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略号一覧

略号	内容
ALP	Alkaline phosphatase（アルカリホスファターゼ）
ALT	Alanine aminotransferase（アラニンアミノトランスフェラーゼ）
AST	Aspartate aminotransferase（アスパラギン酸アミノトランスフェラーゼ）
$AUC_{0-\infty}$	Area under the curve from time zero to infinity （無限大時間時間までの濃度-時間曲線下面積）
CI	Confidence interval（信頼区間）
CL_{CR}	Creatinine clearance（クレアチニンクリアランス）
C_{max}	Maximum plasma concentration（最高血漿中濃度）
CYP	Cytochrome P450（シトクロム P450）
DBP	Diastolic blood pressure（拡張期血圧）
HBV	Hepatitis B virus carrier（B 型肝炎ウイルス）
HCV	Hepatitis C virus carrier（C 型肝炎ウイルス）
IBLS	ITP Bleeding Score
ITP	Idiopathic trombocytopenic purpura（特発性血小板減少性紫斑病）
KPS	Karnofsky Performance Status
LDH	Lactate dehydrogenase（乳酸脱水素酵素）
MedDRA	Medical Dictionary for Regulatory Activities Terminology（ICH 国際医薬用語集）
PT	Preferred term（基本語）
R788	Fostamatinib（ホスタマチニブナトリウム水和物）
RA	Rheumatoid arthritis（関節リウマチ）
SBP	Systolic blood pressure（収縮期血圧）
SD	Standard deviation（標準偏差）
SMQ	Standardised MedDRA Queries（MedDRA 標準検索式）
SOC	System organ class（器官別大分類）
Syk	Spleen tyrosine kinase（脾臓チロシンキナーゼ）
TPO	Thrombopoietin（トロンボポエチン）

2.7.4 臨床的安全性

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

特発性血小板減少性紫斑病（ITP）患者に対する R788 の安全性は、国内第 III 相臨床試験（R788-1301）、海外第 III 相臨床試験（1）（C788-047）、海外第 III 相臨床試験（2）（C788-048）、海外第 III 相継続投与試験（C788-049）及び海外第 II 相臨床試験（D4300-022）の 5 試験を評価資料とし、これらの試験成績に基づき評価した。

健康成人及び特別な患者集団に対する R788 の安全性は、第 I 相臨床試験 5 試験（C406-001、C788-001、C788-003、D4300-007 及び D4300-032）、バイオアベイラビリティ評価試験（D4300-027）、マスバランス試験（C788-014）、腎機能低下者試験（D4300-009）、肝機能低下者試験（D4300-010）、薬物相互作用試験 10 試験（C788-004、C788-018、D4300-011、D4300-012、D4300-013、D4300-014、D4300-015、D4300-019、D4300-026 及び D4300-039）、QT/QTc 評価試験（C788-013）及び生物学的同等性試験 2 試験（D4300-020 及び C788-054）の計 22 試験により評価し、そのうち、日本人の健康成人を対象とした D4300-007 及び D4300-032 試験を評価資料とした。

その他、日本人を含むアジア人の関節リウマチ（RA）患者を対象とした 2 試験（D4300-008 及び D4300-029）についても参考資料として安全性を評価する臨床試験に含めた。

海外第 III 相臨床試験の 3 試験については、プラセボと R788 の比較を目的とした C788-047 及び C788-048 試験の 2 試験の統合解析、並びに長期投与時の評価を目的とした C788-047、C788-048 及び C788-049 試験の 3 試験の統合解析を実施した。

なお、R788-1301 試験は、20[redacted] 年 [redacted] 月 [redacted] 日のデータカットオフ時点までのデータを対象とした。評価は、第 I 期のデータを評価したプラセボ対照期、第 I 期で R788 に割り付けられた被験者を対象に第 II 期のデータも含めて評価した R788 長期投与時、第 I 期又は第 II 期のいずれかで R788 を投与した被験者の第 III 期までの R788 の全投与期間を評価した R788 投与期、並びに休薬期に移行した被験者の休薬期データを評価した休薬期を対象とした。各評価は、プラセボと R788 の比較を目的としてプラセボ対照期、R788 を長期間投与した際の臨床検査及びバイタルサインの評価を目的として R788 長期投与時、R788 を長期間投与した際の有害事象の評価を目的として R788 投与期、並びに R788 を休薬した際に与える影響の評価を目的として休薬期をそれぞれ設定した。

評価資料とする臨床試験の一覧を表 2.7.4.1.1-1 及び表 2.7.4.1.1-2 に示す。

表 2.7.4.1.1-1　　臨床的安全性試験の要約（評価資料）～患者対象試験

試験番号 添付資料番号	国内/海外 施設数	試験デザイン	対象	投与量 投与方法	安全性解析対象集団/登録時の被験者数	投与期間	安全性評価項目
R788-1301 5.3.5.1.1	国内 42 施設	第 I 期： 二重盲検 無作為化 プラセボ対照 第 II 期、休薬期、第 III 期： 非盲検	慢性 ITP 患者	第 I 期： R788 100 mg 又は 150 mg（血小板数を基に増量） プラセボ 1 日 2 回投与 第 II 期： R788 100 mg 又は 150 mg（第 I 期の血小板数を基に決定） 1 日 2 回投与 休薬期： 治験薬を投与しない 第 III 期： R788 100 mg 又は 150 mg（第 II 期の最終の用法・用量） 1 日 2 回投与	第 I 期： R788 群　22/22 例 プラセボ群　12/12 例 第 II 期（継続投与例）： 第 I 期 R788 群　10/10 例 第 I 期プラセボ群　4/4 例 第 II 期（早期移行例） 第 I 期 R788 群　9/9 例 第 I 期プラセボ群　7/7 例 休薬期　12/12 例 第 III 期　22/22 例 （第 III 期はデータカットオフ時点）	第 I 期：24 週間 第 II 期：28 週間 休薬期：4 週間 第 III 期：製造販売承認まで	・有害事象 ・臨床検査 ・免疫グロブリン検査 ・ITP Bleeding Score ・ECOG Performance Status ・バイタルサイン ・12 誘導心電図
C788-047 5.3.5.1.2	海外 35 施設	二重盲検 無作為化 プラセボ対照	持続性/慢性 ITP 患者	R788 100 mg 又は 150 mg（血小板数を基に増量） プラセボ 1 日 2 回経口投与	R788 群　51/51 例 プラセボ群　25/25 例	24 週間	・有害事象 ・臨床検査 ・免疫グロブリン検査 ・Karnofsky Performance Status ・バイタルサイン ・12 誘導心電図
C788-048 5.3.5.1.3	海外 23 施設	二重盲検 無作為化 プラセボ対照	持続性/慢性 ITP 患者	R788 100 mg 又は 150 mg（血小板数を基に増量） プラセボ 1 日 2 回経口投与	R788 群　51/50 例 プラセボ群　23/24 例	24 週間	・有害事象 ・臨床検査 ・免疫グロブリン検査 ・Karnofsky Performance Status ・バイタルサイン ・12 誘導心電図

試験番号 添付資料番号	国内/海外 施設数	試験デザイン	対象	投与量 投与方法	安全性解析対象集団/登録時の被験者数	投与期間	安全性評価項目
D4300-022 5.3.5.2.1	海外 2 施設	非盲検 用量漸増	難治性 ITP 患者	R788 75～175 mg 1 日 2 回経口投与	R788 群　18/18 例	3 ヵ月間（継続可能）	・有害事象 ・臨床検査 ・バイタルサイン ・12 誘導心電図
C788-049 5.3.5.2.2	海外 54 施設	非盲検	C788-047 及び C788-048 試験を終了した持続性/慢性 ITP 患者	R788 100 mg 又は 150 mg（前試験の血小板数を基に決定） 1 日 2 回投与	R788 群　123/123 例	5 年間又は製造販売承認後上市まで	・有害事象 ・臨床検査 ・免疫グロブリン検査 ・Karnofsky Performance Status ・バイタルサイン ・12 誘導心電図

表 2.7.4.1.1-2　臨床的安全性試験の要約（評価資料）～第 I 相臨床試験及び臨床薬理試験

試験番号 添付資料番号	国内/海外 施設数	試験デザイン	対象	投与量 投与方法	投与例数	投与期間
D4300-007 5.3.3.3.1	海外 1 施設	無作為化 二重盲検 プラセボ対照	日本人又は白人健康成人	R788 50 mg 1 日 2 回 R788 100 mg 1 日 2 回 R788 150 mg 1 日 1 回 R788 200 mg 1 日 2 回 プラセボ 単回投与後、7 日間反復投与	R788 50 mg 群　6 例 R788 100 mg 群　6 例 R788 150 mg 群　24 例 R788 200 mg 群　6 例 プラセボ群　14 例	単回投与後、7 日間反復投与
D4300-032 5.3.3.3.2	海外 1 施設	非盲検	日本人健康成人	R788 100 mg 1 日 2 回 R788 200 mg 1 日 2 回 単回投与後、7 日間反復投与	R788 100 mg 群　12 例 R788 200 mg 群　12 例	単回投与後、7 日間反復投与

本薬の安全性評価項目は有害事象、副作用、臨床検査、バイタルサイン及び 12 誘導心電図であり、ITP 患者を対象とした臨床試験では ITP Bleeding Score（IBLS）（海外第 III 相臨床試験では ITP Bleeding Score 及び WHO Bleeding Scale scores を有効性評価として実施）及び ECOG Performance Status（海外第 III 相臨床試験は Karnofsky Performance Status）を併せて評価した。

有害事象は、症例報告書に記載された症状・項目名を「ICH 国際医薬用語集（MedDRA）」に準じて基本語へ読み替えた。各試験で使用した MedDRA のバージョンは、各試験の「2.7.6 個々の試験のまとめ」に示した。統合解析では、統合する試験の有害事象を MedDRA Ver.18.1 で読み替えて集計した。

有害事象とは、被験者に生じたあらゆる好ましくない、又は意図しない徴候、症状、合併症の悪化又は病気のことであり、当該治験薬との因果関係の有無は問わないこととした。また、治験薬投与前に発現した事象のうち、治験薬投与後に症状又は検査値が悪化した場合も、新たに発現した有害事象として扱った。

R788-1301 試験において、有害事象発現時の治験薬に対する処置は、「中止」、「休薬」、「減量」、「投与量変更せず」、「不明」及び「該当せず」に分類して評価した（詳細は表 2.7.4.1.1-3 参照）。

R788-1301 試験において、有害事象と治験薬との因果関係は、「有」又は「無」の 2 段階で評価し、「有」を副作用とした。C788-047、C788-048 及び C788-049 試験において、有害事象と治験薬との因果関係は、「おそらく関連あり（Probable）」、「関連があるかもしれない（Possible）」又は「おそらく関連なし（Unlikely）」の 3 段階で評価し、「おそらく関連あり」及び「関連あるかもしれない」を副作用とした。D4300-022 試験において、有害事象と治験薬との因果関係は、「おそらく関連あり（Probable）」、「関連があるかもしれない（Possible）」、「おそらく関連なし（Unlikely）」又は「関連なし（Not Related）」の 4 段階で評価し、「おそらく関連あり」及び「関連があるかもしれない」を副作用とした。すべての臨床試験で有害事象の程度は、「軽度（Mild）」、「中等度（Moderate）」又は「高度（Severe）」の 3 段階で評価した。

表 2.7.4.1.1-3　　有害事象発現時の治験薬に対する処置

処置	定義
中止	被験者の申し出も含めて、当該有害事象により治験薬の投与を中止した場合
休薬	被験者の申し出も含めて、当該有害事象により治験薬を休薬した場合
減量	被験者の申し出も含めて、当該有害事象により治験薬を減量した場合 増量基準に該当したが、当該有害事象により治験薬を増量できなかった場合
投与量変更せず	治験薬に対する処置を行わずに投与を継続した場合
不明	治験薬に対する処置が確認できない場合
該当せず	当該有害事象発現前に治験薬の投与終了又は投与中止されていた場合

2.7.4.1.2 全般的な曝露状況

2.7.4.1.2.1 治験薬への曝露状況

2.7.4.1.2.1.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験の曝露状況を表 2.7.4.1.2.1.1-1 に示す。

R788-1301 試験に無作為割付けされた例数は、R788 群 22 例及びプラセボ群 12 例であった。また、R788 長期投与時 22 例（第 I 期 R788 群 22 例）、R788 投与期 33 例、休薬期 12 例及び第

III 期 22 例を解析対象とした。

全被験者のプラセボ対照期の曝露期間の中央値は R788 群 99 日（範囲：42～170 日）及びプラセボ群 88 日（範囲：16～169 日）であった。R788 群の曝露期間はプラセボ群と比較してやや長かった。R788 群の 1 日平均投与量の中央値は 236 mg（範囲：143～283 mg）であり、プラセボ群ではR788 の投与量に相当する集計として 267 mg（範囲：200～283 mg）であった。R788 投与期の 33 例中 22 例は、第 I 期から R788 が投与されており、11 例は第 I 期でプラセボが投与された後に第 II 期で R788 が投与された。R788 投与期の曝露期間の中央値は 365 日（範囲：42～785 日）であった。

曝露期間及び 1 日平均投与量の中央値は、海外第 III 相臨床試験の結果と同様の傾向を示した。

表 2.7.4.1.2.1.1-1 国内第 III 相臨床試験（R788-1301）の曝露状況

Variable	Period I		R788 Treatment Period (N=33)
	R788 (N=22)	Placebo (N=12)	
Duration of Exposure (days)			
Median	99	88	365
Min, Max	42, 170	16, 169	42, 785
Duration of Exposure Category, n (%)			
< 4 weeks	0 (0.0)	1 (8.3)	0 (0.0)
≥ 4 weeks, < 8 weeks	1 (4.5)	0 (0.0)	1 (3.0)
≥ 8 weeks, < 12 weeks	1 (4.5)	0 (0.0)	1 (3.0)
≥ 12 weeks, < 24 weeks	20 (90.9) [a]	11 (91.7) [a]	3 (9.1)
≥ 24 weeks, < 52 weeks	---	---	11 (33.3)
≥ 52 weeks	---	---	17 (51.5)
Average Daily Dose (mg)			
Median	236	267	237
Min, Max	143, 283	200, 283	145, 295

a プラセボ対照期に曝露期間が 12 週以上であった被験者
(Source: 5.3.5.1.1, 表 12.1.1-1、表 12.1.1-2、表 12.1.3-1、表 12.1.3-2、Table 14.1.2.2.1 及び Table 14.3.2.2.1 改編)

2.7.4.1.2.1.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047、C788-048 及び C788-049 試験の曝露状況を表 2.7.4.1.2.1.2-1 に示す。

C788-047 試験に無作為割付けされた例数は、R788 群 51 例及びプラセボ群 25 例であった。C788-048 試験に無作為割付けされた例数は、R788 群 50 例及びプラセボ群 24 例であったが、プラセボ群に割り付けられた 1 例において Week 2 に誤って R788 が投与されたため、安全性解析対象集団では投与された治験薬に従い R788 群として集計した。また、C788-047 及び C788-048 試験に無作為に割り付けられた計 150 例をプラセボ対照期（Placebo-Controlled Period）として統合解析を実施した。

プラセボ対照期の曝露期間の中央値は R788 群 12.29 週（範囲：1.1～26.1 週）及びプラセボ群 12.14 週（範囲：2.3～24.7 週）であった。R788 群の 1 日投与量の中央値は 258.84 mg（範囲：40.0～389.7 mg）であり、プラセボ群では R788 の投与量に相当する集計として 258.97 mg（範囲：131.3～270.2 mg）であった。

C788-047、C788-048 又は C788-049 試験のいずれかの試験で R788 が投与された 146 例が R788 投与期（Fostamatinib Exposure Period）の解析対象となった。146 例中 102 例は C788-047 又は C788-048 試験から R788 が投与されており、44 例は C788-047 又は C788-048 試験でプラセボが投与された後に C788-049 試験で R788 が投与された。R788 投与期の曝露期間の中央値は 29.14

週（範囲：1.1～268.1 週）であった。

表 2.7.4.1.2.1.2-1　海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の曝露状況

Variable	Placebo-Controlled Period [a] (N=150)		Fostamatinib Exposure Period [b] (N=146)
	R788 (N=102)	Placebo (N=48)	
Duration of Exposure (weeks)			
Median	12.29	12.14	29.14
Min, Max	1.1, 26.1	2.3, 24.7	1.1, 268.1
Duration of Exposure Category, n (%) [c]			
< 4 weeks (< 28 days)	4 (3.9)	3 (6.3)	4 (2.7)
≥ 4 weeks (≥ 28 days)	98 (96.1)	45 (93.8)	142 (97.3)
≥ 8 weeks (≥ 56 days)	93 (91.2)	45 (93.8)	134 (91.8)
≥ 12 weeks (≥ 84 days)	78 (76.5)	38 (79.2)	125 (85.6)
≥ 24 weeks (≥ 168 days)	20 (19.6)	2 (4.2)	98 (67.1)
≥ 48 weeks (≥ 336 days)	---	---	58 (39.7)
Average Daily Dose (mg)			
Median	258.84	258.97	265.41
Min, Max	40.0, 389.7	131.3, 270.2	40.0 - 665.7

a　Duration of exposure was defined as study drug stop date minus study drug start date plus 1.
b　Duration of exposure was defined as the sum of all available R788 treatment durations within each study (Studies C788-047, C788-048, C788-049) for a given subject.
c　Subjects can appear in more than one category.
(Source: 5.3.5.3.2, Table 3.2.1, 3.2.2 改編)

2.7.4.1.2.1.3 国内第 III 相臨床試験（R788-1301）及び海外第 III 相臨床試験（C788-047 及び C788-048）の Stable platelet response のレスポンダー及びノンレスポンダーの曝露状況

R788-1301、C788-047 及び C788-048 試験における R788 群の Stable platelet response のレスポンダー及びノンレスポンダー、並びにプラセボ群の治験薬投与量の維持用量（投与期間における各被験者の最頻度投与量）及び最高用量（投与期間における各被験者の最高投与量）の分布を表 2.7.4.1.2.1.3-1～表 2.7.4.1.2.1.3-4 に示す。

国内外の第 III 相臨床試験の R788 100 mg 1 日 2 回及び 150 mg 1 日 2 回のいずれにおいても Stable platelet response のレスポンダーが認められた。

表 2.7.4.1.2.1.3-1　国内第 III 相臨床試験（R788-1301）の維持用量

Period I

Group	N	100 mg 1 日 1 回		150 mg 1 日 1 回		100 mg 1 日 2 回		150 mg 1 日 2 回	
		n	%	n	%	n	%	n	%
Placebo	12	0	0.0	0	0.0	1	8.3	11	91.7
R788 Non-responder	14	0	0.0	0	0.0	9	64.3	5	35.7
R788 Responder	8	0	0.0	1	12.5	4	50.0	3	37.5

（Source: 1.13.3-4, C-12-2 表 52）

表 2.7.4.1.2.1.3-2　国内第 III 相臨床試験（R788-1301）の最高用量

Period I

Group	N	100 mg 1 日 1 回		150 mg 1 日 1 回		100 mg 1 日 2 回		150 mg 1 日 2 回	
		n	%	n	%	n	%	n	%
Placebo	12	0	0.0	0	0.0	1	8.3	11	91.7
R788 Non-responder	14	0	0.0	0	0.0	3	21.4	11	78.6
R788 Responder	8	0	0.0	0	0.0	4	50.0	4	50.0

（Source: 1.13.3-4, C-12-2 表 53）

表 2.7.4.1.2.1.3-3 海外第 III 相臨床試験（C788-047 及び C788-048）の維持用量

C788-047 試験
Placebo-Controlled Period

Group	N	100 mg 1 日 1 回		150 mg 1 日 1 回		100 mg 1 日 2 回		150 mg 1 日 2 回	
		n	%	n	%	n	%	n	%
Placebo	25	0	0.0	0	0.0	6	24.0	19	76.0
R788 Non-responder	42	0	0.0	0	0.0	17	40.5	25	59.5
R788 Responder	9	0	0.0	0	0.0	3	33.3	6	66.7

C788-048 試験
Placebo-Controlled Period

Group	N	100 mg 1 日 1 回		150 mg 1 日 1 回		100 mg 1 日 2 回		150 mg 1 日 2 回	
		n	%	n	%	n	%	n	%
Placebo	24	0	0.0	0	0.0	6	25.0	18	75.0
R788 Non-responder	41	0	0.0	1	2.4	6	14.6	34	82.9
R788 Responder	9	0	0.0	1	11.1	4	44.4	4	44.4

（Source: 1.13.3-4, C-12-2 表 54、表 56）

表 2.7.4.1.2.1.3-4 海外第 III 相臨床試験（C788-047 及び C788-048）の最高用量

C788-047 試験
Placebo-Controlled Period

Group	N	100 mg 1 日 1 回		150 mg 1 日 1 回		100 mg 1 日 2 回		150 mg 1 日 2 回	
		n	%	n	%	n	%	n	%
Placebo	25	0	0.0	0	0.0	1	4.0	24	96.0
R788 Non-responder	42	0	0.0	0	0.0	5	11.9	37	88.1
R788 Responder	9	0	0.0	0	0.0	2	22.2	7	77.8

C788-048 試験
Placebo-Controlled Period

Group	N	100 mg 1 日 1 回		150 mg 1 日 1 回		100 mg 1 日 2 回		150 mg 1 日 2 回	
		n	%	n	%	n	%	n	%
Placebo	24	0	0.0	0	0.0	2	8.3	22	91.7
R788 Non-responder	41	0	0.0	0	0.0	1	2.4	40	97.6
R788 Responder	9	0	0.0	0	0.0	5	55.6	4	44.4

（Source: 1.13.3-4, C-12-2 表 55、表 57）

2.7.4.1.2.1.4 海外第 II 相臨床試験（D4300-022）

D4300-022 試験には 18 例が登録され、6 例が試験を完了し、12 例が中止した。治療期間の平均は 538.72 日（範囲：28～1192 日）であり、初期投与量は、75 mg 1 日 2 回から 150 mg 1 日 2 回であった。漸増後の最大用量は、全被験者が 100 mg 1 日 2 回以上であり、8 例（44.4%）が 175 mg 1 日 2 回に到達した。

表 2.7.4.1.2.1.4-1 投与期間及び投与量

Parameter	R788 PO N=18
Treatment duration (days)[a]	
Mean (SD)	538.72 (449.612)
Median	452.50
Range	28.0-1192.0
Initial dose of R788, n (%)	
75 mg bid	3 (16.7)
100 mg bid	5 (27.8)
125 mg bid	6 (33.3)
150 mg bid	4 (22.2)
Highest achieved dose of R788, n (%)	
100 mg bid	1 (5.6)
125 mg bid	2 (11.1)
275 mg qd	1 (5.6)
150 mg bid	6 (33.3)
175 mg bid	8 (44.4)

PO = orally; SD = standard deviation; bid = twice daily; qd = once daily.
a: last dosing date – first dosing date +1. If the patient was continuing dosing with R788 at the time ofdatabase lock, then the last visit date was assumed to be the last available dosing date.
(Source: 5.3.5.2.1, Table 12-1)

2.7.4.1.2.2 第 I 相臨床試験及び臨床薬理試験

第 I 相臨床試験及び臨床薬理試験で検討した用法・用量は、R788 の投与量が 50 mg から 600 mg の範囲であり、投与回数が単回投与、並びに 1 日 1 回及び 1 日 2 回の反復投与であった。各試験の詳細は「2.7.6 個々の試験のまとめ」に示す。

2.7.4.1.3 治験対象集団の人口統計学的特性及びその他の特性

1) 国内第 III 相臨床試験（R788-1301）

R788-1301 試験の被験者背景を表 2.7.4.1.3-1 及び表 2.7.4.1.3-2 に示す。

R788-1301 試験に無作為割付けされた被験者の背景は、男性 23.5%（8/34 例）、女性 76.5%（26/34 例）、年齢 63 歳（25～81 歳）（中央値（範囲）、以下同様）、ベースラインの血小板数 18000/μL（1000～28000/μL）、ITP の罹病期間 12 年（1～41 年）及び脾摘の施行歴あり 20.6%（7/34 例）であった。また、ITP 治療薬の内訳（重複あり）は、副腎皮質ステロイド 97.1%（33/34 例）、トロンボポエチン（TPO）受容体作動薬 52.9%（18/34 例）及びリツキシマブ 14.7%（5/34）であった。

表 2.7.4.1.3-1 国内第 III 相臨床試験（R788-1301）の人口統計学的特性 – プラセボ対照期

Variable	R788 (N=22)	Placebo (N=11)	Overall (N=34)
Age (years), n (%)			
Median	61	64	63
Min, Max	25, 81	31, 76	25, 81
Age Category (years)			
<65	12 (54.5)	7 (58.3)	19 (55.9)
≥65	10 (45.5)	5 (41.7)	15 (44.1)
Gender, n (%)			
Male	4 (18.2)	4 (33.3)	8 (23.5)
Female	18 (81.8)	8 (66.7)	26 (76.5)

(Source: 5.3.5.1.1, 表 11.2-1、表 11.2-2 改編)

表 2.7.4.1.3-2　　国内第 III 相臨床試験（R788-1301）の基準値の特性 – プラセボ対照期

Variable	R788 (N=22)	Placebo (N=11)	Overall (N=34)
Splenectomy, n (%)			
Yes	5 (22.7)	2 (16.7)	7 (20.6)
No	17 (77.3)	10 (83.3)	27 (79.4)
Duration of ITP, years			
Median	12	12	12
Min, Max	1, 41	1, 38	1, 41
Baseline Platelet count(/μL)			
Median	19000	18000	18000
Min, Max	3000, 28000	1000, 27000	1000, 28000
Prior ITP Medication, n (%)			
Corticosteroid	21 (95.5)	12 (100.0)	33 (97.1)
Rituximab	1 (4.5)	4 (33.3)	5 (14.7)
Thrombopoietin Medication	11 (50.0)	7 (58.3)	18 (52.9)

(Source: 5.3.5.1.1, 表 11.2-1、表 11.2-2 改編)

2)　海外第 III 相臨床試験（C788-047 及び C788-048）

C788-047 及び C788-048 試験の被験者背景を表 2.7.4.1.3-3 及び表 2.7.4.1.3-4 に示す。

C788-047 及び C788-048 試験を統合したプラセボ対照期の被験者の背景は、男性 39.3%（59/150 例）、女性 60.7%（91/150 例）、年齢の中央値（範囲）は 53.5 歳（20～88 歳）であった。被験者の人種はほとんどが白人（92.7%）であり、民族はほとんどがヒスパニック系又はラテン系以外（97.3%）であった。

被験者の ITP の分類はほとんどが慢性 ITP（93.3%）であり、脾摘の施行歴のある被験者は 35.3%であった。ITP の罹病期間は 8.45 年（0.3～53.0 年）（中央値（範囲）、以下同様）であり、ベースラインの血小板数は 16000.0/μL（1000～156000/μL）であった。また、ITP 治療薬の内訳（重複あり）は、副腎皮質ステロイド 94.0%（141/150 例）、リツキシマブ 32.0%（48/150 例）及び TPO 受容体作動薬 47.3%（71/150 例）であった。

表 2.7.4.1.3-3　　海外第 III 相臨床試験（C788-047 及び C788-048 試験）の人口統計学的特性

Variable	R788 (N=102)	Placebo (N=48)	Overall (N=150)
Age (years), n (%)			
Median	53.5	54.0	53.5
Min, Max	20, 88	20, 78	20, 88
Age Category (years)			
<50	42 (41.2)	21 (43.8)	63 (42.0)
50 – <65	32 (31.4)	16 (33.3)	48 (32.0)
≥65	28 (27.5)	11 (22.9)	39 (26.0)
65 – <75	17 (16.7)	7 (14.6)	24 (16.0)
≥75	11 (10.8)	4 (8.3)	15 (10.0)
Gender, n (%)			
Male	41 (40.2)	18 (37.5)	59 (39.3)
Female	61 (59.8)	30 (62.5)	91 (60.7)
Race, n (%)			
Asian	3 (2.9)	2 (4.2)	5 (3.3)
Black or African American	2 (2.0)	2 (4.2)	4 (2.7)
White	95 (93.1)	44 (91.7)	139 (92.7)
Other	2 (2.0)	0 (0.0)	2 (1.3)
Ethnicity, n (%)			
Hispanic or Latino	3 (2.9)	1 (2.1)	4 (2.7)
Not Hispanic or Latino	99 (97.1)	47 (97.9)	146 (97.3)

Abbreviations: Max = maximum value; Min = minimum value; SD = standard deviation.
(Source: 5.3.5.3.2, Table 2.1.1 改編)

表 2.7.4.1.3-4　　海外第 III 相臨床試験（C788-047 及び C788-048）の基準値の特性

Variable	R788 (N=102)	Placebo (N=48)	Overall (N=150)
Type of ITP [a], n (%)			
Persistent ITP	6 (5.9)	4 (8.3)	10 (6.7)
Chronic ITP	96 (94.1)	44 (91.7)	140 (93.3)
Splenectomy, n (%)			
Yes	34 (33.3)	19 (39.6)	53 (35.3)
No	68 (66.7)	29 (60.4)	97 (64.7)
Duration of ITP, years			
Median	8.70	7.10	8.45
Min, Max	0.3, 53.0	0.4, 45.0	0.3, 53.0
Baseline Platelet count(/μL)			
Median	15000.0	17550.0	16000.0
Min, Max	1000, 51000	1000, 156000 [b]	1000, 156000 [b]
Prior ITP Medication, n (%)			
Corticosteroid	94 (92.2)	47 (97.9)	141 (94.0)
Rituximab	34 (33.3)	14 (29.2)	48 (32.0)
Thrombopoietin Medication	47 (46.1)	24 (50.0)	71 (47.3)

Abbreviations: Max = maximum value; Min = minimum value; SD = standard deviation
a　Persistent ITP defined as 3 to 12 months since diagnosis. Chronic ITP defined as > 12 months since diagnosis
b　Platelet count of 156000 obtained shortly after rescue treatment with IVIg
(Source: 5.3.5.3.2, Table 2.2.1, Table 2.2.2 改編)

以上より、ITP に対して使用された薬剤の内訳について、副腎皮質ステロイド及び TPO 受容体作動薬の割合は R788-1301 試験と、C788-047 及び C788-048 試験の統合解析において同様であったが、リツキシマブの割合が C788-047 及び C788-048 試験と比較して R788-1301 試験で低かった。その他、R788-1301 試験と、C788-047 試験及び C788-048 試験の被験者背景に大きな違いは認められなかった。

2.7.4.2 有害事象

2.7.4.2.1 有害事象の解析

2.7.4.2.1.1 比較的よく見られる有害事象

国内第 III 相臨床試験（R788-1301/5.3.5.1.1）、並びに海外第 III 相臨床試験（1）（C788-047/5.3.5.1.2）、海外第 III 相臨床試験（2）（C788-048/5.3.5.1.3）及び海外第 III 相継続投与試験（C788-049/5.3.5.2.2）の統合解析、海外第 II 相臨床試験（D4300-022/5.3.5.2.1）及び第 I 相臨床試験（D4300-007/5.3.3.3.1 及び D4300-032/5.3.3.3.2）において、比較的よく見られる有害事象及び副作用を記載した。

2.7.4.2.1.1.1 R788 投与期

2.7.4.2.1.1.1.1 国内第 III 相臨床試験（R788-1301）における有害事象及び副作用

R788-1301 試験の R788 投与期に 10%以上認められた有害事象及び副作用を表 2.7.4.2.1.1.1.1-1 に示す。

有害事象発現率は 97.0%（32/33 例）、副作用発現率は 72.7%（24/33 例）であった。

10%以上認められた有害事象は、高血圧 30.3%（10/33 例）、便秘 15.2%（5/33 例）、下痢 39.4%（13/33 例）、湿疹 15.2%（5/33 例）及び肝機能検査値上昇 12.1%（4/33 例）であった。10%以上認められた副作用は、高血圧 27.3%（9/33 例）及び下痢 30.3%（10/33 例）であった。

重篤な有害事象は 21.2%（7/33 例）、重篤な副作用は 6.1%（2/33 例）認められた。有害事象の多くは軽度（57.6%（19/33 例））又は中等度（33.3%（11/33 例））であり、高度の有害事象は 6.1%（2/33 例）認められた。高度の副作用の内訳は下痢 3.0%（1/33 例）であった。

表 2.7.4.2.1.1.1.1-1　有害事象（10%以上）及び副作用（R788-1301 試験 R788 投与期）

	有害事象	副作用
System Organ Class Preferred Term	R788 (N=33) n (%)	R788 (N=33) n (%)
全体	32 (97.0)	24 (72.7)
血管障害	10 (30.3)	9 (27.3)
高血圧	10 (30.3)	9 (27.3)
胃腸障害	20 (60.6)	11 (33.3)
便秘	5 (15.2)	0 (0.0)
下痢	13 (39.4)	10 (30.3)
皮膚および皮下組織障害	14 (42.4)	1 (3.0)
湿疹	5 (15.2)	0 (0.0)
臨床検査	15 (45.5)	12 (36.4)
肝機能検査値上昇	4 (12.1)	3 (9.1)

(Source: 5.3.5.1.1, 表 12.2.2.3-1 改編)

2.7.4.2.1.1.1.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の統合解析における有害事象及び副作用

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期に認められた有害事象及び副作用を表 2.7.4.2.1.1.1.2-1、表 2.7.4.9-1 及び表 2.7.4.9-4 に示す。

有害事象発現率は 89.0%（130/146 例）、副作用発現率は 65.8%（96/146 例）であった。

10%以上認められた有害事象は下痢 36.3%（53/146 例）、悪心 19.2%（28/146 例）、上気道感染 12.3%（18/146 例）、鼻出血 18.5%（27/146 例）、頭痛 15.1%（22/146 例）、浮動性めまい 12.3%（18/146 例）、点状出血 15.1%（22/146 例）、高血圧 21.9%（32/146 例）及び挫傷 11.6%（17/146 例）であった。10%以上認められた副作用は下痢 31.5%（46/146 例）、悪心 12.3%（18/146 例）及び高血圧 14.4%（21/146 例）であった。

重篤な有害事象は 30.8%（45/146 例）、重篤な副作用は 6.8%（10/146 例）認められた。有害事象の多くは軽度（21.2%（31/146 例））又は中等度（40.4%（59/146 例））であり、高度の有害事象は 27.4%（40/146 例）認められた。高度の副作用の内訳は、下痢及び呼吸困難各 1.4%（2/146 例）、並びに血圧上昇、トランスアミナーゼ上昇、高血圧クリーゼ、浮動性めまい、胸痛、インフルエンザ様疾患、低酸素症、好中球減少症、再生不良性貧血、発熱性好中球減少症、肺炎、硬結性紅斑、敗血症、結核及び関節痛各 0.7%（1/146 例）であった。

表 2.7.4.2.1.1.1.2-1　有害事象（10%以上）及び副作用（C788-047、C788-048 及び C788-049 試験 R788 投与期）

System Organ Class Preferred Term	有害事象 R788 (N=146) n (%)	副作用 R788 (N=146) n (%)
全体	130 (89.0%)	96 (65.8%)
胃腸障害	85 (58.2%)	58 (39.7%)
下痢	53 (36.3%)	46 (31.5%)
悪心	28 (19.2%)	18 (12.3%)
感染症および寄生虫症	64 (43.8%)	11 (7.5%)
上気道感染	18 (12.3%)	1 (0.7%)
呼吸器、胸郭および縦隔障害	50 (34.2%)	14 (9.6%)
鼻出血	27 (18.5%)	5 (3.4%)
神経系障害	47 (32.2%)	18 (12.3%)
頭痛	22 (15.1%)	7 (4.8%)
浮動性めまい	18 (12.3%)	9 (6.2%)
皮膚および皮下組織障害	45 (30.8%)	13 (8.9%)
点状出血	22 (15.1%)	3 (2.1%)
血管障害	40 (27.4%)	23 (15.8%)
高血圧	32 (21.9%)	21 (14.4%)
傷害、中毒および処置合併症	24 (16.4%)	1 (0.7%)
挫傷	17 (11.6%)	1 (0.7%)

(Source: 5.3.5.3.2, Table 4.2.1.2.1, Table 4.2.1.2.2 改編)

2.7.4.2.1.1.2 プラセボ対照期

2.7.4.2.1.1.2.1 国内第 III 相臨床試験（R788-1301）における有害事象及び副作用

R788-1301 試験のプラセボ対照期に 10%以上認められた有害事象及び副作用を表 2.7.4.2.1.1.2.1-1 に示す。

有害事象発現率は R788 群で 90.9%（20/22 例）及びプラセボ群で 66.7%（8/12 例）、副作用発現率は R788 群で 77.3%（17/22 例）及びプラセボ群で 8.3%（1/12 例）であった。

R788 群で 10%以上認められた有害事象は、高血圧（R788 群 31.8%（7/22 例）及びプラセボ群 8.3%（1/12 例）（以下同順））、下痢（40.9%（9/22 例）及び 0.0%（0/12 例））、並びに好中球数減少（13.6%（3/22 例）及び 0.0%（0/12 例））であった。R788 群で 10%以上認められた副作用は、高血圧（27.3%（6/22 例）及び 8.3%（1/12 例））、下痢（31.8%（7/22 例）及び 0.0%（0/12 例））、並びに好中球数減少（13.6%（3/22 例）及び 0.0%（0/12 例））であった。

重篤な有害事象は R788 群で 9.1%（2/22 例）及びプラセボ群で 8.3%（1/12 例）、重篤な副作用は R788 群で 9.1%（2/22 例）であり、プラセボ群では認められなかった。有害事象の多くは軽度（R788 群 63.6%（14/22 例）及びプラセボ群 58.3%（7/12 例）（以下同順））又は中等度（22.7%（5/22 例）及び 8.3%（1/12 例））であり、高度の有害事象は R788 群で 4.5%（1/22 例）であり、プラセボ群では認められなかった。R788 群で認められた高度の副作用の内訳は、下痢（R788 群 4.5%（1/22 例）及びプラセボ群 0.0%（0/12 例））であった。

表 2.7.4.2.1.1.2.1-1　有害事象（R788 群で 10%以上）及び副作用（R788-1301 試験プラセボ対照期）

System Organ Class Preferred Term	有害事象		副作用	
	R788 (N=22) n (%)	Placebo (N=12) n (%)	R788 (N=22) n (%)	Placebo (N=12) n (%)
全体	20 (90.9)	8 (66.7)	17 (77.3)	1 (8.3)
血管障害	7 (31.8)	1 (8.3)	6 (27.3)	1 (8.3)
高血圧	7 (31.8)	1 (8.3)	6 (27.3)	1 (8.3)
胃腸障害	11 (50.0)	0 (0.0)	9 (40.9)	0 (0.0)
下痢	9 (40.9)	0 (0.0)	7 (31.8)	0 (0.0)
臨床検査	9 (40.9)	1 (8.3)	8 (36.4)	0 (0.0)
好中球数減少	3 (13.6)	0 (0.0)	3 (13.6)	0 (0.0)

(Source: 5.3.5.1.1, 表 12.2.2.1-1 改編)

2.7.4.2.1.1.2.2 海外第 III 相臨床試験（C788-047 及び C788-048）の統合解析における有害事象及び副作用

C788-047 及び C788-048 試験を統合したプラセボ対照期に認められた有害事象及び副作用を表 2.7.4.2.1.1.2.2-1、表 2.7.4.9-5 及び表 2.7.4.9-8 に示す。

有害事象発現率は R788 群で 83.3%（85/102 例）及びプラセボ群で 75.0%（36/48 例）、副作用発現率は R788 群で 58.8%（60/102 例）及びプラセボ群で 27.1%（13/48 例）であった。

R788 群で 10%以上認められた有害事象は、下痢（R788 群 29.4%（30/102 例）及びプラセボ群 14.6%（7/48 例）（以下同順））、悪心（18.6%（19/102 例）及び 8.3%（4/48 例））、頭痛（10.8%（11/102 例）及び 18.8%（9/48 例））、浮動性めまい（10.8%（11/102 例）及び 8.3%（4/48 例））、アラニンアミノトランスフェラーゼ（ALT）増加（10.8%（11/102 例）及び 0.0%（0/48 例））、鼻出血（15.7%（16/102 例）及び 10.4%（5/48 例））、並びに高血圧（19.6%（20/102 例）及び 8.3%（4/48 例））であった。R788 群で 10%以上認められた副作用は、下痢（26.5%（27/102 例）及び 12.5%（6/48 例））、悪心（14.7%（15/102 例）及び 6.3%（3/48 例））、並びに高血圧（15.7%（16/102 例）及び 4.2%（2/48 例））であった。

重篤な有害事象は R788 群で 12.7%（13/102 例）及びプラセボ群で 20.8%（10/48 例）、重篤な副作用は R788 群で 3.9%（4/102 例）及びプラセボ群で 2.1%（1/48 例）認められた。有害事象の多くは軽度（R788 群 32.4%（33/102 例）及びプラセボ群 41.7%（20/48 例）（以下同順））又は中等度（35.3%（36/102 例）及び 18.8%（9/48 例））であり、高度の有害事象は R788 群で 15.7%（16/102 例）及びプラセボ群で 14.6%（7/48 例）認められた。R788 群で認められた高度の副作用の内訳は、呼吸困難（R788 群 2.0%（2/102 例）及びプラセボ群 0.0%（0/48 例））、並びに下痢、血圧上昇、高血圧クリーゼ、浮動性めまい、低酸素症、好中球減少症、発熱性好中球減少症、胸痛、インフルエンザ様疾患、関節痛及び肺炎（各 R788 群 1.0%（1/102 例）及びプラセボ群 0.0%（0/48 例））であった。

