった（ISS update Table 2. 6 10）。

NMSC

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の NMSC の発現状況を表 2.7. .7- 7 に示す。

プラセボ対照併合解析集団（投与 2 週時）の NMSC の発現割合（PT はいずれも基底細胞癌）は，ウパダシチニブ 15 mg 併合群で 0.2%（1/6 0 名），ウパダシチニブ 30 mg 併合群で 0.5%（3/6 1 名），プラセボ併合群で 0 2%（1/635 名）であった。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，NMSC は発現しなかった（J-ISS Table 2. 1.1. 1.6 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の NMSC の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7- 8 に示す。

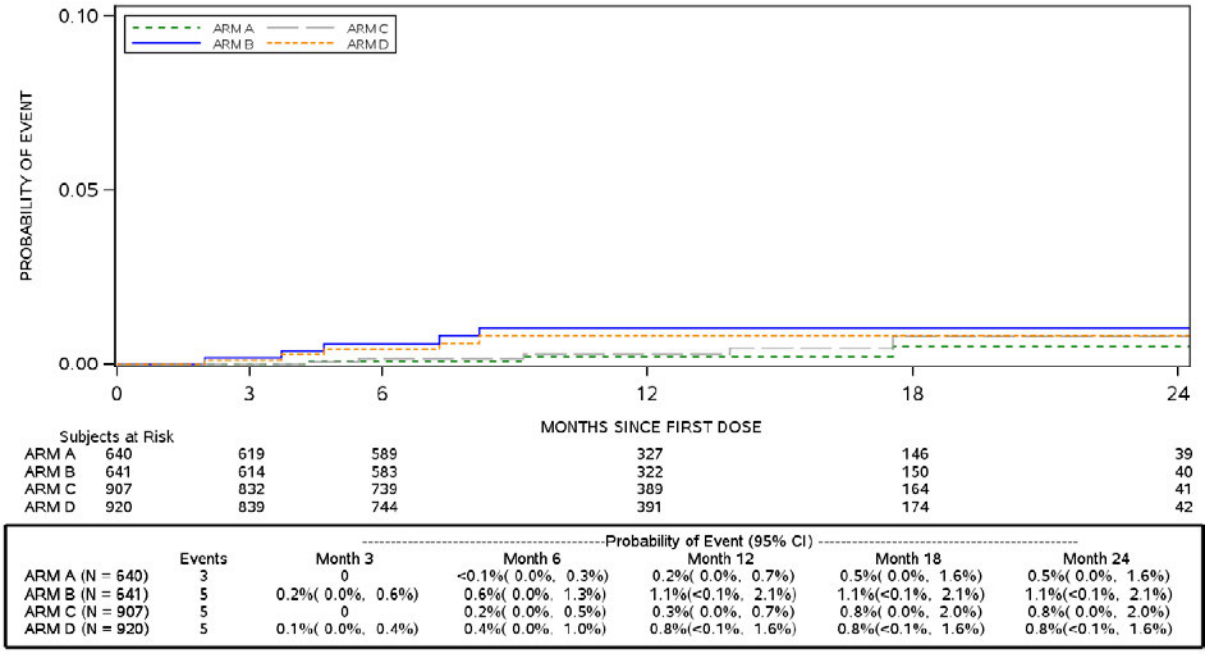
全ウパダシチニブ併合解析集団（長期）の NMSC の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群でいずれも 0.6 名/100 人年（5 名）であった。100 人年あたりの発現被験者数が最も多かった事象は，いずれの投与群でも基底細胞癌（全ウパダシチニブ 15 mg 併合群：0.5 名/100 人年，30 mg 併合群：0. 名/100 人年）であった。なお，全ウパダシチニブ 30 mg 併合群の 2 名で発現した事象（1 名は扁平上皮癌及び基底扁平上皮癌各 1 件を発現，他の 1 名は扁平上皮癌 1 件を発現）は，メディカルレビューにより NMSC と判断されたため，表 2.7. .7- 8 の NMSC のデータには含まれていない。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，NMSC は発現しなかった（J-ISS Table 2. 1.2. 1.6 J）。

全ウパダシチニブ併合解析集団（長期）の NMSC の Kaplan-Meier プロットを図 2.7. - に示す。

ウパダシチニブ 15 mg を投与された被験者では，NMSC が発現するリスクの経時的な増加は認められなかった。

図 2 7. - . 全ウパダシチニブ併合解析集団（長期）の NMSC の Kap an-Meier プロット



Note: ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.
Patients could be included in more than one treatment group.

相互参照：ISS Figure 2. 1.2.9.

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの NMSC の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0. 名/100 人年（2 名），全ウパダシチニブ 30 mg 群で 0.8 名/100 人年（ 名），アダリムマブ群で 0.5 名/100 人年（2 名）であった（M15-572 試験 CSR W2 Table 1 .3 1.1.2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の NMSC の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-11 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の NMSC の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.7 名/100 人年（9 名），全ウパダシチニブ 30 mg 併合群で 0.6 名/100 人年（7 名）であった。100 人年あたりの発現被験者数が最も多かった事象は，いずれの投与群でも基底細胞癌（全ウパダシチニブ 15 mg 併合群：0.6 名/100 人年，30 mg 併合群：0. 名/100 人年）であった。なお，申請時データカットオフで，メディカルレビューにより悪性腫瘍（NMSC を除く）ではなく NMSC と判断された 3 件のうち，扁平上皮癌の 1 件（全ウパダシチニブ 30 mg 併合群）が，20[redacted]年[redacted]月[redacted]日データカットオフで皮

膚有棘細胞癌に更新され，NMSC に再分類された（他の 2 件は表 2.7. .7-11 に含まれていない）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，NMSC は発現しなかった（J-ISS update Table 2. 1.2. .1 6 J）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の NMSC の Kaplan-Meier プロットを ISS update Figure 2. 8. に示す。

アダリムマブとの比較（M15-572 試験［20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ］）

M15-572 試験（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）での NMSC の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0.5 名 100 人年（ 名），全ウパダシチニブ 30 mg 群で 0. 名/100 人年（3 名），アダリムマブ群で 0. 名/100 人年（2 名）であった（ISS update Table 2. 2.8）。投与 2 週時データカットオフから新たに NMSC を発現した被験者は，全ウパダシチニブ 15 mg 群の 2 名であり，全ウパダシチニブ 30 mg 群及びアダリムマブ群では認められなかった。なお，投与 2 週時データカットオフまでに NMSC を発現した被験者は，全ウパダシチニブ 30 mg 群で 名と報告されたが，20[redacted] 年 [redacted] 月 [redacted] 日データカットオフでは 3 名と報告された。投与 2 週時データカットオフでは，1 名に皮膚有棘細胞癌が発現し，NMSC に分類されたが，20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ時点では PT は空欄でコード化されなかった。本事象は，データカットオフ後に皮膚有棘細胞癌に再コード化された。

リンパ腫

プラセボ対照併合解析集団（投与 2 週時）のリンパ腫の発現状況を表 2.7. .7- 9，全ウパダシチニブ併合解析集団（長期）のリンパ腫の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-50 に示す。

全ウパダシチニブ併合解析集団（長期）のリンパ腫の発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.2 名/100 人年（2 名）であり，全ウパダシチニブ 30 mg 併合群では発現しなかった。全ウパダシチニブ 15 mg 併合群で発現したリンパ腫は，いずれもリンパ球形態異常であり，PT のリンパ腫は発現しなかった。この 2 名の被験者は，いずれも日本人であった（J-ISS Table 2. 1.2. .1.8 J）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）のリンパ腫の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-115 に示す。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）のリンパ腫の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.2 名/100 人年（2 名）であり，全ウパダシチニブ 30 mg 併合群では発現しなかった。全ウパダシチニブ 15 mg 併合群で発現した

リンパ腫は，いずれも投与 2 週時データカットオフまでに認められたリンパ球形態異常であり，PT のリンパ腫は発現しなかった（ISS update Table 2. 6.11）。

2.7. .2.1.5.1.6 薬物性肝障害

	全体集団（SS）		日本人部分集団（J-ISS）	
項目	Table	F gure	Table	F gure
プラセボ対照併合解析集団の発現被験者数及び発現割合				
薬物性肝障害	2. 1 1. .1.9	--	2. 1.1. 1 9 J	--
重篤な薬物性肝障害	2. 1 1. .2.7	--	--	--
Grade 3 以上の薬物性肝障害	2. 1 1. .3.9	--	--	--
治験薬の投与中止に至った薬物性肝障害	2. 1 1. . .9	--	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数				
薬物性肝障害	2. 1 2. .1.9 Update 2. .1.9	--	2. 1.2. 1 9 J Update 2 1 2 1 9 J	--
重篤な薬物性肝障害	2 1 2 2 7 Update 2. .2.7	--	--	--
Grade 3 以上の薬物性肝障害	2. 1 2. .3.9 Update 2. .3.9	--	--	--
治験薬の投与中止に至った薬物性肝障害	2. 1 2. . .9 Update 2. . .9	--	--	--
薬物性肝障害の一覧表				
プラセボ対照併合解析集団	2 1 1 8 12	--	--	--
全ウパダシチニブ併合解析集団	2 1 2 8 12 Update 2. 6 12	--	--	--
臨床検査値のベースラインからの平均変化量				
プラセボ対照併合解析集団	2.5 1.1.1	--	2.5 1.1 1 J	--
全ウパダシチニブ併合解析集団	2.5 1.2.1 Update 2 5 1	--	2.5 1.2 1 J Update 2.5 1.2 1 J	--
肝機能検査値上昇の基準に該当した被験者数及び割合				
プラセボ対照併合解析集団	2 5 1 1 5 1	--	2 5 1 1 5 1 J	--

項目	全体集団（SS）		日本人部分集団（J-ISS）	
	Table	F gure	Table	F gure
全ウパダシチニブ併合解析集団	2.5 1 2.5.1 Update 2 5 1	--	2.5 1.2 5 1 J Update 2.5 1.2.5 1 J	--
肝機能検査値上昇の基準に該当した被験者の一覧表				
プラセボ対照併合解析集団	2.5 1 1.5.2	--	--	--
全ウパダシチニブ併合解析集団	2.5 1 2.5.2 Update 2.5 .2	--	--	--
臨床検査値のベースラインからの平均変化量の推移				
全ウパダシチニブ併合解析集団	--	2.5 1 2.6 Update 2.5 5	--	2.5 1.2.6 J Update 2.5 1.2.6 J
総ビリルビンのベースライン後の最大値対 ALT のベースライン後の最大値の eDISH プロット				
プラセボ対照併合解析集団	--	2.5 1 1.7	--	2.5 1.1.7 J
全ウパダシチニブ併合解析集団	--	2.5 1 2.8 Update 2 5 6	--	2.5 1.2.8 J Update 2.5 1.2.8 J
総ビリルビンのベースライン後の最大値対 AST のベースライン後の最大値の eDISH プロット				
全ウパダシチニブ併合解析集団	--	Update 2.5 9	--	--
ALT 及び AST が最初に ULN の 3 倍以上になるまでの時間の Kaplan-Meier プロット				
全ウパダシチニブ併合解析集団	--	2.5 1 2.7	--	--

M15-572 試験及び M15-55 試験では，トランスアミナーゼに関する選択基準として，スクリーニング時の ALT 及び AST を基準値上限（以下「ULN」）の 2 倍未満とした。また，治験実施計画書では，次の場合に治験薬の投与を中断すると規定した。

- ALT 又は AST が ULN の 3 倍を上回り，かつ総ビリルビンが ULN の 2 倍を上回るか，国際標準化比（INR）が 1.5 を上回った場合。
- ALT 又は AST が ULN の 3 倍を上回り，かつ関連する臨床症状又は好酸球増加症（5%を上回る）が確認された場合。

- ALT 又は AST が ULN の 5 倍を上回り，2 週間を超えて継続することが確認された場合。
- ALT 又は AST が ULN の 8 倍を上回った場合。

基準に該当した場合，治験薬以外の原因を検討し，必要に応じて医学的に管理した。
本項では，ウパダシチニブを投与した被験者の肝機能検査値の上昇について示す。また，表 2.7. - の定義を用いて特定した薬物性肝障害に関する有害事象を検討した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時の ALT 及び AST のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群が 6.3 U/L 及び 6.0 U/L，ウパダシチニブ 30 mg 併合群が 8.3 U L 及び 7.5 U/L，プラセボ併合群が–0.9 U/L 及び–0.8 U/L であった（ISS T 1 2 5 1 1 1）。
ウパダシチニブ併合群で認められた ALT，AST 又はビリルビン増加は，多くが Grade 2 であった（ISS T 1 2 5 1 1 1）。

プラセボ対照併合解析集団（投与 2 週時）で肝機能検査値上昇の基準に該当した被験者数を表 2.7. -62 に示す。
ALT 及び AST が ULN の 3 倍以上であった被験者の割合は，ウパダシチニブ 15 mg 併合群で 3.0%（19/635 名）及び 1. %（9/635 名），ウパダシチニブ 30 mg 併合群で .9%（31/638 名）及び 1.9%（12/637 名），プラセボ併合群で 2.7%（17/626 名）及び 2.2%（1 /626 名）であった。ALT 及び AST が ULN の 5 倍以上であった被験者の割合は，プラセボ併合群の ALT で 1. %（9/626 名）であったが，プラセボ併合群の AST，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群ではいずれも 1.0%以下であった。ALT が ULN の 10 倍以上であった被験者は，ウパダシチニブ 30 mg 併合群で 2 名，プラセボ併合群で 1 名認められた。また，AST が ULN の 10 倍以上であった被験者は，ウパダシチニブ 30 mg 併合群のみで 3 名認められた。ウパダシチニブ 15 mg 併合群では，ALT 又は AST が ULN の 10 倍以上であった被験者は認められなかった。AST が ULN の 20 倍以上であった被験者がウパダシチニブ 30 mg 併合群で 1 名認められたが，これは有害事象の食中毒の後に発現したものであった。
ウパダシチニブ 15 mg 併合群及び 30 mg 併合群では，プラセボ対照期間中に Hy’s Law の生化学検査値基準に該当した被験者はいなかった（ISS Figure 2.5 1.1.7）。

表 2.7.4-62. プラセボ対照併合解析集団（投与 24 週時）で肝機能検査値上昇の基準に該当した被験者数

Criteria	Placebo (N = 635) n/N_OBS (%) [SSA %]	Upadacitinib 15 mg QD (N = 640) n/N_OBS (%) [SSA %]	Upadacitinib 30 mg QD (N = 641) n/N_OBS (%) [SSA %]	Treatment Comparison (95% CI) [A] 15 mg QD - Placebo	Treatment Comparison (95% CI) [A] 30 mg QD - Placebo
ALT >= 3 x ULN	17/626 (2.7) [2.7]	19/635 (3.0) [3.0]	31/638 (4.9) [4.9]	0.3 (-1.6, 2.1)	2.2 (0.1, 4.3)
ALT >= 5 x ULN	9/626 (1.4) [1.4]	6/635 (0.9) [0.9]	6/638 (0.9) [0.9]	-0.5 (-1.7, 0.7)	-0.5 (-1.7, 0.7)
ALT >= 10 x ULN	1/626 (0.2) [0.2]	0/635	2/638 (0.3) [0.3]	-0.2 (-0.5, 0.2)	0.2 (-0.4, 0.7)
ALT >= 20 x ULN	0/626	0/635	0/638	0.0	0.0
AST >= 3 x ULN	14/626 (2.2) [2.2]	9/635 (1.4) [1.4]	12/637 (1.9) [1.9]	-0.8 (-2.3, 0.7)	-0.4 (-1.9, 1.2)
AST >= 5 x ULN	4/626 (0.6) [0.6]	2/635 (0.3) [0.3]	4/637 (0.6) [0.6]	-0.3 (-1.1, 0.4)	-0.0 (-0.9, 0.9)
AST >= 10 x ULN	0/626	0/635	3/637 (0.5) [0.5]	0.0	0.5 (-0.1, 1.0)
AST >= 20 x ULN	0/626	0/635	1/637 (0.2) [0.2]	0.0	0.2 (-0.2, 0.5)
TBL >= 2 x ULN	2/627 (0.3) [0.3]	3/635 (0.5) [0.5]	4/638 (0.6) [0.6]	0.2 (-0.5, 0.8)	0.3 (-0.4, 1.1)

Note: N OBS indicates the number of subjects with both baseline and post-baseline values up to Week 24 for the respective parameter.
SSA = Study size adjusted.
ULN = Upper limit of the normal range.
TBL = Total bilirubin.
[A] Study size adjusted risk difference between treatment groups.

Criteria	Placebo (N = 635) n/N OBS (%) SSA %]	Upadacitinib 15 mg QD (N = 640) n/N OBS (%) [SSA %]	Upadacitinib 30 mg QD N = 641) n/N OBS (%) [SSA %]	Treatment Comparison 95% CI) [A] 15 mg QD - Placebo	Treatment Comparison 95% CI) [A] 30 mg QD - Placebo
Alkaline phosphatase >= 1 5 x ULN	8/627 (1 3) [1 3]	4/635 0 6) 0 6]	8/638 1 3) [1 2]	-0 7 (-1 7, 0 4)	-0 0 (-1 3, 1 2)
ALT and/or AST >= 3 x ULN and concurrent TBL >= 1 5 x ULN	0/627	0/635	0/638	0 0	0 0
ALT and/or AST >= 3 x ULN and concurrent TBL >= 2 x ULN	0/627	0/635	0/638	0 0	0 0

Note N OBS indicates the number of subjects with both baseline and post-baseline values up to Week 24 for the respective parameter
SSA = Study size adjusted
ULN = Upper limit of the normal range
TBL = Total bilirubin
A] Study size adjusted risk difference between treatment groups

相互参照：ISS T 1 2 5 1 1 5 1

プラセボ対照併合解析集団（投与 2 週時）の薬物性肝障害の発現状況を表 2.7. .7-51 に示す。

プラセボ対照併合解析集団（投与 2 週時）の薬物性肝障害の発現割合は，ウパダシチニブ 15 mg 併合群で 6.7%（ 3/6 0 名），ウパダシチニブ 30 mg 併合群で 10.9%（70/6 1 名），プラセボ併合群で 3.0%（19/635 名）であった。発現した薬物性肝障害は，主に軽度又は中等度のトランスアミナーゼの上昇であった（表 2.7. .7-51 及び ISS Table 2. 1.1. .3.9）。非アルコール性脂肪性肝炎及び非アルコール性脂肪性肝疾患がプラセボ併合群で各 1 名（0.2%）に発現し，脂肪性肝炎がウパダシチニブ 15 mg 併合群で 2 名（0 3%）に発現した。重篤な薬物性肝障害は発現しなかった（ISS Table 2. 1.1. .2.7）。治験薬の投与中止に至った薬物性肝障害は，ウパダシチニブ 15 mg 併合群で 2 名（0.3%），ウパダシチニブ 30 mg 併合群で 6 名（0.9%），プラセボ併合群で 1 名（0.2%）に発現した（ISS Table 2. 1.1. . .9）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 以上の ALT 及び AST 増加は認められなかった（J-ISS T 1 2 5 1 1 1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，薬物性肝障害の発現割合は，ウパダシチニブ 15 mg 併合群で 17.6%（3/17 名），ウパダシチニブ 30 mg 併合群で 5.6%（1/18 名）であり，プラセボ併合群では発現しなかった（J-ISS Table 2. 1.1. .1.9 J）。

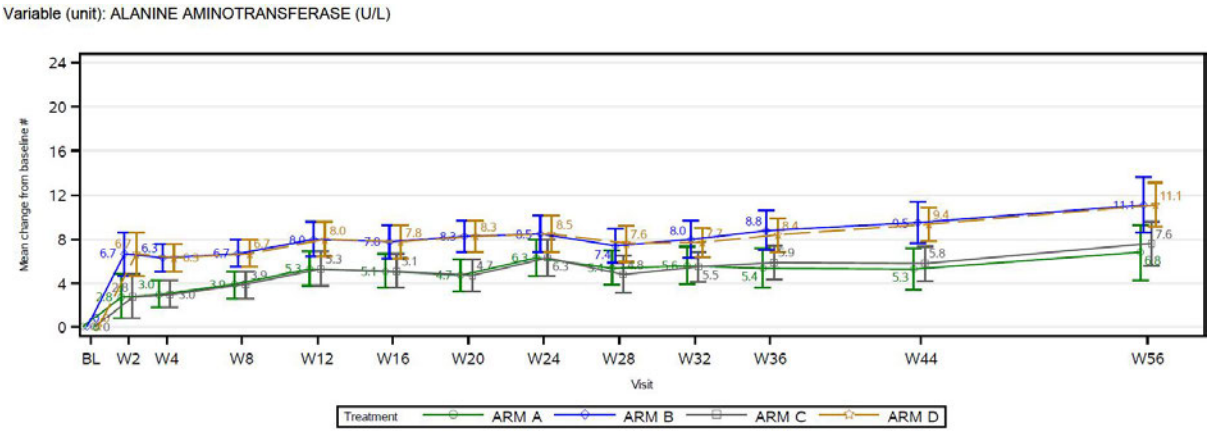
全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）では，投与 56 週時の ALT 及び AST のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 7.5 U/L 及び 6.2 U/L，全ウパダシチニブ 30 mg 併合群で 11 2 U/L 及び 8.9 U/L であった（ISS Table 2.5 1 2.1）。

全ウパダシチニブ併合解析集団（長期）での ALT 及び AST のベースラインからの平均変化量の推移を図 2.7. -5 に示す。

ALT 及び AST のベースラインからの平均変化量の増加は，投与 2 週時からプラトーに達し始めた。

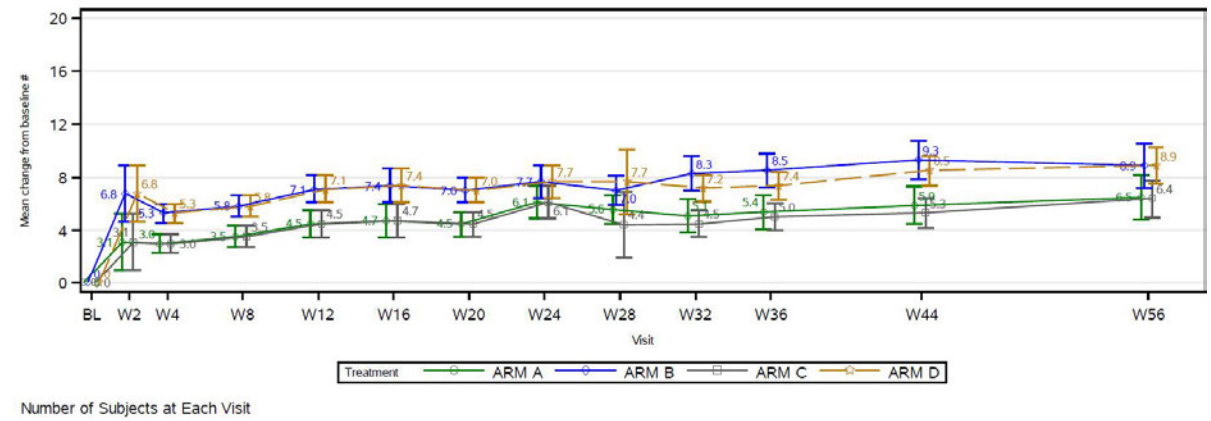
図 2 7. -5. 全ウパダシチニブ併合解析集団での ALT 及び AST のベースラインからの平均変化量の推移



Number of Subjects at Each Visit

ARM A	635	623	621	621	610	602	589	572	528	477	441	361	269
ARM B	638	628	629	620	613	601	588	571	530	466	432	359	269
ARM C	877	623	621	621	610	602	589	572	768	693	644	525	391
ARM D	896	628	629	620	613	601	588	571	783	695	648	530	396

ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo), ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo), ARM C = Any Upadacitinib 15 mg QD, ARM D = Any Upadacitinib 30 mg QD.
Note: Patients could be included in more than one treatment group.
Baseline mean includes subjects with non-missing baseline and at least one post-baseline value.
LS mean is based on ANCOVA model with treatment as a main factor, and baseline and study as covariates.



Number of Subjects at Each Visit

ARM A	635	621	618	619	610	602	588	568	528	475	438	360	268
ARM B	637	624	625	619	610	599	587	566	529	464	430	357	269
ARM C	877	621	618	619	610	602	588	568	767	690	641	524	389
ARM D	895	624	625	619	610	599	587	566	780	692	646	527	395

ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo), ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo), ARM C = Any Upadacitinib 15 mg QD, ARM D = Any Upadacitinib 30 mg QD.
Note: Patients could be included in more than one treatment group.
Baseline mean includes subjects with non-missing baseline and at least one post-baseline value.
LS mean is based on ANCOVA model with treatment as a main factor, and baseline and study as covariates.

相互参照：ISS Figure 2.5 1.2.6

全ウパダシチニブ併合解析集団（長期）で肝機能検査値上昇の基準に該当した被験者数を表 2.7. -63 に示す。

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ALT 及び AST が ULN の 3 倍以上であった被験者の割合は，全ウパダシチニブ 15 mg 併合群で 3.8%（33/878 名）及び 2 2%（19 878 名），全ウパダシチニブ 30 mg 併合群で 5.9%（53/896 名）及び 3. %（30/895 名）であった。ALT 及び AST が ULN の 5 倍以上であった被験者の割合は，いずれの投与群も 1 0%以下であった。ALT 及び AST が ULN の 10 倍以上であった被験者は，全ウパダシチニブ 30 mg 併合群でそれぞれ 3 名及び　名認められたが，全ウパダシチニブ 15 mg 併合群では認められなかった。全ウパダシチニブ 30 mg 併合群では，食中毒により，AST が ULN の 20 倍以上となった 1 名に加え，ALT 及び AST が ULN の 20 倍以上であった被験者が新たに 1 名認められた。本被験者は胃腸炎を発現していたが，ALT 及び AST は約 3 週間後に基準範囲内に回復した（ISS Table 2.5　1.2.5.2）。

表 2.7.4-63. 全ウパダシチニブ併合解析集団（長期）で肝機能検査値上昇の基準に該当した被験者数

Criteria	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) n/N OBS (%) [SSA %]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) n/N OBS (%) [SSA %]	Upadacitinib Any 15 mg QD (N = 907) n/N OBS (%) [SSA %]	Upadacitinib Any 30 mg QD (N = 920) n/N OBS (%) [SSA %]
ALT >= 3 x ULN	24/635 (3.8) [3.8]	42/638 (6.6) [6.6]	33/878 (3.8) [3.7]	53/896 (5.9) [5.9]
ALT >= 5 x ULN	8/635 (1.3) [1.3]	7/638 (1.1) [1.1]	9/878 (1.0) [1.0]	8/896 (0.9) [0.9]
ALT >= 10 x ULN	0/635	2/638 (0.3) [0.3]	0/878	3/896 (0.3) [0.3]
ALT >= 20 x ULN	0/635	0/638	0/878	1/896 (0.1) [0.1]
AST >= 3 x ULN	14/635 (2.2) [2.2]	21/637 (3.3) [3.3]	19/878 (2.2) [2.2]	30/895 (3.4) [3.4]
AST >= 5 x ULN	4/635 (0.6) [0.6]	8/637 (1.3) [1.3]	6/878 (0.7) [0.7]	9/895 (1.0) [1.0]
AST >= 10 x ULN	0/635	3/637 (0.5) [0.5]	0/878	4/895 (0.4) [0.5]

Note: Patients could be included in more than one treatment group.
N_OBS indicates the number of subjects with both baseline and post-baseline values for the respective parameter.
SSA = Study size adjusted.
ULN = Upper limit of the normal range.
TBL = Total bilirubin.

Criteria	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) n/N OBS (%) [SSA %]	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 641) n/N OBS (%) [SSA %]	Upadacitinib Any 15 mg QD (N = 907) n/N OBS (%) SSA %]	Upadacitinib Any 30 mg QD (N = 920) n/N OBS (%) SSA %]
AST >= 20 x ULN	0/635	1/637 0 2) 0 2]	0/878	2/895 (0 2) 0 2]
TBL >= 2 x ULN	3/635 0 5) 0 5]	5/638 0 8) 0 8]	6/878 0 7) 0 7]	6/896 (0 7) 0 7]
Alkaline phosphatase >= 1 5 x ULN	4/635 0 6) 0 6]	9/638 1 4) 1 4]	4/878 0 5) 0 5]	10/896 (1 1) 1 1]
ALT and/or AST >= 3 x ULN and concurrent TBL >= 1 5 x ULN	0/635	0/638	0/878	0/896
ALT and/or AST >= 3 x ULN and concurrent TBL >= 2 x ULN	0/635	0/638	0/878	0/896

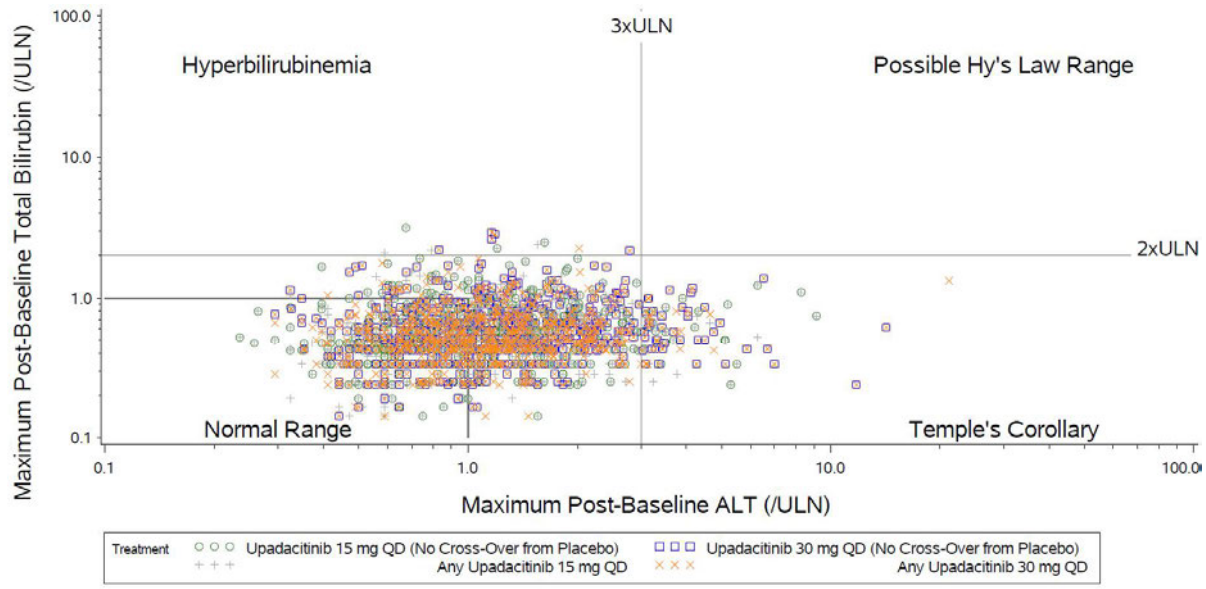
Note Patients could be included in more than one treatment group
N OBS indicates the number of subjects with both baseline and post-baseline values for the respective parameter
SSA = Study size adjusted
ULN = Upper limit of the normal range
TBL = Total bilirubin

相互参照：ISS Table 2.5 1.2.5.1

全ウパダシチニブ併合解析集団（長期）での総ビリルビンのベースライン後の最大値対 ALT のベースライン後の最大値の eDISH プロットを図 2.7. -6 に示す。

全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群では，Hy's Law の生化学検査値基準に該当した被験者はいなかった。

図 2 7. -6. 全ウパダシチニブ併合解析集団（長期）での総ビリルビンのベースライン後の最大値対 ALT のベースライン後の最大値の eDISH プロット



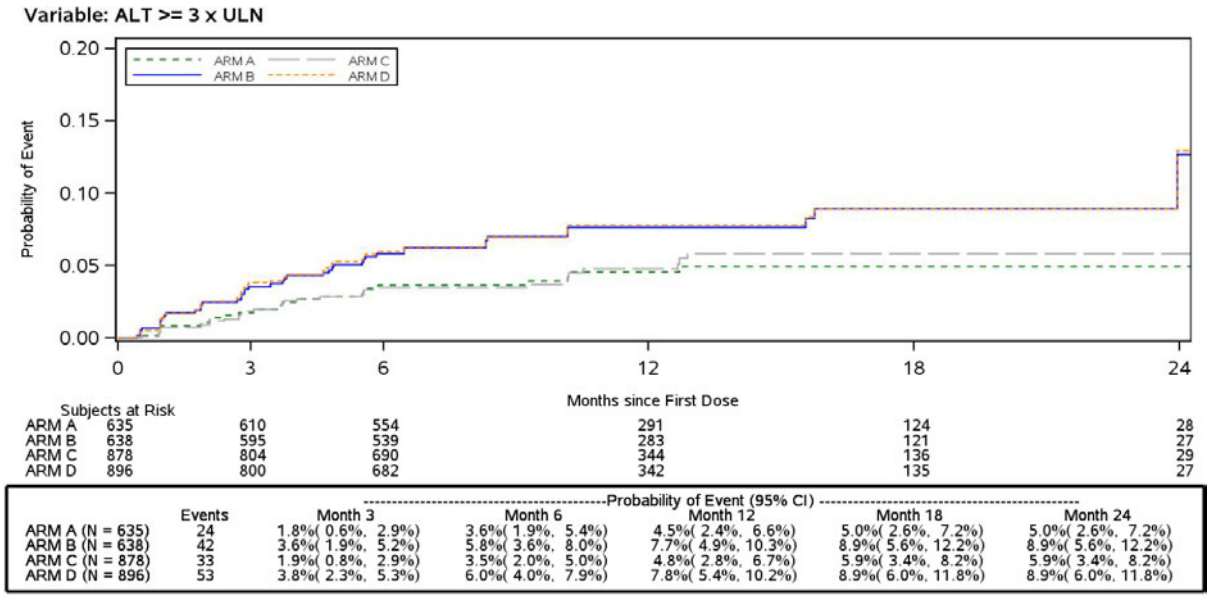
Note: Patients could be included in more than one treatment group.
ULN = Upper limit of the normal range.

相互参照：ISS Figure 2.5 1.2.8

全ウパダシチニブ併合解析集団（長期）で，ALT 及び AST が最初に ULN の 3 倍以上になるまでの時間の Kaplan-Meier プロットを図 2.7. -7 に示す。

全ウパダシチニブ併合解析集団（長期）では，ULN の 3 倍以上の ALT 又は AST が発現するリスクは一定で推移した。

図 2.7.4-7. 全ウパダシチニブ併合解析集団（長期）の ALT 及び AST が最初に ULN の 3 倍以上になるまでの時間の Kaplan-Meier プロット

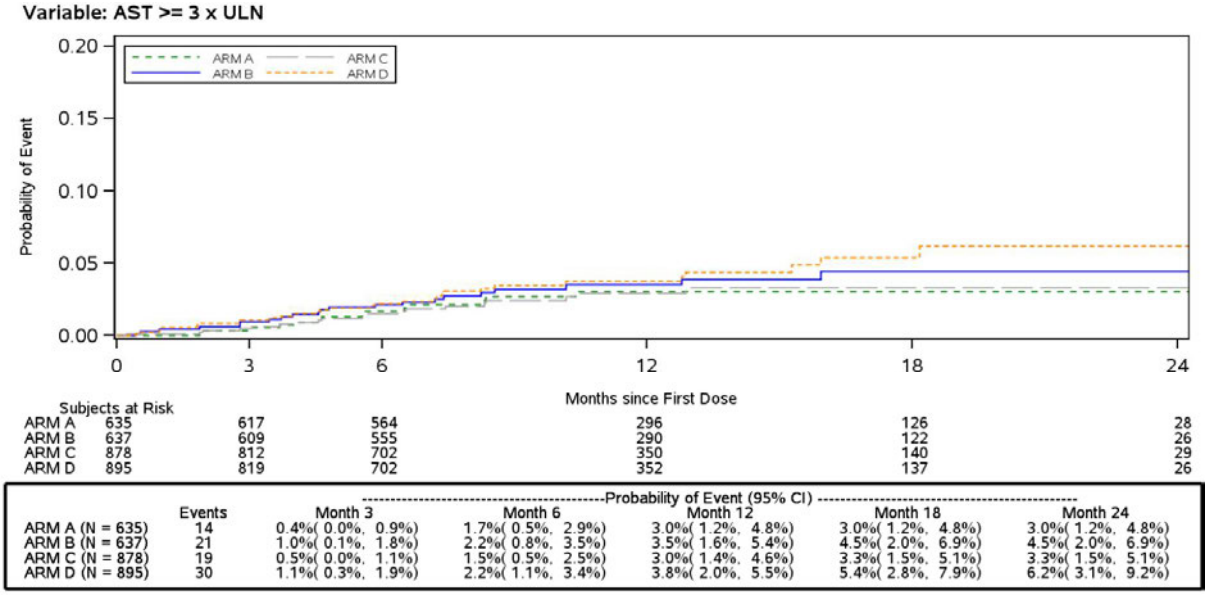


Subjects at Risk

ARM A	635	610	554	291	124	28
ARM B	638	595	539	283	121	27
ARM C	878	804	690	344	136	29
ARM D	896	800	682	342	135	27

	Events	Probability of Event (95% CI) Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 635)	24	1.8%(0.6%, 2.9%)	3.6%(1.9%, 5.4%)	4.5%(2.4%, 6.6%)	5.0%(2.6%, 7.2%)	5.0%(2.6%, 7.2%)
ARM B (N = 638)	42	3.6%(1.9%, 5.2%)	5.8%(3.6%, 8.0%)	7.7%(4.9%, 10.3%)	8.9%(5.6%, 12.2%)	8.9%(5.6%, 12.2%)
ARM C (N = 878)	33	1.9%(0.8%, 2.9%)	3.5%(2.0%, 5.0%)	4.8%(2.8%, 6.7%)	5.9%(3.4%, 8.2%)	5.9%(3.4%, 8.2%)
ARM D (N = 896)	53	3.8%(2.3%, 5.3%)	6.0%(4.0%, 7.9%)	7.8%(5.4%, 10.2%)	8.9%(6.0%, 11.8%)	8.9%(6.0%, 11.8%)

Note: Patients could be included in more than one treatment group.
N indicates the number of subjects with both baseline and post-baseline values for the respective parameter.
ULN = Upper limit of the normal range.
ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.



	Events	Probability of Event (95% CI) Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 635)	14	0.4%(0.0%, 0.9%)	1.7%(0.5%, 2.9%)	3.0%(1.2%, 4.8%)	3.0%(1.2%, 4.8%)	3.0%(1.2%, 4.8%)
ARM B (N = 637)	21	1.0%(0.1%, 1.8%)	2.2%(0.8%, 3.5%)	3.5%(1.6%, 5.4%)	4.5%(2.0%, 6.9%)	4.5%(2.0%, 6.9%)
ARM C (N = 878)	19	0.5%(0.0%, 1.1%)	1.5%(0.5%, 2.5%)	3.0%(1.4%, 4.6%)	3.3%(1.5%, 5.1%)	3.3%(1.5%, 5.1%)
ARM D (N = 895)	30	1.1%(0.3%, 1.9%)	2.2%(1.1%, 3.4%)	3.8%(2.0%, 5.5%)	5.4%(2.8%, 7.9%)	6.2%(3.1%, 9.2%)

Note: Patients could be included in more than one treatment group.
N indicates the number of subjects with both baseline and post-baseline values for the respective parameter.
ULN = Upper limit of the normal range.
ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.

相互参照：ISS Figure 2.5 1.2.7

全ウパダシチニブ併合解析集団（長期）の薬物性肝障害の発現状況（100 人年あたりの発現件数）を表 2.7. .7-52 に示す。

全ウパダシチニブ併合解析集団（長期）の薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 16.3 件/100 人年（133 件），全ウパダシチニブ 30 mg 併合群で 22.3 件/100 人年（183 件）であった。発現した薬物性肝障害は，主に軽度又は中等度のトランスアミナーゼの上昇であった（表 2.7. .7-52 及び ISS Table 2. 1.2. .3 9）。全ウパダシチニブ 30 mg 併合群の 1 名（被験者番号 [redacted]）で非重篤の薬物性肝障害（PT）が認められたが，治験責任医師により，治験薬と関連なしであり，レフルノミドによるものと判断された（ISS T 1 2 1 2 8 12）。重篤な薬物性肝障害は発現しなかった（ISS T 1 2 1 2 2 7）。治験薬の投与中止に至った薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.2 件 100 人年（2 件），全ウパダシチニブ 30 mg 併合群で 1.3 件 100 人年（11 件）であった（ISS Table 2. 1.2. . .9）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 以上の ALT 及び AST 増加は認められなかった（J-ISS Table 2.5 1.2. .1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 21.7 件 100 人年（5 件），全ウパダシチニブ 30 mg 併合群で 1 .2 件/100 人年（ 件）であった（J-ISS Table 2. 1 2. 1.9 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの Grade 3 の ALT 増加及び AST 増加の発現割合は，全ウパダシチニブ 15 mg 群で 1.2%（7/593 名）及び 0.5%（3/593 名），全ウパダシチニブ 30 mg 群で 1.0%（6/593 名）及び 0.8%（5/593 名），アダリムマブ群で 1.2%（5/ 27 名）及び 0.5%（2/ 26 名）であった（M15-572 試験 CSR W2 T 1 1 3 3 2 1 2）。Grade の ALT 増加及び AST 増加は，全ウパダシチニブ 30 mg 群でのみ発現した（ALT：0.2%［1/593 名］，AST：0.3%［2/593 名］）。

投与 2 週時データカットオフまでの薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 22 5 件/100 人年（118 件），全ウパダシチニブ 30 mg 群で 2 .3 件/100 人年（128 件），アダリムマブ群で 30.9 件/100 人年（122 件）であった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，投与 56 週時の ALT 及び AST のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 7.3 U/L 及び 6.3 U/L，全ウパダシチニブ 30 mg 併合群で 11.8 U/L 及び 9.3 U/L であった（ISS update T 1 2 5 1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）での ALT 及び AST のベースラインからの平均変化量の推移を ISS upda e Figure 2.5 5 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）で肝機能検査値上昇の基準に該当した被験者数を表 2.7. -6 に示す。

ALT 及び AST が ULN の 5 倍以上であった被験者の割合は，全ウパダシチニブ 15 mg 併合群で 1.2%（11/901 名）及び 0.7%（6/901 名），全ウパダシチニブ 30 mg 併合群で 1 6%（15/918 名）及び 1.7%（16/917 名）であった。ALT 及び AST が ULN の 10 倍以上であった被験者の割合は，全ウパダシチニブ 30 mg 併合群で 0. %（ /918 名）及び 0. %（ /917 名）であり，全ウパダシチニブ 15 mg 併合群では認められなかった。

表 2 7. -6 . 全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）で肝機能検査値上昇の基準に該当した被験者数

Criteria	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) n/N OBS (%) [SSA %]	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 641) n/N OBS (%) [SSA %]	Upadacitinib Any 15 mg QD (N = 907) n/N OBS (%) SSA %]	Upadacitinib Any 30 mg QD (N = 921) n/N OBS (%) SSA %]
ALT >= 3 x ULN	32/635 5 0) 5 0]	48/638 7 5) 7 5]	46/901 5 1) 5 1]	67/918 (7 3) 7 3]
ALT >= 5 x ULN	9/635 1 4) 1 4]	12/638 1 9) 1 9]	11/901 1 2) 1 2]	15/918 (1 6) 1 6]
ALT >= 10 x ULN	0/635	3/638 0 5) 0 5]	0/901	4/918 (0 4) 0 4]
ALT >= 20 x ULN	0/635	0/638	0/901	1/918 (0 1) 0 1]
AST >= 3 x ULN	15/635 2 4) 2 4]	32/637 5 0) 5 0]	24/901 2 7) 2 7]	44/917 (4 8) 4 8]
AST >= 5 x ULN	4/635 0 6) 0 6]	13/637 2 0) 2 0]	6/901 0 7) 0 7]	16/917 (1 7) 1 7]
AST >= 10 x ULN	0/635	3/637 0 5) 0 5]	0/901	4/917 (0 4) 0 4]

Note Patients could be included in more than one treatment group
N OBS indicates the number of subjects with both baseline and post-baseline values for the respective parameter
SSA = Study size adjusted
ULN = Upper limit of the normal range
TBL = Total bilirubin

Criteria	Upadacitinib 15 mg QD No Cross-Over from Placebo) N = 640) n/N OBS (%) [SSA %]	Upadacitinib 30 mg QD No Cross-Over from Placebo) (N = 641) n/N OBS (%) [SSA %]	Upadacitinib Any 15 mg QD (N = 907) n/N OBS (%) SSA %]	Upadacitinib Any 30 mg QD (N = 921) n/N OBS (%) SSA %]
AST >= 20 x ULN	0/635	1/637 0 2) 0 2]	0/901	2/917 (0 2) 0 2]
TBL >= 2 x ULN	3/635 0 5) 0 5]	6/638 0 9) 0 9]	6/901 0 7) 0 7]	7/918 (0 8) 0 8]
Alkaline phosphatase >= 1 5 x ULN	4/635 0 6) 0 6]	12/638 1 9) 1 9]	4/901 0 4) 0 4]	14/918 (1 5) 1 5]
ALT and/or AST >= 3 x ULN and concurrent TBL >= 1 5 x ULN	0/635	1/638 0 2) 0 2]	0/901	1/918 (0 1) 0 1]
ALT and/or AST >= 3 x ULN and concurrent TBL >= 2 x ULN	0/635	1/638 0 2) 0 2]	0/901	1/918 (0 1) 0 1]

Note Patients could be included in more than one treatment group
N OBS indicates the number of subjects with both baseline and post-baseline values for the respective parameter
SSA = Study size adjusted
ULN = Upper limit of the normal range
TBL = Total bilirubin

相互参照：ISS update Table 2 5 .1

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）での総ビリルビンのベースライン後の最大値対 AST のベースライン後の最大値の eDISH プロットを ISS update Figure 2.5 9 に示す。

全ウパダシチニブ 15 mg 併合群では，Hy's Law の生化学検査値基準に該当した被験者はいなかった。全ウパダシチニブ 30 mg 併合群では，1 名（被験者番号 [redacted]）が Hy's law の生化学検査値基準（AST 及びビリルビン値に基づく）に該当したが，メディカルレビューにより，AST 増加及び総ビリルビン増加の別の原因が特定されたことから，真の Hy's law とは判断されなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の薬物性肝障害の発現状況（100 人年あたりの発現件数）を表 2.7. .7-116 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 13.6 件/100 人年（169 件），全ウパダシチニブ 30 mg 併合群で 18.6 件/100 人年（23 件）であった。申請時データカットオフ以降に，新たに薬物性肝障害（PT）を発現した被験者が全ウパダシチニブ 30 mg 併合群で 2 名（3 件）認められた。このうち，1 名に 2 件発現した薬物性肝障害（1 件は重篤）は治験薬と関連ありと判断された（ISS upda e Table 2. 6.12）。重篤な薬物性肝障害は，全ウパダシチニブ 30 mg 併合群で 2 件（薬物性肝障害及び肝臓血管腫）発現した（ISS update Table 2. .2.7）。治験薬の投与中止に至った薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.2 件/100 人年（2 件），全ウパダシチニブ 30 mg 併合群で 1.0 件/100 人年（12 件）であった（ISS update Table 2. . .9）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 以上の ALT 及び AST 増加が全ウパダシチニブ 30 mg 併合群で各 1 名に認められた（J-ISS update Table 2.5 1.2. .1 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 1 .2 件/100 人年（5 件），全ウパダシチニブ 30 mg 併合群で 17 5 件/100 人年（7 件）であった（J-ISS update T 1 2 1 2 1 9 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 3 の ALT 増加及び AST 増加の発現割合は，全ウパダシチニブ 15 mg 群で 1.3%（8/613 名）及び 0.5%（3/613 名），全ウパダシチニブ 30 mg 群で 1.8%（11/611 名）及び 1.5%（9/611 名），アダリムマブ群で 1.9%（8/ 27 名）及び 0.7%（3/ 26 名）であった（ISS update Table 2.5 5. ）。Grade の ALT 増加及び AST 増加は，全ウパダシチニブ 30 mg 群でのみ発現した（ALT：0.2%［1 611 名］，AST：0.3%［2/611 名］）。

薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 18.5 件/100 人年（1 9 件），全ウパダシチニブ 30 mg 群で 19.6 件/100 人年（159 件），アダリムマブ群で 26.6 件/100 人年（1 6 件）であった（ISS update Table 2. 8.13）。

2.7. .2.1.5.1.7 消化管穿孔

	全体集団（SS）	日本人部分集団（J-ISS）
項目	Tab e	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合		
消化管穿孔	2. 1.1. 1 10	2. 1.1. 1 10 J
重篤な消化管穿孔	2. 1.1. .2.8	--
Grade 3 以上の消化管穿孔	2. 1.1. 3 10	--
治験薬の投与中止に至った消化管穿孔	2. 1.1. . 10	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数		
消化管穿孔	2. 1.2. 1 10 Update 2. .1.10	2. 1.2. 1 10 J Update 2. 1 2. .1.10 J
重篤な消化管穿孔	2. 1.2. .2.8 Update 2. 2.8	--
Grade 3 以上の消化管穿孔	2. 1.2. 3 10 Update 2. .3.10	--
治験薬の投与中止に至った消化管穿孔	2. 1.2. . 10 Update 2. . .10	--
消化管穿孔の一覧表		
プラセボ対照併合解析集団	2 1 1 8 13	--
全ウパダシチニブ併合解析集団	2 1 2 8 13 Update 2. 6.13	--

M15-572 試験及び M15-55 試験では，消化管穿孔（虫垂炎又は貫通性損傷を除く）若しくは憩室炎の既往歴を有する患者又は治験責任医師により消化管穿孔のリスクが高いと判断された患者は除外した。ただし，憩室炎を伴わない憩室症の既往歴を有する患者は除外しなかった。

消化管穿孔に関する有害事象は，表 2.7. - の定義を用いて特定し，そのうちメディカルレビューで判定された事象とした。消化管穿孔の判定は，臨床試験実施部門から独立した社内専門家が，消化管穿孔の可能性のある事象を事前に規定した定義に基づき盲検下で行った。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の消化管穿孔の発現状況を表 2.7. .7-53 に示す。

プラセボ対照併合解析集団（投与 2 週時）では，消化管穿孔は発現しなかった。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の消化管穿孔の発現状況（100 人年あたりの発現件数）を表 2.7. .7-5 に示す。

全ウパダシチニブ併合解析集団（長期）では，消化管穿孔は全ウパダシチニブ 15 mg 併合群で 1 件（0.1 件/100 人年）発現し，全ウパダシチニブ 30 mg 併合群では発現しなかった。全ウパダシチニブ 15 mg 併合群で発現した事象は穿孔性胃潰瘍であり，重篤で本事象により治験薬の投与が中止された（表 2.7. .7-2 ）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，消化管穿孔は発現しなかった（J-ISS Table 2. 1.2. .1.10 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでに消化管穿孔が全ウパダシチニブ 15 mg 群で 1 名に発現した（PT：穿孔性胃潰瘍）。全ウパダシチニブ 30 mg 群及びアダリムマブ群では，消化管穿孔は発現しなかった（M15-572 試験 CSR W2 Table 1 .3 1.1.2.2.2，Table 1 .3 2 8.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の消化管穿孔の発現状況（100 人年あたりの発現件数）を表 2.7. .7-117 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，消化管穿孔は，全ウパダシチニブ 15 mg 併合群で 1 件（0 1 件未満/100 人年）発現し，全ウパダシチニブ 30 mg 併合群では発現しなかった。全ウパダシチニブ 15 mg 併合群で発現した事象は申請時データカットオフまでに発現したものであり，新たに発現した消化管穿孔はなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，消化管穿孔は発現しなかった（J-ISS update Table 2. 1 2. 1.10 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）では，消化管穿孔が全ウパダシチニブ 15 mg 群で 1 名に発現し，全ウパダシチニブ 30 mg 群及びアダリムマブ群では発現しなかった（ISS update Table 2. 8.1 ）。

2.7. .2.1.5.1.8 貧血

	全体集団（ISS）		日本人部分集団（J-ISS）	
項目	Tab e	Figure	Table	F gure
プラセボ対照併合解析集団の発現被験者数及び発現割合				
貧血	2 1 1 1 11	--	2 1 1 1 11 J	--
重篤な貧血	2 1 1 2 9	--	--	--
Grade 3 以上の貧血	2. 1.1. 3 11	--	--	--
治験薬の投与中止に至った貧血	2. 1.1. . 11	--	--	--
全ウパダシチニブ併合解析集団の100 人年あたりの発現件数				
貧血	2. 1.2. 1 11 Update 2. .1 11	--	2. 1 2. .1.11 J Update 2. 1 2. .1.11 J	--
重篤な貧血	2. 1.2. .2.9 Update 2 2 9	--	--	--
Grade 3 以上の貧血	2 1 2 3 11 Update 2. .3 11	--	--	--
治験薬の投与中止に至った貧血	2. 1.2. . 11 Update 2. . 11	--	--	--
貧血の一覧表				
プラセボ対照併合解析集団	2. 1.1 8 1	--	--	--
全ウパダシチニブ併合解析集団	2. 1.2 8 1 Update 2. 6.1	--	--	--
臨床検査値のベースラインからの平均変化量				
プラセボ対照併合解析集団	2 5 1.1.1	--	2.5 1 1 1 J	--
全ウパダシチニブ併合解析集団	2 5 1.2.1 Update 2 5 1	--	2.5 1 2 1 J Update 2.5 1 2 1 J	--

項目	全体集団（ISS）		日本人部分集団（J-ISS）	
	Tab e	Figure	Table	F gure
臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数及び割合				
プラセボ対照併合解析集団	2 5 1.1.3.1	--	2.5 1 1 3.1 J	--
全ウパダシチニブ併合解析集団	2 5 1.2.3.1 Update 2.5 2 1	--	2.5 1 2 3.1 J Update 2.5 1 2 3.1 J	--
臨床的に意義があると判断した血液学的検査値の基準に該当した被験者の一覧表				
プラセボ対照併合解析集団	2 5 1.1.3.2	--	--	--
全ウパダシチニブ併合解析集団	2 5 1.2.3.2 Update 2.5 2 2	--	--	--
臨床検査値のベースラインからの平均変化量の推移				
全ウパダシチニブ併合解析集団	--	2 5 1.2.6 Update 2.5 5	--	2.5 1.2 6 J Update 2.5 1.2 6 J

M15-572 試験及び M15-55 試験では，スクリーニング時にヘモグロビン値が 10 g/dL（100 g/L）未満であった患者は除外した。治験実施計画書では，ヘモグロビン値が 8 g dL（80 g/L）未満又は特定の原因がなくベースラインから 3 g/dL（30 g/L）以上減少した場合，再検査で確認し，基準値又はベースライン値に回復するまで治験薬の投与を中断することとした。

本項では，ヘモグロビン値のベースラインからの平均変化量及び臨床的に意義があると判断したヘモグロビン値（CTCAE 基準の Grade 2 及び Grade 3 に該当）が認められた被験者数の結果を示す。なお，CTCAE 基準では Grade のヘモグロビン減少の定量的基準がないことから，臨床的に意義があると判断したヘモグロビン値については，Grade 2 及び Grade 3 のみを示した。また，表 2.7. - の定義を用いて特定した貧血に関する有害事象を検討した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時のヘモグロビン値のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群で–1 6 g L，ウパダシチニブ 30 mg 併合群で–3.6 g/L，プラセボ併合群で–0.2 g/L であった（ISS Table 2.5 1.1.1）。

プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断したヘモグロビン値の基準に該当した被験者数を表 2.7. -65 に示す。

プラセボ対照併合解析集団（投与 24 週時）での Grade 3 のヘモグロビン減少の発現割合は，ウパダシチニブ 30 mg 併合群で 0.5%（3/638 名）であり，ウパダシチニブ 15 mg 併合群及びプラセボ併合群では認められなかった。

表 2 7. -65. プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断したヘモグロビン値の基準に該当した被験者数

Variable (unit) Criteria	Placebo N = 635) n/N OBS (%) [SSA %]	---- Upadacitinib ----- 15 mg QD (N = 640) n/N OBS (%) SSA %]	30 mg QD (N = 641) n/N OBS (%) SSA %]	--Treatment Comparison (95% CI) A]-- 15 mg QD - Placebo	30 mg QD - Placebo
HEMOGLOBIN (G/L)					
GRADE 2 (80-<100)	12/627 (1 9) [1 9]	10/635 (1 6) 1 6]	19/638 3 0) 3 0]	-0 3 (-1 8, 1 1)	1 0 (-0 7, 2 7)
GRADE 3 (<80)	0/627	0/635	3/638 0 5) 0 5]	0 0	0 5 (-0 1, 1 0)

Note Toxicity grading scale is based on NCI Common Terminology Criteria version 4 03 Grade must also be more extreme than the baseline grade
N OBS indicates the number of subjects with both baseline and post-baseline values up to Week 24 for the respective parameter
SSA = Study size adjusted
A] Study size adjusted risk difference between treatment groups

相互参照：ISS T 1 2 5 1 1 3 1

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プラセボ対照併合解析集団（投与 2 週時）の貧血の発現状況を表 2.7. .7-55 に示す。

プラセボ対照併合解析集団（投与 2 週時）の貧血の発現割合は，ウパダシチニブ 15 mg 併合群で 1.1%（7/6 0 名），ウパダシチニブ 30 mg 併合群で 5.3%（3 /6 1 名），プラセボ併合群で 0.9%（6/635 名）であった。重篤な貧血は，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名（0 2%）に発現し，プラセボ併合群では発現しなかった（ISS Table 2. 1.1. .2 9）。治験薬の投与中止に至った貧血は，ウパダシチニブ 15 mg 併合群で 2 名（0.3%），ウパダシチニブ 30 mg 併合群で 3 名（0.5%）に発現し，プラセボ併合群では発現しなかった（ISS Table 2. 1.1. . .11）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 のヘモグロビン減少の発現割合は，ウパダシチニブ 30 mg 併合群で 11.1%（2/18 名）であり，ウパダシチニブ 15 mg 併合群及びプラセボ併合群では認められなかった（J-ISS T 1 2 5 1 1 3 1 J）。

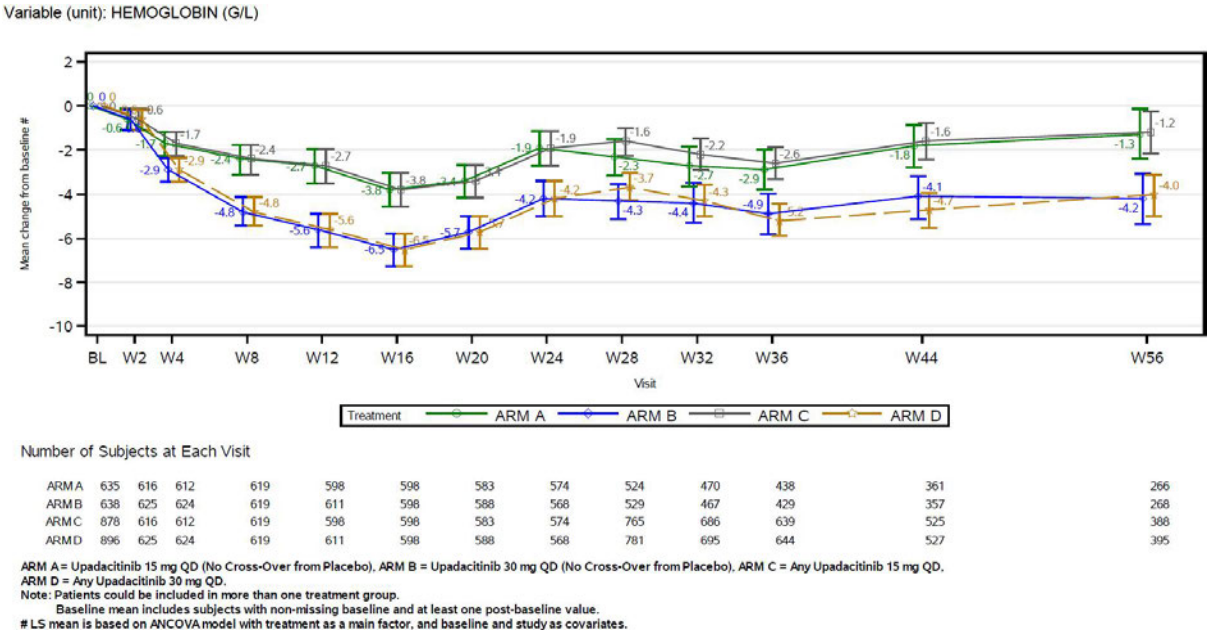
プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，貧血の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 11.1%（2/18 名）であり，プラセボ併合群では発現しなかった（J-ISS Table 2. 1.1. .1 11 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）でのヘモグロビン値のベースラインからの平均変化量の推移を図 2.7. -8 に示す。

全ウパダシチニブ併合解析集団（長期）のヘモグロビン値の平均変化量は，ウパダシチニブ 15 mg 及び 30 mg を投与開始後の最初の 16 週間で経時的に減少し，その後，ウパダシチニブの投与を継続しても投与 56 週時までおおむね一定で推移した。投与 56 週時のヘモグロビン値のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で–1.0 g/L，全ウパダシチニブ 30 mg 併合群で–3.7 g/L であった（ISS T 1 2 5 1 2 1）。

図 2 7. -8. 全ウパダシチニブ併合解析集団（長期）でのヘモグロビン値のベースラインからの平均変化量の推移



相互参照：ISS Figure 2.5 1.2.6

全ウパダシチニブ併合解析集団（長期）では，Grade 3 のヘモグロビン減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.1%（1/879 名），全ウパダシチニブ 30 mg 併合群で 0.7%（6/896 名）であった（ISS Table 2.5 1.2.3.1）。

全ウパダシチニブ併合解析集団（長期）で，Grade 3 のヘモグロビン減少が認められた全ウパダシチニブ 15 mg 併合群の 1 名及び 30 mg 併合群の 6 名では，1 名を除いて関連する別の要因が認められた。このうち 1 名（全ウパダシチニブ 30 mg 併合群，被験者番号 [redacted]）では，単位の誤りにより Grade 3 のヘモグロビン減少が報告された。しかし，単位を訂正した場合は正常値であった。別の要因が認められなかった 1 名（全ウパダシチニブ 30 mg 併合群）は，ウイルス性気道感染，リンパ球減少症及び正色素性貧血が認められ，これらの 3 事象等により，治験薬の投与を中止した。別の要因が認められた残りの 5 名のうち 1 名（全ウパダシチニブ 30 mg 併合群）は，尿路感染のために治験薬の投与を中止し，その後，卵巣癌及び子宮内膜癌と診断され，輸血を必要とする手術を受けた。本被験者では，治験薬の投与中止から約 20 日後に Grade 3 のヘモグロビン減少が認められた。他の 1 名（全ウパダシチニブ 30 mg 併合群）は小腸潰瘍により治験薬の投与を中止し，残りの 2 名（全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 1 名）は，それぞれ上部消化管出血及び出血性十二指腸潰瘍を発現した。全ウパダシチニブ 30 mg 併合群の 1 名（被験者番号 [redacted] は，ニューモシスチス・イロベチイ肺炎，播種性血管内凝固，脳梗塞及び十二指腸潰瘍を発現後に汎血球減少症により死亡した（詳細は 2.7. .2.1.2 項を参照）。

全ウパダシチニブ併合解析集団（長期）の貧血の発現状況（100 人年あたりの発現件数）を表 2.7. .7-56 に示す。

全ウパダシチニブ併合解析集団（長期）の貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.8 件/100 人年（23 件），全ウパダシチニブ 30 mg 併合群で 6.9 件 100 人年（57 件）であった。重篤な貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0 1 件 100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 0. 件 100 人年（3 件）であった（ISS Table 2. 1.2. .2.9）。治験薬の投与中止に至った貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群のいずれも 0. 件/100 人年（3 件）であった（ISS Table 2. 1.2. . .11）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 のヘモグロビン減少の発現割合は，全ウパダシチニブ 30 mg 併合群で 11.5%（3/26 名）であり，全ウパダシチニブ 15 mg 併合群では認められなかった（J-ISS T 1 2 5 1 2 3 1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で .3 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 7 1 件/100 人年（2 件）であった（J-ISS Table 2. 1.2. .1.11 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの Grade 3 のヘモグロビン減少の発現割合は，全ウパダシチニブ 15 mg 群で 0.2%（1/59 名），全ウパダシチニブ 30 mg 群で 0.3%（2/593 名），アダリムマブ群で 0.5%（2/ 27 名）であった（M15-572 試験 CSR W2 Table 1 3 .3 1.1.2）。

投与 2 週時データカットオフまでの貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 2.9 件/100 人年（15 件），全ウパダシチニブ 30 mg 群で 7.2 件/100 人年（38 件），アダリムマブ群で 1 5 件/100 人年（6 件）であった（M15-572 試験 CSR W2 T 1 1 3 1 1 2 2 2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）のヘモグロビン値のベースラインからの平均変化量の推移を ISS update Figure 2 5 5 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）のヘモグロビン値のベースラインからの平均変化量は，申請時データカットオフと同様に，最初の 16 週間で経時的に減少し，その後，ウパダシチニブの投与を継続してもおおむね一定で推移した。投与 56 週時のヘモグロビン値のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で–0 9 g/L，全ウパダシチニブ 30 mg 併合群で–3.6 g/L であった（ISS upda e Table 2.5 1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の Grade 3 のヘモグロビン減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.2%（2/901 名），全ウパダシチニブ 30 mg 併合群で 0.5%（5/918 名）であった（ISS update Table 2.5 2.1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の貧血の発現状況（100 人年あたりの発現件数）を表 2.7. .7-118 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.2 件 100 人年（28 件），全ウパダシチニブ 30 mg 併合群で 5 6 件/100 人年（70 件）であった。重篤及び治験薬の投与中止に至った貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.1 件未満/100 人年（1 件）及び 0.2 件/100 人年（3 件），全ウパダシチニブ 30 mg 併合群で 0.2 件/100 人年（3 件）及び 0.2 件/100 人年（3 件）であり，申請時データカットオフ以降に新たに発現した事象はなかった（ISS update T 1 2 2 9，ISS update T 1 2 11）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 のヘモグロビン減少の発現割合は，全ウパダシチニブ 30 mg 併合群で 11.5%（3/26 名）であり，全ウパダシチニブ 15 mg 併合群では認められなかった（J-ISS update Table 2.5 1.2.3.1 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2 8 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 7.5 件/100 人年（3 件）であった（J-ISS update Table 2. 1.2. .1.11 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 3 のヘモグロビン減少の発現割合は，全ウパダシチニブ 15 mg 群で 0.2%（1/613 名），全ウパダシチニブ 30 mg 群で 0.2%（1/611 名），アダリムマブ群で 0 5%（2/ 27 名）であった（ISS update Table 2.5 5 2）。

貧血の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 2. 件/100 人年（19 件），全ウパダシチニブ 30 mg 群で 5.8 件/100 人年（ 7 件），アダリムマブ群で 1.6 件/100 人年（9 件）であった（ISS upda e Table 2. 8.15）。

2.7. .2.1.5.1.9 好中球減少症

項目	全体集団 (ISS)		日本人部分集団 (J-ISS)	
	Tab e	Figure	Table	Figure
プラセボ対照併合解析集団の発現被験者数及び発現割合				
好中球減少症	2. 1.1. 1.12	--	2. 1.1. 1 12 J	--
重篤な好中球減少症	2. 1.1. 2.10	--	--	--
Grade 3 以上の好中球減少症	2. 1.1. 3.12	--	--	--
治験薬の投与中止に至った好中球減少症	2. 1.1. . .12	--	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数				
好中球減少症	2. 1.2. 1.12 Upda e 2. 1 12	--	2. 1.2. 1 12 J Update 2. 1.2. 1 12 J	--
重篤な好中球減少症	2. 1.2. 2.10 Upda e 2. 2 10	--	--	--
Grade 3 以上の好中球減少症	2. 1.2. 3.12 Upda e 2. 3 12	--	--	--
治験薬の投与中止に至った好中球減少症	2. 1.2. . .12 Upda e 2. . 12	--	--	--
好中球減少症の一覧表				
プラセボ対照併合解析集団	2 1 1 8 15	--	--	--
全ウパダシチニブ併合解析集団	2 1 2 8 15 Upda e 2. 6.15	--	--	--
臨床検査値のベースラインからの平均変化量				
プラセボ対照併合解析集団	2.5 1.1.1	--	2.5 1.1.1 J	--
全ウパダシチニブ併合解析集団	2.5 1.2.1 Update 2 5 1	--	2.5 1.2.1 J Update 2.5 1.2.1 J	--
臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数及び割合				
プラセボ対照併合解析集団	2.5 1.1.3.1	--	2 5 1.1.3.1 J	--
全ウパダシチニブ併合解析集団	2.5 1.2.3.1 Update 2.5 2.1	--	2 5 1.2.3.1 J Update 2 5 1 2 3 1 J	--

	全体集団 (ISS)		日本人部分集団 (J-ISS)	
項目	Tab e	Figure	Table	Figure
臨床的に意義があると判断した血液学的検査値の基準に該当した被験者の一覧表				
プラセボ対照併合解析集団	2.5 1.1.3.2	--	--	--
全ウパダシチニブ併合解析集団	2.5 1.2.3.2 Update 2.5 2.2	--	--	--
臨床検査値のベースラインからの平均変化量の推移				
全ウパダシチニブ併合解析集団	-	2.5 1.2 6 Update 2 5 5	--	2.5 1.2.6 J Update 2 5 1 2 6 J

M15-572 試験及び M15-55 試験では，スクリーニング時に好中球数（絶対値）が 1500/μL 未満であった患者は除外した。治験実施計画書では，再検査で好中球数が 1000/μL 未満であった場合，基準値又はベースライン値に回復するまで治験薬の投与を中断することとした。再検査で確認された好中球数が 500/μL 未満の場合，治験薬の投与を中止することとした。

本項では，好中球数のベースラインからの平均変化量及び臨床的に意義があると判断した好中球数減少（CTCAE 基準の Grade 2 から に該当）が認められた被験者数の結果を示す。また，表 2.7. - の定義を用いて特定した好中球減少症に関する有害事象を検討した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時の好中球数のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群で–0. 2 × 10^9/L，ウパダシチニブ 30 mg 併合群で–0.758 × 10^9 L，プラセボ併合群で 0.018 × 10^9/L であった（ISS Table 2.5 1.1.1）。

プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断した好中球数の基準に該当した被験者数を表 2.7. -66 に示す。

プラセボ対照併合解析集団（投与 2 週時）で認められた好中球数減少の多くは，Grade 2 であった。Grade 3 の好中球数減少の発現割合は，ウパダシチニブ 15 mg 併合群で 0.6%（ /635 名），ウパダシチニブ 30 mg 併合群で 1.6%（10/638 名），プラセボ併合群で 0 3%（2/627 名）であった。Grade の好中球数減少は認められなかった。

表 2 7. -66. プラセボ対照併合解析集団（投与 2 週時）の臨床的に意義があると判断した好中球数の基準に該当した被験者数

Variable (unit) Criteria	Placebo N = 635) n/N OBS (%) [SSA %]	---- Upadacitinib ----- 15 mg QD (N = 640) n/N OBS (%) SSA %]	30 mg QD (N = 641) n/N OBS (%) SSA %]	--Treatment Comparison (95% CI) A]-- 15 mg QD - Placebo	30 mg QD - Placebo
NEUTROPHILS (10^9/L)					
GRADE 2 (1 0-<1 5)	5/627 (0 8) [0 8]	20/635 (3 1) 3 2]	43/638 6 7) 6 7]	2 4 (0 8, 3 9)	6 0 (3 9, 8 0)
GRADE 3 (0 5-<1 0)	2/627 (0 3) [0 3]	4/635 (0 6) 0 6]	10/638 1 6) 1 6]	0 3 (-0 4, 1 1)	1 2 (0 2, 2 3)
GRADE 4 (<0 5)	0/627	0/635	0/638	0 0	0 0
>= GRADE 3	2/627 (0 3) [0 3]	4/635 (0 6) 0 6]	10/638 1 6) 1 6]	0 3 (-0 4, 1 1)	1 2 (0 2, 2 3)

Note Toxicity grading scale is based on NCI Common Terminology Criteria version 4 03 Grade must also be more extreme than the baseline grade
N OBS indicates the number of subjects with both baseline and post-baseline values up to Week 24 for the respective parameter
SSA = Study size adjusted
A] Study size adjusted risk difference between treatment groups

相互参照：ISS Table 2.5 1.1.3.1

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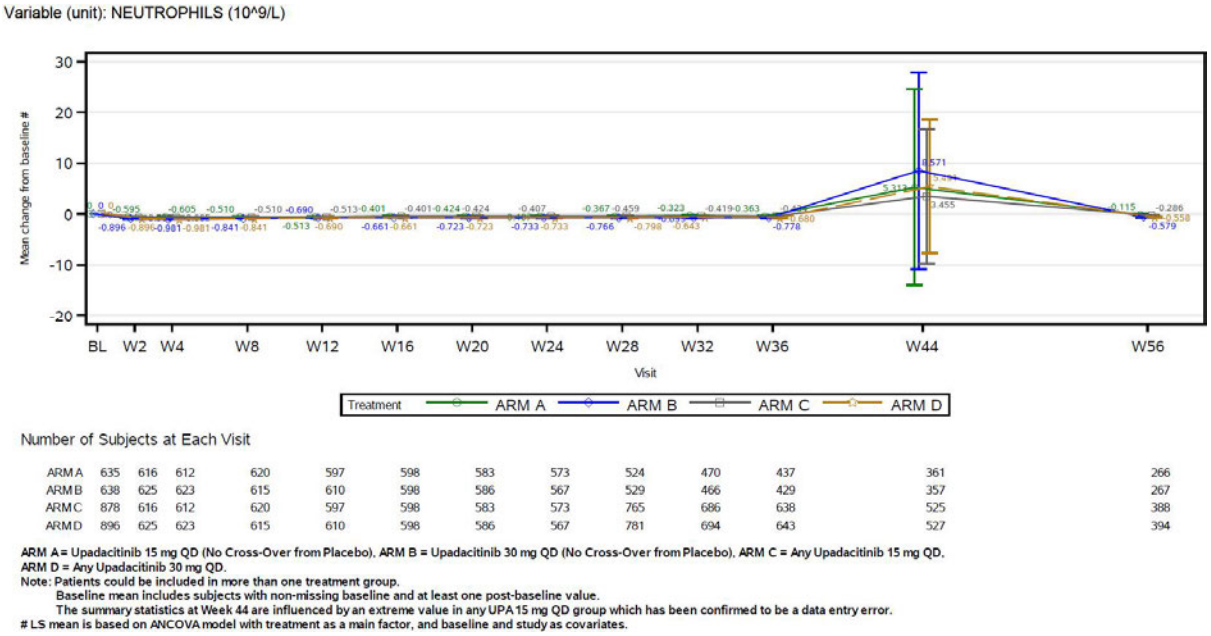
プラセボ対照併合解析集団（投与 2 週時）の好中球減少症の発現状況を表 2.7. .7-57 に示す。
プラセボ対照併合解析集団（投与 2 週時）の好中球減少症の発現割合は，ウパダシチニブ 15 mg 併合群で 0.9%（6/6 0 名），ウパダシチニブ 30 mg 併合群で 2%（27 6 1 名），プラセボ併合群で 0.3%（2/635 名）であった。重篤な好中球減少症及び治験薬の投与中止に至った好中球減少症は発現しなかった（ISS Table 2. 1.1. .2 10 及び Table 2. 1 1. . .12）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 の好中球数減少の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 5.6%（1/18 名）であり，プラセボ併合群では認められなかった。Grade の好中球数減少は認められなかった（J-ISS Table 2.5 1 1.3 1 J）。
プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，好中球減少症の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 5.6%（1/18 名）であり，プラセボ併合群では発現しなかった（J-ISS T 1 2 1 1 1 12 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）での好中球数のベースラインからの平均変化量の推移を図 2.7. -9 に示す。
全ウパダシチニブ併合解析集団（長期）で，投与期間中に認められた好中球数の平均変化量の若干の減少は，ウパダシチニブの投与に伴うものであると考えられた。ただし，投与 週時に認められた好中球数の平均変化量の増加は，データ入力ミスによるものであった。このデータ入力ミスは，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の各 1 名に認められた。いずれも好中球数の検査値に小数点がなく，全ウパダシチニブ 15 mg 併合群の被験者（被験者番号 [redacted] では 2.7 5 × 10^9/L が 27 5 × 10^9/L として，全ウパダシチニブ 30 mg 併合群の被験者（被験者番号 [redacted]）では .070 × 10^9 L が 070 × 10^9/L として入力された。投与 56 週時の好中球数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で–0 360 × 10^9/L，全ウパダシチニブ 30 mg 併合群で–0.531 × 10^9/L であった（ISS Table 2.5 1.2.1）。

図 2 7. -9. 全ウパダシチニブ併合解析集団（長期）での好中球数のベースラインからの平均変化量の推移



相互参照：ISS Figure 2.5 1.2.6

全ウパダシチニブ併合解析集団（長期）での Grade 3 の好中球数減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.7%（6/879 名），全ウパダシチニブ 30 mg 併合群で 1.7%（15/896 名）であった（ISS Table 2.5 1.2.3.1）。これらの値の多くは一過性であり，申請時データカットオフまでの投与期間中に治験薬の投与を中止することなく，ベースライン値又は基準範囲内に回復した（ISS Table 2.5 1.2.3.2）。Grade の好中球数減少は認められなかった。

全ウパダシチニブ併合解析集団（長期）の好中球減少症の発現状況（100 人年あたりの発現件数）を表 2.7. .7-58 に示す。
全ウパダシチニブ併合解析集団（長期）の好中球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.2 件/100 人年（18 件），全ウパダシチニブ 30 mg 併合群で 6.2 件/100 人年（51 件）であった。重篤な好中球減少症及び治験薬の投与中止に至った好中球減少症は発現しなかった（ISS Table 2. 1.2. .2 10 及び Table 2. 1 2. . .12）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 の好中球数減少の発現割合は，全ウパダシチニブ 15 mg 併合群で .3%（1/23 名），全ウパダシチニブ 30 mg 併合群で 3.8%（1/26 名）であった。Grade の好中球数減少は認められなかった（J-ISS Table 2.5 1.2.3.1 J）。

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全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，好中球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で .3 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 3.6 件/100 人年（1 件）であった（J-ISS Table 2. 1 2. 1.12 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの Grade 3 の好中球数減少の発現割合は，全ウパダシチニブ 15 mg 群で 0 5%（3/59 名），全ウパダシチニブ 30 mg 群で 1.7%（10/593 名），アダリムマブ群で 0.5%（2/ 26 名）であった。Grade の好中球数減少は認められなかった（M15-572 試験 CSR W2 T 1 1 3 3 1 1 2）。

投与 2 週時データカットオフまでの好中球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 2.7 件/100 人年（1 件），全ウパダシチニブ 30 mg 群で 7. 件 100 人年（39 件），アダリムマブ群で 5 8 件/100 人年（23 件）であった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の好中球数のベースラインからの平均変化量の推移を ISS update Figure 2 5 5 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，好中球数のベースラインからの平均変化量で投与 週時まで若干の減少が認められた。投与 週時の好中球数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 6.739 × 10^9/L，全ウパダシチニブ 30 mg 併合群で–0.867 × 10^9/L であった（ISS update T 1 2 5 1）。データ入力ミスにより，投与 週時から 116 週時までに外れ値があったことから，投与 週時以降のデータの解釈は困難であった。この外れ値を報告した治験実施医療機関にクエリーを出したが，COVID-19 パンデミックにより，20[redacted]年[redacted]月[redacted]日データカットオフまでに修正することができなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の Grade 3 の好中球数減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.8%（7/901 名），全ウパダシチニブ 30 mg 併合群で 2.1%（19/918 名）であった（ISS update Table 2.5 2.1）。Grade の好中球数減少は認められなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の好中球減少症の発現状況（100 人年あたりの発現件数）を表 2.7. .7-119 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の好中球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 1 8 件/100 人年（22 件），全ウパダシチニブ 30 mg 併合群で 5.1 件/100 人年（6 件）であった。重篤な好中球減少症及び治験薬

の投与中止に至った好中球減少症は発現しなかった（ISS update Table 2. .2.10 及び Table 2. . .12）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 の好中球数減少の発現割合は，全ウパダシチニブ 15 mg 併合群で .3%（1/23 名），全ウパダシチニブ 30 mg 併合群で 3 8%（1/26 名）であった。Grade の好中球数減少は認められなかった（J-ISS update Table 2 5 1.2 3.1 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，好中球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.8 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 2.5 件/100 人年（1 件）であった（J-ISS update Table 2. 1.2. .1.12 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 3 の好中球数減少の発現割合は，全ウパダシチニブ 15 mg 群で 0.7%（ /613 名），全ウパダシチニブ 30 mg 群で 2.1%（13/611 名），アダリムマブ群で 0.7%（3/ 26 名）であった。Grade の好中球数減少は認められなかった（ISS update Table 2.5 5 2）。

好中球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 2 2 件/100 人年（18 件），全ウパダシチニブ 30 mg 群で 6.3 件/100 人年（51 件），アダリムマブ群で .7 件/100 人年（26 件）であった（ISS update Table 2. 8.16）。

2.7. .2.1.5.1.10 リンパ球減少症

	全体集団（ISS）		日本人部分集団（J-ISS）	
項目	Tab e	Figure	Table	Figure
プラセボ対照併合解析集団の発現被験者数及び発現割合				
リンパ球減少症	2 1 1 1 13	--	2 1 1 1 13 J	--
重篤なリンパ球減少症	2 1 1 2 11	--	--	--
Grade 3 以上のリンパ球減少症	2 1 1 3 13	--	--	--
治験薬の投与中止に至ったリンパ球減少症	2. 1.1. . .13	--	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数				
リンパ球減少症	2 1 2 1 13 Upda e 2. 1 13	--	2 1 2 1 13 J Update 2. 1.2. 1 13 J	--

項目	全体集団 (ISS)		日本人部分集団 (J-ISS)	
	Tab e	Figure	Table	Figure
重篤なリンパ球減少症	2. 1.2. 2.11 Upda e 2. 2 11	--	--	--
Grade 3 以上のリンパ球減少症	2. 1.2. 3.13 Upda e 2 3 13	--	--	--
治験薬の投与中止に至ったリンパ球減少症	2 1 2 13 Upda e 2. . 13	--	--	--
リンパ球減少症の一覧表				
プラセボ対照併合解析集団	2. 1.1 8 16	--	--	--
全ウパダシチニブ併合解析集団	2. 1.2 8 16 Upda e 2 6 16	--	--	--
臨床検査値のベースラインからの平均変化量				
プラセボ対照併合解析集団	2.5 1.1.1	--	2.5 1.1.1 J	--
全ウパダシチニブ併合解析集団	2.5 1.2.1 Update 2.5 1	--	2.5 1.2.1 J Update 2.5 1.2.1 J	--
臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数及び割合				
プラセボ対照併合解析集団	2.5 1.1.3.1	--	2 5 1.1.3.1 J	--
全ウパダシチニブ併合解析集団	2.5 1.2.3.1 Update 2.5 2.1	--	2 5 1.2.3.1 J Update 2 5 1.2.3.1 J	--
臨床的に意義があると判断した血液学的検査値の基準に該当した被験者の一覧表				
プラセボ対照併合解析集団	2.5 1.1.3.2	--	--	--
全ウパダシチニブ併合解析集団	2.5 1.2.3.2 Update 2 5 2 2	--	--	--
臨床検査値のベースラインからの平均変化量の推移				
全ウパダシチニブ併合解析集団	-	2 5 1 2 6 Update 2 5 5	--	2 5 1 2 6 J Update 2.5 1.2.6 J

M15-572 試験及び M15-55 試験では，スクリーニング時にリンパ球数（絶対値）が 800/μL 未満であった患者は除外した。治験実施計画書では，再検査でリンパ球数が 500/μL 未満であった場合，基準値又はベースライン値に回復するまで治験薬の投与を中断することとした。

本項では，リンパ球数のベースラインからの平均変化量及び臨床的に意義があると判断したリンパ球数減少（CTCAE 基準の Grade 2 から に該当）が認められた被験者数の結果を示す。また，表 2.7. - の定義を用いて特定したリンパ球減少症に関する有害事象を検討した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時のリンパ球数の平均変化量は，ウパダシチニブ 15 mg 併合群で 0.035 × 10^9/L，ウパダシチニブ 30 mg 併合群で 0.075 × 10^9/L，プラセボ併合群で 0 0 2 × 10^9/L であった（ISS Table 2.5 1.1.1）。

プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断したリンパ球数の基準に該当した被験者数を表 2.7. -67 に示す。

プラセボ対照併合解析集団（投与 2 週時）で認められたリンパ球数減少の多くは，Grade 2 であった。Grade 3 のリンパ球数減少の発現割合は，ウパダシチニブ 15 mg 併合群で 0 8%（5/635 名），ウパダシチニブ 30 mg 併合群で 1.7%（11/638 名），プラセボ併合群で 0 2%（1/627 名）であった。Grade のリンパ球数減少は認められなかった。

表 2 7. -67. プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断したリンパ球数の基準に該当した被験者数

Variable (unit) Criteria	Placebo N = 635) n/N OBS (%) [SSA %]	---- Upadacitinib ----- 15 mg QD (N = 640) n/N OBS (%) SSA %]	30 mg QD (N = 641) n/N OBS (%) SSA %]	--Treatment Comparison (95% CI) A]-- 15 mg QD - Placebo	30 mg QD - Placebo
LYMPHOCYTES (10^9/L)					
GRADE 2 (0 5-<0 8)	24/627 (3 8) [3 8]	32/635 (5 0) 5 0]	54/638 8 5) 8 5]	1 2 (-1 1, 3 5)	4 6 (2 0, 7 3)
GRADE 3 (0 2-<0 5)	1/627 (0 2) [0 2]	5/635 (0 8) 0 8]	11/638 1 7) 1 7]	0 6 (-0 1, 1 4)	1 6 (0 5, 2 6)
GRADE 4 (<0 2)	0/627	0/635	0/638	0 0	0 0
>= GRADE 3	1/627 (0 2) [0 2]	5/635 (0 8) 0 8]	11/638 1 7) 1 7]	0 6 (-0 1, 1 4)	1 6 (0 5, 2 6)

Note Toxicity grading scale is based on NCI Common Terminology Criteria version 4 03 Grade must also be more extreme than the baseline grade
N OBS indicates the number of subjects with both baseline and post-baseline values up to Week 24 for the respective parameter
SSA = Study size adjusted
A] Study size adjusted risk difference between treatment groups

相互参照：ISS Table 2 5 1.1.3.1

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プラセボ対照併合解析集団（投与 2 週時）のリンパ球減少症の発現状況を表 2.7. .7-59 に示す。

プラセボ対照併合解析集団（投与 2 週時）のリンパ球減少症の発現割合は，ウパダシチニブ 15 mg 併合群で 1.3%（8/6 0 名），ウパダシチニブ 30 mg 併合群で 2.7%（17 6 1 名），プラセボ併合群で 0.8%（5/635 名）であった。重篤なリンパ球減少症は発現しなかった（ISS Table 2. 1.1. .2.11）。治験薬の投与中止に至ったリンパ球減少症は，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 2 名（0.3%）に発現し，プラセボ併合群では発現しなかった（ISS Table 2. 1.1. . .13）。Grade 3 以上のリンパ球減少症は，ウパダシチニブ 15 mg 併合群で 名（0.6%），ウパダシチニブ 30 mg 併合群で 2 名（0.3%），プラセボ併合群で 1 名（0.2%）に発現した（ISS Table 2. 1.1. .3.13）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 以上のリンパ球数減少は認められなかった（J-ISS T 1 2 5 1 1 3 1 J）。

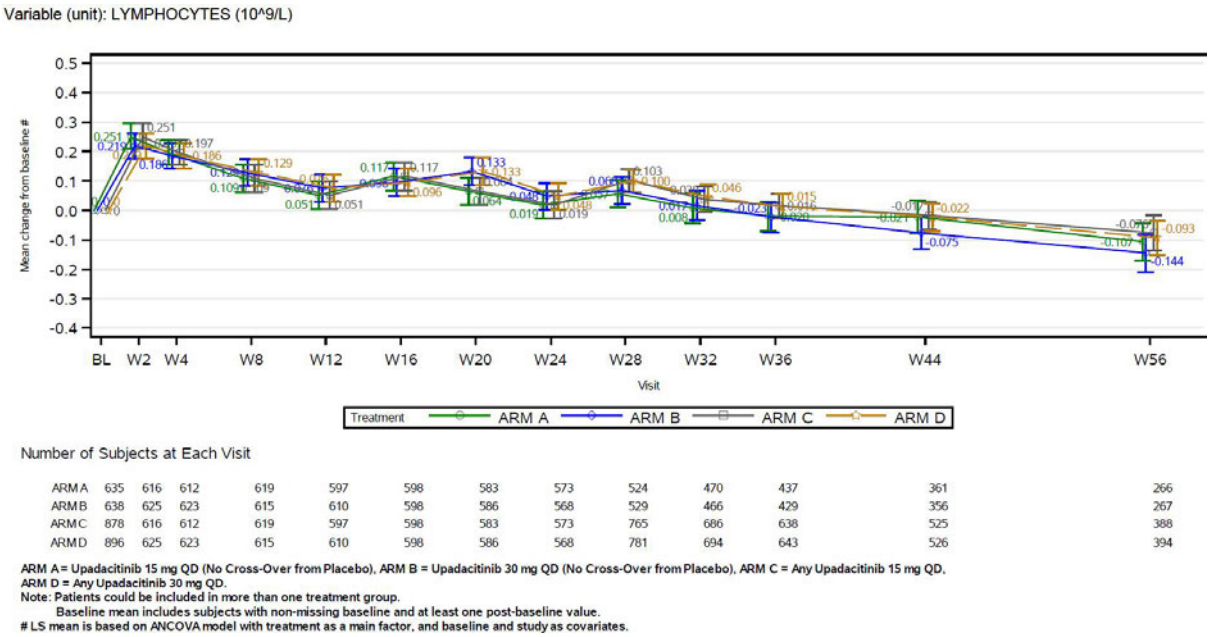
プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，リンパ球減少症の発現割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 11.1%（2/18 名）であり，プラセボ併合群では発現しなかった（J-ISS Table 2. 1.1. .1.13 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）でのリンパ球数のベースラインからの平均変化量の推移を図 2.7. -10 に示す。

全ウパダシチニブ併合解析集団（長期）では，リンパ球数のベースラインからの平均変化量で投与 36 週時まで若干の増加が認められ，その後，ベースライン付近又はベースラインをやや下回る値まで減少した。投与 56 週時のリンパ球数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で–0.077 × 10^9/L，全ウパダシチニブ 30 mg 併合群で–0.08 × 10^9/L であった（ISS T 1 2 5 1 2 1）。

図 2 7. -10. 全ウパダシチニブ併合解析集団（長期）でのリンパ球数のベースラインからの平均変化量の推移



相互参照：ISS Figure 2.5 1.2.6

全ウパダシチニブ併合解析集団（長期）での Grade 3 のリンパ球数減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 1.3%（11/879 名），全ウパダシチニブ 30 mg 併合群で 2.7%（2 /896 名）であった（ISS Table 2.5 1.2.3.1）。Grade 3 のリンパ球数減少の多くは一過性であり，その後 90 日以内に回復した。Grade のリンパ球数減少は，全ウパダシチニブ 30 mg 併合群で 1 名（0.1%）に認められた。本被験者（被験者番号 [redacted]）は MTX を併用しており，85 日目から Grade 2 のリンパ球数減少が発現したが，Grade のリンパ球数減少は 5 0 日目のみであった（ISS Table 2 5 1.2 3.2）。本被験者は非重篤の上気道の炎症及び重篤な気管支炎を発現したため，治験薬の投与は中断された。抗生物質を投与し，MTX を減量した。リンパ球数は，申請時データカットオフまでに Grade 2 に改善した。

全ウパダシチニブ併合解析集団（長期）のリンパ球減少症の発現状況（100 人年あたりの発現件数）を表 2.7. .7-60 に示す。

全ウパダシチニブ併合解析集団（長期）のリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2. 件/100 人年（20 件），全ウパダシチニブ 30 mg 併合群で 3.5 件/100 人年（29 件）であった。重篤なリンパ球減少症は発現しなかった（ISS T 1 2 1 2 2 11）。治験薬の投与中止に至ったリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.2 件/100 人年（2 件），全ウパダシチニブ 30 mg 併合群

で 0. 件/100 人年（3 件）であった（ISS Table 2. 1.2. . 13）。Grade 3 以上のリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.6 件/100 人年（5 件），全ウパダシチニブ 30 mg 併合群で 0.5 件 100 人年（ 件）であった（ISS Table 2. 1.2. .3 13）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 及び Grade のリンパ球数減少の発現割合は，全ウパダシチニブ 30 mg 併合群で 7.7%（2/26 名）及び 3.8%（1/26 名）であり，全ウパダシチニブ 15 mg 併合群では Grade 3 以上のリンパ球数減少は認められなかった（J-ISS Table 2.5 1.2.3.1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，リンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で .3 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 1 .2 件/100 人年（ 件）であった（J-ISS Table 2. 1 2. 1.13 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの Grade 2 のリンパ球数減少の発現割合は，全ウパダシチニブ 15 mg 群で 7.1%（ 2/59 名），全ウパダシチニブ 30 mg 群で 8.8%（52/593 名），アダリムマブ群で 0.9%（ / 26 名）であった。アダリムマブ群で Grade 3 以上のリンパ球数減少は認められなかった（M15-572 試験 CSR W2 Table 1 .3 3.1 1.2）。

投与 2 週時データカットオフまでのリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 3 2 件/100 人年（17 件），全ウパダシチニブ 30 mg 群で .8 件/100 人年（25 件），アダリムマブ群で 0 3 件 100 人年（1 件）であった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）のリンパ球数のベースラインからの平均変化量の推移を ISS update Figure 2.5 5 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，リンパ球数のベースラインからの平均変化量で投与 36 週時まで若干の増加が認められた。投与 36 週時のリンパ球数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 0.078 × 10^9/L，全ウパダシチニブ 30 mg 併合群で 0.065 × 10^9/L であった（ISS update Table 2 5 1）。データ入力ミ

[redacted]

[redacted] 2 及び Grade 3 のリンパ球数減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 9.5%（86/901 名）及び 1.7%（15/901 名），全ウパダシチニブ 30 mg 併合群で 12.3%（113/918 名）及び 3.2%（29/918 名）で

あった（ISS update Table 2 5 2.1）。Grade のリンパ球数減少は，全ウパダシチニブ 30 mg 併合群で 1 名（0.1%）に認められたが，申請時データカットオフ以降に新たに発現したものはなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）のリンパ球減少症の発現状況（100 人年あたりの発現件数）を表 2.7. .7-120 に示す。
全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）のリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.2 件/100 人年（27 件），全ウパダシチニブ 30 mg 併合群で 3.0 件/100 人年（38 件）であった。重篤なリンパ球減少症は発現しなかった（ISS update Table 2. .2.11）。治験薬の投与中止に至ったリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0 1 件未満/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 0 2 件/100 人年（3 件）であった（ISS update T 1 2 13）。Grade 3 以上のリンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群とも 0. 件/100 人年（5 件）であった（ISS update Table 2. 3.13）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 及び Grade のリンパ球数減少の発現割合は，全ウパダシチニブ 30 mg 併合群で 7.7%（2/26 名）及び 3.8%（1/26 名）であり，全ウパダシチニブ 15 mg 併合群では Grade 3 以上のリンパ球数減少は認められなかった（J-ISS update Table 2.5 1.2.3.1 J）。
全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，リンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 2.8 件 100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 10 0 件/100 人年（ 件）であった（J-ISS update Table 2. 1.2. .1.13 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 2 のリンパ球数減少の発現割合は，全ウパダシチニブ 15 mg 群で 9.3%（57/613 名），全ウパダシチニブ 30 mg 群で 10.6%（65/611 名），アダリムマブ群で 1.2%（5/ 26 名）であった。アダリムマブ群では，Grade 3 以上のリンパ球数減少は認められなかった（ISS update Table 2.5 5.2）。
リンパ球減少症の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 3.0 件/100 人年（2 件），全ウパダシチニブ 30 mg 群で 3. 件/100 人年（28 件），アダリムマブ群で 0.2 件/100 人年（1 件）であった（ISS update Table 2. 8.17）。

2.7. .2.1.5.1.11 クレアチンホスホキナーゼ（CPK）増加

項目	全体集団（SS） Tab e	日本人部分集団（J-ISS） Table
プラセボ対照併合解析集団の発現被験者数及び発現割合		
CPK 増加	2. 1.1. 1 15	2. 1.1. 1 15 J
重篤な CPK 増加	2. 1.1. 2 13	--
Grade 3 以上の CPK 増加	2. 1.1. 3 15	--
治験薬の投与中止に至った CPK 増加	2. 1.1. . 15	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数		
CPK 増加	2 1 2 1 15 Update 2. .1.15	2 1 2 1 15 J Update 2. 1 2. .1.15 J
重篤な CPK 増加	2. 1.2. 2 13 Update 2 2 13	--
Grade 3 以上の CPK 増加	2 1 2 3 15 Update 2. .3.15	--
治験薬の投与中止に至った CPK 増加	2. 1.2. . 15 Update 2 15	--
CPK 増加の一覧表		
プラセボ対照併合解析集団	2. 1.1 8 18	--
全ウパダシチニブ併合解析集団	2. 1.2 8 18 Update 2. 6.18	--
臨床検査値のベースラインからの平均変化量		
プラセボ対照併合解析集団	2 5 1 1 1	2 5 1 1 1 J
全ウパダシチニブ併合解析集団	2 5 1 2 1 Update 2.5 1	2 5 1 2 1 J Update 2.5 1 2 1 J
臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数及び割合		
プラセボ対照併合解析集団	2 5 1.1. .1	2 5 1.1. .1 J
全ウパダシチニブ併合解析集団	2 5 1.2. .1 Update 2 5 3 1	2 5 1.2. .1 J Update 2 5 1 2 1 J

M15-572 試験及び M15-55 試験の治験実施計画書では，CPK 値が ULN の 倍以上であり，筋炎又は横紋筋融解症を示唆する症状を伴う場合，治験薬の投与を中断することとした。

本項では，CPK のベースラインからの平均変化量及び臨床的に意義があると判断した CPK 増加（CTCAE 基準の Grade 2 から に該当）が認められた被験者数の結果を示す。また，表 2.7. - の定義を用いて特定した CPK 増加に関する有害事象を検討した。

2 2

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時の CPK 値のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群で 111.1 U/L，ウパダシチニブ 30 mg 併合群で 139.5 U L，プラセボ併合群で 7.5 U L であった（ISS Table 2 5 1.1 1）。

プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断した CPK 値の基準に該当した被験者数を表 2.7. -68 に示す。

プラセボ対照併合解析集団（投与 2 週時）での Grade 3 及び Grade の CPK 増加 臨床検査値）の発現割合は，ウパダシチニブ 15 mg 併合群で 1.1%（7/635 名）及び 0.3%（2 635 名），ウパダシチニブ 30 mg 併合群で 1.9%（12/638 名）及び 0.6%（ /638 名），プラセボ併合群で 0.6%（ /627 名）及び 0.5%（3 627 名）であった。

表 2 7. -68. プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断した CPK 値の基準に該当した被験者数

Variable (unit) Criteria	Placebo N = 635) n/N OBS (%) [SSA %]	---- Upadacitinib ----- 15 mg QD (N = 640) n/N OBS (%) SSA %]	30 mg QD (N = 641) n/N OBS (%) SSA %]	--Treatment Comparison (95% CI) A]-- 15 mg QD - Placebo	30 mg QD - Placebo
CREATINE KINASE (U/L)					
GRADE 2 (>2 5-5 0 xULN)	8/627 (1 3) [1 3]	35/635 (5 5) 5 5]	48/638 7 5) 7 5]	4 2 (2 3, 6 2)	6 2 (4 0, 8 5)
GRADE 3 (>5 0-10 0 xULN)	4/627 (0 6) [0 6]	7/635 (1 1) 1 1]	12/638 1 9) 1 9]	0 5 (-0 6, 1 5)	1 2 (0 0, 2 5)
GRADE 4 (>10 0 xULN)	3/627 (0 5) [0 5]	2/635 (0 3) 0 3]	4/638 0 6) 0 6]	-0 2 (-0 9, 0 5)	0 2 (-0 7, 1 0)
>= GRADE 3	7/627 (1 1) [1 1]	9/635 (1 4) 1 4]	16/638 2 5) 2 5]	0 3 (-0 9, 1 5)	1 4 (-0 1, 2 9)

Note Toxicity grading scale is based on NCI Common Terminology Criteria version 4 03 Grade must also be more extreme than the baseline grade
N OBS indicates the number of subjects with both baseline and post-baseline values up to Week 24 for the respective parameter
xULN = Times upper limit of the normal range
SSA = Study size adjusted
A] Study size adjusted risk difference between treatment groups

相互参照：ISS Table 2.5 1.1. .1

プラセボ対照併合解析集団（投与 2 週時）の CPK 増加（有害事象）の発現状況を表 2.7. .7-61 に示す。
プラセボ対照併合解析集団（投与 2 週時）の CPK 増加（有害事象）の発現割合は，ウパダシチニブ 15 mg 併合群で 6.6%（ 2/6 0 名），ウパダシチニブ 30 mg 併合群で 8.3%（53/6 1 名），プラセボ併合群で 1.6%（10/635 名）であった。重篤な CPK 増加は発現しなかった（ISS Table 2. 1.1. .2.13）。治験薬の投与中止に至った CPK 増加は，ウパダシチニブ 30 mg 併合群で 2 名（0 3%），プラセボ併合群で 1 名（0 2%）に発現し，ウパダシチニブ 15 mg 併合群では発現しなかった（ISS Table 2. 1 1. . .15）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 以上の CPK 増加臨床検査値）は認められなかった（J-ISS Table 2.5 1.1. .1 J）。
プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，CPK 増加（有害事象）の発現割合は，ウパダシチニブ 15 mg 併合群で 11 8%（2/17 名），ウパダシチニブ 30 mg 併合群で 16.7%（3/18 名）であり，プラセボ併合群では発現しなかった（J-ISS Table 2. 1.1. .1.15 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）では，投与 56 週時の CPK 値のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 82.6 U L，全ウパダシチニブ 30 mg 併合群で 137.9 U L であった（ISS Table 2 5 1.2 1）。

全ウパダシチニブ併合解析集団（長期）での Grade 3 及び Grade の CPK 増加（臨床検査値）の発現割合は，全ウパダシチニブ 15 mg 併合群で 1.6%（1 /878 名）及び 0.8%（7/878 名），全ウパダシチニブ 30 mg 併合群で 1.9%（17/896 名）及び 1 0%（9/896 名）であった（ISS T 1 2 5 1 2 1）。

全ウパダシチニブ併合解析集団（長期）の CPK 増加（有害事象）の発現状況（100 人年あたりの発現件数）を表 2.7. .7-62 に示す。
全ウパダシチニブ併合解析集団（長期）の CPK 増加（有害事象）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 11. 件/100 人年（93 件），全ウパダシチニブ 30 mg 併合群で 17.0 件/100 人年（1 0 件）であった。重篤な CPK 増加は発現しなかった（ISS Table 2. 1.2. .2.13）。治験薬の投与中止に至った CPK 増加の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.1 件/100 人年（1 件），全ウパダシチニブ 30 mg 併合群で 0.2 件/100 人年（2 件）であった（ISS Table 2. 1.2. . .15）。横紋筋融解症は発現しなかった。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 の CPK 増加（臨床検査値）の発現割合は，全ウパダシチニブ 15 mg 併合群で .3%（1/23 名）であり，全ウパダシチ

ニブ 30 mg 併合群では認められなかった。Grade の CPK 増加 臨床検査値）は認められなかった（J-ISS Table 2 5 1.2. .1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，CPK 増加（有害事象）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 17. 件/100 人年（ 件），全ウパダシチニブ 30 mg 併合群で 17.8 件 100 人年（5 件）であった（J-ISS Table 2. 1 2. 1.15 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの Grade 3 及び Grade の CPK 増加 臨床検査値）の発現割合は，全ウパダシチニブ 15 mg 群で 1.9%（11/593 名）及び 0.7%（ /593 名），全ウパダシチニブ 30 mg 群で 2 0%（12 593 名）及び 1.5%（9 593 名），アダリムマブ群で 0.5%（2/ 26 名）及び 0.7%（3/ 26 名）であった（M15-572 試験 CSR W2 Table 1 .3 3.2 1.2）。

投与 2 週時データカットオフまでの CPK 増加（有害事象）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 1 .3 件/100 人年（75 件），全ウパダシチニブ 30 mg 群で 21 5 件/100 人年（113 件），アダリムマブ群で 9 1 件/100 人年（36 件）であった（M15-572 試験 CSR W2 Table 1 .3 1.1.2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，投与 56 週時の CPK 値のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 8 .1 U/L，全ウパダシチニブ 30 mg 併合群で 138.0 U/L であった（ISS update T 1 2 5 1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 3 及び Grade の CPK 増加（臨床検査値）の発現割合は，全ウパダシチニブ 15 mg 併合群で 2.0%（18/901 名）及び 0 9%（8/901 名），全ウパダシチニブ 30 mg 併合群で 2.8%（26/918 名）及び 1.6%（15/918 名）であった（ISS update Table 2.5 3.1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の CPK 増加（有害事象）の発現状況（100 人年あたりの発現件数）を表 2.7. .7-121 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の CPK 増加（有害事象）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 9.1 件/100 人年（113 件），全ウパダシチニブ 30 mg 併合群で 13.8 件/100 人年（173 件）であった。重篤な CPK 増加は発現しなかった（ISS update Table 2. .2.13）。治験薬の投与中止に至った CPK 増加の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.2 件/100 人年（2 件），全ウパダシチニブ 30 mg 併合群で 0.3 件/100 人年（ 件）であった（ISS update Table 2. . .15）。横紋筋融解症は発現しなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 の CPK 増加（臨床検査値）の発現割合は，全ウパダシチニブ 15 mg 併合群で .3%（1/23 名）であり，全ウパダシチニブ 30 mg 併合群では認められなかった（J-ISS update Table 2.5 1.2. .1 J）。Grade の CPK 増加 臨床検査値）の発現割合は，全ウパダシチニブ 30 mg 併合群で 3.8%（1/26 名）であり，全ウパダシチニブ 15 mg 併合群では認められなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，CPK 増加（有害事象）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 11. 件/100 人年（ 件），全ウパダシチニブ 30 mg 併合群で 15.0 件 100 人年（6 件）であった（J-ISS update Table 2. 1 2. 1.15 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 3 及び Grade の CPK 増加 臨床検査値）の発現割合は，全ウパダシチニブ 15 mg 群で 2.1%（13/613 名）及び 0.8%（5/613 名），全ウパダシチニブ 30 mg 群で 3. %（21 611 名）及び 2.0%（12/611 名），アダリムマブ群で 0.7%（3/ 26 名）及び 0.9%（ / 26 名）であった（ISS update Table 2.5 5. ）。

CPK 増加（有害事象）の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 11.3 件/100 人年（91 件），全ウパダシチニブ 30 mg 群で 16.7 件/100 人年（136 件），アダリムマブ群で 7 5 件/100 人年（ 1 件）であった（ISS update Table 2. 8.19）。

2.7. .2.1.5.1.12 腎機能障害

	全体集団（ISS）		日本人部分集団（J-ISS）	
項目	Tab e	Figure	Table	Figure
プラセボ対照併合解析集団の発現被験者数及び発現割合				
腎機能障害	2. 1.1. 1.16	--	2. 1.1. 1 16 J	--
重篤な腎機能障害	2 1 1 2 1	--	--	--
Grade 3 以上の腎機能障害	2 1 1 3 16	--	--	--
治験薬の投与中止に至った腎機能障害	2 1 1 16	--	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現件数				
腎機能障害	2. 1.2. 1.16 Upda e 2. 1 16	--	2. 1.2. 1 16 J Update 2. 1.2. 1 16 J	--
重篤な腎機能障害	2. 1.2. 2.1 Upda e 2. 2 1	--	--	--

	全体集団 (ISS)		日本人部分集団 (J-ISS)	
項目	Tab e	Figure	Table	Figure
Grade 3 以上の腎機能障害	2. 1.2. 3.16 Upda e 2. 3 16	--	--	--
治験薬の投与中止に至った腎機能障害	2. 1.2. . .16 Upda e 2 16	--	--	--
腎機能障害の一覧表				
プラセボ対照併合解析集団	2. 1.1 8 19	--	--	--
全ウパダシチニブ併合解析集団	2. 1.2 8 19 Upda e 2. 6.19	--	--	--
臨床検査値のベースラインからの平均変化量				
プラセボ対照併合解析集団	2.5 1.1.1	--	2.5 1.1.1 J	--
全ウパダシチニブ併合解析集団	2.5 1.2.1 Update 2.5 1	--	2.5 1.2.1 J Update 2.5 1.2.1 J	--
臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数及び割合				
プラセボ対照併合解析集団	2 5 1 1 1	--	2 5 1 1 1 J	--
全ウパダシチニブ併合解析集団	2 5 1 2 1 Update 2.5 3.1	--	2 5 1 2 1 J Update 2 5 1.2. .1 J	--
臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者の一覧表				
プラセボ対照併合解析集団	2.5 1.1. .2	--	--	--
全ウパダシチニブ併合解析集団	2.5 1.2. .2 Update 2.5 3.2	--	--	--
臨床検査値のベースラインからの平均変化量の推移				
全ウパダシチニブ併合解析集団	-	2.5 1.2 6 Update 2 5 5	--	2.5 1.2.6 J Update 2 5 1 2 6 J

M15-572 試験及び M15-55 試験では，スクリーニング時に糸球体濾過率が 0 mL/min/1.73 m^2 未満の患者は除外した。治験実施計画書では，再検査でクレアチニン値がベースライン値の 1.5

倍を上回り，かつ ULN を上回った場合，又はクレアチニン値が 2 mg dL 以上であった場合，基準値又はベースライン値に回復するまで治験薬の投与を中断することとした。

本項では，クレアチニン値のベースラインからの平均変化量及び臨床的に意義があると判断したクレアチニン増加（CTCAE 基準の Grade 2 から に該当）が認められた被験者数の結果を示す。また，表 2.7. - の定義を用いて特定した腎機能障害に関する有害事象を検討した。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時のクレアチニン値のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群で .7 µmol L，ウパダシチニブ 30 mg 併合群で 6.0 µmol/L，プラセボ併合群で 1.8 µmol/L であった（ISS Table 2 5 1.1.1）。

プラセボ対照併合解析集団（投与 2 週時）で臨床的に意義があると判断した血液生化学検査値（クレアチニン値を含む）の基準に該当した被験者数を表 2.7. .7-63 に示す。

プラセボ対照併合解析集団（投与 2 週時）での Grade 3 のクレアチニン増加の発現割合は，ウパダシチニブ 30 mg 併合群で 0.2%（1/638 名）であり，ウパダシチニブ 15 mg 併合群及びプラセボ併合群では発現しなかった。このウパダシチニブ 30 mg 併合群の 1 名（被験者番号 [redacted] で認められた Grade 3 のクレアチニン増加は 57 日目に発現し，72 日目にベースライン値付近に回復した（ISS Table 2.5 1.1. .2）。Grade のクレアチニン増加は認められなかった。

プラセボ対照併合解析集団（投与 2 週時）の腎機能障害の発現状況を表 2.7. .7-6 に示す。

プラセボ対照併合解析集団（投与 2 週時）の腎機能障害の発現割合は，ウパダシチニブ 30 mg 併合群で 0.2%（1/6 1 名），プラセボ併合群で 0.3%（2/635 名）であり，ウパダシチニブ 15 mg 併合群では発現しなかった。内訳は，ウパダシチニブ 30 mg 併合群では急性腎障害（1 名），プラセボ併合群では急性腎障害（2 名）及び腎不全（1 名）であった（1 名が腎不全及び急性腎障害を発現）。重篤な腎機能障害は，ウパダシチニブ 30 mg 併合群及びプラセボ併合群で各 1 名（0.2%）に発現した（ISS T 1 2 1 1 2 1 ）。内訳は，いずれも急性腎障害であった。治験薬の投与中止に至った腎機能障害は発現しなかった（ISS Table 2. 1.1. . 16）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 以上のクレアチニン増加は認められなかった（J-ISS Table 2.5 1 1. 1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，腎機能障害は発現しなかった（J-ISS Table 2. 1.1. .1.16 J）。

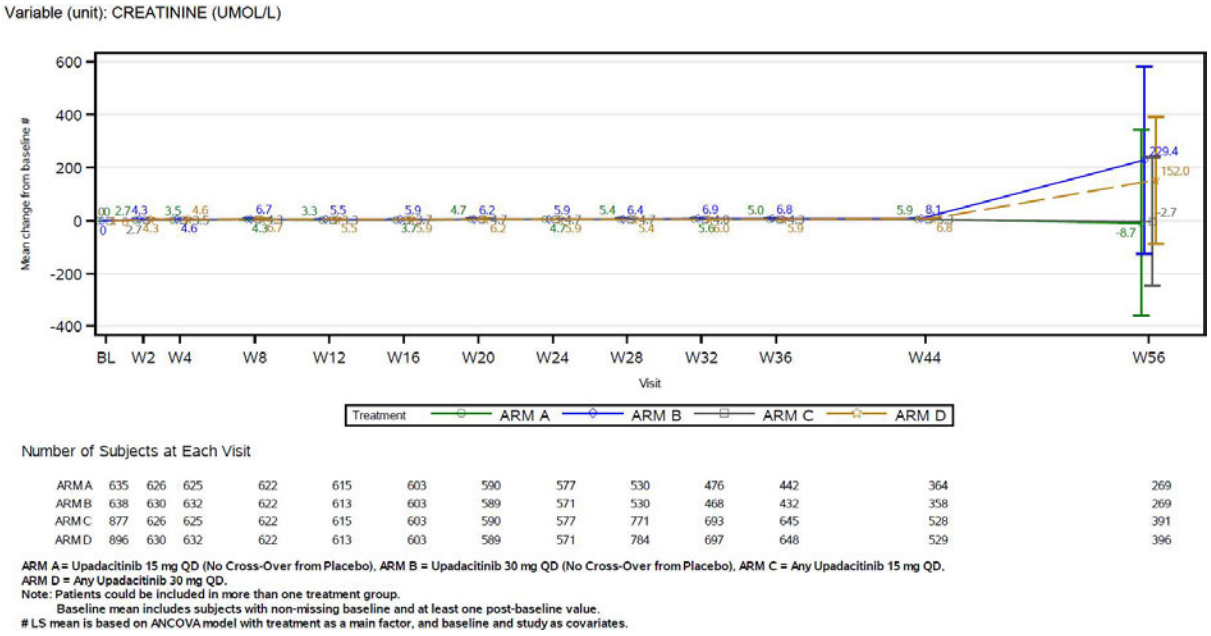
全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）でのクレアチニン値のベースラインからの平均変化量の推移を図 2.7. -11 に示す。

全ウパダシチニブ併合解析集団（長期）で，投与期間中に認められたクレアチニン値の平均変化量の若干の増加は，おおむねウパダシチニブの投与に伴うものであると考えられた。投与

週時のクレアチニン値のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 5.1 µmol/L，全ウパダシチニブ 30 mg 併合群で 6.9 µmol/L であった（ISS Table 2 5 1.2.1）。しかし，投与 56 週時のクレアチニン値のベースラインからの平均変化量は，全ウパダシチニブ 30 mg 併合群で著しく増加した（177.6 µmol/L）。データベースロック後のクエリーに基づくと，この著しい増加は，治験実施医療機関が誤って入力した 1 つの非常に大きな外れ値（被験者番号 [redacted] によるものであった。

図 2 7. -11. 全ウパダシチニブ併合解析集団（長期）でのクレアチニン値のベースラインからの平均変化量の推移



相互参照：ISS Figure 2.5 1.2.6

全ウパダシチニブ併合解析集団（長期）で臨床的に意義があると判断した血液生化学検査値（クレアチニン値を含む）の基準に該当した被験者数を表 2.7. .7-65 に示す。

全ウパダシチニブ併合解析集団（長期）での Grade 3 及び Grade のクレアチニン増加の発現割合は，全ウパダシチニブ 30 mg 併合群で 0.2%（2/896 名）及び 0.1%（1/896 名）であり，全ウパダシチニブ 15 mg 併合群では，Grade 3 以上のクレアチニン増加は認められなかった。ただし，全ウパダシチニブ 30 mg 併合群の 1 名に認められた Grade のクレアチニン増加は，上記のデータ入力ミスによるものであった（被験者番号 [redacted] 。

全ウパダシチニブ併合解析集団（長期）の腎機能障害の発現状況（100 人年あたりの発現件数）を表 2.7. .7-66 に示す。

全ウパダシチニブ併合解析集団（長期）では，腎機能障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.2 件/100 人年（2 件），全ウパダシチニブ 30 mg 併合群で 0.1 件/100 人年（1 件）であった。重篤な腎機能障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 0.1 件 100 人年（1 件）であった（ISS Table 2. 1.2. .2.1 ）。これらの重篤な腎機能障害（PT はいずれも急性腎障害）は，治験責任医師により，いずれも治験薬と関連なしと判断された（ISS Table 2. 1.2.8.19）。治験薬の投与中止に至った腎機能障害は発現しなかった（ISS Table 2. 1.2. . .16）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 のクレアチニン増加の発現割合は，全ウパダシチニブ 30 mg 併合群で 3.8%（1/26 名）であり，全ウパダシチニブ 15 mg 併合群では認められなかった。Grade のクレアチニン増加は認められなかった（J-ISS T 1 2 5 1 2 1 J）。
全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，腎機能障害はいずれの投与群でも発現しなかった（J-ISS Table 2. 1.2. .1.16 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでに Grade 3 のクレアチニン増加は認められなかった。Grade のクレアチニン増加の発現割合は，全ウパダシチニブ 30 mg 群で 0.2%（1/593 名），アダリムマブ群で 0.5%（2/ 27 名）であり，全ウパダシチニブ 15 mg 群では認められなかった（M15-572 試験 CSR W2 Table 1 .3 .3.2.1.2）。
投与 2 週時データカットオフまでに腎機能障害が全ウパダシチニブ 15 mg 群で 1 件発現し，全ウパダシチニブ 30 mg 群及びアダリムマブ群では発現しなかった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）でのクレアチニン値のベースラインからの平均変化量の推移を ISS upda e Figure 2.5 5 に示す。
投与期間中に認められたクレアチニン値の平均変化量の若干の増加は，おおむねウパダシチニブの投与に伴うものであると考えられた。投与 68 週時のクレアチニン値のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 6.3 µmol L，全ウパダシチニブ 30 mg 併合群で 8 2 µmol/L であった（ISS upda e Table 2.5 1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）で臨床的に意義があると判断した血液生化学検査値（クレアチニン値を含む）の基準に該当した被験者数を表 2.7. .7-122 に示す。
全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）での Grade 3 及び Grade のクレアチニン増加の発現割合は，全ウパダシチニブ 15 mg 併合群で 0 1%（1/901 名）

及び 0.2%（2/901 名），全ウパダシチニブ 30 mg 併合群で 0. %（ /918 名）及び 0.2%（2/918 名）であった。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の腎機能障害の発現状況（100 人年あたりの発現件数）を表 2.7. .7-123 に示す。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，腎機能障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群で 0.2 件/100 人年（3 件），全ウパダシチニブ 30 mg 併合群で 0.2 件/100 人年（3 件）であった。重篤な腎機能障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 0.2 件/100 人年（2 件）であった（ISS update Table 2. 2.1 ）。申請時データカットオフ以降に新たに発現した腎機能障害は 3 件（重篤：2 件，非重篤：1 件）であった。この重篤な腎機能障害のうち，全ウパダシチニブ 30 mg 併合群の 1 件は治験責任医師により治験薬と関連ありと判断され，全ウパダシチニブ 15 mg 併合群の 1 件は治験薬と関連なしと判断された（ISS update T 1 2 6 19）。治験薬の投与中止に至った腎機能障害は発現しなかった（ISS update Table 2. . .16）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，Grade 3 のクレアチニン増加の発現割合は，全ウパダシチニブ 30 mg 併合群で 3.8%（1/26 名）であり，全ウパダシチニブ 15 mg 併合群では認められなかった。Grade のクレアチニン増加は認められなかった（J-ISS update Table 2.5 1 2. 1 J）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，腎機能障害はいずれの投与群でも発現しなかった（J-ISS update Table 2. 1 2. .1.16 J）。

アダリムマブとの比較（M15-572 試験［20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ］）

M15-572 試験（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）での Grade 3 のクレアチニン増加の発現割合は，全ウパダシチニブ 30 mg 群で 0.3%（2/611 名）であり，全ウパダシチニブ 15 mg 群及びアダリムマブ群では認められなかった。Grade のクレアチニン増加の発現割合は，全ウパダシチニブ 30 mg 群で 0.3%（2 611 名），アダリムマブ群で 0 5%（2/ 27 名）であり，全ウパダシチニブ 15 mg 群では認められなかった（ISS update Table 2.5 5. ）。

腎機能障害は，全ウパダシチニブ 15 mg 群で 1 件，全ウパダシチニブ 30 mg 群で 2 件発現し，アダリムマブ群では発現しなかった（ISS update Table 2. 8.20）。

2.7. .2.1.5.1.13 主要心血管イベント及びその他の委員会判定された心血管イベント

項目	全体集団 (ISS)		日本人部分集団 (J ISS)
	Table	Figure	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合			
MACE 及びその他の委員会判定された心血管イベント	2. 1.1. .1.18	--	2. 1 1. .1.18 J
重篤な MACE 及びその他の委員会判定された心血管イベント	2. 1.1. .2.16	--	--
Grade 3 以上の MACE 及びその他の委員会判定された心血管イベント	2. 1.1. .3.18	--	--
治験薬の投与中止に至った MACE 及びその他の委員会判定された心血管イベント	2. 1.1. . .18	--	--
全ウパダシチニブ併合解析集団の 100 人年あたりの発現被験者数			
MACE 及びその他の委員会判定された心血管イベント	2. 1.2. .1.18 Update 2 1 18	--	2. 1 2. .1.18 J Update 2 1 2 1 18 J
重篤な MACE 及びその他の委員会判定された心血管イベント	2 1 2 2 16 Update 2. 2 16	--	--
Grade 3 以上の MACE 及びその他の委員会判定された心血管イベント	2. 1.2. .3.18 Update 2 3 18	--	--
治験薬の投与中止に至った MACE 及びその他の委員会判定された心血管イベント	2. 1.2. . .18 Update 2. . 18	--	--
MACE 及びその他の委員会判定された心血管イベントの一覧表			
プラセボ対照併合解析集団	2. 1.1.8.21	--	--
全ウパダシチニブ併合解析集団	2 1 2 8 21 Update 2. 6 21	--	--
MACE 及びその他の委員会判定された心血管イベントの Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2. 1.2.9.6 Update 2. 8 6	--

心血管イベントは，独立した外部委員会である CAC により，その設置要綱の定義に基づき判定された。本項では，委員会判定された心血管イベントを以下のカテゴリーに分類して示す。なお，委員会判定された血栓症の結果は 2.7. .2 1.5 1.1 項に示す。

- MACE（心血管イベントによる死亡，非致死性心筋梗塞及び非致死性脳卒中と定義）
- 死亡（原因未特定 / 不明）
- その他の委員会判定された心血管イベント（心血管手術，入院を必要とする不安定狭心症，心不全のための入院治療及び一過性脳虚血発作）
- 血栓症

プラセボ対照併合解析集団及び全ウパダシチニブ併合解析集団のいずれも，人口統計学的特性及びベースライン時に心血管系のリスク因子を有した被験者の割合は，投与群間で同様であった。本試験対象集団の主な心血管系のリスク因子は，高血圧，糖尿病，脂質異常症及び肥満であった（表 2.7. -29 及び表 2.7. -31）。

M15-572 試験及び M15-55 試験では，過去 6 ヵ月以内に脳血管障害の発作，心筋梗塞又は冠動脈ステント留置の既往歴を有した患者，コントロールされていない高血圧を有した患者又は本試験の参加によりリスクが生じる患者（治験責任医師の判断）は除外した。また，M15-572 試験では，対照薬としてアダリムマブを投与するため，ニューヨーク心臓協会の心機能分類クラス III 又は IV に該当するうっ血性心不全の既往歴を有する患者も除外した。

MACE 及びその他の委員会判定された心血管イベントは，相互に関連する事象から構成される項目であるため，全ウパダシチニブ併合解析集団での結果は 100 人年あたりの発現被験者数で示した。

<u>プラセボ対照併合解析集団</u>

プラセボ対照併合解析集団（投与 2 週時）の MACE 及びその他の委員会判定された心血管イベントの発現状況を表 2.7. .7-67 に示す。

プラセボ対照併合解析集団（投与 2 週時）の MACE の発現割合は，ウパダシチニブ 15 mg 併合群で 0.2%（1/6 0 名），プラセボ併合群で 0 2%（1/635 名）であり，ウパダシチニブ 30 mg 併合群では発現しなかった。発現した MACE は，いずれも非致死性心筋梗塞であった。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，MACE は発現しなかった（J-ISS Table 2. 1.1. 1.18 J）。

<u>全ウパダシチニブ併合解析集団</u>

全ウパダシチニブ併合解析集団（長期）の MACE 及びその他の委員会判定された心血管イベントの発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-68 に示す。

全ウパダシチニブ併合解析集団（長期）の MACE の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.5 名/100 人年（ 名），全ウパダシチニブ 30 mg 併合群で 0.2 名

/100 人年（2 名）であった。内訳は，非致死性心筋梗塞及び非致死性脳卒中であり，いずれも全ウパダシチニブ 15 mg 併合群で各 2 名（0.2 名/100 人年），全ウパダシチニブ 30 mg 併合群で各 1 名（0 1 名/100 人年）に発現した。死亡に至った MACE は認められなかった。

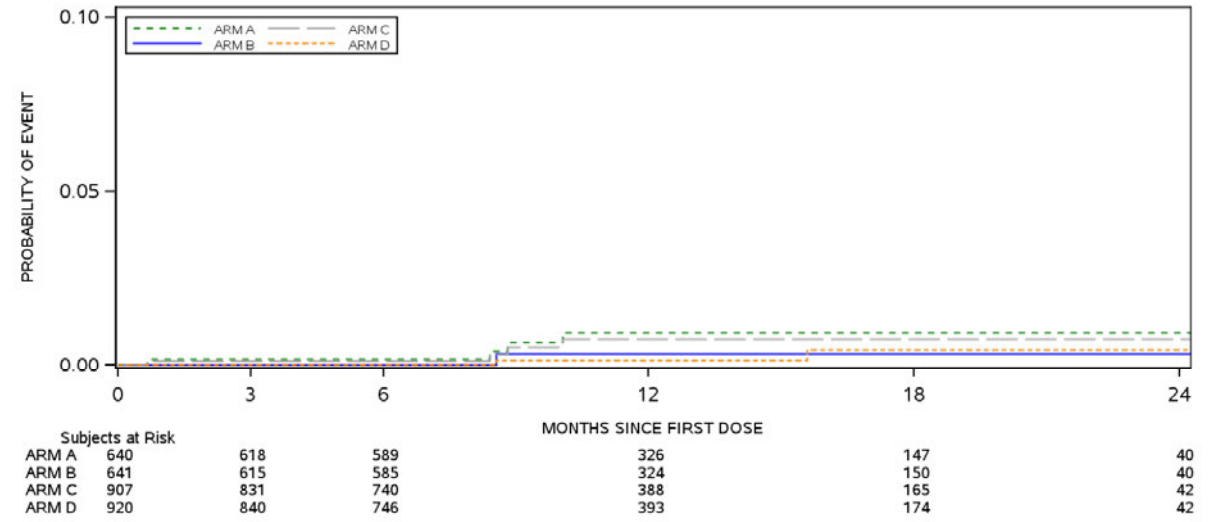
MACE を発現した被験者は，いずれも基礎疾患である乾癬性関節炎に加えて，既存の心血管系疾患，高脂血症，糖尿病，喫煙歴，肥満など，複数の心血管リスク因子を有していた。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，MACE は全ウパダシチニブ 30 mg 併合群で 1 名（3.6 名/100 人年）に発現した（非致死性脳卒中）（J-ISS Table 2. 1.2. .1.18 J）。

全ウパダシチニブ併合解析集団（長期）の MACE の Kaplan-Meier プロットを図 2.7. -12 に示す。

全ウパダシチニブ併合解析集団（長期）では，MACE が発現するリスクは比較的一定に推移しており，MACE の発現までの期間に明らかな傾向は認められなかった。

図 2 7. -12. 全ウパダシチニブ併合解析集団（長期）の MACE の Kap an-Meier プロット



Subjects at Risk

ARM A	640	618	589	326	147	40
ARM B	641	615	585	324	150	40
ARM C	907	831	740	388	165	42
ARM D	920	840	746	393	174	42

	Events	Probability of Event (95% CI)				
		Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 640)	4	0.2%(0.0%, 0.5%)	0.2%(0.0%, 0.5%)	0.9%(0.0%, 2.0%)	0.9%(0.0%, 2.0%)	0.9%(0.0%, 2.0%)
ARM B (N = 641)	1	0	0	0.3%(0.0%, 1.0%)	0.3%(0.0%, 1.0%)	0.3%(0.0%, 1.0%)
ARM C (N = 907)	4	0.1%(0.0%, 0.4%)	0.1%(0.0%, 0.4%)	0.7%(0.0%, 1.6%)	0.7%(0.0%, 1.6%)	0.7%(0.0%, 1.6%)
ARM D (N = 920)	2	0	0	0.1%(0.0%, 0.5%)	0.5%(0.0%, 1.4%)	0.5%(0.0%, 1.4%)

Note: ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.
Patients could be included in more than one treatment group.

相互参照：ISS F 2 1 2 9 6

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの MACE の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0 6 名/100 人年（3 名），全ウパダシチニブ 30 mg 群で 0.2 名/100 人年（1 名），アダリムマブ群で 0.8 名/100 人年（3 名）であった（M15-572 試験 CSR W2 Table 1 3 1.1 2.2 2）。アダリムマブ群で発現した MACE は，非致死性心筋梗塞が 1 件，非致死性脳卒中が 2 件であった（M15-572 試験 CSR W2 Table 1 .3 2.16.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の MACE 及びその他の委員会判定された心血管イベントの発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-12 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の MACE の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.3 名/100 人年（ 名），全ウパダシチニブ 30 mg 併合群で 0 2 名 100 人年（3 名）であった。このうち，申請時データカットオフ以降に新たに MACE を発現した被験者は，全ウパダシチニブ 30 mg 併合群の 1 名であり，事象名は非致死性心筋梗塞であった。死亡に至った MACE は認められなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，MACE は全ウパダシチニブ 30 mg 併合群で 1 名（2.5 名/100 人年）に発現した（非致死性脳卒中）（J-ISS update T 1 2 1 2 1 18 J）。申請時データカットオフ以降に新たに発現した MACE は認められなかった。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の MACE の Kaplan-Meier プロットを ISS update Figure 2. 8.6 に示す。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）での MACE の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0. 名 100 人年（3 名），全ウパダシチニブ 30 mg 群で 0.2 名/100 人年（2 名），アダリムマブ群で 0.5 名/100 人年（3 名）であった（ISS update Table 2. 2.8）。アダリムマブ群では，投与 2 週時データカットオフ以降に新たに発現した MACE は認められなかった（ISS upda e Table 2. 8.22）。

死亡（原因未特定 / 不明）

プラセボ対照併合解析集団（投与 24 週時）及び全ウパダシチニブ併合解析集団（申請時）

プラセボ対照併合解析集団（投与 2 週時）では，プラセボ併合群で心停止が 1 名（0.2%）に発現した（被験者番号 [redacted] 。本事象は，CAC により死亡（原因未特定 / 不明）と判定された（ISS Table 2. 1.1. .1.18，Table 2. 1.1.8.21）。本被験者の詳細は，2.7. .2 1.2 項に示す。

全ウパダシチニブ併合解析集団（長期）では，死亡（原因未特定 / 不明）と判定された事象は発現しなかった（ISS Table 2. 1 2. 1.18）

プラセボ対照併合解析集団（投与 2 週時）及び全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，死亡（原因未特定 / 不明）と判定された事象は発現しなかった（J-ISS Table 2. 1.1. .1.18 J，Table 2. 1.2. .1.18 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでにアダリムマブ群で死亡（原因未特定 / 不明）と判定された事象は発現しなかった（M15-572 試験 CSR W2 T 1 1 3 2 16 2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，死亡（原因未特定 / 不明）と判定された事象は発現しなかった（ISS update Table 2. .1.18）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，死亡（原因未特定 / 不明）と判定された事象は発現しなかった（J-ISS update Table 2. 1.2. .1.18 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）のアダリムマブ群で死亡（原因未特定 / 不明）と判定された事象は発現しなかった（ISS update Table 2. 8.22）。

その他の委員会判定された心血管イベント

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）では，その他の委員会判定された心血管イベントが発現した被験者は，ウパダシチニブ 30 mg 併合群で 6 1 名中 3 名（0.5%），プラセボ併合群で 635 名中 1 名（0.2%）であり，ウパダシチニブ 15 mg 併合群では発現しなかった。内訳は，ウパダシチニブ 30 mg 併合群では心血管手術（2 名）及び一過性脳虚血発作（1 名）であり，プラセボ併合群では入院を必要とする不安定狭心症（1 名）であった（表 2.7. .7-67）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，その他の委員会判定された心血管イベントは発現しなかった（J-ISS Table 2. 1.1. .1.18 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）では，その他の委員会判定された心血管イベントの 100 人年あたりの発現被験者数は，全ウパダシチニブ 30 mg 併合群で 0.5 名/100 人年（ 名）であり，全ウパダシチニブ 15 mg 併合群では発現しなかった（表 2.7. .7-68）。内訳は，心血管手術（2 名［0.2 名/100 人年］）及び一過性脳虚血発作（2 名［0.2 名/100 人年］）であった。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，その他の委員会判定された心血管イベントは発現しなかった（J-ISS Table 2. 1 2. 1.18 J）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでに，その他の委員会判定された心血管イベントが全ウパダシチニブ 30 mg 群及びアダリムマブ群で各 2 件発現し，全ウパダシチニブ 15 mg 群では発現しなかった。内訳は，全ウパダシチニブ 30 mg 群及びアダリムマブ群とも，心血管手術及び一過性脳虚血発作（各 1 件）であった（M15-572 試験 CSR W2 T 1 1 3 2 16 2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，その他の委員会判定された心血管イベントの 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.1 名未満/100 人年（1 名），全ウパダシチニブ 30 mg 併合群で 0.5 名/100 人年（6 名）であった（ISS update Table 2. .1.18）。このうち，申請時データカットオフ以降にその他の委員会判定された心血管イベントを新たに発現した被験者は，全ウパダシチニブ 15 mg 併合群の 1 名（心血管手術）及び全ウパダシチニブ 30 mg 併合群の 2 名（心血管手術：1 名，心不全のための入院治療：1 名）であった（ISS update Table 2. 6.21）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，その他の委員会判定された心血管イベントは発現しなかった（J-ISS update T 1 2 1 2 1 18 J）。

アダリムマブとの比較（M15-572 試験［20[redacted]年[redacted]月[redacted]日データカットオフ］）

M15-572 試験（20[redacted]年[redacted]月[redacted]日データカットオフ）では，その他の委員会判定された心血管イベントが全ウパダシチニブ 30 mg 群及びアダリムマブ群で各 2 件発現し，全ウパダシチニブ 15 mg 群では発現しなかった。アダリムマブ群では，投与 2 週時データカットオフ以降に新たに発現した，その他の委員会判定された心血管イベントは認められなかった（ISS update Table 2. 8.22）。

2.7. .2.1.5.1.1 血栓症

	全体集団（ISS）		日本人部分集団（J-ISS）
項目	Tab e	F gure	Table
プラセボ対照併合解析集団の発現被験者数及び発現割合			
血栓症	2 1 1 1 19	--	2 1 1 1 19 J
重篤な血栓症	2 1 1 2 17	--	--
Grade 3 以上の血栓症	2 1 1 3 19	--	--

項目	全体集団（ISS）		日本人部分集団（J-ISS）
	Tab e	F gure	Table
治験薬の投与中止に至った血栓症	2. 1.1. . 19	--	--
全ウパダシチニブ併合解析集団の100 人年あたりの発現被験者数			
血栓症	2. 1.2. 1 19 Update 2 1 19	--	2. 1 2. .1.19 J Update 2 1 2 1 19 J
重篤な血栓症	2 1 2 2 17 Update 2. .2.17	--	--
Grade 3 以上の血栓症	2. 1.2. 3 19 Update 2 3 19	--	--
治験薬の投与中止に至った血栓症	2 1 2 19 Update 2. . .19	--	--
血栓症の一覧表			
プラセボ対照併合解析集団	2. 1.1.8 22	--	--
全ウパダシチニブ併合解析集団	2. 1.2.8 22 Update 2. 6.22	--	--
血栓症の Kaplan-Meier プロット			
全ウパダシチニブ併合解析集団	--	2. 1 2 9.7 Upda e 2 8 7	--

静脈血栓塞栓症は，深部静脈血栓症及び致死性 / 非致死性の肺塞栓症と定義した。

関節リウマチの臨床開発プログラムでは，判定された静脈血栓塞栓症の発現率は，ウパダシチニブ群とプラセボ群又は実薬対照群（MTX，アダリムマブ等）で同様であった。静脈血栓塞栓症の発現率，発現までの時間の傾向又は血小板数との関連性では，用量相関性は認められなかった。

静脈及び動脈血栓症が疑われるすべての事象について，独立した外部委員会の CAC が判定した結果を本項に示す。

プラセボ対照併合解析集団

プラセボ対照併合解析集団（投与 2 週時）の血栓症の発現状況を表 2.7. .7-69 に示す。

プラセボ対照併合解析集団（投与 2 週時）の静脈血栓塞栓症の発現割合は，ウパダシチニブ 15 mg 併合群で 0.2%（1 6 0 名），ウパダシチニブ 30 mg 併合群で 0.2%（1/6 1 名），プラセボ併合群で 0 2%（1/635 名）であった。事象名は，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群が肺塞栓症，プラセボ併合群が深部静脈血栓症であった。発現した静脈血栓塞栓症はいずれも重篤であり（ISS Table 2. 1.1. .2.17），肺塞栓症（2 件）では治験薬の投与を中止した（ISS Table 2. 1.1. . .19）。

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プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，静脈血栓塞栓症は発現しなかった（J-ISS Table 2. 1.1. .1.19 J）。

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）の血栓症の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-70 に示す。

全ウパダシチニブ併合解析集団（長期）の静脈血栓塞栓症の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.5 名/100 人年（ 名），全ウパダシチニブ 30 mg 併合群で 0.2 名/100 人年（2 名）であった。死亡に至った静脈血栓塞栓症は発現しなかった。重篤な静脈血栓塞栓症は，全ウパダシチニブ 15 mg 併合群で 3 名（0. 名/100 人年），全ウパダシチニブ 30 mg 併合群で 2 名（0.2 名/100 人年）に発現した（ISS Table 2. 1.2. .2 17）。治験薬の投与中止に至った静脈血栓塞栓症は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 2 名（0.2 名/100 人年）に発現した（ISS Table 2. 1.2. . .19）。

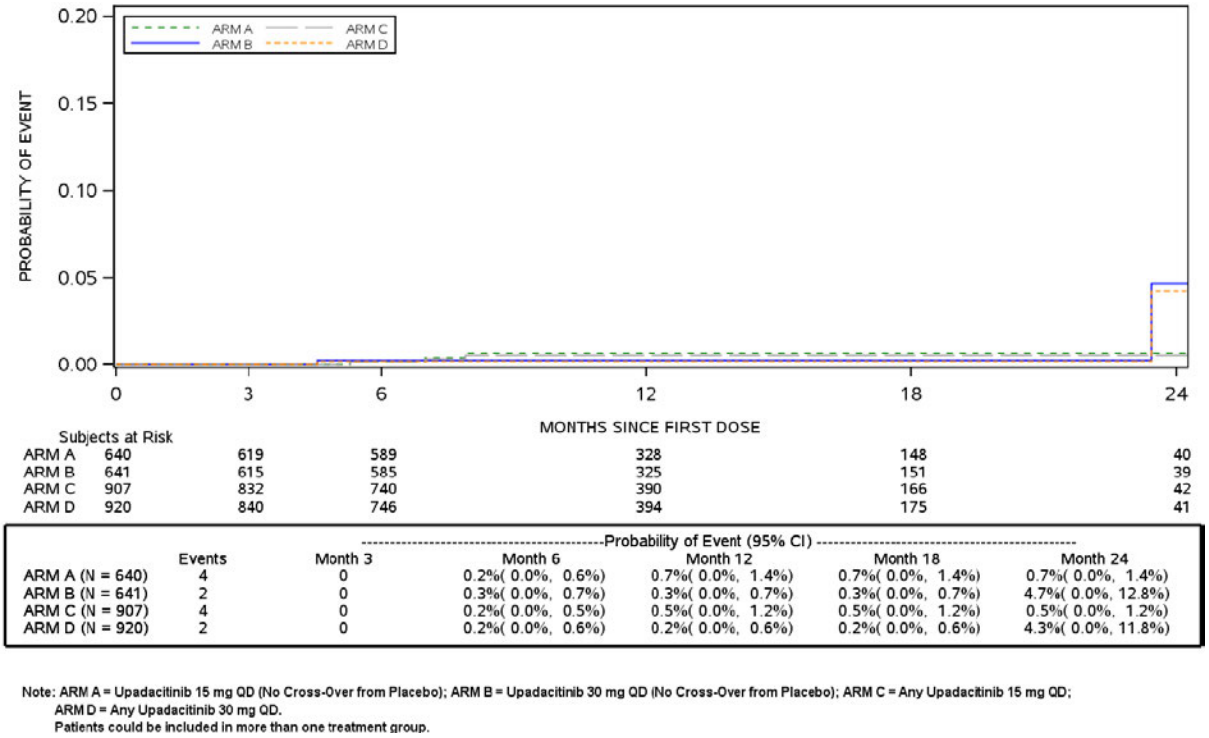
静脈血栓塞栓症を発現した被験者は，いずれも高血圧，高脂血症，肥満，喫煙歴又は併存疾患（心房細動，感染症等）等の静脈血栓塞栓症のリスク因子を 1 つ以上有していた。静脈血栓塞栓症の発現までの期間では，明らかな傾向は認められなかった（ウパダシチニブの投与期間の範囲：138–808 日，ISS Table 2. 1.2 8.22）。死亡に至った静脈血栓塞栓症は発現しなかった。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，静脈血栓塞栓症は発現しなかった（J-ISS Table 2. 1 2. 1.19 J）。

全ウパダシチニブ併合解析集団（長期）の静脈血栓塞栓症の Kaplan-Meier プロットを図 2.7. -13 に示す。

全ウパダシチニブ併合解析集団（長期）では，静脈血栓塞栓症が発現するリスクは比較的一定に推移しており，発現までの期間に明らかな傾向は認められなかった。

図 2 7. -13. 全ウパダシチニブ併合解析集団（長期）の静脈血栓塞栓症の Kaplan-Me er プロット



Subjects at Risk

ARM A	640	619	589	328	148	40
ARM B	641	615	585	325	151	39
ARM C	907	832	740	390	166	42
ARM D	920	840	746	394	175	41

	Events	Probability of Event (95% CI)				
		Month 3	Month 6	Month 12	Month 18	Month 24
ARM A (N = 640)	4	0	0.2%(0.0%, 0.6%)	0.7%(0.0%, 1.4%)	0.7%(0.0%, 1.4%)	0.7%(0.0%, 1.4%)
ARM B (N = 641)	2	0	0.3%(0.0%, 0.7%)	0.3%(0.0%, 0.7%)	0.3%(0.0%, 0.7%)	4.7%(0.0%, 12.8%)
ARM C (N = 907)	4	0	0.2%(0.0%, 0.5%)	0.5%(0.0%, 1.2%)	0.5%(0.0%, 1.2%)	0.5%(0.0%, 1.2%)
ARM D (N = 920)	2	0	0.2%(0.0%, 0.6%)	0.2%(0.0%, 0.6%)	0.2%(0.0%, 0.6%)	4.3%(0.0%, 11.8%)

Note: ARM A = Upadacitinib 15 mg QD (No Cross-Over from Placebo); ARM B = Upadacitinib 30 mg QD (No Cross-Over from Placebo); ARM C = Any Upadacitinib 15 mg QD; ARM D = Any Upadacitinib 30 mg QD.
Patients could be included in more than one treatment group.

相互参照：ISS Figure 2. 1.2.9.7

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでの静脈血栓塞栓症の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0.6 名/100 人年（3 名），全ウパダシチニブ 30 mg 群で 0. 名/100 人年（2 名），アダリムマブ群で 0.5 名/100 人年（2 名）であった（M15-572 試験 CSR W2 Table 1 .3 1 1.2 2.2）。アダリムマブ群で発現した事象は，いずれも深部静脈血栓症であった（M15-572 試験 CSR W2 Table 1 .3 2.17.2）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の血栓症の発現状況（100 人年あたりの発現被験者数）を表 2.7. .7-125 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の静脈血栓塞栓症の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 併合群で 0.3 名/100 人年（ 名），全ウパダシチニブ 30 mg 併合群で 0.2 名/100 人年（3 名）であった。このうち，申請時データカットオフ以降に新たに発現した静脈血栓塞栓症は，全ウパダシチニブ 30 mg 併合群の 1 名に発現した肺塞栓症（重篤）であった。死亡に至った静脈血栓塞栓症は発現しなかった。重篤な静

脈血栓塞栓症は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 3 名（0.2 名/100 人年）に発現した（ISS update Table 2. .2.17）。治験薬の投与中止に至った静脈血栓塞栓症は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群で各 2 名（0.2 名/100 人年）に発現した（ISS update Table 2. . .19）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，静脈血栓塞栓症は発現しなかった（J-ISS update Table 2. 1.2. .1.19 J）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の静脈血栓塞栓症の Kaplan-Meier プロットを ISS update Figure 2. 8.7 に示す。

アダリムマブとの比較（M15-572 試験［20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ］）

M15-572 試験（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）での静脈血栓塞栓症の 100 人年あたりの発現被験者数は，全ウパダシチニブ 15 mg 群で 0. 名/100 人年（3 名），全ウパダシチニブ 30 mg 群で 0.2 名/100 人年（2 名），アダリムマブ群で 0. 名/100 人年（2 名）であった（ISS update Table 2. 2.8）。M15-572 試験では，投与 2 週時データカットオフ以降に新たに発現した静脈血栓塞栓症は認められなかった（ISS update Table 2. 8.23）。

その他の静脈血栓症及び動脈血栓塞栓症

全ウパダシチニブ併合解析集団

全ウパダシチニブ併合解析集団（長期）では，その他の静脈血栓症及び動脈血栓塞栓症は発現しなかった（表 2.7. .7-70）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，アダリムマブ群の 1 名（本態性血小板血症［JAK2 遺伝子変異］及び門脈血栓症の病歴あり）で門脈血栓症が発現し，その他の非致死性静脈血栓症と判定された（M15-572 試験 CSR W2 Table 1 .3 2.18.16.2）。アダリムマブ群の他の 1 名（左心室瘤及び血栓，末梢血管疾患並びに腸骨大腿動脈バイパスの病歴あり）では，左心室瘤を伴う左心室の血栓の再発が認められ，非致死性動脈血栓塞栓症（非心臓性，非神経性）と判定された。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，その他の静脈血栓症及び動脈血栓塞栓症は発現しなかった（表 2.7. .7-125）。

アダリムマブとの比較（M15-572 試験［20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ］）

M15-572 試験（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，その他の静脈血栓症及び動脈血栓塞栓症がアダリムマブ群で各 1 名に発現した（ISS update Table 2. 8.23）。M15-572 試験では，

投与 2 週時データカットオフ以降に新たに発現したその他の静脈血栓症及び動脈血栓塞栓症は認められなかった。

2.7. .2.2 個別有害事象の文章による説明

M15-572 試験及び M15-55 試験での死亡例及び重篤な有害事象発現例の詳細（叙述）は，2.7.6 項並びに各試験の CSR W2 （M15-572 試験：1 .3__3 項，M15-55 試験：1 .3__3 項）及び CSR W56（M15-572 試験：1 .3__3 項，M15-55 試験：1 3__3 項）に示す。

2.7. .3 臨床検査値の評価

2.7. .3.1 血液学的検査

安全性併合解析について，特に注目すべき有害事象で評価した血液学的検査（ヘモグロビン，好中球数及びリンパ球数）に関する結果は，2.7. .2.1.5.1.8 項（貧血），2.7. .2 1.5 1.9 項（好中球減少症）及び 2.7. .2.1.5.1.10 項（リンパ球減少症）に示した。本項では，血小板数について評価した。

M15-572 試験及び M15-55 試験の解析では，血液学的検査の全項目について評価した。

2.7. .3.1.1 プラセボ対照併合解析

<u>全体集団</u>

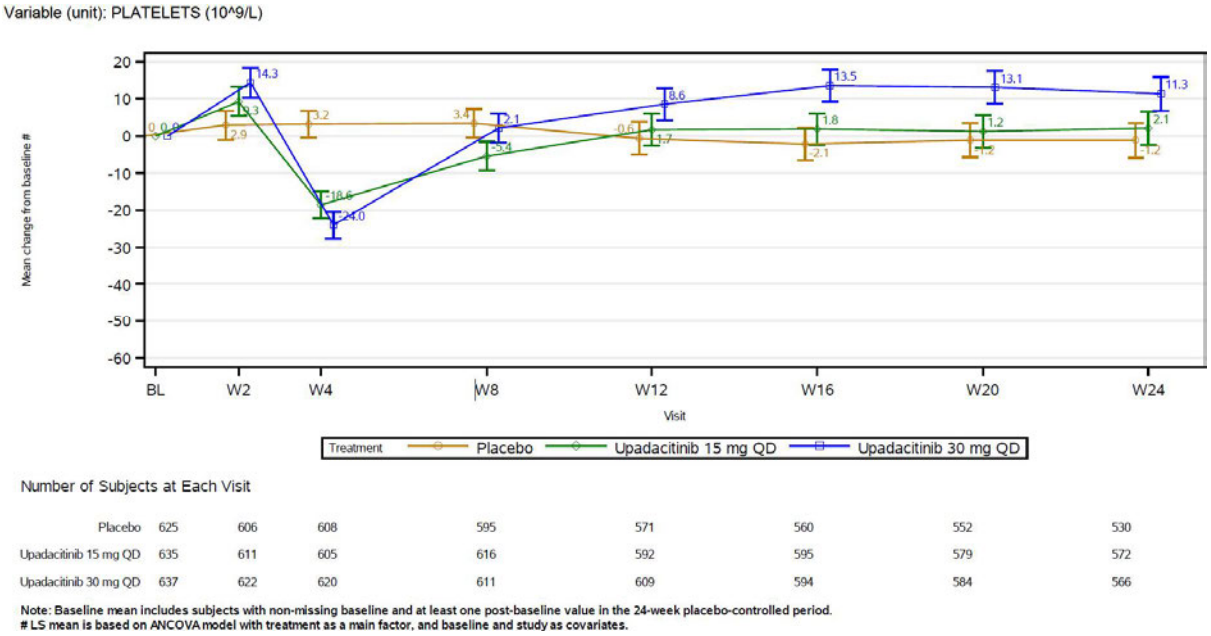
プラセボ対照併合解析集団（投与 2 週時）での血小板数のベースラインからの平均変化量の推移を図 2.7. -1 に示す。

プラセボ対照併合解析集団（投与 2 週時）では，投与 2 週時の血小板数のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群で 1.3×10^9 L，ウパダシチニブ 30 mg 併合群で 10.6×10^9/L，プラセボ併合群で -2.7×10^9/L であった（ISS Table 2.5 1.1.1）。

プラセボ対照併合解析集団（投与 2 週時）では，Grade 3 の血小板数減少はウパダシチニブ 30 mg 併合群のみで 637 名中 1 名（0.2%）に認められた。Grade の血小板数減少は認められなかった（ISS Table 2.5 1.1.3.1）。

プラセボ対照併合解析集団（投与 2 週時）では，有害事象の血小板減少症，血小板増加症又は血小板数増加を発現した被験者は各投与群でいずれも 3 名以下であり，血小板数減少は発現しなかった（ISS Table 2. 1.1.3.1）。

図 2 7. -1 . プラセボ対照併合解析集団（投与 2 週時）での血小板数のベースラインからの平均変化量の推移



Number of Subjects at Each Visit

Placebo	625	606	608	595	571	560	552	530
Upadacitinib 15 mg QD	635	611	605	616	592	595	579	572
Upadacitinib 30 mg QD	637	622	620	611	609	594	584	566

Note: Baseline mean includes subjects with non-missing baseline and at least one post-baseline value in the 24-week placebo-controlled period.
LS mean is based on ANCOVA model with treatment as a main factor, and baseline and study as covariates.