表 2.7.4.2.1.1.2.2-1　有害事象（R788 群で 10%以上）及び副作用（C788-047 及び C788-048 試験プラセボ対照期）

System Organ Class Preferred Term	有害事象		副作用	
	R788 (N=102) n (%)	Placebo (N=48) n (%)	R788 (N=102) n (%)	Placebo (N=48) n (%)
全体	85 (83.3%)	36 (75.0%)	60 (58.8%)	13 (27.1%)
胃腸障害	49 (48.0%)	16 (33.3%)	38 (37.3%)	9 (18.8%)
下痢	30 (29.4%)	7 (14.6%)	27 (26.5%)	6 (12.5%)
悪心	19 (18.6%)	4 (8.3%)	15 (14.7%)	3 (6.3%)
神経系障害	26 (25.5%)	13 (27.1%)	14 (13.7%)	2 (4.2%)
頭痛	11 (10.8%)	9 (18.8%)	4 (3.9%)	0 (0.0%)
浮動性めまい	11 (10.8%)	4 (8.3%)	9 (8.8%)	2 (4.2%)
臨床検査	28 (27.5%)	5 (10.4%)	19 (18.6%)	1 (2.1%)
アラニンアミノトランスフェラーゼ増加	11 (10.8%)	0 (0.0%)	10 (9.8%)	0 (0.0%)
呼吸器、胸郭および縦隔障害	23 (22.5%)	10 (20.8%)	9 (8.8%)	0 (0.0%)
鼻出血	16 (15.7%)	5 (10.4%)	4 (3.9%)	0 (0.0%)
血管障害	24 (23.5%)	9 (18.8%)	17 (16.7%)	2 (4.2%)
高血圧	20 (19.6%)	4 (8.3%)	16 (15.7%)	2 (4.2%)

(Source: 5.3.5.3.2, Table 4.2.1.1.1, Table 4.2.1.1.2 改編)

2.7.4.2.1.1.3 休薬期

2.7.4.2.1.1.3.1 国内第 III 相臨床試験（R788-1301）における有害事象及び副作用

R788-1301 試験の休薬期に認められた有害事象及び副作用を表 2.7.4.2.1.1.3.1-1 に示す。

有害事象発現率は 50.0%（6/12 例）、副作用発現率は 0.0%（0/12 例）であった。

認められた有害事象は、白癬感染、ウイルス感染、高血糖、不眠症、腹部不快感、上腹部痛、肝嚢胞、紅斑、紅斑性皮疹及び酒さ各 8.3%（1/12 例）であった。

重篤な有害事象は認められなかった。有害事象は軽度（41.7%（5/12 例））又は中等度（8.3%（1/12 例））であり、高度の有害事象は認められなかった。

表 2.7.4.2.1.1.3.1-1　有害事象及び副作用（R788-1301 試験休薬期）

System Organ Class Preferred Term	有害事象	副作用
	R788 (N=12) n (%)	R788 (N=12) n (%)
全体	6 (50.0)	0 (0.0)
感染症および寄生虫症	2 (16.7)	0 (0.0)
白癬感染	1 (8.3)	0 (0.0)
ウイルス感染	1 (8.3)	0 (0.0)
代謝および栄養障害	1 (8.3)	0 (0.0)
高血糖	1 (8.3)	0 (0.0)
精神障害	1 (8.3)	0 (0.0)
不眠症	1 (8.3)	0 (0.0)
胃腸障害	2 (16.7)	0 (0.0)
腹部不快感	1 (8.3)	0 (0.0)
上腹部痛	1 (8.3)	0 (0.0)
肝胆道系障害	1 (8.3)	0 (0.0)
肝嚢胞	1 (8.3)	0 (0.0)
皮膚および皮下組織障害	3 (25.0)	0 (0.0)
紅斑	1 (8.3)	0 (0.0)
紅斑性皮疹	1 (8.3)	0 (0.0)
酒さ	1 (8.3)	0 (0.0)

(Source: 5.3.5.1.1, 表 12.2.2.4-1)

2.7.4.2.1.1.4 発現時期別の有害事象

2.7.4.2.1.1.4.1 国内第 III 相臨床試験（R788-1301）における発現時期別の有害事象

R788-1301 試験の R788 投与期における、R788 が投与された被験者の全体で 10%以上認められた発現時期別の有害事象を表 2.7.4.2.1.1.4.1-1、表 2.7.4.9-9 及び表 2.7.4.9-114 に示す。

各発現時期の有害事象の発現率は、≤Week 4 が 60.6%（20/33 例）、≤Week 12 が 75.8%（25/33 例）、Week 12< ≤Week 24 が 58.1%（18/31 例）、Week 24< ≤Week 36 が 61.5%（16/26 例）、Week 36< ≤Week 48 が 34.8%（8/23 例）、Week 48< ≤Week 72 が 44.4%（8/18 例）及び Week 72< が 42.9%（3/7 例）であった。

投与開始後早期（Week 12 以前）を含む特定の時期で高頻度に発現した有害事象はなく、長期投与によって遅発的に発現する有害事象は認められなかった。また、死亡に至った有害事象、その他の重篤な有害事象及び中止に至った有害事象も、遅発的に発現する傾向は認められなかった。

表 2.7.4.2.1.1.4.1-1　国内第 III 相臨床試験（R788-1301）の R788 投与期における発現時期別の有害事象（10%以上）

Time to Onset	Overall	≤Week 4	≤Week 12	Week 12< ≤24	Week 24< ≤36	Week 36< ≤48	Week 48< ≤72	>Week 72
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N	33	33	33	31	26	23	18	7
有害事象	32 (97.0)	20 (60.6)	25 (75.8)	18 (58.1)	16 (61.5)	8 (34.8)	8 (44.4)	3 (42.9)
Overall で 10%以上に認められた有害事象								
血管障害	10 (30.3)	7 (21.2)	9 (27.3)	1 (3.2)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	10 (30.3)	7 (21.2)	9 (27.3)	1 (3.2)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	20 (60.6)	9 (27.3)	15 (45.5)	7 (22.6)	3 (11.5)	3 (13.0)	2 (11.1)	0 (0.0)
便秘	5 (15.2)	1 (3.0)	3 (9.1)	1 (3.2)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
下痢	13 (39.4)	7 (21.2)	11 (33.3)	4 (12.9)	0 (0.0)	0 (0.0)	1 (5.6)	0 (0.0)
皮膚および皮下組織障害	14 (42.4)	2 (6.1)	4 (12.1)	2 (6.5)	2 (7.7)	1 (4.3)	3 (16.7)	1 (14.3)
湿疹	5 (15.2)	1 (3.0)	2 (6.1)	2 (6.5)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	15 (45.5)	5 (15.2)	10 (30.3)	5 (16.1)	3 (11.5)	0 (0.0)	1 (5.6)	0 (0.0)
肝機能検査値上昇	4 (12.1)	0 (0.0)	2 (6.1)	1 (3.2)	1 (3.8)	0 (0.0)	1 (5.6)	0 (0.0)

(Source: 5.3.5.1.1, 表 12.2.2.3-1, Table 14.3.4.1.6.1, Table 14.3.4.1.8.1 改編)

2.7.4.2.1.1.4.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の統合解析における発現時期別の有害事象

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期における、R788 が投与された被験者の全体で 10%以上認められた発現時期別の有害事象を表 2.7.4.2.1.1.4.2-1、表 2.7.4.9-10 及び表 2.7.4.9-115 に示す。

各発現時期の有害事象の発現率は、≤Week 12 が 76.7%（112/146 例）、Week 12< ≤Week 24 が 48.4%（62/128 例）、Week 24< ≤Week 36 が 43.6%（44/101 例）、Week 36< ≤Week 48 が 44.6%（29/65 例）、Week 48< ≤Month 18 が 56.9%（33/58 例）、Month 18< ≤Month 24 が 50.0%（25/50 例）、Month 24< ≤Month 30 が 36.2%（17/47 例）、Month 30< ≤Month 36 が 42.2%（19/45 例）、Month 36< ≤Month 42 が 32.5%（13/40 例）、Month 42< ≤Month 48 が 34.2%（13/38 例）及び Month 48<が 30.4%（7/23 例）であった。

投与開始後早期（Week 12 以前）を含む特定の時期で高頻度に発現した有害事象はなく、投与期間の延長に伴い有害事象の発現頻度が減少する傾向が認められ、長期投与によって遅発的に発現する有害事象は認められなかった。また、死亡に至った有害事象、その他の重篤な有害事象及び中止に至った有害事象も、遅発的に発現する傾向は認められなかった。

表 2.7.4.2.1.1.4.2-1　海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の R788 投与期における発現時期別の有害事象（10%以上）

Time to Onset	Overall	≤Week 12	Week 12< ≤24	Week 24< ≤36	Week 36< ≤48	Week 48< ≤Month 18	Month 18< ≤24	Month 24< ≤30	Month 30< ≤36	Month 36< ≤42	Month 42< ≤48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N	146	146	128	101	65	58	50	47	45	40	38	23
有害事象	130 (89.0%)	112 (76.7%)	62 (48.4%)	44 (43.6%)	29 (44.6%)	33 (56.9%)	25 (50.0%)	17 (36.2%)	19 (42.2%)	13 (32.5%)	13 (34.2%)	7 (30.4%)
死亡に至った有害事象	5 (3.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (4.3%)
その他重篤な有害事象	42 (28.8%)	19 (13.0%)	12 (9.4%)	4 (4.0%)	4 (6.2%)	2 (3.4%)	3 (6.0%)	1 (2.1%)	3 (6.7%)	4 (10.0%)	4 (10.5%)	3 (13.0%)
中止に至った有害事象	28 (19.2%)	13 (8.9%)	5 (3.9%)	2 (2.0%)	1 (1.5%)	3 (5.2%)	1 (2.0%)	1 (2.1%)	2 (4.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Overall で 10%以上に認められた有害事象												
胃腸障害	85 (58.2%)	65 (44.5%)	29 (22.7%)	17 (16.8%)	7 (10.8%)	13 (22.4%)	7 (14.0%)	4 (8.5%)	5 (11.1%)	4 (10.0%)	5 (13.2%)	6 (26.1%)
下痢	53 (36.3%)	31 (21.2%)	19 (14.8%)	10 (9.9%)	2 (3.1%)	9 (15.5%)	3 (6.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	2 (5.3%)	2 (8.7%)
悪心	28 (19.2%)	23 (15.8%)	4 (3.1%)	3 (3.0%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
感染症および寄生虫症	64 (43.8%)	27 (18.5%)	16 (12.5%)	13 (12.9%)	8 (12.3%)	14 (24.1%)	10 (20.0%)	10 (21.3%)	12 (26.7%)	8 (20.0%)	4 (10.5%)	3 (13.0%)
上気道感染	18 (12.3%)	6 (4.1%)	2 (1.6%)	5 (5.0%)	1 (1.5%)	1 (1.7%)	4 (8.0%)	1 (2.1%)	1 (2.2%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
呼吸器、胸郭および縦隔障害	50 (34.2%)	29 (19.9%)	13 (10.2%)	7 (6.9%)	7 (10.8%)	6 (10.3%)	2 (4.0%)	2 (4.3%)	3 (6.7%)	3 (7.5%)	2 (5.3%)	1 (4.3%)
鼻出血	27 (18.5%)	17 (11.6%)	9 (7.0%)	3 (3.0%)	2 (3.1%)	3 (5.2%)	0 (0.0%)	2 (4.3%)	2 (4.4%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
神経系障害	47 (32.2%)	29 (19.9%)	12 (9.4%)	2 (2.0%)	3 (4.6%)	9 (15.5%)	1 (2.0%)	2 (4.3%)	2 (4.4%)	2 (5.0%)	3 (7.9%)	3 (13.0%)
頭痛	22 (15.1%)	12 (8.2%)	5 (3.9%)	2 (2.0%)	1 (1.5%)	4 (6.9%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	2 (5.0%)	2 (5.3%)	2 (8.7%)
浮動性めまい	18 (12.3%)	13 (8.9%)	5 (3.9%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
皮膚および皮下組織障害	45 (30.8%)	23 (15.8%)	13 (10.2%)	10 (9.9%)	3 (4.6%)	7 (12.1%)	4 (8.0%)	4 (8.5%)	3 (6.7%)	2 (5.0%)	3 (7.9%)	1 (4.3%)
点状出血	22 (15.1%)	7 (4.8%)	7 (5.5%)	5 (5.0%)	2 (3.1%)	3 (5.2%)	2 (4.0%)	2 (4.3%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
血管障害	40 (27.4%)	29 (19.9%)	5 (3.9%)	3 (3.0%)	5 (7.7%)	3 (5.2%)	5 (10.0%)	2 (4.3%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	1 (4.3%)
高血圧	32 (21.9%)	22 (15.1%)	4 (3.1%)	2 (2.0%)	4 (6.2%)	3 (5.2%)	4 (8.0%)	2 (4.3%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
傷害、中毒および処置合併症	24 (16.4%)	8 (5.5%)	2 (1.6%)	4 (4.0%)	4 (6.2%)	4 (6.9%)	2 (4.0%)	0 (0.0%)	2 (4.4%)	2 (5.0%)	3 (7.9%)	2 (8.7%)
挫傷	17 (11.6%)	8 (5.5%)	1 (0.8%)	2 (2.0%)	0 (0.0%)	2 (3.4%)	2 (4.0%)	0 (0.0%)	2 (4.4%)	2 (5.0%)	1 (2.6%)	1 (4.3%)

(Source: 5.3.5.3.2, Table 4.5.1.1 改編)

2.7.4.2.1.1.5 海外第 II 相臨床試験（D4300-022）における有害事象及び副作用

D4300-022 試験において認められた有害事象及び副作用を表 2.7.4.2.1.1.5-1 及び 2.7.6.26.2.4 に示す。

有害事象発現率は 100%（18/18 例）、副作用発現率は 100%（18/18 例）であった。

50%以上認められた有害事象は血中ブドウ糖増加、血圧上昇及び斑状出血各 72.2%（13/18 例）、点状出血及び下痢各 66.7%（12/18 例）、アスパラギン酸アミノトランスフェラーゼ（AST）増加及び血中ブドウ糖減少各 61.1%（11/18 例）、並びに鼻出血 50.0%（9/18 例）であった。50%以上認められた副作用は血中ブドウ糖増加、血圧上昇及び斑状出血各 66.7%（12/18 例）、AST 増加、点状出血及び下痢各 61.1%（11/18 例）、並びに血中ブドウ糖減少 55.6%（10/18 例）であった。

重篤な有害事象は 44.4%（8/18 例）、重篤な副作用は 11.1%（2/18 例）認められた。有害事象の多くは軽度（5.6%（1/18 例））又は中等度（61.1%（11/18 例））であり、高度の有害事象は 33.3%（6/18 例）認められた。高度の有害事象の内訳は点状出血、血性水疱、下痢、歯肉出血、嘔吐、口腔内出血、胃炎、無酸素性脳症、片頭痛、鼻咽頭炎、上気道感染、筋骨格痛、血栓症、深部静脈血栓症、挫傷、動悸、うっ血性心不全、耳痛、膣出血及び自然流産各 5.6%（1/18 例）であった。

表 2.7.4.2.1.1.5-1 有害事象及び副作用（Total 10%以上）

System Organ Class [a] Preferred Term [b] Number of Patients, (%)	R788 Total (N=18)				
	Total	Probable	Possible	Unlikely	Not Related
Subjects with Treatment Emergent Adverse Events	18 (100.0)	3 (16.7)	15 (83.3)	0 (0.0)	0 (0.0)
臨床検査	18 (100.0)	0 (0.0)	18 (100.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	13 (72.2)	0 (0.0)	12 (66.7)	0 (0.0)	1 (5.6)
血圧上昇	13 (72.2)	0 (0.0)	12 (66.7)	0 (0.0)	1 (5.6)
アスパラギン酸アミノトランスフェラーゼ増加	11 (61.1)	0 (0.0)	11 (61.1)	0 (0.0)	0 (0.0)
血中ブドウ糖減少	11 (61.1)	0 (0.0)	10 (55.6)	1 (5.6)	0 (0.0)
血中アルカリホスファターゼ増加	8 (44.4)	0 (0.0)	8 (44.4)	0 (0.0)	0 (0.0)
アラニンアミノトランスフェラーゼ増加	7 (38.9)	0 (0.0)	7 (38.9)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	6 (33.3)	0 (0.0)	6 (33.3)	0 (0.0)	0 (0.0)
血中コレステロール増加	5 (27.8)	0 (0.0)	4 (22.2)	0 (0.0)	1 (5.6)
総蛋白減少	5 (27.8)	0 (0.0)	5 (27.8)	0 (0.0)	0 (0.0)
血中ビリルビン減少	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
血中ビリルビン増加	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
血中カルシウム減少	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
血中カリウム減少	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
血中尿素増加	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
心拍数増加	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
アニオンギャップ増加	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
抱合ビリルビン	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
血中カルシウム増加	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
血中クロール減少	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
血中クレアチニン増加	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
血中マグネシウム減少	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
血中ナトリウム減少	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
グロブリン増加	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
体重増加	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	17 (94.4)	0 (0.0)	17 (94.4)	0 (0.0)	0 (0.0)

System Organ Class [a] Preferred Term [b]	R788 Total (N=18)				
斑状出血	13 (72.2)	0 (0.0)	12 (66.7)	0 (0.0)	1 (5.6)
点状出血	12 (66.7)	0 (0.0)	11 (61.1)	0 (0.0)	1 (5.6)
発疹	6 (33.3)	0 (0.0)	4 (22.2)	1 (5.6)	1 (5.6)
血性水疱	4 (22.2)	0 (0.0)	2 (11.1)	0 (0.0)	2 (11.1)
そう痒症	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
皮膚出血	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
蕁麻疹	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
胃腸障害	16 (88.9)	2 (11.1)	13 (72.2)	1 (5.6)	0 (0.0)
下痢	12 (66.7)	2 (11.1)	9 (50.0)	0 (0.0)	1 (5.6)
悪心	7 (38.9)	1 (5.6)	4 (22.2)	1 (5.6)	1 (5.6)
歯肉出血	5 (27.8)	0 (0.0)	5 (27.8)	0 (0.0)	0 (0.0)
口内炎	5 (27.8)	0 (0.0)	5 (27.8)	0 (0.0)	0 (0.0)
嘔吐	5 (27.8)	1 (5.6)	3 (16.7)	1 (5.6)	0 (0.0)
痔核	3 (16.7)	0 (0.0)	2 (11.1)	1 (5.6)	0 (0.0)
口腔内痛	3 (16.7)	0 (0.0)	2 (11.1)	1 (5.6)	0 (0.0)
直腸出血	3 (16.7)	0 (0.0)	1 (5.6)	1 (5.6)	1 (5.6)
腹痛	2 (11.1)	0 (0.0)	1 (5.6)	1 (5.6)	0 (0.0)
上腹部痛	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
便秘	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
口腔内出血	2 (11.1)	0 (0.0)	0 (0.0)	1 (5.6)	1 (5.6)
呼吸器、胸郭および縦隔障害	14 (77.8)	0 (0.0)	13 (72.2)	0 (0.0)	1 (5.6)
鼻出血	9 (50.0)	0 (0.0)	7 (38.9)	2 (11.1)	0 (0.0)
咳嗽	5 (27.8)	0 (0.0)	3 (16.7)	2 (11.1)	0 (0.0)
口腔咽頭痛	5 (27.8)	0 (0.0)	3 (16.7)	1 (5.6)	1 (5.6)
呼吸困難	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
鼻閉	3 (16.7)	0 (0.0)	0 (0.0)	3 (16.7)	0 (0.0)
鼻漏	3 (16.7)	0 (0.0)	2 (11.1)	1 (5.6)	0 (0.0)
神経系障害	13 (72.2)	0 (0.0)	12 (66.7)	0 (0.0)	1 (5.6)
頭痛	8 (44.4)	0 (0.0)	7 (38.9)	0 (0.0)	1 (5.6)
浮動性めまい	3 (16.7)	0 (0.0)	2 (11.1)	1 (5.6)	0 (0.0)
傾眠	3 (16.7)	0 (0.0)	3 (16.7)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	12 (66.7)	0 (0.0)	11 (61.1)	1 (5.6)	0 (0.0)
疲労	7 (38.9)	0 (0.0)	6 (33.3)	1 (5.6)	0 (0.0)
発熱	5 (27.8)	0 (0.0)	4 (22.2)	1 (5.6)	0 (0.0)
末梢性浮腫	4 (22.2)	0 (0.0)	3 (16.7)	1 (5.6)	0 (0.0)
疼痛	3 (16.7)	0 (0.0)	1 (5.6)	0 (0.0)	2 (11.1)
胸痛	2 (11.1)	0 (0.0)	1 (5.6)	1 (5.6)	0 (0.0)
感染症および寄生虫症	10 (55.6)	0 (0.0)	7 (38.9)	0 (0.0)	3 (16.7)
上咽頭炎	5 (27.8)	0 (0.0)	5 (27.8)	0 (0.0)	0 (0.0)
帯状疱疹	2 (11.1)	0 (0.0)	1 (5.6)	1 (5.6)	0 (0.0)
インフルエンザ	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
上気道感染	2 (11.1)	0 (0.0)	1 (5.6)	0 (0.0)	1 (5.6)
筋骨格系および結合組織障害	9 (50.0)	0 (0.0)	7 (38.9)	1 (5.6)	1 (5.6)
関節痛	4 (22.2)	0 (0.0)	2 (11.1)	1 (5.6)	1 (5.6)
筋痙縮	4 (22.2)	0 (0.0)	4 (22.2)	0 (0.0)	0 (0.0)
筋骨格硬直	3 (16.7)	0 (0.0)	1 (5.6)	2 (11.1)	0 (0.0)
四肢痛	3 (16.7)	0 (0.0)	0 (0.0)	3 (16.7)	0 (0.0)
背部痛	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
代謝および栄養障害	7 (38.9)	0 (0.0)	4 (22.2)	3 (16.7)	0 (0.0)
痛風	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
血管障害	6 (33.3)	1 (5.6)	4 (22.2)	1 (5.6)	0 (0.0)
高血圧	3 (16.7)	0 (0.0)	2 (11.1)	1 (5.6)	0 (0.0)
出血	2 (11.1)	0 (0.0)	0 (0.0)	2 (11.1)	0 (0.0)
血栓症	2 (11.1)	0 (0.0)	1 (5.6)	1 (5.6)	0 (0.0)
傷害、中毒および処置合併症	5 (27.8)	0 (0.0)	2 (11.1)	2 (11.1)	1 (5.6)
挫傷	4 (22.2)	0 (0.0)	1 (5.6)	2 (11.1)	1 (5.6)
心臓障害	4 (22.2)	0 (0.0)	1 (5.6)	2 (11.1)	1 (5.6)
動悸	2 (11.1)	0 (0.0)	1 (5.6)	1 (5.6)	0 (0.0)
眼障害	4 (22.2)	0 (0.0)	4 (22.2)	0 (0.0)	0 (0.0)

System Organ Class [a] Preferred Term [b]	R788 Total (N=18)				
眼出血	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
霧視	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
耳および迷路障害	3 (16.7)	0 (0.0)	2 (11.1)	1 (5.6)	0 (0.0)
耳痛	2 (11.1)	0 (0.0)	1 (5.6)	1 (5.6)	0 (0.0)

(a) Patients may have had more than 1 event within a system organ class. They are summarized according to the highest relationship.
(b) Patients may have had more than 1 event with the same preferred term. They are summarized according to the highest relationship.
MedDRA: Version 13.0
(Source: 5.3.5.2.1, Table 14.3.1.5.1 改編)

2.7.4.2.1.1.6 日本人及び白人を対象とした第 I 相臨床試験（D4300-007）における有害事象及び副作用

D4300-007 試験において認められた有害事象及び副作用を 2.7.6.9.2.3 に示す。

単回投与期間中、有害事象はプラセボ群の日本人被験者で 10.0%（1/10 例）認められた。反復投与期間中、有害事象はプラセボ群の日本人被験者で 50.0%（5/10 例）、R788 50 mg 1 日 2 回投与群の日本人被験者で 33.3%（2/6 例）、R788 100 mg 1 日 2 回投与群の日本人被験者で 16.7%（1/6 例）、並びに R788 150 mg 1 日 1 回投与群の白人被験者で 33.3%（4/12 例）認められた。

単回投与期間中、副作用は認められなかった。反復投与期間中、副作用はプラセボ群の日本人被験者で 20.0%（2/10 例）（耳鳴及び下痢各 1 例）、R788 50 mg 1 日 2 回投与群の日本人被験者で 16.7%（1/6 例）（下痢及び腹部不快感 1 例）、並びに R788 150 mg 1 日 1 回投与群の白人被験者で 8.3%（1/12 例）（頭痛 1 例）認められた。

重篤な有害事象及び副作用は認められなかった。有害事象はいずれも軽度であった。

2.7.4.2.1.1.7 日本人を対象とした第 I 相臨床試験（D4300-032）における有害事象及び副作用

D4300-032 試験において認められた有害事象及び副作用を 2.7.6.10.2.3 に示す。

単回投与期間中、有害事象は認められなかった。反復投与期間中、有害事象は R788 100 mg 1 日 2 回投与群で 8.3%（1/12 例）、R788 200 mg 1 日 2 回投与群で 16.7%（2/12 例）認められた。

単回投与期間中、副作用は認められなかった。反復投与期間中、副作用は R788 100 mg 1 日 2 回投与群で 8.3%（1/12 例）（熱感 1 例）、並びに R788 200 mg 1 日 2 回投与群で 16.7%（2/12 例）（ほてり 1 例、並びに腹痛、下痢、悪心及び頭痛 1 例）認められた。

重篤な有害事象及び副作用は認められなかった。有害事象はいずれも軽度であった。

2.7.4.2.1.1.8 その他の第 I 相臨床試験及び臨床薬理試験における有害事象及び副作用

D4300-007 及び D4300-032 試験以外の第 I 相臨床試験及び臨床薬理試験において認められた有害事象及び副作用を「2.7.6 個々の試験のまとめ」の各試験に示す。

R788 の忍容性は良好であり、最も多く共通して認められた有害事象は頭痛であった。

2.7.4.2.1.2 死亡

海外第 II 相及び第 III 相臨床試験（D4300-022、C788-047、C788-048 及び C788-049）の死亡一覧を表 2.7.4.2.1.2-1 に示す。その他の臨床試験において、死亡は認められなかった。

表 2.7.4.2.1.2-1　死亡一覧（海外臨床試験）

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/非重篤	治験薬の処置	転帰 転帰日	因果関係
C788-047 [redacted]	プラセボ	白人 女性 7[redacted]歳	敗血症	Day 65 プラセボ	高度	重篤	該当せず	死亡 Day 74	おそらく関連なし
C788-048 [redacted]	R788	白人 女性 6[redacted]歳	形質細胞性骨髄腫	Day 18 100 mg 1 日 2 回	中等度	重篤	中止	死亡 Day 90	おそらく関連なし
C788-049 [redacted]	R788/R788	白人 女性 5[redacted]歳	敗血症	Day 124 150 mg 1 日 2 回	高度	重篤	中止	死亡 Day 58	おそらく関連なし
C788-049 [redacted]	R788/R788	白人 男性 7[redacted]歳	肺炎	Day 469 100 mg 1 日 2 回	高度	重篤	変更なし	死亡 Day 294	おそらく関連なし
C788-049 [redacted]	R788/R788	白人 女性 8[redacted]歳	細菌性心内膜炎	Day 1516 100 mg 1 日 2 回	高度	重篤	変更なし	死亡 Day 1345	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 男性 8[redacted]歳	心肺停止	Day 1507 150 mg 1 日 2 回	高度	重篤	変更なし	死亡 Day 1340	おそらく関連なし
D4300-022 [redacted]	R788	白人 男性 8[redacted]歳	無酸素性脳症	Day 418 75 mg 1 日 2 回	高度	重篤	中止	死亡 Day 426	関連なし

（Source : 5.3.5.1.2, 14.3.3; 5.3.5.1.3, 14.3.3; 5.3.5.2.1, 14.3.3; 5.3.5.2.2, 14.3.3 改編）

2.7.4.2.1.2.1 国内第 III 相臨床試験（R788-1301）

死亡は認められなかった。

2.7.4.2.1.2.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

1)　C788-047 及び C788-048 試験の統合解析

死亡は R788 群で 1.0%（1/102 例）及びプラセボ群で 2.1%（1/48 例）認められたが、いずれも治験薬との因果関係なしと判定された。2 例の詳細は以下のとおり。

– R788 群の 1 例（被験者 [redacted]）は、6[redacted] 歳の白人女性で、C788-048 試験の治療開始から 18 日目に、重篤な有害事象である形質細胞性骨髄腫を発現し、治験薬投与を中止した。被験者は、形質細胞性骨髄腫が原因で、治験薬最終投与から 72 日後に死亡した。
– プラセボ群の 1 例（被験者 [redacted]）は、鼻出血のために C788-047 試験を中止した後、敗血症により死亡した。

2)　C788-049 試験

死亡は 3.3%（4/123 例）認められたが、いずれも治験薬との因果関係なしと判定された。4 例の詳細は以下のとおり。

– 被験者 [redacted] は、6 年間の ITP 罹患歴を有する 5[redacted] 歳の白人女性で、敗血症により死亡した。被験者は、C788-047 試験の開始当初から R788 の投与を受けており、C788-049 試験の 39 日目（R788 投与 124 日目）に敗血症になった。血液培養で肺炎球菌陽性、尿培養でカンジダを認め、サイトメガロウイルス-DNA が陽性（低値）であった。当該事象により治験薬投与は中止された。被験者は治験薬最終投与から 19 日後に死亡した。治験担当医師は、別の要因として併発疾患を挙げ、当該事象と治験薬との因果関係はおそらく関連

なしと判定したが、治験依頼者は R788 の増悪関与は否定できないと判定した。

- 被験者 [redacted] は、大葉性肺炎により死亡した。被験者は、C788-047 試験において R788 による 24 週間の投与（4 週時までは 100 mg 1 日 2 回、4 週時から 24 週時までは 150 mg 1 日 2 回）を受け、C788-049 試験では R788 150 mg 1 日 2 回の投与を継続した。C788-049 試験の 294 日目（R788 投与 469 日目）に、被験者は死亡したと報告された。剖検により両側性肺炎が明らかとなった。R788 は、腓骨神経麻痺（因果関係なし）のため、死亡の 21 日前に中止された。治験担当医師は、当該事象と治験薬との因果関係はおそらく関連なしと判定した。
- 被験者 [redacted] は、C788-047 試験の開始当初から R788 の投与を受けており、C788-049 試験の 1345 日目（R788 投与 1516 日目）に、脈拍不検出及び末期呼吸不全状態で発見され、蘇生処置を行ったが、細菌性心内膜炎のため死亡した。治験担当医師は、当該事象と治験薬との因果関係はおそらく関連なしと判定した。
- 被験者 [redacted] は、C788-048 試験でプラセボの投与を受けており、C788-049 試験の 1340 日目（プラセボ投与開始から 1507 日目）に、心肺停止のため死亡した。治験担当医師は、当該事象と治験薬との因果関係はおそらく関連なしと判定した。

2.7.4.2.1.2.3 海外第 II 相臨床試験（D4300-022）

死亡は 5.6%（1/18 例）認められたが、治験薬との因果関係なしと判定された。1 例の詳細は以下のとおり。

被験者[redacted] は、ITP 並びに心房細動、冠動脈疾患、高血圧、うっ血性心不全及び四枝バイパス心臓手術を含む多発性心血管障害の既往歴を有する 8[redacted] 歳の白人男性であった。被験者は複数の併用薬を服用していた。R788 による治療開始後、被験者は心房細動及び自動植込み型心臓除細動器の留置のため入院した。装置の機械的破損が起こり、経食道心エコー像ガイド下心臓除細動を試みた。処置の間、心血管ショックを発症した被験者は、蘇生及び人工換気された。被験者はその後、心室細動を発症し、翌日死亡した。治験担当医師は、重篤な有害事象（うっ血性心不全及び高血圧に続発する心肺停止及び無酸素性脳症）を高度と評価し、本事象は治験薬と関連なしと判定した。治験依頼者も本事象は治験薬と関連なしと判定した。

2.7.4.2.1.2.4 その他の第 I 相臨床試験及び臨床薬理試験

死亡は認められなかった。

2.7.4.2.1.3 その他の重篤な有害事象

2.7.4.2.1.3.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験において認められた重篤な有害事象を表 2.7.4.2.1.3.1-1 に示す。

R788 投与期において、重篤な有害事象は 21.2%（7/33 例）認められた。このうち治験薬との因果関係ありと判定されたのは 6.1%（2/33 例）であり、重篤な副作用の内訳は血小板減少症及び下痢各 3.0%（1/33 例）であった。2 例以上認められた重篤な有害事象はなかった。重篤な出血関連有害事象は認められなかった。

プラセボ対照期において、重篤な有害事象は R788 群で 9.1%（2/22 例）及びプラセボ群で 8.3%（1/12 例）認められた。このうち治験薬との因果関係ありと判定されたのは R788 群の

9.1%（2/22 例）であり、重篤な副作用の内訳は下痢及び血小板減少症各 4.5%（1/22 例）であった。いずれかの投与群で 2 例以上認められた重篤な有害事象はなかった。重篤な出血関連有害事象は、R788 群では認められず、プラセボ群で 8.3%（1/12 例）認められた。

休薬期において、重篤な有害事象は認められなかった。

表 2.7.4.2.1.3.1-1 重篤な有害事象（R788-1301 試験）

試験番号 被験者識別コード	第 I 期 投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
R788-1301 [redacted]	R788	日本人 女性 5[redacted]歳	下痢	Day 19 100 mg 1 日 2 回	高度	重篤	減量	回復 Day 26	関連あり
R788-1301 [redacted]	プラセボ	日本人 女性 7[redacted]歳	橈骨骨折	Day 263 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 393	関連なし
R788-1301 [redacted]	R788	日本人 女性 5[redacted]歳	大腸ポリープ	Day 246 150 mg 1 日 2 回	軽度	重篤	変更なし	回復 Day 351	関連なし
R788-1301 [redacted]	プラセボ	日本人 女性 6[redacted]歳	蜂巣炎	Day 251 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 269	関連なし
			自己免疫性肝炎	Day 264 150 mg 1 日 2 回	中等度	重篤	減量	回復 Day 379	関連なし
R788-1301 [redacted]	プラセボ	日本人 男性 6[redacted]歳	心房細動	Day 549 150 mg 1 日 2 回	高度	重篤	変更なし	未回復	関連なし
R788-1301 [redacted]	R788	日本人 女性 5[redacted]歳	血小板減少症	Day 50 休薬中	中等度	重篤	変更なし	軽快	関連あり
R788-1301 [redacted]	プラセボ	日本人 女性 6[redacted]歳	帯状疱疹	Day 258 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 305	関連なし
			腰部脊柱管狭窄症	Day 328 150 mg 1 日 2 回	中等度	重篤	変更なし	軽快	関連なし
R788-1301 [redacted]	プラセボ	日本人 女性 7[redacted]歳	胆管結石	Day 26 プラセボ	中等度	重篤	変更なし	回復 Day 91	関連なし
			処置による出血	Day 136 プラセボ	中等度	重篤	変更なし	回復 Day 148	関連なし

(Source : 5.3.5.1.1, 表 12.3.2.2-1, 14.3.3, Listing 14.4.4.1.1, Listing 16.2.7-1 改編)

2.7.4.2.1.3.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047、C788-048 及び C788-049 試験において認められた重篤な有害事象を表 2.7.4.2.1.3.2-1 及び表 2.7.4.2.1.3.2-2 に示す。

1) C788-047 及び C788-048 試験の統合解析

重篤な有害事象は R788 群で 12.7%（13/102 例）及びプラセボ群で 20.8%（10/48 例）認められた。このうち治験薬との因果関係ありと判定されたのは R788 群で 3.9%（4/102 例）及びプラセボ群で 2.1%（1/48 例）であり、R788 群で認められた重篤な副作用の内訳は発熱性好中球減少症、下痢、肺炎及び高血圧クリーゼ各 1.0%（1/102 例）であった。

いずれかの投与群で 2 例以上認められた重篤な有害事象は、血小板減少症（R788 群 1.0%（1/102 例）及びプラセボ群 4.2%（2/48 例）（以下同順））、鼻出血（2.0%（2/102 例）及び 2.1%

（1/48 例））、並びに月経過多（0.0%（0/102 例）及び 4.2%（2/48 例））であった。重篤な出血関連有害事象は、R788 群で 4.9%（5/102 例）及びプラセボ群で 10.4%（5/48 例）認められた。

2) C788-049 試験

重篤な有害事象は 27.6%（34/123 例）認められた。このうち治験薬との因果関係ありと判定されたのは 4.9%（6/123 例）であり、重篤な副作用の内訳は敗血症、下痢、硬結性紅斑、結核、トランスアミナーゼ上昇、心房細動、発熱及び上気道感染各 0.8%（1/123 例）であった。

2 例以上認められた重篤な有害事象は、血小板減少症 6.5%（8/123 例）、鼻出血 2.4%（3/123 例）、並びに敗血症、胃腸出血及びトランスアミナーゼ上昇各 1.6%（2/123 例）であった。重篤な出血関連有害事象は、8.9%（11/123 例）認められた。

表 2.7.4.2.1.3.2-1 重篤な有害事象（C788-047 及び C788-048 試験）

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
C788-047 [redacted]	R788	ヒスパニック 男性 5[redacted]歳	失神	Day 32 150 mg 1 日 2 回	高度	重篤	中止	回復 Day 37	おそらく関連なし
C788-047 [redacted]	R788	ヒスパニック 女性 4[redacted]歳	肺炎	Day 23 100 mg 1 日 2 回	高度	重篤	中止	回復 Day 36	おそらく関連あり
C788-047 [redacted]	R788	白人 女性 7[redacted]歳	下痢	Day 54 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 63	関連があるかもしれない
C788-047 [redacted]	R788	白人 男性 3[redacted]歳	発熱性好中球減少症	Day 103 150 mg 1 日 1 回	高度	重篤	休薬	回復 Day 108	関連があるかもしれない
C788-047 [redacted]	R788	白人 女性 4[redacted]歳	膣出血	Day 27 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 37	おそらく関連なし
C788-047 [redacted]	R788	白人 男性 6[redacted]歳	血小板減少症	Day 4 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 5	おそらく関連なし
			血小板減少症	Day 17 100 mg 1 日 2 回	高度	重篤	中止	回復 Day 85	おそらく関連なし
C788-047 [redacted]	R788	白人 女性 8[redacted]歳	免疫性血小板減少性紫斑病	Day 134 休薬中	軽度	重篤	変更なし	回復 Day 139	おそらく関連なし
C788-047 [redacted]	R788	白人 男性 7[redacted]歳	鼻出血	Day 40 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 40	おそらく関連なし
			鼻出血	Day 46 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 50	おそらく関連なし
			網膜裂孔	Day 45 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 50	おそらく関連なし

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
C788-047 [redacted]	プラセボ	黒人 女性 3[redacted]歳	うっ血性心不全	Day 5 プラセボ	中等度	重篤	休薬	回復 Day 10	おそらく関連なし
C788-047 [redacted]	プラセボ	アフリカ系アメリカ人 男性 6[redacted]歳	胃腸出血	Day 45 プラセボ	高度	重篤	変更なし	回復 Day 48	おそらく関連なし
			貧血	Day 52 プラセボ	高度	重篤	変更なし	回復 Day 77	おそらく関連なし
			貧血	Day 110 プラセボ	高度	重篤	変更なし	回復 Day 112	おそらく関連なし
			胃腸出血	Day 115 プラセボ	高度	重篤	変更なし	回復 Day 127	おそらく関連なし
C788-047 [redacted]	プラセボ	白人 女性 7[redacted]歳	鼻出血	Day 43 プラセボ	中等度	重篤	変更なし	回復 Day 45	おそらく関連なし
			敗血症	Day 65 プラセボ	高度	重篤	該当せず	死亡 Day 74	おそらく関連なし
C788-047 [redacted]	プラセボ	アジア人 女性 3[redacted]歳	月経過多	Day 56 プラセボ	高度	重篤	変更なし	回復 Day 59	おそらく関連なし
C788-047 [redacted]	プラセボ	白人 女性 5[redacted]歳	慢性閉塞性肺疾患	Day 21 プラセボ	中等度	重篤	変更なし	回復したが残存症状あり Day 24	おそらく関連なし
C788-048 [redacted]	R788	白人 男性 2[redacted]歳	挫傷	Day 29 100 mg 1 日 2 回	高度	重篤	変更なし	回復したが残存症状あり Day 31	おそらく関連なし
C788-048 [redacted]	R788	白人 女性 7[redacted]歳	高血圧クリーゼ	Day 21 100 mg 1 日 2 回	高度	重篤	休薬	回復 Day 25	おそらく関連あり
C788-048 [redacted]	R788	白人 女性 6[redacted]歳	鼻出血	Day 15 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 15	おそらく関連なし
			形質細胞性骨髄腫	Day 18 100 mg 1 日 2 回	中等度	重篤	中止	死亡 Day 90	おそらく関連なし
C788-048 [redacted]	R788	白人 女性 5[redacted]歳	血小板数減少	Day 46 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 47	おそらく関連なし
			気管支炎	Day 62 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 67	おそらく関連なし
C788-048 [redacted]	R788	白人 女性 6[redacted]歳	一過性脳虚血発作	Day 80 150 mg 1 日 1 回	軽度	重篤	変更なし	回復 Day 83	おそらく関連なし
C788-048 [redacted]	プラセボ	白人 女性 2[redacted]歳	感染	Day 70 プラセボ	中等度	重篤	変更なし	回復 Day 72	おそらく関連なし
C788-048 [redacted]	プラセボ	白人 女性 2[redacted]歳	月経過多	Day 38 プラセボ	中等度	重篤	変更なし	回復したが残存症状あり Day 41	関連があるかもしれない
C788-048 [redacted]	プラセボ	白人 男性 5[redacted]歳	筋断裂	Day 73 プラセボ	高度	重篤	変更なし	回復 Day 168	おそらく関連なし