相互参照：ISS Figure 2.5 1.1.6

プラセボ対照併合解析集団（投与 2 週時）での血小板数のベースラインから投与後のシフトテーブルを ISS Table 2.5 1.1.2 に示す。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，投与 2 週時の血小板数のベースラインからの平均変化量は，ウパダシチニブ 15 mg 併合群で 3. × 10^9/L，ウパダシチニブ 30 mg 併合群で 3 .7 × 10^9/L，プラセボ併合群で –6.9 × 10^9/L であった（J-ISS Table 2.5 1.1.1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，Grade 3 及び Grade の血小板数減少は認められなかった（J-ISS Table 2.5 1.1.3.1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団での血小板数のベースラインから投与後のシフトテーブルを J-ISS Table 2.5 1.1.2 J に示す。

2.7. .3.1.2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

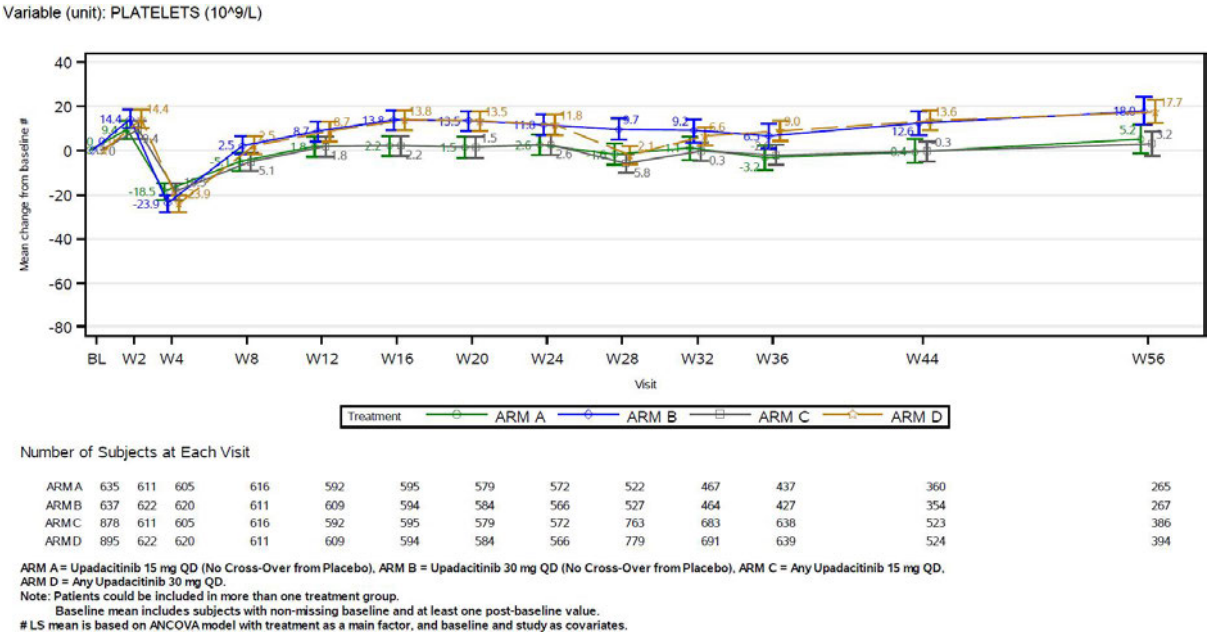
全ウパダシチニブ併合解析集団（長期）での血小板数のベースラインからの平均変化量の推移を図 2.7. -15 に示す。

全ウパダシチニブ併合解析集団（長期）では，投与 56 週時の血小板数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 2.1 × 10^9/L，全ウパダシチニブ 30 mg 併合群で 17.7 × 10^9/L であった（ISS Table 2.5 1.2 1）。

全ウパダシチニブ併合解析集団（長期）では，Grade 3 の血小板数減少は全ウパダシチニブ 30 mg 併合群のみで 895 名中 1 名（0.1%）に認められた。Grade の血小板数減少は，全ウパダシチニブ 15 mg 併合群で 879 名中 1 名（0.1%），全ウパダシチニブ 30 mg 併合群で 895 名中 1 名（0.1%）に認められた（ISS Table 2 5 1.2 3.1）。

全ウパダシチニブ併合解析集団（長期）では，有害事象の血小板減少症，血小板増加症及び血小板数増加の 100 人年あたりの発現件数は各投与群でいずれも 0.7 件/100 人年以下であり，血小板数減少は発現しなかった（ISS Table 2. 1.2.3.2）。

図 2 7. -15. 全ウパダシチニブ併合解析集団（長期）での血小板数のベースラインからの平均変化量の推移



相互参照：ISS Figure 2.5 1.2.6

全ウパダシチニブ併合解析集団（長期）での血小板数のベースラインから投与後のシフトテーブルを ISS Table 2 5 1.2 2 に示す。

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，投与 56 週時の血小板数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 0.1 × 10^9/L，全ウパダシチニブ 30 mg 併合群で 28. × 10^9/L であった（J-ISS Table 2 5 1.2 1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，Grade 3 の血小板数減少は認められず，Grade の血小板数減少は全ウパダシチニブ 30 mg 併合群で 26 名中 1 名（3.8%）に認められた（J-ISS Table 2.5 1.2.3.1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団での血小板数のベースラインから投与後のシフトテーブルを J-ISS T 1 2 5 1 2 2 J に示す。

266

20[redacted]年[redacted]月[redacted]日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）での血小板数のベースラインからの平均変化量の推移を ISS update Figure 2.5 5 に示す。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，投与 36 週時の血小板数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で–2.3 × 10^9/L，全ウパダシチニブ 30 mg 併合群で 10.0 × 10^9/L であった（ISS update T 1 2 5 1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，Grade 3 の血小板数減少は，全ウパダシチニブ 30 mg 併合群のみで 918 名中 1 名（0.1%）に認められた。Grade の血小板数減少は，全ウパダシチニブ 15 mg 併合群で 901 名中 1 名（0.1%），全ウパダシチニブ 30 mg 併合群で 918 名中 1 名（0.1%）に認められた（ISS update Table 2 5 2.1）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）での血小板数のベースラインから投与後のシフトテーブルを ISS-J update Table 2.5 1.2.2 に示す。

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，投与 56 週時の血小板数のベースラインからの平均変化量は，全ウパダシチニブ 15 mg 併合群で 3.6 × 10^9/L，全ウパダシチニブ 30 mg 併合群で 32.0 × 10^9/L であった（J-ISS update Table 2.5 1.2.1 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団では，Grade 3 の血小板数減少は認められず，Grade の血小板数減少は全ウパダシチニブ 30 mg 併合群で 26 名中 1 名（3.8%）に認められた（J-ISS update Table 2.5 1 2.3 1 J）。

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）の日本人部分集団での血小板数のベースラインから投与後のシフトテーブルを J-ISS update Table 2 5 1.2.2 J に示す。

2.7. .3.1.3 M15-572 試験

投与 2 週時

M15-572 試験の投与 2 週時までの血液学的検査値及びベースラインからの平均変化量をそれぞれ M15-572 試験 CSR W2 Table 1 .3 1.1 1 及び Table 1 .3 1. 1 に示す。

ヘモグロビンでは，投与 2 週時にベースラインからの平均変化量の減少がウパダシチニブ 15 mg 群（–0.7 g/L）及びウパダシチニブ 30 mg 群（–2.7 g/L）のみで認められた。投与 2 週時

のベースラインからの平均変化量は，アダリムマブ群では 2.7 g/L，プラセボ群では 0.0 g/L であった。ウパダシチニブ群でのヘモグロビンの変化は，用量依存的と考えられた。平均変化量の減少は投与 16 週時に最大となり，その後の来院時から徐々に小さくなり，ベースライン値に近づいた。

リンパ球数では，ベースラインから投与 2 週時までの平均変化量は，投与 8 週時のプラセボ群を除き，ウパダシチニブ 15 mg 群，30 mg 群，アダリムマブ群及びプラセボ群でおおむね同様であった。投与 2 週時のベースラインからの平均変化量の増加は，ウパダシチニブ 15 mg 群（0.06 × 10^9 L），ウパダシチニブ 30 mg 群（0.1 3 × 10^9/L）及びプラセボ群（0.095 × 10^9/L）と比較してアダリムマブ群（0. 3 × 10^9/L）の方が大きかった。

好中球数では，ベースラインから投与 2 週時までの平均変化量は，ウパダシチニブ 15 mg 群，30 mg 群，アダリムマブ群及びプラセボ群でおおむね同様であり，臨床的に意味はないと考えられた。投与 2 週時のベースラインからの平均変化量は，ウパダシチニブ 15 mg 群で-0.515 × 10^9/L，ウパダシチニブ 30 mg 群で–0.83 × 10^9/L，アダリムマブ群で–1.015 × 10^9/L であり，プラセボ群では 0 052 × 10^9/L であった。

血小板数では，ベースラインからの平均変化量の減少は，ウパダシチニブ 15 mg 群（-21.7 × 10^9/L），ウパダシチニブ 30 mg 群（–25.2 × 10^9/L），アダリムマブ群（–27.9 × 10^9/L）では投与 週時で最も大きく，プラセボ群の投与 週時のベースラインからの平均変化量は-0.8 × 10^9 L であった。投与 2 週時のベースラインからの平均変化量は，ウパダシチニブ 15 mg 群で–2.1 × 10^9/L，ウパダシチニブ 30 mg 群で 6.7 × 10^9/L，アダリムマブ群で–20.3 × 10^9/L，プラセボ群で– .7 × 10^9 L であった。血小板数のベースラインから投与 2 週時までの平均変化量は，臨床的に意味はないと考えられた。

投与 2 週時までに，臨床的に意義があると判断した臨床検査値の基準に該当した被験者数を M15-572 試験 CSR W2 Table 1 3 .3 1.1 1 に示す。

Grade 3 のヘモグロビン減少及び血小板数減少がウパダシチニブ 30 mg 群で各 1 名（0.2%），Grade 3 の白血球数減少が 2 名（0 5%）に認められた。Grade 3 の好中球数減少及びリンパ球数減少が認められた被験者は，ウパダシチニブ 15 mg 群（2 名［0 5%］及び 名［0.9%］），アダリムマブ群（1 名［0.2%］及び 0 名），プラセボ群（1 名［0.2%］及び 1 名［0.2%］）と比較してウパダシチニブ 30 mg 群（6 名［1. %］及び 9 名［2.1%］）の方が多かった。Grade の血小板数減少，白血球数減少，好中球数減少及びリンパ球数減少は認められなかった。

M15-572 試験の日本人部分集団での投与 2 週時までの血液学的検査値を M15-572 試験 JSA Table 1 3 .1.1.1 J，臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数を M15-572 試験 JSA Table 1 .3 .3.1.1 1 J に示す。

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの血液学的検査値及びベースラインからの平均変化量をそれぞれ M15-572 試験 CSR W56 Table 1 .3 1.1，Table 1 3 .1. 及び Figure 1 .3 5 1 に示す。

ヘモグロビンでは，ウパダシチニブ投与時にベースラインからの平均変化量の減少が認められ，用量依存的と考えられた。ウパダシチニブ 15 mg では，平均変化量の減少は最大で 3 g/L 未満であり，ウパダシチニブの投与 12–16 週後に認められたが，その後平均値はやや回復し，一定となった。ウパダシチニブ 30 mg では，平均変化量の減少は最大で 6 g/L 未満であり，ウパダシチニブの投与 16–20 週後に認められたが，その後平均値はやや回復し，一定となった。投与 56 週時のベースラインからの平均変化量の減少は，プラセボ→ウパダシチニブ 15 mg 群で-0.7 g/L，ウパダシチニブ 15 mg 群で–0.7 g/L，プラセボ→ウパダシチニブ 30 mg 群で–2.9 g/L，ウパダシチニブ 30 mg 群で–2.7 g/L であった。アダリムマブ群では，投与 56 週時にベースラインからの平均変化量の増加（3 8 g/L）が認められた。

リンパ球数では，ウパダシチニブ投与後の最初の 週間以内にベースラインからの平均変化量の増加が認められたが，用量依存的ではないと考えられた。平均変化量の増加後に減少が認められたため，投与 56 週時のベースラインからの平均変化量は小さく（プラセボ→ウパダシチニブ 15 mg 群：0.017 × 10^9/L，ウパダシチニブ 15 mg 群：–0.107 × 10^9/L，プラセボ→ウパダシチニブ 30 mg 群：0.0 9 × 10^9/L，ウパダシチニブ 30 mg 群：–0.0 6 × 10^9/L），アダリムマブ群（0. 20 × 10^9/L）と比較して小さかった。リンパ球数の変化は，いずれの投与群でも臨床的に意味はないと考えられた。

好中球数では，ウパダシチニブ投与後の最初の 週間以内にベースラインからの平均変化量の減少が認められ，用量依存的と考えられた。平均変化量は減少後にやや回復し，一定となったため，投与 56 週時のベースラインからの平均変化量は小さく（プラセボ→ウパダシチニブ 15 mg 群：–0.729 × 10^9/L，ウパダシチニブ 15 mg 群：–0.571 × 10^9/L，プラセボ→ウパダシチニブ 30 mg 群：–0.629 × 10^9/L，ウパダシチニブ 30 mg 群：–0.871 × 10^9/L），アダリムマブ群（-0.968 × 10^9/L）と同様であった。好中球数の変化は，いずれの投与群でも臨床的に意味はないと考えられた。

血小板数では，平均測定値の経時的な推移で臨床的に意味のある傾向は認められなかった。

投与 56 週時データカットオフまでに，臨床的に意義があると判断した臨床検査値の基準に該当した被験者数を M15-572 試験 CSR W56 Table 1 .3 .3.1.1 に示す。

Grade 3 のヘモグロビン減少が認められた被験者の割合は，全ウパダシチニブ 15 mg 群（0.2%［1 名］），全ウパダシチニブ 30 mg 群（0.2%［1 名］）及びアダリムマブ群（0.5%［2 名］）で同様であった。アダリムマブ群の 1 名では，単発の Grade 3 のヘモグロビン減少が 1 時点で認められ，全ウパダシチニブ 30 mg 群の 1 名では，最後の 2 回の評価で，単発の Grade 2 のヘモグロビン減少に続いて単発の Grade 3 のヘモグロビン減少が認められた（M15-572 試験 CSR W56 Table 1 .3 .3.1.2）。他の 2 名については，全ウパダシチニブ 15 mg 群の 1 名では上部消化管

出血（重篤）の発現時の検査で，アダリムマブ群の 1 名では十二指腸潰瘍（重篤）及びびらん性胃炎（非重篤）の発現時の検査で，Grade 3 のヘモグロビン減少が認められた（M15-572 試験 CSR W56 Table 1 .3 .3.1.2 及び Appendix 16.2 7.1.1）。

Grade 3 の血小板数減少は，全ウパダシチニブ 30 mg 群の 1 名で単発のものが認められた（M15-572 試験 CSR W56 Table 1 .3 .3.1.2）。Grade の血小板数減少は，全ウパダシチニブ 15 mg 群で 6 名，全ウパダシチニブ 30 mg 群で 名，アダリムマブ群で 3 名に認められたが，データベースロック後に，全ウパダシチニブ 15 mg 群の 1 名を除く全被験者で治験実施医療機関のデータ入力ミスによるものであったことが判明した。入力ミスとされた血小板数は，いずれも臨床的に意味はないと考えられた。全ウパダシチニブ 15 mg 群の 1 名（被験者番号 ）は，投与 221 日目に健康状態不良のため試験を中止し，投与 2 0 日目から Grade の血小板数減少が複数回認められた。当該被験者は，Grade の血小板数減少の発現経過で，裂孔ヘルニア，憩室炎，胃炎，消化性潰瘍，血小板減少症，貧血及び骨髄異形成症候群を発現していた（M15-572 試験 CSR W56 16 2 7 1 1）。当該被験者の血小板数は，併発の有害事象の治療期間中（抗生物質及び輸血等）の投与 2 9 日目までにベースライン値に戻った（M15-572 試験 CSR W56 Appendix 16 2 7.3）。

Grade 3 の白血球数減少が 名（全ウパダシチニブ 30 mg 群）に認められ，いずれも単発のものであった（M15-572 試験 CSR W56 Table 1 .3 .3.1.2）。Grade の白血球数減少は，全ウパダシチニブ 15 mg 群で 名，全ウパダシチニブ 30 mg 群で 3 名，アダリムマブ群で 1 名に認められたが，データベースロック後に，全被験者で治験実施医療機関のデータ入力ミスによるものであったことが判明した。入力ミスとされた白血球数は，いずれも臨床的に意味はないと考えられた。

Grade 3 の好中球数減少が認められた被験者の割合は，全ウパダシチニブ 15 mg 群（0.5%［3 名］）とアダリムマブ群（0.7%［3 名］）で同様であり，全ウパダシチニブ 30 mg 群（2.3%［1 名］）で高かった。Grade 3 の好中球数減少の多くは，単発のものであった（M15-572 試験 CSR W56 Table 1 .3 .3.1.2）。Grade の好中球数減少は，全ウパダシチニブ 15 mg 群で 名，全ウ

ade 3 のリンパ球数減少の多くは，単発のものであった（M15-572 試験 CSR W56 Table 14.3 4.3.1.2）。Grade 4 のリンパ球数減少は，全ウパダシチニブ 15 mg 群で 4 名，全ウパダシチニブ 30 mg 群で 3 名，アダリムマブ群で 1 名に認められたが，データベースロック後に，全被験者で治験実施医療機関のデータ入力ミスによるものであったことが判明した。入力ミスとされたリンパ球数は，いずれも臨床的に意味はないと考えられた。

M15-572 試験の日本人部分集団での投与 56 週時データカットオフまでの血液学的検査値を M15-572 試験 JSA W56 Table 1 .3 .1.1 J，臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数を M15-572 試験 JSA W56 Table 1 .3 .3.1.1 J に示す。

2.7. .3.1. M15-55 試験

投与２ 週時

M15-55 試験の投与 2 週時までの血液学的検査値及びベースラインからの平均変化量をそれぞれ M15-55 試験 CSR W2 Table 1 .3 1.1 1 及び Table 1 .3 1. 1 に示す。

ヘモグロビンでは，投与 2 週時のベースラインからの平均変化量の減少は，プラセボ群（-0.7 g/L）と比較して，ウパダシチニブ 15 mg 群（–3.6 g/L）及びウパダシチニブ 30 mg 群（-5.5 g/L）の方が大きかった。ヘモグロビンの変化は，用量依存的と考えられた。ベースラインからの平均変化量の減少は投与 16 週時に最大となり，その後，徐々に小さくなり，ベースライン値に近づいた。

リンパ球数では，ウパダシチニブ群で投与 2 週時からベースラインからの平均変化量の増加が認められ，その後，徐々に減少し，投与 2 週時のベースラインからの平均変化量ではプラセボ群と同様の値に近づいた（ウパダシチニブ 15 mg 群：–0.028 × 10^9/L，ウパダシチニブ 30 mg 群：–0.057 × 10^9 L，プラセボ群：–0.076 × 10^9/L）。投与 2 週時までの平均変化量は，用量依存的ではなく，臨床的に意味はないと考えられた。

好中球数では，投与 2 週時のベースラインからの平均変化量の減少は，プラセボ群（-0.056 × 10^9/L）と比較して，ウパダシチニブ 15 mg 群（–0.286 × 10^9 L）及び 30 mg 群（-0.610 × 10^9/L）の方が大きかった。好中球数の平均変化量は，用量依存的であると考えられた。平均変化量の減少は投与 週時に最大となり，その後，徐々に小さくなり，ベースライン値に近づいた。

血小板数では，ウパダシチニブ群で投与 週時にベースラインからの平均変化量の減少が認められ，その後，ベースライン値に近づいた。投与 2 週時のベースラインからの平均変化量の増加は，プラセボ群（1.7 × 10^9/L）と比較して，ウパダシチニブ 15 mg 群（8. × 10^9/L）及び 30 mg 群（18.3 × 10^9/L）の方が大きかった。投与 2 週時までの平均変化量の増加は，臨床的に意味はないと考えられた。

投与 2 週時までに，臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数を M15-55 試験 CSR W2 Table 1 .3 3.1 1.1 に示す。

ウパダシチニブ 30 mg 群では，Grade 3 のヘモグロビン減少が 2 名（0.9%）に認められた。プラセボ群では，Grade 3 の白血球数減少が 1 名（0.5%）に認められた。Grade 3 の好中球数減少が認められた被験者は，ウパダシチニブ 15 mg 群（2 名［1 0%］）及びプラセボ群（1 名［0.5%］）と比較してウパダシチニブ 30 mg 群（ 名［1.8%］）の方が多かった。Grade の血小板数減少，白血球数減少，好中球数減少及びリンパ球数減少は認められなかった。

M15-55 試験の日本人部分集団での投与 2 週時までの臨床検査値のベースラインからの変化量を M15-55 試験 JSA Table 1 .3 .1. .1 J，臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数を M15-55 試験 JSA Table 1 .3 .3.1.1.1 J に示す。

投与 56 週時

M15-55 試験の投与 56 週時までの血液学的検査値及びベースラインからの平均変化量をそれぞれ M15-55 試験 CSR W56 Table 1 .3 1.1，Table 1 3 .1. 及び Figure 1 .3 5 1 に示す。

ヘモグロビンでは，ウパダシチニブ投与時にベースラインからの平均変化量の減少が認められ，用量依存的と考えられた。平均変化量の減少は最大で 9 g/L 未満であり，ウパダシチニブの投与 12–20 週後に認められたが，その後平均値はやや回復し，一定となった。投与 56 週時のベースラインからの平均変化量の減少は，プラセボ→ウパダシチニブ 15 mg 群で–1.5 g/L，ウパダシチニブ 15 mg 群で–3.0 g/L，プラセボ→ウパダシチニブ 30 mg 群で–6.8 g/L，ウパダシチニブ 30 mg 群で–5. g/L であった。

リンパ球数では，ウパダシチニブ投与後の 週間以内にベースラインからの平均変化量の増加が認められたが，用量依存的ではないと考えられた。平均変化量の増加後に減少が認められたため，投与 56 週時のベースラインからの平均変化量は小さく（プラセボ→ウパダシチニブ 15 mg 群：0.111 × 10^9/L，ウパダシチニブ 15 mg 群：0.0 9 × 10^9/L，プラセボ→ウパダシチニブ 30 mg 群：–0.11 × 10^9/L，ウパダシチニブ 30 mg 群：–0.1 5 × 10^9/L），臨床的に意味はないと考えられた。

好中球数では，ウパダシチニブ投与後の最初の 週間以内にベースラインからの平均変化量の減少が認められ，用量依存的と考えられた。平均変化量の減少後に増加が認められたため，投与 56 週時のベースラインからの平均変化量は小さく（プラセボ→ウパダシチニブ 15 mg 群：-0.37 × 10^9/L，ウパダシチニブ 15 mg 群：–0.355 × 10^9/L，プラセボ→ウパダシチニブ 30 mg 群：–0.520 × 10^9/L，ウパダシチニブ 30 mg 群：–0.61 × 10^9/L），臨床的に意味はないと考えられた。

血小板数では，平均測定値の経時的な推移で臨床的に意味のある傾向は認められなかった。

投与 56 週時データカットオフまでに，臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数を M15-55 試験 CSR W56 Table 1 .3 .3 1.1 に示す。

血液学的検査値では，Grade 3 以上の減少が認められた被験者はわずかであった。

Grade 3 のヘモグロビン減少及び好中球数減少が認められた被験者の割合は，全ウパダシチニブ 15 mg 群（それぞれ 0.3%［1 名］及び 1.0%［3 名］）と比較して，全ウパダシチニブ 30 mg 群（それぞれ 1.3%［ 名］及び 2.0%［6 名］）の方が高かった。全ウパダシチニブ 30 mg 群の 1 名（被験者番号 [redacted] では，Grade の血小板数減少（治験薬の投与中止 7 日後から発現），Grade の白血球数減少（治験薬の投与中止 21 日後から発現）及び Grade 3 のヘモグロビン減少（治験薬の投与中止 1 日後から発現）が発現し，これらは死亡に至った有害事象（汎血球減少

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症）と同時期に認められた（M15-55 試験 CSR W56 Table 1 .3 3.1 2 及び 2.7. .2 1.2 項参照）。本被験者以外に Grade の血液学的検査値が認められた被験者はいなかった。Grade 3 の血小板数減少及び白血球数減少は認められなかった。

その他の Grade 3 のヘモグロビン減少は，関連する重篤な有害事象と同時期に認められた（M15-55 試験 CSR W56 Table 1 .3 .3.1.2 及び Appendix 16 2 7.1 1）。これらの被験者のうち 3 名ではヘモグロビン値が Grade 2 に改善又は正常となったが，残りの 1 名（被験者番号 [redacted] では Grade 3 のヘモグロビン減少が最後の 2 回の評価で連続して認められた。

Grade 3 の好中球数減少及びリンパ球数減少の多くは，単発のものであった。Grade 3 の好中球数減少は，いずれもその後の評価で Grade 2 に改善又は正常となった（M15-55 試験 CSR W56 Table 1 .3 .3.1.2）。また，Grade 3 のリンパ球数減少の多くは，その後の評価で Grade 2 に改善又は正常となった。全ウパダシチニブ 30 mg 群の 1 名（被験者番号 [redacted] では，同意撤回による治験薬の投与中止 6 日後に単発の Grade 3 のリンパ球数減少が認められ，同時期に重篤な有害事象である急性腎障害及び菌血症が発現した（M15-55 試験 CSR W56 16 2 1 1 及び Appendix 16.2 7 1.1）。本被験者を除き，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に，関連する重篤な有害事象は発現しなかった。

M15-55 試験の日本人部分集団での投与 56 週時までの臨床検査値のベースラインからの変化量を M15-55 試験 JSA W56 Table 1 .3 .1. J，投与 56 週時データカットオフまでの臨床的に意義があると判断した血液学的検査値の基準に該当した被験者数を M15-55 試験 JSA W56 Table 1 3 .3.1.1 J に示す。

2.7. .3.2 血液生化学検査

安全性併合解析について，特に注目すべき有害事象で評価した血液生化学検査（肝機能検査項目［AST，ALT 及び総ビリルビン等］，CPK 及びクレアチニン）に関する結果は，2.7. .2.1.5.1.6 項（薬物性肝障害），2.7. .2.1.5.1.11 項（CPK 増加）及び 2.7. .2 1.5 1.12 項（腎機能障害）に示した。本項では，プラセボ対照併合解析集団の脂質（総コレステロール，HDL-C，LDL-C 及びトリグリセリド）について評価した。

M15-572 試験及び M15-55 試験の解析では，血液生化学検査の全項目について評価した。

関節リウマチ及び乾癬性関節炎の第 III 相臨床開発プログラムでは，総コレステロール，HDL-C 及び LDL-C を測定し，脂質に対するウパダシチニブの影響を評価した。トリグリセリドも測定したが，ウパダシチニブの臨床試験では，臨床検査前に絶食を必須としなかったことから，直近の食事による影響を受けている可能性があった。関節リウマチの臨床開発プログラムでは，ウパダシチニブの投与で用量依存的な脂質上昇が認められたが，JAK 阻害薬による脂質パラメータの上昇が心血管イベントの罹患率及び死亡率に影響を及ぼすかについては，現時点で不明である。

プラセボ対照併合解析集団（投与 2 週時）では，ベースライン時に LDL-C 上昇（≥3 36 mmol/L）がウパダシチニブ 15 mg 併合群で 28.1%（180/6 0 名），ウパダシチニブ 30 mg 併合群で 28.1%（180/6 1 名），プラセボ併合群で 27.9%（177/635 名）に認められ，HDL-C 低下（≤ 1.55 mmol/L）がウパダシチニブ 15 mg 併合群で 70.2%（ 9/6 0 名），ウパダシチニブ 30 mg 併合群で 69 3%（ /6 1 名），プラセボ併合群で 71.7%（ 55 635 名）に認められた（表 2.7. -25）。

2.7. .3.2.1 プラセボ対照併合解析

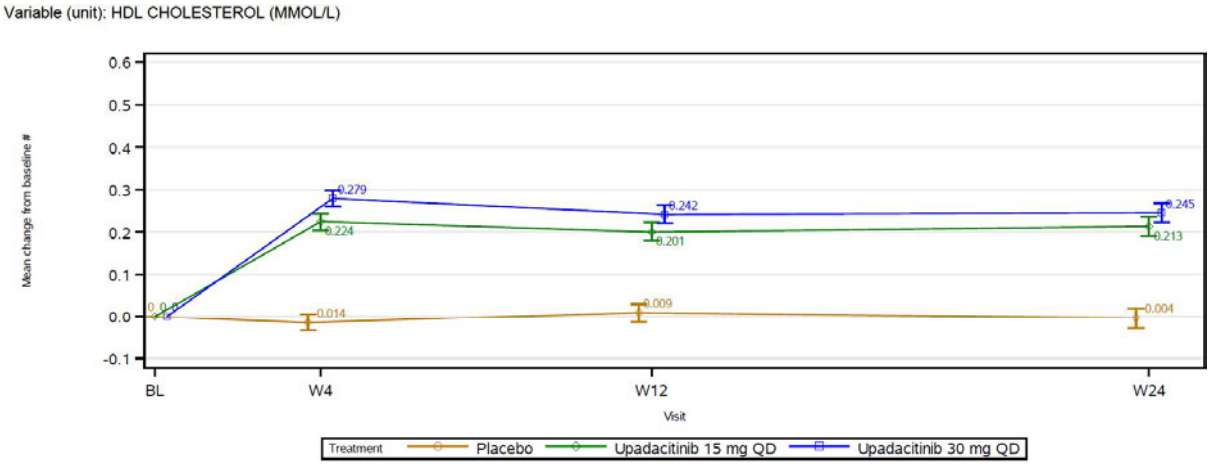
全体集団

プラセボ対照併合解析集団（投与 2 週時）での HDL-C，LDL-C 及び LDL-C / HDL-C 比のベースラインからの平均変化量の推移をそれぞれ図 2.7. -16，図 2.7. -17 及び図 2.7. -18 に示す。

プラセボ対照併合解析集団（投与 2 週時）では，プラセボ併合群，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群での投与 2 週時の脂質パラメータのベースラインからの平均変化量は，総コレステロールが 0 009 mmol/L，0.651 mmol/L 及び 0.773 mmol/L，HDL-C が–0.001 mmol/L，0.215 mmol/L 及び 0.2 7 mmol/L，LDL-C が 0.018 mmol L，0.350 mmol/L 及び 0. 9 mmol/L であった（ISS Table 2.5 1.1.1）。

プラセボ併合群，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群での投与 2 週時の各脂質の比のベースラインからの平均変化量は，総コレステロール / HDL-C 比が -0.010 mmol/L ， -0.095 mmol/L 及び 0.015 mmol L ， LDL-C / HDL-C 比が-0.006 mmol/L，-0.078 mmol/L 及び–0.013 mmol/L であった（ISS Table 2.5 1.1.1）。

図 2 7. -16. プラセボ対照併合解析集団（投与 2 週時）での HDL-C のベースラインからの平均変化量の推移



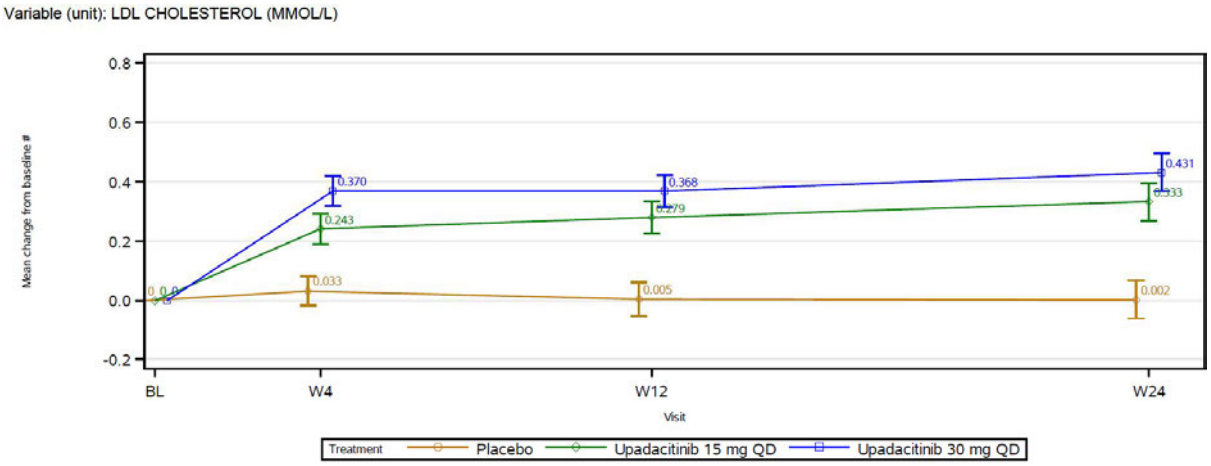
Number of Subjects at Each Visit

Placebo	609	603	565	532
Upadacitinib 15 mg QD	622	613	606	569
Upadacitinib 30 mg QD	631	630	606	563

Note: Baseline mean includes subjects with non-missing baseline and at least one post-baseline value in the 24-week placebo-controlled period.
LS mean is based on ANCOVA model with treatment as a main factor, and baseline and study as covariates.

相互参照：ISS Figure 2.5 1.1.6

図 2 7. -17. プラセボ対照併合解析集団（投与 2 週時）での LDL-C のベースラインからの平均変化量の推移



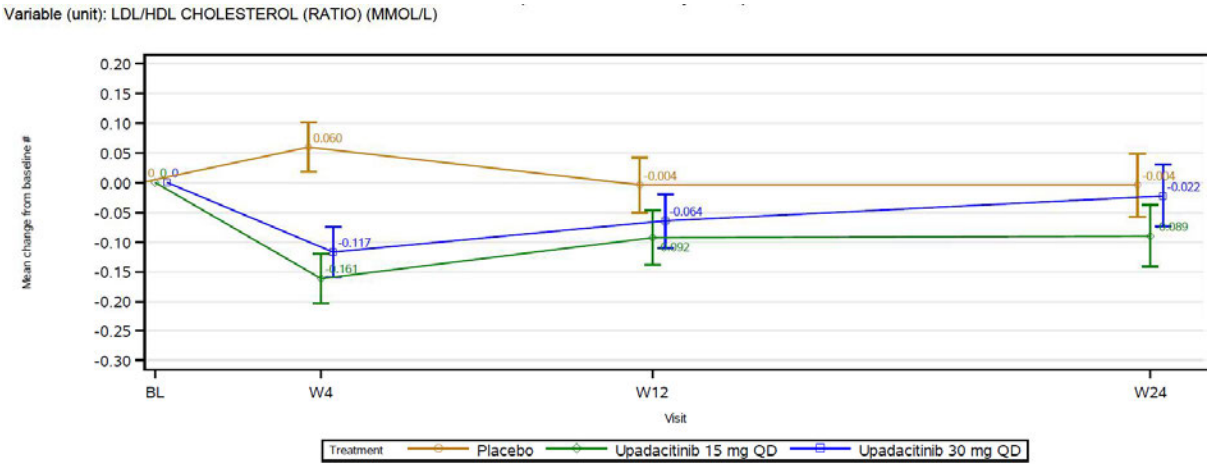
Number of Subjects at Each Visit

Placebo	601	591	546	516
Upadacitinib 15 mg QD	607	589	582	548
Upadacitinib 30 mg QD	616	605	577	538

Note: Baseline mean includes subjects with non-missing baseline and at least one post-baseline value in the 24-week placebo-controlled period.
LS mean is based on ANCOVA model with treatment as a main factor, and baseline and study as covariates.

相互参照：ISS Figure 2.5 1.1.6

図 2 7. -18. プラセボ対照併合解析集団（投与 2 週時）での LDL-C / HDL-C 比のベースラインからの平均変化量の推移



Number of Subjects at Each Visit

Placebo	601	591	546	516
Upadacitinib 15 mg QD	607	589	582	548
Upadacitinib 30 mg QD	616	605	577	538

Note: Baseline mean includes subjects with non-missing baseline and at least one post-baseline value in the 24-week placebo-controlled period.
LS mean is based on ANCOVA model with treatment as a main factor, and baseline and study as covariates.

相互参照：ISS Figure 2.5 1.1.6

プラセボ対照併合解析集団（投与 2 週時）での臨床検査値のベースラインから投与後のシフトテーブルを表 2.7. .7-71 に示す。全米コレステロール教育プログラム成人治療第 3 委員会脂質カテゴリーを用いて，脂質のシフト解析を実施した。

プラセボ対照併合解析集団（投与 2 週時）では，総コレステロールがベースラインの 5.17 mmol/L 未満（望ましい値）から 6.21 mmol/L 以上（高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 8 0%（51/6 0 名），ウパダシチニブ 30 mg 併合群で 12.3%（79/6 1 名），プラセボ併合群で 2.5%（16/635 名）であった。

HDL-C は，多くの被験者でベースライン及び投与後ともに 1.03 mmol/L 以上（良好な高値）であり，その割合はウパダシチニブ 15 mg 併合群で 79. %（508/6 0 名），ウパダシチニブ 30 mg 併合群で 78.9%（506/6 1 名），プラセボ併合群で 7 0%（ 70/635 名）であった。HDL-C がベースラインの 1.03 mmol/L 未満（低値）から 1.03 mmol L 以上（良好な高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 1 . %（92/6 0 名），ウパダシチニブ 30 mg 併合群で 16 1%（103/6 1 名），プラセボ併合群で 9.0%（57/635 名）であった。

LDL-C がベースラインの 3 36 mmol/L 未満（適正値及びほぼ適正値）から 1 mmol/L 以上（高値及び非常に高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 7.5%（ 8 6 0 名），ウパダシチニブ 30 mg 併合群で 9. %（60/6 1 名），プラセボ併合群で 3.1%（20/635 名）であった。

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トリグリセリドがベースラインの 1.69 mmol/L 未満（正常値）から 2.26 mmol/L 以上（高値及び非常に高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 9.2%（59/6 0 名），ウパダシチニブ 30 mg 併合群で 11.1%（71/6 1 名），プラセボ併合群で 5.0%（32/635 名）であった。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，プラセボ併合群，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の投与 2 週時の脂質パラメータのベースラインからの平均変化量は，総コレステロールが–0.103 mmol/L，0 638 mmol/L 及び 1.355 mmol/L，HDL-C が 0.011 mmol/L，0.319 mmol/L 及び 0. 1 mmol/L，LDL-C が–0 201 mmol/L，0.2 0 mmol/L 及び 0.902 mmol/L であった（J-ISS T 1 2 5 1 1 1 J）。

プラセボ併合群，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の投与 2 週時での各脂質の比のベースラインからの平均変化量は，総コレステロール / HDL-C 比が 0.018 mmol/L ， -0 323 mmol/L 及び 0.011 mmol/L ， LDL-C / HDL-C 比が-0.109 mmol/L，-0.317 mmol/L 及び 0 108 mmol/L であった（J-ISS Table 2 5 1.1.1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団での臨床検査値のベースラインから投与後のシフトテーブルを表 2.7. .7-72 に示す。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，総コレステロールがベースラインの 5.17 mmol/L 未満（望ましい値）から 6.21 mmol L 以上（高値）に変化した被験者は，ウパダシチニブ 15 mg 併合群で 17.6%（3/17 名），ウパダシチニブ 30 mg 併合群で 33.3%（6/18 名）であり，プラセボ併合群では認められなかった。

HDL-C は，多くの被験者でベースライン及び投与後ともに 1.03 mmol/L 以上（良好な高値）であり，その割合はウパダシチニブ 15 mg 併合群で 76.5%（13/17 名），ウパダシチニブ 30 mg 併合群で 88.9%（16/18 名），プラセボ併合群で 86.7%（13/15 名）であった。HDL-C がベースラインの 1.03 mmol/L 未満（低値）から 1 03 mmol/L 以上（良好な高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 17 6%（3/17 名），ウパダシチニブ 30 mg 併合群で 5.6%（1/18 名）であり，プラセボ併合群では認められなかった。

LDL-C がベースラインの 3 36 mmol/L 未満（適正値及びほぼ適正値）から 1 mmol/L 以上（高値及び非常に高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 11.8%（2/17 名），ウパダシチニブ 30 mg 併合群で 33.3%（6/18 名）であり，プラセボ併合群では認められなかった。

トリグリセリドがベースラインの 1.69 mmol/L 未満（正常値）から 2.26 mmol/L 以上（高値及び非常に高値）に変化した被験者の割合は，ウパダシチニブ 15 mg 併合群で 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群で 16.7%（3/18 名）であり，プラセボ併合群では認められなかった。

スタチン製剤の使用

プラセボ対照併合解析集団（投与 2 週時）のプラセボ対照期間中に，ベースライン後にスタチン製剤の投与を開始した被験者は，ウパダシチニブ 15 mg 併合群で 9 名，ウパダシチニブ 30 mg 併合群で 21 名，プラセボ併合群で 13 名であった（ISS F gure 2 5 1.1 8）。少数の被験者からのデータであるが，スタチン投与後に LDL-C がベースライン値付近まで低下する傾向が認められた。このデータから，ウパダシチニブを投与された被験者のうち，脂質の変動のためにスタチン製剤を投与する必要があった患者はわずかであり，スタチン製剤をウパダシチニブと併用投与した場合，スタチン製剤は LDL-C の低下に有効であることが示唆された。

2.7. .3.2.2 M15-572 試験

投与 2 週時

M15-572 試験の投与 2 週時までの血液生化学検査値及びベースラインからの平均変化量をそれぞれ M15-572 試験 CSR W2 Table 1 .3 .1.2.1 及び Table 1 .3 .1. .1 に示す。

ALT 及び AST では，投与 2 週時のベースラインからの平均変化量は，アダリムマブ群（5.0 U L 及び 2.9 U/L）及びプラセボ群（–1.0 U/L 及び–1.1 U/L）と比較して，ウパダシチニブ 15 mg 群（6.1 U/L 及び 5.7 U/L）及び 30 mg 群（7.9 U/L 及び 7.1 U/L）の方が大きかった。ALT 及び AST の平均変化量の増加は用量依存的であるが，臨床的に意味はないと考えられた。

クレアチニンでは，投与 2 週時のベースラインからの平均変化量の増加は，アダリムマブ群（ .1 µmol/L）及びプラセボ群（1.6 µmol/L）と比較して，ウパダシチニブ 15 mg 群（ .7 µmol/L）及びウパダシチニブ 30 mg 群（6.3 µmol/L）の方が大きかった。

CPK では，投与 2 週時のベースラインからの平均変化量の増加は，アダリムマブ群（25.8 U/L）及びプラセボ群（20.0 U/L）と比較して，ウパダシチニブ 15 mg 群（85.2 U/L）及び 30 mg 群（1 0 0 U/L）の方が大きかった。

コレステロール（コレステロール，HDL-C 及び LDL-C）では，投与 2 週時のベースラインからの平均変化量の増加は，アダリムマブ群（0.152 mmol/L，0 080 mmol/L 及び 0.03 mmol/L）及びプラセボ群（0.02 mmol/L，0.003 mmol/L 及び 0.025 mmol/L）と比較して，ウパダシチニブ 15 mg 群（0.702 mmol/L，0.223 mmol/L 及び 0. 08 mmol/L）及び 30 mg 群（0.78 mmol/L，0.2 9 mmol/L 及び 0. 7 mmol/L）の方が大きかった。ウパダシチニブ群での LDL-C / HDL-C 比及び総コレステロール / HDL-C 比は，ベースラインから基本的に変化しなかった。

投与 2 週時までに，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-572 試験 CSR W2 Table 1 .3 .3.2.1.1 に示す。

Grade 3 の ALT 増加は，ウパダシチニブ 15 mg 群で 名（0 9%），ウパダシチニブ 30 mg 群で 5 名（1.2%），アダリムマブ群で 名（0.9%），プラセボ群で 7 名（1.7%）に認められた。

Grade 3 の AST 増加は，ウパダシチニブ 30 mg 群で 3 名（0.7%），アダリムマブ群で 1 名（0.2%），プラセボ群で 2 名（0 5%）に認められ，ウパダシチニブ 15 mg 群では認められなか

った。ウパダシチニブ群では Grade 3 の ALT 増加又は AST 増加の多くは単発のものであり，以降の検査では回復していた（M15-572 試験 CSR W2 Table 1 .3 .3.2.2.1）。また，Grade 3 の ALT 増加の多くは AST 増加を伴うものであり，このうち多くは有害事象として報告された（M15-572 試験 CSR W2 Table 1 .3 .3.2.2.1，Appendix 16.2 7.1.1）。ウパダシチニブを投与された被験者のうち，Grade 3 の ALT 又は AST 増加により治験薬の投与を中止した被験者はいなかった（M15-572 試験 CSR W2 Table 1 .3 2.18.2.1）。Grade の ALT 増加は認められなかったが，Grade の AST 増加は，ウパダシチニブ 30 mg 群で 1 名（0 2%）に 1 時点のみ認められた（M15-572 試験 CSR W2 Table 1 .3 .3.2.2.1）。Hy's law の基準に該当した被験者はいなかった（M15-572 試験 CSR W2 Table 1 .3 . .1.1）。

Grade 3 の CPK 増加は，ウパダシチニブ 15 mg 群で 6 名（1. %），ウパダシチニブ 30 mg 群で 7 名（1.7%），アダリムマブ群で 1 名（0.2%），プラセボ群で 3 名（0.7%）に認められた。Grade の CPK 増加は，ウパダシチニブ 15 mg 群で 1 名（0.2%），ウパダシチニブ 30 mg 群で 名（1.0%），アダリムマブ群で 2 名（0.5%），プラセボ群で 1 名（0.2%）に認められた。筋肉痛を伴っていたウパダシチニブ 30 mg 群の 1 名を除き，その他の被験者では Grade 3 又は Grade の CPK 増加に伴う筋肉痛及び横紋筋融解症の症状は認められなかった（M15-572 試験 CSR W2 Table 1 .3 .3.2.2.1，Appendix 16.2 7.1.2）。Grade 3 及び Grade の CPK 増加の多くは最終来院時までに回復しており，治験薬の投与中止に至った Grade 3 及び Grade の CPK 増加は認められなかった。

ウパダシチニブ群では，Grade 3 又は Grade のクレアチニン増加は認められなかった。

Grade 3 のコレステロール増加がウパダシチニブ 30 mg 群で 2 名（0.5%）に認められたが，これらの被験者にコレステロール増加に関連する有害事象は認められなかった（M15-572 試験 CSR W2 Appendix 16.2 7.1.1）。

M15-572 試験の日本人部分集団での血液生化学検査値を M15-572 試験 JSA Table 1 3 .1 2.1 J，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-572 試験 JSA Table 1 .3 3.2 1.1 J，肝機能検査値上昇の基準に該当した被験者数を M15-572 試験 JSA Table 1 3 . 1.1 J に示す。

投与 56 週時

M15-572 試験の投与 56 週時データカットオフまでの血液生化学検査値及びベースラインからの平均変化量をそれぞれ M15-572 試験 CSR W56 Table 1 .3 1.2 及び Table 1 .3 .1. に示す。

ALT 及び AST では，ウパダシチニブ及びアダリムマブ投与時のベースラインからの平均変化量の増加は小さかった。ウパダシチニブ投与時の変化量は用量依存的と考えられた。投与 56 週時の ALT 及び AST のベースラインからの平均変化量の増加は，プラセボ→ウパダシチニブ 15 mg 群で 7.5 U/L 及び 5.7 U/L，ウパダシチニブ 15 mg 群で 6.8 U/L 及び 6.3 U/L，プラセボ→ウパダシチニブ 30 mg 群で 9.7 U/L 及び 8.0 U/L，ウパダシチニブ 30 mg 群で 10.3 U/L 及び 8.2 U/L，

アダリムマブ群で 6.2 U/L 及び 3.8 U L であった。ALT 及び AST の変化は，いずれの投与群でも臨床的に意味はないと考えられた。

クレアチニンでは，ウパダシチニブ投与時のベースラインからの平均変化量は投与 56 週時まで経時的に徐々に増加し，増加は用量依存的である可能性があった。投与 56 週時のベースラインからの平均変化量の増加は，プラセボ→ウパダシチニブ 15 mg 群で 5.1 µmol/L，ウパダシチニブ 15 mg 群で 6 2 µmol/L，プラセボ→ウパダシチニブ 30 mg 群で 7.7 µmol/L，ウパダシチニブ 30 mg 群で 8 8 µmol/L であり，アダリムマブ群（3.3 µmol/L）と比較して大きかった。クレアチニンの変化は，いずれの投与群でも臨床的に意味はないと考えられた。

CPK では，ウパダシチニブ投与時にベースラインからの平均変化量の増加が認められ，用量依存的と考えられた。平均変化量の増加は，いずれの投与群でもウパダシチニブの投与 12–32 週後に最大となり，その後は一定で推移した。投与 56 週時のベースラインからの平均変化量の増加は，プラセボ→ウパダシチニブ 15 mg 群で 88.2 U/L，ウパダシチニブ 15 mg 群で 87 8 U/L，プラセボ→ウパダシチニブ 30 mg 群で 1 7 6 U/L，ウパダシチニブ 30 mg 群で 119.2 U/L であり，アダリムマブ群（2 .3 U/L）と比較して大きかった。CPK の変化は，いずれの投与群でも臨床的に意味はないと考えられた。

投与 56 週時データカットオフまでに，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-572 試験 CSR W56 Table 1 .3 .3.2.1 に示す。

Grade 3 の ALT 増加が認められた被験者の割合は，全ウパダシチニブ 15 mg 群で 1.3%（8 名），全ウパダシチニブ 30 mg 群で 2.0%（12 名），アダリムマブ群で 2.1%（9 名）であり，Grade 3 の AST 増加が認められた被験者の割合は，全ウパダシチニブ 15 mg 群で 0 5%（3 名），全ウパダシチニブ 30 mg 群で 1.6%（10 名），アダリムマブ群で 0.7%（3 名）であった。全ウパダシチニブ 30 mg 群の 1 名で Grade の ALT 増加及び AST 増加が認められ，全ウパダシチニブ 30 mg 群の 1 名で Grade の AST 増加が認められた（M15-572 試験 CSR W56 Table 1 3 .3 2.2）。Grade 3 のビリルビン増加がアダリムマブ群の 1 名に，Grade のビリルビン増加が全ウパダシチニブ 15 mg 群の 1 名に認められた。Grade 3 及び Grade の ALT 増加，AST 増加及びビリルビン増加の多くは単発のものであり，これらは改善したか，投与 56 週時データカットオフ前の最終来院時での発現であった。Hy's law は特定されなかった。

Grade 3 の CPK 増加が認められた被験者の割合は，全ウパダシチニブ 30 mg 群（3 6%［22 名］）で最も高く，次いで全ウパダシチニブ 15 mg 群（2.1%［13 名］），アダリムマブ群（0.9%［ 名］）であった。Grade の CPK 増加が認められた被験者の割合は，全ウパダシチニブ 15 mg 群（0.8%［5 名］）とアダリムマブ群（0.9%［ 名］）で同様であり，全ウパダシチニブ 30 mg 群（2.1%［13 名］）で最も高かった。Grade 3 及び Grade の CPK 増加の多くは単発のものであり，これらは改善したか，投与 56 週時データカットオフ前の最終来院時での発現であった（M15-572 試験 CSR W56 Table 1 .3 .3.2.2）。全ウパダシチニブ 30 mg 群の 2 名で，Grade の CPK 増加が連続で認められた。このうち 1 名（被験者番号 [redacted]）では，Grade の CPK 増加が投与 197 日目（2997 U/L）及び投与 202 日目（28 U/L）に認められ，同時期に

重篤な有害事象である気管支炎が発現した（M15-572 試験 CSR W56 Appendix 16.2 7.1.1）。気管支炎の発現のため，治験薬の投与は中止されたが，その後，重篤な有害事象として間質性肺疾患及び皮膚筋炎が発現し，最終投与 52 日後に間質性肺疾患により死亡した（2.7. .2.1.2 項参照）。他の 1 名（被験者番号 [redacted] では，Grade の CPK 増加が投与 57 日目（5363 U/L）及び投与 58 日目（3825 U/L）に認められ，同時期に重篤な有害事象である菌血症が発現した（M15-572 試験 CSR W56 Appendix 16.2 7.1.1）。治験薬の投与は中止され，CPK 値は投与終了後 29 日目までに基準範囲内に回復した。横紋筋融解症が発現した被験者はいなかった。

Grade 3 のクレアチニン増加が 2 名（全ウパダシチニブ 30 mg 群），Grade のクレアチニン増加が 1 名（アダリムマブ群）に認められた。全ウパダシチニブ 30 mg 群の 1 名（被験者番号 [redacted] では，Grade 3 のクレアチニン増加が，重篤な有害事象である急性腎障害と同日に発現した（M15-572 試験 CSR W56 Table 1 .3 3.2 2，Appendix 16.2 7.1.1）。当該被験者は，この重篤な有害事象が発現した後，同意を撤回したため，それ以降のクレアチニン値は報告されなかった。全ウパダシチニブ 30 mg 群の 1 名（被験者番号 [redacted] では，Grade 3 のクレアチニン増加が単発で認められ，治験薬の投与を中止することなく，次の来院日にベースライン値付近まで改善した。

M15-572 試験の日本人部分集団での投与 56 週時データカットオフまでの血液生化学検査値を M15-572 試験 JSA W56 Table 1 .3 .1.2 J，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-572 試験 JSA W56 Table 1 .3 3.2 1 J，肝機能検査値上昇の基準に該当した被験者数を M15-572 試験 JSA W56 Table 1 .3 . .1 J に示す。

2.7. .3.2.3 M15-55 試験

投与 2 週時

M15-55 試験の投与 2 週時までの血液生化学検査値及びベースラインからの平均変化量をそれぞれ M15-55 試験 CSR W2 T 1 1 3 1 2 1 及び T 1 1 3 1 1 に示す。

ALT 及び AST では，投与 2 週時のベースラインからの平均変化量は，プラセボ群（–0.7 U/L 及び–0.1 U/L）と比較して，ウパダシチニブ 15 mg 群（6 8 U/L 及び 6.5 U/L）及び 30 mg 群（9.1 U L 及び 8.3 U/L）の方が大きかった。ALT 及び AST の平均変化量の増加は，用量依存的であるが，臨床的に意味はないと考えられた。

クレアチニンでは，投与 2 週時のベースラインからの平均変化量の増加は，プラセボ群（2.2 µmol/L）と比較して，ウパダシチニブ 15 mg 群（ .7 µmol/L）及び 30 mg 群（5.3 µmol/L）の方が大きかった。

CPK では，投与 2 週時のベースラインからの平均変化量の増加は，プラセボ群（–19.9 U/L）と比較して，ウパダシチニブ 15 mg 群（166.8 U/L）及び 30 mg 群（138.7 U/L）の方が大きかった。

コレステロール（コレステロール，HDL-C 及び LDL-C）では，投与 2 週時のベースラインからの平均変化量の増加は，プラセボ群（–0.023 mmol/L，–0.008 mmol/L 及び 0.003 mmol/L）と比較して，ウパダシチニブ 15 mg 群（0 539 mmol/L，0.199 mmol/L 及び 0.219 mmol/L）及び 30 mg 群（0.752 mmol/L，0.2 3 mmol/L 及び 0. 53 mmol/L）の方が大きかった。ウパダシチニブ群での LDL-C / HDL-C 比及び総コレステロール / HDL-C 比は，ベースラインから基本的に変化しなかった。

投与 2 週時までに，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-55 試験 CSR W2 Table 1 .3 .3.2.1.1 に示す。

Grade 3 の ALT 増加は，ウパダシチニブ 15 mg 群で 2 名（1 0%），ウパダシチニブ 30 mg 群で 1 名（0.5%），プラセボ群で 1 名（0 5%）に認められた。ウパダシチニブ群では，Grade 3 の ALT 増加は単発のものであった（M15-55 試験 CSR W2 T 1 1 3 3 2 2 1）。また，Grade 3 の ALT 増加は AST 増加を伴うものもあり，多くは有害事象として報告された（M15-55 試験 CSR W2 Table 1 3 .3.2.2.1，Appendix 16 2 7.1 1）。ウパダシチニブ 30 mg 群の 1 名で，Grade 3 の ALT 増加により治験薬の投与を中止した。また，ウパダシチニブ 15 mg 群の 1 名では，重篤な有害事象（全身性エリテマトーデス）により治験薬の投与を中止した後，Grade 3 の ALT 増加が認められた。Grade の ALT 増加は認められなかった。

Grade 3 の AST 増加は，ウパダシチニブ 15 mg 群で 2 名（1.0%），プラセボ群で 1 名（0.5%）に認められ，ウパダシチニブ 30 mg 群では認められなかった。Grade 3 の AST 増加はすべて単発のものであった（M15-55 試験 CSR W2 Table 1 .3 .3.2.2.1）。Grade 3 のビリルビン増加がウパダシチニブ 15 mg 群の 1 名（0.5%）で認められたが，その他の肝酵素上昇を伴うものではなかった（M15-55 試験 CSR W2 Table 1 3 .3 2.2 1）。Grade の AST 増加は認められなかった。Hy's law の基準に該当した被験者はいなかった（M15-55 試験 CSR W2 Table 1 3 . .1.1）。

Grade 3 の CPK 増加は，ウパダシチニブ 15 mg 群で 1 名（0 5%），ウパダシチニブ 30 mg 群で 5 名（2.3%），プラセボ群で 1 名（0 5%）に認められた。Grade の CPK 増加は，ウパダシチニブ 15 mg 群で 1 名（0.5%），プラセボ群で 2 名（1.0%）に認められた。ウパダシチニブ 15 mg 群で 1 名に認められた Grade の CPK 増加は単発の発現であり，AST 及び ALT の上昇を伴っていた（M15-55 試験 CSR W2 T 1 1 3 3 2 2 1， 16 2 8 2 1）。本被験者では，有害事象として肝酵素上昇が報告された。Grade 3 又は Grade の CPK 増加を伴う筋肉痛又は横紋筋融解症の症状が認められた被験者はいなかった（M15-55 試験 CSR W2 Appendix 16.2 7 1.1）。Grade 3 及び Grade の CPK 増加の多くは回復し，治験薬の投与中止に至った Grade 3 及び Grade の CPK 増加はなかった。

Grade 3 のクレアチニン増加はウパダシチニブ 30 mg 群で 1 名（0.5%）に認められた。これは単発の発現であり，完全に回復した（M15-55 試験 CSR W2 Table 1 .3 .3.2.2.1）。Grade のクレアチニン増加は認められなかった。

Grade 3 のコレステロール増加はウパダシチニブ 30 mg 群の 2 名（0.9%）に認められ，Grade のコレステロール増加はウパダシチニブ 15 mg 群の 1 名（0.5%）に認められた。

M15-55 試験の日本人部分集団での投与 2 週時までの臨床検査値のベースラインからの平均変化量を M15-55 試験 JSA Table 1 .3 .1. .1 J，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-55 試験 JSA Table 1 .3 .3.2.1.1 J，肝機能検査値上昇の基準に該当した被験者数を M15-55 試験 JSA Table 1 3 . 1.1 J に示す。

投与 56 週時

M15-55 試験の投与 56 週時までの血液生化学検査値及びベースラインからの平均変化量をそれぞれ M15-55 試験 CSR W56 T 1 1 3 1 2 及び T 1 1 3 1 に示す。

ALT 及び AST では，ウパダシチニブ投与時のベースラインからの平均変化量の増加は小さかった。ALT 及び AST ともに，投与 56 週時のベースラインからの平均変化量の増加は，いずれの投与群でも 13 U/L 以下であった。これらの経時的な変化は，臨床的に意味はないと考えられた。

クレアチニンでは，ウパダシチニブ投与時にベースラインからの平均変化量の増加が認められ，投与後の最初の 2 時間は用量依存的である可能性があった。平均変化量の増加は，いずれの投与群でもウパダシチニブの投与 8–32 週後に最大となり，その後は一定で推移した後，いくつかの投与群ではベースライン値に向かって減少した。投与 56 週時のベースラインからの平均変化量の増加は，プラセボ→ウパダシチニブ 15 mg 群で 6. µmol/L，ウパダシチニブ 15 mg 群で 5.5 µmol/L，プラセボ→ウパダシチニブ 30 mg 群で 2 5 µmol/L，ウパダシチニブ 30 mg 群で 7.1 µmol/L であった。これらの経時的な変化は，臨床的に意味はないと考えられた。

CPK では，ウパダシチニブ投与時にベースラインからの平均変化量の増加が認められた。平均変化量の増加は，いずれの投与群でもウパダシチニブの投与 8–32 週後に最大となり，その後は一定で推移した。投与 56 週時のベースラインからの平均変化量の増加は，プラセボ→ウパダシチニブ 15 mg 群で 70. U/L，ウパダシチニブ 15 mg 群で 95. U/L，プラセボ→ウパダシチニブ 30 mg 群で 67 6 U/L，ウパダシチニブ 30 mg 群で 170 3 U/L であった。これらの経時的な変化は，臨床的に意味はないと考えられた。

投与 56 週時データカットオフまでに，臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-55 試験 CSR W56 Table 1 .3 .3.2.1 に示す。

Grade の ALT 増加，AST 増加及びビリルビン増加は認められなかった。Grade 3 の ALT 増加，AST 増加及びビリルビン増加のほとんどは単発のものであり，これらは改善したか，最終来院時での発現であった。全ウパダシチニブ 30 mg 群の 1 名が 1 時点のみで Hy's law の基準（AST 及びビリルビン値に基づく）に該当したが（M15-55 試験 CSR W56 Table 1 .3 . .1，Table 1 3 . .2），メディカルレビューにより，真の Hy's law とは判断されなかった。

Grade 3 以上の CPK 増加は各投与群で 8 名に認められた。多くは単発のものであり，その後の評価で Grade 2 に改善又は正常となった（M15-55 試験 CSR W56 Table 1 .3 3.2 2）。全ウパダシチニブ 15 mg 群の 2 名では，Grade 3 以上の CPK 増加が連続で認められ，いずれも激しい身体活動によるものであった（M15-55 試験 CSR W56 Appendix 16.2 7.1.2）。Grade 3 又は の CPK 増加に伴う横紋筋融解症は認められなかった（M15-55 試験 CSR W56 Table 1 .3 .3.2.2, Appendix 16.2 7 1.1, Appendix 16.2 7 1.2）。

Grade 3 以上のクレアチニン増加は各投与群で 2 名に認められた。全ウパダシチニブ 15 mg 群の 1 名では，重篤な有害事象（卵巣癌）のために治験薬の投与を中止した後，最終評価時に Grade 3 のクレアチニン増加が単発で 1 回発現した（M15-55 試験 CSR W56 Table 1 .3 .3 2.2, Appendix 16.2 7.1.1）。他の 1 名では，Grade 3 及び のクレアチニン増加が連続して認められ（その後 Grade 2 に改善），同時期に重篤な有害事象として胃腸炎，脱水，急性腎障害及び低ナトリウム血症が発現した。全ウパダシチニブ 30 mg 群の 1 名では，投与 57 日目に Grade 3 のクレアチニン増加が単発で 1 回発現し，次の評価時（投与 72 日目）に正常値に戻った。他の 1 名は Grade 3 のクレアチニン増加が 2 回連続で認められ，同時期に死亡に至った有害事象（汎血球減少症）が発現した（2.7. .2.1 2 項参照）。

M15-55 試験の日本人部分集団での臨床検査値のベースラインから投与 56 週時までの平均変化量を M15-55 試験 JSA W56 Table 1 .3 1. J，投与 56 週時データカットオフまでの臨床的に意義があると判断した血液生化学検査値の基準に該当した被験者数を M15-55 試験 JSA W56 Table 1 .3 .3.2.1 J，肝機能検査値上昇の基準に該当した被験者数を M15-55 試験 JSA W56 Table 1 .3 . .1 J に示す。

2.7. . バイタルサイン，身体的所見及び安全性に関連する他の観察項目

2.7. . .1 プラセボ対照併合解析

全体集団

プラセボ対照併合解析集団（投与 2 週時）では，臨床的に意義があると判断した収縮期血圧（160 mmHg 以上かつ 20 mmHg 以上上昇）及び拡張期血圧（100 mmHg 以上かつ 10 mmHg 以上上昇）の基準に該当した被験者の割合は，ウパダシチニブ 15 mg 併合群で 9%（31/635 名）及び 2.7%（17/635 名），ウパダシチニブ 30 mg 併合群で 3. %（22/638 名）及び 3. %（22/638 名），プラセボ併合群で 2.7%（17 626 名）及び 3.2%（20/626 名）であった（ISS Table 2.6 1.1.2.1）。

プラセボ対照併合解析集団（投与 2 週時）では，体重増加（7%超の増加）が認められた被験者の割合は，ウパダシチニブ 15 mg 併合群で 10. %（66 635 名），ウパダシチニブ 30 mg 併合群で 12 2%（78/638 名），プラセボ併合群で 5.3%（33 626 名）であった（ISS Table 2.6 1.1.2.1）。体重減少（7%超の減少）が認められた被験者の割合は，ウパダシチニブ 15 mg 併合群で 3.1%

（20 635 名），ウパダシチニブ 30 mg 併合群で .9%（31/638 名），プラセボ併合群で .5%（28/626 名）であった。

プラセボ対照併合解析集団（投与 2 週時）のバイタルサインのベースラインからの平均変化量を ISS Table 2.6 1.1.1 に示す。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団では，臨床的に意義があると判断した収縮期血圧（160 mmHg 以上かつ 20 mmHg 以上上昇）及び拡張期血圧（100 mmHg 以上かつ 10 mmHg 以上上昇）の基準に該当した被験者の割合は，ウパダシチニブ 15 mg 併合群ではいずれも 5.9%（1/17 名），ウパダシチニブ 30 mg 併合群ではいずれも 5.6%（1/18 名），プラセボ併合群では 13.3%（2/15 名）及び 20 0%（3/15 名）であった（J-ISS T 1 2 6 1 1 2 1 J）。

プラセボ対照併合解析集団（投与 2 週時）では，体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，ウパダシチニブ 30 mg 併合群で 11.1%（2/18 名）及び 5.6%（1/18 名）であり，ウパダシチニブ 15 mg 併合群及びプラセボ併合群では認められなかった（J-ISS Table 2.6 1 1.2 1 J）。

プラセボ対照併合解析集団（投与 2 週時）の日本人部分集団でのバイタルサインのベースラインからの平均変化量を J-ISS Table 2.6 1.1.1 J に示す。

2.7. . .2 全ウパダシチニブ併合解析

申請時データカットオフ

全体集団

全ウパダシチニブ併合解析集団（長期）では，臨床的に意義があると判断した収縮期血圧（160 mmHg 以上かつ 20 mmHg 以上上昇）及び拡張期血圧（100 mmHg 以上かつ 10 mmHg 以上上昇）の基準に該当した被験者の割合は，全ウパダシチニブ 15 mg 併合群で 5.8%（51/877 名）及び 3.9%（3 /877 名），全ウパダシチニブ 30 mg 併合群で .2%（38/896 名）及び .7%（ 2/896 名］）であった（ISS Table 2.6 1 2.1 1）。

有害事象の高血圧の発現割合は，全ウパダシチニブ 15 mg 併合群で .7%（ 3/907 名），全ウパダシチニブ 30 mg 併合群で 3 8%（35/920 名）であった（ISS Table 2. 1.2.3.1）。治験薬の投与中止に至った高血圧は発現しなかった（ISS Table 2. 1.2 3.6）。

全ウパダシチニブ併合解析集団（長期）では，体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，全ウパダシチニブ 15 mg 併合群で 17.8%（156/877 名）及び 7.8%（68/877 名），全ウパダシチニブ 30 mg 併合群で 20 3%（182 896 名）及び 7.9%（71/896 名）であった（ISS Table 2.6 1 2.1 1）。

有害事象の体重増加の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.8%（7/907 名），全ウパダシチニブ 30 mg 併合群で 0.9%（8/920 名）であった。また，有害事象の体重減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.2%（2 907 名），全ウパダシチニブ 30 mg 併合群で 0.1%（1/920 名）であった（ISS Table 2. 1.2.3.1）。体重増加及び体重減少のいずれも，重篤又は治験薬の投与中止に至った事象は認められなかった（ISS Table 2. 1.2.8.1，Table 2. 1.2.8.2）。

アダリムマブとの比較（M15-572 試験［長期］）

M15-572 試験では，投与 2 週時データカットオフまでに体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，全ウパダシチニブ 15 mg 群で 17.7%（105/593 名）及び 7.6%（ 5/593 名），全ウパダシチニブ 30 mg 群で 18 9%（112 593 名）及び 7.6%（ 5/593 名），アダリムマブ群で 10.5%（ 5/ 27 名）及び 8. %（36/ 27 名）であった（M15-572 試験 CSR W2 Table 1 .3 .5.2.2）。

日本人部分集団

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，臨床的に意義があると判断した収縮期血圧（160 mmHg 以上かつ 20 mmHg 以上上昇）及び拡張期血圧（100 mmHg 以上かつ 10 mmHg 以上上昇）の基準に該当した被験者の割合は，全ウパダシチニブ 15 mg 併合群で 8.7%（2/23 名）及び 17. %（ /23 名），全ウパダシチニブ 30 mg 併合群で 3.8%（1/26 名）及び 11.5%（3/26 名）であった（J-ISS Table 2.6 1.2.1.1 J）。

全ウパダシチニブ併合解析集団（長期）の日本人部分集団では，体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，全ウパダシチニブ 15 mg 併合群で 8.7%（2/23 名）及び .3%（1/23 名），ウパダシチニブ 30 mg 併合群で 23.1%（6 26 名）及び 7.7%（2/26 名）であった（J-ISS Table 2.6 1 2.1 1 J）。

20[redacted]年[redacted]月[redacted]日データカットオフ

全体集団

全ウパダシチニブ併合解析集団（20[redacted]年[redacted]月[redacted]日データカットオフ）では，臨床的に意義があると判断した収縮期血圧（160 mmHg 以上かつ 20 mmHg 以上上昇）及び拡張期血圧（100 mmHg 以上かつ 10 mmHg 以上上昇）の基準に該当した被験者の割合は，全ウパダシチニ

ブ 15 mg 併合群で 6.5%（59/901 名）及び 5. %（ 9/901 名），全ウパダシチニブ 30 mg 併合群で 6.0%（55/918 名）及び 6.1%（56/918 名］）であった（ISS update Table 2.6 1.1）。

有害事象の高血圧の発現割合は，全ウパダシチニブ 15 mg 併合群で 6. %（58/907 名），全ウパダシチニブ 30 mg 併合群で 5 3%（ 9/921 名）であった（ISS upda e Table 2. 3.1）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）では，体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，全ウパダシチニブ 15 mg 併合群で 2 . %（220/901 名）及び 9.9%（89/901 名），全ウパダシチニブ 30 mg 併合群で 28.3%（260/918 名）及び 10.6%（97/918 名）であった（ISS update Table 2.6 1 1）。

有害事象の体重増加の発現割合は，全ウパダシチニブ 15 mg 併合群で 1.1%（10/907 名），全ウパダシチニブ 30 mg 併合群で 1.0%（9/921 名）であった。また，有害事象の体重減少の発現割合は，全ウパダシチニブ 15 mg 併合群で 0.2%（2/907 名），全ウパダシチニブ 30 mg 併合群で 0.1%（1/921 名）であった（ISS update Table 2. 3 1）。

アダリムマブとの比較（M15-572 試験［20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ］）

M15-572 試験では，20[redacted] 年 [redacted] 月 [redacted] 日データカットオフまでに体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，全ウパダシチニブ 15 mg 群で 2 .8%（152/613 名）及び 9.8%（60/613 名），全ウパダシチニブ 30 mg 群で 27.5%（168/611 名）及び 10.5%（6 /611 名），アダリムマブ群で 17.8%（76/ 27 名）及び 11.2%（ 8/ 27 名）であった（ISS update Table 2 6 2.1）。

日本人部分集団

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，臨床的に意義があると判断した収縮期血圧（160 mmHg 以上かつ 20 mmHg 以上上昇）及び拡張期血圧（100 mmHg 以上かつ 10 mmHg 以上上昇）の基準に該当した被験者の割合は，全ウパダシチニブ 15 mg 併合群で 8.7%（2/23 名）及び 21.7%（5/23 名），全ウパダシチニブ 30 mg 併合群で 7.7%（2/26 名）及び 15. %（ /26 名）であった（J-ISS update Table 2.6 1 2.1 1 J）。

全ウパダシチニブ併合解析集団（20[redacted] 年 [redacted] 月 [redacted] 日データカットオフ）の日本人部分集団では，体重増加（7%超の増加）及び体重減少（7%超の減少）が認められた被験者の割合は，全ウパダシチニブ 15 mg 併合群で 8.7%（2/23 名）及び .3%（1/23 名），ウパダシチニブ 30 mg 併合群で 38.5%（10/26 名）及び 11 5%（3/26 名）であった（J-ISS update Table 2.6 1.2.1.1 J）。

2.7. . .3 M15-572 試験

投与 2 週時

投与 2 週時までの臨床的に意義があると判断したバイタルサインの基準に該当した被験者の割合は，体重増加（7%超の増加）を除き，いずれの投与群でも低く，おおむね同様であった（M15-572 試験 CSR W2 Table 1 .3 .5.2.1）。投与 2 週時までにベースラインから 7%を超える体重増加が認められた被験者の割合は，アダリムマブ群（5. %）及びプラセボ群（ 8%）と比較してウパダシチニブ 15 mg 群（11.3%）及び 30 mg 群（11 9%）の方が高かった。

M15-572 試験の全体集団のバイタルサインの結果を M15-572 試験 CSR W2 Table 1 .3 .5.1.1 に示す。

M15-572 試験の日本人部分集団のバイタルサインの結果を M15-572 試験 JSA Table 1 3 .5.1.1 J，臨床的に意義があると判断したバイタルサインの基準に該当した被験者数を M15-572 試験 JSA Table 1 .3 .5.2.1 J に示す。