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
C788-048 [redacted]	プラセボ	白人 男性 4[redacted]歳	血小板減少症	Day 85 プラセボ	高度	重篤	変更なし	回復 Day 86	おそらく関連なし
C788-048 [redacted]	プラセボ	白人 女性 5[redacted]歳	点状出血	Day 31 プラセボ	高度	重篤	変更なし	回復 Day 34	おそらく関連なし
			血小板減少症	Day 70 プラセボ	高度	重篤	変更なし	回復 Day 72	おそらく関連なし
			点状出血	Day 85 プラセボ	高度	重篤	変更なし	回復 Day 86	おそらく関連なし
C788-048 [redacted]	プラセボ	白人 女性 4[redacted]歳	血小板減少症	Day 18 プラセボ	高度	重篤	変更なし	回復 Day 25	おそらく関連なし
			血小板減少症	Day 32 プラセボ	高度	重篤	変更なし	回復 Day 33	おそらく関連なし
			血小板減少症	Day 42 プラセボ	高度	重篤	変更なし	回復 Day 46	おそらく関連なし
			血小板減少症	Day 53 プラセボ	高度	重篤	変更なし	回復 Day 56	おそらく関連なし
			血小板減少症	Day 64 プラセボ	高度	重篤	変更なし	回復 Day 68	おそらく関連なし
			血小板減少症	Day 74 プラセボ	高度	重篤	変更なし	回復 Day 81	おそらく関連なし

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(Source: 5.3.5.1.2, Table 12-5, 14.3.3; 5.3.5.1.3, Table 12-5, 14.3.3 改編)

表 2.7.4.2.1.3.2-2 重篤な有害事象（C788-049 試験）

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
C788-049 [redacted]	R788/ R788	白人 女性 7[redacted]歳	乳様突起炎	Day 1422 150 mg 1 日 2 回	高度	重篤	休薬	回復 Day 1526	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 8[redacted]歳	胃前庭部毛細血管拡張症	Day 96 100 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 99	おそらく関連なし
			大動脈狭窄	Day 97 100 mg 1 日 2 回	高度	重篤	変更なし	回復[b] Day 148	おそらく関連なし
			胃腸出血[a]	Day 319 100 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 324	おそらく関連なし
			メレナ[a]	Day 668 100 mg 1 日 2 回	高度	重篤	休薬	回復 Day 675	おそらく関連なし
			トランスアミナーゼ上昇	Day 719 100 mg 1 日 2 回	高度	重篤	休薬	回復 Day 730	おそらく関連なし
			尿路性敗血症	Day 724 100 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 730	おそらく関連なし
			敗血症	Day 890 100 mg 1 日 2 回	高度	重篤	休薬	回復 Day 896	関連があるかもしれない
			尿路性敗血症	Day 1319 100 mg 1 日 2 回	高度	重篤	休薬	回復 Day 1326	おそらく関連なし

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
			細菌性心内膜炎	Day 1345 100 mg 1 日 2 回	高度	重篤	変更なし	死亡 Day 1345	おそらく関連なし
C788-049 [redacted]	R788/ R788	黒人 女性 4[redacted]歳	ウイルス感染	Day 991 100 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 1009	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 5[redacted]歳	敗血症	Day 39 150 mg 1 日 2 回	高度	重篤	休薬	死亡 Day 58	おそらく関連なし
C788-049 [redacted]	R788/ R788	フィリピン人 女性 8[redacted]歳	ピロリン酸カルシウム結晶性軟骨石灰化症	Day 108 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 131	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 7[redacted]歳	鼻出血[a]	Day 36 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 37	おそらく関連なし
			血小板減少症	Day 77 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 81	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 8[redacted]歳	胃腸炎	Day 81 150 mg 1 日 2 回	中等度	重篤	休薬	回復 Day 93	おそらく関連なし
			下痢	Day 351 150 mg 1 日 2 回	中等度	重篤	中止	回復 Day 358	おそらく関連あり
C788-049 [redacted]	R788/ R788	白人 男性 7[redacted]歳	肺炎	Day 294 150 mg 1 日 2 回	高度	重篤	発現前に中止	死亡 Day 294	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 3[redacted]歳	血小板減少症	Day 15 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 16	おそらく関連なし
			血小板減少症	Day 95 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 96	おそらく関連なし
C788-049 [redacted]	R788/ R788	アジア人 女性 4[redacted]歳	硬結性紅斑	Day 1196 150 mg 1 日 2 回	高度	重篤	変更なし	回復 1354 Day	関連があるかもしれない
			結核	Day 1208 150 mg 1 日 2 回	高度	重篤	変更なし	回復 1452 Day	関連があるかもしれない
C788-049 [redacted]	R788/ R788	白人 女性 4[redacted]歳	痔核	Day 1010 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 1012	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 5[redacted]歳	鼻出血[a]	Day 73 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 82	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 5[redacted]歳	トランスアミナーゼ上昇	Day 29 100 mg 1 日 2 回	高度	重篤	中止	回復 Day 41	おそらく関連あり
C788-049 [redacted]	R788/ R788	白人 女性 5[redacted]歳	胸椎骨折	Day 77 150 mg 1 日 2 回	軽度	重篤	変更なし	回復 Day 80	おそらく関連なし
			血小板減少症	Day 966 150 mg 1 日 2 回	軽度	重篤	変更なし	回復 Day 967	おそらく関連なし
			尿路感染	Day 1108 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 1113	おそらく関連なし

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
			血小板減少症	Day 1200 150 mg 1 日 2 回	軽度	重篤	変更なし	回復 Day 1203	おそらく関連なし
			血小板減少症	Day 1343 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 1344	おそらく関連なし
			血小板減少症	Day 1375 150 mg 1 日 2 回	軽度	重篤	変更なし	回復 Day 1377	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 4[redacted]歳	頭痛	Day 1376 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 1380	おそらく関連なし
C788-049 [redacted]	R788/ R788	白人 女性 6[redacted]歳	口腔内出血 [a,d]	Day 45 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 47	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	白人 女性 7[redacted]歳	直腸出血 [a]	Day 37 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 37	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	白人 男性 4[redacted]歳	腎結石症	Day 182 150 mg 1 日 2 回	高度	重篤	変更なし	回復 [b] Day 193	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	白人 男性 2[redacted]歳	血便排泄 [a]	Day 90 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 91	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	黒人 女性 3[redacted]歳	口腔カンジダ症	Day 86 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 88	おそらく関連なし
			鼻出血 [a]	Day 89 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 93	おそらく関連なし
C788-049 [redacted] [c]	プラセボ /R788	黒人 男性 6[redacted]歳	胃腸出血 [a,c]	Day −5 プラセボ	高度	重篤	変更なし	回復 Day 8	おそらく関連なし
			胃腸出血 [a]	Day 30 100 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 35	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	アジア人 女性 4[redacted]歳	血小板減少症	Day 677 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 688	おそらく関連なし
			血小板減少症	Day 698 150 mg 1 日 2 回	高度	重篤	中止	回復 Day 712	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	アジア人 女性 3[redacted]歳	月経過多 [a]	Day 212 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 215	おそらく関連なし
			粘膜出血 [a]	Day 611 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 616	おそらく関連なし
			粘膜出血 [a]	Day 634 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 636	おそらく関連なし
			粘膜出血 [a]	Day 1017 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 1018	おそらく関連なし
C788-049 [redacted]	プラセボ /R788	白人 女性 7[redacted]歳	心房細動	Day 150 150 mg 1 日 2 回	中等度	重篤	休薬	回復 Day 151	関連があるかもしれない
C788-049 [redacted]	プラセボ /R788	白人 女性 6[redacted]歳	胆嚢炎	Day 330 100 mg 1 日 2 回	高度	重篤	休薬	回復 Day 340	おそらく関連なし

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/ 非重篤	治験薬の処置	転帰 転帰日	因果関係
C788-049 [redacted]	プラセボ/R788	白人 女性 2[redacted]歳	発熱	Day 68 150 mg 1日2回	中等度	重篤	変更なし	回復 Day 70	関連があるかもしれない
			上気道感染	Day 68 150 mg 1日2回	中等度	重篤	変更なし	回復 Day 70	関連があるかもしれない
C788-049 [redacted]	プラセボ/R788	白人 男性 8[redacted]歳	心肺停止	Day 1340 150 mg 1日2回	高度	重篤	変更なし	死亡 Day 1340	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 男性 7[redacted]歳	ブドウ球菌性蜂巣炎	Day 637 150 mg 1日2回	高度	重篤	変更なし	回復 Day 780	おそらく関連なし
			うっ血性心不全	Day 1253 150 mg 1日2回	高度	重篤	変更なし	回復 Day 1258	おそらく関連なし
			腹水	Day 1271 150 mg 1日2回	中等度	重篤	変更なし	回復 Day 1276	おそらく関連なし
C788-049 [redacted][c]	プラセボ/R788	白人 男性 5[redacted]歳	筋断裂[c]	Day -12 プラセボ	高度	重篤	変更なし	回復 Day 83	おそらく関連なし
			意識消失	Day 319 150 mg 1日2回	軽度	重篤	休薬	回復 Day 324	おそらく関連なし
			血小板減少症	Day 1393 150 mg 1日2回	高度	重篤	変更なし	回復 Day 1399	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 男性 4[redacted]歳	血小板減少症	Day 1 100 mg 1日2回	高度	重篤	変更なし	回復 Day 2	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 女性 5[redacted]歳	点状出血[a]	Day 1 100 mg 1日2回	高度	重篤	変更なし	回復 Day 2	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 女性 4[redacted]歳	血小板減少症	Day 76 150 mg 1日2回	高度	重篤	変更なし	回復 Day 77	おそらく関連なし
			血小板減少症	Day 97 150 mg 1日2回	高度	重篤	変更なし	回復 Day 103	おそらく関連なし
			紫斑[a]	Day 161 150 mg 1日2回	高度	重篤	変更なし	回復 Day 166	おそらく関連なし
			血小板減少症	Day 1360 150 mg 1日2回	高度	重篤	変更なし	回復 Day 1362	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 男性 6[redacted]歳	血小板減少症	Day 29 150 mg 1日1回	高度	重篤	変更なし	未回復 Day 55	おそらく関連なし
C788-049 [redacted]	プラセボ/R788	白人 男性 6[redacted]歳	胸痛	Day 59 100 mg 1日2回	軽度	重篤	発現前に中止	回復 Day 60	おそらく関連なし

Abbreviations: EDC = electronic data capture; SAE = serious adverse event; y = years.
a Bleeding-related SAEs.
b Resolved with sequelae.
c SAE onset occurred in parent study (either CSR C788-047 or C788-048) and resolved in CSR788-049.
d SAE was reported as petechiae in the EDC but recorded as a mouth hemorrhage in the database; the difference in terminology was not resolved.
MedDRA version.18.1
(Source: 5.3.5.2.2, Table 12-6, 14.3.3.2 改編)

2.7.4.2.1.3.3 海外第 II 相臨床試験（D4300-022）

D4300-022 試験において認められた重篤な有害事象を表 2.7.4.2.1.3.3-1 に示す。

重篤な有害事象は 44.4%（8/18 例）認められた。このうち治験薬との因果関係ありと判定されたのは 11.1%（2/18 例）であり、重篤な副作用の内訳は悪心、嘔吐、下痢及び深部静脈血栓症各 5.6%（1/18 例）であった。

2 例以上認められた重篤な有害事象は、下痢、悪心及び嘔吐各 11.1%（2/18 例）であった。重篤な出血関連有害事象は、16.7%（3/18 例）認められた。

表 2.7.4.2.1.3.3-1 重篤な有害事象（D4300-022 試験）

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/非重篤	治験薬の処置	転帰 転帰日	因果関係
D4300-022 [redacted]	R788	ヒスパニック 女性 3[redacted]歳	自然流産	Day 1128 175 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 1129	関連なし
D4300-022 [redacted]	R788	白人 女性 5[redacted]歳	胃腸出血	Day 173 175 mg 1 日 2 回	中等度	重篤	中止	回復 Day 177	関連なし
D4300-022 [redacted]	R788	白人 男性 7[redacted]歳	嘔吐	Day 56 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 65	おそらく関連なし
			下痢	Day 56 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 65	おそらく関連なし
			脱水	Day 56 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 65	おそらく関連なし
			動悸	Day 56 150 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 65	おそらく関連なし
			悪心	Day 80 150 mg 1 日 2 回	中等度	重篤	休薬	回復 Day 88	おそらく関連あり
			嘔吐	Day 80 150 mg 1 日 2 回	中等度	重篤	休薬	回復 Day 88	おそらく関連あり
			下痢	Day 80 150 mg 1 日 2 回	中等度	重篤	休薬	回復 Day 88	おそらく関連あり
D4300-022 [redacted]	R788	白人 男性 8[redacted]歳	うっ血性心不全	Day 314 朝 100 mg/ 夕 75 mg	高度	重篤	変更なし	回復したが残存症状あり Day 316	関連なし
			無酸素性脳症	Day 418 75 mg 1 日 2 回	高度	重篤	不明	死亡 Day 426	関連なし
D4300-022 [redacted]	R788	白人 女性 5[redacted]歳	点状出血	Day 479 50 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 482	関連なし
			歯肉出血	Day 479 50 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 482	関連なし
			直腸出血	Day 479 50 mg 1 日 2 回	中等度	重篤	変更なし	回復 Day 482	関連なし
D4300-022 [redacted]	R788	白人 女性 8[redacted]歳	尿路感染	Day 17 125 mg 1 日 2 回	中等度	重篤	変更なし (ER 内で 1 回不服用)	回復 Day 20	関連なし
			深部静脈血栓症	Day 30 150 mg 1 日 2 回	高度	重篤	該当なし	回復 Day 227	おそらく関連あり
D4300-022 [redacted]	R788	中東人 女性 6[redacted]歳	悪心	Day 794 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 797	関連なし
			嘔吐	Day 794 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 797	関連なし
			下痢	Day 794 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 797	関連なし

試験番号 被験者識別コード	投与群	人種 性別 年齢	事象名 (PT)	発現時期 発現時投与量	程度	重篤/非重篤	治験薬の処置	転帰 転帰日	因果関係
			浮動性めまい	Day 794 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 797	関連なし
			口腔内出血	Day 957 150 mg 1 日 2 回	高度	重篤	変更なし	回復 Day 962	関連なし
D4300-022 [redacted]	R788	白人 男性 8[redacted]歳	肺炎	Day 111 150 mg 1 日 2 回	中等度	重篤	変更なし（入院中、何回か不服用）	回復 Day 117	関連なし

MedDRA Version 13.0
(Source: 5.3.5.2.1, 12.3.2 改編)

2.7.4.2.1.3.4 日本人を対象とした第 I 相臨床試験（D4300-007 及び D4300-032）

D4300-007 及び D4300-032 試験において、重篤な有害事象は認められなかった。

2.7.4.2.1.3.5 その他の第 I 相臨床試験及び臨床薬理試験

D4300-007 及び D4300-032 試験以外の第 I 相臨床試験及び臨床薬理試験において認められた重篤な有害事象は、肝機能低下者試験（D4300-010）で 3.1%（1/32 例）、薬物相互作用試験（ピオグリタゾン）（D4300-014）で 6.7%（1/15 例）認められた。このうち治験薬との因果関係ありと判定されたのは D4300-014 試験の 6.7%（1/15 例）であり、重篤な副作用の内訳は上部消化管出血であった。

重篤な出血関連有害事象は、D4300-014 試験で 6.7%（1/15 例）認められた。

2.7.4.2.1.4 その他の重要な有害事象

2.7.4.2.1.4.1 減量又は休薬に至った有害事象

2.7.4.2.1.4.1.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験において認められた治験薬の減量に至った有害事象及び治験薬の休薬に至った有害事象を表 2.7.4.2.1.4.1.1-1～表 2.7.4.2.1.4.1.1-4 に示す。

R788 投与期中、治験薬の減量に至った有害事象は 60.6%（20/33 例）、治験薬の休薬に至った有害事象は 3.0%（1/33 例）であった。

プラセボ対照期中、治験薬の減量に至った有害事象は R788 群で 45.5%（10/22 例）及びプラセボ群で 0.0%（0/12 例）であり、治験薬の休薬に至った有害事象は認められなかった。

表 2.7.4.2.1.4.1.1-1　治験薬の減量に至った有害事象（R788-1301 試験 プラセボ対照期）

Period I

System Organ Class Preferred Term	R788 N=22 n (%)	プラセボ N=12 n (%)
Any Adverse Events Leading to Dose Reduction	10 (45.5)	0 (0.0)
血液およびリンパ系障害	1 (4.5)	0 (0.0)
好中球減少症	1 (4.5)	0 (0.0)
血管障害	1 (4.5)	0 (0.0)
高血圧	1 (4.5)	0 (0.0)
胃腸障害	3 (13.6)	0 (0.0)
下痢	3 (13.6)	0 (0.0)
肝胆道系障害	1 (4.5)	0 (0.0)
肝機能異常	1 (4.5)	0 (0.0)
臨床検査	5 (22.7)	0 (0.0)
血中クレアチンホスホキナーゼ増加	1 (4.5)	0 (0.0)
血圧上昇	1 (4.5)	0 (0.0)
肝機能検査異常	1 (4.5)	0 (0.0)
好中球数減少	2 (9.1)	0 (0.0)

(Source : 5.3.5.1.1, Table 14.1.4.1.3.7)

表 2.7.4.2.1.4.1.1-2　治験薬の減量に至った有害事象（R788-1301 試験 R788 投与期）

R788 Treatment Period

System Organ Class Preferred Term	R788 N=33 n (%)
Any Adverse Events Leading to Dose Interruption	20 (60.6)
感染症および寄生虫症	1 (3.0)
ウイルス感染	1 (3.0)
血液およびリンパ系障害	2 (6.1)
好中球減少症	2 (6.1)
血管障害	4 (12.1)
高血圧	4 (12.1)
胃腸障害	5 (15.2)
腹部不快感	1 (3.0)
下痢	4 (12.1)
肝胆道系障害	2 (6.1)
自己免疫性肝炎	1 (3.0)
肝機能異常	1 (3.0)
一般・全身障害および投与部位の状態	1 (3.0)
末梢性浮腫	1 (3.0)
臨床検査	8 (24.2)
アラニンアミノトランスフェラーゼ増加	1 (3.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (3.0)
血中クレアチンホスホキナーゼ増加	1 (3.0)
血圧上昇	2 (6.1)
肝機能検査異常	1 (3.0)
肝機能検査値上昇	1 (3.0)
好中球数減少	2 (6.1)

(Source : 5.3.5.1.1, Table 14.3.4.1.3.7)

表 2.7.4.2.1.4.1.1-3　治験薬の休薬に至った有害事象（R788-1301 試験 R788 投与期）

R788 Treatment Period

System Organ Class Preferred Term	R788 N=33 n (%)
Any Adverse Events Leading to Dose Interruption	1 (3.0)
胃腸障害	1 (3.0)
悪心	1 (3.0)

(Source : 5.3.5.1.1, Table 14.3.4.1.3.9)

表 2.7.4.2.1.4.1.1-4　治験薬の減量又は休薬に至った有害事象（R788-1301 試験）

被験者識別コード	第 I 期の治験薬	発現時期	PT	治験薬の処置（期）	転帰	因果関係
発現時治験薬：R788						
[redacted]	R788	II	好中球減少症	休薬（II） 減量（III）	回復	有
		III	好中球減少症	減量（III）	回復	有
[redacted]	R788	I	高血圧	減量（I） 変更なし（II） 減量（III）	軽快	有
		I	下痢	減量（I）	回復	有
[redacted]	R788	I	下痢	減量（I）	回復	有
[redacted]	R788	I	肝機能異常	減量（I）	回復	有
[redacted]	Placebo	II	自己免疫性肝炎	休薬（II） 減量（III）	回復	無
[redacted]	Placebo	II	高血圧	減量（II）	回復	有
		II	下痢	減量（II） 減量（III）	回復	有
[redacted]	R788	I	下痢	減量（I）	回復	有
		I	下痢	減量（I）	回復	有
[redacted]	R788	I	腹部不快感	変更なし（I） 減量（II）	回復	有
[redacted]	R788	I	肝機能検査異常	減量（I）	回復	有
	R788	II	末梢性浮腫	減量（II）	回復	有
	R788	I	好中球数減少	減量（I）	回復	有
	R788	I	血圧上昇	減量（I）	回復	有
[redacted]	Placebo	II	肝機能検査値上昇	減量（II） 減量（III）	未回復	有
[redacted]	R788	I	好中球減少症	減量（I）	回復	無
		III	好中球減少症	減量（III）	回復	無
[redacted]	Placebo	II	高血圧	減量（II）	回復	有
[redacted]	R788	I	高血圧	変更なし（I） 減量（II）	未回復	無
		I	好中球数減少	減量（I）	回復	有
		II	好中球数減少	減量（II）	回復	有
[redacted]	Placebo	II	アラニンアミノトランスフェラーゼ増加	減量（II）	回復	有
		II	アスパラギン酸アミノトランスフェラーゼ増加	減量（II）	回復	有
[redacted]	R788	II	血圧上昇	減量（II） 変更なし（III）	未回復	有
[redacted]	R788	I	血中クレアチンホスホキナーゼ増加	減量（I） 変更なし（II）	回復	無
		II	悪心	変更なし（II） 休薬（III）	未回復	無
休薬期発現事象						
[redacted]	R788	休薬期	ウイルス感染	減量（III）	回復	無

(Source : 5.3.5.1.1, 表 12.3.2.3.1-1 改編)

2.7.4.2.1.4.1.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の統合解析

C788-047、C788-048 及び C788-049 試験において認められた治験薬の減量に至った有害事象及び治験薬の休薬に至った有害事象を表 2.7.4.2.1.4.1.2-1、表 2.7.4.2.1.4.1.2-2、表 2.7.4.2.1.4.1.2-3 及び表 2.7.4.2.1.4.1.2-4 に示す。

R788 投与期中、治験薬の減量に至った有害事象は 11.0%（16/146 例）、治験薬の休薬に至った有害事象は 26.0%（38/146 例）認められた。2 例以上認められた治験薬の減量に至った有害事象は、下痢 2.7%（4/146 例）及び高血圧 1.4%（2/146 例）であった。2 例以上認められた治験薬の休薬に至った有害事象は、ALT 増加及び下痢各 3.4%（5/146 例）、並びに肝酵素上昇、腹痛、敗血症、高血圧及びインフルエンザ様疾患各 1.4%（2/146 例）であった。

プラセボ対照期中、治験薬の減量に至った有害事象は R788 群で 8.8%（9/102 例）及びプラセボ群で 2.1%（1/48 例）、治験薬の休薬に至った有害事象は R788 群で 17.6%（18/102 例）及びプラセボ群で 10.4%（5/48 例）認められた。R788 群で 2 例以上認められた治験薬の減量に至った有害事象は、下痢（R788 群 2.0%（2/102 例）及びプラセボ群 0.0%（0/48 例）（以下同順））、並びに高血圧（2.0%（2/102 例）及び 0.0%（0/48 例））であった。R788 群で 2 例以上認められた治験薬の休薬に至った有害事象は、ALT 増加（R788 群 4.9%（5/102 例）及びプラセボ群 0.0%（0/48 例）（以下同順））、下痢（2.9%（3/102 例）及び 0.0%（0/48 例））、並びにインフルエンザ様疾患（2.0%（2/102 例）及び 0.0%（0/48 例））であった。

表 2.7.4.2.1.4.1.2-1　治験薬の減量に至った有害事象（C788-047、C788-048 及び C788-049 試験 R788 投与期）

System Organ Class Preferred Term	R788 (N=146) n (%)
Any Adverse Events Leading to Dose Reduction	16 (11.0)
臨床検査	5 (3.4)
アラニンアミノトランスフェラーゼ増加	1 (0.7)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7)
肝酵素上昇	1 (0.7)
肝機能検査異常	1 (0.7)
好中球数減少	1 (0.7)
胃腸障害	4 (2.7)
下痢	4 (2.7)
血管障害	3 (2.1)
高血圧	2 (1.4)
コントロール不良の血圧	1 (0.7)
血液およびリンパ系障害	2 (1.4)
発熱性好中球減少症	1 (0.7)
血小板増加症	1 (0.7)
感染症および寄生虫症	2 (1.4)
肺炎	1 (0.7)
気道感染	1 (0.7)
一般・全身障害および投与部位の状態	1 (0.7)
胸痛	1 (0.7)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.4.2.1)

表 2.7.4.2.1.4.1.2-2　治験薬の休薬に至った有害事象（C788-047、C788-048 及び C788-049 試験 R788 投与期）

System Organ Class Preferred Term	R788 (N=146) n (%)
Any Adverse Events Leading to Dose Interruption	38 (26.0)
臨床検査	11 (7.5)
アラニンアミノトランスフェラーゼ増加	5 (3.4)
肝酵素上昇	2 (1.4)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7)
血中ビリルビン増加	1 (0.7)
好中球数減少	1 (0.7)
血小板数増加	1 (0.7)
トランスアミナーゼ上昇	1 (0.7)
胃腸障害	8 (5.5)
下痢	5 (3.4)
腹痛	2 (1.4)
嘔吐	1 (0.7)
感染症および寄生虫症	7 (4.8)
敗血症	2 (1.4)
胃腸炎	1 (0.7)
下気道感染	1 (0.7)
乳様突起炎	1 (0.7)
鼻咽頭炎	1 (0.7)
歯感染	1 (0.7)
尿路性敗血症	1 (0.7)
血管障害	4 (2.7)
高血圧	2 (1.4)
高血圧クリーゼ	1 (0.7)
末梢静脈疾患	1 (0.7)
一般・全身障害および投与部位の状態	3 (2.1)
インフルエンザ様疾患	2 (1.4)
末梢腫脹	1 (0.7)
血液およびリンパ系障害	2 (1.4)
発熱性好中球減少症	1 (0.7)
血小板増加症	1 (0.7)
神経系障害	2 (1.4)
意識消失	1 (0.7)
失神寸前の状態	1 (0.7)
呼吸器、胸郭および縦隔障害	2 (1.4)
呼吸困難	1 (0.7)
鼻出血	1 (0.7)
心臓障害	1 (0.7)
心房細動	1 (0.7)
肝胆道系障害	1 (0.7)
胆嚢炎	1 (0.7)
免疫系障害	1 (0.7)
薬物過敏症	1 (0.7)
代謝および栄養障害	1 (0.7)
低カリウム血症	1 (0.7)
筋骨格系および結合組織障害	1 (0.7)
関節痛	1 (0.7)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.5.2.1)

表 2.7.4.2.1.4.1.2-3　治験薬の減量に至った有害事象（C788-047 及び C788-048 試験プラセボ対照期）

System Organ Class Preferred Term	R788 (N=102) n (%)	Placebo (N=48) n (%)
Any Adverse Events Leading to Dose Reduction	9 (8.8)	1 (2.1)
臨床検査	3 (2.9)	1 (2.1)
アラニンアミノトランスフェラーゼ増加	1 (1.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.0)	0 (0.0)
好中球数減少	1 (1.0)	0 (0.0)
血小板数増加	0 (0.0)	1 (2.1)
血液およびリンパ系障害	2 (2.0)	0 (0.0)
発熱性好中球減少症	1 (1.0)	0 (0.0)
血小板増加症	1 (1.0)	0 (0.0)
胃腸障害	2 (2.0)	0 (0.0)
下痢	2 (2.0)	0 (0.0)
血管障害	2 (2.0)	0 (0.0)
高血圧	2 (2.0)	0 (0.0)
一般・全身障害および投与部位の状態	1 (1.0)	0 (0.0)
胸痛	1 (1.0)	0 (0.0)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.4.1.1)

表 2.7.4.2.1.4.1.2-4　治験薬の休薬に至った有害事象（C788-047 及び C788-048 試験プラセボ対照期）

System Organ Class Preferred Term	R788 (N=102) n (%)	Placebo (N=48) n (%)
Any Adverse Events Leading to Dose Interruption	18 (17.6)	5 (10.4)
臨床検査	7 (6.9)	1 (2.1)
アラニンアミノトランスフェラーゼ増加	5 (4.9)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (1.0)	0 (0.0)
血中ビリルビン増加	1 (1.0)	0 (0.0)
好中球数減少	1 (1.0)	0 (0.0)
血小板数増加	0 (0.0)	1 (2.1)
胃腸障害	3 (2.9)	2 (4.2)
下痢	3 (2.9)	0 (0.0)
消化不良	0 (0.0)	1 (2.1)
胃腸出血	0 (0.0)	1 (2.1)
一般・全身障害および投与部位の状態	2 (2.0)	0 (0.0)
インフルエンザ様疾患	2 (2.0)	0 (0.0)
筋骨格系および結合組織障害	1 (1.0)	1 (2.1)
関節痛	1 (1.0)	0 (0.0)
筋骨格痛	0 (0.0)	1 (2.1)
呼吸器、胸郭および縦隔障害	2 (2.0)	0 (0.0)
呼吸困難	1 (1.0)	0 (0.0)
鼻出血	1 (1.0)	0 (0.0)
血管障害	2 (2.0)	0 (0.0)
高血圧クリーゼ	1 (1.0)	0 (0.0)
末梢静脈疾患	1 (1.0)	0 (0.0)
血液およびリンパ系障害	1 (1.0)	0 (0.0)
発熱性好中球減少症	1 (1.0)	0 (0.0)
心臓障害	0 (0.0)	1 (2.1)
うっ血性心不全	0 (0.0)	1 (2.1)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system

organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.5.1.1)

2.7.4.2.1.4.1.3 海外第 II 相臨床試験（D4300-022）

D4300-022 試験において、治験薬の減量又は休薬に至った有害事象は認められなかった。

2.7.4.2.1.4.1.4 第 I 相臨床試験（D4300-007 及び D4300-032）

D4300-007 及び D4300-032 試験において、治験薬の減量又は休薬に至った有害事象は認められなかった。

2.7.4.2.1.4.2 中止に至った有害事象

2.7.4.2.1.4.2.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験において認められた治験薬の中止に至った有害事象を表 2.7.4.2.1.4.2.1-1 に示す。

R788 投与期中、治験薬の中止に至った有害事象は 12.1%（4/33 例）であった。治験薬の中止に至った有害事象は、肝機能異常 2 例、感情不安定、高血圧、下痢各 1 例であった。

プラセボ対照期中、治験薬の中止に至った有害事象は R788 群で 13.6%（3/22 例）認められ、プラセボ群では認められなかった。治験薬の中止に至った有害事象は、肝機能異常 2 例、高血圧及び下痢各 1 例であった。

休薬期中、治験薬の中止に至った有害事象は認められなかった。

表 2.7.4.2.1.4.2.1-1　治験薬の中止に至った有害事象（R788-1301 試験）

被験者識別コード	第 I 期の治験薬	発現時期	PT	治験薬の処置（期）	転帰	因果関係
発現時治験薬：R788						
[redacted]	R788	I	肝機能異常	中止（I）	回復	有
[redacted]	R788	I	感情不安定	変更なし（I） 中止（II）	回復	無
[redacted]	R788	I	下痢	中止（I）	回復	有
		I	高血圧	中止（I）	回復	有
[redacted]	R788	I	肝機能異常	中止（I）	軽快	有

(Source : 5.3.5.1.1, 表 12.3.2.3.1-1 改編)

2.7.4.2.1.4.2.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の統合解析

C788-047、C788-048 及び C788-049 試験において認められた治験薬の中止に至った有害事象を表 2.7.4.2.1.4.2.2-1 及び表 2.7.4.2.1.4.2.2-2 に示す。

R788 投与期中、治験薬の中止に至った有害事象は 19.2%（28/146 例）認められた。2 例以上認められた治験薬の中止に至った有害事象は、下痢 4.1%（6/146 例）、好中球減少症 2.1%（3/146 例）、並びに肝酵素上昇及び血小板減少症各 1.4%（2/146 例）であった。

プラセボ対照期中、治験薬の中止に至った有害事象は R788 群で 10.8%（11/102 例）及びプラセボ群で 8.3%（4/48 例）認められた。R788 群で 2 例以上認められた治験薬の中止に至った有害事象は、好中球減少症（R788 群 2.0%（2/102 例）及びプラセボ群 0.0%（0/48 例））であった。

表 2.7.4.2.1.4.2.2-1　治験薬の中止に至った有害事象（C788-047、C788-048 及び C788-049 試験 R788 投与期）

System Organ Class Preferred Term	R788 (N=146) n (%)
Any Adverse Events Leading to Drug Withdrawal	28 (19.2)
胃腸障害	8 (5.5)
下痢	6 (4.1)
腹痛	1 (0.7)
上腹部痛	1 (0.7)
臨床検査	7 (4.8)
肝酵素上昇	2 (1.4)
アラニンアミノトランスフェラーゼ増加	1 (0.7)
血中ビリルビン増加	1 (0.7)
血圧上昇	1 (0.7)
血小板数減少	1 (0.7)
トランスアミナーゼ上昇	1 (0.7)
血液およびリンパ系障害	5 (3.4)
好中球減少症	3 (2.1)
血小板減少症	2 (1.4)
神経系障害	3 (2.1)
頭痛	1 (0.7)
腓骨神経麻痺	1 (0.7)
失神	1 (0.7)
心臓障害	1 (0.7)
頻脈	1 (0.7)
一般・全身障害および投与部位の状態	1 (0.7)
胸痛	1 (0.7)
感染症および寄生虫症	1 (0.7)
肺炎	1 (0.7)
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 (0.7)
形質細胞性骨髄腫	1 (0.7)
皮膚および皮下組織障害	1 (0.7)
発疹	1 (0.7)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.6.2.1)

表 2.7.4.2.1.4.2.2-2　治験薬の中止に至った有害事象（C788-047 及び C788-048 試験プラセボ対照期）

System Organ Class Preferred Term	R788 (N=102) n (%)	Placebo (N=48) n (%)
Any Adverse Events Leading to Drug Withdrawal	11 (10.8)	4 (8.3)
胃腸障害	2 (2.0)	2 (4.2)
下痢	1 (1.0)	1 (2.1)
腹部不快感	0 (0.0)	1 (2.1)
腹痛	1 (1.0)	0 (0.0)
血液およびリンパ系障害	3 (2.9)	0 (0.0)
好中球減少症	2 (2.0)	0 (0.0)
血小板減少症	1 (1.0)	0 (0.0)
神経系障害	2 (2.0)	0 (0.0)
頭痛	1 (1.0)	0 (0.0)
失神	1 (1.0)	0 (0.0)
一般・全身障害および投与部位の状態	1 (1.0)	0 (0.0)
胸痛	1 (1.0)	0 (0.0)
感染症および寄生虫症	1 (1.0)	0 (0.0)
肺炎	1 (1.0)	0 (0.0)
臨床検査	1 (1.0)	0 (0.0)

System Organ Class Preferred Term	R788 (N=102) n (%)	Placebo (N=48) n (%)
アラニンアミノトランスフェラーゼ増加	1 (1.0)	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）	1 (1.0)	0 (0.0)
形質細胞性骨髄腫	1 (1.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	0 (0.0)	1 (2.1)
鼻出血	0 (0.0)	1 (2.1)
血管障害	0 (0.0)	1 (2.1)
高血圧	0 (0.0)	1 (2.1)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.6.1.1)

2.7.4.2.1.4.2.3 海外第 II 相臨床試験（D4300-022）

D4300-022 試験において、治験薬の中止に至った有害事象は 27.8%（5/18 例）認められた。初期治療期に 22.2%（4/18 例）、継続投与期に 15.4%（2/13 例）認められた。なお、25 ヵ月以降に治験薬の中止に至った有害事象は認められなかった。

表 2.7.4.2.1.4.2.3-1　治験薬の中止に至った有害事象（D4300-022 試験）

System Organ Class[a] Preferred Term[b]	R788 N=18 n (%)
Any AE leading to discontinuation	5 (27.8)
胃腸障害	2 (11.1)
下痢	1 (5.6)
悪心	1 (5.6)
感染症および寄生虫症	1 (5.6)
尿路感染	1 (5.6)
臨床検査	1 (5.6)
トランスアミナーゼ上昇	1 (5.6)
神経系障害	1 (5.6)
無酸素性脳症	1 (5.6)
血管障害	1 (5.6)
深部静脈血栓症	1 (5.6)

Note: MedDRA (Version 13.0) was used for AE coding and percentages were calculated using the population total as the denominator. Events were sorted in order of descending overall incidence of system organ class and then in descending order by preferred term within system organ class.
a Patients may have had more than 1 event within a system organ class. They were counted once in the system organ class summary.
b Patients may have had more than 1 event with the same preferred term. They were counted once in the preferred term summary.
(Source: 5.3.5.2.1, Table 12-5)

2.7.4.2.1.4.2.4 第 I 相臨床試験（D4300-007 及び D4300-032）

D4300-007 及び D4300-032 試験において、治験薬の中止に至った有害事象は認められなかった。

2.7.4.2.1.4.3 注目すべき有害事象

出血関連有害事象、胃腸障害（非感染性下痢 SMQ、悪心、嘔吐及び腹痛）、高血圧、肝機能障害（薬物関連肝障害 SMQ）、好中球減少症、並びに血栓症・塞栓症・血栓塞栓症については、MedDRA 標準検索式（SMQ）に基づいて抽出した。感染症については、器官別大分類（SOC）「感染症および寄生虫症」に分類された事象を対象とした。注目すべき有害事象の定義を表 2.7.4.2.1.4.3-1 に示す。

国内第 III 相臨床試験（R788-1301）において認められた注目すべき有害事象を R788 投与期

は表 2.7.4.9-11～表 2.7.4.9-16 に、プラセボ対照期は表 2.7.4.9-17～表 2.7.4.9-22 に、休薬期は表 2.7.4.9-63 にそれぞれ示す。また、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）において認められた注目すべき有害事象を R788 投与期は表 2.7.4.9-23～表 2.7.4.9-31 に、プラセボ対照期は表 2.7.4.9-32～表 2.7.4.9-40 にそれぞれ示す。

表 2.7.4.2.1.4.3-1 国内及び海外第 III 相臨床試験における注目すべき有害事象の定義

項目	定義
出血関連有害事象	MedDRA の SMQ「Haemorrhages（出血）」の狭域に該当する有害事象
胃腸障害	
非感染性下痢 SMQ	MedDRA の SMQ「Noninfectious diarrhea（非感染性下痢）」の狭域に該当する有害事象
悪心	MedDRA の SMQ「Gastrointestinal nonspecific inflammation and dysfunctional conditions（消化管の非特異的炎症および機能障害）」の狭域に該当する有害事象のうち、「nausea」を含む有害事象
嘔吐	MedDRA の SMQ「Gastrointestinal nonspecific inflammation and dysfunctional conditions（消化管の非特異的炎症および機能障害）」の狭域に該当する有害事象のうち、「vomit」を含む有害事象、及び以下に示す有害事象 ・Retching（レッチング）
腹痛	MedDRA の SMQ「Gastrointestinal nonspecific inflammation and dysfunctional conditions（消化管の非特異的炎症および機能障害）」の狭域に該当する有害事象のうち、「abdominal」を含む有害事象
高血圧	MedDRA の SMQ「Hypertension（高血圧）」の狭域に該当する有害事象
肝機能障害	MedDRA の SMQ「Drug related hepatic disorders - comprehensive search（薬剤に関連する肝障害 - 包括的検索）」の狭域に該当する有害事象
好中球減少症	MedDRA の SMQ「Haematopoietic leucopenia（造血障害による白血球減少症）」の狭域に該当する有害事象のうち、「neutro」を含む有害事象
感染症	MedDRA のプライマリーSOC が「Infections and infestations（感染症及び寄生虫症）」に該当する有害事象及び以下に示す有害事象 ・Influenza like illness（インフルエンザ様疾患） ・Upper respiratory tract inflammation（上気道の炎症）
血栓症・塞栓症・血栓塞栓症	MedDRA の SMQ「Embolic and thrombotic events（塞栓および血栓）」の狭域に該当する有害事象

2.7.4.2.1.4.3.1 出血関連有害事象

国内第 III 相臨床試験（R788-1301）において認められた中等度及び高度の出血関連有害事象を R788 投与期は表 2.7.4.2.1.4.3.1-1 に、プラセボ対照期は表 2.7.4.2.1.4.3.1-3 にそれぞれ示す。また、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）において認められた中等度及び高度の出血関連有害事象を R788 投与期は表 2.7.4.2.1.4.3.1-2 に、プラセボ対照期は表 2.7.4.2.1.4.3.1-4 にそれぞれ示す。

1) R788 投与期

R788-1301 試験の R788 投与期において、出血関連有害事象は 18.2%（6/33 例）、副作用は 3.0%（1/33 例）認められた。重篤な出血関連有害事象は認められなかった。出血関連有害事象は軽度（12.1%（4/33 例））又は中等度（6.1%（2/33 例））のみであり、高度は認められなかった。出血関連有害事象による R788 の減量、休薬又は中止は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、出血関連有害事象は 41.1%（60/146 例）、副作用は 6.2%（9/146 例）認められた。重篤な出血関連有害事象は 11.0%（16/146 例）認められ、そのうち治験薬との因果関係ありと判定されたものはなかった。出血関連有害事象の多くは軽度（21.2%（31/146 例））又は中等度（15.1%（22/146 例））であり、

高度は 4.8%（7/146 例）認められた。高度の出血関連有害事象は、点状出血及び挫傷各 1.4%（2/146 例）、並びに紫斑、胃腸出血、血便排泄、直腸出血、メレナ、月経過多、結膜出血、粘膜出血、脳出血及び出血性卒中各 0.7%（1/146 例）であった。出血関連有害事象による R788 の休薬は 0.7%（1/146 例）であり、減量又は中止は認められなかった。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、出血関連有害事象は R788 群で 13.6%（3/22 例）及びプラセボ群で 16.7%（2/12 例）、副作用は R788 群で 4.5%（1/22 例）及びプラセボ群で 0.0%（0/12 例）であった。重篤な出血関連有害事象はプラセボ群で 8.3%（1/12 例）認められ、治験薬との因果関係ありと判定されたものはなかった。出血関連有害事象は軽度（R788 群 9.1%（2/22 例）及びプラセボ群 8.3%（1/12 例）（以下同順））又は中等度（4.5%（1/22 例）及び 8.3%（1/12 例））のみであり、高度は認められなかった。出血関連有害事象による治験薬の減量、休薬又は中止は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、出血関連有害事象は R788 群で 28.4%（29/102 例）及びプラセボ群で 35.4%（17/48 例）、副作用は R788 群で 3.9%（4/102 例）及びプラセボ群で 6.3%（3/48 例）認められた。重篤な出血関連有害事象は R788 群で 4.9%（5/102 例）及びプラセボ群で 10.4%（5/48 例）認められ、そのうち治験薬との因果関係ありと判定されたのはプラセボ群の 2.1%（1/48 例）であった。出血関連有害事象の多くは軽度（R788 群 18.6%（19/102 例）及びプラセボ群 18.8%（9/48 例）（以下同順））又は中等度（8.8%（9/102 例）及び 10.4%（5/48 例））であり、高度は R788 群で 1.0%（1/102 例）及びプラセボ群で 6.3%（3/48 例）であった。R788 群で認められた高度の出血関連有害事象は、挫傷（R788 群 1.0%（1/102 例）及びプラセボ群 0.0%（0/48 例））であった。出血関連有害事象による治験薬の休薬は R788 群で 1.0%（1/102 例）及びプラセボ群で 2.1%（1/48 例）、中止は R788 群で 0.0%（0/102 例）及びプラセボ群で 2.1%（1/48 例）であり、減量は認められなかった。