投与 56 週時

投与 56 週時データカットオフまでの臨床的に意義があると判断したバイタルサインの基準に該当した被験者の割合は，体重増加（7%超の増加）を除き，いずれの投与群でも低く，おおむね投与群間で同様であった（M15-572 試験 CSR W56 Table 1 .3 .5.2）。いずれの投与群でも体重増加が認められ，ベースラインから 7%を超える体重増加が認められた被験者の割合は，全ウパダシチニブ 15 mg 群で 25.8%，全ウパダシチニブ 30 mg 群で 28.5%，アダリムマブ群で 18.7%であった。

M15-572 試験の全体集団の投与 56 週時データカットオフまでのバイタルサインの結果を M15-572 試験 CSR W56 Table 1 3 .5 1 に示す。

M15-572 試験の日本人部分集団の投与 56 週時データカットオフまでのバイタルサインの結果を M15-572 試験 JSA W56 Table 1 .3 .5.1 J，臨床的に意義があると判断したバイタルサインの基準に該当した被験者数を M15-572 試験 JSA W56 Table 1 3 .5 2 J に示す。

2.7. . . M15-55 試験

投与 2 週時

投与 2 週時までの臨床的に意義があると判断したバイタルサインの基準に該当した被験者の割合は，体重増加（7%超の増加）を除き，いずれの投与群でも低く，おおむね同様であった（M15-55 試験 CSR W2 Table 1 .3 .5.2.1）。投与 2 週時までにベースラインから 7%を超え

る体重増加が認められた被験者の割合は，プラセボ群（6 3%）と比較してウパダシチニブ 15 mg 群（8.6%）及び 30 mg 群（12.9%）の方が高かった。

M15-55 試験の全体集団の投与 2 週時までのバイタルサインの結果を M15-55 試験 CSR W2 Table 1 .3 .5.1.1 に示す。

M15-55 試験の日本人部分集団の投与 2 週時までのバイタルサインの結果を M15-55 試験 JSA Table 1 .3 .5.1.1 J，臨床的に意義があると判断したバイタルサインの基準に該当した被験者数を M15-55 試験 JSA Table 1 .3 .5.2.1 J に示す。

投与 56 週時

投与 56 週時データカットオフまでの臨床的に意義があると判断したバイタルサインの基準に該当した被験者の割合は，体重増加（7%超の増加）を除き，いずれの投与群でも低く，おおむね投与群間で同様であった（M15-55 試験 CSR W56 Table 1 .3 .5.2）。ウパダシチニブの投与時に体重増加が認められ，ベースラインから 7%を超える体重増加が認められた被験者の割合は，全ウパダシチニブ 15 mg 群で 22.9%，30 mg 群で 30.0%であった。

M15-55 試験の全体集団の投与 56 週時までのバイタルサインの結果を M15-55 試験 CSR W56 Table 1 .3 .5.1 に示す。

M15-55 試験の日本人部分集団の投与 56 週時までのバイタルサインの結果を M15-55 試験 JSA W56 Table 1 .3 .5.1 J，投与 56 週時データカットオフまでの臨床的に意義があると判断したバイタルサインの基準に該当した被験者数を M15-55 試験 JSA W56 Table 1 3 .5 2 J に示す。

2.7. .5 特別な患者集団及び状況下における安全性

2.7. .5.1 日本人患者の結果

本項では，M15-572 試験及び M15-55 試験の日本人部分集団の結果を示す。

2.7. .5.1.1 M15-572 試験

2.7. .5.1.1.1 全般的な曝露状況

M15-572 試験の日本人部分集団では，投与 2 週時までの曝露期間の平均値は，ウパダシチニブ 15 mg 群で 168.5 日，ウパダシチニブ 30 mg 群で 167.5 日，アダリムマブ群で 168.3 日，プラセボ群で 167.0 日であった（M15-572 試験 JSA Table 1 .1 8.1 J）。

M15-572 試験の日本人部分集団では，投与 56 週時データカットオフまでの曝露期間の平均値は，全ウパダシチニブ 15 mg 群で 37.6 日，全ウパダシチニブ 30 mg 群で 725.7 日，アダリムマブ群で 653 3 日であった（M15-572 試験 JSA W56 Table 1 .1 3 J）。

2.7. .5.1.1.2 有害事象

2.7. .5.1.1.2.1 有害事象の概要及び比較的よく見られる有害事象

投与 2 週時

M15-572 試験の日本人部分集団の投与 2 週時までの有害事象の概要を表 2.7. -69，全体集団の結果を表 2.7. - 1 に示す。また，日本人部分集団の投与 2 週時データカットオフまでの有害事象の概要を表 2.7. .7-73 及び表 2.7. .7-7 （100 人年あたりの発現状況）に示す。

日本人部分集団の投与 2 週時までの有害事象の発現割合は，ウパダシチニブ 15 mg 群で 100%（ / 名），ウパダシチニブ 30 mg 群で 100%（ / 名），アダリムマブ群で 75.0%（3/ 名），プラセボ群で 66.7%（2/3 名）であった。重篤な有害事象，Grade 3 以上の有害事象及び治験薬の投与中止に至った有害事象は，アダリムマブ群のみで発現した（それぞれ 1 名，2 名及び 1 名）。

日本人部分集団では，投与 2 週時までに死亡した被験者はいなかった。

日本人部分集団での投与 2 週時データカットオフまでの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 3 2.9 件/100 人年（12 件），全ウパダシチニブ 30 mg 群で 1 .6 件/100 人年（3 件），アダリムマブ群で 153.8 件/100 人年（8 件）であった。重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 群で 2 . 件/100 人年（2 件），アダリムマブ群で 19.2 件/100 人年（1 件）であり，全ウパダシチニブ 15 mg 群では発現しなかった。Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 群で 36.6 件/100 人年（3 件），アダリムマブ群で 57.7 件/100 人年（3 件）であり，全ウパダシチニブ 15 mg 群では発現しなかった。治験薬の投与中止に至った有害事象はアダリムマブ群のみで発現し，100 人年あたりの発現件数は 19.2 件/100 人年（1 件）であった。

日本人部分集団では，投与 2 週時データカットオフまでに死亡した被験者はいなかった。

表 2 7. -69. 投与 2 週時までの有害事象の概要（安全性解析対象集団，日本人部分集団）：M15-572 試験

	Placebo (N = 3) n (%)	ADA 40 mg EOW (N = 4) n (%)	---- UPA ------ 15 mg QD N = 4) n (%)	30 mg QD (N = 4) n (%)	-- UPA VS Placebo (95% CI)[A] -- 15 mg QD VS Placebo	30 mg QD VS Placebo	-- UPA VS ADA 95% CI) A] -- 15 mg QD VS ADA	30 mg QD VS ADA
Subjects with								
Any adverse event AE)	2 (66 7)	3 75 0)	4 (100)	4 100)	33 3 (-20 0, 86 7)	33 3 (-20 0, 86 7)	25 0 (-17 4, 67 4)	25 0 (-17 4, 67 4)
Any serious AE (SAE)	0	1 25 0)	0	0	0 0	0 0	-25 0 (-67 4, 17 4)	-25 0 (-67 4, 17 4)
Any AE leading to discontinuation of study drug	0	1 25 0)	0	0	0 0	0 0	-25 0 (-67 4, 17 4)	-25 0 (-67 4, 17 4)
Any severe AE	0	2 50 0)	0	0	0 0	0 0	-50 0 (-99 0, -1 0)	-50 0 (-99 0, -1 0)
Any AE with reasonable possibility of being related to study drug$	2 (66 7)	2 50 0)	2 50 0)	3 (75 0)	-16 7 (-89 1, 55 8)	8 3 (-59 8, 76 5)	0 0	25 0 (-39 8, 89 8)
Any AE leading to death	0	0	0	0	0 0	0 0	0 0	0 0
Deaths								
Occurring <= 30 days (ADA for 70 days) after last dose	0	0	0	0	0 0	0 0	0 0	0 0
Occurring > 30 days ADA for 70 days) after last dose	0	0	0	0	0 0	0 0	0 0	0 0

Note Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug

A] The point estimate and 95% CI are based on normal approximation to binomial distribution

$ As assessed by investigator

相互参照：M15-572 試験 JSA T 1 1 3 1 1 1 J

M15-572 試験の日本人部分集団の投与 24 週時までの有害事象を表 2.7.4.7-75，全体集団の結果を表 2.7.4-46 に示す。また，日本人部分集団の投与 24 週時までの治験薬と関連ありの有害事象を表 2.7.4.7-76，全体集団の結果を表 2.7.4-47 に示す。

日本人部分集団では，投与 24 週時までに各投与群で 2 名以上に発現した有害事象は，ウパダシチニブ 30 mg 群の血中クレアチンホスホキナーゼ増加（2 名）のみであった。投与 24 週時までの SOC 別で発現が最も多かった有害事象は，ウパダシチニブ 15 mg 群では感染症および寄生虫症並びに臨床検査（各 2 名），ウパダシチニブ 30 mg 群では臨床検査（3 名）であった。アダリムマブ群及びプラセボ群では，2 名以上に発現した SOC はなかった。

日本人部分集団では，投与 24 週時までに各投与群で 2 名以上に発現した治験薬と関連ありの有害事象はなかった。各投与群で発現した治験薬と関連ありの有害事象は，ウパダシチニブ 15 mg 群では悪心，上咽頭炎，肝機能検査値上昇及び上気道の炎症，ウパダシチニブ 30 mg 群では好中球減少症，血中クレアチンホスホキナーゼ増加，リンパ球数減少，骨髄球存在及び白血球数減少，アダリムマブ群では注射部位反応及び高トリグリセリド血症（各 1 名）であった。

M15-572 試験の日本人部分集団の投与 24 週時までの Grade 3 以上の有害事象を表 2.7.4.7-77，全体集団の結果を表 2.7.4.7-14 に示す。

投与 56 週時

M15-572 試験の日本人部分集団の投与 56 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況）を表 2.7.4-70，全体集団の結果を表 2.7.4-42 に示す。

日本人部分集団の投与 56 週時データカットオフまでの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 283.3 件/100 人年（17 件），全ウパダシチニブ 30 mg 群で 302.5 件/100 人年（36 件），アダリムマブ群で 138.9 件/100 人年（10 件）であった。重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 群で 16.8 件/100 人年（2 件），アダリムマブ群で 13.9 件/100 人年（1 件）であり，全ウパダシチニブ 15 mg 群では発現しなかった。Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 群で 25.2 件/100 人年（3 件），アダリムマブ群で 41.7 件/100 人年（3 件）であり，全ウパダシチニブ 15 mg 群では発現しなかった。治験薬の投与中止に至った有害事象はアダリムマブ群のみで発現し，100 人年あたりの発現件数は 13.9 件/100 人年（1 件）であった。

日本人部分集団では，投与 56 週時データカットオフまでに死亡した被験者はいなかった。

表 2.7.4-70. 投与 56 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況，安全性解析対象集団，日本人部分集団）：M15-572 試験

	UPA 15 mg QD (N = 5) (PYs = 6.0)	UPA 30 mg QD (N = 6) (PYs = 11.9)	ADA 40 mg EOW (N = 4) (PYs = 7.2)	-- UPA VS ADA (95% CI)[A] -- 15 mg QD VS ADA	30 mg QD VS ADA
Exposure-adjusted event rate	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)		
Any adverse event (AE)	17 (283.3)	36 (302.5)	10 (138.9)	144.4 (-15.4, 304.3)	163.6 (32.6, 294.7)
Any serious AE (SAE)	0	2 (16.8)	1 (13.9)	-13.9 (-41.1, 13.3)	2.9 (-32.9, 38.7)
Any AE leading to discontinuation of study drug	0	0	1 (13.9)	-13.9 (-41.1, 13.3)	-13.9 (-41.1, 13.3)
Any severe AE	0	3 (25.2)	3 (41.7)	-41.7 (-88.8, 5.5)	-16.5 (-71.6, 38.7)
Any AE with reasonable possibility of being related to study drug$	8 (133.3)	18 (151.3)	3 (41.7)	91.7 (-12.1, 195.4)	109.6 (25.3, 193.9)
Any AE leading to death	0	0	0	0.0	0.0
Exposure-adjusted incidence rate	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)		
All deaths	0/6.0	0/11.9	0/7.2	0.0	0.0
Occurring <= 30 days (ADA for 70 days) after last dose	0/6.0	0/11.9	0/7.2	0.0	0.0
Occurring > 30 days (ADA for 70 days) after last dose	0/6.0	0/11.9	0/7.2	0.0	0.0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A]: The point estimate and 95% CI are based on normal approximation to poisson distribution.
$ As assessed by investigator.

相互参照：M15-572 試験 JSA W56 Table 14.3__1.1.1_J

M15-572 試験の日本人部分集団の投与 56 週時データカットオフまでの有害事象（100 人年あたりの発現件数）を表 2.7. .7-126，全体集団の結果を M15-572 試験（投与 56 週時）2.7.6 項に示す。また，日本人部分集団の投与 56 週時データカットオフまでの治験薬と関連ありの有害事象（100 人年あたりの発現件数）を表 2.7. .7-127，全体集団の結果を M15-572 試験（投与 56 週時）2.7.6 項に示す。

日本人部分集団では，投与 56 週時データカットオフまでに各投与群で 2 件以上発現した有害事象は，全ウパダシチニブ 15 mg 群では悪心，上咽頭炎及び皮膚乳頭腫（各 2 件），全ウパダシチニブ 30 mg 群では上咽頭炎及び白血球数減少（各 3 件），帯状疱疹，上気道感染，血中クレアチンホスホキナーゼ増加，リンパ球数減少及び起立性低血圧（各 2 件）であった。アダリムマブ群で 2 件以上発現した有害事象はなかった。投与 56 週時データカットオフまでの SOC 別で発現件数が最も多かった有害事象は，全ウパダシチニブ 15 mg 群及び 30 mg 群では感染症および寄生虫症（それぞれ 6 件及び 10 件）であり，アダリムマブ群では臨床検査（3 件）であった。

日本人部分集団では，投与 56 週時データカットオフまでに各投与群で 2 件以上発現した治験薬と関連ありの有害事象は，全ウパダシチニブ 15 mg 群では上咽頭炎（2 件），全ウパダシチニブ 30 mg 群では白血球数減少（3 件），帯状疱疹及びリンパ球数減少（各 2 件）であった。アダリムマブ群で 2 件以上発現した治験薬との関連ありの有害事象はなかった。

M15-572 試験の日本人部分集団の投与 56 週時データカットオフまでの Grade 3 以上の有害事象（100 人年あたりの発現件数）を表 2.7. .7-128，全体集団の結果を表 2.7. .7-9 に示す。

2.7. .5.1.1.2.2 死亡

M15-572 試験の日本人部分集団では，投与 2 週時データカットオフまでに死亡した被験者はいなかった（M15-572 試験 JSA Table 1 3 2.3.2 J）。

M15-572 試験の日本人部分集団では，投与 56 週時データカットオフまでに死亡した被験者はいなかった（M15-572 試験 JSA W56 T 1 1 3 2 3 J）。

2.7. .5.1.1.2.3 その他の重篤な有害事象

M15-572 試験の日本人部分集団の投与 2 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7. .7-78，全体集団の結果を表 2.7. .7-22 に示す。

日本人部分集団では，投与 2 週時までに重篤な有害事象がアダリムマブ群の 1 名のみに発現した（表 2.7. -69）。事象名は子宮癌であった（表 2.7. .7-23）。

日本人部分集団の投与 2 週時データカットオフまでの重篤な有害事象は，全ウパダシチニブ 30 mg 群で 2 件（気管支炎 1 件，帯状疱疹 1 件），アダリムマブ群で 1 件（子宮癌 1 件）発現した。

M15-572 試験の日本人部分集団の投与 56 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7. .7-129，全体集団の結果を表 2.7. .7-99 に示す。
日本人部分集団では，投与 56 週時データカットオフまでに重篤な有害事象が全ウパダシチニブ 30 mg 群で 2 件（気管支炎 1 件，帯状疱疹 1 件），アダリムマブ群で 1 件（子宮癌 1 件）発現した。いずれも投与 2 週時データカットオフまでに発現した事象であった。

2.7. .5.1.1.2. その他の重要な有害事象

M15-572 試験の日本人部分集団では，投与 2 週時までに治験薬の投与中止に至った有害事象がアダリムマブ群の 1 名のみに発現した（表 2.7. -69）。事象名は子宮癌であった（M15-572 試験 CSR W2 Table 1 .3 2 18.2.1）。

M15-572 試験の日本人部分集団の投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を表 2.7. .7-130，全体集団での結果を表 2.7. .7-10 に示す。
M15-572 試験の日本人部分集団では，投与 56 週時データカットオフまでに治験薬の投与中止に至った有害事象がアダリムマブ群の 1 名（子宮癌）のみに発現した。本事象は投与 2 週時データカットオフまでに発現したものであった。

2.7. .5.1.2 M15-55 試験

2.7. .5.1.2.1 全般的な曝露状況

M15-55 試験の日本人部分集団では，投与 2 週時までの曝露期間の平均値は，ウパダシチニブ 15 mg 群で 152.5 日，30 mg 群で 150.2 日，プラセボ群で 156.9 日であった（M15-55 試験 JSA Table 1 1 8.1 J）。

M15-55 試験の日本人部分集団では，投与 56 週時データカットオフまでの曝露期間の平均値は，全ウパダシチニブ 15 mg 群で 569 5 日，30 mg 群で 500.5 日であった（M15-55 試験 JSA W56 Table 1 .1 3 J）。

2.7.4.5.1.2.2 有害事象

2.7.4.5.1.2.2.1 有害事象の概要及び比較的よく見られる有害事象

投与 24 週時

M15-554 試験の日本人部分集団の投与 24 週時までの有害事象の概要を表 2.7.4-71，全体集団の結果を表 2.7.4-43 に示す。また，日本人部分集団の投与 24 週時データカットオフまでの有害事象の概要を表 2.7.4.7-79 及び表 2.7.4.7-80（100 人年あたりの発現状況）に示す。

日本人部分集団の投与 24 週時までの有害事象の発現割合は，ウパダシチニブ 15 mg 群で 76.9%（10/13 名），30 mg 群で 85.7%（12/14 名），プラセボ群で 58.3%（7/12 名）であった。重篤な有害事象，Grade 3 以上の有害事象及び治験薬の投与中止に至った有害事象は，ウパダシチニブ群のみで発現した（15 mg 群で各 1 名，30 mg 群で各 3 名）。

日本人部分集団では，投与 24 週時までに死亡した被験者はいなかった。

日本人部分集団での投与 24 週時データカットオフまでの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 389.7 件/100 人年（76 件），全ウパダシチニブ 30 mg 群で 628.1 件/100 人年（125 件）であった。重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 20.5 件/100 人年（4 件），全ウパダシチニブ 30 mg 群で 70.4 件/100 人年（14 件）であった。Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 15.4 件/100 人年（3 件），全ウパダシチニブ 30 mg 群で 80.4 件/100 人年（16 件）であった。治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 5.1 件/100 人年（1 件），全ウパダシチニブ 30 mg 群で 25.1 件/100 人年（5 件）であった。

日本人部分集団では，投与 24 週時から投与 24 週時データカットオフまでに，死亡が全ウパダシチニブ 30 mg 群で 1 名に認められた。

表 2 7. -71. 投与 2 週時までの有害事象の概要（安全性解析対象集団，日本人部分集団）：M15-55 試験

	Placebo N = 12) n (%)	------- UPA ------- 15 mg QD N = 13) n (%)	30 mg QD (N = 14) n (%)	------ UPA VS Placebo 95% CI) [A] ------- 15 mg QD VS Placebo	30 mg QD VS Placebo
Subjects with					
Any adverse event AE)	7 58 3)	10 76 9)	12 (85 7)	18 6 (-17 5, 54 7)	27 4 (-6 0, 60 8)
Any serious AE (SAE)	0	1 7 7)	3 (21 4)	7 7 (-6 8, 22 2)	21 4 (-0 1, 42 9)
Any AE leading to discontinuation of study drug	0	1 7 7)	3 (21 4)	7 7 (-6 8, 22 2)	21 4 (-0 1, 42 9)
Any severe AE	0	1 7 7)	3 (21 4)	7 7 (-6 8, 22 2)	21 4 (-0 1, 42 9)
Any AE with reasonable possibility of being related to study drug$	3 25 0)	5 38 5)	9 (64 3)	13 5 (-22 6, 49 5)	39 3 (4 2, 74 4)
Any AE leading to death	0	0	0	0 0	0 0
Deaths					
Occurring <= 30 days after last dose	0	0	0	0 0	0 0
Occurring > 30 days after last dose	0	0	0	0 0	0 0

Note Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing
Severe adverse events are defined as events with grade 3 or above based on the Common Terminology Criteria for Adverse Events CTCAE) version 5 0
$ As assessed by investigator
A] The point estimate and 95% CI are based on normal approximation to binomial distribution

相互参照：M15-55 試験 JSA T 1 1 3 1111 J

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M15-554 試験の日本人部分集団の投与 24 週時までの有害事象を表 2.7.4.7-81，全体集団の結果を表 2.7.4-48 に示す。また，日本人部分集団の投与 24 週時までの治験薬と関連ありの有害事象を表 2.7.4.7-82，全体集団の結果を表 2.7.4-49 に示す。

日本人部分集団では，投与 24 週時までに各投与群で 2 名以上に発現した有害事象は，ウパダシチニブ 15 mg 群では上咽頭炎（5 名），腹部不快感及び便秘（各 2 名），ウパダシチニブ 30 mg 群では上咽頭炎（4 名）及び胃腸炎（2 名），プラセボ群では上咽頭炎（3 名）であった。投与 24 週時までの SOC 別で発現割合が最も高かった有害事象は，いずれの投与群でも感染症および寄生虫症であり，発現割合はウパダシチニブ 15 mg 群で 53.8%（7/13 名），ウパダシチニブ 30 mg 群で 71.4%（10/14 名），プラセボ群で 33.3%（4/12 名）であった。

日本人部分集団では，投与 24 週時までに各投与群で 2 名以上に発現した治験薬と関連ありの有害事象はなかった。各投与群で発現した治験薬と関連ありの有害事象は，ウパダシチニブ 15 mg 群では回転性めまい，細菌性膣症，帯状疱疹，上咽頭炎，足部白癬，リンパ球数減少，高脂血症，筋肉痛，乾癬性関節症及びざ瘡，ウパダシチニブ 30 mg 群では貧血，リンパ球減少症，小腸潰瘍，嘔吐，肝損傷，単純ヘルペス，帯状疱疹，咽頭炎，肺炎，足部白癬，尿路感染及び血中クレアチンホスホキナーゼ増加（各 1 名）であった。

M15-554 試験の日本人部分集団の投与 24 週時までの Grade 3 以上の有害事象を表 2.7.4.7-83，全体集団の結果を表 2.7.4.7-15 に示す。

投与 56 週時

M15-554 試験の日本人部分集団の投与 56 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況）を表 2.7.4-72，全体集団の結果を表 2.7.4-44 に示す。

日本人部分集団の投与 56 週時データカットオフまでの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 359.4 件/100 人年（101 件），全ウパダシチニブ 30 mg 群で 580.3 件/100 人年（159 件）であった。重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 17.8 件/100 人年（5 件），全ウパダシチニブ 30 mg 群で 69.3 件/100 人年（19 件）であり，Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 14.2 件/100 人年（4 件），全ウパダシチニブ 30 mg 群で 87.6 件/100 人年（24 件）であった。また，治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 3.6 件/100 人年（1 件），全ウパダシチニブ 30 mg 群で 25.5 件/100 人年（7 件）であった。

日本人部分集団では，死亡が全ウパダシチニブ 30 mg 群で 1 名に認められたが，本事象は投与 24 週時データカットオフまでに報告されたものであった。

表 2 7. -72. 投与 56 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況，安全性解析対象集団，日本人部分集団）：M15-55 試験

	UPA 15 mg QD (N = 18) (PYs = 28 1)	UPA 30 mg QD (N = 20) (PYs = 27 4)
Exposure-adjusted event rate	Events (E/100 PYs)	Events (E/100 PYs)
Any adverse event (AE)	101 359 4)	159 580 3)
Any serious AE SAE)	5 (17 8)	19 69 3)
Any AE leading to discontinuation of study drug	1 3 6)	7 (25 5)
Any severe AE	4 (14 2)	24 87 6)
Any AE with reasonable possibility of being related to study drug$	28 99 6)	63 (229 9)
Any AE leading to death	0	1 3 6)
Exposure-adjusted incidence rate	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
All deaths	0/28 1	1/27 5 3 6)
Occurring <= 30 days after last dose	0/28 1	1/27 5 3 6)
Occurring > 30 days after last dose	0/28 1	0/27 4

Note Treatment emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study
Subjects in UPA 15 mg QD/30 mg QD group include those who started UPA 15 mg QD/30 mg QD at the beginning of the study and those who switched to UPA 15 mg QD/30 mg QD at Week 24
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5 0 will be counted as severe
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug
E/100 PYs = Events per 100 patient-years n/100 PYs = Number of subjects with at least one event per 100 patient-years
$ As assessed by investigator

相互参照：M15-55 試験 JSA W56 Table 1 3 1.1.1 J

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M15-55 試験の日本人部分集団の投与 56 週時データカットオフまでの有害事象（100 人年あたりの発現件数）を表 2.7. .7-131，全体集団の結果を M15-55 試験（投与 56 週時）2.7.6 項に示す。また，日本人部分集団の投与 56 週時データカットオフまでの治験薬と関連ありの有害事象（100 人年あたりの発現件数）を表 2.7. .7-132，全体集団の結果を M15-55 試験（投与 56 週時）2.7.6 項に示す。

日本人部分集団では，投与 56 週時データカットオフまでに各投与群で 10 件/100 人年以上発現した有害事象は，全ウパダシチニブ 15 mg 群では上咽頭炎（ 6.3 件/100 人年［13 件］），便秘（17.8 件/100 人年［5 件］），腹部不快感（1 .2 件/100 人年［ 件］），帯状疱疹，口腔ヘルペス，血中クレアチンホスホキナーゼ増加及び不眠症（各 10.7 件/100 人年［3 件］），全ウパダシチニブ 30 mg 群では上咽頭炎（ 7. 件/100 人年［13 件］），口内炎及び帯状疱疹（各 21.9 件/100 人年［6 件］），口腔ヘルペス（18.2 件/100 人年［5 件］），毛包炎及び血中クレアチンホスホキナーゼ増加（各 1 .6 件/100 人年［ 件］），薬物性肝障害，咽頭炎及び薬疹（各 10.9 件/100 人年［3 件］）であった。投与 56 週時データカットオフまでの SOC 別で 100 人年あたりの発現件数が最も多かった有害事象は，いずれの投与群でも感染症および寄生虫症であり，100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 117. 件/100 人年（33 件），全ウパダシチニブ 30 mg 群で 233 6 件/100 人年（6 件）であった。

日本人部分集団では，投与 56 週時データカットオフまでに各投与群で 10 件/100 人年以上発現した治験薬と関連ありの有害事象は，全ウパダシチニブ 15 mg 群では帯状疱疹及び口腔ヘルペス（各 10.7 件/100 人年［3 件］），全ウパダシチニブ 30 mg 群では帯状疱疹（21.9 件/100 人年［6 件］），上咽頭炎及び口腔ヘルペス（各 1 .6 件/100 人年［ 件］），口内炎及び血中クレアチンホスホキナーゼ増加（各 10.9 件/100 人年［3 件］）であった。

M15-55 試験の日本人部分集団の投与 56 週時データカットオフまでの Grade 3 以上の有害事象（100 人年あたりの発現件数）を表 2.7. .7-133，全体集団の結果を表 2.7. .7-95 に示す。

2.7. .5.1.2.2.2 死亡

M15-55 試験の日本人部分集団では，投与 2 週時までに死亡した被験者はいなかった（M15-55 試験 JSA Table 1 .3 2.3.1 J）。投与 2 週時から投与 2 週時データカットオフまでに，死亡が全ウパダシチニブ 30 mg 群で 1 名に認められた。死亡に至った有害事象は汎血球減少症であり，治験薬と関連ありと判断された（M15-55 試験 JSA Table 1 3 2.3 2 J，詳細は 2.7. .2.1.2 項参照）。なお，本被験者について，治験責任医師は死亡原因を汎血球減少症と報告したが，死亡診断書には，診断医により急性呼吸窮迫症候群及び右気胸と記載されていた。

M15-55 試験の日本人部分集団では，投与 56 週時データカットオフまでに死亡が全ウパダシチニブ 30 mg 群で 1 名に認められた（M15-55 試験 JSA W56 Table 1 .3 2 3 J）。本事象は投与

24 週時データカットオフまでに報告されたものであり，上述の汎血球減少症を発現した被験者であった。

2.7.4.5.1.2.2.3 その他の重篤な有害事象

M15-554 試験の日本人部分集団の投与 24 週時までの重篤な有害事象を表 2.7.4.7-84，全体集団での結果を表 2.7.4.7-25，投与 24 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-85，全体集団での結果を表 2.7.4.7-26 に示す。

日本人部分集団では，投与 24 週時までに重篤な有害事象がウパダシチニブ群のみに発現した（15 mg 群：1 名，30 mg 群：3 名）。内訳は，全ウパダシチニブ 15 mg 群では乾癬性関節症（1 名），30 mg 群では小腸潰瘍，肺炎，尿路感染及び卵巣癌（各 1 名）であった。

日本人部分集団では，投与 24 週時データカットオフまでの重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 20.5 件/100 人年（4 件），全ウパダシチニブ 30 mg 群で 70.4 件/100 人年（14 件）であった。各投与群で 2 件以上に発現した重篤な有害事象はなかった。

M15-554 試験の日本人部分集団の投与 56 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数）を表 2.7.4.7-134，全体集団の結果を表 2.7.4.7-101 に示す。

日本人部分集団では，投与 56 週時データカットオフまでの重篤な有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 17.8 件/100 人年（5 件），全ウパダシチニブ 30 mg 群で 69.3 件/100 人年（19 件）であった。各投与群で 2 件以上発現した重篤な有害事象は，全ウパダシチニブ 15 mg 群では乾癬性関節症（2 件），全ウパダシチニブ 30 mg 群では肺炎（2 件）であった。

2.7.4.5.1.2.2.4 その他の重要な有害事象

M15-554 試験の日本人部分集団の投与 24 週時までの治験薬の投与中止に至った有害事象を表 2.7.4.7-86，全体集団での結果を表 2.7.4.7-33 に示す。

日本人部分集団では，投与 24 週時までに治験薬の投与中止に至った有害事象がウパダシチニブ群のみに発現した（15 mg 群：1 名，30 mg 群：3 名）。内訳は，全ウパダシチニブ 15 mg 群では乾癬性関節症（1 名），30 mg 群では小腸潰瘍，肺炎及び尿路感染（各 1 名）であった。

M15-554 試験の日本人部分集団の投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象（100 人年あたりの発現件数）を表 2.7.4.7-135，全体集団での結果を表 2.7.4.7-105 に示す。

M15-554 試験の日本人部分集団では，投与 56 週時データカットオフまでの治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群で 3.6 件/100 人年

（1 件），全ウパダシチニブ 30 mg 群で 25.5 件/100 人年（7 件）であった。各投与群で 2 件以上発現した治験薬の投与中止に至った有害事象はなかった。

2.7. .5.2 内因性要因

有害事象の概要，特に注目すべき有害事象の概要及び全有害事象について，プラセボ対照併合解析集団及び全ウパダシチニブ併合解析集団を用いて，内因性要因（人種，年齢，性別，ベースライン時の BMI 及び腎機能障害）を因子とした部分集団解析を実施した。日本人部分集団では，年齢及びベースライン時の BMI について実施した。なお，帯状疱疹についての部分集団解析の結果は，2.7. .2.1.5.1 3 項に示す。

2.7. .5.2.1 人種

安全性併合解析では，大部分（約 90%）の被験者が白人であり，白人以外の被験者が白人の被験者と比較して少なかったことから，結果の解釈には注意が必要である。

プラセボ対照併合解析集団（投与 2 週時）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，白人（ウパダシチニブ 15 mg 併合群：6 .1%及び 30 9%，30 mg 併合群：72.9%及び 38 9%。以下，同順で記載）と比較して，白人以外（80.3%及び 50.7%，85.3%及び 61.8%）の方が高かった（ISS Table 2. 1.1.5.1.1）。治験薬の投与中止に至った有害事象は，ウパダシチニブ 15 mg 併合群では白人以外（1. %）と比較して白人（ .7%）の方が高く，30 mg 併合群では白人（6.1%）と白人以外（8.8%）で同様であった。重篤な有害事象及び Grade 3 以上の有害事象の発現割合は，ウパダシチニブ 30 mg 併合群では白人（6.3%及び 5.9%）と比較して白人以外（11.8%及び 13.2%）の方が高く，15 mg 併合群では白人（ .2%及び 5.3%）と白人以外（2.8%及び 5 6%）で同様であった。

全ウパダシチニブ併合解析集団（長期，申請時）でも同様に，有害事象及び治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，白人（全ウパダシチニブ 15 mg 併合群：300.9 件/100 人年及び 101. 件/100 人年，30 mg 併合群：356.7 件/100 人年及び 1 0.0 件/100 人年。以下，同順で記載）と比較して，白人以外（376.7 件/100 人年及び 186.0 件/100 人年，565 6 件/100 人年及び 257.1 件/100 人年）の方が多かった（ISS T 1 2 1 2 5 1 1）。治験薬の投与中止に至った有害事象は，全ウパダシチニブ 15 mg 併合群では白人以外（2.3 件/100 人年）と比較して白人（9.2 件/100 人年）の方が多く，30 mg 併合群では白人（9.1 件/100 人年）と白人以外（12.3 件/100 人年）で同様であった。重篤な有害事象及び Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 30 mg 併合群では白人（12 0 件 100 人年及び 1 .9 件/100 人年）と比較して，白人以外（38.0 件/100 人年及び 5 8 件/100 人年）の方が多く，15 mg 併合群では白人（11.2 件 100 人年及び 12.7 件/100 人年）と白人以外（8.2 件/100 人年及び 9. 件 100 人年）で同様であった。

人種の部分集団間では，両併合解析対象集団とも，発現した有害事象及び特に注目すべき有害事象の種類に差が認められたが，白人以外の被験者が少なかったことから，明確な結論を見出せなかった（ISS Table 2. 1.1 5.3 1，Table 2. 1.1.5.2.1，Table 2. 1.2.5.3.1，Table 2. 1.2.5.2.1）。

2.7. .5.2.2 年齢

全体集団

安全性併合解析では，65 歳未満の被験者と比較して，65 歳以上 75 歳未満の被験者が少なかったことから，結果の解釈には注意が必要である。75 歳以上の被験者は著しく少なかったため，誤解を招く解釈を避けるために他の部分集団との比較は行わなかった。

プラセボ対照併合解析集団（投与 2 週時）では，有害事象，重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の発現割合（以下，同順で記載）は，ウパダシチニブ 15 mg 併合群では 65 歳未満（65. %，3 0%，3.1%，. %）と比較して 65 歳以上 75 歳未満（68.7%，9.6%，9 6%，9.6%）の方が高かった。また，30 mg 併合群でも同様に，65 歳未満（73.3%，5.9%，5.5%，6.1%）と比較して，65 歳以上 75 歳未満（81 0%，13 1%，11.9%，11.9%）の方が高かった（ISS Table 2. 1 1.5 1.2）。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 15 mg 併合群では 65 歳未満（3 .2%）と比較して 65 歳以上 75 歳未満（27.7%）の方が低かったが，ウパダシチニブ 30 mg 併合群では 65 歳未満（ 1. %）と 65 歳以上 75 歳未満（ 1.7%）で同様であった。

全ウパダシチニブ併合解析集団（長期，申請時）でも同様に，有害事象，重篤な有害事象，治験薬の投与中止に至った有害事象，Grade 3 以上の有害事象及び治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群では 65 歳未満（297 5 件/100 人年，8.1 件/100 人年，5.9 件/100 人年，9.3 件/100 人年，110.1 件/100 人年）と比較して，65 歳以上 75 歳未満（358.2 件/100 人年，22.5 件/100 人年，2 . 件/100 人年，26. 件/100 人年，118.1 件/100 人年）の方が多かった。また，30 mg 併合群でも同様に，65 歳未満（360.3 件/100 人年，13.2 件/100 人年，8 1 件/100 人年，17.6 件/100 人年，151 3 件/100 人年）と比較して，65 歳以上 75 歳未満（ 87.9 件/100 人年，2 3 件/100 人年，16.2 件/100 人年，2 .3 件/100 人年，169. 件/100 人年）の方が多かった（ISS Table 2. 1.2.5.1.2）。

プラセボ対照併合解析集団（投与 2 週時）及び全ウパダシチニブ併合解析集団（長期，申請時）ともに，特に注目すべき有害事象の重篤な感染症，帯状疱疹及び悪性腫瘍の発現割合及び 100 人年あたりの発現件数（以下，同順で記載）は，ウパダシチニブ 15 mg 併合群では 65 歳未満（0.6%及び 2 0 件/100 人年，1.3%及び 3. 件/100 人年，0. %及び 0.9 名/100 人年）と比較して，65 歳以上 75 歳未満（3.6%及び 3.9 件/100 人年，0%及び .9 件/100 人年，1.2%及び 2.9 名/100 人年）の方がおおむね高かった。また，30 mg 併合群でも同様に，65 歳未満（2.0%及び 5.7 件/100

人年，1.5%及び 7.6 件/100 人年，0 9%及び 1.2 名/100 人年）と比較して，65 歳以上 75 歳未満（6.0%及び 7 3 件 100 人年，6.0%及び 10 5 件 100 人年，1.2%及び 2. 名/100 人年）の方がおおむね高かった（ISS Table 2. 1 1.5 2.2，Table 2. 1 2.5.2.2）。しかし，悪性腫瘍については，各部分集団の悪性腫瘍の発現件数が比較的少なかった結果に基づくものであった。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）及び全ウパダシチニブ併合解析集団（長期，申請時）の日本人部分集団では，多くの被験者が 65 歳未満であり，65 歳以上 75 歳未満の被験者は少なく，最も高い年齢区分（75 歳以上）の被験者はいなかった（J-ISS Table 2. 1.1.5.1.2 J 及び Table 2. 1.2.5.1.2 J）。

2.7. .5.2.3 性別

プラセボ対照併合解析集団（投与 2 週時）では，有害事象，重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の発現割合は，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群（以下，同順で記載）ともに，男性（59.9%及び 71. %，3.8%及び 6.6%，2. %及び 7.6%，5 2%及び 6.6%）と比較して女性（70.9%及び 76 6%， .3%及び 7.1%，6.0%及び 5. %，5. %及び 6.8%）の方が高い傾向が認められた（ISS Table 2. 1.1.5.1.3）。

全ウパダシチニブ併合解析集団（長期，申請時）では，有害事象及び治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群（以下，同順で記載）ともに，男性（2 6 3 及び 317.6 件/100 人年，90 0 及び 139. 件/100 人年）と比較して女性（365.6 及び 29.9 件/100 人年，128.7 及び 163.6 件/100 人年）の方が多い傾向が認められた。重篤な有害事象，治験薬の投与中止に至った有害事象及び Grade 3 以上の有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群ともに，男性（10.0 及び 16.0 件/100 人年，5 1 及び 10.8 件 100 人年，11.3 及び 20.8 件/100 人年）と女性（11.7 及び 13.9 件/100 人年，11. 及び 8. 件/100 人年，13.3 及び 16.1 件/100 人年）でおおむね同様であった（ISS T 1 2 1 2 5 1 3）。尿路感染の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群ともに，男性（1.8 及び 1.6 件/100 人年）と比較して女性（1 .7 及び 16 3 件/100 人年）の方が多かった（ISS T 1 2 1 2 5 3 3）。

プラセボ対照併合解析集団（投与 2 週時）と全ウパダシチニブ併合解析集団（長期，申請時）の間及び各投与群間で，多くの特に注目すべき有害事象の発現状況は，男性と女性で同様であった。（ISS Table 2. 1.1.5.2.3，Table 2. 1.2 5.2 3）。

2.7. .5.2. BMI

全体集団

ベースライン時の BMI が 18 5 kg/m^2 未満の被験者は，BMI がより高い被験者と比較して非常に少数であったため，結果の解釈には注意が必要である。

プラセボ対照併合解析集団（投与 2 週時）では，有害事象，重篤な有害事象，Grade 3 以上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，BMI の部分集団間でおおむね同様であった（ISS Table 2. 1.1.5.1. ）。

全ウパダシチニブ併合解析集団（長期，申請時）では，すべての種類の有害事象で BMI の部分集団間に明らかな傾向は認められなかった（ISS Table 2. 1.2.5.1. ）。

プラセボ対照併合解析集団（投与 2 週時）と全ウパダシチニブ併合解析集団（長期，申請時）の間では，発現した有害事象及び特に注目すべき有害事象の種類で BMI の部分集団間に明らかな傾向は認められなかった（ISS Table 2. 1.1.5.3. ，Table 2. 1.1 5.2. ，Table 2. 1.2.5.3. ，Table 2. 1.2.5.2. ）。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）及び全ウパダシチニブ併合解析集団（長期，申請時）の日本人部分集団では，BMI の各部分集団の被験者が少なかった（J-ISS Table 2. 1.1.5.1. J 及び Table 2. 1.2.5.1. J）。

2.7. .5.2.5 ベースライン時の腎機能障害

ベースライン時に中等度の腎機能障害を有した被験者は，ベースライン時に腎機能が正常又は軽度の腎機能障害を有した被験者と比較して少なかったため，結果の解釈には注意が必要である。

プラセボ対照併合解析集団（投与 2 週時）では，有害事象，重篤な有害事象，Grade 3 以上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，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群（以下，同順で記載）ともに，ベースライン時に中等度の腎機能障害を有した被験者（73.7%及び 79.2%，13.2%及び 12.5%，10.5%及び 12 5%，10.5%及び 29.2%）で最も高く，ベースライン時に腎機能が正常（63 5%及び 71. %，3 0%及び 6.1%， .3%及び 5.8%，2.6%及び 5. %）及び軽度の腎機能障害を有した被験者（67.3%及び 76. %， 0%及び 7.1%，5.7%及び 7 1%，5. %及び 5.6%）では同様であった（ISS Table 2. 1.1.5.1.7）。

全ウパダシチニブ併合解析集団（長期，申請時）でも同様に，有害事象，重篤な有害事象，Grade 3 以上の有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群（以下，同順で記載）ともに，ベースライン時に中等度の腎機能障害を有した被験者（ 36. 及び 601.1 件/100 人年， 9.0 及び 36 2 件/100 人

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年， 0.1 及び 18.1 件/100 人年，11.1 及び 67.8 件/100 人年）で最も多く，ベースライン時に腎機能が正常（278.2 及び 3 2. 件/100 人年，6.2 及び 13.7 件/100 人年，8.3 及び 17 5 件/100 人年， .7 及び 7.0 件/100 人年）及び軽度の腎機能障害を有した被験者（325.1 及び 06.3 件/100 人年，11.2 及び 1 9 件/100 人年，13 3 及び 19.1 件/100 人年，12.0 及び 8.8 件/100 人年）では同様であった（ISS Table 2. 1.2.5.1.8）。

プラセボ対照併合解析集団（投与 2 週時）と全ウパダシチニブ併合解析集団（長期，申請時）の間では，発現した有害事象の種類で腎機能障害の部分集団間に明らかな傾向は認められなかった（ISS Table 2. 1.1.5.3.7，Table 2. 1.2.5.3.8）。

ベースライン時の腎機能が正常又は軽度若しくは中等度の腎機能障害を有した被験者では，ウパダシチニブ 30 mg 併合群の貧血の発現割合を除き，プラセボ対照併合解析集団（投与 2 週時）と全ウパダシチニブ併合解析集団（長期，申請時）の間及び各投与群間で，特に注目すべき有害事象の種類に一定の傾向は認められなかった。ウパダシチニブ 30 mg 併合群の貧血の発現割合及び 100 人年あたりの発現件数は，ベースライン時に中等度の腎機能障害を有した被験者（8.3%及び 13 6 件/100 人年）が最も高く，次いで軽度の腎機能障害（5.9%及び 9.3 件/100 人年），腎機能が正常の被験者（ . %及び .2 件/100 人年）の順であった（ISS Table 2. 1.1.5.2.7，Table 2. 1.2.5.2.8）。

2.7. .5.3 外因性要因

有害事象の概要，特に注目すべき有害事象の概要及び全有害事象について，プラセボ対照併合解析集団及び全ウパダシチニブ併合解析集団を用いて，外因性要因（ウパダシチニブの単独又は併用投与，ベースライン時の non-bDMARD 併用投与，前治療の bDMARD で効果不十分又は忍容性なし）を因子とした部分集団解析を実施した。更に，M15-572 試験及び M15-55 試験の各試験のデータを用いて，2 つの試験集団間での長期安全性（申請時）の比較（non-bDMARD 又は bDMARD で効果不十分若しくは忍容性なし）を行った。日本人部分集団では，ウパダシチニブの単独又は併用投与，ベースライン時の non-bDMARD 併用投与について実施した。なお，帯状疱疹についての部分集団解析の結果は，2.7. .2.1.5.1.3 項に示す。

2.7. .5.3.1 ウパダシチニブの単独又は併用投与

全体集団

プラセボ対照併合解析集団（投与 2 週時）と全ウパダシチニブ併合解析集団（長期，申請時）の間及びウパダシチニブ各用量群間で，有害事象，重篤な有害事象，Grade 3 以上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及び 100 人年あたりの発現件数は，単独投与と併用投与でおおむね同様であった（ISS Table 2. 1.1.5.1.6，Table 2. 1.2.5.1.6）。

プラセボ対照併合解析集団（投与 2 週時）では，特に注目すべき有害事象の発現割合は単独投与と併用投与でおおむね同様であったが，各部分集団の発現件数が少なかったため，明確な結論を見出せなかった（ISS Table 2. 1 1.5 2.6）。

全ウパダシチニブ併合解析集団（長期，申請時）では，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群（以下，同順で記載）のいずれでも，重篤な感染症（単独：1.3 及び 3 件/100 人年，併用：2.7 及び 6.7 件/100 人年），薬物性肝障害（単独：7 9 及び 12 2 件 100 人年，併用：19.5 及び 26.7 件 100 人年），CPK 増加（単独：7.9 及び 11.5 件/100 人年，併用：12.7 及び 19.5 件/100 人年），好中球減少症（単独：0.9 及び 3.6 件/100 人年，併用：2.7 及び 7. 件/100 人年），貧血（単独：2.2 及び 5.9 件/100 人年，併用：3 1 及び 7. 件/100 人年）及びリンパ球減少症（単独：1.3 及び 1.6 件/100 人年，併用：2.9 及び . 件/100 人年）の 100 人年あたりの発現件数は，単独投与と比較して併用投与の方が多かった（ISS Table 2. 1.2.5.2.6）。これらの所見は，併用薬剤の一般的な相加毒性を考慮すると予期しないものではなかった。その他の特に注目すべき有害事象の 100 人年あたりの発現件数は，単独投与と併用投与でおおむね同様であった（ISS Table 2. 1.2.5.2.6）。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）及び全ウパダシチニブ併合解析集団（長期，申請時）の日本人部分集団では，ウパダシチニブの単独投与及び併用投与の被験者が少なかった（J-ISS Table 2. 1.1.5.1.6 J 及び Table 2. 1.2.5.1.6 J）。

2.7. .5.3.2 ベースライン時の non-bDMARD 併用投与

ベースライン時の non-bDMARD 併用投与のカテゴリーは，MTX 単独，MTX 及び MTX 以外の non-bDMARD，MTX 以外の non-bDMARD であった。

乾癬性関節炎の臨床試験に組み入れられた被験者の多くは，MTX を単独投与しており，他の部分集団の被験者は比較的少なかったことから，結果の解釈には注意が必要である。

プラセボ対照併合解析集団（投与 2 週時）では，ウパダシチニブ 15 mg 併合群，30 mg 併合群及びプラセボ併合群（以下，同順で記載）の有害事象の発現割合は，MTX 及び MTX 以外の non-bDMARD（73 1%，81 3%，72.7%），MTX 以外の non-bDMARD（75.0%，80.3%，68.1%）と比較して，MTX 単独（63.7%，72.7%，55.8%）の方が低かった（ISS Table 2. 1.1.5.1.5）。

全ウパダシチニブ併合解析集団（長期，申請時）でも同様に，全ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の有害事象の 100 人年あたりの発現件数は，MTX 及び MTX 以外の non-bDMARD（ 06.1 及び 11.0 件/100 人年），MTX 以外の non-bDMARD（337. 及び 36.5 件/100 人年）と比較して，MTX 単独（292.7 及び 369. 件/100 人年）の方が少なかった（ISS Table 2. 1.2.5.1.5）。

プラセボ対照解析対象集団（投与 2 週時）では，non-bDMARD の部分集団間での重篤な有害事象の発現割合は，プラセボ併合群とウパダシチニブ 15 mg 併合群では同様であった（ISS Table 2. 1.1.5.1.5）。ウパダシチニブ 30 mg 併合群の重篤な有害事象の発現割合は，MTX 及び MTX 以外の non-bDMARD（0%）及び MTX 以外の non-bDMARD（ .2%）と比較して，MTX 単独（9. %）の方が高かった。全ウパダシチニブ併合解析集団（長期，申請時）では，重篤な有害事象の 100 人年あたりの発現件数で，non-bDMARD の部分集団間に明らかな傾向は認められなかった（ISS Table 2. 1 2.5 1.5）。

プラセボ対照併合解析集団及び全ウパダシチニブ併合解析集団では，ウパダシチニブ 15 mg 併合群及び 30 mg 併合群の治験薬の投与中止に至った有害事象，Grade 3 以上の有害事象，治験薬と関連ありの有害事象の発現状況で，non-bDMARD の部分集団間に明らかな傾向は認められなかった（ISS Table 2. 1 1.5 1.5，Table 2. 1.2.5.1.5）。

プラセボ対照解析対象集団（投与 2 週時）では，特に注目すべき有害事象の発現割合は non-bDMARD の部分集団間でおおむね同様であったが，各部分集団で発現した事象が少なかったため，明確な結論を見出せなかった（ISS Table 2. 1.1.5.2.5）。

全ウパダシチニブ併合解析集団（長期，申請時）では，全ウパダシチニブ 15 mg 併合群の重篤な感染症の 100 人年あたりの発現件数は，MTX 単独（2.6 件/100 人年）及び MTX 以外の non-bDMARD（2.2 件/100 人年）と比較して，MTX 及び MTX 以外の non-bDMARD（5.8 件/100 人年）の方が多かった（ISS Table 2. 1.2.5.2 5）。全ウパダシチニブ 30 mg 併合群では，重篤な感染症の 100 人年あたりの発現件数は，non-bDMARD の部分集団間で同様であった。薬物性肝障害の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群では，MTX 及び MTX 以外の non-bDMARD（17.3 件/100 人年），MTX 以外の non-bDMARD（11.1 件/100 人年）と比較して，MTX 単独（21. 件/100 人年）の方が多かった（ISS Table 2. 1.2.5.2.5）。全ウパダシチニブ 30 mg 併合群では，MTX 及び MTX 以外の non-bDMARD（18.5 件/100 人年）と比較して，MTX 単独（27.2 件/100 人年）及び MTX 以外の non-bDMARD（28.2 件/100 人年）の方が多かった。帯状疱疹の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 併合群では non-bDMARD の部分集団間で同様であった（ISS Table 2. 1.2 5.2.5）。全ウパダシチニブ 30 mg 併合群では，MTX 単独（6.7 件/100 人年）及び MTX 以外の non-bDMARD（5. 件/100 人年）と比較して，MTX 及び MTX 以外の non-bDMARD（13 9 件 100 人年）の方が多かった。他の特に注目すべき有害事象では，non-bDMARD の部分集団間で明らかな傾向は認められず，100 人年あたりの発現件数も同様であった（ISS Table 2. 1.2.5.2.5）。

以上より，全体的な安全性プロファイルは，ウパダシチニブと non-bDMARD を併用した被験者と併用しなかった被験者で同様であった。

日本人部分集団

プラセボ対照併合解析集団（投与 2 週時）及び全ウパダシチニブ併合解析集団（長期，申請時）の日本人部分集団では，ベースライン時の non-bDMARD 併用投与の各部分集団の被験者が少なかった（J-ISS Table 2. 1.1.5.1.5 J 及び Table 2. 1.2 5.1 5 J）。

2.7. .5.3.3 前治療の bDMARD で効果不十分の被験者又は忍容性のない被験者

M15-55 試験の長期データ（申請時）に基づき，前治療の bDMARD で効果不十分の被験者及び bDMARD で忍容性のない被験者について，部分集団解析を実施した。

前治療の bDMARD で効果不十分の被験者（全ウパダシチニブ 15 mg 群：26 名，30 mg 群：286 名）と比較して，忍容性のない被験者（全ウパダシチニブ 15 mg 群：25 名，30 mg 群：22 名）が非常に少なかったことから，発現した有害事象の種類及び特に注目すべき有害事象について明確な結論を見出せなかった（ISS Table 2. 1.2 5.1.7，ISS Table 2. 1 2.5 2.7）。

2.7. .5.3. non-bDMARD 又は bDMARD で効果不十分若しくは忍容性のない被験者

乾癬性関節炎の臨床開発プログラムは，異なる病期の患者を対象とするために計画した。M15-572 試験では 1 種類以上の non-bDMARD で効果不十分又は忍容性のない被験者（以下「non-bDMARD-IR」）を組み入れ，M15-55 試験では 1 種類以上の bDMARD で効果不十分又は忍容性のない被験者（以下「bDMARD-IR」）を組み入れた。ただし，non-bDMARD-IR の被験者数（1705 名）は，bDMARD-IR の被験者数（6 2 名）と比較して多かった（M15-572 試験 CSR W2 Table 1 .1 1.1，M15-55 試験 CSR W2 Table 1 .1 1.1）。

この 2 試験では，non-bDMARD-IR と bDMARD-IR の長期安全性プロファイル（申請時）はおおむね同様であった（M15-572 試験 CSR W2 Table 1 .3 1.1.1.2.2 及び M15-55 試験 CSR W2 Table 1 3 1.1 1.2.2）。重篤な有害事象及び治験薬の投与中止に至った有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群及び 30 mg 群のいずれでも，non-bDMARD-IR（15 mg 群：8.6 及び 5.9 件/100 人年，30 mg 群：12.9 及び 7. 件/100 人年）と比較して，bDMARD-IR（15 mg 群：15.0 及び 13.0 件/100 人年，30 mg 群：18.2 及び 13.2 件/100 人年）の方が多かった。治験薬と関連ありの有害事象の 100 人年あたりの発現件数は，全ウパダシチニブ 15 mg 群及び 30 mg 群のいずれでも，bDMARD-IR（15 mg 群：70.7 件/100 人年，30 mg 群：116.8 件/100 人年）と比較して，non-bDMARD-IR（15 mg 群：132. 件/100 人年，30 mg 群：173.0 件/100 人年）の方が多かった。

特に注目すべき有害事象のうち，多くの事象では，100 人年あたりの発現件数又は発現被験者数は，全ウパダシチニブ 15 mg 群及び 30 mg 群のいずれでも，non-bDMARD-IR と bDMARD-IR で同様であった。ただし，薬物性肝障害，好中球減少症，リンパ球減少症及び CPK 増加（全ウパダシチニブ 15 mg 群及び 30 mg 群の順に記載）では，bDMARD-IR（薬物性肝障害：5.1 及び 18.6 件/100 人年，好中球減少症：1. 及び .1 件/100 人年，リンパ球減少症：1.0 及び 1. 件/100 人年，CPK 増加：6.1 及び 9.1 件/100 人年）と比較して，non-bDMARD-IR（薬物性肝障害：22.5

及び 2 .3 件/100 人年，好中球減少症：2.7 及び 7. 件/100 人年，リンパ球減少症：3.2 及び .8 件/100 人年，CPK 増加：1 .3 及び 21.5 件/100 人年）の方が多く，悪性腫瘍では non-bDMARD-IR（0.8 及び 1.1 名/100 人年）と比較して，bDMARD-IR（2. 及び 2 0 名/100 人年）の方が多かった（M15-572 試験 CSR W2 Table 1 .3 1.1.2.2.2，M15-55 試験 CSR W2 Table 1 .3 1.1.2.2.2）。臨床検査値に関連する特に注目すべき有害事象の 100 人年あたりの発現件数は，bDMARD-IR と比較して non-bDMARD-IR の方が多かったが，好中球数減少，リンパ球数減少，CPK 増加及び ALT / AST 増加の臨床検査値異常（Grade 3 又は Grade の異常値）では，全ウパダシチニブ 15 mg 群と 30 mg 群のいずれでも，各試験集団の間に一定の相関は認められず，有害事象での結果を支持するものではなかった。この相違は，2 試験が異なる国又は治験責任医師により実施されたため，臨床検査値異常を有害事象として報告する判断に影響を及ぼした可能性があった。また，基礎療法の疾患修飾性抗リウマチ薬（以下「DMARD」）の使用頻度が 2 つの試験集団間で異なり，1 種類以上の non-bDMARD を併用した被験者の割合は，bDMARD-IR（ 8.8%）と比較して non-bDMARD-IR（82.3%）の方が高かった（M15-572 試験 CSR W2 T 1 1 1 7 2 M15-55 試験 CSR W2 Table 1 .1 7.2）。bDMARD-IR と比較して，多くの non-bDMARD-IR はウォッシュアウトせずに最後に投与されていた治療を継続したと考えられることから，このような基礎療法の non-bDMARD の使用頻度の差は予測されたことであった。

長期投与時（申請時）の悪性腫瘍（NMSC を除く）の 100 人年あたりの発現被験者数は，non-bDMARD-IR（全ウパダシチニブ 15 mg 群：0.6 名/100 人年，30 mg 群：0. 名/100 人年）と比較して bDMARD-IR（全ウパダシチニブ 15 mg 群：1. 名/100 人年，30 mg 群：1.7 名/100 人年）の方が多いようにみられたが，各試験集団で報告された悪性腫瘍の発現被験者数が少ないこと，悪性腫瘍（NMSC を除く）のうち，特定の種類の悪性腫瘍で，non-bDMARD-IR と bDMARD-IR の間に明らかな傾向が認められなかったことから，明確な結論を見出せなかった（M15-572 試験 CSR W2 Table 1 .3 1.1 2.2 2，M15-55 試験 CSR W2 Table 1 .3 1.1.2.2.2）。NMSC の 100 人年あたりの発現被験者数でも，2 つの試験集団の全ウパダシチニブ 15 mg 群及び 30 mg 群の間で一定の傾向が認められなかったことから，偶発的な所見であると考えられ，non-bDMARD-IR と bDMARD-IR との間の差を示唆するものではないと考えられた。

non-bDMARD-IR 及び bDMARD-IR の安全性の結果の詳細は，M15-572 試験 CSR W2 及び M15-55 試験 CSR W2 に示す。

2.7. .5. 薬物相互作用

ウパダシチニブと一般に用いられる併用薬及び CYP 酵素のプローブ基質との薬物相互作用の可能性を第 I 相試験で評価した。これらの試験結果から，CYP3A の強力な誘導剤（リファンピシン等）は，ウパダシチニブの血漿中曝露量を約半分に減少させることが示された。CYP3A の強力な阻害薬（ケトコナゾール等）は，ウパダシチニブの血漿中濃度－時間曲線下面積（AUC）を 75%増加させ，最高血漿中濃度（以下「C_{max}」）を 70%増加させた。強力な CYP2D6 阻害薬，OATP 1B 阻害薬，MTX，pH 調整効果を有する薬剤又はスタチンを併用しても，ウパダシチニブの血漿中曝露量に影響を及ぼさなかった。ウパダシチニブは，MTX，エチニルエストラジオー

ル，レボノルゲストレル，スタチン又は CYP1A2，CYP2B6，CYP2D6，CYP2C19，CYP2C9 若しくは CYP3A の基質として代謝される薬剤の血漿中曝露量に対して，臨床的に意義のある影響を及ぼさなかった。

これらの試験結果は，関節リウマチに対するウパダシチニブの承認申請で提出しており，新たな薬物相互作用試験は実施しなかった。

乾癬性関節炎患者を対象とした第 III 相試験では，ウパダシチニブの血漿中曝露量は，アプレミラスト，ヒドロキシクロロキン，スルファサラジン，レフルノミド及び MTX を併用投与した被験者と，併用しなかった被験者で同程度であり，これらの DMARD がウパダシチニブの薬物動態に影響を及ぼさないことが示された。詳細は，2.7.2 項に記載した。

2.7.4.5.5 妊娠及び授乳時の使用

主な結果

- 20[redacted] 年 [redacted] 月 [redacted] 日時点で，関節リウマチ，乾癬性関節炎，アトピー性皮膚炎，潰瘍性大腸炎及びクローン病患者を対象とした臨床試験で，ウパダシチニブを投与されたと判断された女性被験者で妊娠が合計 39 件報告された。
- 39 件中 3 件は，乾癬性関節炎を対象とした臨床試験に参加した女性被験者の報告であり，妊娠の転帰は子宮外妊娠，自然流産及び妊娠継続であった。
- 39 件中 13 件では，ウパダシチニブを投与された女性被験者が生児を出産しており，妊娠 4 週から 8 週までに先天性異常は報告されなかった。様々なリスク因子（35 歳超，妊娠中の MTX 曝露など）を有する妊婦では，12 件の自然流産が確認され，その自然流産の発生率は，MTX 投与中のリウマチ性疾患患者で報告されたものと同様であった。選択的中絶を実施した 4 名では，胎児異常は報告されなかった。子宮外妊娠が 1 件，転帰不明が 1 件，妊娠継続中が 8 件であった。

背景

乾癬性関節炎で妊娠転帰が得られた試験は限られており，被験者数も少ない。乾癬性関節炎の女性患者での妊娠期間中のデータが不足していることから，臨床医は最も情報が得られている関節リウマチの試験結果から，乾癬性関節炎の女性患者に一般化する傾向がある [4]。慢性炎症性関節炎と妊娠転帰の全体的な観点から，関節リウマチの女性では，関節リウマチのない女性と比較して，早産及び在胎不当過小児を出産するリスクが増加することが報告されている [5–7]。しかし，乾癬性関節炎の女性ではこれらの転帰に関する文献に一貫性はなく，一部の研究では，乾癬性関節炎のない妊婦と比較して，乾癬性関節炎の妊婦で早産及び在胎不当過小児を出産するリスクが増加することが示されているが，他の研究では，これらのリスクは同様であると報告されている [4, 8–14]。乾癬性関節炎の女性の妊娠で，先天性奇形，自然流産又は死産の発現率が一般集団と比べて高いという報告は認められていない [8–11, 13, 14]。

ウパダシチニブと妊娠

非臨床の胚・胎児発生試験では，ウパダシチニブがラット及びウサギの両方で催奇形性を有することが示されている。ウパダシチニブの投与により，ラットでは母体毒性を伴わない骨格奇形が現れ，ウサギでは母体毒性を伴う心奇形が発現した。ラットの出生前及び出生後の発生試験では，ウパダシチニブは，母体パラメータ，生殖パラメータ及び出生児の発育に影響を及ぼさなかった。これらの試験は，関節リウマチに対するウパダシチニブの承認申請で提出した。

ウパダシチニブ臨床開発プログラムでは，授乳中及び妊娠中の女性は試験から除外され，妊娠可能な女性被験者はすべて治験実施計画書で規定された避妊法を使用しなければならないこととした。試験中に妊娠が判明した女性被験者は，治験薬の投与を直ちに中止することとした。試験中に発生し報告されたすべての妊娠症例について，妊娠及び胎児の転帰に関するデータを収集した。

20[redacted] 年 [redacted] 月 [redacted] 日までに収集した累積報告について，米国アッヴィ社のグローバル安全性データベースを検索した。検索方法は，MedDRA version 22.0 の company MedDRA query（以下「CMQ」）「in utero exposure（子宮内曝露）」を用い，妊娠報告タイプを「子宮内曝露，プロスペクティブ，レトロスペクティブ」，妊娠フラグを「はい」とした。

母胎内曝露

ウパダシチニブの臨床試験では，被験者 48 名で合計 52 件の妊娠が報告されている。臨床試験参加中に報告された 52 件の妊娠のうち，39 件は受胎前 1 ヵ月以内及び妊娠第一期にウパダシチニブに曝露されていたと判断された（乾癬性関節炎，関節リウマチ及びクローン病は非盲検下での報告，潰瘍性大腸炎及びアトピー性皮膚炎は盲検下での報告）。残りの 13 件はウパダシチニブに曝露されていなかった。

ウパダシチニブに曝露されていなかった妊娠 13 件（関節リウマチ 11 件，潰瘍性大腸炎 1 件及びアトピー性皮膚炎 1 件）は以下の 11 名で報告された。

- 6 名は対照薬を投与されていた（MTX：先天性異常のない生児を出産，胎児欠損症なし / 不明の選択的中絶，自然流産，妊娠継続中。アダリムマブ：胎児欠損症なし / 不明の選択的中絶，子宮外妊娠）。
- 1 名はウパダシチニブ投与前に妊娠した（胎児欠損症なし / 不明の選択的中絶）。
- 4 名（妊娠 6 件）はウパダシチニブの投与中止後 1 ヵ月以上経過してから妊娠した。
  - 1 名（被験者番号 [redacted]）は，関節リウマチを対象とした M15-555 試験でウパダシチニブの最終投与 10 ヵ月，16 ヵ月及び 24 ヵ月後に 3 回妊娠した（自然流産，枯死卵のため選択的中絶及び妊娠継続中）。
  - 転帰不明：1 名
  - 妊娠継続中：2 名

ウパダシチニブに曝露されたと考えられる 38 名で 39 件の妊娠が報告された。適応症の内訳は，関節リウマチが 26 件，アトピー性皮膚炎が 5 件，潰瘍性大腸炎が 4 件，乾癬性関節炎が 3 件，クローン病が 1 件であった。関節リウマチを対象とした M14-465 試験で，ウパダシチニブを投与された 1 名（被験者番号 [redacted]）に妊娠が 2 件報告された。本被験者は自然流産し，その 1 年後に 2 回目の妊娠をしたが，先天性異常のない生児を出産した。

臨床試験参加中に報告された 39 件の妊娠の転帰を表 2.7.4-73 及び表 2.7.4-74 に示す。

表 2.7.4-73. ウパダシチニブ臨床開発プログラムでの母胎内曝露妊娠の累積の報告

Pregnancy outcomes for maternal exposure reports	N = 39
Total live births:	13
Live birth without congenital anomaly	13*
Live birth with congenital anomaly	0
Total fetal deaths:	17
Spontaneous Abortion	12
Stillbirth without fetal defects	0
Stillbirth with fetal defects	0
Ectopic pregnancy	1
Elective termination (no fetal defects)	4
Elective termination (with fetal defects)	0
Outcome Unknown	1
Ongoing Pregnancy	8
Other (Molar and blighted ovum pregnancies)	0

*: Includes one infant born premature at 28 weeks gestation with no other reported complications.
Note: Based on cumulative exposure through [redacted] 20[redacted]

表 2.7.4-74. ウパダシチニブ臨床開発プログラムでの妊娠転帰（母胎内曝露妊娠）

Study	Subject	Age	Indication	Treatment Assignment at Time of Pregnancy	Pregnancy Outcome	Comment
M15-554	[redacted]	4[redacted]	PsA	Upadacitinib 30 mg QD	Ectopic pregnancy	Advanced maternal age, Subject had an IUD
M15-572	[redacted]	3[redacted]	PsA	Upadacitinib 15 mg QD	Ongoing pregnancy	--

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Study	Subject	Age	Indication	Treatment Assignment at Time of Pregnancy	Pregnancy Outcome	Comment
M15-554	[redacted]	2[redacted]	PsA	Upadacitinib 30 mg QD	Spontaneous Abortion	Poorly controlled diabetes type 1, occurred at approximately 4-8 weeks gestation
M13-538	[redacted]	3[redacted]	RA	Upadacitinib 6 mg BID	Live birth without congenital anomaly	Full term infant without complications
M13-538	[redacted]	3[redacted]	RA	Upadacitinib 12 mg BID	Live birth without congenital anomaly	Full term infant without complications
M13-549	[redacted]	3[redacted]	RA	Upadacitinib 30 mg QD	Elective termination-no fetal defects or unknown	Reason for elective termination not reported
M13-538	[redacted]	3[redacted]	RA	Upadacitinib 12 mg BID	Elective termination-no fetal defects or unknown	Subject decision due to unknown teratogenic effects
M15-555	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	Advanced maternal age, MTX exposure, occurred at approximately 4 weeks gestation
M14-465	[redacted]	2[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	MTX exposure, Occurred at unknown gestational age. First pregnancy during study
M14-465	[redacted]	2[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Second pregnancy during study
M14-465	[redacted]	2[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	MTX exposure, small benign myoma, occurred during first trimester
M14-465	[redacted]	2[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Full term infant without complications

Study	Subject	Age	Indication	Treatment Assignment at Time of Pregnancy	Pregnancy Outcome	Comment
M14-465	[redacted]	2[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	MTX exposure, obesity, smoker (3 PPD × 3 years), hypothyroidism, occurred at approximately 5 weeks gestation
M15-555	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	MTX exposure, occurred at approximately 4 weeks gestation
M15-555	[redacted]	3[redacted]	RA	Upadacitinib 30 mg QD	Live birth without congenital anomaly	Premature infant born at 28 weeks without any reported complications. Other risk factors or maternal medical complications during delivery were not reported
M13-542	[redacted]	3[redacted]	RA	Upadacitinib 30 mg QD	Spontaneous Abortion	Advanced maternal age, obesity, MTX exposure, occurred at approximately 2 weeks gestation
M14-465	[redacted]	2[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	MTX exposure, Smoker (1 PPD x 9 years), Occurred at approximately 6 weeks gestation
M13-545	[redacted]	3[redacted]	RA	Upadacitinib 30 mg QD	Live birth without congenital anomaly	Full term infant without complications
M15-555	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Full term infant without complications
M14-465	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Full term infant without complications
M13-545	[redacted]	4[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Full term infant without complications

Study	Subject	Age	Indication	Treatment Assignment at Time of Pregnancy	Pregnancy Outcome	Comment
M13-545	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Full term infant without complications
M15-925	[redacted]	4[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	Advanced maternal age, MTX exposure, obesity, uterine myoma, occurred at approximately 8 weeks gestation
M15-557	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Elective termination-no fetal defects or unknown	Reason for elective termination not reported
M13-545	[redacted]	3[redacted]	RA	Upadacitinib 30 mg QD	Spontaneous Abortion	2 prior SABs, occurred at approximately 3-4 weeks gestation
M15-555	[redacted]	4[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	Advanced maternal age, occurred during first trimester
M15-925	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Spontaneous Abortion	Advanced maternal age, MTX exposure, occurred at approximately 6 weeks gestation
M14-465	[redacted]	3[redacted]	RA	Upadacitinib 15 mg QD	Live birth without congenital anomaly	Full term infant without complications
M13-549	[redacted]	2[redacted]	RA	Upadacitinib 30 mg QD	Ongoing pregnancy	--
M13-740	[redacted]	2[redacted]	CD	Upadacitinib 24 mg QD	Live birth without congenital anomaly	Full term infant without complications
M14-234	[redacted]	2[redacted]	UC	Blinded	Live birth without congenital anomaly	Full term infant without complications
M14-533	[redacted]	2[redacted]	UC	Blinded	Ongoing pregnancy	--
M14-533	[redacted]	3[redacted]	UC	Blinded	Unknown	--
M14-234	[redacted]	3[redacted]	UC	Blinded	Ongoing pregnancy	--

Study	Subject	Age	Indication	Treatment Assignment at Time of Pregnancy	Pregnancy Outcome	Comment
M16-046	[redacted]	3[redacted]	AD	Blinded	Ongoing pregnancy	--
M16-045	[redacted]	2[redacted]	AD	Blinded	Elective termination-no fetal defects or unknown	Reason for elective termination not reported
M16-045	[redacted]	3[redacted]	AD	Blinded	Ongoing pregnancy	--
M18-891	[redacted]	--	AD	Blinded	Ongoing pregnancy	--
M16-047	[redacted]	4[redacted]	AD	Blinded	Ongoing pregnancy	--

AD = atopic dermatitis, BID = twice daily, CD = Crohn's disease, IUD = intrauterine device, MTX = methotrexate, PPD = purified protein derivative (tuberculin), PsA = psoriatic arthritis, QD = once daily, RA = rheumatoid arthritis, UC = ulcerative colitis

上記の臨床試験での報告の他に，若年性関節リウマチ及び炎症性腸疾患の病歴を有する 3[redacted] 歳の妊娠に関する市販後の自発報告が 1 件あった。妊娠は継続中であり，ウパダシチニブの曝露時期は報告されていない。

妊娠第一期の自然流産は，一般集団では 15%–20%に起こり，約半数は胎児の染色体異常によるものである [15]。その他のリスク因子及び原因が流産の 50%を占めており，これには高齢妊娠，母体の疾患（糖尿病，甲状腺疾患，栓友病，肥満，子宮の構造的異常及び精神的ストレス等），催奇形性物質（MTX 等）及び感染の曝露が含まれた [16]。自然流産のリスクは，高齢妊娠（> 35 歳）及び流産の既往歴により増加する [15, 17, 18]。高齢妊娠は，自然流産の最も重要なリスク因子である [19]。

乾癬性関節炎の治療に使用される医薬品の中には催奇形性を有すると考えられるものがあり，自然流産と関連している。乾癬性関節炎の治療に使用可能な MTX は自然流産のリスク増加に関連しており，催奇形性が知られている [20]。レフルノミドは動物では催奇形性及び胚毒性が認められているが，複数の試験では，レフルノミド投与中の妊娠女性での自然流産及び先天性異常のリスク増加は示唆されていない [21-24]。British Society for Rheumatology Biologics Register が収集したデータでは，MTX 又はレフルノミドの併用下で腫瘍壊死因子（以下「TNF」）阻害薬を投与された関節リウマチ患者の自然流産の割合は 33%であったが，MTX 又はレフルノミドの非併用下で TNF 阻害薬を投与された患者では 24%であった [25]。別の試験で，リウマチ性疾患を有する妊娠女性に対し，受胎後に MTX を投与した被験者と投与しなかった被験者を比較した結果，自

然流産の割合は MTX 投与集団で 42.5%，疾患をマッチさせた MTX 未投与集団で 22.5%であった[26]。ただし，MTX は選択的中絶のために意図的に投与されることがある[27, 28]。

臨床試験で報告された自然流産 12 件は，いずれも自然流産のリスクを増加させる可能性のあるリスク因子の影響を受けたと考えられた。レフルノミドを併用している患者はいなかったが，受胎前後又は妊娠第一期に MTX を併用していた患者は 9 名認められた。その他の交絡因子は，高齢妊娠（> 35 歳）（5 件），肥満（3 件），喫煙中（2 件），自然流産歴（1 件），コントロール不良の 1 型糖尿病（1 件），甲状腺機能低下症（1 件）及び子宮筋腫（2 件）であった。この他，子宮外妊娠の 1 件は子宮内避妊具及び高齢妊娠によるものであった。妊娠 39 件中 13 件では先天性異常のない生児を出産しており，4 件は胎児欠損症の報告がない選択的中絶であったが，中絶理由は，催奇形性の懸念によるもの又は中絶理由の報告がなかった。

ウパダシチニブの臨床試験で報告された自然流産の発現率（約 31%，多くが MTX を併用投与）は，MTX を投与されたリウマチ性疾患の妊婦を対象とした文献で報告されたものと同様であった。

ウパダシチニブは動物試験で催奇形性が認められているが，臨床試験でウパダシチニブを投与された妊婦が出産した生児では，先天性異常は認められなかった。生児のウパダシチニブへの子宮内曝露は，妊娠 4 週から 8 週までの期間であった。