3) 休薬期

R788-1301 試験の休薬期において、出血関連有害事象は認められなかった。

表 2.7.4.2.1.4.3.1-1　中等度及び高度の出血関連有害事象（R788-1301 試験 R788 投与期）

	R788 Treatment Period (R788-1301) (N=33)	
Preferred Term	Moderate n (%)	Severe n (%)
挫傷	1 (3.0)	0 (0.0)
鼻出血	1 (3.0)	0 (0.0)
皮下出血	1 (3.0)	0 (0.0)

(Source : 5.3.5.1.1, Table 14.3.4.1.5.2 改編)

表 2.7.4.2.1.4.3.1-2　中等度及び高度の出血関連有害事象（C788-047、C788-048 及び C788-049 試験 R788 投与期）

	Fostamatinib Exposure Period (C788-047, C788-048, C788-049) (N = 146)	
Preferred Term	Moderate n (%)	Severe n (%)
点状出血	6 (4.1)	2 (1.4)
血性水疱	1 (0.7)	1 (0.7)
斑状出血	1 (0.7)	0 (0.0)
皮下出血	1 (0.7)	0 (0.0)
紫斑	1 (0.7)	1 (0.7)
鼻出血	10 (6.8)	0 (0.0)
喀血	1 (0.7)	0 (0.0)
胃腸出血	2 (1.4)	1 (0.7)
歯肉出血	2 (1.4)	0 (0.0)
口腔内出血	2 (1.4)	0 (0.0)
直腸出血	1 (0.7)	1 (0.7)
血便排泄	0 (0.0)	1 (0.7)
メレナ	0 (0.0)	1 (0.7)
膣出血	3 (2.1)	0 (0.0)
月経過多	1 (0.7)	1 (0.7)
挫傷	2 (1.4)	2 (1.4)
血腫	1 (0.7)	0 (0.0)
出血	1 (0.7)	0 (0.0)
内出血発生の増加傾向	1 (0.7)	0 (0.0)
耳出血	1 (0.7)	0 (0.0)
結膜出血	1 (0.7)	1 (0.7)
粘膜出血	0 (0.0)	1 (0.7)
脳出血	0 (0.0)	1 (0.7)
出血性卒中	0 (0.0)	1 (0.7)

Subjects are counted only once in each preferred term category based on their most severe AE in the category.
MedDRA version 18.1
(Source: 5.3.5.3.2, Table 4.3.3.1.2)

表 2.7.4.2.1.4.3.1-3　中等度及び高度の出血関連有害事象（R788-1301 試験プラセボ対照期）

	Period I (R788-1301)			
	R788 (N=22)		Placebo (N=12)	
Preferred Term	Moderate n (%)	Severe n (%)	Moderate n (%)	Severe n (%)
鼻出血	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)
処置による出血	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)

(Source : 5.3.5.1.1, Table 14.1.4.1.5.2 改編)

表 2.7.4.2.1.4.3.1-4　中等度及び高度の出血関連有害事象（C788-047 及び C788-048 試験プラセボ対照期）

	Placebo-Controlled Period (C788-047 and C788-048)			
	R788 (N = 102)		Placebo (N = 48)	
Preferred Term	Moderate n (%)	Severe n (%)	Moderate n (%)	Severe n (%)
鼻出血	4 (3.9)	0 (0.0)	3 (6.3)	0 (0.0)
点状出血	2 (2.0)	0 (0.0)	2 (4.2)	1 (2.1)
月経過多	1 (1.0)	0 (0.0)	1 (2.1)	1 (2.1)
膣出血	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
胃腸出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
メレナ	0 (0.0)	0 (0.0)	1 (2.1)	0 (0.0)
出血	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)

Subjects are counted only once in each preferred term category based on their most severe AE in the category.
MedDRA version 18.1
(Source: 5.3.5.3.2, Table 4.3.3.1.1)

2.7.4.2.1.4.3.2 胃腸障害

2.7.4.2.1.4.3.2.1 非感染性下痢 SMQ

1)　R788 投与期

R788-1301 試験の R788 投与期において、非感染性下痢 SMQ の有害事象は 39.4%（13/33 例）、副作用は 30.3%（10/33 例）認められた。重篤な非感染性下痢 SMQ の有害事象は 3.0%（1/33 例）認められ、治験薬との因果関係ありと判定された。非感染性下痢 SMQ の有害事象の多くは軽度（30.3%（10/33 例））又は中等度（6.1%（2/33 例））であり、高度は 3.0%（1/33 例）認められた。非感染性下痢 SMQ の有害事象による R788 の減量は 12.1%（4/33 例）、中止は 3.0%（1/33 例）であり、休薬は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、非感染性下痢 SMQ の有害事象は 36.3%（53/146 例）、副作用は 31.5%（46/146 例）認められた。重篤な非感染性下痢 SMQ は 1.4%（2/146 例）認められ、そのうち治験薬との因果関係ありと判定されたのは 1.4%（2/146 例）であった。非感染性下痢 SMQ の有害事象の多くは軽度（17.1%（25/146 例））又は中等度（17.1%（25/146 例））であり、高度は 2.1%（3/146 例）認められた。非感染性下痢 SMQ の有害事象による R788 の減量は 2.7%（4/146 例）、休薬は 3.4%（5/146 例）、中止は 4.1%（6/146 例）であった。

2)　プラセボ対照期

R788-1301 試験のプラセボ対照期において、非感染性下痢 SMQ の有害事象は R788 群で 40.9%（9/22 例）及びプラセボ群で 0.0%（0/12 例）、副作用は R788 群で 31.8%（7/22 例）及びプラセボ群で 0.0%（0/12 例）であった。重篤な非感染性下痢 SMQ は R788 群で 4.5%（1/22 例）認められ、治験薬との因果関係ありと判定された。非感染性下痢 SMQ の有害事象の多くは軽度（R788 群 27.3%（6/22 例）及びプラセボ群 0.0%（0/12 例）（以下同順））又は中等度（9.1%（2/22 例）及び 0.0%（0/12 例））であり、高度は R788 群で 4.5%（1/22 例）認められた。非感染性下痢 SMQ の有害事象による治験薬の減量は R788 群で 13.6%（3/22 例）及びプラセボ群で 0.0%（0/12 例）、中止は R788 群で 4.5%（1/22 例）及びプラセボ群で 0.0%（0/12 例）であり、

休薬は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、非感染性下痢 SMQ の有害事象は R788 群で 31.4%（32/102 例）及びプラセボ群で 14.6%（7/48 例）、副作用は R788 群で 27.5%（28/102 例）及びプラセボ群で 12.5%（6/48 例）認められた。重篤な非感染性下痢 SMQ は R788 群で 1.0%（1/102 例）認められ、治験薬との因果関係ありと判定された。非感染性下痢 SMQ の有害事象の多くは軽度（R788 群 20.6%（21/102 例）及びプラセボ群 12.5%（6/48 例）（以下同順））又は中等度（9.8%（10/102 例）及び 2.1%（1/48 例））であり、高度は R788 群で 1.0%（1/102 例）認められ、プラセボ群では認められなかった。非感染性下痢 SMQ の有害事象による治験薬の減量又は休薬は R788 群で 2.0%（2/102 例）又は 2.9%（3/102 例）認められ、プラセボ群では認められなかった。非感染性下痢 SMQ の有害事象による治験薬の中止は、R788 群で 1.0%（1/102 例）及びプラセボ群で 2.1%（1/48 例）であった。

3) R788-1301 試験で投与量調節の基準により下痢を管理した被験者の詳細

R788-1301 試験では、CTCAE v5.0（表 2.7.4.2.1.4.3.2.1-1）に基づき下痢の Grade を判定した。治験実施計画書の管理基準において、治験薬の処置が必要となる Grade 3 以上の下痢が発現した被験者は 2 例であった。いずれも本薬の減量・休薬、ロペラミドの投与により、回復した（表 2.7.4.2.1.4.3.2.1-2）。

表 2.7.4.2.1.4.3.2.1-1 下痢の Grade（CTCAE v5.0）

Grade	判定基準
Grade 1	・ ベースラインと比べて＜4 回/日の排便回数増加 ・ ベースラインと比べて人工肛門からの排泄量が軽度に増加
Grade 2	・ ベースラインと比べて 4-6 回/日の排便回数増加 ・ ベースラインと比べて人工肛門からの排泄量の中等度増加 ・ 身の回り以外の日常生活動作の制限
Grade 3	・ ベースラインと比べて 7 回以上/日の排便回数増加 ・ 入院を要する ・ ベースラインと比べて人工肛門からの排泄量の高度増加 ・ 身の回りの日常生活動作の制限
Grade 4	・ 生命を脅かす，緊急の措置を要する
Grade 5	・ 死亡

出典：
有害事象共通用語規準 v5.0 日本語訳 JCOG 版より引用
JCOG ホームページ http://www.jcog.jp/

表 2.7.4.2.1.4.3.2.1-2 Grade 3 以上の下痢の発現例（2 例）

被験者 ID	発現時投与量	発現日（R788 投与後）	程度／Grade	R788 の処置	その他の処置	転帰／転帰日（発現後）	因果関係
[redacted]	100 mg BID	3 日	軽度／1	投与量変更せず	－	回復／2 日	関連あり
	100 mg BID	78 日	中等度／2→3→1	休薬、減量	Loperamide hydrochloride	回復／42 日	関連あり
	150 mg QD	128 日	軽度／2→1	投与量変更せず（I 期、II 期）	Loperamide hydrochloride	回復／238 日	関連あり
[redacted]	100 mg BID	19 日	高度（SAE）／3→1	休薬、減量	Loperamide hydrochloride	回復／8 日	関連あり
	100 mg QD	37 日	軽度／1	投与量変更せず	Loperamide hydrochloride rehydration	回復／4 日	関連あり

（Source: 1.13.3-4, C-15 表 71）

2.7.4.2.1.4.3.2.2 悪心

1) R788 投与期

R788-1301 試験の R788 投与期において、悪心の有害事象は 3.0%（1/33 例）、副作用は 3.0%（1/33 例）認められた。重篤な悪心は認められなかった。悪心の有害事象は軽度（3.0%（1/33 例））であった。悪心の有害事象による R788 の休薬は 3.0%（1/33 例）であり、減量又は中止は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、悪心の有害事象は 19.2%（28/146 例）、副作用は 12.3%（18/146 例）認められた。重篤な悪心は認められなかった。悪心の有害事象は軽度（17.1%（25/146 例））又は中等度（2.1%（3/146 例））であり、高度は認められなかった。悪心の有害事象による R788 の減量、休薬又は中止は認められなかった。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、悪心の有害事象は R788 群で 4.5%（1/22 例）及びプラセボ群で 0.0%（0/12 例）、副作用は R788 群で 4.5%（1/22 例）及びプラセボ群で 0.0%（0/12 例）であった。重篤な悪心は認められなかった。悪心の有害事象は軽度（R788 群 4.5%（1/22 例）及びプラセボ群 0.0%（0/12 例））であった。悪心の有害事象による治験薬の減量、休薬又は中止は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、悪心の有害事象は R788 群で 18.6%（19/102 例）及びプラセボ群で 8.3%（4/48 例）、副作用は R788 群で 14.7%（15/102 例）及びプラセボ群で 6.3%（3/48 例）認められた。重篤な悪心は認められなかった。悪心の有害事象は軽度（R788 群 15.7%（16/102 例）及びプラセボ群 8.3%（4/48 例）（以下同順））又は中等度（2.9%（3/102 例）及び 0.0%（0/48 例））であり、高度は認められなかった。悪心の有害事象による治験薬の減量、休薬又は中止は認められなかった。

2.7.4.2.1.4.3.2.3 嘔吐

1) R788 投与期

R788-1301 試験の R788 投与期において、嘔吐の有害事象は 3.0%（1/33 例）であり、副作用は認められなかった。重篤な嘔吐は認められなかった。嘔吐の有害事象は軽度（3.0%（1/33 例））であった。嘔吐の有害事象による R788 の減量、休薬又は中止は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、嘔吐の有害事象は 9.6%（14/146 例）、副作用は 2.7%（4/146 例）認められた。重篤な嘔吐は認められなかった。嘔吐の有害事象は軽度（8.9%（13/146 例））又は中等度（0.7%（1/146 例））であり、高度は認められなかった。嘔吐の有害事象による R788 の休薬は 0.7%（1/146 例）であり、減量又は中止は認められなかった。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、嘔吐の有害事象は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、嘔吐の有害事象は R788 群で 3.9%（4/102 例）及びプラセボ群で 6.3%（3/48 例）、副作用は R788 群で 2.0%（2/102 例）及びプラセボ群で 2.1%（1/48 例）認められた。重篤な嘔吐は認められなかった。嘔吐の有害事象は軽度（R788 群 3.9%（4/102 例）及びプラセボ群 4.2%（2/48 例）（以下同順））又は中等度

（0.0%（0/102 例）及び 2.1%（1/48 例））であり、高度は認められなかった。嘔吐の有害事象による治験薬の減量、休薬又は中止は認められなかった。

2.7.4.2.1.4.3.2.4 腹痛

1) R788 投与期

R788-1301 試験の R788 投与期において、腹痛の有害事象は 15.2%（5/33 例）、副作用は 3.0%（1/33 例）認められた。重篤な腹痛は認められなかった。腹痛の有害事象は軽度（15.2%（5/33 例））であった。腹痛の有害事象による R788 の減量は 3.0%（1/33 例）であり、休薬又は中止は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、腹痛の有害事象は 13.0%（19/146 例）、副作用は 6.8%（10/146 例）認められた。重篤な腹痛は認められなかった。腹痛の有害事象は軽度（11.0%（16/146 例））又は中等度（2.1%（3/146 例））であり、高度は認められなかった。腹痛の有害事象による R788 の休薬は 1.4%（2/146 例）、中止は 1.4%（2/146 例）であり、減量は認められなかった。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、腹痛の有害事象は R788 群で 9.1%（2/22 例）及びプラセボ群で 0.0%（0/12 例）、副作用は R788 群で 4.5%（1/22 例）及びプラセボ群で 0.0%（0/12 例）であった。重篤な腹痛は認められなかった。腹痛の有害事象は軽度（R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例））であった。腹痛の有害事象による治験薬の減量、休薬又は中止は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、腹痛の有害事象は R788 群で 6.9%（7/102 例）及びプラセボ群で 4.2%（2/48 例）、副作用は R788 群で 4.9%（5/102 例）及びプラセボ群で 4.2%（2/48 例）認められた。重篤な腹痛は認められなかった。腹痛の有害事象は軽度（R788 群 5.9%（6/102 例）及びプラセボ群 4.2%（2/48 例）（以下同順））又は中等度（1.0%（1/102 例）及び 0.0%（0/48 例））であり、高度は認められなかった。腹痛による治験薬の中止は R788 群で 1.0%（1/102 例）及びプラセボ群で 2.1%（1/48 例）であり、減量又は休薬は認められなかった。

2.7.4.2.1.4.3.2.5 消化管障害

国内第 III 相試験（R788-1301）及び海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）で認められた胃腸障害を詳細に評価するため、消化管障害に関連する有害事象を以下の定義で抽出した。

- MedDRA の SMQ「Gastrointestinal nonspecific inflammation and dysfunctional conditions（消化管の非特異的炎症および機能障害）」の狭域に該当する有害事象

R788-1301 試験、並びに C788-047、C788-048 及び C788-049 試験において認められた消化管障害を表 2.7.4.9-64～表 2.7.4.9-95 に、並びに重篤又は重症度が中等度以上の消化管障害の一覧表を表 2.7.4.9-100 及び表 2.7.4.9-101 にそれぞれ示す。

R788-1301 試験の R788 投与期では、消化管障害の有害事象は 66.7%（22/33 例）、副作用は 42.4%（14/33 例）認められ、重症度はほとんどが軽度であった。消化管障害の有害事象による

休薬は3.0%（1/33例）、減量は15.2%（5/33例）、中止は3.0%（1/33例）であった。C788-047、C788-048及びC788-049試験を統合したR788投与期では、消化管障害の有害事象は55.5%（81/146例）、副作用は39.0%（57/146例）認められ、重症度はほとんどが軽度又は中等度であった。消化管障害の有害事象による休薬は5.5%（8/146例）、減量は2.7%（4/146例）、中止は5.5%（8/146例）であった。いずれの試験も、主に認められた消化管障害の有害事象は下痢であった。

重篤又は重症度が中等度以上の消化管障害について、R788-1301試験のR788投与期では、重篤又は重症度が中等度以上の消化管障害の副作用が3例5件に認められたが、いずれも治験薬を中止することなく、治験薬の処置（休薬又は減量）により回復した。また、C788-047、C788-048及びC788-049試験を統合したR788投与期では、重篤又は重症度が中等度以上の消化管障害の副作用が26例40件に認められたが、20件が治験薬の処置を必要とせず回復、7件が休薬又は減量により回復、7件が中止により回復しており、転帰が回復ではない被験者はいずれも治験薬の処置を必要とせず投与継続可能であった。

2.7.4.2.1.4.3.3 高血圧

2.7.4.2.1.4.3.3.1 高血圧SMQ

R788-1301試験、並びにC788-047、C788-048及びC788-049試験において認められた重篤又は重症度が中等度以上の高血圧SMQの一覧表を表 2.7.4.9-102及び表 2.7.4.9-103にそれぞれ示す。

1) R788投与期

R788-1301試験のR788投与期において、高血圧SMQの有害事象は36.4%（12/33例）、副作用は33.3%（11/33例）認められた。重篤な高血圧SMQは認められなかった。高血圧SMQの有害事象は軽度（33.3%（11/33例））又は中等度（3.0%（1/33例））であった。高血圧SMQの有害事象による治験薬の減量は18.2%（6/33例）、中止は3.0%（1/33例）であり、休薬は認められなかった。治験薬との因果関係が否定できない重症度が中等度の高血圧が1例1件に認められたが、本薬の減量後に回復した。

C788-047、C788-048及びC788-049試験を統合したR788投与期において、高血圧SMQの有害事象は29.5%（43/146例）、副作用は19.2%（28/146例）認められた。重篤な高血圧SMQは0.7%（1/146例）認められ、治験薬との因果関係ありと判定された。高血圧SMQの有害事象の多くは軽度（17.8%（26/146例））又は中等度（9.6%（14/146例））であり、高度は2.1%（3/146例）認められた。高血圧SMQの有害事象による治験薬の減量は2.1%（3/146例）、休薬は2.1%（3/146例）、中止は0.7%（1/146例）であった。治験薬との因果関係が否定できない重篤又は重症度が中等度以上の高血圧は11例12件に認められた。重篤な高血圧として高血圧クリーゼが1例に認められ、治験薬との因果関係ありと判断され、本薬の休薬後に回復した。その他の10件については本薬の休薬・減量後に回復又は本薬の処置なしで回復し、転帰が回復でなかった1件は本薬の処置を必要とせず投与継続可能で、本薬の投与中止を要する高血圧は認められなかった。

R788-1301試験では、海外第III相臨床試験（C788-047、C788-048及びC788-049）と比較して高血圧の発現割合が高かったが、ほとんどの事象の重症度が軽度であり、治験実施計画書で規

定した投与量調節の基準により適切な処置を行うことで本薬による治療継続が可能であった。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、高血圧 SMQ の有害事象は R788 群で 36.4%（8/22 例）及びプラセボ群で 8.3%（1/12 例）、副作用は R788 群で 31.8%（7/22 例）及びプラセボ群で 8.3%（1/12 例）認められた。重篤な高血圧 SMQ の有害事象は認められなかった。高血圧 SMQ の有害事象は軽度（R788 群 36.4%（8/22 例）及びプラセボ群 8.3%（1/12 例））であった。高血圧 SMQ の有害事象による治験薬の減量は R788 群で 9.1%（2/22 例）及びプラセボ群で 0.0%（0/12 例）、中止は R788 群で 4.5%（1/22 例）及びプラセボ群で 0.0%（0/12 例）であり、休薬は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、高血圧 SMQ の有害事象は R788 群で 27.5%（28/102 例）及びプラセボ群で 12.5%（6/48 例）、副作用は R788 群で 21.6%（22/102 例）及びプラセボ群で 4.2%（2/48 例）認められた。重篤な高血圧 SMQ は R788 群で 1.0%（1/102 例）認められ、治験薬との因果関係ありと判定された。高血圧 SMQ の有害事象の多くは軽度（R788 群 16.7%（17/102 例）及びプラセボ群 10.4%（5/48 例）（以下同順））又は中等度（8.8%（9/102 例）及び 0.0%（0/48 例））であり、高度は R788 群で 2.0%（2/102 例）及びプラセボ群で 2.1%（1/48 例）認められた。高血圧 SMQ の有害事象による治験薬の減量又は休薬は、R788 群で 2.0%（2/102 例）又は 1.0%（1/102 例）認められ、プラセボ群では認められなかった。高血圧 SMQ の有害事象による治験薬の中止は、プラセボ群で 2.1%（1/48 例）認められ、R788 群では認められなかった。

3) R788-1301 試験で投与量調節の基準により高血圧を管理した被験者の詳細

- 収縮期血圧 140 mmHg 以上又は拡張期血圧 90 mmHg 以上に上昇した被験者（SBP 140 mmHg/DBP 90 mmHg 以上への上昇例）

R788 投与後に SBP 140 mmHg/DBP 90 mmHg 以上への上昇例は 20 例であった（表 2.7.4.2.1.4.3.3.1-1、該当被験者の血圧の一覧は表 2.7.4.9-96 参照）。また、当該血圧上昇が有害事象と判断されたのは 11 例であった（表 2.7.4.2.1.4.3.3.1-2）。

SBP 140 mmHg/DBP 90 mmHg 以上への上昇例のうち高血圧の合併症を有していた被験者は 9 例であり、当該血圧上昇に対して行われた処置は、降圧剤の増量や変更、別の降圧剤の追加等が 3 例、従来の降圧治療に加えて本薬の減量が 1 例、処置なしが 5 例であった。高血圧の合併症を有していない被験者は 11 例であり、降圧治療の開始が 4 例、本薬の休薬・減量が 2 例、処置なしが 5 例であった。上記の処置により、4 例（被験者 [redacted]、[redacted]、[redacted] 及び [redacted]）を除く被験者で血圧上昇が回復・軽快した。3 例は血圧高値の状態が継続しているものの、第 III 期でも継続して本薬を投薬中であり、1 例（被験者 [redacted]）は早期第 II 期 8 週で有効性の欠如により試験を中止した。

SBP 140 mmHg/DBP 90 mmHg 以上に上昇しても医師の判断により処置が行われず、回復・軽快している被験者もいることから、添付文書には、目安として血圧上昇への対処方法を提供することが妥当と考えられた。

表 2.7.4.2.1.4.3.3.1-1 SBP 140 mmHg/DBP 90 mmHg 以上への上昇例（20 例）

被験者 ID	合併症（血圧関連）	併用薬（血圧関連）	有害事象に該当	当該血圧上昇に対する処置 a)
[redacted]	高血圧	Amlodipine besilate	No	降圧剤の増量
[redacted]	高血圧	Olmesartan medoxomil	Yes	本薬の減量
[redacted]	高血圧	Amlodipine besilate Azilsartan	Yes	降圧剤の増量
[redacted]	高血圧	Benidipine hydrochloride	No	なし
[redacted]	―	―	Yes	降圧療法の開始
[redacted]	―	―	Yes	降圧療法の開始
[redacted]	―	―	No	なし
[redacted]	―	―	Yes	降圧療法の開始
[redacted]	―	―	No	なし
[redacted]	高血圧	Amlodipine besilate Candesartan cilexetil	Yes	降圧剤の増量
[redacted]	―	―	Yes	本薬の減量、降圧療法の開始
[redacted]	高血圧	Amlodipine besilate	No	なし
[redacted]	―	―	Yes	なし
[redacted]	―	―	Yes	なし
[redacted]	高血圧	Amlodipine besilate	No	なし
[redacted]	高血圧	Amlodipine besilate Candesartan cilexetil	No	なし
[redacted]	高血圧	Azelnidipine Olmesartan medoxomil	No	なし
[redacted]	―	―	No	なし
[redacted]	―	―	Yes	本薬の休薬、減量、降圧剤の増量
[redacted]	―	―	Yes	降圧療法の開始

a) モニタリングによる確認内容を含む。
（Source: 1.13.3-4, C-15 表 72）

表 2.7.4.2.1.4.3.3.1-2 SBP 140 mmHg/DBP 90 mmHg 以上に上昇例のうち、有害事象と判断された被験者

被験者 ID	発現時投与量	発現日（R788 投与後）	程度	R788 の処置	その他の処置	転帰／転帰日（発現後）	因果関係
[redacted]	100 mg BID	15 日	軽度	減量（I 期）	Amlodipine besilate	軽快／継続中	関連あり
[redacted]	100 mg BID	19 日	軽度	投与量変更せず	―	回復／5 日	関連あり
	100 mg QD	32 日	軽度	投与量変更せず	―	回復／10 日	関連あり
	150 mg QD	217 日	軽度	投与量変更せず（II 期）	Amlodipine besilate	未回復／継続中	関連あり
[redacted]	150 mg BID	57 日	軽度	投与量変更せず（I 期、II 期）	Amlodipine besilate	軽快／継続中	関連あり
[redacted]	100 mg BID	8 日	軽度	投与量変更せず（I 期、II 期）	Amlodipine besilate	軽快／継続中	関連あり
[redacted]	100 mg BID	29 日	軽度	投与量変更せず（I 期、II 期）	Amlodipine besilate Carvedilol Azilsartan	回復／296 日	関連あり
[redacted]	100 mg BID	29 日	軽度	減量	Amlodipine besilate	回復／15 日	関連あり
	150 mg BID	71 日	軽度	投与量変更せず	Amlodipine besilate	回復／15 日	関連あり
[redacted]	100 mg BID	4 日	中等度	減量（II 期） 休薬（II 期）	Nicardipine hydrochloride	回復／12 日	関連あり
[redacted]	100 mg BID	16 日	軽度	投与量変更せず（I 期） 減量（II 期）	Amlodipine besilate	未回復／継続中	関連なし
[redacted]	150 mg BID	41 日	軽度	投与量変更せず（I 期、II 期）	Amlodipine besilate Enalapril maleate	未回復／継続中	関連あり
[redacted]	150 mg BID	141 日	軽度	投与量変更せず（II 期）	―	回復／36 日	関連あり
[redacted]	150 mg BID	182 日	軽度	減量（II 期）	Candesartan cilexetil	未回復／継続中	関連あり

（Source: 1.13.3-4, C-15 表 73）

- 収縮期血圧 180 mmHg 以上又は拡張期血圧 110 mmHg 以上に上昇した被験者

R788 投与後に収縮期血圧 180 mmHg 以上又は拡張期血圧 110 mmHg 以上に上昇した被験者は 2 例（被験者 [redacted] 及び [redacted]）であった。

被験者 [redacted] は、合併症に高血圧を有する被験者であり、投与 2 週より血圧上昇が認められ、4 週の 3 回の血圧測定中に収縮期血圧 185 mmHg が 1 回認められたが、本薬の休薬には至らないと判断された。

被験者 [redacted] は、合併症に高血圧を有する被験者であり、早期移行 28 週の 3 回の血圧測定中に収縮期血圧 185 mmHg が 1 回認められたが、降圧薬の飲み忘れによるものであり、本薬の休薬には至らないと判断された。

2.7.4.2.1.4.3.3.2 高血圧の管理

1) 海外第 III 相臨床試験

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）において認められた高血圧の有害事象に対する管理状況を表 2.7.4.9-42 及び表 2.7.4.9-43 に示す。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、28.8%（42/146 例）が高血圧に対する治療介入を必要とした。このうち、12.3%（18/146 例）は併用降圧薬の増量により治療され、25.3%（37/146 例）は新たに降圧薬の投与を開始した。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、R788 群の 20.6%（21/102 例）及びプラセボ群の 16.7%（8/48 例）が高血圧に対する治療介入を必要とした。このうち、R788 群の 10.8%（11/102 例）及びプラセボ群の 6.3%（3/48 例）は併用降圧薬の増量により治療され、R788 群の 17.6%（18/102 例）及びプラセボ群の 14.6%（7/48 例）は新たに降圧剤の投与を開始した。

2) 国内第 III 相臨床試験

R788-1301 試験において認められた高血圧 SMQ の有害事象に対する管理状況を表 2.7.4.9-125 及び表 2.7.4.9-126 に示す。なお、R788-1301 試験では有害事象の処置として降圧薬の増量と新たな介入を特定して収集していないため、併用薬の処置としてまとめて表示した。

第 I 期では、R788 投与群 22.7%（5/22 例）及びプラセボ群 8.3%（1/12 例）が高血圧に対する治療介入を必要とした。

R788 投与期では、27.3%（9/33 例）が高血圧に対する治療介入を必要とした。

2.7.4.2.1.4.3.4 肝機能障害（薬物関連肝障害 SMQ）

R788-1301 試験、並びに C788-047、C788-048 及び C788-049 試験において認められた重篤又は重症度が中等度以上の薬物関連肝障害 SMQ の一覧表を表 2.7.4.9-104 及び表 2.7.4.9-105 にそれぞれ示す。

1) R788 投与期

R788-1301 試験の R788 投与期において、薬物関連肝障害 SMQ の有害事象は 33.3%（11/33 例）、副作用は 30.3%（10/33 例）認められた。高頻度に認められた薬物関連肝障害 SMQ の有害事象は、肝機能検査値上昇 12.1%（4/33 例）であった。重篤な薬物関連肝障害 SMQ は 3.0%（1/33 例）認められ、治験薬との因果関係ありと判定されたものはなかった。薬物関連肝障害 SMQ の有害事象は軽度（27.3%（9/33 例））又は中等度（6.1%（2/33 例））であり、高度は認め

られなかった。薬物関連肝障害 SMQ の有害事象による治験薬の減量は 15.2%（5/33 例）、中止は 6.1%（2/33 例）であり、休薬は認められなかった。重篤な肝機能障害が 1 例に認められたが、治験薬との因果関係は否定された。その他、重症度が高度の肝機能障害は認められず、重症度が中等度の肝機能障害は、1 例 1 件に認められた肝機能検査値異常で、治験薬との因果関係は否定されず、本薬の投与中止後に軽快した。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、薬物関連肝障害 SMQ の有害事象は 19.2%（28/146 例）、副作用は 14.4%（21/146 例）認められた。高頻度に認められた薬物関連肝障害 SMQ の有害事象は、ALT 増加 9.6%（14/146 例）、AST 増加 6.8%（10/146 例）、肝酵素上昇 3.4%（5/146 例）、肝機能検査異常 2.7%（4/146 例）及び血中ビリルビン増加 2.1%（3/146 例）であった。重篤な薬物関連肝障害 SMQ は 2.1%（3/146 例）認められ、そのうち治験薬との因果関係ありと判定されたのはトランスアミナーゼ上昇 0.7%（1/146 例）であった。薬物関連肝障害 SMQ の有害事象の多くは軽度（10.3%（15/146 例））又は中等度（6.8%（10/146 例））であり、高度は 2.1%（3/146 例）認められた。高度の薬物関連肝障害 SMQ の有害事象は、肝酵素上昇 0.7%（1/146 例）及びトランスアミナーゼ上昇 1.4%（2/146 例）であった。薬物関連肝障害 SMQ の有害事象による治験薬の減量は 2.7%（4/146 例）、休薬は 6.2%（9/146 例）、中止は 3.4%（5/146 例）であった。治験薬との因果関係が否定できない重篤な肝機能障害として、トランスアミナーゼ上昇が 1 例に認められ、本薬の投与中止後に回復した。その他、治験薬との因果関係が否定できない重症度が中等度以上の肝機能障害が 10 例 15 件に認められ、このうち 3 件で本薬の投与中止に至ったが、12 件は本薬の休薬・減量後に回復又は本薬の処置を必要とせずに回復し、転帰が回復でない 1 件は本薬の処置を必要とせず投与継続可能であった。

R788-1301 試験では、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）と比較して肝機能障害の発現割合が高かったが、多くは重症度が軽度であり、日本人におけるリスクの増大を示唆するものではないと考えられた。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、薬物関連肝障害 SMQ の有害事象は R788 群で 27.3%（6/22 例）及びプラセボ群で 8.3%（1/12 例）、副作用は R788 群で 27.3%（6/22 例）及びプラセボ群で 0.0%（0/12 例）であった。高頻度に認められた薬物関連肝障害 SMQ の有害事象は、肝機能異常（R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例））であった。重篤な薬物関連肝障害 SMQ の有害事象は認められなかった。薬物関連肝障害 SMQ の有害事象は軽度（R788 群 22.7%（5/22 例）及びプラセボ群 8.3%（1/12 例）（以下同順））又は中等度（4.5%（1/22 例）及び 0.0%（0/12 例））であり、高度は認められなかった。薬物関連肝障害 SMQ の有害事象による治験薬の減量は R788 群で 9.1%（2/22 例）及びプラセボ群で 0.0%（0/12 例）、中止は R788 群で 9.1%（2/22 例）及びプラセボ群で 0.0%（0/12 例）であり、休薬は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、薬物関連肝障害 SMQ の有害事象は R788 群で 15.7%（16/102 例）及びプラセボ群で 2.1%（1/48 例）、副作用は R788 群で 11.8%（12/102 例）及びプラセボ群で 0.0%（0/48 例）であった。高頻度に認められた薬物関連肝障害 SMQ の有害事象は、ALT 増加（R788 群 10.8%（11/102 例）及びプラセボ群 0.0%（0/48

例）（以下同順））、AST 増加（8.8%（9/102 例）及び 0.0%（0/48 例））、並びに血中ビリルビン増加（2.0%（2/102 例）及び 0.0%（0/48 例））であった。重篤な薬物関連肝障害 SMQ の有害事象は認められなかった。薬物関連肝障害 SMQ の有害事象は軽度（R788 群 9.8%（10/102 例）及びプラセボ群 2.1%（1/48 例）（以下同順））又は中等度（5.9%（6/102 例）及び 0.0%（0/48 例））であった。薬物関連肝障害 SMQ の有害事象による治験薬の減量、休薬又は中止は、R788 群で 2.0%（2/102 例）、5.9%（6/102 例）又は 1.0%（1/102 例）であり、プラセボ群では認められなかった。

3) R788-1301 試験で投与量調節の基準により肝機能障害を管理した被験者の詳細

R788 投与後に以下の a) の基準に該当した被験者はいなかった。b) 及び c) の基準に該当した被験者はそれぞれ 1 例及び 2 例であった（表 2.7.4.2.1.4.3.4-1 及び表 2.7.4.2.1.4.3.4-2、肝機能検査値の一覧は表 2.7.4.9-98 及び表 2.7.4.9-99 参照）

a) 以下のいずれも満たす場合

- AST 又は ALT が基準値上限の 3 倍以上
- 総ビリルビンが基準値上限の 2 倍超
- ALP が基準値上限の 2 倍未満

b) 以下のいずれかを満たし、悪心、嘔吐、腹痛が認められる場合

- AST 又は ALT が基準値上限の 3 倍以上
- 総ビリルビンが基準値上限の 2 倍超

被験者 [redacted] は、Week 4 に AST 及び ALT が基準値上限の 3 倍以上となり、腹痛を伴ったため休薬となった。AST 及び ALT が回復後、投与量を 1 段階下げて 150 mg QD にて投与再開となったが、Week 10 に 100 mg BID へ増量後、14 週で再び AST 及び ALT が基準値上限の 3 倍以上となったため、中止となった。

なお、被験者 [redacted] は、早期移行 Week 16 に総ビリルビンが基準値上限の 2 倍超となったが、悪心、嘔吐、腹痛などの症状が認められなかったため、特に処置は行っていない。

表 2.7.4.2.1.4.3.4-1 AST 又は ALT が基準値上限の 3 倍以上で特定の症状を有する被験者（1 例）

被験者 ID	有害事象名	発現時投与量	発現日（R788 投与後）	程度	R788 の処置	転帰／転帰日（発現後）	因果関係
[redacted]	肝機能異常	100 mg BID	29 日	軽度	休薬、減量	回復／22 日	関連あり
	肝機能異常	100 mg BID	99 日	軽度	中止	回復／43 日	関連あり

（Source: 1.13.3-4, C-15 表 75）

c) 以下を満たす場合

- AST 又は ALT が基準値上限の 5 倍超

被験者 [redacted] は、早期移行 Week 24 及び早期移行 Week 28 の間の規定外来院にて AST 及び ALT が基準値上限の 3 倍以上に増加し、その後 AST 及び ALT が基準値上限の 5 倍以上に増加したため早期移行 Week 28 に休薬した。一連の肝機能検査値上昇は、自己免疫性肝炎と判断された。

被験者 [redacted] は、Week 6 に AST 及び ALT が基準値上限の 5 倍以上に該当し、休薬した。Week 8 にて AST 及び ALT は回復傾向ではあるものの、本薬投与再開により、再び AST 及び ALT が上昇する可能性があることから、試験を中止した。

表 2.7.4.2.1.4.3.4-2　AST 又は ALT が基準値上限の 5 倍超の被験者（2 例）

被験者 ID	有害事象名	発現時投与量	発現日（R788 投与後）	程度	R788 の処置	転帰／転帰日（発現後）	因果関係
[redacted]	自己免疫性肝炎	150 mg BID	173 日	中等度	休薬（II 期）	回復／116 日	関連なし
	肝機能異常	100 mg BID	43 日	中等度	休薬、中止	軽快／継続中	関連あり

（Source: 1.13.3-4, C-15 表 76）

2.7.4.2.1.4.3.5 好中球減少症

1)　R788 投与期

R788-1301 試験の R788 投与期において、好中球減少症の有害事象は 15.2%（5/33 例）、副作用は 12.1%（4/33 例）認められた。重篤な好中球減少症は認められなかった。好中球減少症の有害事象は軽度（15.2%（5/33 例））であった。好中球減少症の有害事象による治験薬の減量は 12.1%（4/33 例）であり、休薬又は中止は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、好中球減少症の有害事象は 6.8%（10/146 例）、副作用は 4.8%（7/146 例）認められた。重篤な好中球減少症は 0.7%（1/146 例）認められ、治験薬との因果関係ありと判定された。好中球減少症の有害事象の多くは軽度（2.7%（4/146 例））又は中等度（2.7%（4/146 例））であり、高度は 1.4%（2/146 例）認められた。好中球減少症の有害事象による治験薬の減量は 1.4%（2/146 例）、休薬は 1.4%（2/146 例）、中止は 2.1%（3/146 例）であった。

2)　プラセボ対照期

R788-1301 試験のプラセボ対照期において、好中球減少症の有害事象は R788 群で 18.2%（4/22 例）及びプラセボ群で 0.0%（0/12 例）、副作用は R788 群で 13.6%（3/22 例）及びプラセボ群で 0.0%（0/12 例）であった。重篤な好中球減少症の有害事象は認められなかった。好中球減少症の有害事象は軽度（R788 群 18.2%（4/22 例）及びプラセボ群 0.0%（0/12 例））であった。好中球減少症の有害事象による治験薬の減量は R788 群で 13.6%（3/22 例）及びプラセボ群で 0.0%（0/12 例）であり、中止又は休薬は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、好中球減少症の有害事象は R788 群で 6.9%（7/102 例）及びプラセボ群で 0.0%（0/48 例）、副作用は R788 群で 5.9%（6/102 例）及びプラセボ群で 0.0%（0/48 例）であった。重篤な好中球減少症は R788 群で 1.0%（1/102 例）認められ、治験薬との因果関係ありと判定された。好中球減少症の有害事象は、R788 群において、軽度が 2.9%（3/102 例）、中等度が 2.0%（2/102 例）、高度が 2.0%（2/102 例）であった。好中球減少症の有害事象による治験薬の減量、休薬又は中止は、R788 群で 2.0%（2/102 例）、2.0%（2/102 例）又は 2.0%（2/102 例）であった。好中球減少症が感染と関連することはまれであった。発熱性好中球減少症を発現した R788 群 1 例のほかに、好中球減少症の発現から約 10 日後に上気道感染を発現した R788 群 1 例が認められた。

3) R788-1301 試験で投与量調節の基準により好中球減少症を管理した被験者の詳細

R788 投与後に好中球数が 1000/μL 未満に減少した被験者は 7 例（[redacted]、[redacted]、[redacted]、[redacted]、[redacted]、[redacted] 及び [redacted]）であった（該当被験者の好中球数の一覧は表 2.7.4.9-97 参照）。このうち、5 例では当該好中球数減少は有害事象と判断され、治験実施計画書の投与量調節の基準に従い本薬の休薬・減量の処置がとられた（表 2.7.4.2.1.4.3.5-1）。いずれの被験者も処置により回復した。被験者 [redacted] は休薬により好中球が回復したものの、28 週に有効性の欠如により試験を中止した。

なお、被験者 [redacted] は 2 時点で好中球数 1000/μL 未満となったが、有害事象には該当しないと判断された。

表 2.7.4.2.1.4.3.5-1 好中球数 1000/μL 未満に減少した被験者のうち、有害事象と判断された被験者

被験者 ID	発現時投与量	発現日（R788 投与後）	程度	R788 の処置	転帰／転帰日（発現後）	因果関係
[redacted]	150 mg BID	310 日	軽度	休薬（II 期）	回復／71 日	関連あり
	100 mg BID	29 日	軽度	投与量変更せず	回復／64 日	関連あり
	150 mg BID	128 日	軽度	休薬、減量	回復／14 日	関連あり
	100 mg BID	29 日	軽度	休薬、減量	回復／6 日	関連なし
	150 mg BID	58 日	軽度	休薬、減量	回復／21 日	関連あり
	100 mg BID	141 日	軽度	休薬（II 期）、減量	回復／29 日	関連あり