父性曝露

ウパダシチニブには遺伝毒性がないため，生殖細胞への影響を伴う雄性介在の発生リスクは低いと考えられる。また，実験動物モデルのデータから，化学物質が精液中に移行しても，受胎産物が臨床的に意味のある曝露を受けることはないと考えられる[29]。精液中に分泌されたウパダシチニブの移行及び膣吸収を介した胚・胎児曝露の可能性を評価するため，米国アッヴィ社が文献で記述された方法に基づいて曝露量を算出したところ，妊娠可能な女性パートナー又は妊娠中の女性パートナーを有する男性被験者へのウパダシチニブ投与に伴う受胎産物又は胎児へのリスクは無視できることが示された[30, 31]。

20[redacted] 年 [redacted] 月 [redacted] 日時点で，ウパダシチニブを投与された男性被験者のパートナー12 名の妊娠が報告された。いずれも臨床試験での報告であり，対象疾患の内訳は，関節リウマチが 3 名，クローン病が 6 名，乾癬性関節炎が 2 名，強直性脊椎炎が 1 名であった。これら 12 名のパートナーの妊娠転帰を表 2.7.4-75 に示す。

表 2.7.4-75. ウパダシチニブ臨床開発プログラムでの男性被験者のパートナーの妊娠転帰

Study	Subject	Indication	Treatment Assignment at Time of Partner Pregnancy	Pregnancy Outcome
M15-572	[redacted]	PsA	Unknown- partner refused to provide any information	Unknown
M15-554	[redacted]	PsA	BLINDED	Live birth without congenital anomaly
M13-740	[redacted]	CD	UPA 15 mg QD	Live birth without congenital anomaly
M13-740	[redacted]	CD	UPA 12 mg BID	Live birth without congenital anomaly
M13-740	[redacted]	CD	UPA 12 mg BID	Clinical Study subject lost to follow-up
M14-327	[redacted]	CD	UPA 30 mg QD	Live birth without congenital anomaly
M14-327	[redacted]	CD	UPA 15 mg QD	Unknown
M14-433	[redacted]	CD	BLINDED	Ongoing pregnancy
M16-098	[redacted]	AS	UPA 15 mg QD	Ongoing pregnancy
M14-465	[redacted]	RA	Adalimumab	Live birth without congenital anomaly
M14-465	[redacted]	RA	UPA 15 mg QD	Ongoing pregnancy
M15-555	[redacted]	RA	UPA 30 mg QD	Spontaneous Abortion

AS = ankylosing spondylitis, BID = twice daily, CD = Crohn's disease, PsA = psoriatic arthritis, QD = once daily, RA = rheumatoid arthritis, UPA = upadacitinib

乾癬性関節炎の臨床試験期間中に発生した妊娠，並びにウパダシチニブ投与時に発生した母胎内曝露妊娠及び父性曝露妊娠の累積報告を評価した結果，安全性の懸念は認められなかった。

ウパダシチニブは動物試験で催奇形性が認められているが，臨床試験でウパダシチニブを投与された妊婦が出産した生児では先天性異常は認められなかった。自然流産が認められた妊婦は，いずれも 1 つ以上のリスク因子を有しており（多くが MTX を併用していた），ウパダシチニブの臨床開発プログラムで報告された自然流産の発現率は，MTX を投与されたリウマチ性疾患の妊婦で報告されたものと同様であった。

妊娠の累積報告を評価した結果，ウパダシチニブ臨床開発プログラムにおける乾癬性関節炎，関節リウマチ及びその他の適応症で，新たに子宮内曝露に関する重要な情報は得られなかった。関連資料では，妊娠可能な女性に対してウパダシチニブの投与期間及び最終投与後少なくとも 4 週間までは有効な避妊法を用いることを勧めている。妊娠の報告については，標準化された医薬品安全性監視活動を通してモニタリングを継続する予定である。

20[redacted]年[redacted]月[redacted]日以降に，M15-572 試験で 2 名（全ウパダシチニブ 15 mg 群及びアダリムマブ群）に母胎内曝露妊娠が認められた（詳細は M15-572 試験 CSR W56 12. .1 項参照）。M15-55 試験では新たな妊娠は認められなかった。

授乳に関する報告

ウパダシチニブのヒトでの母乳移行，授乳中の乳児に対する影響及び母乳分泌に対する影響に関するデータは得られていない。ウパダシチニブ及びその代謝産物がヒト母乳中に分泌されるかについては不明である。動物での利用可能な薬力学及び毒性学的データでは，ウパダシチニブの乳汁中排泄が示されている。ウパダシチニブの臨床試験の治験実施計画書では，授乳中の女性は除外されており，関連資料にはウパダシチニブ投与中の授乳は避けるようにガイダンスが提示されている。

20[redacted]年[redacted]月[redacted]日までに収集したすべての報告について，米国アッヴィ社のグローバル安全性データベースを検索した。検索方法は，投与経路を「経乳」とし，MedDRA ers on 22.0 の MedDRA 標準検索式（SMQ）「母乳を介した新生児曝露」を用いた。

この検索により，米国で市販後に 2 件の報告が得られた。新生児での有害事象は報告されなかった。両報告とも，最小限の情報のみであった。

ヒトでの授乳中のウパダシチニブ投与に関するデータが不十分であったことから，結論を見出すことはできなかった。

2.7. .5.6 過量投与

ウパダシチニブの過量投与の報告はなかった（ISS Table 2. 1.1 3.1，Table 2. 1.2.3.1）。

ヒトに投与されたウパダシチニブの最大投与量は，第 I 相試験である M13- 01 試験で即放性製剤を用いた 8 mg の単回投与であった（C_{max} は 120 mg 徐放性製剤と同程度であり，0 時間から無限大時間までの血漿中濃度－時間曲線下面積［AUC_{nf}］は 60 mg 徐放性製剤と同程度であると予測される）。本試験では，ウパダシチニブの忍容性は良好であり，重篤な有害事象又は治験薬の投与中止に至った有害事象は報告されなかった。有害事象の大部分は軽度であった。

過量投与が起きた場合，副作用の徴候及び症状がないか患者をモニタリングすることが推奨される。副作用が発現した患者には適切な治療を行う必要がある。

2.7. .5.7 薬物乱用

臨床試験では，薬物乱用又は依存性の報告はなく，薬物乱用に関連するその他の情報も報告されていない。健康被験者及び関節リウマチ患者を対象としたウパダシチニブの臨床試験（第 I 相から第 III 相），すべての適応症，並びにウパダシチニブの市販予定用法・用量（15 mg 1 日 1 回）又はその付近の用法・用量に対して，薬物乱用傾向の可能性に関連する事象を特定できるように設定した CMQ「Abuse Liability（薬物乱用傾向）」を用いて，包括的な解析を実施した。

解析の結果，ウパダシチニブによる治療は乱用の可能性を伴わないことが示された。ウパダシチニブによる治療が薬物乱用を生じさせる根拠及び予測はない。

2.7.4.5.8 離脱症状及び反跳現象

乾癬性関節炎の臨床開発プログラムのいずれの臨床試験でも，離脱症状及び反跳現象の報告はなかった。

2.7.4.5.9 自動車運転及び機械操作に対する影響又は精神機能の障害

マウス，ラット及びイヌを用いた反復投与一般毒性試験でウパダシチニブを評価するとともに，臨床評価を行った。ウパダシチニブを 3 種の動物に反復投与したときの平均 C_{max} は，0.0103–13.5 µg/mL であった。これは，乾癬性関節炎患者での推奨用量である 15 mg（1 日 1 回）を投与したときの定常状態 C_{max} である 0.0376 µg/mL の 0.27–360 倍であった（又は乾癬性関節炎患者に 30 mg［1 日 1 回］を投与したときの定常状態 C_{max} である 0.074 µg/mL の 0.14–180 倍）。いずれの試験（関節リウマチに対するウパダシチニブの承認申請で提出済み）でも，観察された一般状態所見は中枢神経系作用と関連しないと考えられるもの，若しくはウパダシチニブの高用量投与に伴う一般的な病的状態の一部として，致死量又は致死量に近い用量を投与したときにのみ生じたものと考えられた。

SOC の神経系障害及び精神障害の有害事象を検討した結果，投与 24 週時までの発現割合でウパダシチニブ 15 mg，ウパダシチニブ 30 mg 及びプラセボの間に差は認められなかった。

ウパダシチニブが自動車運転及び機械操作に影響を及ぼす又は精神機能に障害を生じさせる根拠及び予測はない。

2.7.4.6 市販後データ

2019 年 8 月 16 日（国際誕生日），米国で関節リウマチに対するウパダシチニブ 15 mg の 1 日 1 回投与が初めて承認された。20[redacted] 年 [redacted] 月 [redacted] 日時点で，ウパダシチニブは 41 ヵ国で承認されており，推定累積曝露数は 9 ヵ国で 3138 人年であった。アッヴィ社は，通常の医薬品安全性監視を通して，新たな潜在的安全性シグナルのモニタリングを継続している。この調査には，市販後報告，すべての情報源（文献を含む）からの重篤及び非重篤な事象の報告，並びに臨床試験で発現した重篤な有害事象の週 1 回の評価，米国食品医薬品局有害事象報告システムデータベースから得られたデータマイニングスコアの四半期ごとの評価，特に注目すべき有害事象の結果を要約した項を含む規定期間ごとの定期報告（定期的安全性最新報告，治験安全性最新報告，定期副作用報告等）及び市販後調査が含まれる。

ウパダシチニブ 15 mg の 1 日 1 回投与の安全性は，2019 年 8 月 16 日から 20[redacted] 年 [redacted] 月 [redacted] 日までに収集した市販後報告（自発報告，非自発的な報告及び文献）をもとに評価した。アッヴィ社のグローバル安全性データベースを検索し，1573 件の報告情報を得た。報告の 90%は非重篤

な事象であり，95%は非自発的な報告からの情報であった。最も発現割合が高かった MedDRA の SOC は感染症および寄生虫症であり，その中で報告数が多かった事象は，上咽頭炎，副鼻腔炎及び上気道感染であった。すべての報告の中で発現割合が高かった事象は，頭痛（7%），嘔吐（7%），薬効欠如（6%），疲労（6%）及び関節痛（5%）であった。市販後に発現した事象の多くは，ウパダシチニブ投与で予測できる事象，又は一般集団若しくは関節リウマチ患者でよくみられる事象であった。薬効欠如は，発現割合が高かった事象として示しているが，市販後の製品で予想できないものではなかった。

最も発現割合が高かった重篤な有害事象は肺炎（1%）であり，その他の重篤な有害事象はいずれも検索された報告の 0.5%未満であった。報告された重篤な有害事象の種類及び発現傾向は，関節リウマチを対象としたウパダシチニブの臨床試験で認められたものとおおむね同様であった。これらの報告では利用可能な情報が限られていることから，報告数が少なかった過敏症 / アナフィラキシー反応のウパダシチニブとの因果関係について，評価することはできなかった。

市販後報告を評価した結果，中等症から重症の活動性関節リウマチを有する患者に対するウパダシチニブの投与で新たな安全性リスクは認められなかった。なお，本邦では，2020 年 4 月 24 日より販売開始されたばかりであり，本申請時点では報告できる市販後調査結果はない。

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2.7.4.7 付録

表 2.7.4.7-1. プラセボ対照併合解析集団（投与 24 週時）の有害事象の概要（100 人年あたりの発現状況）

TABLE 2.4__1.1.1.2

Overview of Treatment-Emergent Adverse Events
in Exposure-Adjusted Rate per 100 Patient Years
(PBO-Controlled Analysis Set)

		----- Upadacitinib -----			-Treatment Comparison (95% CI) [A]-	
	Placebo (N = 635)	15 mg QD (N = 640)	30 mg QD (N = 641)	Adalimumab 40 mg EOW (N = 429)	15 mg QD - Placebo	30 mg QD - Placebo
Exposure-adjusted event rate:	(PYs = 268.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 281.9) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 281.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 189.6) Events (E/100 PYs)		
Any adverse event (AE)	946 (352.1) [352.8]	1245 (441.6) [441.6]	1541 (548.0) [547.9]	833 (439.3)	88.8 (55.5, 122.1)	195.0 (159.6, 230.4)
Any serious AE	22 (8.2) [8.2]	41 (14.5) [14.6]	51 (18.1) [18.0]	19 (10.0)	6.3 (0.7, 12.0)	9.8 (3.8, 15.8)
Any AE leading to discontinuation of study drug	33 (12.3) [12.4]	45 (16.0) [16.0]	56 (19.9) [19.8]	32 (16.9)	3.6 (-2.8, 9.9)	7.3 (0.6, 14.0)
Any severe AE	39 (14.5) [14.6]	49 (17.4) [17.4]	61 (21.7) [21.7]	32 (16.9)	2.8 (-3.9, 9.5)	7.0 (-0.1, 14.1)
Any AE with reasonable possibility of being related to study drug$	320 (119.1) [118.9]	481 (170.6) [170.6]	670 (238.3) [239.2]	410 (216.2)	51.7 (31.6, 71.7)	120.3 (97.9, 142.6)
Any AE leading to death	3 (1.1) [1.1]	0	0	0	-1.1 (-2.4, 0.1)	-1.1 (-2.4, 0.1)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 2.4__1.1.1.2

Overview of Treatment-Emergent Adverse Events
in Exposure-Adjusted Rate per 100 Patient Years
(PBO-Controlled Analysis Set)

		----- Upadacitinib -----			-Treatment Comparison (95% CI) [A]-	
	Placebo (N = 635)	15 mg QD (N = 640)	30 mg QD (N = 641)	Adalimumab 40 mg EOW (N = 429)	15 mg QD - Placebo	30 mg QD - Placebo
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		
Deaths#	2/268.7 (0.7) [0.8]	0/281.9	0/281.2	0/189.6	-0.8 (-1.8, 0.3)	-0.8 (-1.8, 0.3)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A] Study size adjusted risk difference between treatment groups.
Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-2. プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の有害事象の概要（100 人年あたりの発現状況）

TABLE 2.4__1.1.1.2_J

Overview of Treatment-Emergent Adverse Events
in Exposure-Adjusted Rate per 100 Patient Years
(PBO-Controlled Analysis Set, Japanese Population)

		----- Upadacitinib -----			-Treatment Comparison (95% CI) [A]-	
	Placebo (N = 15)	15 mg QD (N = 17)	30 mg QD (N = 18)	Adalimumab 40 mg EOW (N = 4)	15 mg QD - Placebo	30 mg QD - Placebo
Exposure-adjusted event rate:	(PYs = 6.5) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 7.3) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 7.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 1.8) Events (E/100 PYs)		
Any adverse event (AE)	21 (323.1) [316.0]	47 (643.8) [648.5]	53 (697.4) [697.6]	6 (333.3)	332.6 (103.0, 562.2)	381.7 (150.2, 613.1)
Any serious AE	0	1 (13.7) [14.1]	4 (52.6) [53.1]	1 (55.6)	14.1 (-13.5, 41.6)	53.1 (1.1, 105.1)
Any AE leading to discontinuation of study drug	0	1 (13.7) [14.1]	3 (39.5) [39.8]	1 (55.6)	14.1 (-13.5, 41.6)	39.8 (-5.2, 84.8)
Any severe AE	0	1 (13.7) [14.1]	5 (65.8) [66.3]	3 (166.7)	14.1 (-13.5, 41.6)	66.3 (8.2, 124.5)
Any AE with reasonable possibility of being related to study drug$	9 (138.5) [138.1]	15 (205.5) [206.0]	18 (236.8) [236.4]	2 (111.1)	67.8 (-70.3, 205.9)	98.3 (-43.5, 240.1)
Any AE leading to death	0	0	0	0	0.0	0.0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 2.4__1.1.1.2_J

Overview of Treatment-Emergent Adverse Events
in Exposure-Adjusted Rate per 100 Patient Years
(PBO-Controlled Analysis Set, Japanese Population)

		----- Upadacitinib -----			-Treatment Comparison (95% CI) [A]-	
	Placebo (N = 15)	15 mg QD (N = 17)	30 mg QD (N = 18)	Adalimumab 40 mg EOW (N = 4)	15 mg QD - Placebo	30 mg QD - Placebo
Exposure-adjusted incidence rate:	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs)		
Deaths#	0/6.5	0/7.3	0/7.6	0/1.8	0.0	0.0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. SSA = Study size adjusted.
n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A] Study size adjusted risk difference between treatment groups.
Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-3.　　全ウパダシチニブ併合解析集団（長期）の有害事象の概要

TABLE 2.4__1.2.1.1

Overview of Number and Percentage of Subjects
with Treatment-Emergent Adverse Events
(Any Upadacitinib Analysis Set)

	Upadacitinib					Treatment Comparison (95% CI) [A]	
	15 mg QD (No Cross-Over from Placebo) (N = 640) n (%) [SSA %]	30 mg QD (No Cross-Over from Placebo) (N = 641) n (%) [SSA %]	Any 15 mg QD (N = 907) n (%) [SSA %]	Any 30 mg QD (N = 920) n (%) [SSA %]	Adalimumab 40 mg EOW (N = 429) n (%)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Subjects with:							
Any adverse event (AE)	498 (77.8) [77.8]	527 (82.2) [82.2]	648 (71.4) [71.5]	682 (74.1) [74.1]	334 (77.9)	4.4 (-0.0, 8.7)	2.6 (-1.5, 6.6)
Any serious AE	50 (7.8) [7.8]	76 (11.9) [11.8]	61 (6.7) [6.8]	93 (10.1) [10.1]	36 (8.4)	4.0 (0.8, 7.3)	3.3 (0.8, 5.9)
Any AE leading to discontinuation of study drug	41 (6.4) [6.4]	54 (8.4) [8.4]	51 (5.6) [5.7]	60 (6.5) [6.5]	30 (7.0)	2.0 (-0.9, 4.8)	0.8 (-1.3, 3.0)
Any severe AE	61 (9.5) [9.5]	83 (12.9) [12.9]	72 (7.9) [8.0]	99 (10.8) [10.7]	43 (10.0)	3.4 (-0.1, 6.8)	2.8 (0.1, 5.4)
Any AE with reasonable possibility of being related to study drug$	272 (42.5) [42.5]	337 (52.6) [52.6]	338 (37.3) [37.3]	417 (45.3) [45.3]	201 (46.9)	10.1 (4.7, 15.6)	8.1 (3.6, 12.6)
Any AE leading to death	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]	0	-0.2 (-0.5, 0.1)	-0.0 (-0.3, 0.3)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 2.4__1.2.1.1

Overview of Number and Percentage of Subjects
with Treatment-Emergent Adverse Events
(Any Upadacitinib Analysis Set)

	Upadacitinib					Treatment Comparison (95% CI) [A]	
	15 mg QD (No Cross-Over from Placebo) (N = 640) n (%) [SSA %]	30 mg QD (No Cross-Over from Placebo) (N = 641) n (%) [SSA %]	Any 15 mg QD (N = 907) n (%) [SSA %]	Any 30 mg QD (N = 920) n (%) [SSA %]	Adalimumab 40 mg EOW (N = 429) n (%)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Deaths#	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]	0	0.0 (-0.4, 0.4)	0.1 (-0.3, 0.5)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.
Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-4.　　全ウパダシチニブ併合解析集団（長期）の日本人部分集団の有害事象の概要

TABLE 2.4__1.2.1.1_J

Overview of Number and Percentage of Subjects
with Treatment-Emergent Adverse Events
(Any Upadacitinib Analysis Set, Japanese Population)

	Upadacitinib					Treatment Comparison (95% CI) [A]	
	15 mg QD (No Cross-Over from Placebo) (N = 17) n (%) [SSA %]	30 mg QD (No Cross-Over from Placebo) (N = 18) n (%) [SSA %]	Any 15 mg QD (N = 23) n (%) [SSA %]	Any 30 mg QD (N = 26) n (%) [SSA %]	Adalimumab 40 mg EOW (N = 4) n (%)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Subjects with:							
Any adverse event (AE)	16 (94.1) [94.1]	18 (100) [100.0]	21 (91.3) [91.2]	26 (100) [100]	3 (75.0)	5.9 (-5.2, 17.1)	8.8 (-2.6, 20.2)
Any serious AE	3 (17.6) [17.8]	6 (33.3) [33.3]	4 (17.4) [17.2]	8 (30.8) [30.9]	1 (25.0)	15.5 (-12.5, 43.4)	13.7 (-9.4, 36.7)
Any AE leading to discontinuation of study drug	1 (5.9) [5.9]	3 (16.7) [16.5]	1 (4.3) [4.3]	4 (15.4) [15.5]	1 (25.0)	10.6 (-9.4, 30.6)	11.2 (-4.7, 27.1)
Any severe AE	2 (11.8) [11.9]	5 (27.8) [27.8]	3 (13.0) [12.9]	8 (30.8) [30.7]	2 (50.0)	15.9 (-9.7, 41.5)	17.8 (-4.4, 40.0)
Any AE with reasonable possibility of being related to study drug$	9 (52.9) [53.0]	15 (83.3) [83.5]	11 (47.8) [47.8]	20 (76.9) [76.9]	2 (50.0)	30.5 (1.6, 59.4)	29.1 (3.1, 55.1)
Any AE leading to death	0	0	0	1 (3.8) [3.9]	0	0.0	3.9 (-3.5, 11.3)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.
$ As assessed by investigator.

Program Source Code: [redacted]

TABLE 2.4__1.2.1.1_J

Overview of Number and Percentage of Subjects
with Treatment-Emergent Adverse Events
(Any Upadacitinib Analysis Set, Japanese Population)

	Upadacitinib					Treatment Comparison (95% CI) [A]	
	15 mg QD (No Cross-Over from Placebo) (N = 17) n (%) [SSA %]	30 mg QD (No Cross-Over from Placebo) (N = 18) n (%) [SSA %]	Any 15 mg QD (N = 23) n (%) [SSA %]	Any 30 mg QD (N = 26) n (%) [SSA %]	Adalimumab 40 mg EOW (N = 4) n (%)	30 mg QD - 15 mg QD (No Cross-Over from Placebo)	Any 30 mg QD - Any 15 mg QD
Deaths#	0	0	0	1 (3.8) [3.9]	0	0.0	3.9 (-3.5, 11.3)

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo, and no more than 70 days after the last dose of adalimumab.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
SSA = Study size adjusted.
[A] Study size adjusted risk difference between treatment groups.
Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-5. 投与 24 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況，安全性解析対象集団）：M15-572 試験

[redacted]
ABT-494 (PSA)
STUDY M15-572 - WEEK 24 (DATA CUTOFF - [redacted]20[redacted])
R&D/19/0849 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.1.2.2

Overview of Treatment-Emergent Adverse Events in Exposure Adjusted Rate per 100 Patient Years - Long Term
(Safety Analysis Set)

	UPA			-- UPA VS ADA (95% CI)[A] --	
	15 mg QD (N = 617) (PYs = 524.1)	30 mg QD (N = 612) (PYs = 526.0)	ADA 40 mg EOW (N = 429) (PYs = 394.5)	15 mg QD VS ADA	30 mg QD VS ADA
Exposure-adjusted event rate	Events (E/100 PYs)	Events (E/100 PYs)	Events (E/100 PYs)		
Any adverse event (AE)	1683 (321.1)	2015 (383.1)	1294 (328.0)	-6.9 (-30.4, 16.7)	55.1 (30.6, 79.5)
Any serious AE (SAE)	45 (8.6)	68 (12.9)	43 (10.9)	-2.3 (-6.4, 1.8)	2.0 (-2.5, 6.5)
Any AE leading to discontinuation of study drug	31 (5.9)	39 (7.4)	40 (10.1)	-4.2 (-8.0, -0.5)	-2.7 (-6.6, 1.2)
Any severe AE	55 (10.5)	83 (15.8)	51 (12.9)	-2.4 (-6.9, 2.1)	2.9 (-2.1, 7.8)
Any AE with reasonable possibility of being related to study drug$	694 (132.4)	910 (173.0)	594 (150.6)	-18.2 (-33.8, -2.5)	22.4 (5.9, 39.0)
Any AE leading to death	1 (0.2)	0	0	0.2 (-0.2, 0.6)	0.0
Exposure-adjusted incidence rate	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)		
Deaths					
Occurring <= 30 days (ADA for 70 days) after last dose	0/524.1	0/526.0	0/394.5	0.0	0.0
Occurring > 30 days (ADA for 70 days) after last dose	1/524.3 (0.2)	1/526.1 (0.2)	0/394.5	0.2 (-0.2, 0.6)	0.2 (-0.2, 0.6)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
[A]: The point estimate and 95% CI are based on normal approximation to poisson distribution.
$ As assessed by investigator.

Program Source Code: [redacted]

表 2.7.4.7-6. 投与 24 週時データカットオフまでの有害事象の概要（安全性解析対象集団）：M15-572 試験

TABLE 14.3__1.1.1.2_J

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events - Long Term
(Safety Analysis Set)

	---- UPA ------			-- UPA VS ADA (95% CI)[A] --	
	15 mg QD (N = 617) n (%)	30 mg QD (N = 612) n (%)	ADA 40 mg EOW (N = 429) n (%)	15 mg QD VS ADA	30 mg QD VS ADA
Subjects with:					
Any adverse event (AE)	427 (69.2)	433 (70.8)	334 (77.9)	-8.6 (-14.0, -3.3)	-7.1 (-12.4, -1.8)
Any serious AE (SAE)	34 (5.5)	55 (9.0)	36 (8.4)	-2.9 (-6.1, 0.3)	0.6 (-2.9, 4.1)
Any AE leading to discontinuation of study drug	26 (4.2)	32 (5.2)	30 (7.0)	-2.8 (-5.7, 0.1)	-1.8 (-4.8, 1.2)
Any severe AE	44 (7.1)	60 (9.8)	43 (10.0)	-2.9 (-6.4, 0.6)	-0.2 (-3.9, 3.5)
Any AE with reasonable possibility of being related to study drug$	234 (37.9)	282 (46.1)	201 (46.9)	-8.9 (-15.0, -2.8)	-0.8 (-6.9, 5.4)
Any AE leading to death	1 (0.2)	0	0	0.2 (-0.2, 0.5)	0.0
Deaths					
Occurring <= 30 days (ADA for 70 days) after last dose	0	0	0	0.0	0.0
Occurring > 30 days (ADA for 70 days) after last dose	1 (0.2)	1 (0.2)	0	0.2 (-0.2, 0.5)	0.2 (-0.2, 0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
[A]: The point estimate and 95% CI are based on normal approximation to binomial distribution.
$ As assessed by investigator.

Program Source Code: [redacted]

表 2.7.4.7-7. 投与 24 週時データカットオフまでの有害事象の概要（100 人年あたりの発現状況，安全性解析対象集団）：M15-554 試験

[redacted]
ABT-494 (PSA)
STUDY M15-554 - WEEK 24 (DATA CUTOFF - [redacted]20[redacted])
R&D/19/0848 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.1.2.2

Overview of Treatment-Emergent Adverse Events in Exposure Adjusted Rate per 100 Patient Years - Long Term
(Safety Analysis Set)

	UPA	
	15 mg QD (N = 290) (PYs = 292.8)	30 mg QD (N = 308) (PYs = 296.2)
Exposure-adjusted event rate	Events (E/100 PYs)	Events (E/100 PYs)
Any adverse event (AE)	840 (286.9)	1105 (373.1)
Any serious AE (SAE)	44 (15.0)	54 (18.2)
Any AE leading to discontinuation of study drug	38 (13.0)	39 (13.2)
Any severe AE	46 (15.7)	67 (22.6)
Any AE with reasonable possibility of being related to study drug$	207 (70.7)	346 (116.8)
Any AE leading to death	0	1 (0.3)
Exposure-adjusted incidence rate	n/PYs (n/100 PYs)	n/PYs (n/100 PYs)
Deaths		
Occurring <= 30 days after last dose	0/292.8	1/296.3 (0.3)
Occurring > 30 days after last dose	0/292.8	0/296.2

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study. Severe AEs are defined as events with grade 3 or above based on the Common Terminology Criteria for AEs (CTCAE) version 5.0.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
$ As assessed by investigator.

Program Source Code: [redacted]

表 2.7.4.7-8. 投与 24 週時データカットオフまでの有害事象の概要（安全性解析対象集団）：M15-554 試験

[redacted]
ABT-494 (PSA)
STUDY M15-554 - WEEK 24 (DATA CUTOFF - [redacted]20[redacted])
R&D/19/0848 - CLINICAL/STATISTICAL

TABLE 14.3__1.1.1.2_J

Overview of Number and Percentage of Subjects with Treatment-Emergent Adverse Events - Long Term
(Safety Analysis Set)

	------- UPA -------	
	15 mg QD (N = 290) n (%)	30 mg QD (N = 308) n (%)
Subjects with:		
Any adverse event (AE)	221 (76.2)	249 (80.8)
Any serious AE (SAE)	27 (9.3)	38 (12.3)
Any AE leading to discontinuation of study drug	25 (8.6)	28 (9.1)
Any severe AE	28 (9.7)	39 (12.7)
Any AE with reasonable possibility of being related to study drug$	104 (35.9)	135 (43.8)
Any AE leading to death	0	1 (0.3)
Deaths		
Occurring <= 30 days after last dose	0	1 (0.3)
Occurring > 30 days after last dose	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of UPA and up to 30 days after the last dose of UPA, if subject discontinued prematurely from the study.
Subjects in UPA 15 mg QD/30mg QD group include those who started UPA 15 mg QD/30mg QD at the beginning of the study and those who switched to UPA 15 mg/30mg QD at Week 24.
Severe adverse events are defined as events with grade 3 or above based on the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.
$ As assessed by investigator.

Program Source Code: [redacted]

表 2.7.4.7-9.　　プラセボ対照併合解析集団（投与 24 週時）の治験薬と関連ありの有害事象

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
Any adverse event	173 (27.2) [27.2]	212 (33.1) [33.1]	265 (41.3) [41.4]
血液およびリンパ系障害	10 (1.6) [1.6]	22 (3.4) [3.4]	44 (6.9) [6.9]
貧血	2 (0.3) [0.3]	3 (0.5) [0.5]	11 (1.7) [1.7]
大球性貧血	0	0	1 (0.2) [0.2]
失血性貧血	0	1 (0.2) [0.2]	0
骨髄浮腫	0	0	1 (0.2) [0.2]
赤血球減少症	0	0	1 (0.2) [0.2]
顆粒球減少症	0	0	1 (0.2) [0.2]
内出血発生の増加傾向	0	0	1 (0.2) [0.2]
鉄欠乏性貧血	0	0	1 (0.2) [0.2]
白血球増加症	1 (0.2) [0.2]	0	1 (0.2) [0.2]
白血球減少症	2 (0.3) [0.3]	10 (1.6) [1.6]	11 (1.7) [1.7]
リンパ節症	2 (0.3) [0.3]	1 (0.2) [0.2]	0
リンパ球増加症	0	0	1 (0.2) [0.2]
リンパ組織過形成	0	0	1 (0.2) [0.2]
リンパ球減少症	3 (0.5) [0.5]	5 (0.8) [0.8]	13 (2.0) [2.0]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
血液およびリンパ系障害 (Cont.)			
好中球減少症	1 (0.2) [0.2]	5 (0.8) [0.8]	17 (2.7) [2.7]
好中球増加症	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]
正色素性貧血	0	0	1 (0.2) [0.2]
血小板減少症	1 (0.2) [0.2]	0	2 (0.3) [0.3]
血小板増加症	1 (0.2) [0.2]	0	0
心臓障害	0	3 (0.5) [0.5]	1 (0.2) [0.2]
心房細動	0	1 (0.2) [0.2]	0
心肺停止	0	1 (0.2) [0.2]	0
動悸	0	1 (0.2) [0.2]	0
発作性頻脈	0	0	1 (0.2) [0.2]
心室細動	0	1 (0.2) [0.2]	0
先天性、家族性および遺伝性障害	1 (0.2) [0.2]	0	0
ミトコンドリアミオパチー	1 (0.2) [0.2]	0	0
耳および迷路障害	3 (0.5) [0.5]	1 (0.2) [0.2]	0
耳痛	3 (0.5) [0.5]	0	0
回転性めまい	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
内分泌障害	0	1 (0.2) [0.2]	0
アンドロゲン欠乏症	0	1 (0.2) [0.2]	0
眼障害	2 (0.3) [0.3]	3 (0.5) [0.5]	3 (0.5) [0.5]
一過性黒内障	0	0	1 (0.2) [0.2]
眼瞼痙攣	0	1 (0.2) [0.2]	0
ドライアイ	0	0	1 (0.2) [0.2]
眼痛	0	1 (0.2) [0.2]	0
虹彩毛様体炎	0	0	1 (0.2) [0.2]
瞼板腺炎	0	1 (0.2) [0.2]	0
眼充血	1 (0.2) [0.2]	0	0
霧視	0	1 (0.2) [0.2]	0
視力障害	0	1 (0.2) [0.2]	0
硝子体剥離	1 (0.2) [0.2]	0	0
胃腸障害	28 (4.4) [4.4]	33 (5.2) [5.1]	38 (5.9) [5.9]
腹部不快感	3 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
腹部膨満	0	0	2 (0.3) [0.3]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
胃腸障害 (Cont.)			
腹痛	0	1 (0.2) [0.2]	2 (0.3) [0.3]
上腹部痛	1 (0.2) [0.2]	4 (0.6) [0.6]	4 (0.6) [0.6]
口角口唇炎	0	1 (0.2) [0.2]	0
アフタ性潰瘍	0	1 (0.2) [0.2]	0
根尖肉芽腫	0	0	1 (0.2) [0.2]
大腸炎	0	0	1 (0.2) [0.2]
便秘	2 (0.3) [0.3]	3 (0.5) [0.5]	1 (0.2) [0.2]
下痢	9 (1.4) [1.4]	7 (1.1) [1.1]	7 (1.1) [1.1]
口内乾燥	2 (0.3) [0.3]	1 (0.2) [0.2]	1 (0.2) [0.2]
消化不良	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.5) [0.5]
びらん性十二指腸炎	0	1 (0.2) [0.2]	0
変色便	0	1 (0.2) [0.2]	0
鼓腸	3 (0.5) [0.5]	0	1 (0.2) [0.2]
胃出血	0	0	1 (0.2) [0.2]
胃炎	0	0	3 (0.5) [0.5]
びらん性胃炎	0	3 (0.5) [0.5]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
胃腸障害 (Cont.)			
胃十二指腸出血	0	1 (0.2) [0.2]	0
胃十二指腸潰瘍	0	0	1 (0.2) [0.2]
胃腸障害	1 (0.2) [0.2]	0	0
胃食道逆流性疾患	0	1 (0.2) [0.2]	0
舌炎	1 (0.2) [0.2]	0	0
痔核	0	1 (0.2) [0.2]	1 (0.2) [0.2]
過敏性腸症候群	1 (0.2) [0.2]	0	0
口腔内潰瘍形成	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.5) [0.5]
悪心	8 (1.3) [1.3]	7 (1.1) [1.1]	7 (1.1) [1.1]
食道潰瘍	0	0	1 (0.2) [0.2]
口腔障害	0	0	1 (0.2) [0.2]
口腔粘膜水疱形成	0	0	1 (0.2) [0.2]
膵炎	0	1 (0.2) [0.2]	0
歯周の炎症	0	1 (0.2) [0.2]	0
小腸出血	0	0	1 (0.2) [0.2]
小腸潰瘍	0	0	1 (0.2) [0.2]

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SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
胃腸障害 (Cont.)			
口内炎	0	0	1 (0.2) [0.2]
舌腫脹	1 (0.2) [0.2]	0	0
舌潰瘍	0	1 (0.2) [0.2]	1 (0.2) [0.2]
歯の障害	0	1 (0.2) [0.2]	0
歯痛	0	1 (0.2) [0.2]	0
嘔吐	2 (0.3) [0.3]	0	5 (0.8) [0.8]
一般・全身障害および投与部位の状態	14 (2.2) [2.2]	11 (1.7) [1.7]	19 (3.0) [3.0]
無力症	2 (0.3) [0.3]	1 (0.2) [0.2]	1 (0.2) [0.2]
胸痛	1 (0.2) [0.2]	1 (0.2) [0.2]	0
悪寒	0	2 (0.3) [0.3]	0
疲労	3 (0.5) [0.5]	3 (0.5) [0.5]	4 (0.6) [0.6]
インフルエンザ様疾患	2 (0.3) [0.3]	0	2 (0.3) [0.3]
注射部位血腫	1 (0.2) [0.2]	0	0
注射部位疼痛	1 (0.2) [0.2]	0	1 (0.2) [0.2]
注射部位反応	0	0	1 (0.2) [0.2]
倦怠感	1 (0.2) [0.2]	1 (0.2) [0.2]	0

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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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
一般・全身障害および投与部位の状態 (Cont.)			
非心臓性胸痛	0	0	1 (0.2) [0.2]
疼痛	1 (0.2) [0.2]	0	1 (0.2) [0.2]
末梢腫脹	1 (0.2) [0.2]	1 (0.2) [0.2]	0
発熱	2 (0.3) [0.3]	2 (0.3) [0.3]	6 (0.9) [0.9]
腫脹	0	0	1 (0.2) [0.2]
全身性炎症反応症候群	0	0	1 (0.2) [0.2]
肝胆道系障害	2 (0.3) [0.3]	7 (1.1) [1.1]	8 (1.2) [1.3]
胆道仙痛	1 (0.2) [0.2]	0	0
胆石症	1 (0.2) [0.2]	0	0
肝機能異常	0	3 (0.5) [0.5]	3 (0.5) [0.5]
脂肪肝	0	0	1 (0.2) [0.2]
肝毒性	0	1 (0.2) [0.2]	1 (0.2) [0.2]
高ビリルビン血症	0	2 (0.3) [0.3]	1 (0.2) [0.2]
肝障害	0	0	1 (0.2) [0.2]
肝損傷	0	0	1 (0.2) [0.2]
脂肪性肝炎	0	1 (0.2) [0.2]	0

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Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
免疫系障害	1 (0.2) [0.2]	0	2 (0.3) [0.3]
食物アレルギー	0	0	1 (0.2) [0.2]
過敏症	0	0	1 (0.2) [0.2]
季節性アレルギー	1 (0.2) [0.2]	0	0
感染症および寄生虫症	86 (13.5) [13.5]	123 (19.2) [19.2]	130 (20.3) [20.3]
膿瘍	1 (0.2) [0.2]	0	0
四肢膿瘍	0	0	1 (0.2) [0.2]
急性副鼻腔炎	0	0	1 (0.2) [0.2]
虫垂炎	1 (0.2) [0.2]	0	1 (0.2) [0.2]
異型肺炎	0	0	1 (0.2) [0.2]
菌血症	0	0	1 (0.2) [0.2]
細菌感染	1 (0.2) [0.2]	1 (0.2) [0.2]	0
細菌性前立腺炎	1 (0.2) [0.2]	0	0
細菌性膣症	0	1 (0.2) [0.2]	0
体部白癬	0	1 (0.2) [0.2]	0
乳房蜂巣炎	1 (0.2) [0.2]	0	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
with Reasonable Possibility of Being Related to Study Drug
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(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
気管支炎	3 (0.5) [0.5]	8 (1.3) [1.3]	12 (1.9) [1.9]
細菌性気管支炎	0	0	1 (0.2) [0.2]
蜂巣炎	0	2 (0.3) [0.3]	1 (0.2) [0.2]
眼窩蜂巣炎	1 (0.2) [0.2]	0	0
結膜炎	1 (0.2) [0.2]	1 (0.2) [0.2]	0
ウイルス性結膜炎	0	1 (0.2) [0.2]	0
膀胱炎	3 (0.5) [0.5]	3 (0.5) [0.5]	1 (0.2) [0.2]
サイトメガロウイルス感染	0	0	1 (0.2) [0.2]
毛嚢虫症	0	1 (0.2) [0.2]	1 (0.2) [0.2]
精巣上体炎	0	0	1 (0.2) [0.2]
丹毒	0	1 (0.2) [0.2]	0
大腸菌性尿路感染	1 (0.2) [0.2]	1 (0.2) [0.2]	0
毛包炎	0	6 (0.9) [0.9]	2 (0.3) [0.3]
真菌感染	0	1 (0.2) [0.2]	0
皮膚真菌感染	0	2 (0.3) [0.3]	3 (0.5) [0.5]
せつ	1 (0.2) [0.2]	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

Number and Percentage of Subjects with Treatment-Emergent Adverse Events
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System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
胃腸炎	3 (0.5) [0.5]	1 (0.2) [0.2]	4 (0.6) [0.6]
ウイルス性胃腸炎	1 (0.2) [0.2]	0	1 (0.2) [0.2]
消化管感染	1 (0.2) [0.2]	0	0
陰部ヘルペス	0	2 (0.3) [0.3]	1 (0.2) [0.2]
歯肉炎	0	1 (0.2) [0.2]	2 (0.3) [0.3]
鼠径部膿瘍	0	0	1 (0.2) [0.2]
B型肝炎再活性化	0	1 (0.2) [0.2]	0
C型肝炎	1 (0.2) [0.2]	0	0
単純ヘルペス	1 (0.2) [0.2]	2 (0.3) [0.3]	6 (0.9) [0.9]
ヘルペスウイルス感染	0	1 (0.2) [0.2]	0
帯状疱疹	2 (0.3) [0.3]	7 (1.1) [1.1]	12 (1.9) [1.9]
麦粒腫	0	1 (0.2) [0.2]	0
感染性皮膚嚢腫	1 (0.2) [0.2]	0	0
インフルエンザ	0	9 (1.4) [1.4]	6 (0.9) [0.9]
喉頭炎	1 (0.2) [0.2]	0	1 (0.2) [0.2]
下気道感染	3 (0.5) [0.5]	3 (0.5) [0.5]	1 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
肺感染	1 (0.2) [0.2]	0	1 (0.2) [0.2]
爪感染	1 (0.2) [0.2]	1 (0.2) [0.2]	0
上咽頭炎	9 (1.4) [1.4]	9 (1.4) [1.4]	10 (1.6) [1.6]
口腔カンジダ症	0	1 (0.2) [0.2]	2 (0.3) [0.3]
口腔ヘルペス	4 (0.6) [0.6]	5 (0.8) [0.8]	19 (3.0) [3.0]
口腔感染	1 (0.2) [0.2]	0	0
中咽頭カンジダ症	0	0	1 (0.2) [0.2]
外耳炎	0	0	1 (0.2) [0.2]
中耳炎	0	0	1 (0.2) [0.2]
急性中耳炎	0	0	2 (0.3) [0.3]
爪囲炎	0	2 (0.3) [0.3]	2 (0.3) [0.3]
歯周炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.2) [0.2]
咽頭炎	3 (0.5) [0.5]	2 (0.3) [0.3]	2 (0.3) [0.3]
レンサ球菌性咽頭炎	0	3 (0.5) [0.5]	2 (0.3) [0.3]
ニューモシスチス・イロベチイ肺炎	0	0	1 (0.2) [0.2]
肺炎	1 (0.2) [0.2]	3 (0.5) [0.5]	4 (0.6) [0.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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with Reasonable Possibility of Being Related to Study Drug
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(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
歯髄炎	0	1 (0.2) [0.2]	0
化膿性分泌物	0	0	1 (0.2) [0.2]
膿疱性皮疹	0	0	2 (0.3) [0.3]
気道感染	3 (0.5) [0.5]	7 (1.1) [1.1]	8 (1.2) [1.3]
ウイルス性気道感染	1 (0.2) [0.2]	0	0
鼻炎	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.5) [0.5]
敗血症	0	2 (0.3) [0.3]	0
副鼻腔炎	8 (1.3) [1.3]	5 (0.8) [0.8]	4 (0.6) [0.6]
細菌性副鼻腔炎	2 (0.3) [0.3]	0	0
皮膚カンジダ	0	0	1 (0.2) [0.2]
皮膚感染	0	1 (0.2) [0.2]	0
ブドウ球菌感染	0	1 (0.2) [0.2]	0
ブドウ球菌皮膚感染	0	1 (0.2) [0.2]	0
皮下組織膿瘍	0	0	1 (0.2) [0.2]
白癬感染	0	1 (0.2) [0.2]	0
足部白癬	1 (0.2) [0.2]	2 (0.3) [0.3]	2 (0.3) [0.3]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
癜風	1 (0.2) [0.2]	1 (0.2) [0.2]	0
扁桃炎	0	1 (0.2) [0.2]	4 (0.6) [0.6]
細菌性扁桃炎	0	1 (0.2) [0.2]	1 (0.2) [0.2]
歯膿瘍	0	1 (0.2) [0.2]	0
歯感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.2) [0.2]
気管炎	0	0	2 (0.3) [0.3]
気管気管支炎	0	1 (0.2) [0.2]	0
上気道感染	21 (3.3) [3.3]	28 (4.4) [4.4]	26 (4.1) [4.1]
尿路感染	11 (1.7) [1.7]	16 (2.5) [2.5]	12 (1.9) [1.9]
腸球菌性尿路感染	0	1 (0.2) [0.2]	0
尿路性敗血症	0	0	1 (0.2) [0.2]
腟感染	1 (0.2) [0.2]	0	0
ウイルス感染	2 (0.3) [0.3]	0	1 (0.2) [0.2]
ウイルス性筋炎	0	1 (0.2) [0.2]	0
ウイルス性咽頭炎	0	0	1 (0.2) [0.2]
ウイルス性気管炎	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
ウイルス性上気道感染	1 (0.2) [0.2]	1 (0.2) [0.2]	0
外陰部炎	0	1 (0.2) [0.2]	0
外陰部腟カンジダ症	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.3) [0.3]
外陰腟真菌感染	0	1 (0.2) [0.2]	1 (0.2) [0.2]
傷害、中毒および処置合併症	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.5) [0.5]
節足動物咬傷	0	0	1 (0.2) [0.2]
挫傷	0	0	1 (0.2) [0.2]
仙骨骨折	0	0	1 (0.2) [0.2]
皮膚擦過傷	0	1 (0.2) [0.2]	0
歯牙破折	1 (0.2) [0.2]	0	0
各種物質毒性	1 (0.2) [0.2]	0	0
臨床検査	28 (4.4) [4.4]	56 (8.8) [8.7]	90 (14.0) [14.1]
アラニンアミノトランスフェラーゼ増加	8 (1.3) [1.3]	19 (3.0) [3.0]	28 (4.4) [4.4]
αヒドロキシ酪酸脱水素酵素増加	0	0	1 (0.2) [0.2]
アスパラギン酸アミノトランスフェラーゼ増加	5 (0.8) [0.8]	13 (2.0) [2.0]	18 (2.8) [2.8]
血中アルカリホスファターゼ増加	1 (0.2) [0.2]	0	0

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SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
臨床検査 (Cont.)			
血中ビリルビン増加	0	1 (0.2) [0.2]	0
血中コレステロール減少	1 (0.2) [0.2]	0	0
血中コレステロール増加	0	4 (0.6) [0.6]	2 (0.3) [0.3]
血中クレアチンホスホキナーゼMB増加	1 (0.2) [0.2]	0	0
血中クレアチンホスホキナーゼ増加	8 (1.3) [1.3]	30 (4.7) [4.7]	42 (6.6) [6.6]
血中クレアチニン増加	1 (0.2) [0.2]	2 (0.3) [0.3]	3 (0.5) [0.5]
血中乳酸脱水素酵素増加	0	0	1 (0.2) [0.2]
血中カリウム増加	1 (0.2) [0.2]	0	1 (0.2) [0.2]
血圧上昇	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]
血中トリグリセリド増加	0	0	1 (0.2) [0.2]
血中尿素増加	0	0	2 (0.3) [0.3]
血中尿酸増加	0	0	4 (0.6) [0.6]
ヘマトクリット減少	0	1 (0.2) [0.2]	0
ヘモグロビン減少	2 (0.3) [0.3]	1 (0.2) [0.2]	5 (0.8) [0.8]
肝酵素上昇	2 (0.3) [0.3]	1 (0.2) [0.2]	6 (0.9) [0.9]
高比重リポ蛋白減少	1 (0.2) [0.2]	0	0

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SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
臨床検査 (Cont.)			
高比重リポ蛋白増加	0	2 (0.3) [0.3]	0
未熟顆粒球数増加	0	1 (0.2) [0.2]	0
肝機能検査値上昇	0	3 (0.5) [0.5]	2 (0.3) [0.3]
低比重リポ蛋白増加	0	2 (0.3) [0.3]	1 (0.2) [0.2]
リンパ球数減少	0	3 (0.5) [0.5]	2 (0.3) [0.3]
リンパ球数増加	0	0	1 (0.2) [0.2]
平均赤血球容積増加	0	0	2 (0.3) [0.3]
筋酵素上昇	0	1 (0.2) [0.2]	0
骨髄球数増加	1 (0.2) [0.2]	0	0
骨髄球存在	0	0	1 (0.2) [0.2]
好中球数減少	0	0	8 (1.2) [1.2]
好中球数増加	1 (0.2) [0.2]	0	0
血小板数増加	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.2) [0.2]
尿中蛋白陽性	1 (0.2) [0.2]	0	0
赤血球数減少	0	1 (0.2) [0.2]	3 (0.5) [0.5]
血沈亢進	1 (0.2) [0.2]	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
臨床検査 (Cont.)			
尿中赤血球	1 (0.2) [0.2]	0	0
トランスアミナーゼ上昇	0	0	3 (0.5) [0.5]
超低比重リポ蛋白増加	0	2 (0.3) [0.3]	2 (0.3) [0.3]
体重減少	1 (0.2) [0.2]	0	1 (0.2) [0.2]
体重増加	0	1 (0.2) [0.2]	1 (0.2) [0.2]
白血球数減少	0	2 (0.3) [0.3]	7 (1.1) [1.1]
白血球数増加	1 (0.2) [0.2]	0	0
代謝および栄養障害	8 (1.3) [1.3]	9 (1.4) [1.4]	20 (3.1) [3.1]
脂質異常症	1 (0.2) [0.2]	2 (0.3) [0.3]	4 (0.6) [0.6]
高カルシウム血症	0	0	1 (0.2) [0.2]
高コレステロール血症	0	1 (0.2) [0.2]	7 (1.1) [1.1]
高血糖	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.2) [0.2]
高カリウム血症	1 (0.2) [0.2]	0	0
高脂血症	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.5) [0.5]
高トリグリセリド血症	3 (0.5) [0.5]	1 (0.2) [0.2]	1 (0.2) [0.2]
高尿酸血症	0	1 (0.2) [0.2]	1 (0.2) [0.2]

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Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
代謝および栄養障害 (Cont.)			
低血糖	0	0	1 (0.2) [0.2]
低リン酸血症	0	1 (0.2) [0.2]	0
ビタミンD欠乏	0	0	1 (0.2) [0.2]
筋骨格系および結合組織障害	7 (1.1) [1.1]	12 (1.9) [1.9]	7 (1.1) [1.1]
関節痛	0	1 (0.2) [0.2]	0
背部痛	2 (0.3) [0.3]	0	0
側腹部痛	0	0	1 (0.2) [0.2]
関節雑音	0	0	1 (0.2) [0.2]
関節硬直	0	1 (0.2) [0.2]	0
筋痙縮	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]
筋力低下	0	0	1 (0.2) [0.2]
筋肉痛	0	3 (0.5) [0.5]	1 (0.2) [0.2]
四肢痛	0	1 (0.2) [0.2]	1 (0.2) [0.2]
骨膜炎	1 (0.2) [0.2]	0	0
乾癬性関節症	3 (0.5) [0.5]	3 (0.5) [0.5]	1 (0.2) [0.2]
急速進行性変形性関節症	0	1 (0.2) [0.2]	0

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Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
筋骨格系および結合組織障害 (Cont.)			
脊椎痛	0	1 (0.2) [0.2]	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）	1 (0.2) [0.2]	1 (0.2) [0.2]	4 (0.6) [0.6]
肛門性器疣贅	0	0	1 (0.2) [0.2]
基底細胞癌	0	0	1 (0.2) [0.2]
化膿性肉芽腫	1 (0.2) [0.2]	0	0
直腸腺癌	0	0	1 (0.2) [0.2]
直腸癌	0	1 (0.2) [0.2]	0
皮膚乳頭腫	0	0	1 (0.2) [0.2]
神経系障害	13 (2.0) [2.0]	13 (2.0) [2.0]	23 (3.6) [3.6]
手根管症候群	0	0	1 (0.2) [0.2]
注意力障害	1 (0.2) [0.2]	0	0
浮動性めまい	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.5) [0.5]
頭痛	8 (1.3) [1.3]	7 (1.1) [1.1]	12 (1.9) [1.9]
感覚鈍麻	1 (0.2) [0.2]	1 (0.2) [0.2]	0
嗜眠	0	1 (0.2) [0.2]	0
記憶障害	0	0	1 (0.2) [0.2]

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Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
神経系障害 (Cont.)			
片頭痛	1 (0.2) [0.2]	0	1 (0.2) [0.2]
神経痛	0	0	1 (0.2) [0.2]
錯感覚	0	1 (0.2) [0.2]	1 (0.2) [0.2]
末梢性感覚ニューロパチー	0	0	1 (0.2) [0.2]
ヘルペス後神経痛	0	0	1 (0.2) [0.2]
失神寸前の状態	0	0	1 (0.2) [0.2]
感覚障害	0	0	1 (0.2) [0.2]
傾眠	0	0	1 (0.2) [0.2]
精神障害	3 (0.5) [0.5]	4 (0.6) [0.6]	5 (0.8) [0.8]
感情不安定	0	0	1 (0.2) [0.2]
不安	1 (0.2) [0.2]	0	2 (0.3) [0.3]
うつ病	0	1 (0.2) [0.2]	1 (0.2) [0.2]
不眠症	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]
悪夢	1 (0.2) [0.2]	0	0
睡眠障害	0	1 (0.2) [0.2]	0
腎および尿路障害	2 (0.3) [0.3]	2 (0.3) [0.3]	4 (0.6) [0.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
腎および尿路障害 (Cont.)			
尿路結石	0	0	1 (0.2) [0.2]
慢性腎臓病	0	0	1 (0.2) [0.2]
血尿	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.3) [0.3]
白血球尿	0	1 (0.2) [0.2]	0
頻尿	0	0	1 (0.2) [0.2]
蛋白尿	1 (0.2) [0.2]	0	1 (0.2) [0.2]
生殖系および乳房障害	2 (0.3) [0.3]	5 (0.8) [0.8]	1 (0.2) [0.2]
無月経	0	1 (0.2) [0.2]	0
前立腺結石	0	1 (0.2) [0.2]	0
線維嚢胞性乳腺疾患	0	0	1 (0.2) [0.2]
月経過多	0	1 (0.2) [0.2]	0
不規則月経	0	2 (0.3) [0.3]	0
不正子宮出血	1 (0.2) [0.2]	0	0
子宮出血	1 (0.2) [0.2]	0	0
腟分泌物	1 (0.2) [0.2]	0	0
呼吸器、胸郭および縦隔障害	10 (1.6) [1.6]	12 (1.9) [1.9]	20 (3.1) [3.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)			
急性呼吸不全	0	1 (0.2) [0.2]	1 (0.2) [0.2]
咳嗽	4 (0.6) [0.6]	3 (0.5) [0.5]	9 (1.4) [1.4]
呼吸困難	0	1 (0.2) [0.2]	1 (0.2) [0.2]
労作性呼吸困難	0	1 (0.2) [0.2]	0
鼻出血	2 (0.3) [0.3]	0	0
鼻部不快感	0	1 (0.2) [0.2]	0
鼻の炎症	0	0	1 (0.2) [0.2]
鼻潰瘍	0	0	1 (0.2) [0.2]
閉塞性気道障害	1 (0.2) [0.2]	0	0
口腔咽頭痛	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.5) [0.5]
咽頭の炎症	0	0	1 (0.2) [0.2]
胸膜炎	0	1 (0.2) [0.2]	0
肺塞栓症	0	1 (0.2) [0.2]	1 (0.2) [0.2]
肺線維症	0	0	1 (0.2) [0.2]
アレルギー性鼻炎	0	1 (0.2) [0.2]	0
鼻漏	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
呼吸器、胸郭および縦隔障害 (Cont.)			
副鼻腔うっ血	0	1 (0.2) [0.2]	0
咽喉刺激感	0	0	2 (0.3) [0.3]
上気道の炎症	0	1 (0.2) [0.2]	0
声帯障害	1 (0.2) [0.2]	0	0
皮膚および皮下組織障害	19 (3.0) [3.0]	16 (2.5) [2.5]	21 (3.3) [3.3]
ざ瘡	1 (0.2) [0.2]	4 (0.6) [0.6]	4 (0.6) [0.6]
脱毛症	0	1 (0.2) [0.2]	2 (0.3) [0.3]
水疱	0	0	1 (0.2) [0.2]
皮膚嚢腫	0	1 (0.2) [0.2]	0
皮膚炎	0	1 (0.2) [0.2]	0
ざ瘡様皮膚炎	0	0	1 (0.2) [0.2]
皮膚乾燥	1 (0.2) [0.2]	0	1 (0.2) [0.2]
斑状出血	0	0	1 (0.2) [0.2]
湿疹	0	1 (0.2) [0.2]	0
紅斑	0	0	2 (0.3) [0.3]
毛髪成長異常	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)			
多汗症	1 (0.2) [0.2]	2 (0.3) [0.3]	0
過角化	2 (0.3) [0.3]	0	0
間擦疹	0	1 (0.2) [0.2]	0
爪郭の炎症	0	0	1 (0.2) [0.2]
爪成長異常	0	1 (0.2) [0.2]	0
光線過敏性反応	1 (0.2) [0.2]	0	0
そう痒症	0	0	1 (0.2) [0.2]
乾癬	7 (1.1) [1.1]	2 (0.3) [0.3]	1 (0.2) [0.2]
膿疱性乾癬	0	0	1 (0.2) [0.2]
発疹	6 (0.9) [0.9]	0	4 (0.6) [0.6]
全身性皮疹	0	1 (0.2) [0.2]	0
斑状皮疹	0	0	1 (0.2) [0.2]
斑状丘疹状皮疹	0	1 (0.2) [0.2]	0
皮膚亀裂	1 (0.2) [0.2]	0	0
皮膚刺激	0	0	1 (0.2) [0.2]
皮膚病変	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.4

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
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
皮膚および皮下組織障害 (Cont.)			
顔面腫脹	0	1 (0.2) [0.2]	0
血管障害	5 (0.8) [0.8]	7 (1.1) [1.1]	4 (0.6) [0.6]
深部静脈血栓症	1 (0.2) [0.2]	0	0
ほてり	0	3 (0.5) [0.5]	0
高血圧	4 (0.6) [0.6]	3 (0.5) [0.5]	3 (0.5) [0.5]
高血圧クリーゼ	0	1 (0.2) [0.2]	0
表在性血栓性静脈炎	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.

Program Source Code: [redacted]

表 2.7.4.7-10.　全ウパダシチニブ併合解析集団（長期）の有害事象（100 人年あたりの発現件数）

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	2111 (323.9) [323.9]	2638 (407.7) [407.6]	2523 (308.9) [308.8]	3120 (379.4) [379.5]
血液およびリンパ系障害	67 (10.3) [10.3]	133 (20.6) [20.5]	76 (9.3) [9.3]	156 (19.0) [19.0]
貧血	11 (1.7) [1.7]	30 (4.6) [4.6]	13 (1.6) [1.6]	35 (4.3) [4.3]
大球性貧血	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
自己免疫性貧血	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
失血性貧血	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
骨髄浮腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
血球減少症	0	0	0	2 (0.2) [0.2]
播種性血管内凝固	0	0	0	1 (0.1) [0.1]
赤血球減少症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
顆粒球減少症	0	1 (0.2) [0.2]	0	3 (0.4) [0.4]
内出血発生の増加傾向	3 (0.5) [0.5]	1 (0.2) [0.2]	4 (0.5) [0.5]	1 (0.1) [0.1]
鉄欠乏性貧血	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	3 (0.4) [0.4]
白血球増加症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
白血球減少症	15 (2.3) [2.3]	21 (3.2) [3.2]	16 (2.0) [2.0]	25 (3.0) [3.0]
リンパ節炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
血液およびリンパ系障害 (Cont.)				
リンパ節症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
リンパ球増加症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ組織過形成	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ球減少症	15 (2.3) [2.3]	23 (3.6) [3.6]	16 (2.0) [2.0]	25 (3.0) [3.0]
好中球減少症	13 (2.0) [2.0]	30 (4.6) [4.6]	16 (2.0) [2.0]	35 (4.3) [4.3]
好中球増加症	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
正色素性貧血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
汎血球減少症	0	0	0	1 (0.1) [0.1]
脾肉芽腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
血小板減少症	1 (0.2) [0.2]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
血小板増加症	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
心臓障害	34 (5.2) [5.2]	24 (3.7) [3.7]	37 (4.5) [4.5]	30 (3.6) [3.6]
急性心筋梗塞	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
狭心症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
不安定狭心症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大動脈弁硬化症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)				
不整脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
冠動脈硬化症	0	0	0	1 (0.1) [0.1]
心房細動	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.4) [0.4]	3 (0.4) [0.4]
心房粗動	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
第一度房室ブロック	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
第二度房室ブロック	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
徐脈	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
右脚ブロック	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
心不全	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
うっ血性心不全	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心臓弁硬化症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心肺停止	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
心拡大	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心腎症候群	0	0	0	1 (0.1) [0.1]
冠動脈疾患	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
冠動脈狭窄	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)				
チアノーゼ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
期外収縮	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
左室肥大	0	0	0	1 (0.1) [0.1]
僧帽弁閉鎖不全症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
僧帽弁硬化症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
心筋梗塞	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
心筋虚血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
動悸	10 (1.5) [1.5]	1 (0.2) [0.2]	11 (1.3) [1.3]	1 (0.1) [0.1]
起立性頻脈症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺動脈弁閉鎖不全症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
洞性徐脈	0	2 (0.3) [0.3]	0	3 (0.4) [0.4]
洞性頻脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
上室性頻脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
頻脈	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
発作性頻脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
三尖弁閉鎖不全症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)				
心室細動	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
先天性、家族性および遺伝性障害	0	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
発育性股関節形成不全	0	0	1 (0.1) [0.1]	0
胃腸管動静脈奇形	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
陰嚢水瘤	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
2a型高脂血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
耳および迷路障害	7 (1.1) [1.1]	8 (1.2) [1.2]	11 (1.3) [1.3]	9 (1.1) [1.1]
耳垢栓塞	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
耳閉	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
耳不快感	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
耳痛	0	0	1 (0.1) [0.1]	0
外耳の炎症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
耳鳴	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
回転性めまい	4 (0.6) [0.6]	3 (0.5) [0.5]	5 (0.6) [0.6]	3 (0.4) [0.4]
頭位性回転性めまい	1 (0.2) [0.2]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
前庭障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
内分泌障害	6 (0.9) [0.9]	13 (2.0) [2.0]	7 (0.9) [0.9]	14 (1.7) [1.7]
副腎石灰化	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
アンドロゲン欠乏症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
自己免疫性甲状腺炎	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
甲状腺腫	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
甲状腺機能亢進症	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
甲状腺機能低下症	2 (0.3) [0.3]	4 (0.6) [0.6]	3 (0.4) [0.4]	4 (0.5) [0.5]
甲状腺腫瘤	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
眼障害	31 (4.8) [4.8]	33 (5.1) [5.1]	32 (3.9) [3.9]	39 (4.7) [4.7]
一過性黒内障	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
閉塞隅角緑内障	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
動脈硬化性網膜症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
眼精疲労	0	0	0	1 (0.1) [0.1]
眼瞼炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼瞼痙攣	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
境界域緑内障	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)				
白内障	2 (0.3) [0.3]	10 (1.5) [1.5]	3 (0.4) [0.4]	12 (1.5) [1.5]
霰粒腫	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
結膜出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
結膜充血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
アレルギー性結膜炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
糖尿病網膜症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
複視	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ドライアイ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼痛	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
眼瞼下垂	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
緑内障	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	6 (0.7) [0.7]
虹彩毛様体炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
角膜炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
流涙増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
水晶体脱臼	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
瞼板腺炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)				
眼部不快感	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
眼窩周囲腫脹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
光視症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
後嚢部混濁	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
眼瞼腫脹	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
ぶどう膜炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
霧視	4 (0.6) [0.6]	0	4 (0.5) [0.5]	0
視力低下	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
視力障害	4 (0.6) [0.6]	0	4 (0.5) [0.5]	0
硝子体浮遊物	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃腸障害	207 (31.8) [31.8]	241 (37.2) [37.3]	239 (29.3) [29.3]	284 (34.5) [34.5]
腹部不快感	7 (1.1) [1.1]	3 (0.5) [0.5]	10 (1.2) [1.2]	5 (0.6) [0.6]
腹部膨満	4 (0.6) [0.6]	3 (0.5) [0.5]	5 (0.6) [0.6]	4 (0.5) [0.5]
腹部腫瘤	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腹痛	9 (1.4) [1.4]	7 (1.1) [1.1]	12 (1.5) [1.5]	8 (1.0) [1.0]
下腹部痛	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
上腹部痛	11 (1.7) [1.7]	13 (2.0) [2.0]	14 (1.7) [1.7]	13 (1.6) [1.6]
腹壁嚢胞	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
裂肛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
痔瘻	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口角口唇炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
アフタ性潰瘍	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	4 (0.5) [0.5]
根尖肉芽腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腹水	0	0	0	1 (0.1) [0.1]
バレット食道	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
慢性胃炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
大腸炎	1 (0.2) [0.2]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
結腸異形成	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
便秘	12 (1.8) [1.8]	14 (2.2) [2.2]	12 (1.5) [1.5]	14 (1.7) [1.7]
クローン病	0	0	1 (0.1) [0.1]	0
齲歯	2 (0.3) [0.3]	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
下痢	31 (4.8) [4.8]	43 (6.6) [6.6]	37 (4.5) [4.5]	50 (6.1) [6.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
憩室	1 (0.2) [0.2]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
腸憩室	0	2 (0.3) [0.3]	0	3 (0.4) [0.4]
食道憩室	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口内乾燥	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	4 (0.5) [0.5]
十二指腸潰瘍	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	3 (0.4) [0.4]
出血性十二指腸潰瘍	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
十二指腸炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
排便困難	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
消化不良	10 (1.5) [1.5]	7 (1.1) [1.1]	12 (1.5) [1.5]	10 (1.2) [1.2]
嚥下障害	0	3 (0.5) [0.5]	0	4 (0.5) [0.5]
小腸炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
腸炎	0	0	0	2 (0.2) [0.2]
心窩部不快感	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
びらん性十二指腸炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
びらん性食道炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
おくび	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
変色便	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼓腸	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
食中毒	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
胃出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
穿孔性胃潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃炎	9 (1.4) [1.4]	9 (1.4) [1.4]	9 (1.1) [1.1]	9 (1.1) [1.1]
びらん性胃炎	3 (0.5) [0.5]	1 (0.2) [0.2]	4 (0.5) [0.5]	1 (0.1) [0.1]
胃十二指腸出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃十二指腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胃腸出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
消化器痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胃食道逆流性疾患	7 (1.1) [1.1]	7 (1.1) [1.1]	7 (0.9) [0.9]	8 (1.0) [1.0]
歯肉退縮	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
歯肉腫脹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
潰瘍性歯肉炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
吐血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
血便排泄	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
痔出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
痔核	6 (0.9) [0.9]	2 (0.3) [0.3]	6 (0.7) [0.7]	4 (0.5) [0.5]
裂孔ヘルニア	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	3 (0.4) [0.4]
単径ヘルニア	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
腸閉塞	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
大腸ポリープ	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
口唇乾燥	0	0	1 (0.1) [0.1]	0
口唇潰瘍	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
腰ヘルニア	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
口腔嚢胞	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔内潰瘍形成	5 (0.8) [0.8]	5 (0.8) [0.8]	5 (0.6) [0.6]	8 (1.0) [1.0]
悪心	24 (3.7) [3.7]	34 (5.3) [5.3]	25 (3.1) [3.1]	37 (4.5) [4.5]
食道痙攣	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
食道潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
食道潰瘍出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
口腔挫傷	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
口腔障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔粘膜びらん	0	0	0	1 (0.1) [0.1]
口腔粘膜水疱形成	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
膵臓障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膵脂肪変性	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
膵炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
急性膵炎	0	0	0	1 (0.1) [0.1]
消化性潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
歯周の炎症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
直腸出血	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
直腸潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
吐き戻し	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
レッチング	0	0	1 (0.1) [0.1]	0
小腸出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
小腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
口内炎	3 (0.5) [0.5]	8 (1.2) [1.2]	4 (0.5) [0.5]	10 (1.2) [1.2]
舌潰瘍	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
歯の障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
歯痛	5 (0.8) [0.8]	5 (0.8) [0.8]	7 (0.9) [0.9]	5 (0.6) [0.6]
臍ヘルニア	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
上部消化管出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
嘔吐	13 (2.0) [2.0]	12 (1.9) [1.9]	16 (2.0) [2.0]	15 (1.8) [1.8]
一般・全身障害および投与部位の状態	53 (8.1) [8.1]	77 (11.9) [11.9]	68 (8.3) [8.3]	90 (10.9) [10.9]
医薬品副作用	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
無力症	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	4 (0.5) [0.5]
腋窩痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胸部不快感	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胸痛	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	3 (0.4) [0.4]
悪寒	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
不快感	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
薬物不耐性	2 (0.3) [0.3]	5 (0.8) [0.8]	3 (0.4) [0.4]	6 (0.7) [0.7]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)				
顔面痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
疲労	9 (1.4) [1.4]	10 (1.5) [1.5]	15 (1.8) [1.8]	13 (1.6) [1.6]
歩行障害	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
高熱	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
低体温	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
インフルエンザ様疾患	4 (0.6) [0.6]	5 (0.8) [0.8]	4 (0.5) [0.5]	5 (0.6) [0.6]
注射部位内出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
注射部位疼痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
注射部位反応	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
倦怠感	5 (0.8) [0.8]	0	5 (0.6) [0.6]	0
医療機器使用部位関節腫脹	0	0	0	1 (0.1) [0.1]
小結節	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
非心臓性胸痛	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
浮腫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
末梢性浮腫	3 (0.5) [0.5]	8 (1.2) [1.2]	10 (1.2) [1.2]	11 (1.3) [1.3]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)				
疼痛	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
末梢腫脹	4 (0.6) [0.6]	4 (0.6) [0.6]	4 (0.5) [0.5]	4 (0.5) [0.5]
発熱	10 (1.5) [1.5]	22 (3.4) [3.4]	11 (1.3) [1.3]	25 (3.0) [3.0]
腫脹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
全身性炎症反応症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝胆道系障害	24 (3.7) [3.7]	47 (7.3) [7.3]	34 (4.2) [4.2]	54 (6.6) [6.6]
胆管結石	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胆道仙痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
慢性胆嚢炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胆石症	2 (0.3) [0.3]	8 (1.2) [1.2]	3 (0.4) [0.4]	8 (1.0) [1.0]
薬物性肝障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胆嚢ポリープ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝硬変	0	0	0	1 (0.1) [0.1]
肝嚢胞	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
肝機能異常	9 (1.4) [1.4]	9 (1.4) [1.4]	13 (1.6) [1.6]	12 (1.5) [1.5]
肝腫瘤	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
肝胆道系障害 (Cont.)				
脂肪肝	4 (0.6) [0.6]	12 (1.9) [1.9]	5 (0.6) [0.6]	14 (1.7) [1.7]
肝炎	0	0	1 (0.1) [0.1]	0
肝腫大	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝毒性	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
高ビリルビン血症	2 (0.3) [0.3]	1 (0.2) [0.2]	4 (0.5) [0.5]	1 (0.1) [0.1]
過形成性胆嚢症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
高トランスアミナーゼ血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝障害	0	2 (0.3) [0.3]	0	3 (0.4) [0.4]
肝損傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
非アルコール性脂肪性肝炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
非アルコール性脂肪性肝疾患	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
胆管穿孔	0	0	1 (0.1) [0.1]	0
脂肪性肝炎	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
免疫系障害	6 (0.9) [0.9]	13 (2.0) [2.0]	8 (1.0) [1.0]	14 (1.7) [1.7]
節足動物咬傷アレルギー	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
造影剤アレルギー	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
免疫系障害 (Cont.)				
薬物過敏症	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	4 (0.5) [0.5]
食物アレルギー	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
過敏症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
ダニアレルギー	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
季節性アレルギー	4 (0.6) [0.6]	3 (0.5) [0.5]	6 (0.7) [0.7]	3 (0.4) [0.4]
感染症および寄生虫症	647 (99.3) [99.3]	846 (130.7) [130.7]	809 (99.0) [99.0]	1021 (124.2) [124.2]
腹部膿瘍	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
膿瘍	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
四肢膿瘍	0	5 (0.8) [0.8]	0	5 (0.6) [0.6]
口腔膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ダニ皮膚炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
急性副鼻腔炎	3 (0.5) [0.5]	2 (0.3) [0.3]	5 (0.6) [0.6]	2 (0.2) [0.2]
肛門膿瘍	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
肛門カンジダ症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
肛門直腸蜂巣炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
虫垂炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
細菌性関節炎	0	0	1 (0.1) [0.1]	0
無症候性細菌尿	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
異型肺炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
バベシア症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
菌血症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
細菌感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
細菌性膣症	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
細菌尿	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	3 (0.4) [0.4]
体部白癬	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
細気管支炎	0	0	1 (0.1) [0.1]	0
気管支炎	45 (6.9) [6.9]	58 (9.0) [9.0]	56 (6.9) [6.9]	66 (8.0) [8.0]
細菌性気管支炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
気管支肺アスペルギルス症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
カンジダ感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
カンジダ性尿道炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
気管カンジダ症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
蜂巣炎	8 (1.2) [1.2]	10 (1.5) [1.5]	8 (1.0) [1.0]	11 (1.3) [1.3]
コクシジオイデス症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
結膜炎	4 (0.6) [0.6]	1 (0.2) [0.2]	6 (0.7) [0.7]	2 (0.2) [0.2]
ウイルス性結膜炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
クリプトスポリジウム感染	0	0	1 (0.1) [0.1]	0
膀胱炎	9 (1.4) [1.4]	10 (1.5) [1.5]	11 (1.3) [1.3]	13 (1.6) [1.6]
サイトメガロウイルス感染	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
毛嚢虫症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
爪の皮膚糸状菌症	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
憩室炎	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	3 (0.4) [0.4]
耳感染	6 (0.9) [0.9]	3 (0.5) [0.5]	10 (1.2) [1.2]	3 (0.4) [0.4]
エンテロウイルス感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
精巣上体炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
丹毒	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
大腸菌感染	0	0	1 (0.1) [0.1]	0
大腸菌性尿路感染	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
硬膜外膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
毛包炎	14 (2.1) [2.1]	10 (1.5) [1.5]	14 (1.7) [1.7]	15 (1.8) [1.8]
真菌感染	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
皮膚真菌感染	3 (0.5) [0.5]	11 (1.7) [1.7]	3 (0.4) [0.4]	11 (1.3) [1.3]
せつ	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
胃腸炎	15 (2.3) [2.3]	30 (4.6) [4.6]	22 (2.7) [2.7]	34 (4.1) [4.1]
ウイルス性胃腸炎	6 (0.9) [0.9]	17 (2.6) [2.6]	10 (1.2) [1.2]	19 (2.3) [2.3]
消化管感染	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
ウイルス性消化管感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
性器カンジダ症	0	0	1 (0.1) [0.1]	0
陰部ヘルペス	4 (0.6) [0.6]	4 (0.6) [0.6]	5 (0.6) [0.6]	4 (0.5) [0.5]
陰部帯状疱疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
泌尿生殖器感染	0	0	1 (0.1) [0.1]	0
ジアルジア症	0	0	1 (0.1) [0.1]	0
歯肉膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