（Source: 1.13.3-4, C-15 表 74）

4) 白血球減少

国内第 III 相試験（R788-1301）及び海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）で認められた好中球減少症を詳細に評価するため、白血球減少に関連する有害事象を以下の定義で抽出した。

- MedDRA の SMQ「Haematopoietic thrombocytopenia（造血障害による白血球減少症）」の狭域に該当する有害事象

R788-1301 試験、並びに C788-047、C788-048 及び C788-049 試験において認められた白血球減少を表 2.7.4.9-64～表 2.7.4.9-95 に、並びに重篤又は重症度が中等度以上の白血球減少の一覧表を表 2.7.4.9-100 及び表 2.7.4.9-101 にそれぞれ示す。

R788-1301 試験の R788 投与期では、白血球減少の有害事象は 15.2%（5/33 例）、副作用は 12.1%（4/33 例）認められ、重症度はいずれも軽度であった。白血球減少の有害事象による休薬は 0%（0/33 例）、減量は 12.1%（4/33 例）及び中止は 0.0%（0/33 例）であった。C788-047、C788-048 及び C788-049 試験を統合した R788 投与期では、白血球減少の有害事象は 8.2%（12/146 例）、副作用は 5.5%（8/146）認められ、程度はほとんどが軽度又は中等度であった。白血球減少の副作用による休薬は 1.4%（2/146 例）、減量は 1.4%（2/146 例）、中止は 2.1%（3/146）例であった。主に認められた白血球減少の有害事象はいずれの試験も好中球減少症及び好中球数減少であった。

重篤又は重症度が中等度以上の白血球減少について、R788-1301 試験の R788 投与期では、重篤又は重症度が中等度以上の白血球減少症は認められなかった。C788-047、C788-048 及び C788-049 試験を統合した R788 投与期では、重篤又は重症度が中等度以上の白血球減少症の副作用が 5 例 6 件に認められた。2 件が休薬又は減量により回復、3 件が中止により回復し、転

帰が回復せずであった 1 件は治験薬の処置を必要とせず投与継続可能であった。

2.7.4.2.1.4.3.6 感染症

2.7.4.2.1.4.3.6.1 感染症の有害事象の発現状況

1) R788 投与期

R788-1301 試験の R788 投与期において、感染症の有害事象は 30.3%（10/33 例）であり、副作用は認められなかった。感染症に分類される有害事象で高頻度に認められた事象はなかった。重篤な感染症は 6.1%（2/33 例）認められ、治験薬との因果関係ありと判定されたものはなかった。感染症の有害事象は軽度（21.2%（7/33 例））又は中等度（9.1%（3/33 例））であり、高度は認められなかった。感染症の有害事象による治験薬の減量は 3.0%（1/33 例）であり、休薬又は中止は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、感染症の有害事象は 46.6%（68/146 例）、副作用は 8.2%（12/146 例）認められた。高頻度に認められた感染症の有害事象は、上気道感染 12.3%（18/146 例）、鼻咽頭炎 6.8%（10/146 例）、尿路感染 6.2%（9/146 例）、並びに気管支炎、インフルエンザ様疾患、下気道感染、気道感染及びウイルス感染各 4.1%（6/146 例）であった。重篤な感染症は 8.2%（12/146 例）認められ、そのうち治験薬との因果関係ありと判定されたのは 2.7%（4/146 例）であった。感染症の有害事象の多くは軽度（25.3%（37/146 例））又は中等度（15.1%（22/146 例））であり、高度は 6.2%（9/146 例）認められた。高度の感染症の有害事象は、インフルエンザ様疾患、ウイルス感染、蜂巣炎、ブドウ球菌性蜂巣炎、細菌性心内膜炎、硬結性紅斑、乳様突起炎、結核及び尿路性敗血症各 0.7%（1/146 例）、並びに肺炎及び敗血症各 1.4%（2/146 例）であった。感染症の有害事象による治験薬の減量は 1.4%（2/146 例）、休薬は 6.2%（9/146 例）、中止は 0.7%（1/146 例）であった。

2) プラセボ対照期

R788-1301 試験のプラセボ対照期において、感染症の有害事象は R788 群で 9.1%（2/22 例）及びプラセボ群で 25.0%（3/12 例）であり、副作用は認められなかった。感染症に分類される有害事象で高頻度に認められた事象はなかった。重篤な感染症の有害事象は認められなかった。感染症の有害事象は軽度（R788 群 9.1%（2/22 例）及びプラセボ群 25.0%（3/12 例））であった。感染症の有害事象による治験薬の減量、休薬又は中止は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、感染症の有害事象は R788 群で 30.4%（31/102 例）及びプラセボ群で 20.8%（10/48 例）、副作用は R788 群で 3.9%（4/102 例）及びプラセボ群で 0.0%（0/48 例）であった。最も高頻度に認められた感染症の有害事象は、上気道感染（R788 群 5.9%（6/102 例）及びプラセボ群 4.2%（2/48 例））であった。重篤な感染症は R788 群で 2.0%（2/102 例）及びプラセボ群で 4.2%（2/48 例）認められ、そのうち治験薬との因果関係ありと判定されたのは R788 群の 1.0%（1/102 例）であった。感染症の有害事象の多くは軽度（R788 群 22.5%（23/102 例）及びプラセボ群 14.6%（7/48 例）（以下同順））又は中等度（5.9%（6/102 例）及び 4.2%（2/48 例））であり、高度は R788 群で 2.0%（2/102 例）及びプラセボ群で 2.1%（1/48 例）認められた。R788 群で認められた高度の感染症の有害事象は、インフルエンザ様疾患（R788 群 1.0%（1/102 例）及びプラセボ群 0.0%（0/48 例）（以下同順））並びに肺炎（1.0%（1/102 例）及び 0.0%（0/48 例））であった。感染症の有害事象による

治験薬の減量は認められなかった。感染症の有害事象による治験薬の休薬は R788 群で 2.0%（2/102 例）及びプラセボ群で 0.0%（0/48 例）、中止は R788 群で 1.0%（1/102 例）及びプラセボ群で 0.0%（0/48 例）であった。気道に及ぶ感染は、R788 群で感染事象の 60%、プラセボ群で感染事象の 40%であった。口腔ヘルペス（熱性疱疹として報告）及び口腔カンジダ症（鵞口瘡として報告）が、R788 群で各 1 例報告された。これらの被験者はいずれも、細菌感染の既往歴があり、これらのウイルス及び真菌感染が発生する少し前に、抗菌薬を投与されていた。

2.7.4.2.1.4.3.6.2 白血球数、リンパ球数及び IgG と感染症の関連性

R788-1301 試験、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049 試験の統合）及び海外第 II 相臨床試験（D4300-022）を対象として、白血球数、リンパ球数及び IgG に異常低値が認められた被験者における感染症の発現状況について検討した。各項目の異常低値は、白血球数及びリンパ球数は CTCAE v5.0 の Grade 3 以上に該当した場合（白血球数：<2.0×10^9/L、リンパ球数：<0.5×10^9/L）とし、IgG は基準値下限未満となった場合とした。なお、D4300-022 試験では IgG を測定してないため白血球数及びリンパ球数のみ示す。

1) R788-1301 試験

(1) 臨床検査値の推移

第 I 期の白血球数、リンパ球数及び IgG の測定値及び変化量の推移を表 2.7.4.9-133～表 2.7.4.9-136 に示す。

Week 24 の白血球数のベースラインからの変化量は、R788 群−1.906±1.615×10^9/L 及びプラセボ群−1.210±0.900×10^9/L（平均値±標準偏差、以下同様）であり、両群で軽度に低下した。Week 24 のリンパ球数のベースラインからの変化量は、R788 群−0.019±0.345×10^9/L 及びプラセボ群−0.111±0.608×10^9/L であり、いずれも大きな変動は認められなかった。Week 24 の IgG のベースラインからの変化量は、R788 群−1.804±0.985 g/L 及びプラセボ群 0.065±0.615 g/L であり、R788 群で軽度に低下した。いずれの検査項目も平均値は基準値範囲内の変動であった。

R788 長期投与時及び第 III 期の白血球数及びリンパ球数の要約統計量の推移、R788 長期投与時の IgG の測定値及び変化量の推移を表 2.7.4.9-137～表 2.7.4.9-142 に示す。なお、R788-1301 試験では第 III 期は IgG を測定しなかった。

長期投与時では Week 52 まで、第 III 期では最長で Week 64 まで R788 を投与した結果、白血球数及び IgG は R788 の投与開始後に軽度な低下を認めたが、長期投与に伴うさらなる低下は認められなかった。

(2) 異常低値が認められた被験者

白血球数、リンパ球数及び IgG の異常低値が認められた被験者の割合を表 2.7.4.2.1.4.3.6.2-1 に示す。

第 I 期に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の割合は、白血球数 R788 群 4.5%及びプラセボ群 0.0%、リンパ球数 R788 群 18.2%及びプラセボ群 0.0%、IgG R788 群 22.7%及びプラセボ群 16.7%であった。

R788 投与期に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の割合は、白血球数 9.1%、リンパ球数 21.2%及び IgG 21.2%であった。なお、このうち、IgG の 3 例は、R788

の投与前より異常低値を示していた。

表 2.7.4.2.1.4.3.6.2-1 異常低値が認められた被験者の割合（R788-1301 試験）

検査項目	第 I 期		R788 投与期
	R788 群	Placebo 群	
白血球数	4.5% (1/22 例)	0.0% (0/12 例)	9.1% (3/33 例)
リンパ球数	18.2% (4/22 例)	0.0% (0/12 例)	21.2% (7/33 例)
IgG	22.7% (5/22 例)	16.7% (2/12 例)	21.2% (7/33 例)

（Source: 1.13.3-10, C-02 表 3）

また、R788 の投与中に異常低値が認められた被験者の被験者背景、感染症に関連する有害事象の発現状況の一覧、併用薬の一覧及び病歴の一覧を表 2.7.4.9-143～表 2.7.4.9-145 に示す。

R788 を投与した 33 例中いずれかの異常低値が認められた被験者は 13 例であり、このうち感染症に関連する有害事象（SOC「感染症および寄生虫症」）が 3 例 4 件に認められた。有害事象の内訳は、膀胱炎 1 例 1 件、尿路感染 1 例 1 件及びウイルス感染 2 例 2 件であった。いずれの事象も治験薬との因果関係はないと判断された。

異常低値が認められた被験者の背景及び合併症に一定の傾向は認められなかった。また、R788 の投与中に副腎皮質ステロイドを使用した被験者は試験全体で 18 例であり、そのうち異常低値が認められた被験者は 10 例であった。

2) 海外第 III 相臨床試験

(1) 臨床検査値の推移

プラセボ対照期（C788-047 及び C788-048 試験統合）の白血球数、リンパ球数及び IgG の測定値及び変化量の推移を表 2.7.4.9-146～表 2.7.4.9-148 に示す。

Week 24 の白血球数のベースラインからの変化量は、R788 群−2.768±3.149×10^9/L 及びプラセボ群 1.400±4.243×10^9/L（平均値±標準偏差、以下同様）であり、R788 群で軽度に低下した。Week 24 のリンパ球数のベースラインからの変化量は、R788 群 0.040±0.827×10^9/L 及びプラセボ群−0.160±0.170×10^9/L であり、いずれも大きな変動は認められなかった。Week 24 の IgG のベースラインからの変化量は、R788 群−1.77±3.72 g/L 及びプラセボ群−0.47±0.92 g/L であり、R788 群で軽度に低下した。いずれの検査項目も平均値は基準値範囲内の変動であった。

R788 投与期（C788-047、C788-048 及び C788-049 試験統合）の白血球数、リンパ球数及び IgG の測定値及び変化量の推移を表 2.7.4.9-149～表 2.7.4.9-151 に示す。

白血球数及び IgG は R788 の投与開始後にプラセボ対照期と同程度の低下を認めたが、長期投与に伴うさらなる低下は認められなかった。

(2) 異常低値が認められた被験者

白血球数、リンパ球数及び IgG の異常低値が認められた被験者の割合を表 2.7.4.2.1.4.3.6.2-2 に示す。

プラセボ対照期に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の割合は、白血球数 R788 群 2.0%及びプラセボ群 0.0%、リンパ球数 R788 群 5.9%及びプラセボ群 8.3%、IgG R788 群 8.9%及びプラセボ群 12.5%であった。

R788 投与期に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の割合は、白

血球数 2.1%、リンパ球数 13.0%及び IgG 13.0%であった。なお、このうち、リンパ球数の 1 例及び IgG の 6 例は、R788 投与前より異常低値を示していた。

表 2.7.4.2.1.4.3.6.2-2 異常低値が認められた被験者の割合（海外第 III 相臨床試験）

検査項目	C788-047 及び C788-048 試験		C788-047、C788-048 及び C788-049 試験
	R788 群	Placebo 群	
白血球数	2.0% (2/102 例)	0.0% (0/48 例)	2.1% (3/146 例)
リンパ球数	5.9% (6/102 例)	8.3% (4/48 例)	13.0% (19/146 例)
IgG	8.9% (9/101 例)	12.5% (6/48 例)	13.0% (19/146 例)

（Source: 1.13.3-10, C-02 表 1）

また、R788 の投与中に異常低値が認められた被験者の被験者背景、感染症に関連する有害事象の発現状況の一覧、併用薬の一覧及び病歴の一覧を表 2.7.4.9-152～表 2.7.4.9-154 に示す。

R788 を投与した 146 例中いずれかの異常低値が認められた被験者 35 例に発現した感染症に関連する有害事象（SOC「感染症および寄生虫症」）を表 2.7.4.2.1.4.3.6.2-3 に示した。35 例中、感染症に関連する有害事象は 20 例 73 件、副作用は 7 例 11 件に認められた。副作用の内訳は、ウイルス性関節炎 1 例 1 件、下気道感染 1 例 3 件、口腔カンジダ症 1 例 1 件、肺炎 2 例 2 件、処置後感染 1 例 1 件、気道感染 1 例 1 件、敗血症 1 例 1 件及び上気道感染 1 例 1 件であった。

表 2.7.4.2.1.4.3.6.2-3 異常低値が認められた被験者の感染症に関連する有害事象の発現状況（海外第 III 相臨床試験）

事象名（PT）	有害事象 (N=35)		副作用 (N=35)	
	例数	件数	例数	件数
膿瘍	1	1	0	0
ウイルス性関節炎	1	2	1	1
気管支炎	2	2	0	0
蜂巣炎	1	1	0	0
ブドウ球菌性蜂巣炎	1	2	0	0
憩室炎	1	1	0	0
細菌性心内膜炎	1	1	0	0
大腸菌性尿路感染	1	2	0	0
眼感染	2	3	0	0
真菌感染	1	1	0	0
皮膚真菌感染	1	1	0	0
胃腸炎	1	1	0	0
消化管感染	1	1	0	0
インフルエンザ	1	1	0	0
下気道感染	2	9	1	1
鼻咽頭炎	3	6	0	0
爪真菌症	1	1	0	0
口腔カンジダ症	1	1	1	1
口腔ヘルペス	1	1	0	0
肺炎	4	4	2	2
処置後感染	1	1	1	1
気道感染	2	2	1	1
鼻炎	1	1	0	0
敗血症	1	1	1	1
亜急性心内膜炎	1	1	0	0
白癬感染	1	1	0	0

事象名（PT）	有害事象 (N=35)		副作用 (N=35)	
	例数	件数	例数	件数
上気道感染	5	7	1	1
尿路感染	4	8	0	0
細菌性尿路感染	1	1	0	0
尿路性敗血症	1	2	0	0
ウイルス感染	3	5	0	0
ウイルス性咽頭炎	1	1	0	0

（Source: 1.13.3-10, C-02 表 2）

異常低値が認められた被験者の背景や合併症に一定の傾向は認められなかった。また、R788 の投与中に副腎皮質ステロイドを使用した被験者は試験全体で 85 例であり、そのうち異常低値が認められた被験者は 26 例であった。

3) D4300-022 試験

(1) 臨床検査値の推移

D4300-022 試験の白血球数及びリンパ球数の推移を表 2.7.4.9-155 に示す。

Week 24 の白血球数のベースラインからの変化量は、−0.880±0.8828×10^9/L（平均値±標準偏差、以下同様）、リンパ球数のベースラインからの変化量は、−0.323±0.5002×10^9/L であり R788 の投与後に軽度な低下を認めたが、長期投与に伴うさらなる低下は認められなかった。

(2) 異常低値が認められた被験者

試験中にリンパ球数に異常低値が認められた被験者の割合は 16.7%（3/18 例）であった。白血球数が異常低値を示した被験者は認められなかった。

また、R788 の投与中に異常低値が認められた被験者の被験者背景、感染症に関連する有害事象の発現状況の一覧、併用薬の一覧及び病歴の一覧を表 2.7.4.9-156～表 2.7.4.9-158 に示す。

異常低値が認められた被験者に発現した感染症に関連する有害事象（SOC「感染症および寄生虫症」）は、骨髄炎 1 例 1 件、帯状疱疹 1 例 1 件、インフルエンザ 1 例 1 件、肺炎 1 例 1 件及び歯感染 1 例 1 件であった。このうち副作用はインフルエンザ 1 例 1 件であった。

異常低値が認められた被験者の年齢は 71～80 歳であり、全被験者 18 例の平均値（61.9 歳）と比較し高い傾向が認められた。その他背景や合併症に一定の傾向は認められなかった。また、R788 の投与中に副腎皮質ステロイドを使用した被験者は試験全体で 17 例であり、そのうち異常低値が認められた被験者は 3 例であった。

2.7.4.2.1.4.3.6.3 日和見感染の発現状況

R788-1301 試験の第 I 期及び海外第 III 相臨床試験（C788-047 及び C788-048 試験）における、R788 群及びプラセボ群の日和見感染の発現状況（発現例数及び発現割合）を表 2.7.4.2.1.4.3.6.3-1 に示す。また、R788-1301 試験の R788 投与期、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049 試験）及び D4300-022 試験における、日和見感染の発現状況（発現例数及び発現割合）を表 2.7.4.2.1.4.3.6.3-2 に示す。

日和見感染は以下の定義で抽出した。なお、日和見感染（SMQ）は、海外臨床試験で使用していた MedDRA の Version では設定されていなかったため、R788-1301 試験と同様に、MedDRA Ver 23.0 を使用して抽出した。

- MedDRA の SMQ「Opportunistic infections（日和見感染）」の広域に該当する有害事象

R788-1301 試験の第 I 期及び海外第 III 相臨床試験（C788-047 及び C788-048 試験）における日和見感染の発現状況は、国内外のいずれにおいても R788 群及びプラセボ群で大きな違いは認められなかった。

R788-1301 試験の R788 投与期、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049 試験）及び D4300-022 試験における日和見感染の発現状況について、D4300-022 試験では被験者数が少ないため、発現割合が若干高かった。海外第 III 相試験及び R788-1301 試験では、R788 投与における特徴的な有害事象（下痢、高血圧など）以外の他の有害事象発現割合と同程度であった（5.3.5.1.1 Table 14.3.4.1.3.1、5.3.5.3.2 Table 4.2.1.2.1 参照）。

表 2.7.4.2.1.4.3.6.3-1 日和見感染の発現状況～プラセボ対照

	有害事象				副作用			
	C788-047, 048 統合		R788-1301		C788-047, 048 統合		R788-1301	
	R788 N=102	Placebo N=48	R788 N=22	Placebo N=12	R788 N=102	Placebo N=48	R788 N=22	Placebo N=12
日和見感染 SMQ 広域	2 (2.0)	2 (4.2)	1 (4.5)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔カンジダ症	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

n (%)
（Source: 1.13.3-10, C-02 表 4）

表 2.7.4.2.1.4.3.6.3-2 日和見感染の発現状況～R788 投与期

	有害事象			副作用		
	D4300-022	C788-047, 048, 049 統合	R788-1301	D4300-022	C788-047, 048, 049 統合	R788-1301
	R788 N=18	R788 N=146	R788 N=33	R788 N=18	R788 N=146	R788 N=33
日和見感染 SMQ 広域	3 (16.7)	13 (8.9)	2 (6.2)	3 (16.7)	4 (2.7)	0 (0.0)
ブドウ球菌性蜂巣炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硬結性紅斑	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
大腸菌性尿路感染	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	2 (11.1)	1 (0.7)	2 (6.2)	1 (5.6)	1 (0.7)	0 (0.0)
インフルエンザ	2 (11.1)	1 (0.7)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
クレブシエラ性菌血症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪真菌症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔カンジダ症	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
口腔ヘルペス	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	0 (0.0)	3 (2.1)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
結核	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
尿路性敗血症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

n (%)
（Source: 1.13.3-10, C-02 表 5）

2.7.4.2.1.4.3.7 血栓症、塞栓症、血栓塞栓症

2.7.4.2.1.4.3.7.1 血栓症、塞栓症、血栓塞栓症の有害事象の発現状況

R788-1301 試験の R788 投与期において、血栓症、塞栓症及び血栓塞栓症の有害事象は認められなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、血栓症、塞栓症及び血栓塞栓症の有害事象は 146 例中 1 例（0.7%）に認められ、重篤な有害事象であったが、治験薬との因果関係は否定された。また、程度は軽度であり、治験薬に対する処置は行われなかった（表 2.7.4.9-106 参照）。

R788-1301 試験のプラセボ対照期において、血栓症、塞栓症及び血栓塞栓症の有害事象は認められなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期において、血栓症、塞栓症及び血栓塞栓症の有害事象は R788 群で 102 例中 1 例（1.0%）に認められ（R788 投与期と同一事象）、重篤な有害事象であったが、治験薬との因果関係は否定された。また、程度は軽度であり、治験薬に対する処置は行われなかった（表 2.7.4.9-106 参照）。

海外第 II 相臨床試験（D4300-022）では、血栓症、塞栓症及び血栓塞栓症に関連する有害事象が 3 例に認められ、このうち 2 例は R788 との因果関係が否定されていないものの、1 例目の深部静脈血栓症は高齢及び糖尿病の病歴の要因がある被験者であり、2 例目の血栓症は抗リン脂質抗体症候群、深部静脈血栓症及び血中コレステロール増加の病歴の要因がある被験者であった。また、血小板数が 400000/μL を超えるオーバーシュートは 2 例に認められているが、いずれも一過性であり、R788 の用量調節により血小板数が 400000/μL 以下に減少している。D4300-022 試験で認められた深部静脈血栓症及び血栓症は、血小板数のオーバーシュートを認めた被験者とは別の被験者であり、血栓症、塞栓症及び血栓塞栓症との関連有害事象を発現した被験者の血小板数は必ずしも高値ではないことから、血栓症、塞栓症及び血栓塞栓症との関連有害事象の発現には、血小板数以外の個別の要因が影響している可能性が高い（表 2.7.4.9-107 参照）。

2.7.4.2.1.4.3.7.2 副腎皮質ステロイドを併用した被験者における血栓症、塞栓症、血栓塞栓症の有害事象の発現状況

R788-1301 試験及び海外第 III 相臨床試験（C788−047、C788-048 及び C788-049 試験の統合）の R788 投与期、並びに海外第 II 相臨床試験（D4300−0022 試験））における、副腎皮質ステロイドを併用した被験者割合、副腎皮質ステロイドの併用の有無別における血栓症、塞栓症及び血栓塞栓症の有害事象の発現状況、血小板数の変化量、並びに血小板数のオーバーシュートが認められた被験者割合を表 2.7.4.9-159～表 2.7.4.9-164 に示す。

血栓症、塞栓症及び血栓塞栓症の有害事象及びオーバーシュートは副腎皮質ステロイドの併用例での発現が多い傾向にあったが、これら事象の発現例数自体が少ないことから、副腎皮質ステロイドの併用有無による発生頻度の差異を明確に説明することはできないと考えられた。また、血小板数の変化量（中央値）についても、副腎皮質ステロイドの併用有無による差異は認められなかった。

2.7.4.2.1.4.3.8 発現時期別の注目すべき有害事象

R788-1301 試験の R788 投与期、並びに C788-047、C788-048 及び C788-049 試験を統合した R788 投与期における発現時期別の非感染性下痢 SMQ、高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ の発現状況を表 2.7.4.2.1.4.3.8-1 及び表 2.7.4.2.1.4.3.8-2 に示す。また、R788 の投与開始又は用量変更後 4 週間以内に発現した高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ に関する有害事象のうち治療介入が必要となった事象を表 2.7.4.9-129～表 2.7.4.9-132 に示す。

R788-1301 試験の R788 投与期、並びに C788-047、C788-048 及び C788-049 試験を統合した R788 投与期において、非感染性下痢 SMQ、高血圧 SMQ 及び薬物関連肝障害 SMQ では、≤Week 2、Week 2<≤Week 4、Week 4<≤Week 12 の 3 区分いずれかで発現割合が 10%以上であり、投与早期に発現する傾向が認められた。また、好中球減少症は発現割合が低いことから、上記 3 区分でいずれも 10%以上ではなかったものの、投与早期に発現する傾向が認められた。

R788-1301 試験において R788 の投与開始又は用量変更後 4 週間以内に発現した治療介入が必要であった高血圧 SMQ、好中球数減少症及び薬物関連肝障害 SMQ に関する有害事象は、投与開始後 4 週間以内は 10 例 11 件、用量変更後 4 週間以内は 7 例 7 件であった。海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）においては、投与開始後 4 週間以内は 10 例 11 件、用量変更後 4 週間以内は 11 例 13 件であった。

表 2.7.4.2.1.4.3.8-1　R788-1301 試験の R788 投与期における発現時期別の有害事象（非感染性下痢 SMQ、高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ）

Time to Onset	≤Week 2	Week 2< ≤4	Week 4 < ≤12	Week 12< ≤24	Week 24< ≤36	Week 36< ≤48	Week 48< ≤72	>Week 72	Follow-up
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N	33	33	33	31	26	23	18	7	12
非感染性下痢 SMQ	5 (15.2)	4 (12.1)	8 (24.2)	4 (12.9)	0 (0.0)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)
下痢	5 (15.2)	4 (12.1)	8 (24.2)	4 (12.9)	0 (0.0)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)
高血圧 SMQ	4 (12.1)	4 (12.1)	4 (12.1)	1 (3.2)	2 (7.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	1 (3.0)	1 (3.0)	0 (0.0)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	4 (12.1)	3 (9.1)	3 (9.1)	1 (3.2)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球減少症	0 (0.0)	2 (6.1)	1 (3.0)	2 (6.5)	0 (0.0)	1 (4.3)	1 (5.6)	1 (14.3)	0 (0.0)
好中球減少症	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)	1 (5.6)	1 (14.3)	0 (0.0)
好中球数減少	0 (0.0)	1 (3.0)	1 (3.0)	2 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物関連肝障害 SMQ	0 (0.0)	2 (6.1)	6 (18.2)	3 (9.7)	2 (7.7)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)
ALT 増加	0 (0.0)	1 (3.0)	1 (3.0)	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
AST 増加	0 (0.0)	1 (3.0)	1 (3.0)	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝嚢胞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	1 (3.0)	1 (3.0)	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査異常	0 (0.0)	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査値上昇	0 (0.0)	0 (0.0)	2 (6.1)	1 (3.2)	1 (3.8)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)

（Source: 1.13.3-6, C-05 表 20）

表 2.7.4.2.1.4.3.8-2　C788-047、C788-048 及び C788-049 試験の R788 投与期における発現時期別の有害事象（非感染性下痢 SMQ、高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ）

Time to Onset	≤Week 2	Week 2< ≤4	Week 4< ≤12	Week 12< ≤24	Week 24< ≤36	Week 36< ≤48	Week 48< ≤Month 18	Month 18< ≤24	Month 24< ≤30	Month 30< ≤36	Month 36< ≤42	Month 42< ≤48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N	146	146	143	128	101	65	58	50	47	45	40	38	23
非感染性下痢 SMQ	14 (9.6)	6 (4.1)	20 (14.0)	19 (14.8)	10 (9.9)	2 (3.1)	9 (15.5)	3 (6.0)	1 (2.1)	1 (2.2)	1 (2.5)	2 (5.3)	2 (8.7)
下痢	12 (8.2)	6 (4.1)	20 (14.0)	19 (14.8)	10 (9.9)	2 (3.1)	9 (15.5)	3 (6.0)	1 (2.1)	1 (2.2)	1 (2.5)	2 (5.3)	2 (8.7)
排便回数増加	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧 SMQ	6 (4.1)	6 (4.1)	18 (12.6)	6 (4.7)	3 (3.0)	6 (9.2)	3 (5.2)	4 (8.0)	4 (8.5)	0 (0.0)	3 (7.5)	0 (0.0)	1 (4.3)
拡張期血圧上昇	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
コントロール不良の血圧	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (0.7)	0 (0.0)	3 (2.1)	1 (0.8)	0 (0.0)	1 (1.5)	0 (0.0)	0 (0.0)	2 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
収縮期血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.5)	0 (0.0)	1 (4.3)
高血圧	4 (2.7)	5 (3.4)	14 (9.8)	4 (3.1)	2 (2.0)	4 (6.2)	3 (5.2)	4 (8.0)	2 (4.3)	0 (0.0)	2 (5.0)	0 (0.0)	0 (0.0)
高血圧クリーゼ	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球減少症	0 (0.0)	2 (1.4)	3 (2.1)	5 (3.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)
発熱性好中球減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球減少症	0 (0.0)	1 (0.7)	2 (1.4)	4 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.6)	0 (0.0)
好中球数減少	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物関連肝障害 SMQ	2 (1.4)	1 (0.7)	11 (7.7)	9 (7.0)	2 (2.0)	2 (3.1)	2 (3.4)	1 (2.0)	1 (2.1)	1 (2.2)	1 (2.5)	0 (0.0)	1 (4.3)
ALT 増加	0 (0.0)	0 (0.0)	9 (6.3)	5 (3.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)
AST 増加	1 (0.7)	0 (0.0)	6 (4.2)	3 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.6)	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ-GTP 増加	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)
肝嚢胞	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.8)	1 (1.0)	1 (1.5)	1 (1.7)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)
高ビリルビン血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査異常	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	1 (1.7)	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.3)
門脈圧亢進症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

（Source: 1.13.3-6, C-05 表 21）

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

2.7.4.2.1.5.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験において、R788 が投与された被験者で 10%以上認められた SOC 別の有害事象を表 2.7.4.2.1.5.1-1 及び表 2.7.4.2.1.5.1-2 に示す。

R788-1301 試験の R788 投与期中、25%以上の有害事象が認められた SOC は、胃腸障害 60.6%（20/33 例）、臨床検査 45.5%（15/33 例）、皮膚および皮下組織障害 42.4%（14/33 例）、感染症および寄生虫症 30.3%（10/33 例）及び血管障害 30.3%（10/33 例）であった。

R788-1301 試験のプラセボ対照期中、R788 群で 25%以上の有害事象が認められた SOC は、胃腸障害（R788 群 50.0%（11/22 例）及びプラセボ群 0.0%（0/12 例）（以下同順））、臨床検査（40.9%（9/22 例）及び 8.3%（1/12 例））、並びに血管障害（31.8%（7/22 例）及び 8.3%（1/12 例））であった。

表 2.7.4.2.1.5.1-1 SOC 別の有害事象（10%以上）（R788-1301 試験 R788 投与期）

R788 Treatment Period

System Organ Class	Adverse Events R788 (N=33) n (%)
胃腸障害	20 (60.6)
臨床検査	15 (45.5)
皮膚および皮下組織障害	14 (42.4)
感染症および寄生虫症	10 (30.3)
血管障害	10 (30.3)
筋骨格系および結合組織障害	6 (18.2)
一般・全身障害および投与部位の状態	5 (15.2)
傷害、中毒および処置合併症	5 (15.2)
肝胆道系障害	4 (12.1)
代謝および栄養障害	4 (12.1)

(Source : 5.3.5.1.1, 表 12.2.2.3-1 改編)

表 2.7.4.2.1.5.1-2 SOC 別の有害事象（10%以上）（R788-1301 試験プラセボ対照期）

Period I

System Organ Class	Adverse Events R788 (N=22) n (%)	Adverse Events Placebo (N=12) n (%)
胃腸障害	11 (50.0)	0 (0.0)
臨床検査	9 (40.9)	1 (8.3)
血管障害	7 (31.8)	1 (8.3)
皮膚および皮下組織障害	4 (18.2)	1 (8.3)
血液およびリンパ系障害	3 (13.6)	0 (0.0)
肝胆道系障害	3 (13.6)	1 (8.3)

(Source : 5.3.5.1.1, 表 12.2.2.1-1 改編)

2.7.4.2.1.5.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047、C788-048 及び C788-049 試験において、R788 が投与された被験者で 10%以上認められた SOC 別の有害事象を表 2.7.4.2.1.5.2-1 及び表 2.7.4.2.1.5.2-2 に示す。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期中、25%以上の有害事象が認められた SOC は、胃腸障害 58.2%（85/146 例）、感染症および寄生虫症 43.8%（64/146 例）、呼

吸器、胸郭および縦隔障害 34.2%（50/146 例）、一般・全身障害および投与部位の状態 32.2%（47/146 例）、神経系障害 32.2%（47/146 例）、臨床検査 31.5%（46/146 例）、皮膚および皮下組織障害 30.8%（45/146 例）及び血管障害 27.4%（40/146 例）であった。

C788-047 及び C788-048 試験を統合したプラセボ対照期中、R788 群で 25%以上の有害事象が認められた SOC は、胃腸障害（R788 群 48.0%（49/102 例）及びプラセボ群 33.3%（16/48 例）（以下同順））、臨床検査（27.5%（28/102 例）及び 10.4%（5/48 例））、感染症および寄生虫症（26.5%（27/102 例）及び 20.8%（10/48 例））、並びに神経系障害（25.5%（26/102 例）及び 27.1%（13/48 例））であった。

表 2.7.4.2.1.5.2-1 SOC 別の有害事象（10%以上）（C788-047、C788-048 及び C788-049 試験 R788 投与期）

System Organ Class	Fostamatinib (N=146) n (%)
胃腸障害	85 (58.2)
感染症および寄生虫症	64 (43.8)
呼吸器、胸郭および縦隔障害	50 (34.2)
一般・全身障害および投与部位の状態	47 (32.2)
神経系障害	47 (32.2)
臨床検査	46 (31.5)
皮膚および皮下組織障害	45 (30.8)
血管障害	40 (27.4)
血液およびリンパ系障害	32 (21.9)
筋骨格系および結合組織障害	32 (21.9)
傷害、中毒および処置合併症	24 (16.4)

MedDRA version 18.1
（Source: 5.3.5.3.2, Table 4.2.1.2.1 改編）

表 2.7.4.2.1.5.2-2 SOC 別の有害事象（10%以上）（C788-047 及び C788-048 試験プラセボ対照期）

System Organ Class	Placebo-Controlled Period	
	R788 (N = 102) n (%)	Placebo (N = 48) n (%)
胃腸障害	49 (48.0)	16 (33.3)
臨床検査	28 (27.5)	5 (10.4)
感染症および寄生虫症	27 (26.5)	10 (20.8)
神経系障害	26 (25.5)	13 (27.1)
血管障害	24 (23.5)	9 (18.8)
呼吸器、胸郭および縦隔障害	23 (22.5)	10 (20.8)
皮膚および皮下組織障害	18 (17.6)	5 (10.4)
一般・全身障害および投与部位の状態	17 (16.7)	5 (10.4)
血液およびリンパ系障害	15 (14.7)	4 (8.3)

MedDRA version 18.1
（Source: 5.3.5.3.2, Table 4.2.1.1.1 改編）

2.7.4.2.1.5.2.1 胃腸障害

以下の選択された胃腸障害について要約した（(a) 悪心、(b) 嘔吐、(c) 非感染性下痢 SMQ（PT：下痢及び排便回数増加）、並びに(d) 腹痛（PT：上腹部痛、腹痛及び腹部不快感））。

国内第 III 相臨床試験（R788-1301）の R788 投与期において、選択された胃腸障害の有害事象は 48.5%（16/33 例）、副作用は 33.3%（11/33 例）認められた。高頻度に認められた胃腸障害

の有害事象は、非感染性下痢 SMQ 39.4%（13/33 例）及び腹痛 15.2%（5/33 例）であった。高度と判定された胃腸障害の有害事象は非感染性下痢 SMQ 3.0%（1/33 例）であった。

R788-1301 試験のプラセボ対照期において、選択された胃腸障害の有害事象は R788 群で 50.0%（11/22 例）及びプラセボ群で 0.0%（0/12 例）、副作用は R788 群で 40.9%（9/22 例）及びプラセボ群で 0.0%（0/12 例）であった。高頻度に認められた胃腸障害の有害事象は、非感染性下痢 SMQ（R788 群 40.9%（9/22 例）及びプラセボ群 0.0%（0/12 例））であった。高度と判定された胃腸障害の有害事象は R788 群の非感染性下痢 SMQ 4.5%（1/22 例）であった。

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の R788 投与期において、選択された胃腸障害の有害事象は 47.9%（70/146 例）、副作用は 37.0%（54/146 例）認められた。高頻度に認められた胃腸障害の有害事象は非感染性下痢 SMQ 36.3%（53/146 例）、悪心 19.2%（28/146 例）及び腹痛 13.0%（19/146 例）であった。高度と判定された胃腸障害の有害事象は非感染性下痢 SMQ 2.1%（3/146 例）であった。

海外第 III 相臨床試験（C788-047 及び C788-048）のプラセボ対照期において、選択された胃腸障害の有害事象は R788 群で 41.2%（42/102 例）及びプラセボ群で 20.8%（10/48 例）、副作用は R788 群で 34.3%（35/102 例）及びプラセボ群で 16.7%（8/48 例）認められた。高頻度に認められた胃腸障害の有害事象は、非感染性下痢 SMQ（R788 群 31.4%（32/102 例）及びプラセボ群 14.6%（7/48 例）（以下同順））及び悪心（18.6%（19/102 例）及び 8.3%（4/48 例））であった。高度と判定された胃腸障害の有害事象は R788 群の非感染性下痢 SMQ 1.0%（1/102 例）であった。

2.7.4.2.1.5.2.2 心血管障害

SOC 心血管障害について要約した。高血圧 SMQ は、注目すべき有害事象として 2.7.4.2.1.4.3.3 に記載した。

国内第 III 相臨床試験（R788-1301）の R788 投与期において、心臓障害の有害事象は 3.0%（1/33 例）、副作用は 0.0%（0/33 例）であった。高度と判定された心臓障害の有害事象は心房細動 3.0%（1/33 例）であった。

R788-1301 試験のプラセボ対照期において、心臓障害の有害事象は認められなかった。

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の R788 投与期において、心臓障害の有害事象は 6.8%（10/146 例）、副作用は 1.4%（2/146 例）認められた。高頻度に認められた心臓障害の有害事象は頻脈 2.1%（3/146 例）、心房細動 1.4%（2/146 例）及びうっ血性心不全 1.4%（2/146 例）であった。高度と判定された心臓障害の有害事象は心房細動、うっ血性心不全及び心肺停止各 0.7%（1/146 例）であった。

海外第 III 相臨床試験（C788-047 及び C788-048）のプラセボ対照期において、心臓障害の有害事象は R788 群で 2.9%（3/102 例）及びプラセボ群で 2.1%（1/48 例）、副作用は R788 群で 1.0%（1/102 例）であり、プラセボ群では認められなかった。高頻度に認められた心臓障害の有害事象は頻脈（R788 群 2.9%（3/102 例）及びプラセボ群 0.0%（0/48 例））であった。高度と判定された心臓障害の有害事象は認められなかった。

2.7.4.2.1.5.2.3 肝障害

SOC 肝障害について要約した。トランスアミナーゼ及びビリルビンにおける特定の変化のよ

り詳細な要約は、2.7.4.2.1.4.3.4 に記載する。

国内第 III 相臨床試験（R788-1301）の R788 投与期において、肝障害の有害事象は 12.1%（4/33 例）、副作用は 6.1%（2/33 例）認められた。高頻度に認められた肝障害の有害事象は肝機能異常 6.1%（2/33 例）であった。高度と判定された肝障害の有害事象は認められなかった。

R788-1301 試験のプラセボ対照期において、肝障害の有害事象は R788 群で 13.6%（3/22 例）及びプラセボ群で 8.3%（1/12 例）、副作用は R788 群で 9.1%（2/22 例）であり、プラセボ群では認められなかった。高頻度に認められた肝障害の有害事象は肝機能異常（R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例））であった。高度と判定された肝障害の有害事象は認められなかった。

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の R788 投与期において、肝障害の有害事象は 2.7%（4/146 例）、副作用は 0.7%（1/146 例）認められた。高頻度に認められた肝障害の有害事象はなかった。高度と判定された肝障害の有害事象は胆嚢炎 0.7%（1/146 例）であった。

海外第 III 相臨床試験（C788-047 及び C788-048）のプラセボ対照期において、肝障害の有害事象は R788 群で 1.0%（1/102 例）及びプラセボ群で 0.0%（0/48 例）であり、副作用は認められなかった。高頻度に認められた肝障害の有害事象はなかった。高度と判定された肝障害の有害事象は認められなかった。

2.7.4.2.1.5.2.4 腎障害

SOC 腎障害について要約した。

国内第 III 相臨床試験（R788-1301）の R788 投与期において、腎障害の有害事象は認められなかった。

R788-1301 試験のプラセボ対照期において、腎障害の有害事象は R788 群で 0.0%（0/22 例）及びプラセボ群で 8.3%（1/12 例）であり、副作用は認められなかった。高頻度に認められた腎障害の有害事象はなかった。高度と判定された腎障害の有害事象は認められなかった。

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の R788 投与期において、腎障害の有害事象は 6.2%（9/146 例）、副作用は 0.7%（1/146 例）認められた。高頻度に認められた腎障害の有害事象は腎結石症 2.7%（4/146 例）及び頻尿 1.4%（2/146 例）であった。高度と判定された腎障害の有害事象は腎結石症 1.4%（2/146 例）及び慢性腎臓病 0.7%（1/146 例）であった。