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Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
歯肉炎	3 (0.5) [0.5]	5 (0.8) [0.8]	3 (0.4) [0.4]	6 (0.7) [0.7]
単径部膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
H1N1インフルエンザ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
手足口病	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ヘリコバクター感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
B型肝炎再活性化	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
単純ヘルペス	5 (0.8) [0.8]	16 (2.5) [2.5]	6 (0.7) [0.7]	19 (2.3) [2.3]
ヘルペスウイルス感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
帯状疱疹	21 (3.2) [3.2]	41 (6.3) [6.3]	26 (3.2) [3.2]	57 (6.9) [6.9]
麦粒腫	4 (0.6) [0.6]	3 (0.5) [0.5]	4 (0.5) [0.5]	3 (0.4) [0.4]
膿痂疹	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
伝染性単核症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
インフルエンザ	33 (5.1) [5.1]	31 (4.8) [4.8]	37 (4.5) [4.5]	38 (4.6) [4.6]
腎感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
クレブシエラ感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
喉頭炎	4 (0.6) [0.6]	4 (0.6) [0.6]	5 (0.6) [0.6]	6 (0.7) [0.7]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
潜伏結核	2 (0.3) [0.3]	2 (0.3) [0.3]	7 (0.9) [0.9]	3 (0.4) [0.4]
限局性感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
下気道感染	6 (0.9) [0.9]	3 (0.5) [0.5]	6 (0.7) [0.7]	5 (0.6) [0.6]
肺感染	0	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
リンパ管炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
爪床感染	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
爪感染	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	5 (0.6) [0.6]
鼻ヘルペス	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
上咽頭炎	68 (10.4) [10.4]	83 (12.8) [12.8]	83 (10.2) [10.2]	108 (13.1) [13.1]
食道カンジダ症	0	0	1 (0.1) [0.1]	0
爪真菌症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
口腔カンジダ症	6 (0.9) [0.9]	9 (1.4) [1.4]	6 (0.7) [0.7]	11 (1.3) [1.3]
口腔真菌感染	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
口腔ヘルペス	12 (1.8) [1.8]	47 (7.3) [7.3]	15 (1.8) [1.8]	53 (6.4) [6.5]
口腔感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
中咽頭カンジダ症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
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Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
外耳炎	0	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
中耳炎	0	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
急性中耳炎	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
子宮傍組織炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
爪囲炎	2 (0.3) [0.3]	4 (0.6) [0.6]	3 (0.4) [0.4]	4 (0.5) [0.5]
軟骨膜炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
歯冠周囲炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
歯周炎	4 (0.6) [0.6]	3 (0.5) [0.5]	4 (0.5) [0.5]	3 (0.4) [0.4]
咽頭炎	17 (2.6) [2.6]	14 (2.2) [2.2]	21 (2.6) [2.6]	24 (2.9) [2.9]
レンサ球菌性咽頭炎	5 (0.8) [0.8]	2 (0.3) [0.3]	5 (0.6) [0.6]	3 (0.4) [0.4]
咽頭扁桃炎	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
ニューモシスチス・イロベチイ肺炎	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
肺炎	11 (1.7) [1.7]	9 (1.4) [1.4]	16 (2.0) [2.0]	14 (1.7) [1.7]
細菌性肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
レンサ球菌性肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
処置後蜂巣炎	0	0	1 (0.1) [0.1]	0

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Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

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感染症および寄生虫症 (Cont.)				
前立腺感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
シュードモナス感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
歯髄炎	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
化膿性分泌物	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腎盂腎炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
急性腎盂腎炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膿尿	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
膿疱性皮疹	0	3 (0.5) [0.5]	0	4 (0.5) [0.5]
気道感染	15 (2.3) [2.3]	14 (2.2) [2.2]	17 (2.1) [2.1]	17 (2.1) [2.1]
ウイルス性気道感染	4 (0.6) [0.6]	9 (1.4) [1.4]	6 (0.7) [0.7]	12 (1.5) [1.5]
鼻炎	5 (0.8) [0.8]	8 (1.2) [1.2]	5 (0.6) [0.6]	9 (1.1) [1.1]
卵管炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
敗血症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
副鼻腔炎	23 (3.5) [3.5]	25 (3.9) [3.9]	32 (3.9) [3.9]	30 (3.6) [3.6]
細菌性副鼻腔炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮膚細菌感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]

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TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

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感染症および寄生虫症 (Cont.)				
皮膚カンジダ	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
皮膚感染	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.4) [0.4]	3 (0.4) [0.4]
ブドウ球菌性菌血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ブドウ球菌感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ブドウ球菌性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ブドウ球菌皮膚感染	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
皮下組織膿瘍	0	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
股部白癬	0	0	0	1 (0.1) [0.1]
白癬感染	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
手白癬	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
足部白癬	3 (0.5) [0.5]	6 (0.9) [0.9]	4 (0.5) [0.5]	9 (1.1) [1.1]
癜風	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
扁桃炎	5 (0.8) [0.8]	8 (1.2) [1.2]	8 (1.0) [1.0]	9 (1.1) [1.1]
細菌性扁桃炎	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
歯膿瘍	7 (1.1) [1.1]	2 (0.3) [0.3]	9 (1.1) [1.1]	2 (0.2) [0.2]
歯感染	5 (0.8) [0.8]	7 (1.1) [1.1]	6 (0.7) [0.7]	10 (1.2) [1.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

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TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
気管炎	0	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
気管気管支炎	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
細菌性気管気管支炎	0	0	0	1 (0.1) [0.1]
上気道感染	107 (16.4) [16.4]	124 (19.2) [19.2]	129 (15.8) [15.8]	139 (16.9) [16.9]
尿路感染	59 (9.1) [9.0]	63 (9.7) [9.7]	70 (8.6) [8.6]	80 (9.7) [9.7]
細菌性尿路感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腸球菌性尿路感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
尿路性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腟感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス感染	4 (0.6) [0.6]	9 (1.4) [1.4]	4 (0.5) [0.5]	11 (1.3) [1.3]
ウイルス性筋炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ウイルス性咽頭炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
ウイルス性発疹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス性副鼻腔炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス性扁桃炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ウイルス性気管炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
ウイルス性上気道感染	8 (1.2) [1.2]	8 (1.2) [1.2]	16 (2.0) [2.0]	14 (1.7) [1.7]
外陰部炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
外陰部腟カンジダ症	4 (0.6) [0.6]	7 (1.1) [1.1]	4 (0.5) [0.5]	7 (0.9) [0.9]
外陰腟真菌感染	4 (0.6) [0.6]	11 (1.7) [1.7]	4 (0.5) [0.5]	11 (1.3) [1.3]
傷害、中毒および処置合併症	109 (16.7) [16.7]	101 (15.6) [15.6]	124 (15.2) [15.2]	125 (15.2) [15.2]
動物咬傷	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	5 (0.6) [0.6]
足関節部骨折	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
節足動物咬傷	4 (0.6) [0.6]	2 (0.3) [0.3]	4 (0.5) [0.5]	3 (0.4) [0.4]
節足動物刺傷	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
剥離骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
背部損傷	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
骨亀裂	0	0	1 (0.1) [0.1]	0
第1度熱傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
第2度熱傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
軟骨損傷	0	0	1 (0.1) [0.1]	1 (0.1) [0.1]
頚椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
化学熱傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
鎖骨骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
粉砕骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脳振盪	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
挫傷	13 (2.0) [2.0]	10 (1.5) [1.5]	14 (1.7) [1.7]	12 (1.5) [1.5]
角膜擦過傷	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
上顆炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
眼挫傷	0	0	0	1 (0.1) [0.1]
転倒	9 (1.4) [1.4]	11 (1.7) [1.7]	9 (1.1) [1.1]	14 (1.7) [1.7]
大腿骨頚部骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大腿骨骨折	0	0	0	1 (0.1) [0.1]
腓骨骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
足骨折	7 (1.1) [1.1]	1 (0.2) [0.2]	7 (0.9) [0.9]	1 (0.1) [0.1]
仙骨骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
凍傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
手骨折	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
上腕骨骨折	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
損傷	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
関節脱臼	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
関節損傷	3 (0.5) [0.5]	2 (0.3) [0.3]	4 (0.5) [0.5]	3 (0.4) [0.4]
靭帯損傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
靭帯断裂	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
靭帯捻挫	3 (0.5) [0.5]	6 (0.9) [0.9]	4 (0.5) [0.5]	6 (0.7) [0.7]
四肢圧挫損傷	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
四肢損傷	6 (0.9) [0.9]	1 (0.2) [0.2]	6 (0.7) [0.7]	2 (0.2) [0.2]
口唇損傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腰椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
つち指	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
半月板損傷	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
筋損傷	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
筋断裂	0	0	2 (0.2) [0.2]	0
肉離れ	4 (0.6) [0.6]	4 (0.6) [0.6]	4 (0.5) [0.5]	5 (0.6) [0.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
膝蓋骨骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
椎弓切除後症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
処置後胆汁漏出	0	0	1 (0.1) [0.1]	0
処置後出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
外傷後頚部症候群	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
処置による疼痛	2 (0.3) [0.3]	2 (0.3) [0.3]	3 (0.4) [0.4]	3 (0.4) [0.4]
肋骨骨折	0	3 (0.5) [0.5]	0	4 (0.5) [0.5]
交通事故	3 (0.5) [0.5]	1 (0.2) [0.2]	4 (0.5) [0.5]	2 (0.2) [0.2]
引っかき傷	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮膚擦過傷	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
皮膚裂傷	7 (1.1) [1.1]	4 (0.6) [0.6]	8 (1.0) [1.0]	6 (0.7) [0.7]
脊椎圧迫骨折	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
胸骨骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ストレス骨折	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
滑膜断裂	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腱損傷	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
腱断裂	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	3 (0.4) [0.4]
熱傷	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
胸椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脛骨骨折	0	0	1 (0.1) [0.1]	0
歯牙破折	8 (1.2) [1.2]	5 (0.8) [0.8]	8 (1.0) [1.0]	5 (0.6) [0.6]
各種物質毒性	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
外傷性関節炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
外傷性血腫	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
外傷性血胸	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
上肢骨折	0	1 (0.2) [0.2]	1 (0.1) [0.1]	3 (0.4) [0.4]
創傷	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
手首関節骨折	0	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
臨床検査	239 (36.7) [36.7]	363 (56.1) [56.1]	290 (35.5) [35.5]	414 (50.3) [50.4]
アラニンアミノトランスフェラーゼ増加	43 (6.6) [6.6]	55 (8.5) [8.5]	50 (6.1) [6.1]	63 (7.7) [7.7]
アルドラーゼ増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
抗甲状腺抗体陽性	0	0	1 (0.1) [0.1]	0
アスパラギン酸アミノトランスフェラーゼ増加	29 (4.4) [4.5]	36 (5.6) [5.6]	33 (4.0) [4.0]	43 (5.2) [5.2]
細菌検査陽性	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
血中アルカリホスファターゼ増加	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
血中ビリルビン増加	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
血中コレステロール増加	6 (0.9) [0.9]	5 (0.8) [0.8]	7 (0.9) [0.9]	5 (0.6) [0.6]
血中クレアチン増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中クレアチンホスホキナーゼ増加	78 (12.0) [12.0]	121 (18.7) [18.7]	93 (11.4) [11.4]	140 (17.0) [17.0]
血中クレアチニン増加	3 (0.5) [0.5]	8 (1.2) [1.2]	6 (0.7) [0.7]	8 (1.0) [1.0]
血中葉酸減少	0	0	1 (0.1) [0.1]	0
血中ブドウ糖異常	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
血中ブドウ糖増加	7 (1.1) [1.1]	2 (0.3) [0.3]	7 (0.9) [0.9]	3 (0.4) [0.4]
血中乳酸脱水素酵素増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
血中リン減少	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
血中カリウム増加	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	7 (0.9) [0.9]
血圧上昇	5 (0.8) [0.8]	7 (1.1) [1.1]	7 (0.9) [0.9]	7 (0.9) [0.9]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
収縮期血圧上昇	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
血中テストステロン減少	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
血中甲状腺刺激ホルモン減少	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中トリグリセリド増加	1 (0.2) [0.2]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
血中尿素増加	0	5 (0.8) [0.8]	1 (0.1) [0.1]	5 (0.6) [0.6]
血中尿酸増加	1 (0.2) [0.2]	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
体温上昇	0	0	1 (0.1) [0.1]	0
心雑音	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心電図T波逆転	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
γ－グルタミルトランスフェラーゼ増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ヘマトクリット減少	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
ヘモグロビン減少	2 (0.3) [0.3]	8 (1.2) [1.2]	2 (0.2) [0.2]	8 (1.0) [1.0]
心拍数減少	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ヘリコバクター検査陽性	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝酵素上昇	3 (0.5) [0.5]	8 (1.2) [1.2]	5 (0.6) [0.6]	10 (1.2) [1.2]
高比重リポ蛋白増加	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
未熟顆粒球数増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
深吸気量減少	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼圧上昇	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝機能検査値上昇	7 (1.1) [1.1]	7 (1.1) [1.1]	7 (0.9) [0.9]	9 (1.1) [1.1]
低比重リポ蛋白増加	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	3 (0.4) [0.4]
リンパ球数減少	4 (0.6) [0.6]	3 (0.5) [0.5]	4 (0.5) [0.5]	4 (0.5) [0.5]
リンパ球数増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ球形態異常	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
平均赤血球容積増加	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	6 (0.7) [0.7]
筋酵素上昇	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
骨髄球存在	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
好中球数減少	2 (0.3) [0.3]	11 (1.7) [1.7]	2 (0.2) [0.2]	13 (1.6) [1.6]
好中球数増加	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
血小板数増加	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
前立腺特異性抗原異常	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
総蛋白増加	0	0	1 (0.1) [0.1]	0

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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

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by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
尿中蛋白陽性	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
赤血球数減少	1 (0.2) [0.2]	5 (0.8) [0.8]	1 (0.1) [0.1]	5 (0.6) [0.6]
血沈亢進	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
血清フェリチン減少	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
トランスアミナーゼ上昇	5 (0.8) [0.8]	11 (1.7) [1.7]	7 (0.9) [0.9]	13 (1.6) [1.6]
尿検査異常	0	0	0	1 (0.1) [0.1]
超低比重リポ蛋白増加	2 (0.3) [0.3]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
体重減少	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
体重増加	4 (0.6) [0.6]	8 (1.2) [1.2]	7 (0.9) [0.9]	8 (1.0) [1.0]
白血球数減少	3 (0.5) [0.5]	14 (2.2) [2.2]	4 (0.5) [0.5]	16 (1.9) [1.9]
白血球数増加	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
代謝および栄養障害	79 (12.1) [12.1]	81 (12.5) [12.5]	91 (11.1) [11.1]	92 (11.2) [11.2]
異常体重減少	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
炭水化物不耐症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
食欲減退	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脱水	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]

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TABLE 2.4__1.2.3.2

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by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)				
糖尿病	10 (1.5) [1.5]	2 (0.3) [0.3]	12 (1.5) [1.5]	3 (0.4) [0.4]
コントロール不良の糖尿病	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脂質異常症	6 (0.9) [0.9]	12 (1.9) [1.9]	6 (0.7) [0.7]	13 (1.6) [1.6]
体液貯留	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
耐糖能障害	1 (0.2) [0.2]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
グルテン過敏症	0	0	0	1 (0.1) [0.1]
痛風	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
高カルシウム血症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
高コレステロール血症	5 (0.8) [0.8]	13 (2.0) [2.0]	7 (0.9) [0.9]	14 (1.7) [1.7]
高血糖	6 (0.9) [0.9]	9 (1.4) [1.4]	8 (1.0) [1.0]	9 (1.1) [1.1]
高カリウム血症	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
高脂血症	10 (1.5) [1.5]	6 (0.9) [0.9]	10 (1.2) [1.2]	8 (1.0) [1.0]
高トリグリセリド血症	3 (0.5) [0.5]	4 (0.6) [0.6]	3 (0.4) [0.4]	5 (0.6) [0.6]
高尿酸血症	6 (0.9) [0.9]	8 (1.2) [1.2]	7 (0.9) [0.9]	9 (1.1) [1.1]
低カルシウム血症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
低血糖	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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TABLE 2.4__1.2.3.2

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代謝および栄養障害 (Cont.)				
低カリウム血症	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
低ナトリウム血症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
低リン酸血症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
空腹時血中ブドウ糖不良	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
食欲亢進	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
インスリン抵抗性	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
鉄欠乏	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
栄養障害	0	0	0	1 (0.1) [0.1]
肥満	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
2型糖尿病	5 (0.8) [0.8]	6 (0.9) [0.9]	6 (0.7) [0.7]	6 (0.7) [0.7]
ビタミンB群欠乏	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
ビタミンB12欠乏	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
ビタミンD欠乏	6 (0.9) [0.9]	5 (0.8) [0.8]	6 (0.7) [0.7]	7 (0.9) [0.9]
筋骨格系および結合組織障害	153 (23.5) [23.5]	145 (22.4) [22.4]	183 (22.4) [22.4]	181 (22.0) [22.0]
関節痛	16 (2.5) [2.5]	15 (2.3) [2.3]	19 (2.3) [2.3]	17 (2.1) [2.1]
背部痛	22 (3.4) [3.4]	24 (3.7) [3.7]	23 (2.8) [2.8]	27 (3.3) [3.3]

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筋骨格系および結合組織障害 (Cont.)				
滑液包炎	7 (1.1) [1.1]	7 (1.1) [1.1]	7 (0.9) [0.9]	8 (1.0) [1.0]
頚部脊柱管狭窄症	0	0	1 (0.1) [0.1]	0
軟骨疾患	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
尾骨痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肋軟骨炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
外骨腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
顎骨の外骨腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
顔面非対称	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
側腹部痛	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
足変形	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
出血性関節症	0	0	1 (0.1) [0.1]	0
高クレアチン血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
椎間板線維輪断裂	0	0	0	1 (0.1) [0.1]
椎間板変性症	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
椎間板障害	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
椎間板突出	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	5 (0.6) [0.6]

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筋骨格系および結合組織障害 (Cont.)				
関節滲出液	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
関節過伸展	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
関節雑音	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
関節硬直	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
関節腫脹	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
腰部脊柱管狭窄症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
筋肉疲労	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
筋痙縮	12 (1.8) [1.8]	5 (0.8) [0.8]	12 (1.5) [1.5]	10 (1.2) [1.2]
筋緊張	0	0	1 (0.1) [0.1]	0
筋力低下	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
筋骨格系胸痛	1 (0.2) [0.2]	2 (0.3) [0.3]	2 (0.2) [0.2]	4 (0.5) [0.5]
筋骨格痛	2 (0.3) [0.3]	1 (0.2) [0.2]	4 (0.5) [0.5]	3 (0.4) [0.4]
筋骨格硬直	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
筋肉痛	5 (0.8) [0.8]	4 (0.6) [0.6]	5 (0.6) [0.6]	4 (0.5) [0.5]
筋膜疼痛症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
筋炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

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by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)				
頚部痛	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	6 (0.7) [0.7]
変形性関節症	5 (0.8) [0.8]	7 (1.1) [1.1]	11 (1.3) [1.3]	8 (1.0) [1.0]
骨端症	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
骨壊死	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	4 (0.5) [0.5]
骨減少症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
骨粗鬆症	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.4) [0.4]	2 (0.2) [0.2]
四肢痛	4 (0.6) [0.6]	5 (0.8) [0.8]	5 (0.6) [0.6]	5 (0.6) [0.6]
関節周囲炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
足底筋膜炎	0	5 (0.8) [0.8]	0	5 (0.6) [0.6]
多発性関節炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
乾癬性関節症	31 (4.8) [4.8]	26 (4.0) [4.0]	36 (4.4) [4.4]	34 (4.1) [4.1]
急速進行性変形性関節症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
関節リウマチ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肩回旋筋腱板症候群	4 (0.6) [0.6]	2 (0.3) [0.3]	4 (0.5) [0.5]	2 (0.2) [0.2]
仙腸骨炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
側弯症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)				
軟部組織腫脹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脊椎不安定	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
変形性脊椎症	2 (0.3) [0.3]	2 (0.3) [0.3]	4 (0.5) [0.5]	5 (0.6) [0.6]
脊椎痛	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
脊椎後方すべり症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脊柱管狭窄症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
滑液嚢腫	5 (0.8) [0.8]	1 (0.2) [0.2]	5 (0.6) [0.6]	2 (0.2) [0.2]
滑膜炎	0	0	1 (0.1) [0.1]	0
全身性エリテマトーデス	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
顎関節症候群	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
腱炎	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
腱鞘炎	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
狭窄性腱鞘炎	0	0	1 (0.1) [0.1]	1 (0.1) [0.1]
胸部脊柱管狭窄症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
弾発指	0	0	1 (0.1) [0.1]	0
椎間孔狭窄	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	16 (2.5) [2.5]	27 (4.2) [4.2]	25 (3.1) [3.1]	29 (3.5) [3.5]
肛門性器疣贅	1 (0.2) [0.2]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
基底細胞癌	2 (0.3) [0.3]	3 (0.5) [0.5]	4 (0.5) [0.5]	3 (0.4) [0.4]
基底扁平上皮癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
副腎の良性新生物	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ボーエン病	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
乳腺線維腫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
大腸腺腫	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
子宮内膜癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
乳管内乳頭腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脂肪腫	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
乳房脂肪腫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
肺腺癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
遠隔転移を伴う肺癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
悪性黒色腫	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
悪性黒色腫第3期	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)				
メラノサイト性母斑	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
単クローン性免疫グロブリン血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
骨髄異形成症候群	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
神経内分泌癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
中咽頭扁平上皮癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
卵巣癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
前立腺癌	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
直腸腺癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
直腸癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脂漏性角化症	0	0	1 (0.1) [0.1]	0
皮膚乳頭腫	1 (0.2) [0.2]	4 (0.6) [0.6]	3 (0.4) [0.4]	4 (0.5) [0.5]
扁平上皮癌	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
皮膚有棘細胞癌	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
子宮平滑筋腫	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
神経系障害	81 (12.4) [12.4]	115 (17.8) [17.8]	98 (12.0) [12.0]	128 (15.6) [15.6]
健忘	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)				
手根管症候群	2 (0.3) [0.3]	7 (1.1) [1.1]	2 (0.2) [0.2]	8 (1.0) [1.0]
中枢性肺胞性低換気	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脳梗塞	0	0	0	1 (0.1) [0.1]
頚髄神経根障害	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
頚腕症候群	2 (0.3) [0.3]	0	4 (0.5) [0.5]	0
認知障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脱髄	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
糖尿病性ニューロパチー	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
注意力障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
浮動性めまい	7 (1.1) [1.1]	11 (1.7) [1.7]	8 (1.0) [1.0]	13 (1.6) [1.6]
体位性めまい	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
味覚異常	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
顔面麻痺	0	0	0	1 (0.1) [0.1]
蟻走感	0	0	1 (0.1) [0.1]	0
頭部不快感	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
頭痛	32 (4.9) [4.9]	34 (5.3) [5.3]	37 (4.5) [4.5]	35 (4.3) [4.3]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)				
知覚過敏	0	0	1 (0.1) [0.1]	0
感覚鈍麻	4 (0.6) [0.6]	4 (0.6) [0.6]	4 (0.5) [0.5]	5 (0.6) [0.6]
肋間神経痛	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
虚血性ニューロパチー	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
虚血性脳卒中	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ラクナ脳卒中	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
嗜眠	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
腰髄神経根障害	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
腰仙部神経根障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
記憶障害	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
片頭痛	3 (0.5) [0.5]	8 (1.2) [1.2]	4 (0.5) [0.5]	10 (1.2) [1.2]
モートン神経痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
神経圧迫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
神経痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
末梢性ニューロパチー	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
錯感覚	3 (0.5) [0.5]	6 (0.9) [0.9]	3 (0.4) [0.4]	6 (0.7) [0.7]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
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神経系障害 (Cont.)				
末梢性感覚ニューロパチー	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
腓骨神経麻痺	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ヘルペス後神経痛	1 (0.2) [0.2]	7 (1.1) [1.1]	2 (0.2) [0.2]	8 (1.0) [1.0]
失神寸前の状態	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
神経根痛	0	0	1 (0.1) [0.1]	0
坐骨神経痛	5 (0.8) [0.8]	3 (0.5) [0.5]	6 (0.7) [0.7]	3 (0.4) [0.4]
感覚障害	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
副鼻腔炎に伴う頭痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
傾眠	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
会話障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
失神	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	4 (0.5) [0.5]
緊張性頭痛	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
胸髄神経根障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
一過性全健忘	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
一過性脳虚血発作	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
振戦	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)				
三叉神経痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
椎骨脳底動脈不全	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
妊娠、産褥および周産期の状態	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
異所性妊娠	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
製品の問題	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
医療機器破損	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
精神障害	43 (6.6) [6.6]	37 (5.7) [5.7]	49 (6.0) [6.0]	47 (5.7) [5.7]
抑うつ気分を伴う適応障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
感情不安定	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
不安	7 (1.1) [1.1]	6 (0.9) [0.9]	9 (1.1) [1.1]	9 (1.1) [1.1]
不安障害	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	2 (0.2) [0.2]
双極性障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
燃え尽き症候群	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
うつ病	8 (1.2) [1.2]	16 (2.5) [2.5]	12 (1.5) [1.5]	18 (2.2) [2.2]
失見当識	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
薬物乱用	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
精神障害 (Cont.)				
全般性不安障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
不眠症	16 (2.5) [2.5]	9 (1.4) [1.4]	16 (2.0) [2.0]	11 (1.3) [1.3]
リビドー減退	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大うつ病	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
精神状態変化	0	0	0	1 (0.1) [0.1]
パニック発作	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
睡眠障害	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
ストレス	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
腎および尿路障害	47 (7.2) [7.2]	39 (6.0) [6.0]	50 (6.1) [6.1]	48 (5.8) [5.8]
急性腎障害	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
膀胱拡大	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膀胱脱	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
膀胱結石	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
尿路結石	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
着色尿	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
慢性腎臓病	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
腎および尿路障害 (Cont.)				
結晶尿	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腺性膀胱炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
糖尿病性腎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
排尿困難	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	4 (0.5) [0.5]
血尿	10 (1.5) [1.5]	7 (1.1) [1.1]	10 (1.2) [1.2]	9 (1.1) [1.1]
緊張性膀胱	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
白血球尿	5 (0.8) [0.8]	3 (0.5) [0.5]	5 (0.6) [0.6]	4 (0.5) [0.5]
尿意切迫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腎結石症	7 (1.1) [1.1]	5 (0.8) [0.8]	7 (0.9) [0.9]	7 (0.9) [0.9]
腎症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
頻尿	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
蛋白尿	4 (0.6) [0.6]	5 (0.8) [0.8]	5 (0.6) [0.6]	7 (0.9) [0.9]
腎盂腎杯拡張症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腎仙痛	3 (0.5) [0.5]	0	4 (0.5) [0.5]	0
腎嚢胞	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
腎機能障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
腎および尿路障害 (Cont.)				
腎静脈圧迫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腹圧性尿失禁	0	0	1 (0.1) [0.1]	0
尿管結石症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
尿失禁	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
尿閉	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
生殖系および乳房障害	38 (5.8) [5.8]	23 (3.6) [3.6]	41 (5.0) [5.0]	27 (3.3) [3.3]
腺筋症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
子宮付属器嚢胞	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
無月経	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
亀頭包皮炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
良性前立腺肥大症	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	6 (0.7) [0.7]
乳房嚢胞	0	0	1 (0.1) [0.1]	0
乳房障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
乳房線維化	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
乳房腫瘤	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
前立腺結石	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
生殖系および乳房障害 (Cont.)				
子宮頚部上皮異形成	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
子宮頚管ポリープ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膀胱瘤	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
機能不全性子宮出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
子宮頚外反	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
子宮内膜増殖症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
精巣上体嚢胞	0	0	1 (0.1) [0.1]	0
勃起不全	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
線維嚢胞性乳腺疾患	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
閉経期症状	0	0	0	1 (0.1) [0.1]
月経過多	4 (0.6) [0.6]	0	4 (0.5) [0.5]	0
不規則月経	5 (0.8) [0.8]	1 (0.2) [0.2]	5 (0.6) [0.6]	1 (0.1) [0.1]
不正子宮出血	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
卵巣嚢胞	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	3 (0.4) [0.4]
骨盤痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
前立腺石灰化	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
生殖系および乳房障害 (Cont.)				
前立腺閉塞	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
前立腺炎	4 (0.6) [0.6]	1 (0.2) [0.2]	4 (0.5) [0.5]	1 (0.1) [0.1]
前立腺腫大	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
精巣障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
子宮出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
子宮ポリープ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
子宮脱	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
腟異形成	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腟出血	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
外陰腟そう痒症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
呼吸器、胸郭および縦隔障害	78 (12.0) [12.0]	94 (14.5) [14.5]	83 (10.2) [10.2]	117 (14.2) [14.2]
急性呼吸不全	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
アレルギー性咽頭炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
喘息	2 (0.3) [0.3]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
無気肺	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
気管支反応性亢進	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)				
慢性気管支炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
気管支痙攣	2 (0.3) [0.3]	0	2 (0.2) [0.2]	1 (0.1) [0.1]
慢性閉塞性肺疾患	3 (0.5) [0.5]	6 (0.9) [0.9]	3 (0.4) [0.4]	9 (1.1) [1.1]
咳嗽	19 (2.9) [2.9]	31 (4.8) [4.8]	20 (2.4) [2.4]	37 (4.5) [4.5]
発声障害	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
呼吸困難	6 (0.9) [0.9]	7 (1.1) [1.1]	6 (0.7) [0.7]	7 (0.9) [0.9]
労作性呼吸困難	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
鼻出血	4 (0.6) [0.6]	1 (0.2) [0.2]	4 (0.5) [0.5]	1 (0.1) [0.1]
間質性肺疾患	0	0	0	1 (0.1) [0.1]
鼻閉	0	2 (0.3) [0.3]	0	3 (0.4) [0.4]
鼻部不快感	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼻の炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
鼻閉塞	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼻潰瘍	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
口腔咽頭痛	11 (1.7) [1.7]	11 (1.7) [1.7]	11 (1.3) [1.3]	15 (1.8) [1.8]
呼吸時疼痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)				
副鼻腔嚢胞	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
咽頭の炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胸水	0	0	0	1 (0.1) [0.1]
胸膜炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
気胸	0	0	0	1 (0.1) [0.1]
自然気胸	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
湿性咳嗽	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺塞栓症	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
肺線維症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺高血圧症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
肺腫瘤	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
逆流性喉頭炎	0	0	0	1 (0.1) [0.1]
呼吸窮迫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
気道うっ血	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
アレルギー性鼻炎	4 (0.6) [0.6]	1 (0.2) [0.2]	6 (0.7) [0.7]	2 (0.2) [0.2]
鼻漏	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.4) [0.4]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)				
副鼻腔うっ血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	2 (0.2) [0.2]
副鼻腔障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
睡眠時無呼吸症候群	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
喀痰増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
咽喉刺激感	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
上気道の炎症	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
皮膚および皮下組織障害	89 (13.7) [13.7]	122 (18.9) [18.9]	104 (12.7) [12.7]	136 (16.5) [16.5]
黒色表皮腫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ざ瘡	9 (1.4) [1.4]	11 (1.7) [1.7]	10 (1.2) [1.2]	15 (1.8) [1.8]
光線性口唇炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
光線角化症	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
脱毛症	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	5 (0.6) [0.6]
血管浮腫	0	0	1 (0.1) [0.1]	0
皮脂欠乏症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
水疱	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	4 (0.5) [0.5]
肝斑	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)				
皮膚嚢腫	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
皮膚炎	4 (0.6) [0.6]	3 (0.5) [0.5]	4 (0.5) [0.5]	4 (0.5) [0.5]
ざ瘡様皮膚炎	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
アレルギー性皮膚炎	2 (0.3) [0.3]	4 (0.6) [0.6]	3 (0.4) [0.4]	4 (0.5) [0.5]
アトピー性皮膚炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
接触皮膚炎	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
薬疹	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
皮膚乾燥	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
異汗性湿疹	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
斑状出血	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
湿疹	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
紅斑	2 (0.3) [0.3]	4 (0.6) [0.6]	2 (0.2) [0.2]	5 (0.6) [0.6]
毛髪成長異常	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
多汗症	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
嵌入爪	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
内方発育毛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)				
間擦疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
汗疹	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
爪郭の炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
爪成長異常	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
爪乾癬	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
寝汗	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
爪痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
爪破損	0	0	1 (0.1) [0.1]	0
爪甲脱落症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
丘疹	0	0	0	1 (0.1) [0.1]
口囲皮膚炎	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
そう痒症	0	2 (0.3) [0.3]	0	3 (0.4) [0.4]
全身性そう痒症	0	0	1 (0.1) [0.1]	0
乾癬	12 (1.8) [1.8]	10 (1.5) [1.5]	13 (1.6) [1.6]	12 (1.5) [1.5]
老人性紫斑	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
膿疱性乾癬	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)				
発疹	3 (0.5) [0.5]	17 (2.6) [2.6]	4 (0.5) [0.5]	17 (2.1) [2.1]
紅斑性皮疹	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
毛孔性皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
全身性皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
斑状皮疹	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
斑状丘疹状皮疹	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
丘疹性皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
そう痒性皮疹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
小水疱性皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
酒さ	4 (0.6) [0.6]	6 (0.9) [0.9]	6 (0.7) [0.7]	7 (0.9) [0.9]
痂皮	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脂漏性皮膚炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
皮膚変色	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
皮膚障害	0	0	0	1 (0.1) [0.1]
皮膚剥脱	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
皮膚亀裂	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)				
皮膚出血	0	0	1 (0.1) [0.1]	0
皮膚色素過剰	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮膚色素減少	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
皮膚刺激	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
皮膚病変	4 (0.6) [0.6]	5 (0.8) [0.8]	5 (0.6) [0.6]	5 (0.6) [0.6]
皮膚潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
顔面腫脹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
蕁麻疹	6 (0.9) [0.9]	6 (0.9) [0.9]	6 (0.7) [0.7]	6 (0.7) [0.7]
社会環境	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
閉経	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
職場でのストレス	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血管障害	53 (8.1) [8.1]	52 (8.0) [8.0]	58 (7.1) [7.1]	61 (7.4) [7.4]
大動脈瘤	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大動脈硬化症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
動脈硬化症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
深部静脈血栓症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
血管障害 (Cont.)				
本態性高血圧症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
四肢壊死	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大腿動脈瘤	0	0	0	1 (0.1) [0.1]
血腫	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
ほてり	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
高血圧	42 (6.4) [6.4]	30 (4.6) [4.6]	47 (5.8) [5.8]	36 (4.4) [4.4]
高血圧クリーゼ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
高血圧切迫症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
低血圧	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
リンパ浮腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
起立性低血圧	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
末梢静脈疾患	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
表在性血栓性静脈炎	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
静脈瘤	0	1 (0.2) [0.2]	0	3 (0.4) [0.4]
血管拡張	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
静脈性高血圧	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.2

Treatment-Emergent Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
血管障害 (Cont.)				
四肢静脈血栓症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-11. 全ウパダシチニブ併合解析集団（長期）の治験薬と関連ありの有害事象（100 人年あたりの発現件数）

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	763 (117.1) [117.2]	1087 (168.0) [167.9]	901 (110.3) [110.2]	1256 (152.7) [152.8]
血液およびリンパ系障害	54 (8.3) [8.3]	99 (15.3) [15.3]	62 (7.6) [7.6]	116 (14.1) [14.1]
貧血	10 (1.5) [1.5]	16 (2.5) [2.5]	11 (1.3) [1.3]	18 (2.2) [2.2]
大球性貧血	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
失血性貧血	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
骨髄浮腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
血球減少症	0	0	0	2 (0.2) [0.2]
播種性血管内凝固	0	0	0	1 (0.1) [0.1]
赤血球減少症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
顆粒球減少症	0	1 (0.2) [0.2]	0	3 (0.4) [0.4]
内出血発生の増加傾向	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
鉄欠乏性貧血	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
白血球増加症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
白血球減少症	14 (2.1) [2.2]	19 (2.9) [2.9]	15 (1.8) [1.8]	23 (2.8) [2.8]
リンパ節炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ節症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
血液およびリンパ系障害 (Cont.)				
リンパ球増加症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ組織過形成	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ球減少症	14 (2.1) [2.2]	19 (2.9) [2.9]	15 (1.8) [1.8]	20 (2.4) [2.4]
好中球減少症	11 (1.7) [1.7]	27 (4.2) [4.2]	14 (1.7) [1.7]	30 (3.6) [3.7]
好中球増加症	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
正色素性貧血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
汎血球減少症	0	0	0	1 (0.1) [0.1]
血小板減少症	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
血小板増加症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
心臓障害	4 (0.6) [0.6]	1 (0.2) [0.2]	4 (0.5) [0.5]	3 (0.4) [0.4]
心房細動	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
心肺停止	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
動悸	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
洞性徐脈	0	0	0	1 (0.1) [0.1]
頻脈	0	0	0	1 (0.1) [0.1]
発作性頻脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)				
心室細動	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
先天性、家族性および遺伝性障害	0	0	1 (0.1) [0.1]	0
陰嚢水瘤	0	0	1 (0.1) [0.1]	0
耳および迷路障害	1 (0.2) [0.2]	0	3 (0.4) [0.4]	0
耳痛	0	0	1 (0.1) [0.1]	0
回転性めまい	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
頭位性回転性めまい	0	0	1 (0.1) [0.1]	0
内分泌障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
アンドロゲン欠乏症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
眼障害	5 (0.8) [0.8]	4 (0.6) [0.6]	5 (0.6) [0.6]	5 (0.6) [0.6]
一過性黒内障	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼瞼痙攣	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
霰粒腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ドライアイ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
虹彩毛様体炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
眼障害 (Cont.)				
瞼板腺炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
眼部不快感	0	0	0	1 (0.1) [0.1]
霧視	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
視力障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃腸障害	60 (9.2) [9.2]	76 (11.7) [11.7]	68 (8.3) [8.3]	88 (10.7) [10.7]
腹部不快感	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	3 (0.4) [0.4]
腹部膨満	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
腹痛	5 (0.8) [0.8]	2 (0.3) [0.3]	7 (0.9) [0.9]	2 (0.2) [0.2]
上腹部痛	5 (0.8) [0.8]	10 (1.5) [1.5]	5 (0.6) [0.6]	10 (1.2) [1.2]
口角口唇炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
アフタ性潰瘍	2 (0.3) [0.3]	0	2 (0.2) [0.2]	1 (0.1) [0.1]
根尖肉芽腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大腸炎	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
便秘	4 (0.6) [0.6]	3 (0.5) [0.5]	4 (0.5) [0.5]	3 (0.4) [0.4]
下痢	8 (1.2) [1.2]	12 (1.9) [1.9]	10 (1.2) [1.2]	14 (1.7) [1.7]
口内乾燥	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
十二指腸潰瘍	0	0	0	1 (0.1) [0.1]
消化不良	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	4 (0.5) [0.5]
小腸炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腸炎	0	0	0	1 (0.1) [0.1]
びらん性十二指腸炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
変色便	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼓腸	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
胃出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胃炎	2 (0.3) [0.3]	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
びらん性胃炎	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
胃十二指腸出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃十二指腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
消化器痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胃食道逆流性疾患	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
潰瘍性歯肉炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
痔核	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
口腔内潰瘍形成	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
悪心	10 (1.5) [1.5]	9 (1.4) [1.4]	10 (1.2) [1.2]	10 (1.2) [1.2]
食道潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔粘膜水疱形成	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
膵脂肪変性	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膵炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
歯周の炎症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
レッチング	0	0	1 (0.1) [0.1]	0
小腸出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
小腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口内炎	1 (0.2) [0.2]	2 (0.3) [0.3]	2 (0.2) [0.2]	4 (0.5) [0.5]
舌潰瘍	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
歯の障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
歯痛	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
嘔吐	0	5 (0.8) [0.8]	1 (0.1) [0.1]	5 (0.6) [0.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態	12 (1.8) [1.8]	26 (4.0) [4.0]	15 (1.8) [1.8]	31 (3.8) [3.8]
無力症	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
胸痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
悪寒	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
疲労	3 (0.5) [0.5]	5 (0.8) [0.8]	5 (0.6) [0.6]	8 (1.0) [1.0]
炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
インフルエンザ様疾患	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
注射部位疼痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
注射部位反応	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
倦怠感	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
非心臓性胸痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
末梢性浮腫	0	0	1 (0.1) [0.1]	0
疼痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
末梢腫脹	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
発熱	2 (0.3) [0.3]	8 (1.2) [1.2]	2 (0.2) [0.2]	9 (1.1) [1.1]
腫脹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)				
全身性炎症反応症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝胆道系障害	13 (2.0) [2.0]	15 (2.3) [2.3]	17 (2.1) [2.1]	18 (2.2) [2.2]
肝機能異常	7 (1.1) [1.1]	7 (1.1) [1.1]	10 (1.2) [1.2]	10 (1.2) [1.2]
肝腫瘤	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脂肪肝	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
肝炎	0	0	1 (0.1) [0.1]	0
肝毒性	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
高ビリルビン血症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
肝障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝損傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
非アルコール性脂肪性肝炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脂肪性肝炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
免疫系障害	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
食物アレルギー	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
過敏症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
感染症および寄生虫症	297 (45.6) [45.6]	403 (62.3) [62.3]	355 (43.5) [43.4]	472 (57.4) [57.4]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
腹部膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膿瘍	0	0	1 (0.1) [0.1]	0
四肢膿瘍	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
急性副鼻腔炎	1 (0.2) [0.2]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
肛門直腸蜂巣炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
虫垂炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
異型肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
菌血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
細菌感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
細菌性膣症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
体部白癬	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
細気管支炎	0	0	1 (0.1) [0.1]	0
気管支炎	16 (2.5) [2.5]	25 (3.9) [3.9]	21 (2.6) [2.6]	27 (3.3) [3.3]
細菌性気管支炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
蜂巣炎	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	4 (0.5) [0.5]
コクシジオイデス症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
結膜炎	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
ウイルス性結膜炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
膀胱炎	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
サイトメガロウイルス感染	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
毛嚢虫症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
憩室炎	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
耳感染	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
精巣上体炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
丹毒	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
大腸菌性尿路感染	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
眼感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
毛包炎	9 (1.4) [1.4]	3 (0.5) [0.5]	9 (1.1) [1.1]	6 (0.7) [0.7]
真菌感染	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
皮膚真菌感染	2 (0.3) [0.3]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
せつ	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
胃腸炎	6 (0.9) [0.9]	8 (1.2) [1.2]	8 (1.0) [1.0]	10 (1.2) [1.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
ウイルス性胃腸炎	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	5 (0.6) [0.6]
消化管感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
陰部ヘルペス	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
歯肉膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
歯肉炎	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
肛径部膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
H1N1インフルエンザ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
B型肝炎再活性化	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
単純ヘルペス	4 (0.6) [0.6]	11 (1.7) [1.7]	4 (0.5) [0.5]	13 (1.6) [1.6]
ヘルペスウイルス感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
帯状疱疹	17 (2.6) [2.6]	37 (5.7) [5.7]	22 (2.7) [2.7]	48 (5.8) [5.8]
麦粒腫	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
膿痂疹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
伝染性単核症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
インフルエンザ	13 (2.0) [2.0]	12 (1.9) [1.9]	14 (1.7) [1.7]	14 (1.7) [1.7]
クレブシエラ感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
喉頭炎	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
潜伏結核	0	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
下気道感染	4 (0.6) [0.6]	2 (0.3) [0.3]	4 (0.5) [0.5]	3 (0.4) [0.4]
肺感染	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
リンパ管炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
爪感染	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	4 (0.5) [0.5]
上咽頭炎	19 (2.9) [2.9]	19 (2.9) [2.9]	24 (2.9) [2.9]	24 (2.9) [2.9]
爪真菌症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔カンジダ症	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	5 (0.6) [0.6]
口腔真菌感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔ヘルペス	7 (1.1) [1.1]	37 (5.7) [5.7]	10 (1.2) [1.2]	41 (5.0) [5.0]
中咽頭カンジダ症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
外耳炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
中耳炎	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
急性中耳炎	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
爪囲炎	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
歯周炎	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
咽頭炎	5 (0.8) [0.8]	5 (0.8) [0.8]	6 (0.7) [0.7]	7 (0.9) [0.9]
レンサ球菌性咽頭炎	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
ニューモシスチス・イロベチイ肺炎	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
肺炎	7 (1.1) [1.1]	5 (0.8) [0.8]	7 (0.9) [0.9]	8 (1.0) [1.0]
細菌性肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
レンサ球菌性肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
シュードモナス感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
歯髄炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
化膿性分泌物	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腎盂腎炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
膿尿	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
膿疱性皮疹	0	3 (0.5) [0.5]	0	4 (0.5) [0.5]
気道感染	11 (1.7) [1.7]	10 (1.5) [1.5]	12 (1.5) [1.5]	10 (1.2) [1.2]
ウイルス性気道感染	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
鼻炎	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	4 (0.5) [0.5]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
卵管炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
敗血症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
副鼻腔炎	9 (1.4) [1.4]	15 (2.3) [2.3]	13 (1.6) [1.6]	16 (1.9) [1.9]
皮膚カンジダ	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
皮膚感染	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
ブドウ球菌性菌血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ブドウ球菌感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ブドウ球菌性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ブドウ球菌皮膚感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮下組織膿瘍	0	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
股部白癬	0	0	0	1 (0.1) [0.1]
白癬感染	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
手白癬	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
足部白癬	2 (0.3) [0.3]	3 (0.5) [0.5]	3 (0.4) [0.4]	3 (0.4) [0.4]
癜風	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
扁桃炎	2 (0.3) [0.3]	5 (0.8) [0.8]	3 (0.4) [0.4]	5 (0.6) [0.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
細菌性扁桃炎	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
歯膿瘍	2 (0.3) [0.3]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
歯感染	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	3 (0.4) [0.4]
気管炎	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
気管気管支炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
細菌性気管気管支炎	0	0	0	1 (0.1) [0.1]
上気道感染	57 (8.7) [8.8]	62 (9.6) [9.6]	66 (8.1) [8.1]	71 (8.6) [8.6]
尿路感染	34 (5.2) [5.2]	29 (4.5) [4.5]	37 (4.5) [4.5]	36 (4.4) [4.4]
細菌性尿路感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腸球菌性尿路感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
尿路性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス感染	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
ウイルス性筋炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ウイルス性咽頭炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス性副鼻腔炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス性気管炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
ウイルス性上気道感染	1 (0.2) [0.2]	1 (0.2) [0.2]	5 (0.6) [0.6]	2 (0.2) [0.2]
外陰部炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
外陰部腟カンジダ症	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
外陰腟真菌感染	2 (0.3) [0.3]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
傷害、中毒および処置合併症	1 (0.2) [0.2]	5 (0.8) [0.8]	1 (0.1) [0.1]	7 (0.9) [0.9]
節足動物咬傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
挫傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大腿骨骨折	0	0	0	1 (0.1) [0.1]
仙骨骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
処置による疼痛	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
皮膚擦過傷	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
歯牙破折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
臨床検査	172 (26.4) [26.4]	267 (41.3) [41.2]	202 (24.7) [24.7]	297 (36.1) [36.1]
アラニンアミノトランスフェラーゼ増加	39 (6.0) [6.0]	43 (6.6) [6.6]	44 (5.4) [5.4]	48 (5.8) [5.8]
αヒドロキシ酪酸脱水素酵素増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
アスパラギン酸アミノトランスフェラーゼ増加	27 (4.1) [4.2]	30 (4.6) [4.6]	29 (3.6) [3.5]	34 (4.1) [4.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
血中アルカリホスファターゼ増加	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
血中ビリルビン増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中コレステロール増加	5 (0.8) [0.8]	5 (0.8) [0.8]	6 (0.7) [0.7]	5 (0.6) [0.6]
血中クレアチン増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中クレアチンホスホキナーゼ増加	57 (8.7) [8.8]	95 (14.7) [14.7]	66 (8.1) [8.1]	107 (13.0) [13.0]
血中クレアチニン増加	3 (0.5) [0.5]	5 (0.8) [0.8]	6 (0.7) [0.7]	5 (0.6) [0.6]
血中ブドウ糖異常	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中ブドウ糖増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中乳酸脱水素酵素増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
血中リン減少	0	0	1 (0.1) [0.1]	0
血中カリウム増加	0	5 (0.8) [0.8]	0	5 (0.6) [0.6]
血圧上昇	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
血中甲状腺刺激ホルモン減少	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血中トリグリセリド増加	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
血中尿素増加	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
血中尿酸増加	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
体温上昇	0	0	1 (0.1) [0.1]	0
ヘマトクリット減少	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ヘモグロビン減少	2 (0.3) [0.3]	5 (0.8) [0.8]	2 (0.2) [0.2]	5 (0.6) [0.6]
肝酵素上昇	1 (0.2) [0.2]	6 (0.9) [0.9]	2 (0.2) [0.2]	7 (0.9) [0.9]
高比重リポ蛋白増加	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
未熟顆粒球数増加	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
深吸気量減少	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝機能検査値上昇	4 (0.6) [0.6]	5 (0.8) [0.8]	4 (0.5) [0.5]	5 (0.6) [0.6]
低比重リポ蛋白増加	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	3 (0.4) [0.4]
リンパ球数減少	4 (0.6) [0.6]	3 (0.5) [0.5]	4 (0.5) [0.5]	4 (0.5) [0.5]
リンパ球数増加	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
平均赤血球容積増加	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	4 (0.5) [0.5]
筋酵素上昇	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
骨髄球存在	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
好中球数減少	2 (0.3) [0.3]	10 (1.5) [1.5]	2 (0.2) [0.2]	12 (1.5) [1.5]
血小板数増加	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査 (Cont.)				
総蛋白増加	0	0	1 (0.1) [0.1]	0
赤血球数減少	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	4 (0.5) [0.5]
血沈亢進	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
トランスアミナーゼ上昇	2 (0.3) [0.3]	5 (0.8) [0.8]	3 (0.4) [0.4]	7 (0.9) [0.9]
尿検査異常	0	0	0	1 (0.1) [0.1]
超低比重リポ蛋白増加	2 (0.3) [0.3]	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
体重減少	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
体重増加	1 (0.2) [0.2]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
白血球数減少	2 (0.3) [0.3]	14 (2.2) [2.2]	3 (0.4) [0.4]	15 (1.8) [1.8]
代謝および栄養障害	14 (2.1) [2.1]	28 (4.3) [4.3]	17 (2.1) [2.1]	32 (3.9) [3.9]
脂質異常症	2 (0.3) [0.3]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
高カルシウム血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
高コレステロール血症	1 (0.2) [0.2]	8 (1.2) [1.2]	2 (0.2) [0.2]	8 (1.0) [1.0]
高血糖	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
高脂血症	3 (0.5) [0.5]	5 (0.8) [0.8]	3 (0.4) [0.4]	7 (0.9) [0.9]
高トリグリセリド血症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
代謝および栄養障害 (Cont.)				
高尿酸血症	3 (0.5) [0.5]	2 (0.3) [0.3]	4 (0.5) [0.5]	3 (0.4) [0.4]
低血糖	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
低カリウム血症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
低リン酸血症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ビタミンD欠乏	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
筋骨格系および結合組織障害	18 (2.8) [2.8]	12 (1.9) [1.9]	21 (2.6) [2.6]	17 (2.1) [2.1]
関節痛	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
背部痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
軟骨疾患	0	0	0	1 (0.1) [0.1]
側腹部痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
関節雑音	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
関節硬直	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
筋痙縮	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
筋力低下	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
筋骨格系胸痛	0	1 (0.2) [0.2]	0	3 (0.4) [0.4]
筋肉痛	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)				
変形性関節症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
四肢痛	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
乾癬性関節症	6 (0.9) [0.9]	2 (0.3) [0.3]	8 (1.0) [1.0]	4 (0.5) [0.5]
急速進行性変形性関節症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脊椎痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	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）	3 (0.5) [0.5]	12 (1.9) [1.9]	6 (0.7) [0.7]	13 (1.6) [1.6]
肛門性器疣贅	0	3 (0.5) [0.5]	0	3 (0.4) [0.4]
基底細胞癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ボーエン病	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大腸腺腫	0	0	1 (0.1) [0.1]	0
遠隔転移を伴う肺癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
メラノサイト性母斑	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
直腸腺癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
直腸癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮膚乳頭腫	0	4 (0.6) [0.6]	2 (0.2) [0.2]	4 (0.5) [0.5]
扁平上皮癌	0	0	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)				
皮膚有棘細胞癌	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
神経系障害	17 (2.6) [2.6]	37 (5.7) [5.7]	23 (2.8) [2.8]	42 (5.1) [5.1]
手根管症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
頚髄神経根障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
浮動性めまい	3 (0.5) [0.5]	3 (0.5) [0.5]	4 (0.5) [0.5]	4 (0.5) [0.5]
顔面麻痺	0	0	0	1 (0.1) [0.1]
頭痛	8 (1.2) [1.2]	17 (2.6) [2.6]	11 (1.3) [1.3]	17 (2.1) [2.1]
感覚鈍麻	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ラクナ脳卒中	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
嗜眠	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
記憶障害	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
片頭痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
神経痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
錯感覚	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
末梢性感覚ニューロパチー	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
ヘルペス後神経痛	1 (0.2) [0.2]	4 (0.6) [0.6]	2 (0.2) [0.2]	5 (0.6) [0.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)				
失神寸前の状態	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
感覚障害	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
傾眠	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
失神	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
緊張性頭痛	0	0	1 (0.1) [0.1]	0
三叉神経痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
精神障害	5 (0.8) [0.8]	7 (1.1) [1.1]	5 (0.6) [0.6]	7 (0.9) [0.9]
感情不安定	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
不安	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
うつ病	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
不眠症	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	3 (0.4) [0.4]
睡眠障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腎および尿路障害	5 (0.8) [0.8]	11 (1.7) [1.7]	6 (0.7) [0.7]	13 (1.6) [1.6]
尿路結石	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
慢性腎臓病	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
糖尿病性腎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
腎および尿路障害 (Cont.)				
排尿困難	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
血尿	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	4 (0.5) [0.5]
緊張性膀胱	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
白血球尿	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
尿意切迫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
頻尿	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
蛋白尿	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
生殖系および乳房障害	6 (0.9) [0.9]	2 (0.3) [0.3]	7 (0.9) [0.9]	3 (0.4) [0.4]
無月経	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
乳房嚢胞	0	0	1 (0.1) [0.1]	0
前立腺結石	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
線維嚢胞性乳腺疾患	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
月経過多	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
不規則月経	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
前立腺炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
呼吸器、胸郭および縦隔障害	24 (3.7) [3.7]	34 (5.3) [5.2]	25 (3.1) [3.1]	39 (4.7) [4.7]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)				
急性呼吸不全	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
気管支反応性亢進	0	0	1 (0.1) [0.1]	0
咳嗽	3 (0.5) [0.5]	13 (2.0) [2.0]	3 (0.4) [0.4]	16 (1.9) [1.9]
発声障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
呼吸困難	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
労作性呼吸困難	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
鼻出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
間質性肺疾患	0	0	0	1 (0.1) [0.1]
鼻部不快感	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼻の炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
鼻潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
口腔咽頭痛	4 (0.6) [0.6]	4 (0.6) [0.6]	4 (0.5) [0.5]	4 (0.5) [0.5]
咽頭の炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胸膜炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
自然気胸	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
湿性咳嗽	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)				
肺塞栓症	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
肺線維症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺高血圧症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
呼吸窮迫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
アレルギー性鼻炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼻漏	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
副鼻腔うっ血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
咽喉刺激感	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
上気道の炎症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
皮膚および皮下組織障害	39 (6.0) [6.0]	38 (5.9) [5.9]	45 (5.5) [5.5]	42 (5.1) [5.1]
ざ瘡	5 (0.8) [0.8]	5 (0.8) [0.8]	5 (0.6) [0.6]	5 (0.6) [0.6]
光線性口唇炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
脱毛症	2 (0.3) [0.3]	3 (0.5) [0.5]	2 (0.2) [0.2]	3 (0.4) [0.4]
水疱	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	3 (0.4) [0.4]
肝斑	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
皮膚嚢腫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)				
皮膚炎	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
ざ瘡様皮膚炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
アレルギー性皮膚炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
アトピー性皮膚炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮膚乾燥	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
異汗性湿疹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
斑状出血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
湿疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
紅斑	0	4 (0.6) [0.6]	0	5 (0.6) [0.6]
毛髪成長異常	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
多汗症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
間擦疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
爪郭の炎症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
爪成長異常	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
寝汗	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
爪破損	0	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

	Upadacitinib			
System Organ Class MedDRA 22.0 Preferred Term	15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
皮膚および皮下組織障害 (Cont.)				
丘疹	0	0	0	1 (0.1) [0.1]
そう痒症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
全身性そう痒症	0	0	1 (0.1) [0.1]	0
乾癬	8 (1.2) [1.2]	2 (0.3) [0.3]	9 (1.1) [1.1]	3 (0.4) [0.4]
膿疱性乾癬	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
発疹	1 (0.2) [0.2]	6 (0.9) [0.9]	2 (0.2) [0.2]	6 (0.7) [0.7]
毛孔性皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
全身性皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
斑状皮疹	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
斑状丘疹状皮疹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
酒さ	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
皮膚剥脱	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
皮膚刺激	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
皮膚病変	3 (0.5) [0.5]	0	4 (0.5) [0.5]	0
顔面腫脹	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血管障害	12 (1.8) [1.8]	8 (1.2) [1.2]	12 (1.5) [1.5]	9 (1.1) [1.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.5

Treatment-Emergent Adverse Events with Reasonable Possibility of Being Related to Study Drug
in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
血管障害 (Cont.)				
深部静脈血栓症	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
ほてり	3 (0.5) [0.5]	0	3 (0.4) [0.4]	0
高血圧	5 (0.8) [0.8]	6 (0.9) [0.9]	5 (0.6) [0.6]	7 (0.9) [0.9]
高血圧クリーゼ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
低血圧	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
表在性血栓性静脈炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-12.　　プラセボ対照併合解析集団（投与 24 週時）の Grade 3 以上の有害事象

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
Any adverse event	24 (3.8) [3.8]	34 (5.3) [5.3]	43 (6.7) [6.7]
血液およびリンパ系障害	1 (0.2) [0.2]	4 (0.6) [0.6]	7 (1.1) [1.1]
貧血	0	0	2 (0.3) [0.3]
失血性貧血	0	1 (0.2) [0.2]	0
鉄欠乏性貧血	0	0	1 (0.2) [0.2]
リンパ組織過形成	0	0	1 (0.2) [0.2]
リンパ球減少症	1 (0.2) [0.2]	3 (0.5) [0.5]	2 (0.3) [0.3]
好中球減少症	0	0	1 (0.2) [0.2]
心臓障害	1 (0.2) [0.2]	4 (0.6) [0.6]	2 (0.3) [0.3]
不安定狭心症	1 (0.2) [0.2]	0	1 (0.2) [0.2]
心房細動	0	1 (0.2) [0.2]	0
心不全	0	1 (0.2) [0.2]	0
心肺停止	0	1 (0.2) [0.2]	0
冠動脈狭窄	0	0	1 (0.2) [0.2]
頻脈	0	1 (0.2) [0.2]	0
心室細動	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
眼障害	0	1 (0.2) [0.2]	1 (0.2) [0.2]
白内障	0	0	1 (0.2) [0.2]
後嚢部混濁	0	1 (0.2) [0.2]	0
胃腸障害	0	5 (0.8) [0.8]	2 (0.3) [0.3]
下痢	0	1 (0.2) [0.2]	1 (0.2) [0.2]
消化不良	0	1 (0.2) [0.2]	0
びらん性胃炎	0	1 (0.2) [0.2]	0
裂孔ヘルニア	0	1 (0.2) [0.2]	0
大腸ポリープ	0	1 (0.2) [0.2]	0
悪心	0	0	1 (0.2) [0.2]
小腸潰瘍	0	0	1 (0.2) [0.2]
一般・全身障害および投与部位の状態	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.3) [0.3]
胸痛	1 (0.2) [0.2]	0	0
浮腫	0	1 (0.2) [0.2]	0
発熱	0	0	1 (0.2) [0.2]
全身性炎症反応症候群	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
肝胆道系障害	0	0	3 (0.5) [0.5]
胆管結石	0	0	1 (0.2) [0.2]
胆石症	0	0	1 (0.2) [0.2]
胆嚢ポリープ	0	0	1 (0.2) [0.2]
感染症および寄生虫症	8 (1.3) [1.3]	11 (1.7) [1.7]	17 (2.7) [2.6]
肛門膿瘍	0	0	1 (0.2) [0.2]
虫垂炎	1 (0.2) [0.2]	0	0
異型肺炎	0	0	2 (0.3) [0.3]
菌血症	0	0	2 (0.3) [0.3]
乳房蜂巣炎	1 (0.2) [0.2]	0	0
気管支炎	1 (0.2) [0.2]	0	1 (0.2) [0.2]
ブドウ球菌感染性滑液包炎	1 (0.2) [0.2]	0	0
蜂巣炎	0	1 (0.2) [0.2]	0
サイトメガロウイルス感染	0	0	1 (0.2) [0.2]
丹毒	0	1 (0.2) [0.2]	0
大腸菌性尿路感染	1 (0.2) [0.2]	0	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
硬膜外膿瘍	0	0	1 (0.2) [0.2]
胃腸炎	2 (0.3) [0.3]	1 (0.2) [0.2]	1 (0.2) [0.2]
歯肉炎	0	0	1 (0.2) [0.2]
帯状疱疹	0	0	1 (0.2) [0.2]
喉頭炎	0	1 (0.2) [0.2]	0
下気道感染	0	1 (0.2) [0.2]	0
肺感染	0	0	1 (0.2) [0.2]
爪感染	0	1 (0.2) [0.2]	0
上咽頭炎	0	0	1 (0.2) [0.2]
ニューモシスチス・イロベチイ肺炎	0	0	1 (0.2) [0.2]
肺炎	1 (0.2) [0.2]	2 (0.3) [0.3]	4 (0.6) [0.6]
敗血症	0	2 (0.3) [0.3]	0
ブドウ球菌感染	0	1 (0.2) [0.2]	0
扁桃炎	0	1 (0.2) [0.2]	0
尿路感染	0	0	1 (0.2) [0.2]
傷害、中毒および処置合併症	6 (0.9) [0.9]	1 (0.2) [0.2]	2 (0.3) [0.3]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
傷害、中毒および処置合併症 (Cont.)			
足関節部骨折	1 (0.2) [0.2]	0	1 (0.2) [0.2]
粉砕骨折	0	0	1 (0.2) [0.2]
腓骨骨折	1 (0.2) [0.2]	0	0
手骨折	1 (0.2) [0.2]	0	0
上腕骨骨折	0	0	1 (0.2) [0.2]
膝蓋骨骨折	0	1 (0.2) [0.2]	0
外傷後疼痛	1 (0.2) [0.2]	0	0
肋骨骨折	1 (0.2) [0.2]	0	0
交通事故	1 (0.2) [0.2]	0	0
各種物質毒性	1 (0.2) [0.2]	0	0
外傷性血胸	1 (0.2) [0.2]	0	0
血管偽動脈瘤	1 (0.2) [0.2]	0	0
臨床検査	4 (0.6) [0.6]	5 (0.8) [0.8]	4 (0.6) [0.6]
アラニンアミノトランスフェラーゼ増加	1 (0.2) [0.2]	2 (0.3) [0.3]	3 (0.5) [0.5]
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.3) [0.3]
血中クレアチンホスホキナーゼ増加	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.3) [0.3]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
臨床検査 (Cont.)			
リンパ球数減少	0	1 (0.2) [0.2]	0
血沈亢進	1 (0.2) [0.2]	0	0
代謝および栄養障害	0	0	2 (0.3) [0.3]
高トリグリセリド血症	0	0	1 (0.2) [0.2]
高尿酸血症	0	0	1 (0.2) [0.2]
筋骨格系および結合組織障害	4 (0.6) [0.6]	3 (0.5) [0.5]	2 (0.3) [0.3]
椎間関節症候群	1 (0.2) [0.2]	0	0
高クレアチン血症	0	0	1 (0.2) [0.2]
椎間板障害	1 (0.2) [0.2]	0	0
椎間板突出	1 (0.2) [0.2]	0	0
変形性関節症	0	1 (0.2) [0.2]	1 (0.2) [0.2]
乾癬性関節症	2 (0.3) [0.3]	1 (0.2) [0.2]	0
急速進行性変形性関節症	0	1 (0.2) [0.2]	0
変形性脊椎症	1 (0.2) [0.2]	0	0
脊柱管狭窄症	1 (0.2) [0.2]	0	0
脊椎すべり症	1 (0.2) [0.2]	0	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
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	3 (0.5) [0.5]	3 (0.5) [0.5]
基底細胞癌	0	0	1 (0.2) [0.2]
神経内分泌癌	0	1 (0.2) [0.2]	0
卵巣癌	0	0	1 (0.2) [0.2]
前立腺癌	0	1 (0.2) [0.2]	0
直腸腺癌	0	0	1 (0.2) [0.2]
直腸癌	0	1 (0.2) [0.2]	0
神経系障害	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]
頚髄神経根障害	0	1 (0.2) [0.2]	0
片頭痛	1 (0.2) [0.2]	0	0
ヘルペス後神経痛	0	0	1 (0.2) [0.2]
失神	0	1 (0.2) [0.2]	0
妊娠、産褥および周産期の状態	0	0	1 (0.2) [0.2]
異所性妊娠	0	0	1 (0.2) [0.2]
精神障害	1 (0.2) [0.2]	0	0
不安	1 (0.2) [0.2]	0	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.3

Number and Percentage of Subjects with Treatment-Emergent Severe Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
腎および尿路障害	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.2) [0.2]
急性腎障害	1 (0.2) [0.2]	0	1 (0.2) [0.2]
腎結石症	0	1 (0.2) [0.2]	0
生殖系および乳房障害	0	1 (0.2) [0.2]	0
前立腺炎	0	1 (0.2) [0.2]	0
呼吸器、胸郭および縦隔障害	1 (0.2) [0.2]	1 (0.2) [0.2]	3 (0.5) [0.5]
急性呼吸不全	0	1 (0.2) [0.2]	0
慢性閉塞性肺疾患	0	0	1 (0.2) [0.2]
閉塞性気道障害	1 (0.2) [0.2]	0	0
肺塞栓症	0	1 (0.2) [0.2]	1 (0.2) [0.2]
肺線維症	0	0	1 (0.2) [0.2]
皮膚および皮下組織障害	1 (0.2) [0.2]	1 (0.2) [0.2]	0
乾癬	1 (0.2) [0.2]	0	0
皮膚病変	0	1 (0.2) [0.2]	0
血管障害	0	1 (0.2) [0.2]	0
高血圧	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

表 2.7.4.7-13. 全ウパダシチニブ併合解析集団（長期）の Grade 3 以上の有害事象（100 人年あたりの発現件数）

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	88 (13.5) [13.5]	118 (18.2) [18.2]	101 (12.4) [12.4]	150 (18.2) [18.2]
血液およびリンパ系障害	5 (0.8) [0.8]	10 (1.5) [1.5]	5 (0.6) [0.6]	14 (1.7) [1.7]
貧血	0	4 (0.6) [0.6]	0	4 (0.5) [0.5]
失血性貧血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血球減少症	0	0	0	1 (0.1) [0.1]
播種性血管内凝固	0	0	0	1 (0.1) [0.1]
鉄欠乏性貧血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ節炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ組織過形成	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ球減少症	4 (0.6) [0.6]	2 (0.3) [0.3]	4 (0.5) [0.5]	3 (0.4) [0.4]
好中球減少症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
汎血球減少症	0	0	0	1 (0.1) [0.1]
心臓障害	8 (1.2) [1.2]	5 (0.8) [0.8]	8 (1.0) [1.0]	5 (0.6) [0.6]
狭心症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
不安定狭心症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心房細動	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)				
心不全	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
うっ血性心不全	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心肺停止	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
冠動脈狭窄	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心筋梗塞	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
上室性頻脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
頻脈	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
心室細動	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
内分泌障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
甲状腺腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼障害	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
白内障	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
後嚢部混濁	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃腸障害	9 (1.4) [1.4]	6 (0.9) [0.9]	10 (1.2) [1.2]	9 (1.1) [1.1]
腹部不快感	0	0	0	1 (0.1) [0.1]
痔瘻	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
大腸炎	0	0	1 (0.1) [0.1]	0
下痢	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
十二指腸潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
出血性十二指腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
消化不良	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
穿孔性胃潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
びらん性胃炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃腸出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
裂孔ヘルニア	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
大腸ポリープ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
悪心	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
小腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
上部消化管出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
一般・全身障害および投与部位の状態	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	5 (0.6) [0.6]
胸痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
浮腫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)				
発熱	0	2 (0.3) [0.3]	0	3 (0.4) [0.4]
全身性炎症反応症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝胆道系障害	0	4 (0.6) [0.6]	1 (0.1) [0.1]	4 (0.5) [0.5]
胆管結石	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胆石症	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
胆嚢ポリープ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
感染症および寄生虫症	20 (3.1) [3.1]	42 (6.5) [6.5]	24 (2.9) [2.9]	52 (6.3) [6.3]
膿瘍	0	0	1 (0.1) [0.1]	0
四肢膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肛門膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
虫垂炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
異型肺炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
菌血症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
細気管支炎	0	0	1 (0.1) [0.1]	0
気管支炎	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	4 (0.5) [0.5]
気管支肺アスペルギルス症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
蜂巣炎	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
サイトメガロウイルス感染	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
憩室炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
丹毒	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
硬膜外膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
せつ	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胃腸炎	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
ウイルス性胃腸炎	0	0	0	1 (0.1) [0.1]
歯肉炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
H1N1インフルエンザ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
帯状疱疹	1 (0.2) [0.2]	5 (0.8) [0.8]	1 (0.1) [0.1]	7 (0.9) [0.9]
インフルエンザ	0	0	1 (0.1) [0.1]	0
喉頭炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
下気道感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
肺感染	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
爪感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
上咽頭炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
外耳炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
中耳炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ニューモシスチス・イロベチイ肺炎	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
肺炎	3 (0.5) [0.5]	4 (0.6) [0.6]	3 (0.4) [0.4]	6 (0.7) [0.7]
レンサ球菌性肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
卵管炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
敗血症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
副鼻腔炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
ブドウ球菌性菌血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ブドウ球菌感染	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ブドウ球菌性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
扁桃炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
上気道感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
尿路感染	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
傷害、中毒および処置合併症	8 (1.2) [1.2]	5 (0.8) [0.8]	10 (1.2) [1.2]	7 (0.9) [0.9]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
足関節部骨折	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
骨亀裂	0	0	1 (0.1) [0.1]	0
頚椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
粉砕骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
上腕骨骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
靭帯捻挫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腰椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
半月板損傷	0	0	0	1 (0.1) [0.1]
膝蓋骨骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
交通事故	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腱損傷	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腱断裂	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胸椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脛骨骨折	0	0	1 (0.1) [0.1]	0
外傷性血胸	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
上肢骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
臨床検査	10 (1.5) [1.5]	10 (1.5) [1.5]	10 (1.2) [1.2]	11 (1.3) [1.3]
アラニンアミノトランスフェラーゼ増加	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	3 (0.4) [0.4]
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.3) [0.3]	2 (0.3) [0.3]	2 (0.2) [0.2]	2 (0.2) [0.2]
血中クレアチンホスホキナーゼ増加	4 (0.6) [0.6]	4 (0.6) [0.6]	4 (0.5) [0.5]	5 (0.6) [0.6]
リンパ球数減少	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
代謝および栄養障害	0	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
糖尿病	0	0	1 (0.1) [0.1]	0
高トリグリセリド血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
高尿酸血症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
筋骨格系および結合組織障害	6 (0.9) [0.9]	6 (0.9) [0.9]	6 (0.7) [0.7]	10 (1.2) [1.2]
関節痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
背部痛	0	1 (0.2) [0.2]	0	4 (0.5) [0.5]
滑液包炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
高クレアチン血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腰部脊柱管狭窄症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
変形性関節症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)				
骨壊死	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
乾癬性関節症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
急速進行性変形性関節症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腱炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	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）	5 (0.8) [0.8]	4 (0.6) [0.6]	7 (0.9) [0.9]	4 (0.5) [0.5]
基底細胞癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
遠隔転移を伴う肺癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
悪性黒色腫	0	0	1 (0.1) [0.1]	0
悪性黒色腫第3期	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
神経内分泌癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
中咽頭扁平上皮癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
卵巣癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
前立腺癌	1 (0.2) [0.2]	0	2 (0.2) [0.2]	0
直腸腺癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
直腸癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
神経系障害	3 (0.5) [0.5]	3 (0.5) [0.5]	3 (0.4) [0.4]	4 (0.5) [0.5]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
神経系障害 (Cont.)				
頚髄神経根障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
糖尿病性ニューロパチー	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
顔面麻痺	0	0	0	1 (0.1) [0.1]
ラクナ脳卒中	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ヘルペス後神経痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
坐骨神経痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
失神	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
妊娠、産褥および周産期の状態	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
異所性妊娠	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
精神障害	0	4 (0.6) [0.6]	1 (0.1) [0.1]	4 (0.5) [0.5]
不安	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
うつ病	0	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
腎および尿路障害	3 (0.5) [0.5]	1 (0.2) [0.2]	3 (0.4) [0.4]	1 (0.1) [0.1]
急性腎障害	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
腎結石症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腎仙痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
生殖系および乳房障害	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
子宮頚部上皮異形成	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
前立腺炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
呼吸器、胸郭および縦隔障害	4 (0.6) [0.6]	6 (0.9) [0.9]	4 (0.5) [0.5]	10 (1.2) [1.2]
急性呼吸不全	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
慢性閉塞性肺疾患	0	2 (0.3) [0.3]	0	4 (0.5) [0.5]
間質性肺疾患	0	0	0	1 (0.1) [0.1]
気胸	0	0	0	1 (0.1) [0.1]
自然気胸	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺塞栓症	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
肺線維症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
皮膚および皮下組織障害	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
血管浮腫	0	0	1 (0.1) [0.1]	0
乾癬	0	0	0	1 (0.1) [0.1]
皮膚病変	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
蕁麻疹	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.4

Treatment-Emergent Severe Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
血管障害	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
深部静脈血栓症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
四肢壊死	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
高血圧	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
静脈瘤	0	0	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-14. 投与 24 週時までの Grade 3 以上の有害事象（安全性解析対象集団）：M15-572 試験

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
Any adverse event	16 (3.8)	28 (6.5)	21 (4.9)	27 (6.4)
血液およびリンパ系障害	1 (0.2)	0	3 (0.7)	7 (1.7)
貧血	0	0	0	2 (0.5)
鉄欠乏性貧血	0	0	0	1 (0.2)
リンパ組織過形成	0	0	0	1 (0.2)
リンパ球減少症	1 (0.2)	0	3 (0.7)	2 (0.5)
好中球減少症	0	0	0	1 (0.2)
心臓障害	0	1 (0.2)	1 (0.2)	0
急性心筋梗塞	0	1 (0.2)	0	0
心不全	0	0	1 (0.2)	0
眼障害	0	0	0	1 (0.2)
白内障	0	0	0	1 (0.2)
胃腸障害	0	1 (0.2)	3 (0.7)	0
十二指腸潰瘍	0	1 (0.2)	0	0
消化不良	0	0	1 (0.2)	0
裂孔ヘルニア	0	0	1 (0.2)	0
大腸ポリープ	0	0	1 (0.2)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
一般・全身障害および投与部位の状態	1 (0.2)	0	1 (0.2)	0
胸痛	1 (0.2)	0	0	0
浮腫	0	0	1 (0.2)	0
肝胆道系障害	0	2 (0.5)	0	1 (0.2)
胆管結石	0	0	0	1 (0.2)
薬物性肝障害	0	1 (0.2)	0	0
門脈血栓症	0	1 (0.2)	0	0
免疫系障害	0	1 (0.2)	0	0
過敏症	0	1 (0.2)	0	0
感染症および寄生虫症	6 (1.4)	6 (1.4)	8 (1.9)	10 (2.4)
肛門膿瘍	0	0	0	1 (0.2)
虫垂炎	1 (0.2)	0	0	0
異型肺炎	0	0	0	2 (0.5)
菌血症	0	0	0	1 (0.2)
骨膿瘍	0	1 (0.2)	0	0
乳房蜂巣炎	1 (0.2)	0	0	0
気管支炎	1 (0.2)	0	0	0
蜂巣炎	0	0	1 (0.2)	0
サイトメガロウイルス感染	0	0	0	1 (0.2)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
感染症および寄生虫症 (Cont.)				
耳感染	0	1 (0.2)	0	0
丹毒	0	1 (0.2)	1 (0.2)	0
大腸菌性尿路感染	1 (0.2)	0	0	0
胃腸炎	1 (0.2)	0	0	1 (0.2)
歯肉炎	0	0	0	1 (0.2)
インフルエンザ	0	1 (0.2)	0	0
喉頭炎	0	0	1 (0.2)	0
下気道感染	0	1 (0.2)	1 (0.2)	0
肺感染	0	0	0	1 (0.2)
上咽頭炎	0	0	0	1 (0.2)
ニューモシスチス・イロベチイ肺炎	0	0	0	1 (0.2)
肺炎	1 (0.2)	0	1 (0.2)	1 (0.2)
敗血症	0	0	2 (0.5)	0
ブドウ球菌感染	0	1 (0.2)	1 (0.2)	0
扁桃炎	0	0	1 (0.2)	0
傷害、中毒および処置合併症	3 (0.7)	1 (0.2)	0	2 (0.5)
足関節部骨折	0	0	0	1 (0.2)
粉砕骨折	0	0	0	1 (0.2)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
傷害、中毒および処置合併症 (Cont.)				
手骨折	1 (0.2)	0	0	0
上腕骨骨折	0	0	0	1 (0.2)
外傷後疼痛	1 (0.2)	0	0	0
腱断裂	0	1 (0.2)	0	0
各種物質毒性	1 (0.2)	0	0	0
臨床検査	3 (0.7)	3 (0.7)	4 (0.9)	3 (0.7)
アラニンアミノトランスフェラーゼ増加	0	1 (0.2)	2 (0.5)	2 (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 (0.2)	1 (0.2)	2 (0.5)
血中クレアチンホスホキナーゼ増加	2 (0.5)	1 (0.2)	2 (0.5)	2 (0.5)
血中ブドウ糖増加	0	1 (0.2)	0	0
血沈亢進	1 (0.2)	0	0	0
代謝および栄養障害	0	1 (0.2)	0	2 (0.5)
高トリグリセリド血症	0	1 (0.2)	0	1 (0.2)
高尿酸血症	0	0	0	1 (0.2)
筋骨格系および結合組織障害	2 (0.5)	3 (0.7)	0	2 (0.5)
高クレアチン血症	0	0	0	1 (0.2)
椎間板障害	1 (0.2)	0	0	0
椎間板突出	0	2 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
筋骨格系および結合組織障害 (Cont.)				
腰部脊柱管狭窄症	0	1 (0.2)	0	0
変形性関節症	0	1 (0.2)	0	1 (0.2)
乾癬性関節症	1 (0.2)	0	0	0
変形性脊椎症	1 (0.2)	0	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	3 (0.7)	1 (0.2)	1 (0.2)
基底細胞癌	0	0	0	1 (0.2)
遠隔転移を伴う結腸癌	0	1 (0.2)	0	0
神経内分泌癌	0	0	1 (0.2)	0
卵巣癌	0	1 (0.2)	0	0
子宮癌	0	1 (0.2)	0	0
神経系障害	1 (0.2)	4 (0.9)	1 (0.2)	0
頚髄神経根障害	0	0	1 (0.2)	0
顔面麻痺	0	1 (0.2)	0	0
肝性脳症	0	1 (0.2)	0	0
片頭痛	1 (0.2)	0	0	0
失神	0	1 (0.2)	0	0
一過性脳虚血発作	0	1 (0.2)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
精神障害	0	1 (0.2)	0	0
不安	0	1 (0.2)	0	0
腎および尿路障害	1 (0.2)	1 (0.2)	0	0
急性腎障害	1 (0.2)	0	0	0
尿管結石症	0	1 (0.2)	0	0
呼吸器、胸郭および縦隔障害	1 (0.2)	0	0	3 (0.7)
慢性閉塞性肺疾患	0	0	0	1 (0.2)
閉塞性気道障害	1 (0.2)	0	0	0
肺塞栓症	0	0	0	1 (0.2)
肺線維症	0	0	0	1 (0.2)
皮膚および皮下組織障害	0	2 (0.5)	1 (0.2)	0
脱毛症	0	1 (0.2)	0	0
皮膚炎	0	1 (0.2)	0	0
皮膚病変	0	0	1 (0.2)	0
血管障害	0	0	1 (0.2)	0
高血圧	0	0	1 (0.2)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Events with unknown toxicity grade or Grade 3 and above based on CTCAE v5.0 will be counted as severe.

Program Source Code: [redacted]

表 2.7.4.7-15. 投与 24 週時までの Grade 3 以上の有害事象（安全性解析対象集団）：M15-554 試験

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
Any adverse event	8 (3.8)	13 (6.2)	16 (7.3)
血液およびリンパ系障害	0	1 (0.5)	0
失血性貧血	0	1 (0.5)	0
心臓障害	1 (0.5)	3 (1.4)	2 (0.9)
不安定狭心症	1 (0.5)	0	1 (0.5)
心房細動	0	1 (0.5)	0
心肺停止	0	1 (0.5)	0
冠動脈狭窄	0	0	1 (0.5)
頻脈	0	1 (0.5)	0
心室細動	0	1 (0.5)	0
眼障害	0	1 (0.5)	0
後嚢部混濁	0	1 (0.5)	0
胃腸障害	0	2 (0.9)	2 (0.9)
下痢	0	1 (0.5)	1 (0.5)
びらん性胃炎	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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.
Severe AE are defined as events with grade 3 or above based on the Common Terminology Criteria for AE (CTCAE) version 5.0.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
胃腸障害 (Cont.)			
悪心	0	0	1 (0.5)
小腸潰瘍	0	0	1 (0.5)
一般・全身障害および投与部位の状態	0	0	2 (0.9)
発熱	0	0	1 (0.5)
全身性炎症反応症候群	0	0	1 (0.5)
肝胆道系障害	0	0	2 (0.9)
胆石症	0	0	1 (0.5)
胆嚢ポリープ	0	0	1 (0.5)
感染症および寄生虫症	2 (0.9)	3 (1.4)	7 (3.2)
菌血症	0	0	1 (0.5)
気管支炎	0	0	1 (0.5)
ブドウ球菌感染性滑液包炎	1 (0.5)	0	0
硬膜外膿瘍	0	0	1 (0.5)
胃腸炎	1 (0.5)	1 (0.5)	0
帯状疱疹	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Severe AE are defined as events with grade 3 or above based on the Common Terminology Criteria for AE (CTCAE) version 5.0.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
感染症および寄生虫症 (Cont.)			
爪感染	0	1 (0.5)	0
肺炎	0	1 (0.5)	3 (1.4)
尿路感染	0	0	1 (0.5)
傷害、中毒および処置合併症	3 (1.4)	1 (0.5)	0
足関節部骨折	1 (0.5)	0	0
腓骨骨折	1 (0.5)	0	0
膝蓋骨骨折	0	1 (0.5)	0
肋骨骨折	1 (0.5)	0	0
交通事故	1 (0.5)	0	0
外傷性血胸	1 (0.5)	0	0
血管偽動脈瘤	1 (0.5)	0	0
臨床検査	1 (0.5)	1 (0.5)	1 (0.5)
アラニンアミノトランスフェラーゼ増加	1 (0.5)	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 (0.5)	0	0
リンパ球数減少	0	1 (0.5)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Severe AE are defined as events with grade 3 or above based on the Common Terminology Criteria for AE (CTCAE) version 5.0.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
筋骨格系および結合組織障害	2 (0.9)	3 (1.4)	0
椎間関節症候群	1 (0.5)	0	0
椎間板突出	1 (0.5)	0	0
変形性関節症	0	1 (0.5)	0
乾癬性関節症	1 (0.5)	1 (0.5)	0
急速進行性変形性関節症	0	1 (0.5)	0
脊柱管狭窄症	1 (0.5)	0	0
脊椎すべり症	1 (0.5)	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	2 (0.9)	2 (0.9)
卵巣癌	0	0	1 (0.5)
前立腺癌	0	1 (0.5)	0
直腸腺癌	0	0	1 (0.5)
直腸癌	0	1 (0.5)	0
神経系障害	0	1 (0.5)	1 (0.5)
ヘルペス後神経痛	0	0	1 (0.5)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
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.
Severe AE are defined as events with grade 3 or above based on the Common Terminology Criteria for AE (CTCAE) version 5.0.

Program Source Code: [redacted]

TABLE 14.3__1.7.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
神経系障害 (Cont.)			
失神	0	1 (0.5)	0
妊娠、産褥および周産期の状態	0	0	1 (0.5)
異所性妊娠	0	0	1 (0.5)
精神障害	1 (0.5)	0	0
不安	1 (0.5)	0	0
腎および尿路障害	0	1 (0.5)	1 (0.5)
急性腎障害	0	0	1 (0.5)
腎結石症	0	1 (0.5)	0
生殖系および乳房障害	0	1 (0.5)	0
前立腺炎	0	1 (0.5)	0
呼吸器、胸郭および縦隔障害	0	1 (0.5)	0
急性呼吸不全	0	1 (0.5)	0
肺塞栓症	0	1 (0.5)	0
皮膚および皮下組織障害	1 (0.5)	0	0
乾癬	1 (0.5)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.
Severe AE are defined as events with grade 3 or above based on the Common Terminology Criteria for AE (CTCAE) version 5.0.

Program Source Code: [redacted]

表 2.7.4.7-16.　全ウパダシチニブ併合解析集団（長期）の発現時期別（3 ヵ月間隔）の有害事象の概要（100 人年あたりの発現状況）

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	0 - < 3 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 640)	30 mg QD (No Cross-Over from Placebo) (N = 641)	Any 15 mg QD (N = 907)	Any 30 mg QD (N = 920)
Exposure-Adjusted Event Rate	(PYs = 155.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 155.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 212.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 215.6) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	743 (477.5) [477.1]	952 (611.8) [611.8]	933 (438.9) [438.6]	1167 (541.3) [541.1]
Any serious AE	23 (14.8) [14.8]	27 (17.4) [17.3]	27 (12.7) [12.8]	31 (14.4) [14.4]
Any AE leading to discontinuation of study drug	24 (15.4) [15.4]	42 (27.0) [26.9]	26 (12.2) [12.2]	44 (20.4) [20.3]
Any severe AE	31 (19.9) [20.0]	30 (19.3) [19.3]	37 (17.4) [17.5]	37 (17.2) [17.2]
Any AE with reasonable possibility of being related to study drug$	303 (194.7) [194.2]	422 (271.2) [271.5]	376 (176.9) [176.2]	503 (233.3) [233.7]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/155.6	0/155.6	0/212.6	0/215.6

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 3 - < 6 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 605)	30 mg QD (No Cross-Over from Placebo) (N = 603)	Any 15 mg QD (N = 796)	Any 30 mg QD (N = 800)
Exposure-Adjusted Event Rate	(PYs = 147.4) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 146.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 188.0) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 189.5) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	591 (400.9) [400.4]	679 (463.2) [463.2]	685 (364.4) [363.9]	776 (409.5) [409.4]
Any serious AE	20 (13.6) [13.6]	26 (17.7) [17.7]	25 (13.3) [13.4]	33 (17.4) [17.3]
Any AE leading to discontinuation of study drug	21 (14.2) [14.5]	18 (12.3) [12.3]	25 (13.3) [13.5]	21 (11.1) [11.0]
Any severe AE	19 (12.9) [12.9]	37 (25.2) [25.2]	24 (12.8) [12.8]	43 (22.7) [22.6]
Any AE with reasonable possibility of being related to study drug$	215 (145.9) [145.5]	287 (195.8) [196.5]	240 (127.7) [127.4]	322 (169.9) [170.5]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/147.4	0/146.6	0/188.0	0/189.5

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 6 - < 9 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 564)	30 mg QD (No Cross-Over from Placebo) (N = 553)	Any 15 mg QD (N = 701)	Any 30 mg QD (N = 701)
Exposure-Adjusted Event Rate	(PYs = 118.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 116.5) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 147.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 147.0) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	406 (342.0) [341.8]	439 (376.8) [377.1]	473 (320.2) [320.1]	510 (346.9) [347.2]
Any serious AE	15 (12.6) [12.6]	14 (12.0) [12.0]	16 (10.8) [10.8]	17 (11.6) [11.6]
Any AE leading to discontinuation of study drug	9 (7.6) [7.6]	5 (4.3) [4.3]	13 (8.8) [8.8]	5 (3.4) [3.4]
Any severe AE	20 (16.8) [16.8]	13 (11.2) [11.2]	21 (14.2) [14.2]	18 (12.2) [12.3]
Any AE with reasonable possibility of being related to study drug$	135 (113.7) [113.5]	186 (159.7) [159.9]	154 (104.3) [104.0]	207 (140.8) [141.2]
Any AE leading to death	1 (0.8) [0.8]	0	1 (0.7) [0.7]	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/118.8	1/116.6(0.9) [0.9]	0/147.8	1/147.1(0.7) [0.7]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 9 - < 12 Month Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 402)	30 mg QD (No Cross-Over from Placebo) (N = 397)	Any 15 mg QD (N = 491)	Any 30 mg QD (N = 491)
Exposure-Adjusted Event Rate	(PYs = 86.9) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 86.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 104.5) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 104.6) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	149 (171.5) [171.4]	234 (271.8) [271.9]	178 (170.3) [170.7]	282 (269.6) [269.2]
Any serious AE	6 (6.9) [6.9]	9 (10.5) [10.5]	8 (7.7) [7.7]	11 (10.5) [10.5]
Any AE leading to discontinuation of study drug	2 (2.3) [2.3]	3 (3.5) [3.5]	2 (1.9) [1.9]	4 (3.8) [3.8]
Any severe AE	6 (6.9) [6.9]	16 (18.6) [18.6]	7 (6.7) [6.7]	20 (19.1) [19.0]
Any AE with reasonable possibility of being related to study drug$	36 (41.4) [41.4]	75 (87.1) [87.1]	44 (42.1) [42.0]	88 (84.1) [84.0]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	1/87.0(1.1) [1.1]	0/86.1	1/104.6(1.0) [0.9]	0/104.6

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 12 - < 15 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 304)	30 mg QD (No Cross-Over from Placebo) (N = 300)	Any 15 mg QD (N = 360)	Any 30 mg QD (N = 364)
Exposure-Adjusted Event Rate	(PYs = 61.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 62.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 73.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 75.1) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	108 (175.0) [175.5]	176 (283.0) [281.5]	127 (173.5) [173.3]	207 (275.6) [274.8]
Any serious AE	2 (3.2) [3.1]	11 (17.7) [17.9]	3 (4.1) [4.0]	13 (17.3) [17.4]
Any AE leading to discontinuation of study drug	0	1 (1.6) [1.6]	0	1 (1.3) [1.3]
Any severe AE	1 (1.6) [1.6]	9 (14.5) [14.7]	1 (1.4) [1.3]	12 (16.0) [16.2]
Any AE with reasonable possibility of being related to study drug$	38 (61.6) [62.2]	64 (102.9) [102.0]	48 (65.6) [65.7]	72 (95.9) [95.4]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/61.7	0/62.2	0/73.2	0/75.1

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 15 - < 18 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 195)	30 mg QD (No Cross-Over from Placebo) (N = 198)	Any 15 mg QD (N = 229)	Any 30 mg QD (N = 239)
Exposure-Adjusted Event Rate	(PYs = 39.7) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 40.8) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 45.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 47.8) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	70 (176.3) [175.1]	93 (227.9) [227.7]	79 (173.2) [171.8]	111 (232.2) [232.8]
Any serious AE	9 (22.7) [22.2]	8 (19.6) [19.3]	9 (19.7) [19.3]	14 (29.3) [29.6]
Any AE leading to discontinuation of study drug	1 (2.5) [2.6]	0	1 (2.2) [2.3]	2 (4.2) [4.3]
Any severe AE	8 (20.2) [19.6]	9 (22.1) [22.2]	8 (17.5) [17.1]	16 (33.5) [34.2]
Any AE with reasonable possibility of being related to study drug$	21 (52.9) [53.1]	30 (73.5) [72.8]	23 (50.4) [50.5]	40 (83.7) [83.7]
Any AE leading to death	0	0	0	1 (2.1) [2.2]
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/39.7	0/40.8	0/45.6	1/47.8(2.1) [2.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 18 - < 21 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 128)	30 mg QD (No Cross-Over from Placebo) (N = 130)	Any 15 mg QD (N = 142)	Any 30 mg QD (N = 146)
Exposure-Adjusted Event Rate	(PYs = 25.1) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 23.8) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 27.8) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 26.3) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	16 (63.7) [63.6]	42 (176.5) [179.7]	20 (71.9) [72.2]	44 (167.3) [169.8]
Any serious AE	0	2 (8.4) [8.0]	0	2 (7.6) [7.2]
Any AE leading to discontinuation of study drug	0	0	0	0
Any severe AE	1 (4.0) [4.2]	3 (12.6) [12.0]	1 (3.6) [3.8]	3 (11.4) [10.9]
Any AE with reasonable possibility of being related to study drug$	6 (23.9) [24.3]	17 (71.4) [72.7]	7 (25.2) [25.7]	18 (68.4) [69.4]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/25.1	0/23.8	0/27.8	0/26.3

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 21 - < 24 Month			
	Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 74)	30 mg QD (No Cross-Over from Placebo) (N = 69)	Any 15 mg QD (N = 81)	Any 30 mg QD (N = 76)
Exposure-Adjusted Event Rate	(PYs = 12.2) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 12.0) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 13.0) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 12.8) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	16 (131.1) [124.9]	18 (150.0) [148.3]	16 (123.1) [118.6]	18 (140.6) [140.0]
Any serious AE	0	1 (8.3) [7.9]	0	1 (7.8) [7.5]
Any AE leading to discontinuation of study drug	0	1 (8.3) [7.9]	0	1 (7.8) [7.5]
Any severe AE	1 (8.2) [7.7]	1 (8.3) [7.9]	1 (7.7) [7.4]	1 (7.8) [7.5]
Any AE with reasonable possibility of being related to study drug$	3 (24.6) [23.2]	4 (33.3) [32.4]	3 (23.1) [22.1]	4 (31.3) [30.7]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/12.2	0/12.0	0/13.0	0/12.8

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

TABLE 2.4__3.1_J

Overview of Treatment-Emergent Adverse Events in Exposure-Adjusted Rate per 100 Patient Years
by Onset of Adverse Events in 3-month Interval
(Any Upadacitinib Analysis Set)

	>= 24 Month Upadacitinib			
	15 mg QD (No Cross-Over from Placebo) (N = 29)	30 mg QD (No Cross-Over from Placebo) (N = 30)	Any 15 mg QD (N = 30)	Any 30 mg QD (N = 30)
Exposure-Adjusted Event Rate	(PYs = 4.4) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 3.6) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 4.5) Events (E/100 PYs) [SSA E/100 PYs]	(PYs = 3.6) Events (E/100 PYs) [SSA E/100 PYs]
Any adverse event (AE)	12 (272.7) [280.3]	5 (138.9) [148.0]	12 (266.7) [278.2]	5 (138.9) [147.6]
Any serious AE	1 (22.7) [24.2]	0	1 (22.2) [24.0]	0
Any AE leading to discontinuation of study drug	2 (45.5) [48.4]	0	2 (44.4) [48.0]	0
Any severe AE	1 (22.7) [24.2]	0	1 (22.2) [24.0]	0
Any AE with reasonable possibility of being related to study drug$	6 (136.4) [142.7]	2 (55.6) [59.2]	6 (133.3) [141.5]	2 (55.6) [59.0]
Any AE leading to death	0	0	0	0
Exposure-Adjusted Incident Rate	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]	n/PYs (n/100 PYs) [SSA n/100 PYs]
Deaths#	0/4.4	0/3.6	0/4.5	0/3.6

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
E/100 PYs = Events per 100 patient-years. n/100 PYs = Number of subjects with at least one event per 100 patient-years.
SSA = Study size adjusted.
Patients could be included in more than one treatment group.
Events with unknown toxicity grade or grade 3 and above based on CTCAE v5.0 will be counted as severe. Events with unknown relationship to study drug is being counted as having a reasonable possibility of being related to study drug.
$ As assessed by investigator.
# Includes both treatment-emergent and non-treatment-emergent deaths.

Program Source Code: [redacted]

表 2.7.4.7-17.　　プラセボ対照併合解析集団（投与 24 週時）の重篤な有害事象

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
Any adverse event	17 (2.7) [2.7]	26 (4.1) [4.1]	44 (6.9) [6.9]
血液およびリンパ系障害	0	1 (0.2) [0.2]	2 (0.3) [0.3]
失血性貧血	0	1 (0.2) [0.2]	0
鉄欠乏性貧血	0	0	1 (0.2) [0.2]
リンパ組織過形成	0	0	1 (0.2) [0.2]
心臓障害	2 (0.3) [0.3]	2 (0.3) [0.3]	5 (0.8) [0.8]
急性心筋梗塞	0	1 (0.2) [0.2]	0
不安定狭心症	1 (0.2) [0.2]	0	1 (0.2) [0.2]
心房細動	0	0	1 (0.2) [0.2]
徐脈	0	0	1 (0.2) [0.2]
心停止	1 (0.2) [0.2]	0	0
心肺停止	0	1 (0.2) [0.2]	0
冠動脈疾患	0	0	1 (0.2) [0.2]
冠動脈狭窄	0	0	1 (0.2) [0.2]
心室細動	0	1 (0.2) [0.2]	0
眼障害	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
眼障害 (Cont.)			
白内障	0	0	1 (0.2) [0.2]
胃腸障害	1 (0.2) [0.2]	4 (0.6) [0.6]	2 (0.3) [0.3]
腹痛	0	0	1 (0.2) [0.2]
下痢	0	0	1 (0.2) [0.2]
消化不良	0	1 (0.2) [0.2]	0
びらん性胃炎	0	2 (0.3) [0.3]	0
胃十二指腸出血	0	1 (0.2) [0.2]	0
胃食道逆流性疾患	0	1 (0.2) [0.2]	0
裂孔ヘルニア	0	1 (0.2) [0.2]	0
腸管ポリープ	1 (0.2) [0.2]	0	0
小腸潰瘍	0	0	1 (0.2) [0.2]
一般・全身障害および投与部位の状態	1 (0.2) [0.2]	1 (0.2) [0.2]	2 (0.3) [0.3]
胸痛	1 (0.2) [0.2]	0	0
発熱	0	1 (0.2) [0.2]	1 (0.2) [0.2]
全身性炎症反応症候群	0	0	1 (0.2) [0.2]
肝胆道系障害	1 (0.2) [0.2]	0	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
肝胆道系障害 (Cont.)			
胆石症	1 (0.2) [0.2]	0	0
感染症および寄生虫症	5 (0.8) [0.8]	6 (0.9) [0.9]	17 (2.7) [2.7]
肛門膿瘍	0	0	1 (0.2) [0.2]
虫垂炎	1 (0.2) [0.2]	0	1 (0.2) [0.2]
異型肺炎	0	0	2 (0.3) [0.3]
菌血症	0	0	2 (0.3) [0.3]
乳房蜂巣炎	1 (0.2) [0.2]	0	0
気管支炎	0	0	1 (0.2) [0.2]
ブドウ球菌感染性滑液包炎	1 (0.2) [0.2]	0	0
丹毒	0	1 (0.2) [0.2]	0
硬膜外膿瘍	0	0	1 (0.2) [0.2]
喉頭炎	0	1 (0.2) [0.2]	0
肺感染	0	0	1 (0.2) [0.2]
ニューモシスチス・イロベチイ肺炎	0	0	1 (0.2) [0.2]
肺炎	2 (0.3) [0.3]	2 (0.3) [0.3]	6 (0.9) [0.9]
敗血症	0	2 (0.3) [0.3]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
感染症および寄生虫症 (Cont.)			
尿路感染	0	0	1 (0.2) [0.2]
尿路性敗血症	0	0	1 (0.2) [0.2]
傷害、中毒および処置合併症	3 (0.5) [0.5]	1 (0.2) [0.2]	4 (0.6) [0.6]
足関節部骨折	0	0	1 (0.2) [0.2]
粉砕骨折	0	0	1 (0.2) [0.2]
転倒	0	1 (0.2) [0.2]	0
大腿骨頚部骨折	0	0	1 (0.2) [0.2]
腓骨骨折	1 (0.2) [0.2]	0	0
手骨折	1 (0.2) [0.2]	0	0
上腕骨骨折	0	0	1 (0.2) [0.2]
肋骨骨折	1 (0.2) [0.2]	0	0
交通事故	1 (0.2) [0.2]	0	0
腱断裂	0	0	1 (0.2) [0.2]
外傷性血胸	1 (0.2) [0.2]	0	0
血管偽動脈瘤	1 (0.2) [0.2]	0	0
臨床検査	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
臨床検査 (Cont.)			
筋酵素上昇	0	1 (0.2) [0.2]	0
筋骨格系および結合組織障害	1 (0.2) [0.2]	6 (0.9) [1.0]	2 (0.3) [0.3]
関節痛	0	0	1 (0.2) [0.2]
側腹部痛	0	1 (0.2) [0.2]	0
変形性関節症	0	1 (0.2) [0.2]	1 (0.2) [0.2]
乾癬性関節症	0	2 (0.3) [0.3]	0
急速進行性変形性関節症	0	1 (0.2) [0.2]	0
脊柱管狭窄症	1 (0.2) [0.2]	0	0
全身性エリテマトーデス	0	1 (0.2) [0.2]	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）	1 (0.2) [0.2]	3 (0.5) [0.5]	3 (0.5) [0.5]
肺腺癌	0	0	1 (0.2) [0.2]
神経内分泌癌	0	1 (0.2) [0.2]	0
卵巣癌	0	0	1 (0.2) [0.2]
前立腺癌	0	1 (0.2) [0.2]	0
直腸腺癌	0	0	1 (0.2) [0.2]
直腸癌	0	1 (0.2) [0.2]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)			
子宮平滑筋腫	1 (0.2) [0.2]	0	0
神経系障害	0	2 (0.3) [0.3]	2 (0.3) [0.3]
頚髄神経根障害	0	1 (0.2) [0.2]	0
脱髄	0	0	1 (0.2) [0.2]
浮動性めまい	0	1 (0.2) [0.2]	0
会話障害	0	1 (0.2) [0.2]	0
一過性全健忘	0	0	1 (0.2) [0.2]
妊娠、産褥および周産期の状態	0	0	1 (0.2) [0.2]
異所性妊娠	0	0	1 (0.2) [0.2]
精神障害	0	1 (0.2) [0.2]	0
失見当識	0	1 (0.2) [0.2]	0
腎および尿路障害	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.2) [0.2]
急性腎障害	1 (0.2) [0.2]	0	1 (0.2) [0.2]
腎結石症	0	2 (0.3) [0.3]	0
生殖系および乳房障害	0	1 (0.2) [0.2]	2 (0.3) [0.3]
良性前立腺肥大症	0	0	1 (0.2) [0.2]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.1.3.2

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 635) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 640) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 641) n (%) [SSA%]
生殖系および乳房障害 (Cont.)			
線維嚢胞性乳腺疾患	0	0	1 (0.2) [0.2]
子宮脱	0	1 (0.2) [0.2]	0
呼吸器、胸郭および縦隔障害	1 (0.2) [0.2]	2 (0.3) [0.3]	4 (0.6) [0.6]
急性呼吸不全	0	1 (0.2) [0.2]	1 (0.2) [0.2]
慢性閉塞性肺疾患	0	0	1 (0.2) [0.2]
閉塞性気道障害	1 (0.2) [0.2]	0	0
肺塞栓症	0	1 (0.2) [0.2]	1 (0.2) [0.2]
肺線維症	0	0	1 (0.2) [0.2]
睡眠時無呼吸症候群	0	1 (0.2) [0.2]	0
皮膚および皮下組織障害	0	2 (0.3) [0.3]	0
接触皮膚炎	0	1 (0.2) [0.2]	0
嵌入爪	0	1 (0.2) [0.2]	0
血管障害	1 (0.2) [0.2]	0	0
深部静脈血栓症	1 (0.2) [0.2]	0	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-18.　　プラセボ対照併合解析集団（投与 24 週時）の日本人部分集団の重篤な有害事象

TABLE 2.4__1.1.3.2_J

Number and Percentage of Subjects with Treatment-Emergent Serious Adverse Events
by Primary MedDRA System Organ Class and Preferred Term
(PBO-Controlled Analysis Set, Japanese Population)

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 15) n (%) [SSA%]	Upadacitinib 15 mg QD (N = 17) n (%) [SSA%]	Upadacitinib 30 mg QD (N = 18) n (%) [SSA%]
Any adverse event	0	1 (5.9) [6.0]	3 (16.7) [16.7]
胃腸障害	0	0	1 (5.6) [5.6]
小腸潰瘍	0	0	1 (5.6) [5.6]
感染症および寄生虫症	0	0	2 (11.1) [11.1]
肺炎	0	0	1 (5.6) [5.6]
尿路感染	0	0	1 (5.6) [5.6]
筋骨格系および結合組織障害	0	1 (5.9) [6.0]	0
乾癬性関節症	0	1 (5.9) [6.0]	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	0	1 (5.6) [5.6]
卵巣癌	0	0	1 (5.6) [5.6]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
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.
SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-19. 全ウパダシチニブ併合解析集団（長期）の重篤な有害事象（100 人年あたりの発現件数）

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	76 (11.7) [11.6]	98 (15.1) [15.1]	89 (10.9) [10.9]	122 (14.8) [14.8]
血液およびリンパ系障害	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	5 (0.6) [0.6]
貧血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
失血性貧血	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
鉄欠乏性貧血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
リンパ組織過形成	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
汎血球減少症	0	0	0	1 (0.1) [0.1]
心臓障害	6 (0.9) [0.9]	8 (1.2) [1.2]	6 (0.7) [0.7]	9 (1.1) [1.1]
急性心筋梗塞	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
狭心症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
不安定狭心症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心房細動	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
徐脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
うっ血性心不全	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心肺停止	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
冠動脈疾患	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
心臓障害 (Cont.)				
冠動脈狭窄	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心筋梗塞	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
上室性頻脈	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
心室細動	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
耳および迷路障害	0	0	1 (0.1) [0.1]	0
頭位性回転性めまい	0	0	1 (0.1) [0.1]	0
内分泌障害	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
甲状腺腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼障害	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	2 (0.2) [0.2]
白内障	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
複視	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
眼瞼下垂	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃腸障害	10 (1.5) [1.5]	7 (1.1) [1.1]	11 (1.3) [1.3]	9 (1.1) [1.1]
腹痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
痔瘻	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
大腸炎	0	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
胃腸障害 (Cont.)				
下痢	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
十二指腸潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	1 (0.1) [0.1]
出血性十二指腸潰瘍	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
消化不良	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
穿孔性胃潰瘍	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
びらん性胃炎	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
胃十二指腸出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃腸出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
胃食道逆流性疾患	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
吐血	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
裂孔ヘルニア	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
鼠径ヘルニア	0	0	0	1 (0.1) [0.1]
小腸潰瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
上部消化管出血	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
一般・全身障害および投与部位の状態	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	5 (0.6) [0.6]
胸痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
一般・全身障害および投与部位の状態 (Cont.)				
発熱	1 (0.2) [0.2]	2 (0.3) [0.3]	1 (0.1) [0.1]	3 (0.4) [0.4]
全身性炎症反応症候群	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肝胆道系障害	0	0	1 (0.1) [0.1]	0
胆石症	0	0	1 (0.1) [0.1]	0
感染症および寄生虫症	15 (2.3) [2.3]	38 (5.9) [5.9]	19 (2.3) [2.3]	48 (5.8) [5.8]
膿瘍	0	0	1 (0.1) [0.1]	0
四肢膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肛門膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
虫垂炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
細菌性関節炎	0	0	1 (0.1) [0.1]	0
異型肺炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
菌血症	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
細気管支炎	0	0	1 (0.1) [0.1]	0
気管支炎	1 (0.2) [0.2]	3 (0.5) [0.5]	1 (0.1) [0.1]	3 (0.4) [0.4]
蜂巣炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
サイトメガロウイルス感染	0	0	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
憩室炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
丹毒	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
硬膜外膿瘍	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
胃腸炎	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
ウイルス性胃腸炎	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
H1N1インフルエンザ	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
帯状疱疹	1 (0.2) [0.2]	4 (0.6) [0.6]	1 (0.1) [0.1]	5 (0.6) [0.6]
喉頭炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
肺感染	0	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
ニューモシスチス・イロベチイ肺炎	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
肺炎	4 (0.6) [0.6]	6 (0.9) [0.9]	4 (0.5) [0.5]	8 (1.0) [1.0]
レンサ球菌性肺炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腎盂腎炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
卵管炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
敗血症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
ブドウ球菌性菌血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
感染症および寄生虫症 (Cont.)				
ブドウ球菌性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
上気道感染	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
尿路感染	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
尿路性敗血症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
ウイルス感染	0	0	0	1 (0.1) [0.1]
ウイルス性上気道感染	0	0	0	1 (0.1) [0.1]
傷害、中毒および処置合併症	8 (1.2) [1.2]	6 (0.9) [0.9]	10 (1.2) [1.2]	7 (0.9) [0.9]
足関節部骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
頚椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
粉砕骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
転倒	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
大腿骨頚部骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
足骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
上腕骨骨折	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
関節脱臼	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
腰椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
処置後胆汁漏出	0	0	1 (0.1) [0.1]	0
交通事故	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
腱断裂	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
胸椎骨折	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脛骨骨折	0	0	1 (0.1) [0.1]	0
外傷性血胸	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
上肢骨折	0	0	0	1 (0.1) [0.1]
臨床検査	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
筋酵素上昇	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
代謝および栄養障害	0	0	1 (0.1) [0.1]	0
糖尿病	0	0	1 (0.1) [0.1]	0
筋骨格系および結合組織障害	7 (1.1) [1.1]	7 (1.1) [1.1]	8 (1.0) [1.0]	8 (1.0) [1.0]
関節痛	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
頚部脊柱管狭窄症	0	0	1 (0.1) [0.1]	0
側腹部痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
椎間板変性症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
筋骨格系および結合組織障害 (Cont.)				
腰部脊柱管狭窄症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
変形性関節症	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	2 (0.2) [0.2]
骨壊死	0	2 (0.3) [0.3]	0	2 (0.2) [0.2]
乾癬性関節症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	1 (0.1) [0.1]
急速進行性変形性関節症	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脊椎後方すべり症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
全身性エリテマトーデス	1 (0.2) [0.2]	0	1 (0.1) [0.1]	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）	5 (0.8) [0.8]	6 (0.9) [0.9]	5 (0.6) [0.6]	6 (0.7) [0.7]
肛門性器疣贅	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺腺癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
遠隔転移を伴う肺癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
悪性黒色腫第3期	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
神経内分泌癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
中咽頭扁平上皮癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
卵巣癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
前立腺癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む） (Cont.)				
直腸腺癌	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
直腸癌	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
子宮平滑筋腫	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
神経系障害	5 (0.8) [0.8]	3 (0.5) [0.5]	5 (0.6) [0.6]	4 (0.5) [0.5]
頚髄神経根障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
脱髄	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
糖尿病性ニューロパチー	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
浮動性めまい	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
顔面麻痺	0	0	0	1 (0.1) [0.1]
虚血性脳卒中	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
ラクナ脳卒中	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
会話障害	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
一過性全健忘	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
妊娠、産褥および周産期の状態	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
異所性妊娠	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
精神障害	1 (0.2) [0.2]	0	2 (0.2) [0.2]	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
精神障害 (Cont.)				
うつ病	0	0	1 (0.1) [0.1]	0
失見当識	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
精神状態変化	0	0	0	1 (0.1) [0.1]
腎および尿路障害	4 (0.6) [0.6]	2 (0.3) [0.3]	4 (0.5) [0.5]	3 (0.4) [0.4]
急性腎障害	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
腎結石症	2 (0.3) [0.3]	1 (0.2) [0.2]	2 (0.2) [0.2]	2 (0.2) [0.2]
腎仙痛	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
生殖系および乳房障害	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
良性前立腺肥大症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
子宮頚部上皮異形成	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
線維嚢胞性乳腺疾患	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
子宮脱	2 (0.3) [0.3]	0	2 (0.2) [0.2]	0
呼吸器、胸郭および縦隔障害	6 (0.9) [0.9]	6 (0.9) [0.9]	6 (0.7) [0.7]	9 (1.1) [1.1]
急性呼吸不全	1 (0.2) [0.2]	1 (0.2) [0.2]	1 (0.1) [0.1]	1 (0.1) [0.1]
慢性閉塞性肺疾患	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
間質性肺疾患	0	0	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 640) (PYs = 651.8) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 641) (PYs = 647.1) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 907) (PYs = 816.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 920) (PYs = 822.3) Events (E/100 PYs) [SSA E/100 PYs]
呼吸器、胸郭および縦隔障害 (Cont.)				
気胸	0	0	0	1 (0.1) [0.1]
自然気胸	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
肺塞栓症	3 (0.5) [0.5]	2 (0.3) [0.3]	3 (0.4) [0.4]	2 (0.2) [0.2]
肺線維症	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
呼吸窮迫	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
睡眠時無呼吸症候群	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
皮膚および皮下組織障害	2 (0.3) [0.3]	0	3 (0.4) [0.4]	0
血管浮腫	0	0	1 (0.1) [0.1]	0
接触皮膚炎	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
嵌入爪	1 (0.2) [0.2]	0	1 (0.1) [0.1]	0
血管障害	0	1 (0.2) [0.2]	0	2 (0.2) [0.2]
表在性血栓性静脈炎	0	1 (0.2) [0.2]	0	1 (0.1) [0.1]
静脈瘤	0	0	0	1 (0.1) [0.1]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-20.　全ウパダシチニブ併合解析集団（長期）の日本人部分集団の重篤な有害事象（100 人年あたりの発現件数）

TABLE 2.4__1.2.3.3_J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set, Japanese Population)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 17) (PYs = 18.2) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 18) (PYs = 20.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 23) (PYs = 23.0) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 26) (PYs = 28.1) Events (E/100 PYs) [SSA E/100 PYs]
Any Adverse Event	3 (16.5) [15.1]	8 (38.3) [38.9]	4 (17.4) [15.8]	16 (56.9) [59.8]
血液およびリンパ系障害	0	0	0	1 (3.6) [3.9]
汎血球減少症	0	0	0	1 (3.6) [3.9]
胃腸障害	0	1 (4.8) [5.2]	0	2 (7.1) [7.7]
十二指腸潰瘍	0	0	0	1 (3.6) [3.9]
小腸潰瘍	0	1 (4.8) [5.2]	0	1 (3.6) [3.9]
感染症および寄生虫症	1 (5.5) [5.0]	5 (23.9) [23.2]	1 (4.3) [3.9]	8 (28.5) [28.8]
気管支炎	0	1 (4.8) [3.8]	0	1 (3.6) [2.8]
サイトメガロウイルス感染	0	0	0	1 (3.6) [3.9]
ウイルス性胃腸炎	1 (5.5) [5.0]	0	1 (4.3) [3.9]	1 (3.6) [3.9]
帯状疱疹	0	2 (9.6) [9.0]	0	2 (7.1) [6.7]
ニューモシスチス・イロベチイ肺炎	0	0	0	1 (3.6) [3.9]
肺炎	0	1 (4.8) [5.2]	0	1 (3.6) [3.9]
尿路感染	0	1 (4.8) [5.2]	0	1 (3.6) [3.9]
傷害、中毒および処置合併症	1 (5.5) [5.0]	0	1 (4.3) [3.9]	0

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

TABLE 2.4__1.2.3.3_J

Treatment-Emergent Serious Adverse Events in Exposure-Adjusted Event Rate per 100 Patient Years
by Primary MedDRA System Organ Class and Preferred Term
(Any Upadacitinib Analysis Set, Japanese Population)

System Organ Class MedDRA 22.0 Preferred Term	Upadacitinib 15 mg QD (No Cross-Over from Placebo) (N = 17) (PYs = 18.2) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib 30 mg QD (No Cross-Over from Placebo) (N = 18) (PYs = 20.9) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 15 mg QD (N = 23) (PYs = 23.0) Events (E/100 PYs) [SSA E/100 PYs]	Upadacitinib Any 30 mg QD (N = 26) (PYs = 28.1) Events (E/100 PYs) [SSA E/100 PYs]
傷害、中毒および処置合併症 (Cont.)				
腱断裂	1 (5.5) [5.0]	0	1 (4.3) [3.9]	0
代謝および栄養障害	0	0	1 (4.3) [3.9]	0
糖尿病	0	0	1 (4.3) [3.9]	0
筋骨格系および結合組織障害	1 (5.5) [5.0]	0	1 (4.3) [3.9]	0
乾癬性関節症	1 (5.5) [5.0]	0	1 (4.3) [3.9]	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	2 (9.6) [10.4]	0	2 (7.1) [7.7]
肛門性器疣贅	0	1 (4.8) [5.2]	0	1 (3.6) [3.9]
卵巣癌	0	1 (4.8) [5.2]	0	1 (3.6) [3.9]
神経系障害	0	0	0	1 (3.6) [3.9]
顔面麻痺	0	0	0	1 (3.6) [3.9]
呼吸器、胸郭および縦隔障害	0	0	0	2 (7.1) [7.7]
間質性肺疾患	0	0	0	1 (3.6) [3.9]
気胸	0	0	0	1 (3.6) [3.9]

Note: Treatment-emergent adverse event (TEAE) is defined as an adverse event with an onset date that is on or after the first dose of oral study drug, and no more than 30 days after the last dose of upadacitinib and placebo.
Patients could be included in more than one treatment group.
E/100 PYs = Events per 100 patient-years; SSA = Study size adjusted.

Program Source Code: [redacted]

表 2.7.4.7-21.　　投与 24 週時までの重篤な有害事象（安全性解析対象集団）：M15-572 試験

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
Any adverse event	13 (3.1)	16 (3.7)	14 (3.3)	26 (6.1)
血液およびリンパ系障害	0	0	0	2 (0.5)
鉄欠乏性貧血	0	0	0	1 (0.2)
リンパ組織過形成	0	0	0	1 (0.2)
心臓障害	1 (0.2)	2 (0.5)	0	1 (0.2)
急性心筋梗塞	0	1 (0.2)	0	0
心房細動	0	1 (0.2)	0	0
心停止	1 (0.2)	0	0	0
冠動脈疾患	0	0	0	1 (0.2)
眼障害	0	0	0	1 (0.2)
白内障	0	0	0	1 (0.2)
胃腸障害	1 (0.2)	0	3 (0.7)	0
消化不良	0	0	1 (0.2)	0
びらん性胃炎	0	0	1 (0.2)	0
胃十二指腸出血	0	0	1 (0.2)	0
胃食道逆流性疾患	0	0	1 (0.2)	0
裂孔ヘルニア	0	0	1 (0.2)	0
腸管ポリープ	1 (0.2)	0	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
一般・全身障害および投与部位の状態	1 (0.2)	0	1 (0.2)	1 (0.2)
胸痛	1 (0.2)	0	0	0
発熱	0	0	1 (0.2)	1 (0.2)
肝胆道系障害	1 (0.2)	1 (0.2)	0	0
胆石症	1 (0.2)	0	0	0
門脈血栓症	0	1 (0.2)	0	0
感染症および寄生虫症	4 (0.9)	3 (0.7)	5 (1.2)	11 (2.6)
肛門膿瘍	0	0	0	1 (0.2)
虫垂炎	1 (0.2)	0	0	1 (0.2)
異型肺炎	0	0	0	2 (0.5)
菌血症	0	0	0	1 (0.2)
骨膿瘍	0	1 (0.2)	0	0
乳房蜂巣炎	1 (0.2)	0	0	0
丹毒	0	1 (0.2)	1 (0.2)	0
喉頭炎	0	0	1 (0.2)	0
肺感染	0	0	0	1 (0.2)
ニューモシスチス・イロベチイ肺炎	0	0	0	1 (0.2)
肺炎	2 (0.5)	1 (0.2)	1 (0.2)	3 (0.7)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
感染症および寄生虫症 (Cont.)				
敗血症	0	0	2 (0.5)	0
ブドウ球菌感染	0	1 (0.2)	0	0
尿路性敗血症	0	0	0	1 (0.2)
傷害、中毒および処置合併症	1 (0.2)	0	0	3 (0.7)
足関節部骨折	0	0	0	1 (0.2)
粉砕骨折	0	0	0	1 (0.2)
手骨折	1 (0.2)	0	0	0
上腕骨骨折	0	0	0	1 (0.2)
腱断裂	0	0	0	1 (0.2)
臨床検査	0	0	1 (0.2)	0
筋酵素上昇	0	0	1 (0.2)	0
筋骨格系および結合組織障害	1 (0.2)	0	0	2 (0.5)
関節痛	0	0	0	1 (0.2)
変形性関節症	0	0	0	1 (0.2)
脊柱管狭窄症	1 (0.2)	0	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	3 (0.7)	1 (0.2)	1 (0.2)
遠隔転移を伴う結腸癌	0	1 (0.2)	0	0
肺腺癌	0	0	0	1 (0.2)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) 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） (Cont.)				
神経内分泌癌	0	0	1 (0.2)	0
卵巣癌	0	1 (0.2)	0	0
子宮癌	0	1 (0.2)	0	0
神経系障害	0	4 (0.9)	1 (0.2)	1 (0.2)
筋萎縮性側索硬化症	0	1 (0.2)	0	0
脳血管発作	0	1 (0.2)	0	0
頚髄神経根障害	0	0	1 (0.2)	0
脱髄	0	0	0	1 (0.2)
肝性脳症	0	1 (0.2)	0	0
一過性脳虚血発作	0	1 (0.2)	0	0
精神障害	0	1 (0.2)	0	0
不安	0	1 (0.2)	0	0
腎および尿路障害	1 (0.2)	1 (0.2)	0	0
急性腎障害	1 (0.2)	0	0	0
尿管結石症	0	1 (0.2)	0	0
生殖系および乳房障害	0	0	1 (0.2)	1 (0.2)
線維嚢胞性乳腺疾患	0	0	0	1 (0.2)
子宮脱	0	0	1 (0.2)	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 423) n (%)	ADA 40 mg EOW (N = 429) n (%)	UPA 15 mg QD (N = 429) n (%)	UPA 30 mg QD (N = 423) n (%)
呼吸器、胸郭および縦隔障害	1 (0.2)	1 (0.2)	1 (0.2)	3 (0.7)
慢性閉塞性肺疾患	0	0	0	1 (0.2)
閉塞性気道障害	1 (0.2)	0	0	0
胸水	0	1 (0.2)	0	0
肺塞栓症	0	0	0	1 (0.2)
肺線維症	0	0	0	1 (0.2)
睡眠時無呼吸症候群	0	0	1 (0.2)	0
皮膚および皮下組織障害	0	1 (0.2)	2 (0.5)	0
皮膚炎	0	1 (0.2)	0	0
接触皮膚炎	0	0	1 (0.2)	0
嵌入爪	0	0	1 (0.2)	0
血管障害	1 (0.2)	1 (0.2)	0	0
深部静脈血栓症	1 (0.2)	1 (0.2)	0	0

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
The sum of the total number of subjects reporting each of the preferred terms should be greater than or equal to the system organ class total. A subject who reports two or more different preferred terms which are in the same system organ class is counted only once in the system organ class total.

Program Source Code: [redacted]

表 2.7.4.7-22. 投与 24 週時データカットオフまでの重篤な有害事象（100 人年あたりの発現件数，安全性解析対象集団）：M15-572 試験

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
Any adverse event	45 (8.6)	68 (12.9)	43 (10.9)
血液およびリンパ系障害	0	3 (0.6)	1 (0.3)
貧血	0	1 (0.2)	0
鉄欠乏性貧血	0	1 (0.2)	0
リンパ組織過形成	0	1 (0.2)	0
正色素性正球性貧血	0	0	1 (0.3)
心臓障害	1 (0.2)	3 (0.6)	4 (1.0)
急性心筋梗塞	0	0	1 (0.3)
心房細動	0	0	1 (0.3)
うっ血性心不全	0	1 (0.2)	0
冠動脈疾患	0	1 (0.2)	1 (0.3)
心筋梗塞	1 (0.2)	1 (0.2)	0
心膜炎	0	0	1 (0.3)
耳および迷路障害	1 (0.2)	0	0
頭位性回転性めまい	1 (0.2)	0	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
眼障害	1 (0.2)	2 (0.4)	0
白内障	0	1 (0.2)	0
複視	0	1 (0.2)	0
眼瞼下垂	1 (0.2)	0	0
胃腸障害	9 (1.7)	2 (0.4)	3 (0.8)
痔瘻	0	1 (0.2)	0
大腸炎	1 (0.2)	0	0
十二指腸潰瘍	0	0	1 (0.3)
出血性十二指腸潰瘍	0	1 (0.2)	0
消化不良	1 (0.2)	0	0
小腸炎	0	0	1 (0.3)
穿孔性胃潰瘍	1 (0.2)	0	0
びらん性胃炎	1 (0.2)	0	0
胃十二指腸出血	1 (0.2)	0	0
胃腸出血	1 (0.2)	0	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
胃腸障害 (Cont.)			
胃食道逆流性疾患	1 (0.2)	0	0
裂孔ヘルニア	1 (0.2)	0	0
上部消化管出血	1 (0.2)	0	0
嘔吐	0	0	1 (0.3)
一般・全身障害および投与部位の状態	1 (0.2)	3 (0.6)	0
胸痛	0	1 (0.2)	0
発熱	1 (0.2)	2 (0.4)	0
肝胆道系障害	0	0	1 (0.3)
門脈血栓症	0	0	1 (0.3)
感染症および寄生虫症	11 (2.1)	29 (5.5)	6 (1.5)
四肢膿瘍	0	1 (0.2)	0
肛門膿瘍	0	1 (0.2)	0
虫垂炎	1 (0.2)	2 (0.4)	0
細菌性関節炎	1 (0.2)	0	0
異型肺炎	0	2 (0.4)	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
菌血症	0	1 (0.2)	0
骨髄炎	0	0	1 (0.3)
気管支炎	1 (0.2)	2 (0.4)	0
蜂巣炎	0	0	2 (0.5)
憩室炎	1 (0.2)	0	0
丹毒	1 (0.2)	0	1 (0.3)
胃腸炎	0	1 (0.2)	0
H1N1インフルエンザ	1 (0.2)	0	0
帯状疱疹	1 (0.2)	4 (0.8)	0
喉頭炎	1 (0.2)	0	0
肺感染	0	1 (0.2)	0
ニューモシスチス・イロベチイ肺炎	0	1 (0.2)	0
肺炎	1 (0.2)	5 (1.0)	1 (0.3)
レンサ球菌性肺炎	0	1 (0.2)	0
腎盂腎炎	0	1 (0.2)	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
感染症および寄生虫症 (Cont.)			
卵管炎	0	1 (0.2)	0
敗血症	2 (0.4)	0	0
ブドウ球菌性菌血症	0	1 (0.2)	0
ブドウ球菌感染	0	0	1 (0.3)
ブドウ球菌性敗血症	0	1 (0.2)	0
尿路感染	0	1 (0.2)	0
尿路性敗血症	0	1 (0.2)	0
ウイルス感染	0	1 (0.2)	0
傷害、中毒および処置合併症	2 (0.4)	6 (1.1)	3 (0.8)
足関節部骨折	0	1 (0.2)	0
粉砕骨折	0	1 (0.2)	0
足骨折	1 (0.2)	0	0
上腕骨骨折	0	1 (0.2)	0
関節脱臼	0	1 (0.2)	0
橈骨骨折	0	0	1 (0.3)

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
傷害、中毒および処置合併症 (Cont.)			
腱断裂	0	1 (0.2)	0
脛骨骨折	1 (0.2)	0	0
上肢骨折	0	1 (0.2)	1 (0.3)
創離開	0	0	1 (0.3)
臨床検査	1 (0.2)	0	0
筋酵素上昇	1 (0.2)	0	0
筋骨格系および結合組織障害	2 (0.4)	7 (1.3)	3 (0.8)
関節痛	0	1 (0.2)	0
頚部脊柱管狭窄症	1 (0.2)	0	0
椎間板変性症	0	1 (0.2)	0
椎間板突出	0	0	1 (0.3)
腰部脊柱管狭窄症	1 (0.2)	0	0
変形性関節症	0	1 (0.2)	1 (0.3)
骨壊死	0	2 (0.4)	0
乾癬性関節症	0	1 (0.2)	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
筋骨格系および結合組織障害 (Cont.)			
脊椎後方すべり症	0	1 (0.2)	0
脊椎すべり症	0	0	1 (0.3)
良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む)	2 (0.4)	2 (0.4)	5 (1.3)
基底細胞癌	0	0	1 (0.3)
遠隔転移を伴う結腸癌	0	0	1 (0.3)
肺腺癌	0	1 (0.2)	0
遠隔転移を伴う肺癌	1 (0.2)	0	0
神経内分泌癌	1 (0.2)	0	0
卵巣癌	0	0	1 (0.3)
遠隔転移を伴う膵癌	0	0	1 (0.3)
子宮癌	0	0	1 (0.3)
子宮平滑筋腫	0	1 (0.2)	0
神経系障害	3 (0.6)	2 (0.4)	6 (1.5)
筋萎縮性側索硬化症	0	0	1 (0.3)
脳血管発作	0	0	2 (0.5)

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
神経系障害 (Cont.)			
頚髄神経根障害	1 (0.2)	0	0
脱髄	0	1 (0.2)	0
糖尿病性ニューロパチー	0	1 (0.2)	0
頭痛	0	0	1 (0.3)
肝性脳症	0	0	1 (0.3)
虚血性脳卒中	1 (0.2)	0	0
ラクナ脳卒中	1 (0.2)	0	0
一過性脳虚血発作	0	0	1 (0.3)
精神障害	1 (0.2)	0	1 (0.3)
不安	0	0	1 (0.3)
うつ病	1 (0.2)	0	0
腎および尿路障害	1 (0.2)	1 (0.2)	2 (0.5)
腎結石症	0	1 (0.2)	1 (0.3)
腎仙痛	1 (0.2)	0	0
尿管結石症	0	0	1 (0.3)

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
生殖系および乳房障害	2 (0.4)	1 (0.2)	2 (0.5)
良性前立腺肥大症	0	0	1 (0.3)
線維嚢胞性乳腺疾患	0	1 (0.2)	0
卵巣嚢胞	0	0	1 (0.3)
子宮脱	2 (0.4)	0	0
呼吸器、胸郭および縦隔障害	4 (0.8)	5 (1.0)	3 (0.8)
慢性閉塞性肺疾患	0	1 (0.2)	0
胸水	0	0	1 (0.3)
自然気胸	0	1 (0.2)	0
肺塞栓症	2 (0.4)	2 (0.4)	0
肺線維症	0	1 (0.2)	0
呼吸窮迫	1 (0.2)	0	0
睡眠時無呼吸症候群	1 (0.2)	0	1 (0.3)
扁桃肥大	0	0	1 (0.3)

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

Program Source Code: [redacted]

TABLE 14.3__2.1.2

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

System Organ Class MedDRA 22.0 Preferred Term	UPA 15 mg QD (N = 617) (PYs = 524.1) Events (E/100 PYs)	UPA 30 mg QD (N = 612) (PYs = 526.0) Events (E/100 PYs)	ADA 40 mg EOW (N = 429) (PYs = 394.5) Events (E/100 PYs)
皮膚および皮下組織障害	3 (0.6)	0	2 (0.5)
血管浮腫	1 (0.2)	0	0
皮膚炎	0	0	1 (0.3)
接触皮膚炎	1 (0.2)	0	0
嵌入爪	1 (0.2)	0	0
膿疱性乾癬	0	0	1 (0.3)
血管障害	0	2 (0.4)	1 (0.3)
深部静脈血栓症	0	0	1 (0.3)
表在性血栓性静脈炎	0	1 (0.2)	0
静脈瘤	0	1 (0.2)	0

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

Program Source Code: [redacted]

表 2.7.4.7-23. 投与 24 週時までの重篤な有害事象の一覧表（安全性解析対象集団）：M15-572 試験

表中記載の説明

転帰：回復 ＝E 欄に日数が記載されており，S 欄に Death of subject の記載がない。継続中 ＝O 欄に YES と記載されているか，E 欄及び O 欄の記載がない。死亡 ＝S 欄に Death of subject と記載されている。

国内の実施医療機関の番号は，[redacted]，[redacted]，[redacted]，[redacted]，[redacted] 及び [redacted] である。

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])									
TRT: ADA 40 mg EOW									
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:96.93 KG								
		PRE	TO -1						
		BLIND	1 TO 172	94	94	R: HEPATIC ENCEPHALOPATHY S: Nervous system disorders P: 肝性脳症 L: Hepatic encephalopathy	I: YES	T: Severe R: Reasonable possibility A: MULTIPLE:(DRUG INTERRUPTED, DRUG WITHDRAWN) O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,MONITORING AMMONIA LEVELS)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: METHOTREXATE A: NO REASONABLE POSSIBILITY
		POST	173 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:82.50 KG							
	PRE	TO -1						
	BLIND	1 TO	35	35	R: WORSENING OF CHOLECYSTOLITHIASIS S: Hepatobiliary disorders P: 胆石症 L: Cholecystolithiasis	E: 37 L: 3 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: SURGERY	S: YES, Hospitalization or prolonged hospitalization O: KNOWN MEDICAL HISTORY A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
		PRE	TO -1					
		BLIND	1 TO 132	132	R: CONTACT ALLERGY DUE TO SLEEP APNEA MASK S: Respiratory, thoracic and mediastinal disorders P: 睡眠時無呼吸症候群 L: Sleep apnea	E: 133 L: 2 DAYS I: YES	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: ALLERGIC REACTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	132	132	R: CONTACT ALLERGY DUE TO SLEEP APNEA MASK S: Skin and subcutaneous tissue disorders P: 接触皮膚炎 L: Allergic contact dermatitis	E: 133 L: 2 DAYS I: YES	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: ALLERGIC REACTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	166	166	R: HAEMORRHAGIC EROSIVE GASTRODUODENOPATHY AND DISTAL EROSIVE REFLUX DISEASE S: Gastrointestinal disorders P: びらん性胃炎 L: Erosive gastroduodenitis	E: 167 L: 2 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	166	166	R: HAEMORRHAGIC EROSIVE GASTRODUODENOPATHY AND DISTAL EROSIVE REFLUX DISEASE S: Gastrointestinal disorders P: 胃十二指腸出血 L: Gastroduodenal haemorrhage	E: 167 L: 2 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	166	166	R: HAEMORRHAGIC EROSIVE GASTRODUODENOPATHY AND DISTAL EROSIVE REFLUX DISEASE S: Gastrointestinal disorders P: 胃食道逆流性疾患 L: Gastrooesophageal reflux disease	E: 167 L: 2 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:2[redacted] SEX:MALE RACE:WHITE WEIGHT:66.00 KG							
	PRE	TO -1						
	BLIND	1 TO	124	124	R: PERIANAL ABSCESS S: Infections and infestations P: 肛門膿瘍 L: Perianal abscess	E: 127 L: 4 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: ANAL FISSURA A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:90.10 KG							
	PRE	TO -1						
	BLIND	1 TO 57	57	57	R: ATYPICAL PNEUMONIA ON BOTH SIDES S: Infections and infestations P: 異型肺炎 L: Atypical pneumonia	E: 85 L: 29 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(HOSPITALISATION, DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: ENVIRONMENT A: REASONABLE POSSIBILITY
	POST	58 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:WHITE WEIGHT:108.80 KG								
		PRE	TO -1						
		BLIND	1 TO 36	16	16	R: DEMYELINATING DISEASE FLARE S: Nervous system disorders P: 脱髄 L: Demyelination disorder NOS	E: 20 L: 5 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: [redacted] 20[redacted] SHE HAD WORKUP FOR WEAKNESS A: NO REASONABLE POSSIBILITY
		POST	37 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:8[redacted] SEX:MALE RACE:WHITE WEIGHT:82.00 KG							
	PRE	TO -1						
	BLIND	1 TO 46						
	POST	47 TO	1	47	R: UROSEPSIS S: Infections and infestations P: 尿路性敗血症 L: Urosepsis	E: 66 L: 20 DAYS	T: Mild R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])									
TRT: UPA 30 mg QD									
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:72.00 KG								
		PRE	TO -1						
		BLIND	1 TO 59	50	50	R: PNEUMOCYSTOSIS S: Infections and infestations P: ニューモシスチス・イロベチイ肺炎 L: Pneumocystosis	O: YES	T: Life threatening R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
		POST	60 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:2[redacted] SEX:FEMALE RACE:MULTIPLE WEIGHT:69.00 KG							
	PRE	TO -1						
	BLIND	1 TO 393	165	165	R: HIATIS HERNIA S: Gastrointestinal disorders P: 裂孔ヘルニア L: Hiatal hernia	E: 182 L: 18 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: DECREASED TONE OF THE LOWER OESOPHAGEAL SPHINCTER A: NO REASONABLE POSSIBILITY
	OL	394 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:55.50 KG							
	PRE	TO -1						
	BLIND	1 TO 399	52	52	R: ACUTE PNEUMOIA S: Infections and infestations P: 肺炎 L: Acute pneumonia	E: 92 L: 41 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	OL	400 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:97.10 KG							
	PRE	TO -1						
	BLIND	1 TO 394	157	157 &	R: WORSENING OF OSTEOARTHRITIS RIGHT HIP S: Musculoskeletal and connective tissue disorders P: 変形性関節症 L: Osteoarthritis aggravated	E: 458 L: 302 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,RIGHT HIP REPLACEMENT SCHEDULED FOR [redacted]-[redacted]-[redacted]	S: YES, Hospitalization or prolonged hospitalization O: SEVERE OSTEOARTHRITIS AND SHE HAS FAILED SEVERAL ATTEMPTS AT CONSERVATIVE TREATMENT. A: NO REASONABLE POSSIBILITY
	OL	395 TO 712						
	POST	713 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:MULTIPLE WEIGHT:90.20 KG							
	PRE	TO -1						
	BLIND	1 TO	132	132	R: ACUTE ANTEROSEPTAL MYOCARDIAL INFARCTION S: Cardiac disorders P: 急性心筋梗塞 L: Acute myocardial infarction	E: 136 L: 5 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening O: LIFESTYLE OF THE PATIENT, OBESITY, HIGH CHOLESTEROL AND TRYGLICERIDE LEVELS, GENETIC INHERITANCE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])									
TRT: ADA 40 mg EOW									
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:81.00 KG								
		PRE	TO -1						
		BLIND	1 TO 391	34	34	R: ATRIAL FIBRILLATION PAROXYSMIC S: Cardiac disorders P: 心房細動 L: Paroxysmal atrial fibrillation	E: 37 L: 4 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
		OL	392 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:83.00 KG							
	PRE	TO -1						
	BLIND	1 TO 56	37	37	R: BACTEREMIA S: Infections and infestations P: 菌血症 L: Bacteremia	E: 71 L: 35 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	57 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:124.70 KG							
	PRE	TO -1						
	BLIND	1 TO	112	112	R: THROMBOSIS IN THE LEFT SUPERFICIAL FEMORAL AND POPLITEAL VEINS S: Vascular disorders P: 深部静脈血栓症 L: Deep vein thrombosis		T: Mild R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: OBESITY LESS MOVEMENT A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:113.50 KG							
	PRE	TO -1						
	BLIND	1 TO 395	60	60	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 65 L: 6 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: LIKELY COMMUNITY ACQUIRED PNEUMONIA. A: NO REASONABLE POSSIBILITY
	OL	396 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])									
TRT: ADA 40 mg EOW									
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:130.00 KG								
		PRE	TO -1						
		BLIND	1 TO 392	134	134	R: RIGHT LOWER LEG ERYSIPELAS S: Infections and infestations P: 丹毒 L: Erysipelas	E: 146 L: 13 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
		OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:65.40 KG							
		PRE	TO -1					
		BLIND	1 TO 43					
		POST	44 TO 4	47	R: ATYPICAL PNEUMONIA S: Infections and infestations P: 異型肺炎 L: Atypical pneumonia	E: 63 L: 17 DAYS	T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,OXYGEN THERAPY,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW									
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:108.30 KG								
		PRE	TO -1						
		BLIND	1 TO	121	121	R: TRANSIENT ISCHEMIC ATTACK S: Nervous system disorders P: 一過性脳虚血発作 L: Transient ischaemic attack	E: 123 L: 3 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: PATIENT TREATED FOR ATRIAL FIBRILLATION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:112.20 KG							
	PRE	TO -1						
	BLIND	1 TO 393	15	15	R: RAISED MUSCLE ENZYMES S: Investigations P: 筋酵素上昇 L: Muscle enzyme increased		T: Mild R: Reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	OL	394 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:111.00 KG							
	PRE	TO -1						
	BLIND	1 TO	3	3	R: C7 RADICULOPATHY S: Nervous system disorders P: 頚髄神経根障害 L: Cervical radiculopathy	E: 49 L: 47 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: SHOULDER PAIN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

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Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:115.00 KG							
	PRE	TO -1						
	BLIND	1 TO 174	153	153	R: BRONCHOPNEUMONIA S: Infections and infestations P: 肺炎 L: Bronchopneumonia	E: 162 L: 10 DAYS	T: Life threatening R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED)	S: YES, Hospitalization or prolonged hospitalization, Persistent or significant disability, Important medical or surgical intervention, Life threatening O: DIABETES DISEASE. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 30 mg QD

[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:115.00 KG

POST 175 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:74.40 KG							
	PRE	TO -1						
	BLIND	1 TO	143	143	R: JOINT PAIN S: Musculoskeletal and connective tissue disorders P: 関節痛 L: Joint pain	E: 157 L: 15 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: PATIENT HAS GENERAL JOINT PAIN DUE TO WORK-RELATED FATIGUE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.70 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.70 KG							
	BLIND	1 TO 13	6	6	R: CECUM CANCER WITH METASTASIS IN RIGHT HEPATIC LOBE. S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 遠隔転移を伴う結腸癌 L: Metastatic colon cancer	O: YES	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: PATIENT DOES NOT HAVE ANY NEW SYMPTOMS, RISK FACTORS ARE ABSENT, PATIENT THOUGHT THAT IT REFERS TO GALLSTONE DISEASE. THE CAUSE OF CECUM CANCER IS UNKNOWN. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.70 KG							
		POST	14 TO					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:140.40 KG							
	PRE	TO -1						
	BLIND	1 TO	64	64	R: 3MM URETERAL CALCULUS S: Renal and urinary disorders P: 尿管結石症 L: Ureteral calculus	E: 66 L: 3 DAYS	T: Life threatening R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,HOSPITALIZED)	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN AT PRESENT A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.70 KG							
	PRE	TO -1						
	BLIND	1 TO	6	6	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 16 L: 11 DAYS	T: Mild R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 30 mg QD

[redacted] AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG							
	BLIND	1 TO 283	135	135	R: MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE) S: Injury, poisoning and procedural complications P: 粉碎骨折 L: Comminuted fracture	E: 228 L: 94 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,GYPSUM TO HOLD FIXEDLY TO TREAT)	S: YES, Hospitalization or prolonged hospitalization O: FELL DOWN THE LOWER STEP A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG							
	BLIND	1 TO 283	135	135	R: MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE) S: Injury, poisoning and procedural complications P: 上腕骨骨折 L: Humerus fracture	E: 228 L: 94 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,GYPSUM TO HOLD FIXEDLY TO TREAT)	S: YES, Hospitalization or prolonged hospitalization O: FELL DOWN THE LOWER STEP A: NO REASONABLE POSSIBILITY
	POST	284 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:102.20 KG							
	PRE	TO -1						
	BLIND	1 TO 58	37	37	R: NEURO-ENDOCRIENE CARCINOMA OF UNKNOWN PRIMARY SITE S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 神経内分泌癌 L: Neuroendocrine carcinoma	O: YES	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,PET SCAN,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: AGE A: NO REASONABLE POSSIBILITY
	POST	59 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:67.20 KG							
	PRE	TO -1						
	BLIND	1 TO	78	78	R: ACUTE APPENDICITIS S: Infections and infestations P: 虫垂炎 L: Acute appendicitis	E: 81 L: 4 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:75.00 KG								
		PRE	TO -1						
		BLIND	1 TO 112	19	19	R: LEFT EYE CATARACT S: Eye disorders P: 白内障 L: Left cataract	E: 19 L: 1 DAY	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY FOR EYE CATARACT WAS PERFORMED.)	S: YES, Hospitalization or prolonged hospitalization O: MEDICAL HISTORY - CATARACT SINCE 20[redacted] A: NO REASONABLE POSSIBILITY
		POST	113 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.10 KG							
	PRE	TO -1						
	BLIND	1 TO	71	71	R: FRACTURE RIGHT ANKLE S: Injury, poisoning and procedural complications P: 足関節部骨折 L: Ankle fracture		T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY, PHYSIOTHERAPY)	S: YES, Hospitalization or prolonged hospitalization O: 'THE PATIENT SLIPPED ON THE STAIRS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:55.00 KG							
	PRE	TO -1						
	BLIND	1 TO 138	138	138	R: PULMONARY EMBOLISM S: Respiratory, thoracic and mediastinal disorders P: 肺塞栓症 L: Pulmonary embolism		T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening A: NO REASONABLE POSSIBILITY
	POST	139 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:64.50 KG

PRE TO -1

BLIND 1 TO 141

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:64.50 KG							
		POST	142 TO 4	145	R: OVARIAN CANCER S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 卵巢癌 L: Ovarian cancer	O: YES	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: DISCONTINUED STUDY	S: YES, Important medical or surgical intervention O: THERE ARE NO MEDICAL CONDITION IN MEDICAL HISTORY THAT ARE IN RELATIONSHIP WITH AE. SUBJECT DONE UNSCHEDULED CT SCAN WERE SUSPECTED OVARIAN CANCER WAS FOUND AFTER IT WAS CONFIRMED BY GYNECOLOGIST. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:2[redacted] SEX:MALE RACE:WHITE WEIGHT:66.20 KG							
	PRE	TO -1						
	BLIND	1 TO	58	58	R: FRACTURE OF THE BONE RECONSTRUCTION OF THE DISTAL PHALANX OF THE LEFT THUMB S: Injury, poisoning and procedural complications P: 手骨折 L: Fractured finger	E: 59 L: 2 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.50 KG								
		PRE	TO -1						
		BLIND	1 TO 217	34	34	R: EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE S: Respiratory, thoracic and mediastinal disorders P: 慢性閉塞性肺疾患 L: Chronic obstructive airways disease exacerbated	E: 45 L: 12 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,NEBULIZATION)	S: YES, Hospitalization or prolonged hospitalization O: EXACERBATION OF EXISTING CONDITION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.50 KG							
		POST	218 TO					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: Placebo to UPA 30 mg QD

[redacted]AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:90.40 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:90.40 KG							
	BLIND	1 TO	153	153	R: ACUTE KIDNEY FAILURE S: Renal and urinary disorders P: 急性腎障害 L: Acute kidney failure	E: 178 L: 26 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,THE PATIENT HAS BEEN REFERRED TO THE HOSPITAL.)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: THIS EVENT IS PROBABLY ASSOCIATED WITH THE NSAID DRUGS AND EVENT: WORSENING OF PSORIATIC ARTHRITIS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:93.80 KG							
	PRE	TO -1						
	BLIND	1 TO 57						
	POST	58 TO	1	58	R: SEPTICEMIA S: Infections and infestations P: 敗血症 L: Septicemia	E: 66 L: 9 DAYS I: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])									
TRT: UPA 15 mg QD									
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:125.60 KG								
		PRE	TO -1						
		BLIND	1 TO 244	36	36	R: FEVER INTERMITTENT S: General disorders and administration site conditions P: 発熱 L: Intermittent fever	I: YES	T: Mild R: Reasonable possibility A: DRUG WITHDRAWN O: NONE	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention A: NO REASONABLE POSSIBILITY
		POST	245 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:100.00 KG							
	PRE	TO -1						
	BLIND	1 TO 37	36	36	R: EXACERBATED OBSTRUCTIVE PULMONARY DISEASE S: Respiratory, thoracic and mediastinal disorders P: 閉塞性気道障害 L: Obstructive airways disorder	E: 65 L: 30 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	38 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:71.90 KG							
	PRE	TO -1						
	BLIND	1 TO 55	21	21	R: AMYOTROPHIC LATERAL SCLEROSIS S: Nervous system disorders P: 筋萎縮性側索硬化症 L: Amyotrophic lateral sclerosis	O: YES	T: Moderate R: No reasonable possibility A: DRUG WITHDRAWN O: DISCONTINUED STUDY	S: YES, Important medical or surgical intervention O: UNKNOWN ETIOLOGY A: NO REASONABLE POSSIBILITY
	POST	56 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:124.70 KG							
		PRE	TO -1					
		BLIND	1 TO 143	143	R: LEFT LEG ERYSIPELAS S: Infections and infestations P: 丹毒 L: Erysipelas	E: 195 L: 53 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,REFER TO HOSPITAL)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:92.50 KG							
	PRE	TO -1						
	BLIND	1 TO 168						
	POST	169 TO	9	177	R: LEFT LAMINAR PLEURAL EFFUSION S: Respiratory, thoracic and mediastinal disorders P: 胸水 L: Pleural effusion	E: 196 L: 20 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: CAUSE IS PROBABLY VERTEBRAL ABSSCESS

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:92.50 KG							
		POST	169 TO 9	177	R: VERTEBRAL ABSCESS S: Infections and infestations P: 骨膿瘍 L: Vertebral abscess		T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
			10	178	R: CEREBROVASCULAR ACCIDENT S: Nervous system disorders P: 脳血管発作 L: Cerebrovascular accident	E: 205 L: 28 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: CAUSE PROBABLY IS DIABETES.