海外第 III 相臨床試験（C788-047 及び C788-048）のプラセボ対照期において、腎障害の有害事象は R788 群で 3.9%（4/102 例）及びプラセボ群で 2.1%（1/48 例）、副作用は R788 群で 1.0%（1/102 例）であり、プラセボ群では認められなかった。高頻度に認められた腎障害の有害事象はなかった。高度と判定された腎障害の有害事象は R788 群の腎結石症 1.0%（1/102 例）であった。

2.7.4.2.1.5.2.5 皮膚および皮下組織障害

皮膚および皮下組織障害について要約した。

国内第 III 相臨床試験（R788-1301）の R788 投与期において、皮膚および皮下組織障害の有害事象は 42.4%（14/33 例）、副作用は 3.0%（1/33 例）認められた。高頻度に認められた皮膚お

よび皮下組織障害の有害事象は湿疹 15.2%（5/33 例）、紅斑、皮下出血、そう痒症及び発疹各 6.1%（2/33 例）であった。高度と判定された皮膚および皮下組織障害の有害事象は認められなかった。

R788-1301 試験のプラセボ対照期において、皮膚および皮下組織障害の有害事象は R788 群で 18.2%（4/22 例）及びプラセボ群で 8.3%（1/12 例）、副作用は R788 群で 4.5%（1/22 例）であり、プラセボ群では認められなかった。高頻度に認められた皮膚および皮下組織障害の有害事象は湿疹（R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例）（以下同順））及びそう痒症（9.1%（2/22 例）及び 0.0%（0/12 例））であった。高度と判定された皮膚および皮下組織障害の有害事象は認められなかった。

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）の R788 投与期において、皮膚および皮下組織障害の有害事象は 30.8%（45/146 例）、副作用は 8.9%（13/146 例）認められた。高頻度に認められた皮膚および皮下組織障害の有害事象は点状出血 15.1%（22/146 例）、発疹 6.8%（10/146 例）、斑状出血 2.7%（4/146 例）、血性水疱、そう痒症及び皮膚病変各 2.1%（3/146 例）であった。高度と判定された皮膚および皮下組織障害の有害事象は点状出血 1.4%（2/146 例）、紫斑 0.7%（1/146 例）及び前癌性皮膚病変 0.7%（1/146 例）であった。

海外第 III 相臨床試験（C788-047 及び C788-048）のプラセボ対照期において、皮膚および皮下組織障害の有害事象は R788 群で 17.6%（18/102 例）及びプラセボ群で 10.4%（5/48 例）、副作用は R788 群で 7.8%（8/102 例）及びプラセボ群で 2.1%（1/48 例）認められた。高頻度に認められた皮膚および皮下組織障害の有害事象は発疹（R788 群 7.8%（8/102 例）及びプラセボ群 2.1%（1/48 例）（以下同順））及び点状出血（3.9%（4/102 例）及び 6.3%（3/48 例））であった。高度と判定された皮膚および皮下組織障害の有害事象は認められなかった。

2.7.4.2.1.5.2.6 眼障害

眼障害について要約した。

国内第 III 相臨床試験（R788-1301 試験）及び海外第 III 相臨床試験（C788-047、C788-048 及び C788-049 試験）で認められた SOC「眼障害」に該当した有害時事象について、重症度別の有害事象及び副作用を表 2.7.4.9-116～表 2.7.4.9-122 に、発現時期別の有害事象を表 2.7.4.9-123 及び表 2.7.4.9-124 に示した。R788-1301 試験では、本薬を投与後に認められた眼関連の有害事象は、いずれも軽度又は中等度の事象であり、重度の事象は認められなかった。海外第 III 相臨床試験では、R788 の投与後に重度の有害事象が 1 例認められているものの、治験薬との因果関係は否定されており、治験薬の用量を変更せず投与継続できている。副作用はいずれも軽度又は中等度の事象であり、重度の事象は認められていない。

さらに、例数が限られているものの、本薬を長期投与した場合に発現割合が顕著に増加した有害事象は認められておらず、本薬の長期投与により、眼障害に関する有害事象の発現リスクが上昇する傾向は認められなかった。

2.7.4.2.2 個別有害事象の文章による説明

死亡、その他の重篤な有害事象及び重要な有害事象の詳細は、各添付資料（治験総括報告書）に記載した。

2.7.4.3 臨床検査値の評価

ITP 患者を対象とした国内及び海外の臨床試験で変動が認められた臨床検査項目は、好中球数、ヘモグロビン、ALT、AST、ビリルビン、アルカリホスファターゼ（ALP）及び乳酸脱水素酵素（LDH）であった。各項目の詳細を以下の項に示す。

2.7.4.3.1 血液学的検査

国内及び海外第 III 相臨床試験のプラセボ対照期における血液学的検査の要約統計量を国内第 III 相臨床試験は表 2.7.4.9-44 に、海外第 III 相臨床試験（C788-047 及び C788-048）は表 2.7.4.9-45 にそれぞれ示す。

2.7.4.3.1.1 好中球数

国内及び海外第 III 相臨床試験の試験期間中に最小値となった好中球数の分布を国内第 III 相臨床試験（R788-1301）は表 2.7.4.3.1.1-1 に、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）は表 2.7.4.3.1.1-2 にそれぞれ示す。

1) 国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期における好中球数のベースラインからの変化量の中央値は、R788 群−1.42～−0.99×10^9/L 及びプラセボ群−1.08～0.18×10^9/L であった。

R788-1301 試験のプラセボ対照期中、多くの被験者（R788 群 50.0%及びプラセボ群 100.0%）が好中球数 1.5×10^9/L 以上を維持した。好中球数が 0.5×10^9/L 以上 1.0×10^9/L 未満まで減少した被験者は、R788 群 13.6%（3/22 例）及びプラセボ群 0.0%（0/11 例）であった。好中球数が 0.5×10^9/L 未満に減少した被験者は、R788 群 4.5%（1/22 例）及びプラセボ群 0.0%（0/11 例）であった。

R788-1301 試験の R788 長期投与時中、多くの被験者（45.5%）が好中球数 1.5×10^9/L 以上を維持した。好中球数 0.5×10^9/L 以上 1.0×10^9/L 未満となった被験者は 22.7%（5/22 例）であり、1.0×10^9/L 以上 1.5×10^9/L 未満となった被験者は 27.3%（6/22 例）であった。好中球数が 0.5×10^9/L 未満に減少した被験者は 4.5%（1/22 例）であった。

表 2.7.4.3.1.1-1 治験薬投与開始後の好中球数の最小値 – 国内第 III 相臨床試験（R788-1301）

Minimum Postbaseline Value	プラセボ対照期		R788 長期投与時
	R788 N = 22 n (%)	Placebo N=12 n (%)	R788 N=22 n (%)
< 0.5×10^9/L	1 (4.5)	0 (0.0)	1 (4.5)
≥ 0.5 to < 1×10^9/L	3 (13.6)	0 (0.0)	5 (22.7)
≥ 1 to < 1.5×10^9/L	7 (31.8)	0 (0.0)	6 (27.3)
≥ 1.5×10^9/L	11 (50.0)	12 (100.0)	10 (45.5)

(Source : 5.3.5.1.1, Table 14.1.4.4.5, Table 14.2.4.4.5 改編)

2) 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験を統合したプラセボ対照期における好中球数のベースラインからの変化量の中央値は、R788 群−1.810～−1.000×10^9/L 及びプラセボ群−0.640～1.300×10^9/L であった。

C788-047 及び C788-048 試験を統合したプラセボ対照期中、ほとんどの被験者（R788 群

91.0%及びプラセボ群 97.9%）が好中球数 1.5×10^9/L 以上を維持した。好中球数が 0.5×10^9/L 以上 1.0×10^9/L 未満まで減少した被験者は、R788 群で 2.0%（2/100 例）認められ、プラセボ群では認められなかった。C788-047、C788-048 及び C788-049 試験を統合した R788 投与期中、ほとんどの被験者（86.6%）が好中球数 1.5×10^9/L 以上を維持した。好中球数 0.5×10^9/L 以上 1.0×10^9/L 未満となった被験者は 3.5%（5/142 例）であり、1.0×10^9/L 以上 1.5×10^9/L 未満となった被験者は 9.9%（14/142 例）であった。好中球が 0.5×10^9/L 未満に減少した被験者はいなかった。

表 2.7.4.3.1.1-2　治験薬投与開始後の好中球数の最小値 – 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

Minimum Postbaseline Value	Placebo-Controlled Period (C788-047 and C788-048)		Fostamatinib Exposure Period
	R788 N = 100 [a] n (%)	Placebo N=48 [a] n (%)	R788 N=142 [a] n (%)
< 0.5 ×10^9/L	0 (0.0)	0 (0.0)	0 (0.0)
≥ 0.5 to < 1 ×10^9/L	2 (2.0)	0 (0.0)	5 (3.5)
≥ 1 to < 1.5 ×10^9/L	7 (7.0)	1 (2.1)	14 (9.9)
≥ 1.5 ×10^9/L	91 (91.0)	47 (97.9)	123 (86.6)

a　Subjects with a neutrophil measurement at baseline and at least 1 post-baseline neutrophil measurement.
（Source: 5.3.5.3.2, Table 5.2.1, Table 5.2.2 改編）

以上より、海外第 III 相臨床試験と比較して R788-1301 試験では、好中球数が 0.5×10^9/L 以上 1.0×10^9/L 未満、又は 0.5×10^9/L 未満となる被験者の割合が高かったが、好中球数の変化量に大きな違いは認められなかった。

2.7.4.3.1.2 ヘモグロビン

1)　国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期におけるヘモグロビンのベースラインからの変化量の中央値は、R788 群−9～3 g/L 及びプラセボ群−8～1 g/L であった。

2)　海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験のプラセボ対照期における 20 週時までのヘモグロビンのベースラインからの変化量の中央値は、R788 群−6.0～3.0 g/L 及びプラセボ群 0.0～11.5 g/L であり、R788 群でわずかに減少したが、プラセボ群ではベースライン値を下回らなかった。R788 群に認められたヘモグロビン減少に伴う出血事象の増加は認められなかった。

以上より、R788-1301 試験と海外第 III 相臨床試験のヘモグロビンの推移に大きな違いは認められなかった。

2.7.4.3.2 血液生化学的検査

国内第 III 相臨床試験（R788-1301）における肝機能検査の要約統計量を表 2.7.4.9-44 に、頻度分布を表 2.7.4.9-46、表 2.7.4.9-47 及び表 2.7.4.9-127 にそれぞれ示す。

また、海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）における肝機能検査の要約統計量を表 2.7.4.9-48 に、頻度分布を表 2.7.4.9-49 及び表 2.7.4.9-50 にそれぞれ示す。

2.7.4.3.2.1 ALT 及び AST

1) 国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期における ALT のベースラインからの変化量の中央値は R788 群 5～14 U/L 及びプラセボ群−5～2 U/L であり、AST のベースラインからの変化量の中央値は R788 群 6～12 U/L 及びプラセボ群−2～2 U/L であった。

R788-1301 試験のプラセボ対照期中、ALT が基準値上限の 3 倍を超えた被験者は R788 群 18.2%（4/22 例）及びプラセボ群 0.0%（0/12 例）、5 倍を超えた被験者は R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例）であり、5 倍を超えた被験者のうち 1 例は基準値上限の 10 倍を超えた。AST が基準値上限の 3 倍を超えた被験者は R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例）であり、このうち 1 例は基準値上限の 5 倍を超えた。

R788-1301 試験の R788 長期投与時中、ALT が基準値上限の 3 倍を超えた被験者は 13.6%（3/22 例）、5 倍を超えた被験者は 9.1%（2/22 例）であり、5 倍を超えた被験者のうち 1 例は基準値上限の 10 倍を超えた。AST が基準値上限の 3 倍を超えた被験者は 9.1%（2/22 例）であり、このうち 1 例は基準値上限の 5 倍を超えた。なお、ALT が基準値上限の 3 倍を超えた 1 例は、第 I 期では医療機関で実施した 80 U/L（基準値：23 U/L 以下）が最大であったが、R788 長期投与時の評価では、第 II 期移行後に集中測定で実施した 88 U/L（基準値：45 U/L 以下）が最大となったことから、基準値上限の 3 倍を超えた被験者から外れている。

R788-1301 試験の R788 投与期中、ALT が基準値上限の 3 倍を超えた被験者は 12.1%（4/33 例）、5 倍を超えた被験者は 9.1%（3/33 例）であり、5 倍を超えた被験者のうち 2 例は基準値上限の 10 倍を超えた。AST が基準値上限の 3 倍を超えた被験者は 12.1%（4/33 例）、5 倍を超えた被験者は 6.1%（2/33 例）であり、5 倍を超えた被験者のうち 1 例は基準値上限の 10 倍を超えた。

基準値上限の 5 倍を超える ALT 及び/又は AST 増加を認めた 3 例の要約を以下に示した。

– 被験者 [redacted] は、ALT が基準値上限の 5 倍を超えた。Week 4 に ALT は 164 U/L（実施医療機関の測定では 183 U/L）に増加し、治験薬を休薬した。治験薬の休薬により、3 週間後に基準値の範囲内に回復し、治験薬の投与を再開した。その後、再度 ALT が増加し、173 U/L（実施医療機関の測定では 175 U/L）まで増加したことから治験薬の投与を中止した。治験薬の投与中止後 3 週間で ALT は 52 U/L（実施医療機関の測定では 48 U/L）まで減少した。

– 被験者 [redacted] は、ALT 及び AST が基準値上限の 10 倍を超えた。第 II 期 Week 24 と Week 28 の間の規定外来院で ALT 及び AST が 157 及び 134 U/L（基準値上限の 5 倍超）となり休薬基準に合致したが、血小板数の急激な減少や出血のリスクを考慮し治験薬の休薬や減量は行わず投与を継続した。その後、第 II 期 Week 28 までに ALT 及び AST は最大で 453 及び 315 U/L となった（基準値上限の 10 倍超）。第 II 期 Week 28 の ALT 及び AST（集中測定）は 296 及び 146 U/L であり、その後休薬期へ移行した。休薬期移行後、血小板数の低下に対する救済薬及び肝機能障害に対する治療としてプレドニン 20 mg/日を開始した。休薬期 Week 2 の 4 日後の規定外来院で ALT 及び AST は 29 及び 15 U/L まで回復し治験薬の再開基準を満たしたため第 III 期として治験薬の投与を再開した。

  当該肝機能検査値の上昇は自己免疫性肝炎と診断された。治験薬の投与開始 5 ヵ月後以降

に発現しており治験薬投与との時間的な相関は認められないこと、またプレドニンの減量や蜂窩織炎に対して複数の薬剤を投与したことが自己免疫性肝炎の発症に関連した可能性が考えられることから因果関係はないと治験責任医師により判断された。
また、第 III 期移行 1 ヵ月後の規定外来院時検査にて院内検査の ALT が 95 U/L（基準値上限の 3 倍超）であり肝機能検査値上昇と診断された。急激な上昇は認められず、自己免疫性肝炎の再燃ではないことから因果関係は有と判断されたが、翌月の院内検査で ALT 及び AST は基準値内に回復し有害事象は回復と判断された。

– 被験者 [redacted] は、ALT が基準値上限の 10 倍を超えており、AST が基準値上限の 5 倍を超えていた。Week 6 に ALT 及び AST はそれぞれ 626 及び 350 U/L に増加し、治験薬を休薬した。治験薬の休薬から 10 日後に ALT 及び AST はそれぞれ 53 及び 24 U/L まで減少したが、肝機能低下に伴う血小板低下の重篤な有害事象を認めたため、治験薬の投与を再開せずに中止した。治験薬の投与中止により ALT 及び AST は基準値の範囲内に回復した。

R788-1301 試験のプラセボ対照期及び R788 長期投与時のいずれの時点においても、薬剤性肝障害に関する Hy's Law の基準（ALT 又は AST が基準値上限の 3 倍超、総ビリルビンが基準値上限の 2 倍超、並びに ALP が基準値上限の 2 倍未満であり、他の肝毒性の原因がない）に該当する被験者は認められなかった。

2) 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験において、プラセボ群と比較して R788 群で ALT 及び AST の増加傾向が認められた。C788-047 及び C788-048 試験を統合したプラセボ対照期における ALT のベースラインからの変化量の中央値は R788 群 1.0～7.0 U/L 及びプラセボ群−1.0～7.0 U/L であり、AST のベースラインからの変化量の中央値は R788 群 2.0～7.0 U/L 及びプラセボ群−1.0～4.0 U/L であった。

海外第 III 相臨床試験のプラセボ対照期及び R788 投与期のいずれの時点においても、薬剤性肝障害に関する Hy's Law の基準に該当する被験者は認められなかった。プラセボ対照期及び R788 投与期のいずれにおいても、トランスアミナーゼ増加と同時にビリルビンが 2 倍に増加した被験者は認められなかった。R788 投与期の 1 例（被験者 [redacted]）では、基準値上限の 3 倍を超える ALT 増加及び基準値上限の 2 倍を超える総ビリルビン増加を認めたが、同時に増加することはなかった。

C788-047 及び C788-048 試験を統合したプラセボ対照期中、ALT が基準値上限の 3 倍を超えた被験者は R788 群 8.8%（9/102 例）、基準値上限の 5 倍を超えた被験者は 5.9%（6/102 例）、基準値上限の 10 倍を超えた被験者は 1.0%（1/102 例）であった。ALT が基準値上限の 3 倍を超えた 9 例のうち 2 例（2.0%）は AST が基準値上限の 3 倍を超えており、1 例（1.0%）は AST が基準値上限の 5 倍を超えていた。プラセボ群では ALT 又は AST が基準値上限の 3 倍を超えた被験者は認められなかった。

基準値上限の 5 倍を超える ALT 及び/又は AST 増加を認めた 6 例の要約を以下に示した。

– Week 6～12 に 4 例（被験者 [redacted]、[redacted]、[redacted] 及び [redacted]）で ALT 増加が認められ、各被験者の ALT の最大値は 194～292 U/L であった。治験薬の休薬

又は減量後の約 1～2 週以内に ALT は低下した。

- 被験者 [redacted] は、Week 6 に基準値上限の 5 倍以上の ALT 増加（178 U/L）が認められ、治験薬の投与を中止した。治験薬の投与中止後 1 ヵ月以内に ALT は基準値の範囲内（30 U/L 未満）に回復した。肝毒性に対するその他の原因は特定されなかった。
- 被験者 [redacted] は、ALT が基準値上限の 10 倍以上であり、AST が基準値上限の 5 倍超であった。Week 6 に ALT 及び AST はそれぞれ 102 及び 72 U/L に増加し、それぞれ最大で 374 及び 255 U/L まで増加した。治験薬の休薬後、AST は Week 8 までに（28 IU/L）、ALT は Week 10 までに（28 U/L）基準値の範囲内に回復した。治験薬は減量して再開しており、ALT は Week 12（35 U/L）及び C788-049 試験の投与後 2 ヵ月にわずかに増加（38 U/L）した。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期中、ALT 値が基準値上限の 3 倍を超えた被験者は 11.8%（17/144 例）であり、基準値上限の 5 倍を超えた被験者は 6.9%（10/144 例）であった。ALT 値が基準値上限の 3 倍を超えた 17 例のうち 2 例（1.4%）は ALT 及び AST の最大値が基準値上限の 10 倍を超えており、1 例（0.7%）は ALT 及び AST の最大値が基準値上限の 20 倍超であった（当該被験者は胆石に起因する肝酵素上昇の有害事象が認められた）。AST の最大値が基準値上限の 3 倍を超えた被験者は 4.2%（6/144 例）であり、基準値上限の 5 倍を超えた被験者は 1.4%（2/144 例）であった。

R788 投与期のみで基準値上限の 5 倍を超える ALT 及び/又は AST 増加を認めた 4 例の要約を以下に示した。

- 被験者 [redacted] は、投与後 24 ヵ月に基準値上限の 5 倍を超える ALT 増加（169 U/L）を認めた。本事象はトランスアミナーゼ上昇の高度 SAE として報告され、治験薬を休薬した。2.5 ヵ月後の規定外来院時に ALT は基準値上限の 3 倍未満となり、その後回復した。
- 被験者 [redacted] は、投与後 26 ヵ月の来院から 10 日後の規定外来院時に基準値上限の 5 倍を超える ALT 増加（297 U/L）を認めた。本事象は肝酵素上昇の有害事象として報告され、治験薬を休薬した。ALT 増加は約 3 ヵ月間継続し、治験薬の投与を中止した（中止時の ALT は 158 U/L）。治験薬の投与中止後 2 週間で ALT は基準値上限の 3 倍未満に回復した。
- 被験者 [redacted] は、投与後 9 ヵ月の来院から 8 日後の規定外来院時に基準値上限の 5 倍を超える ALT 増加（235 U/L）を認めた。本事象は肝酵素上昇の有害事象として報告され、治験薬を減量した。ALT 増加は継続し、約 6 ヵ月後に ALT が 167 U/L に達した。本事象は 2 回目の肝酵素上昇の有害事象として報告され、治験薬の投与を中止した。治験薬の投与中止後 1 ヵ月以内に ALT が 49 U/L となり、基準値値上限（44 U/L）に近い値まで回復した。
- 被験者 [redacted] は、投与後 4 ヵ月に基準値上限の 5 倍を超える ALT 増加（805 U/L）及び AST 増加（849 U/L）を認めた。本事象は肝酵素上昇の有害事象として報告され、治験薬を減量した。治験薬の減量後 2.5 週間以内に ALT 及び AST は基準値の範囲内に回復した。

以上より、R788-1301 試験と海外第 III 相臨床試験の ALT 及び AST の推移に大きな違いは認

められなかった

2.7.4.3.2.2 ビリルビン

1) 国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期における総ビリルビンのベースラインからの変化量の中央値は、R788 群 1.71～3.42 μmol/L 及びプラセボ群−0.86～0.86 μmol/L であった。

R788-1301 試験のプラセボ対照期及び R788 長期投与時中に総ビリルビンが基準値上限の 2 倍を超えた被験者は認められておらず、R788 投与期中にビリルビンが基準値上限の 2 倍を超えた被験者は 6.1%（2/33 例）であり、非抱合（間接）ビリルビンが基準値上限の 2 倍を超えた被験者は 3.0%（1/33 例）であった。AST 及び ALT の上昇を伴わない総ビリルビン又は間接ビリルビン単独の上昇は認められなかった。

2) 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験において、プラセボ群と比較して R788 群で総ビリルビンの増加傾向が認められた。C788-047 及び C788-048 試験を統合したプラセボ対照期における総ビリルビンのベースラインからの変化量の中央値は、R788 群−0.855～3.000 μmol/L 及びプラセボ群−1.710～0.000 μmol/L であった。総ビリルビン値の中央値は、R788 群で Week 2 から Week 24 までベースラインを上回る増加を示した。

C788-047 及び C788-048 試験を統合したプラセボ対照期中、総ビリルビンが基準値上限の 2 倍を超えた被験者は R788 群 1/102 例（1.0%）であり、プラセボ群では認められなかった。当該被験者（被験者 [redacted]）のビリルビン増加はいずれも間接ビリルビンの増加によるものであり、ALT 及び AST の増加は伴わなかった。

C788-047、C788-048 及び C788-049 試験を統合した R788 投与期中、総ビリルビンが基準値上限の 2 倍を超えた被験者は 3/144 例（2.1%）であった。このうち 2 例（被験者 [redacted] 及び [redacted]）は、主に間接ビリルビンの増加によるものであり、ALT 及び AST の増加は伴わなかった。1 例（被験者 [redacted]）は、主に間接ビリルビンの増加によるものであり、基準値上限の 2 倍を超える ALT 増加も認められたが、ALT 増加はビリルビンの変化と同時には認められなかった。当該被験者のビリルビン増加は有害事象として報告されなかった。

以上より、R788-1301 試験と海外第 III 相臨床試験のビリルビンの推移に大きな違いは認められなかった。

2.7.4.3.2.3 アルカリホスファターゼ（ALP）

1) 国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期における ALP のベースラインからの変化量の中央値は、R788 群 33～52 U/L 及びプラセボ群−14～11 U/L であった。

R788-1301 試験のプラセボ対照期中、ALP が基準値上限の 1.5 倍を超えた被験者は R788 群 1/22 例（4.5%）及びプラセボ群 0/12 例（0.0%）であり、R788 投与期中に ALP が基準値上限の 1.5 倍を超えた被験者は 9.1%（3/33 例）であった。

2) 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験において、プラセボ群と比較して R788 群で ALP の増加傾向が認められた。C788-047 及び C788-048 試験を統合したプラセボ対照期における ALP のベースラインからの変化量の中央値は、R788 群−4.0～13.0 U/L 及びプラセボ群−5.0～9.0 U/L であった。

C788-047 及び C788-048 試験を統合したプラセボ対照期間中、ALP が基準値上限の 1.5 倍を超えた被験者は R788 群 4/102 例（3.9%）であり、プラセボ群では認められなかった。

以上より、R788-1301 試験と海外第 III 相臨床試験の ALP の推移に大きな違いは認められなかった。

2.7.4.3.2.4 乳酸脱水素酵素（LDH）

1) 国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期における LDH のベースラインからの変化量の中央値は、R788 群 33～61 U/L 及びプラセボ群−11～6 U/L であった。

2) 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験において、プラセボ群と比較して R788 群で LDH の増加傾向が認められた。C788-047 及び C788-048 試験を統合したプラセボ対照期における LDH のベースラインからの変化量の中央値は、R788 群 5.0～25.0 U/L 及びプラセボ群−4.0～20.0 U/L であった。

以上より、R788-1301 試験と海外第 III 相臨床試験の LDH の推移に大きな違いは認められなかった。

2.7.4.3.3 尿検査

ITP 患者を対象とした国内及び海外の臨床試験において、臨床的に問題となる変動は認められなかった。

2.7.4.4 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

2.7.4.4.1 バイタルサイン

2.7.4.4.1.1 国内第 III 相臨床試験（R788-1301）

1) グレード別の血圧変化

R788 長期投与時における血圧データの要約統計量、治験薬の投与後最大値の頻度集計及び上昇頻度の頻度集計をそれぞれ表 2.7.4.9-51、表 2.7.4.4.1.1-1 及び表 2.7.4.9-53 に示す。また、プラセボ対照期における血圧データの要約統計量、治験薬の投与後最大値の頻度集計及び上昇頻度の頻度集計を表 2.7.4.9-52、表 2.7.4.4.1.1-2 及び表 2.7.4.9-54 に示す。

R788 長期投与時において、収縮期血圧（SBP）及び拡張期血圧（DBP）の上昇傾向を示した。SBP が 120 mmHg 以上 140 mmHg 未満となった被験者は 31.8%（7/22 例）、140 mmHg 以上 160 mmHg 未満となった被験者は 50.0%（11/22 例）、160 mmHg 以上 180 mmHg 未満となった被験者は 13.6%（3/22 例）であった。180 mmHg 以上となった被験者は認められなかった。また、DBP が 80 mmHg 以上 90 mmHg 未満となった被験者は 54.5%（12/22 例）、90 mmHg 以上 100 mmHg 未満となった被験者は 27.3%（6/22 例）、100 mmHg 以上 110 mmHg 未満となった被

験者は 4.5%（1/22 例）であった。110 mmHg 以上となった被験者は認められなかった。SBP 140 mmHg以上又はDBP 90 mmHg以上の血圧上昇を認めた被験者は63.6%（14/22例）であり、2 回以上の来院で認めた被験者は 45.5%（10/22 例）であり、3 回以上の来院で認めた被験者は 40.9%（9/22 例）であった。また、SBP 160 mmHg 以上又は DBP 100 mmHg 以上の血圧上昇を認めた被験者は 9.1%（2/22 例）であった。2 回以上の来院で認めた被験者は認められなかった。

プラセボ対照期中、SBP が 120 mmHg 以上 140 mmHg 未満となった被験者は R788 群 31.8%（7/22 例）及びプラセボ群 66.7%（8/12 例）、140 mmHg 以上 160 mmHg 未満となった被験者は R788 群 54.5%（12/22 例）及びプラセボ群 25.0%（3/12 例）、160 mmHg 以上 180 mmHg 未満となった被験者は R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例）であった。160 mmHg 以上となった被験者は、R788 群及びプラセボ群のいずれにおいても認められなかった。また、DBP が 80 mmHg 以上 90 mmHg 未満となった被験者は R788 群 54.5%（12/22 例）及びプラセボ群 25.0%（3/12 例）、90 mmHg 以上 100 mmHg 未満となった被験者は R788 群 27.3%（6/22 例）及びプラセボ群 25.0%（3/12 例）であった。100 mmHg 以上となった被験者は、R788 群及びプラセボ群のいずれにもいても認められなかった。SBP 140 mmHg 以上又は DBP 90 mmHg 以上の血圧の上昇を認めた被験者は、R788 群 63.6%（14/22 例）及びプラセボ群 33.3%（4/12 例）であり、2 回以上の来院で認めた被験者は R788 群 45.5%（10/22 例）及びプラセボ群 25.0%（3/12 例）であり、3 回以上の来院で認めた被験者は R788 群 36.4%（8/22 例）及びプラセボ群 16.7%（2/12 例）であった。また、SBP 160 mmHg 以上又は DBP 100 mmHg 以上の血圧上昇を認めた被験者は、R788 群 9.1%（2/22 例）及びプラセボ群 0.0%（0/12 例）であった。2 回以上の来院で認めた被験者は、R788 群及びプラセボ群のいずれにおいても認められなかった。

表 2.7.4.4.1.1-1　収縮期血圧及び拡張期血圧の治験薬投与後最大値の頻度集計（R788-1301 試験 R788 長期投与時）

Long-Term Treatment of R788
Parameter: Systolic Blood Pressure (mmHg)

		Maximum Post Day 1									
		<120		120≤, <140		140≤, <160		160≤, <180		≥180	
Group	N	n	%	n	%	n	%	n	%	n	%
R788	22	1	4.5	7	31.8	11	50.0	3	13.6	0	0.0

Parameter: Diastolic Blood Pressure (mmHg)

		Maximum Post Day 1									
		<80		80≤, <90		90≤, <100		100≤, <110		≥110	
Group	N	n	%	n	%	n	%	n	%	n	%
R788	22	3	13.6	12	54.5	6	27.3	1	4.5	0	0.0

(Source : 5.3.5.1.1, Table 14.2.4.6.3)

表 2.7.4.4.1.1-2　収縮期血圧及び拡張期血圧の治験薬投与後最大値の頻度集計（R788-1301 試験 プラセボ対照期）

Period I
Parameter: Systolic Blood Pressure (mmHg)

		Maximum Post Day 1									
		<120		120≤, <140		140≤, <160		160≤, <180		≥180	
Group	N	n	%	n	%	n	%	n	%	n	%
R788	22	1	4.5	7	31.8	12	54.5	2	9.1	0	0.0
Placebo	12	1	8.3	8	66.7	3	25.0	0	0.0	0	0.0

Parameter: Diastolic Blood Pressure (mmHg)

		Maximum Post Day 1									
		<80		80≤, <90		90≤, <100		100≤, <110		≥110	
Group	N	n	%	n	%	n	%	n	%	n	%
R788	22	4	18.2	12	54.5	6	27.3	0	0.0	0	0.0
Placebo	12	6	50.0	3	25.0	3	25.0	0	0.0	0	0.0

(Source : 5.3.5.1.1, Table 14.1.4.6.3)

2.7.4.4.1.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

1)　グレード別の血圧変化

R788 投与期における血圧データの要約統計量及びシフトテーブルを表 2.7.4.9-55 及び表 2.7.4.4.1.2-1 に、プラセボ対照期における血圧データの要約統計量及びシフトテーブルを表 2.7.4.9-56 及び表 2.7.4.4.1.2-2 に示す。また、R788 投与期における連続した来院時の血圧上昇発現を表 2.7.4.9-57 に、プラセボ対照期における連続した来院時の血圧上昇発現を表 2.7.4.9-58 に示す。

R788 投与期中、41.8%（61/146 例）はベースライン時の状態を保持していた。血圧の 1 レベル上昇は 43.8%（64/146 例）、2 レベル上昇は 10.3%（15/146 例）、3 レベル上昇は 2.7%（4/146 例）及び 4 レベル上昇は 0.7%（1/146 例）認められた。ベースライン後の最高血圧で 140/90 mmHg 以上（SBP 又は DBP のいずれかの上昇）が認められたのは、41.1%（60/146 例）であった。ベースライン後の最高血圧が 160/100 mmHg から 180/110 mmHg 未満であったのは 91.8%（134/146 例）であり、ベースライン後の最高血圧が 180/110 mmHg 以上であったのは 2.1%（3/146 例）であった。血圧上昇 140/90 mmHg 以上が 2 回以上の来院で持続した被験者は 14.1%（19/135 例）、血圧上昇 160/100 mmHg 以上が 2 回以上の来院で持続した被験者は 0.7%（1/137 例）、血圧上昇 140/90 mmHg 以上が 3 回以上の来院で持続した被験者は 5.4%（7/129 例）であった。血圧上昇 180/110 mmHg 以上が 2 回以上の来院で持続した被験者は認められなかった。

プラセボ対照期中、R788 群の 44.1%（45/102 例）及びプラセボ群の 58.3%（28/48 例）はベースラインの状態を保持していた。血圧の 1 レベル上昇は R788 群で 44.1%（45/102 例）及びプラセボ群で 37.5%（18/48 例）、2 レベル上昇は R788 群で 8.8%（9/102 例）及びプラセボ群で 2.1%（1/48 例）、3 レベル上昇は R788 群で 2.9%（3/102 例）及びプラセボ群で 0%であり、4 レベル上昇はいずれの群でも認められなかった。ベースライン後の最高血圧で 140/90 mmHg 以上（SBP 又は DBP のいずれかの上昇）が認められたのは、R788 群で 34.3%（35/102 例）及びプラセボ群で 14.6%（7/48 例）であった。ベースライン後の最高血圧が 160/100 mmHg から 180/110 mmHg 未満であったのは R788 群で 91.2%（93/102 例）及びプラセボ群で 100%（48/48 例）であり、ベースライン後の最高血圧が 180/110 mmHg 以上であったのは R788 群で 1.0%（1/102 例）及びプラセボ群で 0%であった。血圧上昇 140/90 mmHg 以上が 2 回以上の来院で持

続した被験者は R788 群で 15.0%（15/100 例）及びプラセボ群で 0%、血圧上昇 140/90 mmHg 以上が 3 回以上の来院で持続した被験者は R788 群で 7.1%（7/99 例）及びプラセボ群で 0%であった。血圧上昇 160/100 mmHg 以上及び血圧上昇 180/110 mmHg 以上が 2 回以上の来院で持続した被験者は認められなかった。

表 2.7.4.4.1.2-1 ベースライン血圧対ベースライン後の最高血圧のシフトテーブル（C788-047、C788-048 及び C788-049 試験 R788 投与期）

Treatment Group	Baseline Blood Pressure (mmHg)	Maximum Post-Baseline Blood Pressure (mmHg)				
		SBP < 120 and DBP < 80 n (%)	SBP >= 120 and/or DBP >= 80 n (%)	SBP>= 140 and/or DBP >= 90 n (%)	SBP>= 160 and/or DBP >= 100 n (%)	SBP>= 180 and/or DBP >= 110 n (%)
R788						
	SBP< 120 and DBP < 80	3 (2.1%)	26 (17.8%)	9 (6.2%)	2 (1.4%)	1 (0.7%)
	SBP>= 120 and/or DBP >= 80	0 (0.0%)	57 (39.0%)	37 (25.3%)	6 (4.1%)	2 (1.4%)
	SBP>= 140 and/or DBP >= 90	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)
	SBP>= 160 and/or DBP >= 100	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)
	SBP>= 180 and/or DBP >= 110	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: The baseline value is the last measurement for the given vital sign prior to the first dose of fostamatinib. For systolic blood pressure and/or diastolic blood pressure, each blood pressure assessment was categorized into one category according to the higher of the levels reached by systolic blood pressure and diastolic blood pressure.
Percentages are based on the number of subjects with non-missing data at the given visit.
（Source: 5.3.5.3.2, Table 6.2.2）

表 2.7.4.4.1.2-2 ベースライン血圧対ベースライン後の最高血圧のシフトテーブル（C788-047 及び C788-048 試験プラセボ対照期）

Treatment Group	Baseline Blood Pressure (mmHg)	Maximum Post-Baseline Blood Pressure (mmHg)				
		SBP < 120 and DBP < 80 n (%)	SBP >= 120 and/or DBP >= 80 n (%)	SBP>= 140 and/or DBP >= 90 n (%)	SBP>= 160 and/or DBP >= 100 n (%)	SBP>= 180 and/or DBP >= 110 n (%)
R788						
	SBP< 120 and DBP < 80	0 (0.0%)	23 (22.5%)	4 (3.9%)	2 (2.0%)	0 (0.0%)
	SBP>= 120 and/or DBP >= 80	0 (0.0%)	44 (43.1%)	21 (20.6%)	5 (4.9%)	1 (1.0%)
	SBP>= 140 and/or DBP >= 90	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)	0 (0.0%)
	SBP>= 160 and/or DBP >= 100	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SBP>= 180 and/or DBP >= 110	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Placebo						
	SBP< 120 and DBP < 80	4 (8.3%)	12 (25.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)
	SBP>= 120 and/or DBP >= 80	1 (2.1%)	24 (50.0%)	6 (12.5%)	0 (0.0%)	0 (0.0%)
	SBP>= 140 and/or DBP >= 90	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SBP>= 160 and/or DBP >= 100	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	SBP>= 180 and/or DBP >= 110	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: The baseline value is the last measurement for the given vital sign prior to the first randomized dose. For systolic blood pressure and/or diastolic blood pressure, each blood pressure assessment was categorized into one category according to the higher of the levels reached by systolic blood pressure and diastolic blood pressure.

Percentages are based on the number of subjects with non-missing data at the given visit within each treatment group.
（Source: 5.3.5.3.2, Table 6.2.1）

2) ベースライン時の降圧薬使用による最高血圧の変化

R788 投与期におけるベースライン時の降圧薬使用別の最高 SBP 及び最高 DBP を表 2.7.4.4.1.2-3 及び表 2.7.4.4.1.2-4、プラセボ対照期におけるベースライン時の降圧薬使用別の最高 SBP 及び最高 DBP を表 2.7.4.4.1.2-5 及び表 2.7.4.4.1.2-6 に示す。

R788 投与期中、ベースライン時に降圧薬の投与を受けていた被験者は 36.3%（53/146 例）、ベースライン時に降圧薬の投与を受けていなかった被験者は 63.7%（93/146 例）であった。ベースライン後の最高 SBP 値 120 mmHg 未満、120 mmHg 以上 140 mmHg 未満、140 mmHg 以上 160 mmHg 未満、160 mmHg 以上 180 mmHg 未満及び 180 mmHg 以上の頻度は、ベースライン時に降圧薬の投与を受けていた被験者と降圧薬の投与を受けていなかった被験者で同程度であった。同様に、ベースライン後の最高 DBP 値 80 mmHg 未満、80 mmHg 以上 90 mmHg 未満、90 mmHg 以上 100 mmHg 未満、100 mmHg 以上 110 mmHg 未満及び 110 mmHg 以上の頻度は、ベースライン時に降圧薬の投与を受けていた被験者と降圧薬の投与を受けていなかった被験者で同程度であった。ベースライン時に降圧薬の投与を受けていなかった被験者でのみ、ベースライン後の最高血圧値（SBP 180 mmHg 以上又は DBP 110 mmHg 以上）が認められた。

プラセボ対照期中、ベースライン時に降圧薬の投与を受けていた被験者は、R788 群で 36.3%（37/102 例）及びプラセボ群で 33.3%（16/48 例）、ベースライン時に降圧薬の投与を受けていなかった被験者は、R788 群で 63.7%（65/102 例）及びプラセボ群で 66.7%（32/48 例）であった。R788 群及びプラセボ群において、ベースライン後の最高 SBP 値 120 mmHg 未満、120 mmHg 以上 140 mmHg 未満、140 mmHg 以上 160 mmHg 未満、160 mmHg 以上 180 mm Hg 未満及び 180 mmHg 以上の頻度は、ベースライン時に降圧薬の投与を受けていた被験者と降圧薬の投与を受けていなかった被験者で同程度であった。プラセボ群では、ベースライン時の降圧薬の投与の有無に関わらず、ベースライン後の最高 SBP 値 160 mmHg 以上の被験者は認められなかった。R788 群において、ベースライン後の最高 DBP 値 80 mmHg 未満、80 mmHg 以上 90 mmHg 未満、90 mmHg 以上 100 mmHg 未満、100 mmHg 以上 110 mmHg 未満及び 110 mmHg 以上の頻度は、ベースライン時に降圧薬の投与を受けていた被験者と降圧薬の投与を受けていなかった被験者で同程度であった。プラセボ群において、ベースライン後の最高 DBP 値 80 mmHg 未満、80 mmHg 以上 90 mmHg 未満、90 mmHg 以上 100 mmHg 未満、100 mmHg 以上 110 mmHg 未満及び 110 mmHg 以上の頻度は、ベースライン時に降圧薬の投与を受けていた被験者と降圧薬の投与を受けていなかった被験者でおおむね同程度であった。ベースライン時に降圧薬の投与を受けていなかった R788 群被験者でのみ、ベースライン後の最高 DBP 値 100 mmHg 以上 110 mmHg 未満が認められた（7.7%（5/65 例））。いずれの群でも、ベースライン後の最高 DBP 値 110 mmHg 以上の被験者は認められなかった。

表 2.7.4.4.1.2-3　ベースライン時の降圧薬使用別の最高 SBP（C788-047、C788-048 及び C788-049 試験 R788 投与期）

Treatment Group	Anti-hypertensive Medication Use at Baseline (1)	Number of Subjects N	Maximum Post-Baseline Systolic Blood Pressure (mmHg)				
			<120	>= 120 - < 140	>= 140 - < 160	>= 160 - < 180	>= 180
			n (%)	n (%)	n (%)	n (%)	n (%)
Fostamatinib	Yes	53	0 (0.0%)	33 (62.3%)	18 (34.0%)	2 (3.8%)	0 (0.0%)
	No	93	3 (3.2%)	62 (66.7%)	23 (24.7%)	3 (3.2%)	2 (2.2%)

Note: Percentages are based on N, the number of subjects in the anti-hypertensive medication use at baseline category in the Fostamatinib Treated Population: Fostamatinib Exposure Period with at least 1 post-baseline systolic blood pressure measurement.

(1) Subjects with anti-hypertensive medication use are those subjects receiving medications with the following ATC codes at baseline: C02 (anti-hypertensives), C03 (diuretics), C04 (peripheral vasodilators), C07 (beta blocking agents), C08 (calcium channel blockers), and C09 (agents acting on the rennin-angiotensin system).

（Source: 5.3.5.3.2, Table 6.3.1.2.3）

表 2.7.4.4.1.2-4　ベースライン時の降圧薬使用別の最高 DBP（C788-047、C788-048 及び C788-049 試験 R788 投与期）

Treatment Group	Anti-hypertensive Medication Use at Baseline (1)	Number of Subjects N	Maximum Post-Baseline Diastolic Blood Pressure (mmHg)				
			<80	>= 80 - < 90	>= 90 - < 100	>= 100 - < 110	>= 110
			n (%)	n (%)	n (%)	n (%)	n (%)
Fostamatinib	Yes	53	7 (13.2%)	36 (67.9%)	10 (18.9%)	0 (0.0%)	0 (0.0%)
	No	93	10 (10.8%)	57 (61.3%)	19 (20.4%)	6 (6.5%)	1 (1.1%)

Note: Percentages are based on N, the number of subjects in the anti-hypertensive medication use at baseline category in the Fostamatinib Treated Population: Fostamatinib Exposure Period with at least 1 post-baseline diastolic blood pressure measurement.

(1) Subjects with anti-hypertensive medication use are those subjects receiving medications with the following ATC codes at baseline: C02 (anti-hypertensives), C03 (diuretics), C04 (peripheral vasodilators), C07 (beta blocking agents), C08 (calcium channel blockers), and C09 (agents acting on the rennin-angiotensin system).

（Source: 5.3.5.3.2, Table 6.3.2.2.3）

表 2.7.4.4.1.2-5　ベースライン時の降圧薬使用別の最高 SBP（C788-047 及び C788-048 試験プラセボ対照期）

Treatment Group	Anti-hypertensive Medication Use at Baseline (1)	Number of Subjects N	Maximum Post-Baseline Systolic Blood Pressure (mmHg)				
			<120	>= 120 - < 140	>= 140 - < 160	>= 160 - < 180	>= 180 n (%)
			n (%)	n (%)	n (%)	n (%)	n (%)
Fostamatinib	Yes	37	0 (0.0%)	24 (64.9%)	11 (29.7%)	2 (5.4%)	0 (0.0%)
	No	65	4 (6.2%)	46 (70.8%)	12 (18.5%)	2 (3.1%)	1 (1.5%)
Placebo	Yes	16	0 (0.0%)	13 (81.3%)	3 (18.8%)	0 (0.0%)	0 (0.0%)
	No	32	5 (15.6%)	25 (78.1%)	2 (6.3%)	0 (0.0%)	0 (0.0%)

Note: For each treatment group, percentages are based on N, the number of such subjects in the anti-hypertensive medication use at baseline category in the Placebo-Controlled Safety Population: Placebo-Controlled Period with at least 1 post-baseline systolic blood pressure measurement.

(1) Subjects with anti-hypertensive medication use are those subjects receiving medications with the following ATC codes at baseline: C02 (anti-hypertensives), C03 (diuretics), C04 (peripheral vasodilators), C07 (beta blocking agents), C08 (calcium channel blockers), and C09 (agents acting on the rennin-angiotensin system).

（Source: 5.3.5.3.2, Table 6.3.1.1.3）

表 2.7.4.4.1.2-6　ベースライン時の降圧薬使用別の最高 DBP（C788-047 及び C788-048 試験プラセボ対照期）

Treatment Group	Anti-hypertensive Medication Use at Baseline (1)	Number of Subjects N	Maximum Post-Baseline Diastolic Blood Pressure (mmHg)				
			<80	>= 80 - < 90	>= 90 - < 100	>= 100 - < 110	>= 110
			n (%)	n (%)	n (%)	n (%)	n (%)
Fostamatinib	Yes	37	6 (16.2%)	25 (67.6%)	6 (16.2%)	0 (0.0%)	0 (0.0%)
	No	65	12 (18.5%)	39 (60.0%)	9 (13.8%)	5 (7.7%)	0 (0.0%)
Placebo	Yes	16	8 (50.0%)	7 (43.8%)	1 (6.3%)	0 (0.0%)	0 (0.0%)
	No	32	9 (28.1%)	21 (65.6%)	2 (6.3%)	0 (0.0%)	0 (0.0%)

Note: For each treatment group, percentages are based on N, the number of such subjects in the anti-hypertensive medication use at baseline category in the Placebo-Controlled Safety Population: Placebo-Controlled Period with at least 1 post-baseline diastolic blood pressure measurement.
(1) Subjects with anti-hypertensive medication use are those subjects receiving medications with the following ATC codes at baseline: C02 (anti-hypertensives), C03 (diuretics), C04 (peripheral vasodilators), C07 (beta blocking agents), C08 (calcium channel blockers), and C09 (agents acting on the rennin-angiotensin system).
（Source: 5.3.5.3.2, Table 6.3.2.1.3）

2.7.4.4.2 12 誘導心電図

2.7.4.4.2.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験では、前観察期、第 I 期（Week 24）、第 II 期（Week 52）、休薬期及び後観察期に心電図データを収集した。

プラセボ対照期、R788 長期投与時、R788 投与期及び休薬期のいずれにおいても臨床的に問題となる心電図異常所見は認められなかった。

2.7.4.4.2.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

C788-047 及び C788-048 試験では、C788-049 試験に移行した被験者について、ベースライン時及び 24 週時に心電図データを収集した。心電図所見は、両試験の多くの被験者で正常であった。ベースライン時及び 24 週時に臨床的に問題となる心電図所見が認められた動脈性高血圧及び無症候性心筋梗塞の既往歴を有する 1 例（被験者[redacted]）を除き、臨床的に問題となる心電図異常所見は認められなかった。C788-049 試験中、ベースライン後の心電図解析は実施されなかった。

2.7.4.4.3 ITP Bleeding score（IBLS）及び WHO Bleeding Scale scores

2.7.4.4.3.1 国内第 III 相臨床試験（R788-1301）

R788-1301 試験のプラセボ対照期における出血スコアの要約を表 2.7.4.4.3.1-1 に示す。

IBLS で 1 つ以上の部位が Grade 2 である被験者は除外基準により試験に参加できなかったことを反映して、Day 1 の IBLS の平均値は、R788 群 0.09 及びプラセボ群 0.07 であり、いずれも極端な低値であった。24 週間の治療期間における IBLS の投与後平均スコアの平均値±標準偏差（SD）は、R788 群 0.07±0.07 及びプラセボ群 0.09±0.08 であり、R788 群とプラセボ群で同様に低値であった。

最大スコアが 0 であった被験者の割合は、R788 群では Day 1 で 36.4%（8/22 例）、Week 12 で 55.0%（11/20 例）、Week 24 で 60.0%（6/10 例）、最終評価時で 59.1%（13/22 例）であり、プラセボ群では Day 1 で 58.3%（7/12 例）、Week 12 で 30.0（3/10 例）、Week 24 で 75.0%（3/4 例）、最終評価時で 33.3%（4/12 例）であった。R788 群では、治験薬投与開始後に最大スコアが 0 となる被験者の割合が増加した。

表 2.7.4.4.3.1-1　出血スコアの要約（R788-1301 試験）

Parameter	R788	Placebo
Average ITP Bleeding Score Across 9 Anatomical Sites at Day 1		
N	22	12
Mean	0.09	0.07
Minimum – Maximum	0.0 – 0.2	0.0 –0.4
Mean of Average ITP Bleeding Score Across Visits After Treatment		
N	22	12
Mean	0.07	0.09
Median	0.1	0.1
SD	0.07	0.08
Minimum – Maximum	0.0 – 0.2	0.0 – 0.3
Maximum ITP Bleeding Score Across 9 Anatomical Sites: Score = 0		
Day 1		
N	22	12
n (%)	8 (36.4)	7 (58.3)
Week 12		
N	20	10
n (%)	11 (55.0)	3 (30.0)
Week 24		
N	10	4
n (%)	6 (60.0)	3 (75.0)
Last Observed Visit		
N	22	12
n (%)	13 (59.1)	4 (33.3)

(Source : 5.3.5.1.1, Table 14.1.4.2.1 改編)

2.7.4.4.3.2 海外第 III 相臨床試験（C788-047 及び C788-048）

C788-047 及び C788-048 試験における出血スコアの要約を表 2.7.4.4.3.2-1、出血関連の中等度/高度の有害事象及び重篤な有害事象の発現率を表 2.7.4.4.3.2-2 に示す。

IBLS が 2 であった被験者は除外基準により試験に参加できなかったことを反映して、ベースライン時の IBLS の平均値は、C788-047 試験では R788 群 0.15 及びプラセボ群 0.13、C788-048 試験では R788 群 0.09 及びプラセボ群 0.06 であり、いずれも極端な低値であった。24 週間の治療期間における IBLS の投与後平均スコアの平均値±SD は、C788-047 試験では R788 群 0.13±0.12 及びプラセボ群 0.14±0.10、C788-048 試験では R788 群 0.04±0.08 及びプラセボ群 0.06±0.07 であり、R788 群とプラセボ群で同様に低値であった。また、24 週間の治療期間における WHO Bleeding Scale scores の投与後平均スコアの平均値±SD は、C788-047 試験では R788 群 0.61±0.66 及びプラセボ群 0.46±0.56、C788-048 試験では R788 群 0.26±0.38 及びプラセボ群 0.38±0.47 であり、R788 群とプラセボ群で同程度であった。

2 つの出血スコアでは、両群間での出血関連有害事象の差異を区別することはできなかったが、中等度又は高度の出血関連有害事象（R788 群 9.9%（10/101 例）及びプラセボ群 16.3%（8/49 例））、並びに重篤な出血関連有害事象（R788 群 5.0%（5/101 例）及びプラセボ群 10.2%（5/49 例））の発現率は、R788 群と比較してプラセボ群で約 2 倍高かった。高度の出血関連有害事象が認められたのは、R788 群では 1 例（挫傷）のみであったが、プラセボ群では 3 例（消化管出血、月経過多及び点状出血）認められた。高度の出血関連有害事象はいずれも入院に至った。

表 2.7.4.4.3.2-1　出血スコアの要約（C788-047 及び C788-048 試験）

Parameter	C788-047		C788-048	
	R788 (N=51)	Placebo (N=25)	R788 (N=50)	Placebo (N=24)
IBLS – Mean score at baseline				
N	51	25	50	24
Mean	0.15	0.13	0.09	0.06
Minimum – Maximum	0.0 - 0.4	0.0 - 0.4	0.0 - 1.0	0.0 - 0.3
IBLS – Efficacy Endpoint: Mean score across 9 anatomical sites and across visits during the 24-week treatment period[a]				
N	51	25	50	24
Mean	0.13	0.14	0.04	0.06
Median	0.09	0.12	0.01	0.02
SD	0.12	0.10	0.08	0.07
Minimum – Maximum	0.0 - 0.5	0.0 - 0.3	0.0 - 0.4	0.0 - 0.2
Difference in Means (R788 - Placebo) and 95% CI[b]	−0.01 (−0.1, 0.0)		−0.01 (−0.05, 0.02)	
p-value[c]	0.6642		0.4927	
WHO – Efficacy Endpoint: Mean of WHO Bleeding Scale scores across visits during the 24-week treatment period[d]				
N	51	25	50	24
Mean	0.61	0.46	0.26	0.38
Median	0.33	0.17	0.00	0.13
SD	0.66	0.56	0.38	0.47
Minimum – Maximum	0.0 - 2.8	0.0 - 2.0	0.0 - 1.1	0.0 - 1.7
Difference in Means (R788 - Placebo) and 95% CI[b]	0.15 (−0.2, 0.5)		−0.12 (−0.32, 0.09)	
p-value[c]	0.3365		0.2499	

CI = confidence interval; IBLS = ITP bleeding scale; SD = standard deviation; WHO = World Health Organization.
a IBLS: At each visit for each subject, 9 anatomical sites were each graded from 0 (none) to 2 (marked bleeding).
At baseline the parameter summarized is the subject's average score across the 9 sites (note: the source table for the baseline values summarizes the total score at baseline, which is divided by 9 to obtain the average score).
The efficacy endpoint summarized is the average across visits of the subject's average score across sites.
b Confidence interval calculated based on the t-distribution.
c p-value from a two-sided two-sample t-test, testing for a difference in means between R788 and placebo.
d WHO bleeding scale: At each visit, each subject's symptoms were graded from 0 (no bleeding) to 4 (debilitating blood loss).
For each subject, the efficacy endpoint summarized is the average score across visits.
(Source: 5.3.5.1.2 Table 14.1.4, Table 14.2.10, Table 14.3.14; 5.3.5.1.3 Table 14.1.4, Table 14.2.10, Table 14.3.14 改編)

表 2.7.4.4.3.2-2　出血関連の中等度/高度の有害事象及び重篤な有害事象の発現率（C788-047 及び C788-048 試験）

Number of Subjects (%) Having Events	R788 (N=101)	Placebo (N=49)
Total, n (%)	10 (9.9%)[a]	8 (16.3%)
Bleeding-related SAEs, n (%)	5 (5.0%)	5 (10.2%)
Moderate or severe bleeding related AEs, n (%)	10 (9.9%)	8 (16.3%)

AE = adverse event; SAE = serious adverse event.
Incidence is determined for each row separately – some subjects contribute to more than one row.
a One R788 subject had a bleeding event on the last day of C788-048/first day of C788-049. This subject's event of moderate epistaxis was recorded in C788-049, but for purposes of evaluating bleeding events, it is being counted in the placebo-controlled period.
(Source: 5.3.5.3.1 Table 5.5.1, Table 5.5.2; 5.3.5.1.2 Listing 16.2.7.2; 5.3.5.1.3 Listing 16.2.7.2 改編)

2.7.4.4.4 ECOG Performance Status 及び Karnofsky Performance Status（KPS）

2.7.4.4.4.1 国内第 III 相臨床試験（R788-1301）

試験中、R788 群又はプラセボ群のいずれの被験者においても、ECOG Performance Status 値のベースラインからの変化は、ほとんどなかった又はなかった。

2.7.4.4.4.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

1) C788-047 試験

試験中、R788 群又はプラセボ群のいずれの被験者においても、KPS 値のベースラインからの変化は、ほとんどなかった又はなかった。

2) C788-048 試験

試験中、R788 群又はプラセボ群のいずれの被験者においても、KPS 値のベースラインからの変化は、ほとんどなかった又はなかった。R788 群又はプラセボ群におけるレスポンダー及びノンレスポンダーについて、KPS 値の平均値又はベースラインからの変化量平均値の差異はほとんどなかった又はなかった。

3) C788-049 試験

ベースライン後の KPS 値において、臨床的に問題となる変化は認められなかった。

2.7.4.4.5 免疫グロブリン検査

2.7.4.4.5.1 国内第 III 相臨床試験（R788-1301）

プラセボ対照期の血清免疫グロブリン濃度（IgM、IgG、IgA）は、プラセボ群では変化が認められなかったのに対して、R788 群では IgG に減少傾向が認められたが、基準値内（870～1700 mg/dL）の変動であった。R788 長期投与時において、Week 24 から Week 52 にかけて更なる IgG の減少は認められなかった。

2.7.4.4.5.2 海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）

海外第 III 相臨床試験では、免疫グロブリンは総量として評価しており、C788-047、C788-048 及び C788-049 試験のいずれの試験においても R788 の投与により減少傾向が認められた。

2.7.4.5 特別な患者集団及び状況下における安全性

2.7.4.5.1 内因性要因

2.7.4.5.1.1 性別

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049 試験）における「男性」及び「女性」の曝露期間を表 2.7.4.9-59 及び表 2.7.4.9-60 に、有害事象の発現状況を表 2.7.4.9-3 及び表 2.7.4.9-7 に、注目すべき有害事象の発現状況を表 2.7.4.9-25 及び表 2.7.4.9-34 にそれぞれ示す。

C788-047 及び C788-048 試験を統合したプラセボ対照期の治験薬に対する曝露期間の中央値（R788 及びプラセボの両投与群で 12.1～12.3 週）及び 1 日投与量の中央値（両投与群で 258.2～263.0 mg）は男性と女性で同程度であった。C788-047、C788-048 及び C788-049 試験を統合した R788 投与期では、曝露期間の中央値は男性（25.9 週）と比較して女性（30.3 週）の方が長かったが、1 日投与量の中央値は男性（257.1 mg）と女性（265.9 mg）で同程度であった。

プラセボ対照期中に発現した有害事象では、悪心（男性 R788 群 7.3%、プラセボ群 0%、女性 R788 群 26.2%、プラセボ群 13.3%）及び頭痛（男性 R788 群 7.3%、プラセボ群 5.6%、女性 R788 群 13.1%、プラセボ群 26.7%）が R788 群及びプラセボ群のいずれも女性で発現頻度が高かった。高血圧は、男性（R788 群 12.2%、プラセボ群 11.1%）と比較して女性（R788 群 24.6%、プラセボ 6.7%）で 10%以上高い群間差が認められた。鼻出血は、女性（R788 群 16.4%、プラ

セボ群 16.7%）と比較して男性（R788 群 14.6%、プラセボ群 0%）で 10%以上高い群間差が認められた。R788 投与期の被験者の 10%以上に認められた有害事象は、プラセボ対照期に認められた有害事象と同様であった。R788 投与期中に発現した有害事象では、悪心（男性 8.5%、女性 26.4%）及び高血圧（男性 13.6%、女性 27.6%）が女性で発現頻度が高かった。

プラセボ対照期中に発現した注目すべき有害事象である胃腸障害は、男性（R788 群 36.6%、プラセボ群 11.1%）と比較して女性（R788 群 44.3%、プラセボ群 26.7%）が R788 群及びプラセボ群のいずれも発現頻度が高かった。R788 投与期中も同様の傾向が認められた。

プラセボ対照期中に発現した注目すべき有害事象である高血圧 SMQ は、女性の方が両投与群で発現頻度が高く、男性（R788 群 17.1%、プラセボ群 11.1%）と比較して、女性（R788 群 34.4%、プラセボ群 13.3%）で 10%以上高い群間差が認められた。また、R788 投与期中の高血圧 SMQ に該当する有害事象の発現頻度は女性が高かった。

プラセボ対照期中に発現した感染症は、プラセボ群の男性（11.1%）と比較して R788 群の男性（34.1%）の発現頻度が高かった。感染症が発現した女性は、R788 群とプラセボ群で同程度であった（R788 群 27.9%、プラセボ群 26.7%）。R788 投与期中に発現した感染症は、男性と女性で発現頻度が同程度であった（男性 42.4%、女性 49.4%）。

プラセボ対照期中に発現した注目すべき有害事象である薬剤性肝障害 SMQ の発現頻度は、男性と女性で同程度であり、プラセボ群（男性 5.6%、女性 0%）と比較して R788 群（男性 14.6%、女性 16.4%）で高かった。R788 投与期中のこれらの事象の発現頻度は男性と女性で同程度であり（男性 18.6%、女性 19.5%）、プラセボ対照期中に認められた発現頻度と同程度であった。

プラセボ対照期中に発現した注目すべき有害事象である好中球減少症の発現頻度は、男性（R788 群 7.3%、プラセボ群 0%）と女性（R788 群 6.6%、プラセボ群 0%）で臨床的に問題となる差は認められなかった。R788 投与期のこれらの事象の発現頻度は男性と女性で同程度であり（男性 6.8%、女性 6.9%）、プラセボ対照期中に認められた発現頻度と同程度であった。

2.7.4.5.1.2 年齢

1) 海外第 III 相臨床試験

海外第 III 相臨床試験（C788-047、C788-048 及び C788-049 試験）における「65 歳未満」及び「65 歳以上」の曝露期間を表 2.7.4.9-61 及び表 2.7.4.9-62 に、有害事象の要約を表 2.7.4.5.1.2-1 に、有害事象の発現状況を表 2.7.4.9-2 及び表 2.7.4.9-6 に、注目すべき有害事象の発現状況を表 2.7.4.9-24、表 2.7.4.9-33、表 2.7.4.9-108 及び表 2.7.4.9-109 にそれぞれ示す。また、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治験薬の休薬に至った有害事象の一覧表を表 2.7.4.9-110～表 2.7.4.9-113 に示す。

C788-047 及び C788-048 試験を統合したプラセボ対照期の治験薬に対する曝露期間の中央値は 65 歳未満（R788 群 12.6 週及びプラセボ群 12.1 週）と 65 歳以上（R788 群 12.1 週及びプラセボ群 12.4 週）で同程度であり、C788-047、C788-048 及び C788-049 試験を統合した R788 投与期では、65 歳以上（24.3 週）と比較して 65 歳未満（31.3 週）の方が長かった。1 日投与量の中央値は、65 歳以上（プラセボ投与期の R788 群 244.1 mg、R788 投与期 249.3 mg）と比較して 65 歳未満（プラセボ投与期の R788 群 260.0 mg、R788 投与期 266.3 mg）の方がわずかに多かった。

プラセボ対照期に発現した有害事象のうち、65 歳未満と比較して 65 歳以上で発現頻度が高かった有害事象は、下痢（65 歳未満 25.7%、65 歳以上 39.3%）、鼻出血（65 歳未満 12.2%、65 歳以上 25.0%）、浮動性めまい（65 歳未満 8.1%、65 歳以上 17.9%）及び低カリウム血症（65 歳未満 0%、65 歳以上 10.7%）であった。R788 群における頭痛はいずれも 65 歳未満の被験者に認められた（65 歳未満 14.9%）。R788 投与期に発現した有害事象の種類は、プラセボ対照期の R788 群とおおむね同様であった。頭痛は 65 歳以上と比較して 65 歳未満の発現頻度が 10%以上高かった（65 歳未満 18.3%、65 歳以上 5.4%）。

プラセボ対照期中に発現した注目すべき有害事象である胃腸障害は、65 歳未満（R788 群 39.2%、プラセボ群 24.3%）と比較して 65 歳以上（R788 群 46.4%、プラセボ群 9.1%）で高い群間差が認められた。R788 投与期中の胃腸障害の発現頻度は両年齢群で同等であった（65 歳未満 47.7%、65 歳以上 48.6%）。

プラセボ対照期中に発現した高血圧 SMQ は、65 歳未満（R788 群 23.0%、プラセボ群 10.8%）と比較して 65 歳以上（R788 群 39.3%、プラセボ群 18.2%）の発現頻度が高った。また、R788 投与期中に発現した高血圧 SMQ は、65 歳未満と比較して 65 歳以上の発現頻度が高かった（65 歳未満 25.7%、65 歳以上 40.5%）。

プラセボ対照期中に発現した感染症は、65 歳以上（R788 群 25.0%、プラセボ群 9.1%）と比較して 65 歳未満（R788 群 32.4%、プラセボ群 24.3%）の発現頻度が高かった。また、R788 投与期中に発現した感染症は、65 歳以上と比較して 65 歳未満の発現頻度が高かった（65 歳未満 52.3%、65 歳以上 29.7%）。

プラセボ対照期中に発現した注目すべき有害事象である薬剤性肝障害 SMQ は、プラセボ群で認められた黄疸眼の 1 例を除いて R788 投与群に認められ、65 歳以上（R788 群 10.7%、プラセボ群 0%）と比較して 65 歳未満（R788 群 17.6%、プラセボ群 2.7%）の発現頻度が高く、主に ALT 増加及び AST 増加の発現頻度が 65 歳未満で高いことに起因していた。R788 投与期中に発現した薬剤性肝障害 SMQ の発現頻度は、65 歳未満と 65 歳以上で同程度であった（65 歳未満 19.3%、65 歳以上 18.9%）。肝機能検査値に年齢による臨床的に問題となる差は認められなかった。

なお、小児を対象とした臨床試験は実施しておらず、国内及び海外臨床試験で 18 歳未満への投与経験はない。

表 2.7.4.5.1.2-1　年齢別（65 歳未満、65 歳以上）の有害事象の要約（C788-047 及び C788-048 試験プラセボ対照期）

	65 歳未満				65 歳以上			
	R788 (N=74)		プラセボ (N=37)		R788 (N=28)		プラセボ (N=11)	
	n	(%)	n	(%)	n	(%)	n	(%)
すべての有害事象	59	79.7	30	81.1	26	92.9	6	54.5
死亡に至った有害事象	0	0.0	0	0.0	1	3.6	1	9.1
重篤な有害事象	7	9.5	9	24.3	6	21.4	1	9.1
治験薬の投与中止に至った有害事象	5	6.8	2	5.4	6	21.4	2	18.2
治験薬の休薬に至った有害事象	12	16.2	5	13.5	6	21.4	0	0.0
治験薬の減量に至った有害事象	7	9.5	1	2.7	2	7.1	0	0.0

（Source: 1.13.3-4, C-09 表 44）

2) 国内第 III 相臨床試験

国内第 III 相臨床試験（R788-1301）における「65 歳未満」及び「65 歳以上」の有害事象の要約を表 2.7.4.5.1.2-2 に、注目すべき有害事象の発現状況を表 2.7.4.9-108 及び表 2.7.4.9-109 に示す。また、治験薬の減量に至った有害事象の一覧表を表 2.7.4.9-113 に示す。

いずれの部分集団解析においても、年齢別の各部分集団の被験者数が少なく、明確な評価は困難であるが、高齢者における特定の傾向は認められなかった。

表 2.7.4.5.1.2-2 年齢別（65 歳未満、65 歳以上）の有害事象の要約（R788-1301 試験プラセボ対照期）

	65 歳未満				65 歳以上			
	R788 (N=12)		プラセボ (N=7)		R788 (N=10)		プラセボ (N=5)	
	n	(%)	n	(%)	n	(%)	n	(%)
すべての有害事象	11	91.7	4	57.1	9	90.0	4	80.0
死亡に至った有害事象	0	0.0	0	0.0	0	0.0	0	0.0
重篤な有害事象	2	16.7	0	0.0	0	0.0	1	20.0
治験薬の投与中止に至った有害事象	2	16.7	0	0.0	1	10.0	0	0.0
治験薬の休薬に至った有害事象	0	0.0	0	0.0	0	0.0	0	0.0
治験薬の減量に至った有害事象	4	33.3	0	0.0	6	60.0	0	0.0

（Source: 1.13.3-4, C-09 表 43）

2.7.4.5.1.3 腎機能

腎機能低下が R406 の薬物動態に及ぼす影響を検討するため腎機能低下者試験（D4300-009）を実施した。クレアチニンクリアランス（CL_{CR}）に基づいて下記の 3 グループに分類して評価した。

- グループ 1：CL_{CR} 80 mL/min 以上（腎機能正常者）
- グループ 3：CL_{CR} 30 mL/min 以上 50 mL/min 未満（中等度腎機能低下者）
- グループ 5：透析を必要とする（末期腎不全患者）

本試験には計 24 例（各群 8 例）の被験者が登録され、全例が試験を完了した。腎機能正常者（グループ 1）における R406 の薬物動態は、健康被験者を対象とした臨床薬理試験の結果と一致していた。本試験の結果は以下のとおりであった。

- 末期腎不全患者及び中等度腎機能低下者における R406 の曝露は、腎機能正常者と比較して高くなかった（2.7.2.2.2.3.3）。
- 死亡、重篤な有害事象、有害事象による中止及びその他の重要な有害事象は認められなかった。
- 有害事象の発現件数は、3 つの投与群間で同等であった。中等度の有害事象は、末期腎不全患者群で 1 例 1 件、中等度腎機能低下者群で 2 例 2 件、及び腎機能正常者群で 1 例 1 件認められた。ほとんどの有害事象は軽度であった。腎機能正常者群の 1 例に治験薬との因果関係があると判定された有害事象が認められた。
- 臨床検査値、バイタルサイン及び心電図所見については、臨床的に問題となる変化は認められなかった。

以上より、中程度腎機能低下者、末期腎不全患者及び腎機能正常者に R788 150 mg を単回投

与したときの安全性に問題は認められなかった。

2.7.4.5.1.4 肝機能

肝機能低下が R406 の薬物動態に及ぼす影響を検討するため肝機能低下者試験（D4300-010）を実施した。本試験は、肝機能正常者 8 例、軽度肝機能低下者 8 例、中等度肝機能低下者 8 例及び重度肝機能低下者 8 例の合計 32 例を対象に実施した。薬物動態の結果から、肝機能正常者と比較して、様々な程度の肝機能低下が R406 の薬物動態に一貫した影響は認められなかった。本試験の結果は以下のとおりであった。

- 軽度及び中等度の肝機能低下者における R406 の曝露は、肝機能正常者と比較して高くなかった。重度の肝機能低下者では、非結合形 $AUC_{0-\infty}$（AUC_u）及び非結合形 C_{max}（$C_{max,u}$）は肝機能正常者の 1.7 及び 1.3 倍であった（2.7.2.2.2.3.4）。
- 死亡、有害事象による中止及びその他の重要な有害事象は認められなかった。
- 重度肝機能低下者群の 1 例（被験者 [redacted]）に重篤な有害事象である肝性脳症の悪化が認められた。治験担当医師により高度と評価されたが、治験薬との因果関係はないと判定された。
- 有害事象の発現件数は、4 つの投与群間で同等であった。重度肝機能低下者群 1 例で中等度の有害事象が 1 件、肝機能正常者群 1 例で中等度の有害事象が 2 件認められた。上記の重篤な有害事象を除いたその他の有害事象はすべて軽度であった。軽度、中等度及び重度肝機能低下者群の各 1 例に治験薬との因果関係があると判定された有害事象が認められた。
- 臨床検査値、バイタルサイン及び心電図所見については、臨床的に問題となる変化は認められなかった。

以上より、軽度、中程度及び重度の肝機能低下者、並びに肝機能正常者に R788 150 mg を単回投与したときの安全性に問題は認められなかった。

日本人を対象とした R788-1301 試験（34 例）及び欧米人を対象とした海外第 III 相臨床試験（C788-047 試験 76 例、C788-048 試験 74 例及び C788-049 試験 123 例）にて、Day 1 の治験薬投与前の値が「医薬品等の副作用の重篤度分類基準について（平成 4 年 6 月 29 日薬安第 80 号）」[1)]の肝障害の重篤度グレード 1 又は 2 に該当する被験者は 6 例であり、そのうち 4 例 7 件（R788-1301 試験に組み入れられた被験者：1 例 2 件、C788-047 試験に組み入れられた被験者：3 例 5 件）で副作用が認められたものの、いずれも軽度であり重篤な事象はなかった（表 2.7.4.5.1.4-1）。

表 2.7.4.5.1.4-1　肝障害の重篤度グレード 1 又は 2 に該当する被験者における副作用

被験者 ID	グレード	事象名（PT）	副作用程度	R788 投与開始日	副作用発現日	副作用消失日	転帰
[redacted]	1	悪心	軽度	Day 1*	Day 3*	Day 9*	回復
		下痢	軽度	Day 1*	Day 104*	Day 108*	回復
[redacted]	1	血中ビリルビン増加	軽度	Day 1*	Day 70*	Day 128*	回復
		血中ビリルビン増加	軽度	Day 1*	Day 133*	Day 203*	回復
[redacted]	1	高血圧	軽度	Day 1*	Day 23*	Day 24*	回復
		高血圧	軽度	Day 1*	Day 36*	Day 37*	回復
[redacted]	2	関節膨張	軽度	Day 1*	Day 143*	—	未回復

グレード 1：Day 1 の治験薬投与前にて、総ビリルビン（1.6 mg/dL 以上 3.0 mg/dL 未満）、AST 及び ALT（50 U/L 以上 100 U/L 未満）、ALP（正常値上限の 1.25 倍以上 2.5 倍未満）のいずれかを満たす症例
グレード 2：Day 1 の治験薬投与前にて、総ビリルビン（3.0 mg/dL 以上 10 mg/dL 未満）、AST 及び ALT（100 U/L 以上 500 U/L 未満）、ALP（正常値上限の 2.5 倍以上 5 倍未満）のいずれかを満たす症例
（Source: 1.13.3-4, A-03 表 6）

重度の肝機能障害を有する患者に対する投与経験は乏しいものの、本薬の忍容性が確認されている第 I 相臨床試験（C406-001、C788-001 及び C788-013）で認められた曝露は、重度肝機能低下者の曝露（D4300-010 試験）及び重度肝機能低下を有する ITP 患者の曝露（C788-049 試験から推定、C_{max} 1053 ng/mL 及び AUC 18700 ng·h/mL）と比較して、それぞれ C_{max} 比 2.10～13.09 倍及び 1.16～7.24 倍、並びに AUC 比 1.41～11.17 倍及び 0.72～5.67 倍であった（2.7.2.3.3.4）。臨床用量の上限である 150 mg 1 日 2 回投与した場合でも、重度の肝機能障害を有する ITP 患者における安全性に大きな問題はないと考えられる。

以上より、国内外の第 III 相臨床試験において重度の肝機能障害を有する患者は組み入れられていないものの、これまでに実施している臨床試験の安全性結果から、重度の肝機能障害を有する患者で、本薬の曝露量増加に伴い副作用のリスクが増大する可能性は低いと考えられる。

2.7.4.5.1.5 B 型肝炎ウイルス及び C 型肝炎ウイルスのキャリア又は既往感染者

海外第 III 相臨床試験（C788-047 及び C788-048 試験）では、B 型肝炎ウイルス（HBV）又は C 型肝炎ウイルス（HCV）陽性の患者は除外されていることから、HBV 又は HCV のキャリア又は既往感染者に関する評価可能なデータはない。

R788-1301 試験では、HBV 又は HCV 陽性の患者は除外ではあるものの、治験参加時の集中測定の結果が以下に該当する被験者は治験に参加可能である。

- HBs 抗体陽性かつ HBV の DNA 定量で定量下限未満であった場合
- HBc 抗体陽性かつ HBV の DNA 定量で定量下限未満であった場合

上記被験者（HBs 抗体陽性又は HBc 抗体陽性かつ HBV DNA 定量下限未満の被験者）を、HBV のキャリアの患者又は既往感染者とした場合、7 例の被験者が該当する。各被験者の本剤の投与期間及び有害事象の発現状況等を表 2.7.4.5.1.5-1 に示す。なお、HCV のキャリアの患者又は既往感染者に関する評価可能なデータはない。

R788-1301 試験に登録された HBV キャリアの患者又は既往感染者の治験薬投与後の HBV DNA 量の測定は実施されていない。治験薬投与後の HBV の再増殖の有無は不明であるものの、肝炎などの有害事象の発現は認められなかった。HBV キャリア又は既往感染者 7 例のうち 1 例（[redacted]）に認められた肝機能値検査値上昇の有害事象は、軽度（最大値、ALT：96 U/L、

＊新薬承認情報提供時に置き換え

AST：84 U/L）であり臨床症状も認められなかった。

表 2.7.4.5.1.5-1　HBV のキャリアの患者又は既往感染者の投与期間と有害事象の発現状況（R788-1301 試験）

被験者 ID	性別/年齢	HBs 抗体	HBc 抗体	HBV DNA	R788 投与期間（Day）	有害事象
[redacted]	F/7[redacted]	Positive	Positive	Not Detected	554	便秘 橈骨骨折
[redacted]	F/5[redacted]	Positive	Positive	Not Detected	211	高血圧 下痢 閉経期症状 筋痙縮 皮下出血 四肢痛 関節痛 点状角膜炎
[redacted]	M/6[redacted]	Positive	Positive	Not Detected	225	好中球数減少
	F/7[redacted]	Negative	Positive	Not Detected	365	上咽頭炎 肝機能検査値上昇
[redacted]	M/3[redacted]	Positive	Negative	Not Detected	296	高血圧 頭痛 血中クレアチンホスホキナーゼ増加 胃腸炎 下痢 血中ビリルビン増加 上咽頭炎
[redacted]	F/7[redacted]	Negative	Positive	Not Detected	407	湿疹
	F/6[redacted]	Positive	Positive	Not Detected	323	口腔咽頭不快感 歯髄炎 歯周炎 帯状疱疹 腰部脊柱管狭窄症

（Source: 1.13.3-10, C-03 表 6）

2.7.4.5.2 外因性要因

D4300-019 試験において R406 の薬物動態に及ぼす高脂肪/高カロリー食の影響が検討された。空腹時投与に対する食後投与の比（90%CI）は、$AUC_{0-\infty}$及び C_{max} でそれぞれ 123.26%（102.13%, 148.77%）及び 114.53%（88.68%, 147.91%）であり、本試験で認められた食事の影響はわずかであった（2.7.2.3.4.1）。

2.7.4.5.3 薬物相互作用

In vitro 試験の結果を踏まえて、11 試験の薬物相互作用試験を実施した（2.7.2.1.2）。

薬物相互作用試験の結果から、R788 の活性本体である R406 の薬物動態は、CYP3A 阻害薬及び CYP3A 誘導薬により影響を受けることが確認された（2.7.2.3.5）。

強い CYP3A 阻害薬であるケトコナゾールとの薬物相互作用を検討した C788-001 試験では R406 の曝露を約 2 倍増加させ、中程度の CYP3A 阻害薬であるベラパミルとの薬物相互作用を検討した D4300-011 試験では R406 の曝露を約 1.4 倍増加させた。また、強い CYP3A 誘導薬であるリファンピシンとの相互作用を検討した D4300-015 試験では R406 の曝露を約 25%まで低下させた。

これらの薬物相互作用試験では、R788 の単独投与時及び併用投与時に有害事象の発現状況、

程度などの安全性に臨床上問題となる事項は認められず、忍容性は良好であった（2.7.6.6、2.7.6.15 及び 2.7.6.19）。

2.7.4.5.4 妊婦及び授乳時の使用

2.7.4.5.4.1 非臨床試験データ

受胎能及び初期胚発生に関する試験では、R788 の高用量を投与した雌ラットで受胎率のわずかな低下と着床後胚死亡率の増加が認められた。受胎能試験では、雄の生殖能に影響は認められなかった。また、胚・胎児発生に関する試験では、腎臓及び尿管の発育遅延あるいは無発生を含む奇形が認められ、さらに主要血管及び骨格発育における変異及び奇形も認められた。R788 の活性本体である R406 は Ret のキナーゼ活性に阻害作用を有することが *in vitro* 試験で確認されており、また、このキナーゼ阻害作用は、ウサギ及びラットの胚・胎児発生に関する試験において同様の変化（泌尿器及び主要血管の欠損）を生じさせることが報告されている。また、ラットを用いた出生前及び出生後の発生に関する試験では、受胎能試験で認められた受胎率の低値、出生前及び出生後の発生に関する試験で認められた着床後胚死亡の高値並びに発育遅延及び奇形と一致する所見が認められた。また、出生後の出生児生存率低下、並びに下部正中線の白色化及び浮腫が哺育中に観察された。これらの所見は薬効標的である Syk 阻害に起因するものと考えられた。R406 の母乳中濃度は母体血漿中濃度よりも高濃度であった。F1 動物では性成熟遅延及び生殖器発達の遅延が認められたが、学習行動及び免疫学的な影響は認められず、F2 胎児には何らの異常も認められなかった。生殖発生毒性試験で認められたすべての異常所見は、F1 動物が子宮内で R406 に曝露されたことに起因すると判断した（2.4.4）。

2.7.4.5.4.2 臨床試験で報告された妊娠

臨床試験では、女性被験者を胚・胎児発生時のリスクから守るため、治験実施計画書に避妊に関する選択基準又は除外基準を設定し、被験者に対する指導を行ったが、海外臨床試験（第 II 相及び第 III 相臨床試験）の実施中に妊娠が発生した。RA 患者又は ITP 患者を対象とした臨床試験から 15 例の妊娠が報告されており、転帰は健康な新生児の出産 3 例、早産 1 例、死産 1 例、自然流産 4 例、並びに人工妊娠中絶 6 例であった（表 2.7.4.5.4.2-1 参照）。これらの妊娠のうち 14 例は RA 患者を対象とした臨床試験で認められ、1 例は ITP 患者を対象とした臨床試験で認められた。これらの被験者のほとんどは、メトトレキサートなどの催奇形性の可能性のある薬物を服用していた。

表 2.7.4.5.4.2-1　臨床試験で報告された妊娠の一覧

対象疾患	試験番号	被験者識別コード	人種	年齢	発現時投与量	治験薬の処置	転帰
RA	D4300-001	[redacted]	ヒスパニック	2[redacted] 歳	100 mg 1 日 2 回	中止	健康な新生児の出産
RA	D4300-005	[redacted]	ヒスパニック	2[redacted] 歳	100 mg 1 日 2 回	中止	健康な新生児の出産
RA	D4300-005	[redacted]	白人	3[redacted] 歳	150 mg 1 日 1 回	中止	健康な新生児の出産
RA	D4300-001	[redacted]	ヒスパニック	2[redacted] 歳	150 mg 1 日 1 回	中止	早産
RA	C788-010	[redacted]	ヒスパニック	3[redacted] 歳	100 mg 1 日 2 回	中止	死産
ITP	D4300-022	[redacted]	ヒスパニック	3[redacted] 歳	175 mg 1 日 2 回	変更なし	自然流産
RA	D4300-021	[redacted]	ヒスパニック	3[redacted] 歳	100 mg 1 日 2 回	休薬	自然流産
RA	D4300-021	[redacted]	ヒスパニック	4[redacted] 歳	100 mg 1 日 2 回	休薬	自然流産
RA	D4300-001	[redacted]	ヒスパニック	2[redacted] 歳	100 mg 1 日 2 回	中止	自然流産
RA	D4300-021	[redacted]	ヒスパニック	3[redacted] 歳	150 mg 1 日 1 回	変更なし	人工妊娠中絶
RA	D4300-021	[redacted]	ヒスパニック	2[redacted] 歳	100 mg 1 日 2 回	中止	人工妊娠中絶
RA	D4300-004	[redacted]	白人	3[redacted] 歳	100 mg 1 日 2 回	中止	人工妊娠中絶
RA	D4300-005	[redacted]	インド人又はパキスタン人	3[redacted] 歳	100 mg 1 日 1 回	休薬	人工妊娠中絶
RA	D4300-005	[redacted]	インド人又はパキスタン人	3[redacted] 歳	100 mg 1 日 2 回	休薬	人工妊娠中絶
RA	D4300-005	[redacted]	白人	4[redacted] 歳	100 mg 1 日 2 回	変更なし	人工妊娠中絶