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:92.50 KG							
	POST	169 TO	28	196	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 253 L: 58 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:60.10 KG							
		PRE	TO -1					
		BLIND	1 TO 133	133	R: PORTAL VEIN THROMBOSIS S: Hepatobiliary disorders P: 門脈血栓症 L: Portal vein thrombosis	E: 142 L: 10 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
		POST	134 TO					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])									
TRT: UPA 30 mg QD									
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:100.00 KG								
		PRE	TO -1						
		BLIND	1 TO 395	156	156	R: RIGHT ACHILLES TENDON TEAR S: Injury, poisoning and procedural complications P: 腱断裂 L: Tendon rupture		T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: PROLONGED AND INTENSIVE MECHANICAL ACTIVITY A: NO REASONABLE POSSIBILITY
		OL	396 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:113.40 KG							
	PRE	TO -1						
	BLIND	1 TO 392	79	79	R: GASTRIC INDIGESTION S: Gastrointestinal disorders P: 消化不良 L: Indigestion	E: 80 L: 2 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: SUBJECT HAD EATEN HEAVY MEAL CONSISTING OF PIZZA AND THEREAFTER COMPLAINED OF LEFT LOWER CHEST PAIN. A: NO REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:131.54 KG							
	PRE	TO -1						
	BLIND	1 TO 56						
	POST	57 TO	6	62	R: CARDIAC ARREST S: Cardiac disorders P: 心停止 L: Cardiac arrest	E: 62 L: 1 DAY	T: Mild R: No reasonable possibility A: DEATH O: DEATH	S: YES, Death of subject O: DIABETES, HYPERLIPIDEMIA, HYPERTENSION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:BLACK OR AFRICAN AMERICAN WEIGHT:114.70 KG							
	PRE	TO -1						
	BLIND	1 TO	136	136	R: ANXIETY CRISIS S: Psychiatric disorders P: 不安 L: Anxiety attack	E: 137 L: 2 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: RELATED TO PRE-EXISTING BIPOLAR DISORDER AND CURRENT PSYCHOSOCIAL PROBLEMS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

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(Safety Analysis Set)

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INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:95.50 KG							
	PRE	TO -1						
	BLIND	1 TO 112	112	112	R: CHEST PAIN S: General disorders and administration site conditions P: 胸痛 L: Chest pain	E: 114 L: 3 DAYS I: YES	T: Life threatening R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: HISTORY OF MYOCARDIAL INFARCTION, ATRIAL FIBRILLATION AND CAROTID ARTERIAL DISEASE. A: NO REASONABLE POSSIBILITY
	POST	113 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

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(Safety Analysis Set)

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INV: [redacted] ([redacted])								
TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:111.13 KG							
	PRE	TO -1						
	BLIND	1 TO 77	73	73	R: LEFT BREAST CELLULITIS S: Infections and infestations P: 乳房蜂巢炎 L: Breast cellulitis	E: 112 L: 40 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	78 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
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INV: [redacted] ([redacted])									
TRT: UPA 15 mg QD									
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:102.06 KG								
		PRE	TO -1						
		BLIND	1 TO 399	77	77	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 81 L: 5 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
		OL	400 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

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INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:5[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:52.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

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(Safety Analysis Set)

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INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:52.00 KG							
	BLIND	1 TO 196	32	32 &	R: CANCER SARCOMA (UTERINE) S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 子宮癌 L: Carcinosarcoma uterus	E: 263 L: 232 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,ABDOMINAL TYPE EXTENSIVE HYSTERECTOMY ADNEXECTOMY(BOTH) LYMPH NODEDISSECTION(PELVIC) PARA-AORTIC LYMPH NODES BIOPSY BILATERAL URETERAL STENT PLACEMENT)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: CONSISTENT WITH GENERAL RISK FACTORS SUCH AS AGE, FEMALE, MENOPAUSE, FIRST BIRTH, AND LESS CHILDBIRTH EXPERIENCE. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:52.00 KG							
		POST	197 TO					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:102.90 KG							
	PRE	TO -1						
	BLIND	1 TO 63	55	55	R: ACUTE SEPSIS S: Infections and infestations P: 敗血症 L: Sepsis	O: YES	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	POST	64 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:71.20 KG							
	PRE	TO -1						
	BLIND	1 TO 83	64	64	R: FEVER OF UNKNOWN ORIGIN S: General disorders and administration site conditions P: 発熱 L: Fever of unknown origin	E: 90 L: 27 DAYS I: YES	T: Moderate R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	POST	84 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:70.00 KG							
	PRE	TO -1						
	BLIND	1 TO 12	12	12	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 28 L: 17 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: THE WEAKNESS OF IMMUNE SYSTEM DUE TO DIABETES, ARTHRITIS PSORIATICA MAY HAVE CAUSED THIS EVENT A: NO REASONABLE POSSIBILITY
	POST	13 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 15 mg QD

[redacted]AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:93.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:93.00 KG							
	BLIND	1 TO 398	51	51	R: CHRONIC LARYNGITIS S: Infections and infestations P: 喉頭炎 L: Chronic laryngitis	E: 52 L: 2 DAYS I: YES	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: BECAUSE OF RETURNING HOARSENESS THAT HAS EXISTED FOR YEARS LARYNGOSCOPY AND OESOPHAGOSCOPY WAS PERFORMED.THE RESULT IS CHRONIC MUCOUS INFLAMMATION. A: NO REASONABLE POSSIBILITY
	OL	399 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day	Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:69.50 KG								
		PRE	TO -1						
		BLIND	1 TO 159						
		POST	160 TO	1	160	R: ADENOCARCINOMA G-3 BRONCHUS S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 肺腺癌 L: Adenocarcinoma lung	O: YES	T: Moderate R: No reasonable possibility A: DRUG WITHDRAWN O: NONE	S: YES, Important medical or surgical intervention O: SMOKER A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW									
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:147.30 KG								
		PRE	TO -1						
		BLIND	1 TO 70	33	33	R: POSSIBLE STAPH INFECTION S: Infections and infestations P: ブドウ球菌感染 L: Staphylococcal infection	O: YES	A: DOSE NOT CHANGED O: HOSPITALIZATION	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
		POST	71 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:76.40 KG								
		PRE	TO -1						
		BLIND	1 TO	21	21	R: ACUTE APPENDICITIS S: Infections and infestations P: 虫垂炎 L: Acute appendicitis	E: 22 L: 2 DAYS	T: Mild R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:83.00 KG							
	PRE	TO -1						
	BLIND	1 TO	79	79	R: TOENAILS INGROWN WORSENING S: Skin and subcutaneous tissue disorders P: 嵌入爪 L: Ingrown toe nail	E: 232 L: 154 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: PARTIAL SURGICAL REMOVAL OF THE BOTH TOENAILS	S: YES, Hospitalization or prolonged hospitalization O: REPETITIVE PRESSURE TO THE FEET A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:74.00 KG							
	PRE	TO -1						
	BLIND	1 TO 72						
	POST	73 TO	18	90	R: IRON DEFICIENT ANAEMIA S: Blood and lymphatic system disorders P: 鉄欠乏性貧血 L: Iron deficiency anaemia		T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: HOSPITALIZED FOR FURTHER INVESTIGATION	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: UNSPECIFIED INFECTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 30 mg QD

[redacted]AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:64.90 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:64.90 KG							
	BLIND	1 TO 392	157	157	R: CORONARY ARTERIAL DISEASE S: Cardiac disorders P: 冠動脈疾患 L: Coronary artery disease		T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED, STOP IMP SINCE [redacted]20[redacted] O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: IN THE JUDGMENT OF THE PRINCIPAL INVESTIGATOR, THE EVENT WAS NOT RELATED TO THE STUDY DRUG AND ANGIOGRAPHY IS A PROCEDURE AND NOT A SURGERY BECAUSE NO INCISION AND SUTURE WAS NEEDED. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:64.90 KG							
		OL	393	TO				

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:104.20 KG							
	PRE	TO -1						
	BLIND	1 TO 6	6	6	R: LIMITED PNEUMOPHIBROSIS OF THE LOWER LOBE OF THE RIGHT LUNG. HYPERPLASIA OF MEDIASTINAL LYMPH NODES S: Blood and lymphatic system disorders P: リンパ組織過形成 L: Lymphoid tissue hyperplasia	O: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: SMOCKING A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:104.20 KG							
	BLIND	1 TO 6	6	6	R: LIMITED PNEUMOPHIBROSIS OF THE LOWER LOBE OF THE RIGHT LUNG. HYPERPLASIA OF MEDIASTINAL LYMPH NODES S: Respiratory, thoracic and mediastinal disorders P: 肺線維症 L: Pulmonary fibrosis	O: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: SMOCKING A: NO REASONABLE POSSIBILITY
	POST	7 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:45.30 KG								
		PRE	TO -1						
		BLIND	1 TO	122	122	R: FIBROCYSTIC MASTOPATHY OF THE LEFT BREAST S: Reproductive system and breast disorders P: 線維嚢胞性乳腺疾患 L: Fibrocystic breast disease	E: 129 L: 8 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: LEFT BREAST' NEOPLASM SURGERY REMOVING	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:108.00 KG							
	PRE	TO -1						
	BLIND	1 TO	113	113	R: INTESTINAL POLYPUS S: Gastrointestinal disorders P: 腸管ポリープ L: Intestinal polyp	E: 125 L: 13 DAYS	T: Mild R: No reasonable possibility A: DOSE NOT CHANGED O: POLYPECTOMY	S: YES, Hospitalization or prolonged hospitalization O: NO OTHER CAUSES A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:77.40 KG							
	PRE	TO -1						
	BLIND	1 TO 13						
	POST	14 TO	2	15	R: DERMATITIS WORSENING S: Skin and subcutaneous tissue disorders P: 皮膚炎 L: Dermatitis NOS aggravated	E: 23 L: 9 DAYS	T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:2[redacted] SEX:FEMALE RACE:WHITE WEIGHT:83.30 KG							
	PRE	TO -1						
	BLIND	1 TO 28						
	POST	29 TO	4	32	R: DEEP VEIN THROMBOSIS OF LEFT SHIN S: Vascular disorders P: 深部静脈血栓症 L: Deep vein thrombosis leg	E: 105 L: 74 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: COMBINATION OF HORMONAL CONTRACEPTION PLUS NIKOTINISM A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 30 mg QD									
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:86.18 KG								
		PRE	TO -1						
		BLIND	1 TO 386	107	107	R: WORSENING OF PRE-EXISTING SPINAL STENOSIS S: Musculoskeletal and connective tissue disorders P: 脊柱管狭窄症 L: Spinal column stenosis	E: 187 L: 81 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,LAMINECTOMY COMPLETED ON [redacted]/[redacted]/[redacted] PT HOSPITALIZED THROUGH[redacted]/[redacted]/[redacted])	S: YES, Hospitalization or prolonged hospitalization O: MEDICAL HISTORY OF SPINAL STENOSIS A: NO REASONABLE POSSIBILITY
		OL	387 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Day	Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:4[redacted] SEX:MALE RACE:ASIAN WEIGHT:70.00 KG								
		PRE	TO -1						
		BLIND	1 TO 64	60	60	R: PULMONARY INFECTION S: Infections and infestations P: 肺感染 L: Lung infection	O: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
		POST	65 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD									
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.50 KG								
		PRE	TO -1						
		BLIND	1 TO	110	110	R: WORSENING OF PROLAPSE OF THE UTERUS S: Reproductive system and breast disorders P: 子宮脱 L: Uterine prolapse	E: 110 L: 1 DAY	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,TRANSVAGINAL ULTRASOUND, VAGINAL COLPOSCOPY, UTERUS ULTRASOUND)	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.1

Listing of Subjects with Treatment-Emergent Serious Adverse Events - up to Week 24
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.50 KG							
	BLIND	1 TO	154	154	R: WORSENING OF PROLAPSE OF THE UTERUS S: Reproductive system and breast disorders P: 子宮脱 L: Uterine prolapse	E: 166 L: 13 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,HOSPITALIZATION)	S: YES, Hospitalization or prolonged hospitalization O: [redacted] 20[redacted] FOLLOW UP- OTHER ETIOLOGY-AFTER BIRTH OF CHILDREN [redacted]20[redacted] OTHER SUSPECTED CAUSES ARE UNKNOWN- NO INFORMATION ON DISCHARGED SUMMARY REPORT OTHER SUSPECTED CAUSES ARE UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug in Period 1 and prior to the Week 24 dose date, or up to 30 days after the last dose of placebo or UPA and up to 70 days for adalimumab, if subject discontinued study drug prematurely before Week 24 dosing.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

表 2.7.4.7-24. 投与 24 週時データカットオフまでの重篤な有害事象の一覧表（安全性解析対象集団）：M15-572 試験

表中記載の説明

転帰：回復 ＝E 欄に日数が記載されており，S 欄に Death of subject の記載がない。継続中 ＝O 欄に YES と記載されているか，E 欄及び O 欄の記載がない。死亡 ＝S 欄に Death of subject と記載されている。
国内の実施医療機関の番号は，[redacted]，[redacted]，[redacted]，[redacted]，[redacted] 及び [redacted] である。

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:87.09 KG							
	PRE	TO -1						
	BLIND	1 TO 393	306	306	R: ISCHEMIC CEREBRAL VASCULAR ACCIDENT S: Nervous system disorders P: 虚血性脳卒中 L: Ischemic stroke	E: 344 L: 39 DAYS I: YES	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: CORONARY ARTERY DISEASE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:87.09 KG							
	OL	394 TO 682	67	460	R: BRONCHITIS S: Infections and infestations P: 気管支炎 L: Bronchitis	E: 481 L: 22 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: SUBJECT WAS OUT OF THE COUNTRY AND BY AGE HE WAS MAY LIABLE TO DIFFERENT TYPES OF BACTERIAL INFECTION A: NO REASONABLE POSSIBILITY
	POST	683 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:89.90 KG							
	PRE	TO -1						
	BLIND	1 TO 385						
	OL	386 TO 809+	423	808	R: PULMONARY EMBOLISM S: Respiratory, thoracic and mediastinal disorders P: 肺塞栓症 L: Pulmonary embolism		T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
+ Subject is ongoing.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:96.93 KG							
	PRE	TO -1						
	BLIND	1 TO 172	94	94	R: HEPATIC ENCEPHALOPATHY S: Nervous system disorders P: 肝性脳症 L: Hepatic encephalopathy	I: YES	T: Severe R: Reasonable possibility A: MULTIPLE:(DRUG INTERRUPTED, DRUG WITHDRAWN) O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,MONITORING AMMONIA LEVELS)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: METHOTREXATE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:96.93 KG

POST 173 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:89.40 KG							
	PRE	TO -1						
	BLIND	1 TO	267	267	R: WORSENING OF CERVICAL DISCUS PROLAPS C7/C8 S: Musculoskeletal and connective tissue disorders P: 椎間板突出 L: Prolapsed cervical disc	E: 271 L: 5 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: PROGRESSION OF A UNDERLYING DISEASE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:89.40 KG							
	BLIND	1 TO	302	302	R: DUODENAL ULCER (FORREST II A) S: Gastrointestinal disorders P: 十二指腸潰瘍 L: Duodenal ulcer	E: 306 L: 5 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED)	S: YES, Hospitalization or prolonged hospitalization O: BIG DOSES OF IBUPROFEN DUE TO SURGERY ON [redacted]-[redacted]-20[redacted] (SEE AE#3), BUT WITHOUT GASTRIC PROTECTION(DUE TO PATIENT) A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:89.40 KG							
	BLIND	1 TO	342	342	R: NORMOCHROMIC-NORMOCYTIC ANEMIA S: Blood and lymphatic system disorders P: 正色素性正球性貧血 L: Normochromic normocytic anemia	E: 345 L: 4 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	PRE	TO -1						
	BLIND	1 TO	132	132	R: CONTACT ALLERGY DUE TO SLEEP APNEA MASK S: Respiratory, thoracic and mediastinal disorders P: 睡眠時無呼吸症候群 L: Sleep apnea	E: 133 L: 2 DAYS I: YES	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: ALLERGIC REACTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	132	132	R: CONTACT ALLERGY DUE TO SLEEP APNEA MASK S: Skin and subcutaneous tissue disorders P: 接触皮膚炎 L: Allergic contact dermatitis	E: 133 L: 2 DAYS I: YES	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: ALLERGIC REACTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	166	166	R: HAEMORRHAGIC EROSIVE GASTRODUODENOPATHY AND DISTAL EROSIVE REFLUX DISEASE S: Gastrointestinal disorders P: びらん性胃炎 L: Erosive gastroduodenitis	E: 167 L: 2 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	166	166	R: HAEMORRHAGIC EROSIVE GASTRODUODENOPATHY AND DISTAL EROSIVE REFLUX DISEASE S: Gastrointestinal disorders P: 胃十二指腸出血 L: Gastroduodenal haemorrhage	E: 167 L: 2 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.30 KG							
	BLIND	1 TO	166	166	R: HAEMORRHAGIC EROSIVE GASTRODUODENOPATHY AND DISTAL EROSIVE REFLUX DISEASE S: Gastrointestinal disorders P: 胃食道逆流性疾患 L: Gastrooesophageal reflux disease	E: 167 L: 2 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:2[redacted] SEX:MALE RACE:WHITE WEIGHT:66.00 KG							
	PRE	TO -1						
	BLIND	1 TO	124	124	R: PERIANAL ABSCESS S: Infections and infestations P: 肛門膿瘍 L: Perianal abscess	E: 127 L: 4 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: ANAL FISSURA A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:2[redacted] SEX:MALE RACE:WHITE WEIGHT:66.00 KG							
	BLIND	1 TO	255	255	R: ANAL FISTULA S: Gastrointestinal disorders P: 痔瘘 L: Anal fistula	E: 309 L: 55 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: ELECTIV ANALFISTULAECTOMIA [redacted] [redacted] 20[redacted]	S: YES, Hospitalization or prolonged hospitalization O: ANAL FISTULA A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:90.10 KG							
	PRE	TO -1						
	BLIND	1 TO 57	57	57	R: ATYPICAL PNEUMONIA ON BOTH SIDES S: Infections and infestations P: 異型肺炎 L: Atypical pneumonia	E: 85 L: 29 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(HOSPITALISATION, DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: ENVIRONMENT A: REASONABLE POSSIBILITY
	POST	58 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:WHITE WEIGHT:108.80 KG							
	PRE	TO -1						
	BLIND	1 TO 36	16	16	R: DEMYELINATING DISEASE FLARE S: Nervous system disorders P: 脱髄 L: Demyelination disorder NOS	E: 20 L: 5 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: [redacted]20[redacted] SHE HAD WORKUP FOR WEAKNESS A: NO REASONABLE POSSIBILITY
	POST	37 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:131.09 KG							
	PRE	TO -1						
	BLIND	1 TO 221	177	177	R: UPPER GI BLEED S: Gastrointestinal disorders P: 上部消化管出血 L: Upper gastrointestinal hemorrhage	E: 178 L: 2 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED)	S: YES, Hospitalization or prolonged hospitalization O: BLEEDING ULCERS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD									
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:131.09 KG								
		POST	222 TO	17	238	R: DIVERTICULITIS S: Infections and infestations P: 憩室炎 L: Diverticulitis	E: 253 L: 16 DAYS I: YES	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: DIVERTICULOSIS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:92.00 KG							
	PRE	TO -1						
	BLIND	1 TO 394						
	OL	395 TO	198	592	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 602 L: 11 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:105.00 KG							
	PRE	TO -1						
	BLIND	1 TO 389	370	370	R: VIRAL INFECTION S: Infections and infestations P: ウイルス感染 L: Viral infection	E: 373 L: 4 DAYS I: YES	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: VIRUS A: NO REASONABLE POSSIBILITY
	OL	390 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:84.00 KG								
		PRE	TO -1						
		BLIND	1 TO 391	260	260	R: MYOCARDIAL INFARCTION S: Cardiac disorders P: 心筋梗塞 L: Myocardial infarction	E: 264 L: 5 DAYS	T: Life threatening R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: THE FIRST MANIFESTATION OF CORONARY HEART DISEASE A: NO REASONABLE POSSIBILITY
		OL	392 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:8[redacted] SEX:MALE RACE:WHITE WEIGHT:82.00 KG							
	PRE	TO -1						
	BLIND	1 TO 46						
	POST	47 TO	1	47	R: UROSEPSIS S: Infections and infestations P: 尿路性敗血症 L: Urosepsis	E: 66 L: 20 DAYS	T: Mild R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:72.00 KG							
		PRE	TO -1					
		BLIND	1 TO 59	50	R: PNEUMOCYSTOSIS S: Infections and infestations P:ニューモシスチス・イロベチイ肺炎 L: Pneumocystosis	O: YES	T: Life threatening R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
		POST	60 TO					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:MULTIPLE WEIGHT:88.00 KG							
	PRE	TO -1						
	BLIND	1 TO 385						
	OL	386 TO	141	526	R: WORSENING OF VERICOSE VEINS BOTH LEGS S: Vascular disorders P: 静脈瘤 L: Varicose veins of lower extremities	E: 532 L: 7 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: BILATERAL VARICOSE VEIN STRIPPING	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: SHE IS A NURSE AND STANDS A LOT A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:2[redacted] SEX:FEMALE RACE:MULTIPLE WEIGHT:69.00 KG							
	PRE	TO -1						
	BLIND	1 TO 393	165	165	R: HIATIS HERNIA S: Gastrointestinal disorders P: 裂孔ヘルニア L: Hiatal hernia	E: 182 L: 18 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: DECREASED TONE OF THE LOWER OESOPHAGEAL SPHINCTER A: NO REASONABLE POSSIBILITY
	OL	394 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:85.00 KG								
		PRE	TO -1						
		BLIND	1 TO 393	233	233 &	R: ATYPICAL CHEST PAIN S: General disorders and administration site conditions P: 胸痛 L: Chest pain	E: 328 L: 96 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: OCCASIONAL DIZZINESS AND ON ONE OCCASION HAD AN EPISODE OF PRESYNCOPE. A: NO REASONABLE POSSIBILITY
		OL	394 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:MULTIPLE WEIGHT:96.50 KG							
	PRE	TO -1						
	BLIND	1 TO 393						
	OL	394 TO	36	429	R: HERPES ZOSTER OF UPPER LEG, BUTTOCK AND LOWER BACK S: Infections and infestations P: 带状疱疹 L: Herpes zoster	E: 446 L: 18 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 15 mg QD

[redacted] AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.83 KG

PRE TO -1

BLIND 1 TO 395

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.83 KG							
	OL	396 TO 563	136	531	R: WORSENING OF LUMBOSACRAL SPINAL STENOSIS S: Musculoskeletal and connective tissue disorders P: 腰部脊柱管狭窄症 L: Lumbosacral spinal stenosis	E: 568 L: 38 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,L4-L5 AND L5-S1 LAMINECTOMY,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: LUMBAR-RADICULOPATHY DUE TO H/O OF LUMBAR SACRAL SPINAL STENOSIS A: NO REASONABLE POSSIBILITY
	POST	564 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:ASIAN WEIGHT:53.10 KG							
	PRE	TO -1						
	BLIND	1 TO 391						
	OL	392 TO	137	528	R: HERPES ZOSTER(RIGHT SIDE CHEST WALL)(RIGHT T4-T6 DERMATOME) S: Infections and infestations P: 带状疱疹 L: Herpes zoster	E: 553 L: 26 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:55.50 KG							
	PRE	TO -1						
	BLIND	1 TO 399	52	52	R: ACUTE PNEUMOIA S: Infections and infestations P: 肺炎 L: Acute pneumonia	E: 92 L: 41 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
			336	336	R: DUODENAL ULCER WITH BLEEDING S: Gastrointestinal disorders P: 出血性十二指腸潰瘍 L: Duodenal ulcer bleeding	E: 342 L: 7 DAYS	T: Life threatening R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: PEPTIC ULCERS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 30 mg QD

[redacted]AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:55.50 KG

OL 400 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:97.10 KG							
	PRE	TO -1						
	BLIND	1 TO 394	157	157 &	R: WORSENING OF OSTEOARTHRITIS RIGHT HIP S: Musculoskeletal and connective tissue disorders P: 変形性関節症 L: Osteoarthritis aggravated	E: 458 L: 302 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,RIGHT HIP REPLACEMENT SCHEDULED FOR [redacted]-[redacted]-[redacted])	S: YES, Hospitalization or prolonged hospitalization O: SEVERE OSTEOARTHRITIS AND SHE HAS FAILED SEVERAL ATTEMPTS AT CONSERVATIVE TREATMENT. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:97.10 KG							
		OL	395 TO 712					
		POST	713 TO 1	713	R: PULMONARY EMBOLISM BILATERAL S: Respiratory, thoracic and mediastinal disorders P: 肺塞栓症 L: Pulmonary embolism	E: 715 L: 3 DAYS	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention, Life threatening A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Day	Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:MULTIPLE WEIGHT:90.20 KG							
	PRE	TO -1						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:MULTIPLE WEIGHT:90.20 KG							
	BLIND	1 TO	132	132	R: ACUTE ANTEROSEPTAL MYOCARDIAL INFARCTION S: Cardiac disorders P: 急性心筋梗塞 L: Acute myocardial infarction	E: 136 L: 5 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening O: LIFESTYLE OF THE PATIENT, OBESITY, HIGH CHOLESTEROL AND TRYGLICERIDE LEVELS, GENETIC INHERITANCE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:60.10 KG							
	PRE	TO -1						
	BLIND	1 TO 231						
	POST	232 TO	28	259	R: OVARIAN CYST S: Reproductive system and breast disorders P: 卵巢囊胞 L: Ovarian cyst	E: 259 L: 1 DAY	T: Mild R: No reasonable possibility A: DOSE NOT CHANGED O: CYSTECTOMIA OVARII	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: POSTMENOPAUSE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:74.40 KG							
	PRE	TO -1						
	BLIND	1 TO 396	303	303	R: APENDICITIS S: Infections and infestations P: 虫垂炎 L: Appendicitis	E: 306 L: 4 DAYS I: YES	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: APENDETOMY	S: YES, Hospitalization or prolonged hospitalization O: INFECTION A: NO REASONABLE POSSIBILITY
	OL	397 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:65.00 KG							
	PRE	TO -1						
	BLIND	1 TO 196	196	196	R: DISSEMINATED PUSTULAR PSORIASIS S: Skin and subcutaneous tissue disorders P: 膿疱性乾癬 L: Pustular psoriasis	E: 203 L: 8 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: IMMUNOSUPPRESSION A: NO REASONABLE POSSIBILITY
	POST	197 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:81.00 KG							
	PRE	TO -1						
	BLIND	1 TO 391	34	34	R: ATRIAL FIBRILLATION PAROXYSMIC S: Cardiac disorders P: 心房細動 L: Paroxysmal atrial fibrillation	E: 37 L: 4 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	OL	392 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:83.00 KG							
	PRE	TO -1						
	BLIND	1 TO 56	37	37	R: BACTEREMIA S: Infections and infestations P: 菌血症 L: Bacteremia	E: 71 L: 35 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	57 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:124.70 KG							
	PRE	TO -1						
	BLIND	1 TO	112	112	R: THROMBOSIS IN THE LEFT SUPERFICIAL FEMORAL AND POPLITEAL VEINS S: Vascular disorders P: 深部静脈血栓症 L: Deep vein thrombosis		T: Mild R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: OBESITY LESS MOVEMENT A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:2[redacted] SEX:FEMALE RACE:WHITE WEIGHT:45.00 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	49	441	R: ACUTE RIGHT-SIDED SALPINGITIS S: Infections and infestations P: 卵管炎 L: Salpingitis	E: 443 L: 3 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: DIAGNOSTIC LAPAROSCOPIC SURGERY	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:52.00 KG							
	PRE	TO -1						
	BLIND	1 TO	392	392	R: LEFT BUTTOCK ABSCESS S: Infections and infestations P: 四肢膿瘍 L: Abscess on buttock	E: 402 L: 11 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SUBJECT HAD OPENING AND DRAINAGE OF THE ABSCESS)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:WHITE WEIGHT:72.30 KG							
	PRE	TO -1						
	BLIND	1 TO 392	199	199	R: APPENDICITIS S: Infections and infestations P: 虫垂炎 L: Appendicitis	E: 200 L: 2 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: PHLAGMONOUS, GANGRENOUS APPENDIX A: NO REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:123.83 KG							
	PRE	TO -1						
	BLIND	1 TO 390	318	318	R: CERVICAL STENOSIS S: Musculoskeletal and connective tissue disorders P: 頚部脊柱管狭窄症 L: Cervical spinal stenosis	E: 321 L: 4 DAYS	T: Mild R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CERVICAL STENOSIS SURGERY)	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY
	OL	391 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:1[redacted] SEX:MALE RACE:WHITE WEIGHT:109.50 KG							
	PRE	TO -1						
	BLIND	1 TO	227	227	R: HABITUAL LUXATION OF THE LEFT SHOULDER S: Injury, poisoning and procedural complications P: 関節脱臼 L: Subluxation shoulder	E: 310 L: 84 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: TRAUMATIC DISLOCATION OF THE LEFT SHOULDER IN 20[redacted] A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:130.00 KG							
	PRE	TO -1						
	BLIND	1 TO 392	134	134	R: RIGHT LOWER LEG ERYSIPELAS S: Infections and infestations P: 丹毒 L: Erysipelas	E: 146 L: 13 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 15 mg QD							
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:74.30 KG						
	PRE	TO -1					
	BLIND	1 TO 392					
	OL	393 TO 170	562	R: POSTURAL VERTIGO S: Ear and labyrinth disorders P: 頭位性回転性めまい L: Vertigo positional		T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:76.80 KG							
	PRE	TO -1						
	BLIND	1 TO 395	234	234	R: LEFT PYELONEPHRITIS S: Infections and infestations P: 腎盂腎炎 L: Pyelonephritis	E: 241 L: 8 DAYS I: YES	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	OL	396 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:108.00 KG

PRE TO -1

BLIND 1 TO 391

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:108.00 KG							
	OL	392 TO 480+	83	474	R: PRIMARY METASTATIC PANCREAS NEOPLASIA S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 遠隔転移を伴う膵癌 L: Pancreatic carcinoma metastatic		T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: LIVER AND PANCREATIC BIOPSY AND ONCOLOGY APPOINTMENT	S: YES, Important medical or surgical intervention

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
+ Subject is ongoing.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:65.40 KG							
	PRE	TO -1						
	BLIND	1 TO 43						
	POST	44 TO	4	47	R: ATYPICAL PNEUMONIA S: Infections and infestations P: 異型肺炎 L: Atypical pneumonia	E: 63 L: 17 DAYS	T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,OXYGEN THERAPY,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:108.30 KG							
	PRE	TO -1						
	BLIND	1 TO	121	121	R: TRANSIENT ISCHEMIC ATTACK S: Nervous system disorders P: 一過性脳虚血発作 L: Transient ischaemic attack	E: 123 L: 3 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: PATIENT TREATED FOR ATRIAL FIBRILLATION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:3[redacted] SEX:MALE RACE:WHITE WEIGHT:83.30 KG							
	PRE	TO -1						
	BLIND	1 TO 391	309	309	R: RECURRING DEPRESSIVE DISORDER S: Psychiatric disorders P: うつ病 L: Recurrent depressive disorder		T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,REFERRED TO PSYCHIATRIST WHO PRESCRIBED CONMEDS)	S: YES, Hospitalization or prolonged hospitalization O: PERSONAL ISSUES A: NO REASONABLE POSSIBILITY
	OL	392 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:112.20 KG							
	PRE	TO -1						
	BLIND	1 TO 393	15	15	R: RAISED MUSCLE ENZYMES S: Investigations P: 筋酵素上昇 L: Muscle enzyme increased		T: Mild R: Reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:112.20 KG							
	BLIND	1 TO 393	254	254	R: RIGHT RENAL COLIC S: Renal and urinary disorders P: 腎仙痛 L: Renal colic	E: 254 L: 1 DAY I: YES	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: SUSPECTED RENAL STONES. CONFIRMED THROUGH SCAN, NO STONES A: NO REASONABLE POSSIBILITY
	OL	394 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:111.00 KG							
	PRE	TO -1						
	BLIND	1 TO	3	3	R: C7 RADICULOPATHY S: Nervous system disorders P: 頚髄神経根障害 L: Cervical radiculopathy	E: 49 L: 47 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: SHOULDER PAIN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 15 mg QD

[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.00 KG							
	BLIND	1 TO 322	289	289	R: GASTRIC ULCER PERFORATION. S: Gastrointestinal disorders P: 穿孔性胃潰瘍 L: Gastric ulcer perforation	E: 309 L: 21 DAYS	T: Severe R: No reasonable possibility A: MULTIPLE:(DRUG INTERRUPTED, DRUG WITHDRAWN) O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: MORE LIKELY CAUSE IS CONCOMITANT THERAPY - NON STEROID ANTI INFLAMMATORY DRUGS AND METHOTREXATE USAGE. A: NO REASONABLE POSSIBILITY
	POST	323 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 30 mg QD

[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:115.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:115.00 KG							
	BLIND	1 TO 174	153	153	R: BRONCHOPNEUMONIA S: Infections and infestations P: 肺炎 L: Bronchopneumonia	E: 162 L: 10 DAYS	T: Life threatening R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED)	S: YES, Hospitalization or prolonged hospitalization, Persistent or significant disability, Important medical or surgical intervention, Life threatening O: DIABETES DISEASE. A: NO REASONABLE POSSIBILITY
	POST	175 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted] TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:105.00 KG							
	PRE	TO -1						
	BLIND	1 TO 367	260	260	R: WORSENING OF PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia aggravated	E: 267 L: 8 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: LOW IMMUNE RESPONSE, DIABETES A: NO REASONABLE POSSIBILITY
	POST	368 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.00 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	24	416	R: RIGHT LOWER ARM FRACTURE S: Injury, poisoning and procedural complications P: 上肢骨折 L: Arm fracture	E: 468 L: 53 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: PATIENT FELL DURING CLIMBING. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:104.00 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	65	457	R: WORSENING OF DIABETIC POLYNEUROPATHY S: Nervous system disorders P: 糖尿病性ニューロパチー L: Diabetic polyneuropathy	E: 470 L: 14 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: REHABILITATION	S: YES, Hospitalization or prolonged hospitalization O: DIABETIC POLYNEUROPATHY A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:104.00 KG							
		OL	393 TO 458	66	R: ANEMIA S: Blood and lymphatic system disorders P: 貧血 L: Anemia		T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,STOPPED TAKING METHOTREXAT)	S: YES, Hospitalization or prolonged hospitalization O: POSSIBLY DUE TO METHOTREXAT TREATMENT A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted] TRT: UPA 15 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:90.72 KG							
	PRE	TO -1						
	BLIND	1 TO 246	239	239	R: LUNG CANCER - LEFT KIDNEY & LIVER METASTASIZE S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 遠隔転移を伴う肺癌 L: Lung cancer metastatic	E: 313 L: 75 DAYS	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: DISCONTINUED STUDY	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention, Death of subject A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 15 mg QD

[redacted] AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:90.72 KG

POST 247 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:112.00 KG							
	PRE	TO -1						
	BLIND	1 TO 392	256	256	R: MYOCARDIAL INFARCTION S: Cardiac disorders P: 心筋梗塞 L: Myocardial infarction	E: 260 L: 5 DAYS	T: Life threatening R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: SUBJECT HAS SMOKING HX AND HYPERTENSION. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])							
TRT: UPA 15 mg QD							
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:112.00 KG						
		OL	393 TO				

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:74.40 KG							
	PRE	TO -1						
	BLIND	1 TO	143	143	R: JOINT PAIN S: Musculoskeletal and connective tissue disorders P: 関節痛 L: Joint pain	E: 157 L: 15 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: PATIENT HAS GENERAL JOINT PAIN DUE TO WORK-RELATED FATIGUE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 15 mg QD								
[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:72.60 KG								
	PRE	TO -1						
	BLIND	1 TO	179	179	R: QUINKE'S EDEMA S: Skin and subcutaneous tissue disorders P: 血管浮腫 L: Quincke's edema	E: 182 L: 4 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening O: ALLERGIC REACTION BECAUSE OF MEDICATION KLOFAN(CLOTRIMAZOL)

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.70 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.70 KG							
	BLIND	1 TO 13	6	6	R: CECUM CANCER WITH METASTASIS IN RIGHT HEPATIC LOBE. S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 遠隔転移を伴う結腸癌 L: Metastatic colon cancer	O: YES	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: PATIENT DOES NOT HAVE ANY NEW SYMPTOMS, RISK FACTORS ARE ABSENT, PATIENT THOUGHT THAT IT REFERS TO GALLSTONE DISEASE. THE CAUSE OF CECUM CANCER IS UNKNOWN. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.70 KG

POST 14 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])							
TRT: ADA 40 mg EOW							
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:140.40 KG						
	PRE	TO -1					
	BLIND	1 TO 64	64	R: 3MM URETERAL CALCULUS S: Renal and urinary disorders P: 尿管結石症 L: Ureteral calculus	E: 66 L: 3 DAYS	T: Life threatening R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,HOSPITALIZED)	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN AT PRESENT A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: Placebo to UPA 30 mg QD

[redacted]AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:90.20 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted] TRT: Placebo to UPA 30 mg QD									
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:90.20 KG								
		BLIND	1 TO 398	300	300	R: WORSENING LEFT UPPER ARM FRACTURE S: Injury, poisoning and procedural complications P: 上肢骨折 L: Arm fracture	E: 308 L: 9 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: UPPER ARM FRACTURE AS A RESULT OF MOTORCYCLE ACCIDENT ON [redacted] [redacted] 20[redacted]. A: NO REASONABLE POSSIBILITY
		OL	399 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.70 KG							
	PRE	TO -1						
	BLIND	1 TO	6	6	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 16 L: 11 DAYS	T: Mild R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.70 KG							
	BLIND	1 TO	223	223	R: WORSENING UTERINE FIBROIDS S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 子宫平滑肌瘤 L: Uterine fibroids aggravated	E: 232 L: 10 DAYS I: YES	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: THE PATIENT UNDERWENT SURGICAL TREATMENT. ADDITIONAL INFORMATION WILL BE RECEIVED AFTER DISCHARGE.	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: INFORMATION WILL BE PROVIDED AFTER DISCHARGE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:107.00 KG							
		PRE	TO -1					
		BLIND	1 TO 398					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:107.00 KG							
	OL	399 TO	350	748	R: STROKE S: Nervous system disorders P: 脳血管発作 L: Stroke	E: 763 L: 16 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Persistent or significant disability, Important medical or surgical intervention O: ARTERIAL HYPERTENSION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

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INV: [redacted]([redacted] TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:106.20 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	43	435	R: RECURRENCE SUPERFICIAL THROMBOPHLEBITIS LEFT LEG S: Vascular disorders P: 表在性血栓性静脈炎 L: Superficial thrombophlebitis of leg	E: 458 L: 24 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGICAL LIGATION)	S: YES, Hospitalization or prolonged hospitalization O: MASSIVE DILATED VARICOSE VEIN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

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(Safety Analysis Set)

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INV: [redacted]([redacted])
TRT: UPA 30 mg QD

[redacted] AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG							
	BLIND	1 TO 283	135	135	R: MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE) S: Injury, poisoning and procedural complications P: 粉碎骨折 L: Comminuted fracture	E: 228 L: 94 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,GYPSUM TO HOLD FIXEDLY TO TREAT)	S: YES, Hospitalization or prolonged hospitalization O: FELL DOWN THE LOWER STEP A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

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(Safety Analysis Set)

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INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG							
	BLIND	1 TO 283	135	135	R: MIDDLE AND LOWER COMMINUTED FRACTURE OF THE RIGHT TIBIA (AO43-A1 TYPE), MIDDLE RIGHT UPPER HUMERUS FRACTURE (AO 41-A1 TYPE) S: Injury, poisoning and procedural complications P: 上腕骨骨折 L: Humerus fracture	E: 228 L: 94 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,GYPSUM TO HOLD FIXEDLY TO TREAT)	S: YES, Hospitalization or prolonged hospitalization O: FELL DOWN THE LOWER STEP A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

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INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:74.00 KG							
	BLIND	1 TO 283	282	282	R: FEVER S: General disorders and administration site conditions P: 発熱 L: Fever	O: YES	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: DISCONTINUED STUDY	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	284 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:80.80 KG							
	PRE	TO -1						
	BLIND	1 TO 240	225	225	R: WORSENING HYPERTROPHY PROSTATE S: Reproductive system and breast disorders P: 良性前立腺肥大症 L: Prostatic hypertrophy	E: 254 L: 30 DAYS	T: Moderate R: No reasonable possibility A: DRUG WITHDRAWN O: TRANSURETHRAL RESECTION OF THE PROSTATE	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: INSUFFICIENT WORKING OFF TAMSULOSINE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
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Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:80.80 KG

POST 241 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:102.20 KG							
		PRE	TO -1					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

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(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:102.20 KG							
	BLIND	1 TO 58	37	37	R: NEURO-ENDOCRIENE CARCINOMA OF UNKNOWN PRIMARY SITE S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 神経内分泌癌 L: Neuroendocrine carcinoma	O: YES	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,PET SCAN,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: AGE A: NO REASONABLE POSSIBILITY
	POST	59 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

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INV: [redacted] ([redacted])								
TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:105.00 KG							
	PRE	TO -1						
	BLIND	1 TO 267						
	POST	268 TO	1	268	R: LACUNAR CEREBRAL VASCULAR ACCIDENT S: Nervous system disorders P: ラクナ脳卒中 L: Lacunar stroke		T: Severe R: Reasonable possibility A: MULTIPLE:(DRUG INTERRUPTED, DRUG WITHDRAWN) O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

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INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:86.50 KG							
	PRE	TO -1						
	BLIND	1 TO	189	189	R: VERTEBRAE L/S SPONDYLOLISTHESIS EXACERBATION S: Musculoskeletal and connective tissue disorders P: 脊椎すべり症 L: Spondylolisthesis	E: 196 L: 8 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY OF LUMBOSACRAL SPINE)	S: YES, Hospitalization or prolonged hospitalization O: VERTEBRAE L5/S1 SLIPPAGE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:75.00 KG							
	PRE	TO -1						
	BLIND	1 TO 112	19	19	R: LEFT EYE CATARACT S: Eye disorders P: 白内障 L: Left cataract	E: 19 L: 1 DAY	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY FOR EYE CATARACT WAS PERFORMED.)	S: YES, Hospitalization or prolonged hospitalization O: MEDICAL HISTORY - CATARACT SINCE 20[redacted]. A: NO REASONABLE POSSIBILITY
	POST	113 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:AMERICAN INDIAN OR ALASKA NATIVE WEIGHT:113.60 KG							
	PRE	TO -1						
	BLIND	1 TO	224	224	R: CELLULITIS RIGHT LOWER LEG S: Infections and infestations P: 蜂巢炎 L: Cellulitis of leg	E: 232 L: 9 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

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INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:99.10 KG							
	PRE	TO -1						
	BLIND	1 TO	71	71	R: FRACTURE RIGHT ANKLE S: Injury, poisoning and procedural complications P: 足関節部骨折 L: Ankle fracture		T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY, PHYSIOTHERAPY)	S: YES, Hospitalization or prolonged hospitalization O: 'THE PATIENT SLIPPED ON THE STAIRS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

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INV: [redacted]([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:55.00 KG							
	PRE	TO -1						
	BLIND	1 TO 138	138	138	R: PULMONARY EMBOLISM S: Respiratory, thoracic and mediastinal disorders P: 肺塞栓症 L: Pulmonary embolism		T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening A: NO REASONABLE POSSIBILITY
	POST	139 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

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INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:108.86 KG							
	PRE	TO -1						
	BLIND	1 TO 394						
	OL	395 TO	208	602	R: GASTROENTERITIS S: Infections and infestations P: 胃腸炎 L: Gastroenteritis	E: 608 L: 7 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

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Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:75.40 KG							
	PRE	TO -1						
	BLIND	1 TO	175	175	R: FRACTURE TIBIA-LEFT S: Injury, poisoning and procedural complications P: 脛骨骨折 L: Tibia fracture	O: YES	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: DURING PLAYING VOLLEYBALL SUBJECT FELL AND BROKE HIS LEG. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:64.50 KG

PRE TO -1

BLIND 1 TO 141

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:64.50 KG							
	POST	142 TO	4	145	R: OVARIAN CANCER S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 卵巢癌 L: Ovarian cancer	O: YES	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: DISCONTINUED STUDY	S: YES, Important medical or surgical intervention O: THERE ARE NO MEDICAL CONDITION IN MEDICAL HISTORY THAT ARE IN RELATIONSHIP WITH AE. SUBJECT DONE UNSCHEDULED CT SCAN WERE SUSPECTED OVARIAN CANCER WAS FOUND AFTER IT WAS CONFIRMED BY GYNECOLOGIST. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])							
TRT: ADA 40 mg EOW							
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:87.80 KG						
		PRE	TO -1				

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:87.80 KG							
	BLIND	1 TO 399	183	183	R: OBSTRUCTIVE SLEEP APNEA S: Respiratory, thoracic and mediastinal disorders P: 睡眠時無呼吸症候群 L: Obstructive sleep apnea syndrome	O: YES	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CPAP [redacted]20[redacted] CORRECTIVE SURGERY FOR OBSTRUCTIVE SLEEP APNEA)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: RESPIRATORY TRACT ANATOMIC ABNORMALITIES A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:87.80 KG							
	BLIND	1 TO 399	369	369	R: SURGICAL WOUND OPENING S: Injury, poisoning and procedural complications P: 創離開 L: Wound dehiscence	E: 369 L: 1 DAY	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGICAL INTERVENTION)	S: YES, Hospitalization or prolonged hospitalization O: SURGICAL INTERVENTION FOR OBSTRUCTIVE SLEEP APNEA A: NO REASONABLE POSSIBILITY
	OL	400 TO 645						
	POST	646 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:82.50 KG							
	PRE	TO -1						
	BLIND	1 TO	257	257	R: WORSENING OF HERPES ZOSTER S: Infections and infestations P: 带状疱疹 L: Herpes zoster	E: 285 L: 29 DAYS	T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,METHOTREXATE INTERRUPTED)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:75.90 KG							
	PRE	TO -1						
	BLIND	1 TO	179	179	R: DUODENAL MUCOSITIS S: Gastrointestinal disorders P: 小腸炎 L: Small intestinal mucositis	E: 182 L: 4 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])							
TRT: UPA 30 mg QD							
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.50 KG						
		PRE	TO -1				

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.50 KG							
	BLIND	1 TO 217	34	34	R: EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE S: Respiratory, thoracic and mediastinal disorders P: 慢性閉塞性肺疾患 L: Chronic obstructive airways disease exacerbated	E: 45 L: 12 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,NEBULIZATION)	S: YES, Hospitalization or prolonged hospitalization O: EXACERBATION OF EXISTING CONDITION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD									
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.50 KG								
		POST	218 TO	1	218	R: BACTEREMIA STAPHYLOCOCCUS EPIDERMIDIS S: Infections and infestations P: ブドウ球菌性菌血症 L: Staphylococcal bacteremia	E: 234 L: 17 DAYS I: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:79.50 KG							
	POST	218 TO	3	220	R: CONGESTIVE HEART FAILURE-WORSENING S: Cardiac disorders P: うっ血性心不全 L: Congestive cardiac failure aggravated	E: 234 L: 15 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: UPPER RESPIRATORY INFECTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:76.60 KG							
	PRE	TO -1						
	BLIND	1 TO 182						
	POST	183 TO	7	189	R: MULTILOBAR PNEUMONIA(GRAM POSITIVE STREPTOCOCCUS) S: Infections and infestations P: レンサ球菌性肺炎 L: Pneumonia due to Streptococcus	E: 198 L: 10 DAYS	T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 15 mg QD

[redacted] AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:81.30 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:81.30 KG							
	BLIND	1 TO 205	205	205	R: H1N1 INFLUENZA S: Infections and infestations P: H1N1インフルエンザ L: H1N1 influenza	O: YES	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization, Persistent or significant disability, Important medical or surgical intervention, Life threatening O: INFLUENZA SEASON IN THE NETHERLANDS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:81.30 KG							
	POST	206 TO	4	209	R: GASTRO INTESTINAL BLEEDING S: Gastrointestinal disorders P: 胃腸出血 L: Gastro intestinal bleeding	E: 211 L: 3 DAYS I: YES	T: Life threatening R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Life threatening O: CONCOMMITENT MEDICATION A: NO REASONABLE POSSIBILITY
			8	213	R: PULMONARY EMBOLISM S: Respiratory, thoracic and mediastinal disorders P: 肺塞栓症 L: Pulmonary embolism	O: YES I: YES	T: Life threatening R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Life threatening A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:109.54 KG							
	PRE	TO -1						
	BLIND	1 TO	186	186	R: UPPER RESPIRATORY DISTRESS S: Respiratory, thoracic and mediastinal disorders P: 呼吸窮迫 L: Respiratory distress	E: 194 L: 9 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:72.50 KG							
	PRE	TO -1						
	BLIND	1 TO	275	275	R: GONARTHROSIS OF THE RIGHT KNEE S: Musculoskeletal and connective tissue disorders P: 変形性関節症 L: Gonarthrosis	E: 282 L: 8 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: WORSENING OF GONARTHROSIS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:93.80 KG							
	PRE	TO -1						
	BLIND	1 TO 57						
	POST	58 TO	1	58	R: SEPTICEMIA S: Infections and infestations P: 敗血症 L: Septicemia	E: 66 L: 9 DAYS I: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:83.00 KG

PRE TO -1

BLIND 1 TO 392

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:83.00 KG							
	OL	393 TO	64	456	R: INJURY: END OF RADIUS FRACTURE - EXTENSION TYPE, LEFT HAND S: Injury, poisoning and procedural complications P: 橈骨骨折 L: Radius fracture		T: Mild R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY-OSTEOSYNTHESIS, DUE TO FRACTURE OF RADIUS, PLANNED HOSPITALIZATION FROM 27.2.-4.3.)	S: YES, Important medical or surgical intervention O: DUE TO AE FRACTURE OF RADIUS THERE WAS BAD HEALING OF THE FRACTURE SUBJECT WAS INVITED TO PLANNED HOSPITALIZATION [redacted] 20[redacted] A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:125.60 KG							
	PRE	TO -1						
	BLIND	1 TO 244	36	36	R: FEVER INTERMITTENT S: General disorders and administration site conditions P: 発熱 L: Intermittent fever	I: YES	T: Mild R: Reasonable possibility A: DRUG WITHDRAWN O: NONE	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention A: NO REASONABLE POSSIBILITY
	POST	245 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:71.90 KG							
	PRE	TO -1						
	BLIND	1 TO 55	21	21	R: AMYOTROPHIC LATERAL SCLEROSIS S: Nervous system disorders P: 筋萎縮性側索硬化症 L: Amyotrophic lateral sclerosis	O: YES	T: Moderate R: No reasonable possibility A: DRUG WITHDRAWN O: DISCONTINUED STUDY	S: YES, Important medical or surgical intervention O: UNKNOWN ETIOLOGY A: NO REASONABLE POSSIBILITY
	POST	56 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:124.70 KG							
	PRE	TO -1						
	BLIND	1 TO	143	143	R: LEFT LEG ERYSIPELAS S: Infections and infestations P: 丹毒 L: Erysipelas	E: 195 L: 53 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,REFER TO HOSPITAL)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:100.00 KG							
	PRE	TO -1						
	BLIND	1 TO 335	329	329	R: ARTHRITIS PURULENTA OF THE RIGHT GLENOHUMERAL JOINT S: Infections and infestations P: 細菌性関節炎 L: Purulent arthritis		T: Moderate R: No reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: MECHANICAL TRAUMA-SUBJET WAS DRIVING TRACTOR FEW DAYS BEFORE ONSET OF AE A: NO REASONABLE POSSIBILITY
	POST	336 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:92.50 KG							
	PRE	TO -1						
	BLIND	1 TO 168						
	POST	169 TO	9	177	R: LEFT LAMINAR PLEURAL EFFUSION S: Respiratory, thoracic and mediastinal disorders P: 胸水 L: Pleural effusion	E: 196 L: 20 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: CAUSE IS PROBABLY VERTEBRAL ABSSCESS

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch	Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW									
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:92.50 KG								
		POST	169 TO	9	177	R: VERTEBRAL ABSCESS S: Infections and infestations P: 骨膿瘍 L: Vertebral abscess		T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
				10	178	R: CEREBROVASCULAR ACCIDENT S: Nervous system disorders P: 脳血管発作 L: Cerebrovascular accident	E: 205 L: 28 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: CAUSE PROBABLY IS DIABETES.

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:92.50 KG							
	POST	169 TO	28	196	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 253 L: 58 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

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INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:89.00 KG							
	PRE	TO -1						
	BLIND	1 TO	240	240	R: HEADACHE WITH VOMITING S: Gastrointestinal disorders P: 嘔吐 L: Vomiting	E: 250 L: 11 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,ADMITTED TO HOSPITAL)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:3[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:89.00 KG							
	BLIND	1 TO	240	240	R: HEADACHE WITH VOMITING S: Nervous system disorders P: 頭痛 L: Headache	E: 250 L: 11 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,ADMITTED TO HOSPITAL)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:60.10 KG							
	PRE	TO -1						
	BLIND	1 TO 133	133	133	R: PORTAL VEIN THROMBOSIS S: Hepatobiliary disorders P: 門脈血栓症 L: Portal vein thrombosis	E: 142 L: 10 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	134 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:100.00 KG							
	PRE	TO -1						
	BLIND	1 TO 395	156	156	R: RIGHT ACHILLES TENDON TEAR S: Injury, poisoning and procedural complications P: 腱断裂 L: Tendon rupture		T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: PROLONGED AND INTENSIVE MECHANICAL ACTIVITY A: NO REASONABLE POSSIBILITY
	OL	396 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 15 mg QD

[redacted] AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:113.40 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:113.40 KG							
	BLIND	1 TO 392	79	79	R: GASTRIC INDIGESTION S: Gastrointestinal disorders P: 消化不良 L: Indigestion	E: 80 L: 2 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: SUBJECT HAD EATEN HEAVY MEAL CONSISTING OF PIZZA AND THEREAFTER COMPLAINED OF LEFT LOWER CHEST PAIN. A: NO REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted]
TRT: UPA 30 mg QD

[redacted]AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:96.00 KG

PRE TO -1

BLIND 1 TO 390

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:96.00 KG							
	OL	391 TO	114	504	R: DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS S: Musculoskeletal and connective tissue disorders P: 椎間板変性症 L: Degenerative disc disease	E: 507 L: 4 DAYS	T: Mild R: No reasonable possibility A: DOSE NOT CHANGED O: L5-S1 TRANSFORAMINAL LUMBAR INTERBODY FUSION	S: YES, Hospitalization or prolonged hospitalization O: LIFESTYLE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:96.00 KG							
	OL	391 TO	114	504	R: DEGENERATIVE DISC DISEASE WITH RETROLISTHESIS S: Musculoskeletal and connective tissue disorders P: 脊椎後方すべり症 L: Retrospondylolisthesis	E: 507 L: 4 DAYS	T: Mild R: No reasonable possibility A: DOSE NOT CHANGED O: L5-S1 TRANSFORAMINAL LUMBAR INTERBODY FUSION	S: YES, Hospitalization or prolonged hospitalization O: LIFESTYLE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:BLACK OR AFRICAN AMERICAN WEIGHT:114.70 KG							
	PRE	TO -1						
	BLIND	1 TO	136	136	R: ANXIETY CRISIS S: Psychiatric disorders P: 不安 L: Anxiety attack	E: 137 L: 2 DAYS	T: Severe R: No reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: RELATED TO PRE-EXISTING BIPOLAR DISORDER AND CURRENT PSYCHOSOCIAL PROBLEMS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:95.10 KG							
	PRE	TO -1						
	BLIND	1 TO 397	172	172	R: DIPLOPIA S: Eye disorders P: 複視 L: Diplopia	E: 177 L: 6 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: CORONARY ARTERY DISEASE A: NO REASONABLE POSSIBILITY
	OL	398 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:77.00 KG							
	PRE	TO -1						
	BLIND	1 TO 191	191	191	R: ACUTE BRONCHITIS S: Infections and infestations P: 気管支炎 L: Acute bronchitis	E: 217 L: 27 DAYS	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,HOSPITALIZATION)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention A: REASONABLE POSSIBILITY
	POST	192 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: Placebo to UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:68.80 KG							
	PRE	TO -1						
	BLIND	1 TO	231	231	R: WORSENING OF MEDICAL CONDITION (COLITIS) S: Gastrointestinal disorders P: 大腸炎 L: Colitis aggravated	E: 237 L: 7 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: WORSENING OF MEDICAL CONDITION (COLITIS) A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:MALE RACE:WHITE WEIGHT:102.06 KG							
	PRE	TO -1						
	BLIND	1 TO 399	77	77	R: PNEUMONIA S: Infections and infestations P: 肺炎 L: Pneumonia	E: 81 L: 5 DAYS	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	OL	400 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:ASIAN WEIGHT:65.20 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	151	543	R: BRONCHITIS S: Infections and infestations P: 気管支炎 L: Bronchitis	E: 568 L: 26 DAYS I: YES	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:ASIAN WEIGHT:65.20 KG							
	OL	393 TO	222	614	R: HERPES ZOSTER S: Infections and infestations P: 带状疱疹 L: Herpes zoster	I: YES	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:5[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:52.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:52.00 KG							
	BLIND	1 TO 196	32	32 &	R: CANCER SARCOMA (UTERINE) S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 子宮癌 L: Carcinosarcoma uterus	E: 263 L: 232 DAYS	T: Severe R: No reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,ABDOMINAL TYPE EXTENSIVE HYSTERECTOMY ADNEXECTOMY(BOTH) LYMPH NODEDISSECTION(PELVIC) PARA-AORTIC LYMPH NODES BIOPSY BILATERAL URETERAL STENT PLACEMENT)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: CONSISTENT WITH GENERAL RISK FACTORS SUCH AS AGE, FEMALE, MENOPAUSE, FIRST BIRTH, AND LESS CHILDBIRTH EXPERIENCE. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted] AGE:5[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:52.00 KG

POST 197 TO

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:131.50 KG							
	PRE	TO -1						
	BLIND	1 TO	276	276	R: RENAL CALCULI S: Renal and urinary disorders P: 腎結石症 L: Renal calculi	E: 277 L: 2 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:71.00 KG							
	PRE	TO -1						
	BLIND	1 TO 388	209	209	R: FRACTURE OF LEFT FOOT S: Injury, poisoning and procedural complications P: 足骨折 L: Foot fracture		T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,PATIENT TO HAVE SURGERY)	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: TWISTED ANKLE AND FELL OVER. A: NO REASONABLE POSSIBILITY
	OL	389 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:56.70 KG							
	PRE	TO -1						
	BLIND	1 TO 392	303	303	R: HYPERTROPHY OF TONSILS S: Respiratory, thoracic and mediastinal disorders P: 扁桃肥大 L: Tonsillar hypertrophy	E: 304 L: 2 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGERY)	S: YES, Hospitalization or prolonged hospitalization O: HYPERTROPHY OF TONSILS A: NO REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:102.90 KG							
	PRE	TO -1						
	BLIND	1 TO 63	55	55	R: ACUTE SEPSIS S: Infections and infestations P: 敗血症 L: Sepsis	O: YES	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	POST	64 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:91.20 KG							
	PRE	TO -1						
	BLIND	1 TO 396	396	396 &	R: LEFT THIGH BASAL CELL CARCINOMA S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 基底細胞癌 L: Basal cell carcinoma	E: 446 L: 51 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Important medical or surgical intervention A: NO REASONABLE POSSIBILITY
	OL	397 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
& Date is estimated.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:71.20 KG							
	PRE	TO -1						
	BLIND	1 TO 83	64	64	R: FEVER OF UNKNOWN ORIGIN S: General disorders and administration site conditions P: 発熱 L: Fever of unknown origin	E: 90 L: 27 DAYS I: YES	T: Moderate R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	POST	84 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: UPA 15 mg QD

[redacted]AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:93.00 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:93.00 KG							
	BLIND	1 TO 398	51	51	R: CHRONIC LARYNGITIS S: Infections and infestations P: 喉頭炎 L: Chronic laryngitis	E: 52 L: 2 DAYS I: YES	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: NONE	S: YES, Hospitalization or prolonged hospitalization O: BECAUSE OF RETURNING HOARSENESS THAT HAS EXISTED FOR YEARS LARYNGOSCOPY AND OESOPHAGOSCOPY WAS PERFORMED.THE RESULT IS CHRONIC MUCOUS INFLAMMATION. A: NO REASONABLE POSSIBILITY
	OL	399 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:WHITE WEIGHT:69.50 KG							
	PRE	TO -1						
	BLIND	1 TO 159						
	POST	160 TO	1	160	R: ADENOCARCINOMA G-3 BRONCHUS S: Neoplasms benign, malignant and unspecified (incl cysts and polyps) P: 肺腺癌 L: Adenocarcinoma lung	O: YES	T: Moderate R: No reasonable possibility A: DRUG WITHDRAWN O: NONE	S: YES, Important medical or surgical intervention O: SMOKER A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:147.30 KG							
	PRE	TO -1						
	BLIND	1 TO 70	33	33	R: POSSIBLE STAPH INFECTION S: Infections and infestations P: ブドウ球菌感染 L: Staphylococcal infection	O: YES	A: DOSE NOT CHANGED O: HOSPITALIZATION	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY
	POST	71 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:76.40 KG							
	PRE	TO -1						
	BLIND	1 TO	21	21	R: ACUTE APPENDICITIS S: Infections and infestations P: 虫垂炎 L: Acute appendicitis	E: 22 L: 2 DAYS	T: Mild R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:83.00 KG							
	PRE	TO -1						
	BLIND	1 TO	79	79	R: TOENAILS INGROWN WORSENING S: Skin and subcutaneous tissue disorders P: 嵌入爪 L: Ingrown toe nail	E: 232 L: 154 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: PARTIAL SURGICAL REMOVAL OF THE BOTH TOENAILS	S: YES, Hospitalization or prolonged hospitalization O: REPETITIVE PRESSURE TO THE FEET A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])							
TRT: UPA 30 mg QD							
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:74.00 KG						
	PRE	TO -1					
	BLIND	1 TO 72					
	POST	73 TO 18	90	R: IRON DEFICIENT ANAEMIA S: Blood and lymphatic system disorders P: 鉄欠乏性貧血 L: Iron deficiency anaemia		T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: HOSPITALIZED FOR FURTHER INVESTIGATION	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: UNSPECIFIED INFECTION A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted]([redacted])
TRT: ADA 40 mg EOW

[redacted]AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:73.90 KG

PRE	TO -1
BLIND	1 TO 392

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:FEMALE RACE:WHITE WEIGHT:73.90 KG							
	OL	393 TO	261	653	R: PERICARDITIS S: Cardiac disorders P: 心膜炎 L: Pericarditis	E: 662 L: 10 DAYS	T: Life threatening R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization, Important medical or surgical intervention O: LONG TERM SMOKER, PSORIATIC ARTHRITIS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:ASIAN WEIGHT:61.30 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	161	553	R: CORONARY ARTERY DISEASE S: Cardiac disorders P: 冠動脈疾患 L: Coronary artery disease		T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 30 mg QD

[redacted] AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:64.90 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:64.90 KG							
	BLIND	1 TO 392	157	157	R: CORONARY ARTERIAL DISEASE S: Cardiac disorders P: 冠動脈疾患 L: Coronary artery disease		T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED, STOP IMP SINCE [redacted] [redacted] 20[redacted]. O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: IN THE JUDGMENT OF THE PRINCIPAL INVESTIGATOR, THE EVENT WAS NOT RELATED TO THE STUDY DRUG AND ANGIOGRAPHY IS A PROCEDURE AND NOT A SURGERY BECAUSE NO INCISION AND SUTURE WAS NEEDED. A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:ASIAN WEIGHT:64.90 KG							
	BLIND	1 TO 392	378	378	R: AVASCULAR NECROSIS OF BILATERAL HIP JOINTS S: Musculoskeletal and connective tissue disorders P: 骨壊死 L: Avascular necrosis of bone	E: 493 L: 116 DAYS	T: Severe R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: SMOKING AND RECEIVING LOCAL TRIAMCINOLONE INJECTION WERE CONSIDERED AS CAUSE OF THE EVENT. A: NO REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Day	Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 30 mg QD

[redacted] AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:104.20 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:104.20 KG							
	BLIND	1 TO 6	6	6	R: LIMITED PNEUMOPHIBROSIS OF THE LOWER LOBE OF THE RIGHT LUNG. HYPERPLASIA OF MEDIASTINAL LYMPH NODES S: Blood and lymphatic system disorders P: リンパ組織過形成 L: Lymphoid tissue hyperplasia	O: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: SMOCKING A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:104.20 KG							
	BLIND	1 TO 6	6	6	R: LIMITED PNEUMOPHIBROSIS OF THE LOWER LOBE OF THE RIGHT LUNG. HYPERPLASIA OF MEDIASTINAL LYMPH NODES S: Respiratory, thoracic and mediastinal disorders P: 肺線維症 L: Pulmonary fibrosis	O: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization O: SMOCKING A: NO REASONABLE POSSIBILITY
	POST	7 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:45.30 KG							
	PRE	TO -1						
	BLIND	1 TO	122	122	R: FIBROCYSTIC MASTOPATHY OF THE LEFT BREAST S: Reproductive system and breast disorders P: 線維嚢胞性乳腺疾患 L: Fibrocystic breast disease	E: 129 L: 8 DAYS	T: Moderate R: Reasonable possibility A: DRUG INTERRUPTED O: LEFT BREAST' NEOPLASM SURGERY REMOVING	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:5[redacted] SEX:MALE RACE:WHITE WEIGHT:77.40 KG							
	PRE	TO -1						
	BLIND	1 TO 13						
	POST	14 TO	2	15	R: DERMATITIS WORSENING S: Skin and subcutaneous tissue disorders P: 皮膚炎 L: Dermatitis NOS aggravated	E: 23 L: 9 DAYS	T: Severe R: Reasonable possibility A: DOSE NOT CHANGED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:FEMALE RACE:WHITE WEIGHT:60.80 KG							
	PRE	TO -1						
	BLIND	1 TO 393	338	338	R: HERPES ZOSTER THORACIS LOCALIZED S: Infections and infestations P: 带状疱疹 L: Herpes zoster	E: 417 L: 80 DAYS	T: Moderate R: Reasonable possibility A: DOSE NOT CHANGED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	OL	394 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:84.10 KG							
	PRE	TO -1						
	BLIND	1 TO 258	257	257	R: STAPHYLOCOCCUS AUREUS SEPSIS S: Infections and infestations P: ブドウ球菌性敗血症 L: Staphylococcus aureus septicemia	E: 642 L: 386 DAYS	T: Life threatening R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CONCOMITANT MEDICATION OR THERAPY DISCONTINUED)	S: YES, Hospitalization or prolonged hospitalization, Life threatening O: POSTRAUMATIC FRACTURE OF RIGHT 5. METACARPAL BONE (AE) A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:MALE RACE:WHITE WEIGHT:84.10 KG							
		POST	259 TO					

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: Placebo to UPA 30 mg QD								
[redacted]	AGE:7[redacted] SEX:FEMALE RACE:WHITE WEIGHT:86.18 KG							
	PRE	TO -1						
	BLIND	1 TO 386	320	320	R: KIDNEY STONE S: Renal and urinary disorders P: 腎結石症 L: Kidney stone	E: 327 L: 8 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,CT SCAN)	S: YES, Hospitalization or prolonged hospitalization O: NATURALLY PREDISPOSED TO KIDNEY STONE DEVELOPMENT A: NO REASONABLE POSSIBILITY
	OL	387 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	RX Day of Day	Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:85.05 KG							
	PRE	TO -1						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted] TRT: UPA 30 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:85.05 KG							
	BLIND	1 TO 392	313	313	R: COLLAPSED AVASCULAR NECROSIS OF THE LEFT HUMERAL HEAD WITHOUT OBVIOUS GLENOID INVOLVEMENT. S: Musculoskeletal and connective tissue disorders P: 骨壊死 L: Avascular necrosis	E: 369 L: 57 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,SURGICAL REPAIR)	S: YES, Hospitalization or prolonged hospitalization O: HEMIARTHROPLASTY OF L SHOULDER A: NO REASONABLE POSSIBILITY
	OL	393 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: ADA 40 mg EOW								
[redacted]	AGE:6[redacted] SEX:MALE RACE:ASIAN WEIGHT:49.00 KG							
	PRE	TO -1						
	BLIND	1 TO 392						
	OL	393 TO	30	422	R: LEFT DORSAL CELLULITIS S: Infections and infestations P: 蜂巢炎 L: Cellulitis	O: YES	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:3[redacted] SEX:MALE RACE:ASIAN WEIGHT:56.00 KG							
	PRE	TO -1						
	BLIND	1 TO	309	309	R: LEFT SPONTANEOUS PNEUMOTHORAX S: Respiratory, thoracic and mediastinal disorders P: 自然気胸 L: Pneumothorax spontaneous	O: YES	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: OXYGEN CURE	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:ASIAN WEIGHT:67.00 KG							
	PRE	TO -1						
	BLIND	1 TO 234+	206	206	R: URINARY TRACT INFECTION S: Infections and infestations P: 尿路感染 L: Urinary tract infection	O: YES	T: Severe R: Reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
+ Subject is ongoing.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted])								
TRT: UPA 30 mg QD								
[redacted]	AGE:4[redacted] SEX:MALE RACE:ASIAN WEIGHT:70.00 KG							
	PRE	TO -1						
	BLIND	1 TO 64	60	60	R: PULMONARY INFECTION S: Infections and infestations P: 肺感染 L: Lung infection	O: YES	T: Severe R: Reasonable possibility A: DRUG WITHDRAWN O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY DISCONTINUED,DISCONTINUED STUDY)	S: YES, Hospitalization or prolonged hospitalization A: REASONABLE POSSIBILITY
	POST	65 TO						

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.
# Subject prematurely discontinued.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality

INV: [redacted] ([redacted])
TRT: UPA 15 mg QD

[redacted]AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.50 KG

PRE TO -1

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.50 KG							
	BLIND	1 TO	110	110	R: WORSENING OF PROLAPSE OF THE UTERUS S: Reproductive system and breast disorders P: 子宮脱 L: Uterine prolapse	E: 110 L: 1 DAY	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,TRANSVAGINAL ULTRASOUND, VAGINAL COLPOSCOPY, UTERUS ULTRASOUND)	S: YES, Hospitalization or prolonged hospitalization O: UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	Name	Epoch Interval	Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted]) TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.50 KG							
	BLIND	1 TO	154	154	R: WORSENING OF PROLAPSE OF THE UTERUS S: Reproductive system and breast disorders P: 子宮脱 L: Uterine prolapse	E: 166 L: 13 DAYS	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: MULTIPLE:(CONCOMITANT MEDICATION OR THERAPY STARTED,HOSPITALIZATION)	S: YES, Hospitalization or prolonged hospitalization O: [redacted] [redacted] 20[redacted] FOLLOW UP- OTHER ETIOLOGY-AFTER BIRTH OF CHILDREN [redacted]20[redacted]: OTHER SUSPECTED CAUSES ARE UNKNOWN- NO INFORMATION ON DISCHARGED SUMMARY REPORT OTHER SUSPECTED CAUSES ARE UNKNOWN A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted] ([redacted] TRT: UPA 15 mg QD								
[redacted]	AGE:6[redacted] SEX:FEMALE RACE:WHITE WEIGHT:82.50 KG							
	BLIND	1 TO	209	209	R: DROOPING EYELIDS S: Eye disorders P: 眼瞼下垂 L: Eyelid ptosis	E: 209 L: 1 DAY	T: Moderate R: No reasonable possibility A: DRUG INTERRUPTED O: CONCOMITANT MEDICATION OR THERAPY STARTED	S: YES, Hospitalization or prolonged hospitalization O: DUE TO AGE A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

TABLE 14.3__2.18.1.2

Listing of Subjects with Treatment-Emergent Serious Adverse Events - Long Term
(Safety Analysis Set)

Subject Number	------ Name	Epoch Interval	---- Day	RX Day of Onset	R: Reported Term S: System Organ Class P: MedDRA 22.0 Preferred Term L: Lower Level Term	E: RX Day Ended O: Ongoing at the End of Study? L: Length I: Intermittent?	T: Toxicity Grade R: Relationship to Study Treatment A: Action Taken with Study Treatment O: Other Actions Taken	S: Serious AE? O: Other Cause of Event A: Abbvie Opinion of Causality
INV: [redacted]([redacted]) TRT: UPA 30 mg QD								
[redacted]	AGE:3[redacted] SEX:MALE RACE:WHITE WEIGHT:95.10 KG							
	PRE	TO -1						
	BLIND	1 TO	174	174	R: HOSPITALIZATION DUE TO PSORIATIC ARTHRITIS ACTIVITY ASSESSMENT S: Musculoskeletal and connective tissue disorders P: 乾癬性関節症 L: Psoriatic arthritis	E: 180 L: 7 DAYS	T: Moderate R: No reasonable possibility A: DOSE NOT CHANGED O: BLOOD EXAMINATION, ABDOMINAL ULTRASOUND	S: YES, Hospitalization or prolonged hospitalization O: PSORIATIC ARTHRITIS A: NO REASONABLE POSSIBILITY

Note: Treatment-emergent AE (TEAE) is defined as an AE with an onset date that is on or after the first dose of study drug and up to 30 days after the last dose of UPA and up to 70 days for adalimumab, if subject discontinued prematurely from the study.
PRE = Screening; BLIND = Blinded treatment; OL = Open label treatment; POST = Post study drug.

Program Source Code: [redacted]

表 2.7.4.7-25.　　投与 24 週時までの重篤な有害事象（安全性解析対象集団）：M15-554 試験

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
Any adverse event	4 (1.9)	12 (5.7)	18 (8.3)
血液およびリンパ系障害	0	1 (0.5)	0
失血性貧血	0	1 (0.5)	0
心臓障害	1 (0.5)	2 (0.9)	4 (1.8)
急性心筋梗塞	0	1 (0.5)	0
不安定狭心症	1 (0.5)	0	1 (0.5)
心房細動	0	0	1 (0.5)
徐脈	0	0	1 (0.5)
心肺停止	0	1 (0.5)	0
冠動脈狭窄	0	0	1 (0.5)
心室細動	0	1 (0.5)	0
胃腸障害	0	1 (0.5)	2 (0.9)
腹痛	0	0	1 (0.5)
下痢	0	0	1 (0.5)
びらん性胃炎	0	1 (0.5)	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
胃腸障害 (Cont.)			
小腸潰瘍	0	0	1 (0.5)
一般・全身障害および投与部位の状態	0	0	1 (0.5)
全身性炎症反応症候群	0	0	1 (0.5)
感染症および寄生虫症	1 (0.5)	1 (0.5)	6 (2.8)
菌血症	0	0	1 (0.5)
気管支炎	0	0	1 (0.5)
ブドウ球菌感染性滑液包炎	1 (0.5)	0	0
硬膜外膿瘍	0	0	1 (0.5)
肺炎	0	1 (0.5)	3 (1.4)
尿路感染	0	0	1 (0.5)
傷害、中毒および処置合併症	2 (0.9)	1 (0.5)	1 (0.5)
転倒	0	1 (0.5)	0
大腿骨頚部骨折	0	0	1 (0.5)
腓骨骨折	1 (0.5)	0	0
肋骨骨折	1 (0.5)	0	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
傷害、中毒および処置合併症 (Cont.)			
交通事故	1 (0.5)	0	0
外傷性血胸	1 (0.5)	0	0
血管偽動脈瘤	1 (0.5)	0	0
筋骨格系および結合組織障害	0	6 (2.8)	0
側腹部痛	0	1 (0.5)	0
変形性関節症	0	1 (0.5)	0
乾癬性関節症	0	2 (0.9)	0
急速進行性変形性関節症	0	1 (0.5)	0
全身性エリテマトーデス	0	1 (0.5)	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	2 (0.9)	2 (0.9)
卵巣癌	0	0	1 (0.5)
前立腺癌	0	1 (0.5)	0
直腸腺癌	0	0	1 (0.5)
直腸癌	0	1 (0.5)	0
子宮平滑筋腫	1 (0.5)	0	0

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

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
神経系障害	0	1 (0.5)	1 (0.5)
浮動性めまい	0	1 (0.5)	0
会話障害	0	1 (0.5)	0
一過性全健忘	0	0	1 (0.5)
妊娠、産褥および周産期の状態	0	0	1 (0.5)
異所性妊娠	0	0	1 (0.5)
精神障害	0	1 (0.5)	0
失見当識	0	1 (0.5)	0
腎および尿路障害	0	2 (0.9)	1 (0.5)
急性腎障害	0	0	1 (0.5)
腎結石症	0	2 (0.9)	0
生殖系および乳房障害	0	0	1 (0.5)
良性前立腺肥大症	0	0	1 (0.5)
呼吸器、胸郭および縦隔障害	0	1 (0.5)	1 (0.5)
急性呼吸不全	0	1 (0.5)	1 (0.5)

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

Program Source Code: [redacted]

TABLE 14.3__2.1.1

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

System Organ Class MedDRA 22.0 Preferred Term	Placebo (N = 212) n (%)	UPA 15 mg QD (N = 211) n (%)	UPA 30 mg QD (N = 218) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)			
肺塞栓症	0	1 (0.5)	0

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

Program Source Code: [redacted]