2.7.4.5.5 過量投与

R788 の過量投与に対する特異的な解毒剤はなく、透析によって排泄される R406 の量はごくわずかである。

ITP 患者を対象とした国内及び海外臨床試験の実施中に過量投与は認められなかった。健康被験者を対象とした第 I 相臨床試験において、C406-001 試験では R406 を最大 600 mg 単回投与し、C788-001 試験では R788 を最大 400 mg 単回投与した。いずれの試験も忍容性に問題は認められなかった。

2.7.4.5.6 薬物乱用

いずれの臨床試験からも、R788 に依存性があることや、違法又は娯楽目的で使用される可能性を示す徴候は認められていない。健康被験者又は ITP 患者を対象とした臨床試験において、R788 の依存性、乱用又は離脱症状を示す有害事象認められなかった。

以上より、R788 に薬物乱用又は依存症の可能性はないと考えられる。

2.7.4.5.7 離脱症状及び反跳現象

国内第 III 相臨床試験（R788-1301）の休薬期に移行した 12 例の評価において、休薬期の最終評価時の血小板数の休薬期開始時からの変化量の中央値は−29000/μL（Q1-Q3: −57000～−16000/μL）であった。休薬期の最終評価時の血小板数のベースラインからの変化量の中央値は 15000/μL（−7000～34000/μL）であった。休薬期に血小板数が減少した被験者は 11 例であったが、ベースラインを下回る血小板数の減少を認めた被験者は 4 例であった。血小板数が 10000/μL 未満かつベースラインから 10000/μL 以上減少となった被験者は認められず、R788 の休薬による血小板数の大幅な減少は認められなかった（2.7.3.2.1.2.4）。また、休薬期に出血関連有害事象の発現も認められず、リバウンド現象と考えられる事象は認められなかった。

その他、いずれの臨床試験からも、R788 の減量又は中止に伴う離脱症状及び反跳現象は報

告されていない。

2.7.4.5.8 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

R788 の主な有害事象である頭痛、浮動性めまい及び疲労を除き、高頻度に認められた副作用はいずれも、身体的能力又は知力に悪影響を及ぼさないと考えられる。

2.7.4.6 その他の適応症

RA を適応症とした開発は中止したが、日本人を含むアジア人 RA 患者を対象としたアジア第 II 相臨床試験（D4300-008）及びアジア長期投与試験（D4300-029）を実施したため、両試験の安全性に関する概要を記載した。

2.7.4.6.1 関節リウマチ患者を対象としたアジア第 II 相臨床試験（D4300-008）

メトトレキサート療法の効果が不十分な活動性 RA を有するアジア人を対象として、多施設共同、無作為化、二重盲検、プラセボ対照、並行群間比較試験により、R788 を 12 週間投与したときの有効性及び安全性を評価した。被験者を以下の各投与群に無作為に割り付けた。

- 用法 A 群：R788 100 mg 1 日 2 回 12 週間
- 用法 B 群：R788 100 mg 1 日 2 回 4 週間、その後 150 mg 1 日 1 回 Week 12 まで
- 用法 C 群：R788 75 mg 1 日 2 回 12 週間
- 用法 D 群：R788 50 mg 1 日 2 回 12 週間
- 用法 E 群：プラセボ 1 日 2 回 12 週間

全体で 163 例（日本人は 66 例）が用法 A 群 31 例、用法 B 群 33 例、用法 C 群 33 例、用法 D 群 33 例及びプラセボ群 33 例に無作為割付けされた。R788 の用法 A 群、用法 B 群、用法 C 群及び用法 D 群でそれぞれ 77.4%、72.7%、63.6%及び 75.8%の被験者が 12 週間の試験投与を完了し、プラセボ群で 75.8%の被験者が 12 週間の試験投与を完了した。最も多い中止理由は、試験の中断（全体で 34 例（20.9%）の被験者、投与群間でばらつきは認められなかった）であった。

有害事象の発現率は、プラセボ群 60.6%（20/33 例）に対して、R788 用法 A 群 74.2%（23/31 例）、用法 B 群 69.7%（23/33 例）、用法 C 群 63.6%（21/33 例）及び用法 D 群 72.7%（24/33 例）であった。いずれかの R788 投与群で発現率 10%以上の有害事象は、高血圧、下痢及び好中球減少症であった。発現した有害事象の程度は、ほとんどが軽度又は中等度であった。

副作用の発現率は、プラセボ群 24.2%（8/33 例）に対して、R788 用法 A 群 58.1%（18/31 例）、用法 B 群 57.6%（19/33 例）、用法 C 群 48.5%（16/33 例）及び用法 D 群 42.4%（14/33 例）であった。いずれかの R788 投与群で発現率 5%以上の副作用は、高血圧、好中球減少症、下痢、上気道感染、鼻咽頭炎、白血球減少症、蜂巣炎及び脱毛症であった。

本試験で死亡例は認められなかった。重篤な有害事象は 6 例に認められ、高血圧（用法 A 群）、ウイルス性喉頭炎（用法 A 群）、下痢（用法 B 群）、手根管症候群（用法 D 群）、骨粗鬆症（用法 D 群）及び関節リウマチ（用法 D 群及びプラセボ群）であったが、因果関係が否定されなかった事象は高血圧及び下痢のみであった。

中止に至った有害事象は 5 例に認められ、膿疱性皮疹（用法 A 群）、糞線虫症（用法 C 群）、好中球減少症（用法 C 群）、斑状皮疹（用法 C 群）及び嘔吐（プラセボ群）であった。

2.7.4.6.2 関節リウマチ患者を対象としたアジア長期投与試験（D4300-029）

D4300-008 試験を完了した RA 患者を対象とした長期継続投与試験であり、非盲検下で全例に、通常のメトトレキサート療法と併用して R788 100 mg を 1 日 1 回経口投与した。

D4300-008 試験を完了し、組入れ対象として適切であると判断された 115 例（日本人は 47 例に R788 を投与した。なお、関節リウマチの適応に対する開発中止により、本試験を中止した。

有害事象の発現率は 62.6%（72/115 例）であり、発現率 5%以上の有害事象は、鼻咽頭炎、高血圧、関節リウマチ及び好中球減少症であった。発現した有害事象の程度は、ほとんどが軽度又は中等度であった。有害事象（脂漏性角化症、頭痛）、又は治験実施計画書に規定された理由（好中球減少症）による中止は 3 例であった。重篤な有害事象は R788 投与中に 4 例 4 件（脂漏性角化症、急性膵炎、骨壊死及び交通事故）認められた。本試験で死亡例は認められなかった。

2.7.4.7 市販後データ

既存治療で効果不十分な成人慢性 ITP 患者の血小板減少治療薬として、2018 年 4 月 17 日に米国で本薬の FDA 承認を取得し、2018 年 5 月 29 日に米国で販売が開始された（製品名：Tavalisse®）。また、既存治療が無効であった成人慢性 ITP 患者を対象として 2020 年 1 月 9 日に EU で EMA 承認を取得し、2020 年 7 月 1 日に EU で初めてドイツで販売が開始された（製品名：Tavlesse®）。その後、欧州をはじめ、各国で順次販売開始されている。

Periodic Safety Update Report を 5.3.6.1 に添付した。米国で承認を取得した 2018 年 4 月 17 日から 20[redacted] 年 [redacted] 月 [redacted] 日までに報告された市販後の副作用として疑われた個別症例安全性報告（ICSR）は 1875 件であった。また、本薬の出荷量から、当該期間に投与された患者数は 2795 人年と推定された。

市販後に報告された有害事象及び全体的な安全性情報は、臨床試験で確認された本薬の安全性プロファイルに一致している。

1) 海外製造販売後における肝機能障害患者への本剤の投与経験の有無及び投与時の安全性

海外製造販売後の自発報告及び ITP 患者を対象とした海外臨床試験（C788-049 試験）において、20[redacted] 年 [redacted] 月 [redacted] 日までに報告された SAE（海外製造販売後の自発報告 589 例 874 件、海外臨床試験の報告 16 例 18 件）を対象に、患者背景に「肝障害（SMQ）」の狭域に該当する事象を抽出し、本剤の安全性を評価した。その結果、10 例 10 件の SAE が認められたが、1 例を除き本薬との因果関係は関連なしと判断されている（表 2.7.4.7-1）。

表 2.7.4.7-1　　肝機能障害患者における SAE 報告

管理番号	患者背景 （肝障害の種類）	発現した有害事象（PT）	発現日	本剤処置	転帰	因果関係 企業判断
[redacted]	肝臓血管腫	血小板減少症	Day 1444*	継続	回復	関連なし
	B 型肝炎	血小板減少症	Day 1425*	継続	回復	関連なし
	B 型肝炎	血小板数減少	Day 1048*	継続	回復	関連なし
	B 型肝炎	血小板減少症	Day 1457*	継続	回復	関連なし
[redacted]	肝腫大	入院*	20[redacted]	継続	不明	関連なし
	トランスアミナーゼ上昇	敗血症	Day 1061*	中止	回復	関連あり
	B 型肝炎	尿路感染	Day 1190*	継続	回復	関連なし
	肝硬変	肺炎	—	継続	不明	関連なし
	肝硬変	前立腺癌	20[redacted]	継続	不明	関連なし
	脂肪肝	腫脹	20[redacted]	不明	不明	関連なし

*検査や治療についての情報はなし
（Source: 1.13.3-6, A-01 表 4）

2)　海外製造販売後における重篤な肝機能障害関連有害事象

海外製造販売後症例について、20[redacted] 年 [redacted] 月 [redacted] 日までの自発報告データより確認された重篤な肝機能障害関連の有害事象の一覧を表 2.7.4.9-128 に示す。自発報告データでは、重篤な肝機能障害関連の有害事象が 9 例 11 件に認められ、そのうちホスタマチニブとの因果関係があると判断されたのは 5 例 7 件であった（自発報告のため発現割合は不明）。因果関係があると判断された患者はいずれもホスタマチニブの投与を中止しており、転帰は回復が 1 例 2 件、軽快が 1 例 1 件であり、その他の事象は転帰不明であった。なお、Hy's Law の基準に合致する症例は確認されなかった。

3)　海外の製造販売後にとられた安全対策措置及び本邦における対応

海外の製造販売後にとられた安全対策措置は以下に示す 1 件であった。

- 対象国：欧州
- 措置内容：SmPC の「4.8 Undesirable effects」に「headache」が追加された

経緯：　Rigel 社は、2020 年 8 月に PRAC preliminary assessment report により、「headache」の累計レビューを実施し Product Information に「headache」を含めることを検討するよう要求された。「headache」の報告頻度は、ウェーバー効果によると思われる最初のピーク以降安定していること、非重篤な事象であること、因果関係を評価するための情報が欠如していること、ホスタマチニブとプラセボで同様の頭痛の発現率を示した文献があることから、Rigel 社はシグナルを否定した。しかし、2021 年 5 月の PRAC Rapporteurs updated assessment report にて、SmPC の「4.8 Undesirable effects」に「Common」の有害事象として「headache」を追加するよう勧告が行われ、2021 年 8 月に SmPC が改訂された。

欧州 SmPC の改訂は、欧州における製造販売後の集積状況に基づくものであり、米国の添付文書では「頭痛」の注意喚起は行われていない。また、国内第 III 相臨床試験では、ホスタマチニブ群で「頭痛」の副作用は認められていないことから、本邦の添付文書に「頭痛」を記載し注意喚起する必要はないと判断した。

＊新薬承認情報提供時に置き換え

4) 海外製造販売後の自発報告データから確認された間質性肺疾患、重篤皮膚障害（TEN、SJS、多形紅斑を含む）、血栓症、塞栓症及び血栓塞栓症の発現状況及び本邦の添付文書における注意喚起の必要性

(1) 間質性肺疾患

– 検索条件：「SMQ：間質性肺疾患」に含まれる事象
– 発現状況確認結果：該当なし
– 注意喚起の必要性：「SMQ：間質性肺疾患」に該当する事象の発現はないため、添付文書における注意喚起は不要と考える。

(2) 重篤皮膚障害（TEN、SJS、多形紅斑を含む）

– 検索条件：「SMQ：重症皮膚障害」、「SOC：皮膚及び皮下組織障害」に含まれる重篤事象
– 発現状況確認結果：以下の表の通り。

副作用の種類（PT）	重篤（件数）
脱毛症	1
水疱	1
血性水疱	1
皮膚血管炎	1
褥瘡性潰瘍	1
紅斑	1
多形紅斑	1
点状出血	1
発疹	3
皮膚変色	1
皮膚障害	1

– 注意喚起の必要性：海外製造販売後において報告された重篤皮膚障害 13 件のうち、多形紅斑の 1 件は、ホスタマチニブ投与と事象発現との間に時間的関連性が認められており、ホスタマチニブとの関連が疑われる症例であった。残り 12 件はホスタマチニブと事象との因果関係判断に必要な十分な情報が得られていないことから、ホスタマチニブとの関連を判断することは困難である。このことから、海外製造販売後に報告された重篤皮膚障害について、ホスタマチニブとの関連が疑われる症例は 1 例のみと判断した。また、最新の PSUR でも、重篤皮膚障害は安全対策の検討が必要とされる安全性シグナルとして検出されていない。国内外第 III 相臨床試験で重篤皮膚障害は認められておらず、海外製造販売後の集積状況を踏まえても、重篤皮膚障害がホスタマチニブのリスクとは考えられないことから、添付文書における注意喚起は不要と判断した。

(3) 血栓症、塞栓症及び血栓塞栓症

– 検索条件：「SMQ：塞栓および血栓」に含まれる事象
– 発現状況確認結果：以下の表の通り。

副作用の種類（PT）	非重篤（件数）	重篤（件数）
冠動脈閉塞	0	1
心筋梗塞	0	4
末梢動脈閉塞性疾患	0	1
無症候性心筋梗塞	0	1
一過性脳虚血発作	1	0
深部静脈血栓症	0	3
肺塞栓症	0	9
脳血栓症	0	1
脳血管発作	1	8
片麻痺	0	1
血栓症	2	10

– 注意喚起の必要性：海外製造販売後において報告された血栓症、塞栓症及び血栓塞栓症 43 件（重篤 39 件、非重篤 4 件）のうち、脳血管発作の重篤 1 件、血栓症の重篤 1 件及び肺塞栓症の 1 件は、ホスタマチニブ投与と事象発現との間に時間的関連性が認められており、ホスタマチニブとの関連が疑われる症例であった。残り 40 件はホスタマチニブと事象との因果関係判断に必要な十分な情報が得られていないことから、ホスタマチニブとの関連を判断することは困難である。このことから、海外製造販売後に報告された血栓症、塞栓症及び血栓塞栓症について、ホスタマチニブとの関連が疑われる症例は 3 例のみと判断した。また、最新の PSUR でも、血栓症、塞栓症及び血栓塞栓症は安全対策の検討が必要とされる安全性シグナルとして検出されていない。

本薬の作用機序は、ITP の抗血小板抗体産生の病的ループを遮断し、血小板の破壊を抑制するものであり、過剰な血小板数の増加が起こり難いと考えられる。国外第 II 相臨床試験（D4300-022 試験）で認められた本剤との関連が否定できない深部静脈血栓症及び血栓症の 2 例は、血小板数のオーバーシュートを認めた被験者とは別の被験者であり、血小板数以外のリスク要因を有していた。国内外第 III 相臨床試験で血栓症、塞栓症及び血栓塞栓症が発現した症例は一過性脳虚血性発作を認めた 1 例のみであった。

以上より、国内外臨床試験で血栓症、塞栓症及び血栓塞栓症が認められたが、作用機序や海外製造販売後の集積状況を踏まえても、血栓症、塞栓症及び血栓塞栓症がホスタマチニブのリスクとは考えられないことから、添付文書における注意喚起は不要と判断した。

ただし、一般的に血小板数が正常範囲を超えると血栓塞栓症の発現リスクが高まることが知られているため、血小板数が 250000/μL 超に増加した場合は、減量・休薬を検討するよう注意喚起する。

2.7.4.8 参考文献

1) 医薬品等の副作用の重篤度分類基準について．平成 4 年 6 月 29 日薬安第 80 号

2.7.4.9 付録

表 2.7.4.9-1 Adverse Events (AEs): Incidence by System Organ Class and Preferred Term (Subject Level) (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Any Adverse Events	130 (89.0%)
GASTROINTESTINAL DISORDERS	85 (58.2%)
Diarrhoea	53 (36.3%)
Nausea	28 (19.2%)
Vomiting	13 (8.9%)
Abdominal Pain	9 (6.2%)
Abdominal Pain Upper	8 (5.5%)
Constipation	8 (5.5%)
Dyspepsia	6 (4.1%)
Flatulence	6 (4.1%)
Gingival Bleeding	6 (4.1%)
Mouth Haemorrhage	6 (4.1%)
Oral Mucosal Blistering	6 (4.1%)
Abdominal Distension	4 (2.7%)
Gastrointestinal Haemorrhage	4 (2.7%)
Haematochezia	4 (2.7%)
Toothache	4 (2.7%)
Dysphagia	3 (2.1%)
Haemorrhoidal Haemorrhage	3 (2.1%)
Rectal Haemorrhage	3 (2.1%)
Abdominal Discomfort	2 (1.4%)
Frequent Bowel Movements	2 (1.4%)
Gastritis	2 (1.4%)
Gastrooesophageal Reflux Disease	2 (1.4%)
Haemorrhoids	2 (1.4%)
Stomatitis	2 (1.4%)
Abdominal Pain Lower	1 (0.7%)
Anal Fissure	1 (0.7%)
Ascites	1 (0.7%)
Bile Acid Malabsorption	1 (0.7%)
Cheilitis	1 (0.7%)
Dry Mouth	1 (0.7%)
Eructation	1 (0.7%)
Gastric Antral Vascular Ectasia	1 (0.7%)
Gastritis Erosive	1 (0.7%)
Gastrointestinal Disorder	1 (0.7%)
Inguinal Hernia	1 (0.7%)
Irritable Bowel Syndrome	1 (0.7%)
Lip Oedema	1 (0.7%)
Melaena	1 (0.7%)
Odynophagia	1 (0.7%)
Oesophageal Pain	1 (0.7%)
Oral Pain	1 (0.7%)
Palatal Disorder	1 (0.7%)
Retching	1 (0.7%)
INFECTIONS AND INFESTATIONS	64 (43.8%)
Upper Respiratory Tract Infection	18 (12.3%)
Nasopharyngitis	10 (6.8%)
Urinary Tract Infection	9 (6.2%)
Bronchitis	6 (4.1%)
Lower Respiratory Tract Infection	6 (4.1%)
Respiratory Tract Infection	6 (4.1%)
Viral Infection	6 (4.1%)
Pneumonia	5 (3.4%)
Gastroenteritis	4 (2.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Pharyngitis	4 (2.7%)
Tooth Infection	4 (2.7%)
Sepsis	3 (2.1%)
Cellulitis	2 (1.4%)
Ear Infection	2 (1.4%)
Eye Infection	2 (1.4%)
Gastrointestinal Infection	2 (1.4%)
Oral Candidiasis	2 (1.4%)
Oral Herpes	2 (1.4%)
Post Procedural Infection	2 (1.4%)
Sinusitis	2 (1.4%)
Abscess	1 (0.7%)
Arthritis Viral	1 (0.7%)
Bacteriuria	1 (0.7%)
Carbuncle	1 (0.7%)
Cellulitis Staphylococcal	1 (0.7%)
Diverticulitis	1 (0.7%)
Endocarditis Bacterial	1 (0.7%)
Erythema Induratum	1 (0.7%)
Escherichia Urinary Tract Infection	1 (0.7%)
Fungal Infection	1 (0.7%)
Fungal Skin Infection	1 (0.7%)
Gingivitis	1 (0.7%)
Herpes Simplex	1 (0.7%)
Herpes Zoster	1 (0.7%)
Infection	1 (0.7%)
Influenza	1 (0.7%)
Klebsiella Bacteraemia	1 (0.7%)
Laryngitis	1 (0.7%)
Mastoiditis	1 (0.7%)
Onychomycosis	1 (0.7%)
Otitis Media	1 (0.7%)
Pulpitis Dental	1 (0.7%)
Pyelonephritis Acute	1 (0.7%)
Rhinitis	1 (0.7%)
Subacute Endocarditis	1 (0.7%)
Tinea Infection	1 (0.7%)
Tonsillitis	1 (0.7%)
Tooth Abscess	1 (0.7%)
Tuberculosis	1 (0.7%)
Urinary Tract Infection Bacterial	1 (0.7%)
Urosepsis	1 (0.7%)
Viral Pharyngitis	1 (0.7%)
Viral Upper Respiratory Tract Infection	1 (0.7%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	50 (34.2%)
Epistaxis	27 (18.5%)
Cough	11 (7.5%)
Dyspnoea	8 (5.5%)
Oropharyngeal Pain	6 (4.1%)
Rhinorrhoea	4 (2.7%)
Nasal Congestion	3 (2.1%)
Dry Throat	2 (1.4%)
Dyspnoea Exertional	2 (1.4%)
Sleep Apnoea Syndrome	2 (1.4%)
Chronic Obstructive Pulmonary Disease	1 (0.7%)
Dysphonia	1 (0.7%)
Haemoptysis	1 (0.7%)
Hypoxia	1 (0.7%)
Nasal Inflammation	1 (0.7%)
Pleural Effusion	1 (0.7%)
Pulmonary Mass	1 (0.7%)
Upper Respiratory Tract Inflammation	1 (0.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	47 (32.2%)
Fatigue	14 (9.6%)
Pyrexia	10 (6.8%)
Chest Pain	9 (6.2%)
Oedema Peripheral	8 (5.5%)
Asthenia	7 (4.8%)
Peripheral Swelling	7 (4.8%)
Influenza Like Illness	6 (4.1%)
Chills	5 (3.4%)
Pain	3 (2.1%)
Chest Discomfort	2 (1.4%)
Feeling Cold	2 (1.4%)
Adverse Drug Reaction	1 (0.7%)
Facial Pain	1 (0.7%)
Gait Disturbance	1 (0.7%)
General Physical Health Deterioration	1 (0.7%)
Glassy Eyes	1 (0.7%)
Mucosal Haemorrhage	1 (0.7%)
Polyp	1 (0.7%)
Vessel Puncture Site Bruise	1 (0.7%)
NERVOUS SYSTEM DISORDERS	47 (32.2%)
Headache	22 (15.1%)
Dizziness	18 (12.3%)
Dysgeusia	4 (2.7%)
Hypoaesthesia	3 (2.1%)
Sciatica	3 (2.1%)
Memory Impairment	2 (1.4%)
Neuralgia	2 (1.4%)
Presyncope	2 (1.4%)
Cerebral Haemorrhage	1 (0.7%)
Disturbance In Attention	1 (0.7%)
Dysarthria	1 (0.7%)
Haemorrhagic Stroke	1 (0.7%)
Hypogeusia	1 (0.7%)
Lethargy	1 (0.7%)
Loss Of Consciousness	1 (0.7%)
Migraine	1 (0.7%)
Neuropathy Peripheral	1 (0.7%)
Paraesthesia	1 (0.7%)
Peroneal Nerve Palsy	1 (0.7%)
Restless Legs Syndrome	1 (0.7%)
Somnolence	1 (0.7%)
Syncope	1 (0.7%)
Transient Ischaemic Attack	1 (0.7%)
INVESTIGATIONS	46 (31.5%)
Alanine Aminotransferase Increased	14 (9.6%)
Aspartate Aminotransferase Increased	10 (6.8%)
Blood Pressure Increased	7 (4.8%)
Platelet Count Decreased	6 (4.1%)
Hepatic Enzyme Increased	5 (3.4%)
Liver Function Test Abnormal	4 (2.7%)
Blood Bilirubin Increased	3 (2.1%)
Blood Lactate Dehydrogenase Increased	3 (2.1%)
Blood Creatinine Increased	2 (1.4%)
Blood Pressure Diastolic Increased	2 (1.4%)
Neutrophil Count Decreased	2 (1.4%)
Transaminases Increased	2 (1.4%)
Weight Decreased	2 (1.4%)
Weight Increased	2 (1.4%)
Angiogram	1 (0.7%)
Blood Alkaline Phosphatase Increased	1 (0.7%)
Blood Bicarbonate Increased	1 (0.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Blood Glucose Increased	1 (0.7%)
Blood Potassium Decreased	1 (0.7%)
Blood Pressure Diastolic Abnormal	1 (0.7%)
Blood Pressure Measurement	1 (0.7%)
Blood Pressure Systolic Increased	1 (0.7%)
Blood Urea Increased	1 (0.7%)
C-Reactive Protein Increased	1 (0.7%)
Cardiac Murmur	1 (0.7%)
Gamma-Glutamyltransferase Increased	1 (0.7%)
Globulins Increased	1 (0.7%)
Haemoglobin Decreased	1 (0.7%)
Heart Rate Increased	1 (0.7%)
Lymphocyte Count Decreased	1 (0.7%)
Platelet Count Increased	1 (0.7%)
Troponin Increased	1 (0.7%)
Vitamin B12 Increased	1 (0.7%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	45 (30.8%)
Petechiae	22 (15.1%)
Rash	10 (6.8%)
Ecchymosis	4 (2.7%)
Blood Blister	3 (2.1%)
Pruritus	3 (2.1%)
Skin Lesion	3 (2.1%)
Dermatitis Allergic	2 (1.4%)
Dry Skin	2 (1.4%)
Eczema	2 (1.4%)
Erythema	2 (1.4%)
Hair Colour Changes	2 (1.4%)
Hyperhidrosis	2 (1.4%)
Purpura	2 (1.4%)
Swelling Face	2 (1.4%)
Actinic Keratosis	1 (0.7%)
Alopecia	1 (0.7%)
Blister	1 (0.7%)
Haemorrhage Subcutaneous	1 (0.7%)
Hypertrichosis	1 (0.7%)
Nail Discolouration	1 (0.7%)
Nail Disorder	1 (0.7%)
Papule	1 (0.7%)
Photosensitivity Reaction	1 (0.7%)
Precancerous Skin Lesion	1 (0.7%)
Rash Erythematous	1 (0.7%)
Rash Macular	1 (0.7%)
Rash Papular	1 (0.7%)
Skin Hypopigmentation	1 (0.7%)
Skin Ulcer	1 (0.7%)
Urticaria	1 (0.7%)
VASCULAR DISORDERS	40 (27.4%)
Hypertension	32 (21.9%)
Haematoma	4 (2.7%)
Haemorrhage	3 (2.1%)
Hypotension	2 (1.4%)
Aortic Stenosis	1 (0.7%)
Blood Pressure Inadequately Controlled	1 (0.7%)
Hot Flush	1 (0.7%)
Hypertensive Crisis	1 (0.7%)
Peripheral Venous Disease	1 (0.7%)
Phlebitis Superficial	1 (0.7%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	32 (21.9%)
Thrombocytopenia	11 (7.5%)
Anaemia	8 (5.5%)
Neutropenia	8 (5.5%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Leukopenia	3 (2.1%)
Increased Tendency To Bruise	2 (1.4%)
Lymphadenopathy	2 (1.4%)
Microcytic Anaemia	2 (1.4%)
Thrombocytosis	2 (1.4%)
Aplastic Anaemia	1 (0.7%)
Febrile Neutropenia	1 (0.7%)
Immune Thrombocytopenic Purpura	1 (0.7%)
Leukocytosis	1 (0.7%)
Polycythaemia	1 (0.7%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	32 (21.9%)
Arthralgia	9 (6.2%)
Myalgia	8 (5.5%)
Back Pain	6 (4.1%)
Muscle Spasms	6 (4.1%)
Joint Swelling	4 (2.7%)
Musculoskeletal Pain	4 (2.7%)
Neck Pain	4 (2.7%)
Pain In Extremity	4 (2.7%)
Arthritis	2 (1.4%)
Chondrocalcinosis Pyrophosphate	2 (1.4%)
Muscular Weakness	2 (1.4%)
Musculoskeletal Chest Pain	2 (1.4%)
Osteoporosis	2 (1.4%)
Ankylosing Spondylitis	1 (0.7%)
Bone Lesion	1 (0.7%)
Bone Pain	1 (0.7%)
Haemarthrosis	1 (0.7%)
Mobility Decreased	1 (0.7%)
Plantar Fasciitis	1 (0.7%)
Rotator Cuff Syndrome	1 (0.7%)
Spinal Column Stenosis	1 (0.7%)
Tendon Sheath Disorder	1 (0.7%)
Tendonitis	1 (0.7%)
Trigger Finger	1 (0.7%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	24 (16.4%)
Contusion	17 (11.6%)
Fall	3 (2.1%)
Animal Bite	2 (1.4%)
Joint Injury	2 (1.4%)
Anaphylactic Transfusion Reaction	1 (0.7%)
Graft Complication	1 (0.7%)
Head Injury	1 (0.7%)
Limb Injury	1 (0.7%)
Muscle Injury	1 (0.7%)
Procedural Pain	1 (0.7%)
Scratch	1 (0.7%)
Skin Wound	1 (0.7%)
Thoracic Vertebral Fracture	1 (0.7%)
METABOLISM AND NUTRITION DISORDERS	14 (9.6%)
Hypokalaemia	5 (3.4%)
Decreased Appetite	3 (2.1%)
Dehydration	1 (0.7%)
Fluid Overload	1 (0.7%)
Glucose Tolerance Impaired	1 (0.7%)
Gout	1 (0.7%)
Hyperglycaemia	1 (0.7%)
Hyperkalaemia	1 (0.7%)
Hypernatraemia	1 (0.7%)
Hyperuricaemia	1 (0.7%)
Hypomagnesaemia	1 (0.7%)
Hypophosphataemia	1 (0.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Iron Deficiency	1 (0.7%)
Vitamin D Deficiency	1 (0.7%)
CARDIAC DISORDERS	10 (6.8%)
Tachycardia	3 (2.1%)
Atrial Fibrillation	2 (1.4%)
Cardiac Failure Congestive	2 (1.4%)
Angina Pectoris	1 (0.7%)
Aortic Valve Incompetence	1 (0.7%)
Cardiac Failure Chronic	1 (0.7%)
Cardio-Respiratory Arrest	1 (0.7%)
Mitral Valve Incompetence	1 (0.7%)
Palpitations	1 (0.7%)
Tricuspid Valve Incompetence	1 (0.7%)
Ventricular Extrasystoles	1 (0.7%)
EYE DISORDERS	9 (6.2%)
Conjunctival Haemorrhage	2 (1.4%)
Eyelid Oedema	2 (1.4%)
Blepharitis	1 (0.7%)
Eye Disorder	1 (0.7%)
Eye Haemorrhage	1 (0.7%)
Eye Pain	1 (0.7%)
Retinal Tear	1 (0.7%)
Vision Blurred	1 (0.7%)
RENAL AND URINARY DISORDERS	9 (6.2%)
Nephrolithiasis	4 (2.7%)
Pollakiuria	2 (1.4%)
Acute Kidney Injury	1 (0.7%)
Chronic Kidney Disease	1 (0.7%)
Haematuria	1 (0.7%)
Hypertonic Bladder	1 (0.7%)
Leukocyturia	1 (0.7%)
Renal Cyst	1 (0.7%)
Renal Failure	1 (0.7%)
PSYCHIATRIC DISORDERS	8 (5.5%)
Insomnia	4 (2.7%)
Anxiety	2 (1.4%)
Depressed Mood	1 (0.7%)
Depression	1 (0.7%)
Mental Status Changes	1 (0.7%)
Restlessness	1 (0.7%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	8 (5.5%)
Vaginal Haemorrhage	3 (2.1%)
Menorrhagia	2 (1.4%)
Breast Mass	1 (0.7%)
Erectile Dysfunction	1 (0.7%)
Uterine Polyp	1 (0.7%)
Vulvovaginal Pain	1 (0.7%)
EAR AND LABYRINTH DISORDERS	6 (4.1%)
Ear Haemorrhage	1 (0.7%)
Excessive Cerumen Production	1 (0.7%)
Otorrhoea	1 (0.7%)
Tinnitus	1 (0.7%)
Tympanic Membrane Disorder	1 (0.7%)
Tympanic Membrane Perforation	1 (0.7%)
Vertigo	1 (0.7%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	6 (4.1%)
Squamous Cell Carcinoma Of Skin	3 (2.1%)
Basal Cell Carcinoma	2 (1.4%)
Basosquamous Carcinoma Of Skin	1 (0.7%)
Cholesteatoma	1 (0.7%)
Plasma Cell Myeloma	1 (0.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
HEPATOBILIARY DISORDERS	4 (2.7%)
Cholecystitis	1 (0.7%)
Hepatic Cirrhosis	1 (0.7%)
Hepatic Cyst	1 (0.7%)
Hyperbilirubinaemia	1 (0.7%)
Portal Hypertension	1 (0.7%)
SURGICAL AND MEDICAL PROCEDURES	3 (2.1%)
Micrographic Skin Surgery	1 (0.7%)
Rotator Cuff Repair	1 (0.7%)
Tooth Extraction	1 (0.7%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	2 (1.4%)
Dacryostenosis Congenital	1 (0.7%)
Hydrocele	1 (0.7%)
IMMUNE SYSTEM DISORDERS	2 (1.4%)
Allergy To Chemicals	1 (0.7%)
Allergy To Metals	1 (0.7%)
Drug Hypersensitivity	1 (0.7%)
ENDOCRINE DISORDERS	1 (0.7%)
Cushingoid	1 (0.7%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.2.1)

表 2.7.4.9-2 Adverse Events (AEs): Incidence by System Organ Class/Preferred Term and Age Group (Subject Level) (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Age < 65 years

System Organ Class Preferred Term	Fostamatinib (N=109) n (%)
Any Adverse Events	95 (87.2%)
GASTROINTESTINAL DISORDERS	62 (56.9%)
Diarrhoea	37 (33.9%)
Nausea	22 (20.2%)
Vomiting	11 (10.1%)
Abdominal Pain	9 (8.3%)
Abdominal Pain Upper	8 (7.3%)
Constipation	6 (5.5%)
Dyspepsia	5 (4.6%)
Flatulence	5 (4.6%)
Mouth Haemorrhage	5 (4.6%)
Oral Mucosal Blistering	5 (4.6%)
Gingival Bleeding	4 (3.7%)
Haematochezia	4 (3.7%)
Abdominal Distension	3 (2.8%)
Gastrointestinal Haemorrhage	3 (2.8%)
Toothache	3 (2.8%)
Abdominal Discomfort	2 (1.8%)
Dysphagia	2 (1.8%)
Gastritis	2 (1.8%)
Gastrooesophageal Reflux Disease	2 (1.8%)
Haemorrhoidal Haemorrhage	2 (1.8%)
Rectal Haemorrhage	2 (1.8%)
Stomatitis	2 (1.8%)
Abdominal Pain Lower	1 (0.9%)
Anal Fissure	1 (0.9%)
Bile Acid Malabsorption	1 (0.9%)
Eructation	1 (0.9%)
Frequent Bowel Movements	1 (0.9%)
Gastritis Erosive	1 (0.9%)
Haemorrhoids	1 (0.9%)
Odynophagia	1 (0.9%)
Oesophageal Pain	1 (0.9%)
Palatal Disorder	1 (0.9%)
Retching	1 (0.9%)
INFECTIONS AND INFESTATIONS	53 (48.6%)
Upper Respiratory Tract Infection	16 (14.7%)
Nasopharyngitis	8 (7.3%)
Urinary Tract Infection	7 (6.4%)
Respiratory Tract Infection	6 (5.5%)
Lower Respiratory Tract Infection	5 (4.6%)
Viral Infection	5 (4.6%)
Bronchitis	4 (3.7%)
Pharyngitis	4 (3.7%)
Pneumonia	4 (3.7%)
Tooth Infection	4 (3.7%)
Gastroenteritis	3 (2.8%)
Ear Infection	2 (1.8%)
Gastrointestinal Infection	2 (1.8%)
Oral Candidiasis	2 (1.8%)
Oral Herpes	2 (1.8%)
Post Procedural Infection	2 (1.8%)
Sepsis	2 (1.8%)
Sinusitis	2 (1.8%)
Arthritis Viral	1 (0.9%)
Carbuncle	1 (0.9%)
Cellulitis	1 (0.9%)

System Organ Class Preferred Term	Fostamatinib (N=109) n (%)
Diverticulitis	1 (0.9%)
Erythema Induratum	1 (0.9%)
Eye Infection	1 (0.9%)
Gingivitis	1 (0.9%)
Herpes Simplex	1 (0.9%)
Herpes Zoster	1 (0.9%)
Infection	1 (0.9%)
Influenza	1 (0.9%)
Klebsiella Bacteraemia	1 (0.9%)
Laryngitis	1 (0.9%)
Pulpitis Dental	1 (0.9%)
Pyelonephritis Acute	1 (0.9%)
Rhinitis	1 (0.9%)
Tonsillitis	1 (0.9%)
Tooth Abscess	1 (0.9%)
Tuberculosis	1 (0.9%)
Viral Pharyngitis	1 (0.9%)
Viral Upper Respiratory Tract Infection	1 (0.9%)
NERVOUS SYSTEM DISORDERS	36 (33.0%)
Headache	20 (18.3%)
Dizziness	10 (9.2%)
Dysgeusia	3 (2.8%)
Hypoaesthesia	2 (1.8%)
Sciatica	2 (1.8%)
Disturbance In Attention	1 (0.9%)
Lethargy	1 (0.9%)
Loss Of Consciousness	1 (0.9%)
Memory Impairment	1 (0.9%)
Migraine	1 (0.9%)
Neuralgia	1 (0.9%)
Neuropathy Peripheral	1 (0.9%)
Presyncope	1 (0.9%)
Restless Legs Syndrome	1 (0.9%)
Syncope	1 (0.9%)
Transient Ischaemic Attack	1 (0.9%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	36 (33.0%)
Petechiae	18 (16.5%)
Rash	7 (6.4%)
Pruritus	3 (2.8%)
Blood Blister	2 (1.8%)
Dry Skin	2 (1.8%)
Eczema	2 (1.8%)
Erythema	2 (1.8%)
Hair Colour Changes	2 (1.8%)
Hyperhidrosis	2 (1.8%)
Purpura	2 (1.8%)
Swelling Face	2 (1.8%)
Actinic Keratosis	1 (0.9%)
Alopecia	1 (0.9%)
Dermatitis Allergic	1 (0.9%)
Ecchymosis	1 (0.9%)
Haemorrhage Subcutaneous	1 (0.9%)
Hypertrichosis	1 (0.9%)
Nail Discolouration	1 (0.9%)
Nail Disorder	1 (0.9%)
Photosensitivity Reaction	1 (0.9%)
Rash Erythematous	1 (0.9%)
Rash Papular	1 (0.9%)
Skin Hypopigmentation	1 (0.9%)
Skin Lesion	1 (0.9%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	35 (32.1%)
Epistaxis	19 (17.4%)

System Organ Class Preferred Term	Fostamatinib (N=109) n (%)
Cough	8 (7.3%)
Dyspnoea	6 (5.5%)
Oropharyngeal Pain	5 (4.6%)
Rhinorrhoea	3 (2.8%)
Dry Throat	2 (1.8%)
Sleep Apnoea Syndrome	2 (1.8%)
Chronic Obstructive Pulmonary Disease	1 (0.9%)
Haemoptysis	1 (0.9%)
Hypoxia	1 (0.9%)
Pulmonary Mass	1 (0.9%)
Upper Respiratory Tract Inflammation	1 (0.9%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	34 (31.2%)
Pyrexia	9 (8.3%)
Fatigue	8 (7.3%)
Chest Pain	7 (6.4%)
Influenza Like Illness	6 (5.5%)
Asthenia	5 (4.6%)
Chills	4 (3.7%)
Oedema Peripheral	4 (3.7%)
Peripheral Swelling	4 (3.7%)
Pain	3 (2.8%)
Feeling Cold	2 (1.8%)
Adverse Drug Reaction	1 (0.9%)
Chest Discomfort	1 (0.9%)
Facial Pain	1 (0.9%)
General Physical Health Deterioration	1 (0.9%)
Mucosal Haemorrhage	1 (0.9%)
Polyp	1 (0.9%)
Vessel Puncture Site Bruise	1 (0.9%)
INVESTIGATIONS	32 (29.4%)
Alanine Aminotransferase Increased	10 (9.2%)
Aspartate Aminotransferase Increased	8 (7.3%)
Hepatic Enzyme Increased	5 (4.6%)
Platelet Count Decreased	4 (3.7%)
Blood Bilirubin Increased	3 (2.8%)
Blood Pressure Increased	3 (2.8%)
Blood Lactate Dehydrogenase Increased	2 (1.8%)
Blood Pressure Diastolic Increased	2 (1.8%)
Liver Function Test Abnormal	2 (1.8%)
Weight Increased	2 (1.8%)
Angiogram	1 (0.9%)
Blood Alkaline Phosphatase Increased	1 (0.9%)
Blood Potassium Decreased	1 (0.9%)
Blood Pressure Diastolic Abnormal	1 (0.9%)
Blood Pressure Systolic Increased	1 (0.9%)
C-Reactive Protein Increased	1 (0.9%)
Cardiac Murmur	1 (0.9%)
Gamma-Glutamyltransferase Increased	1 (0.9%)
Heart Rate Increased	1 (0.9%)
Lymphocyte Count Decreased	1 (0.9%)
Neutrophil Count Decreased	1 (0.9%)
Platelet Count Increased	1 (0.9%)
Transaminases Increased	1 (0.9%)
Vitamin B12 Increased	1 (0.9%)
Weight Decreased	1 (0.9%)
VASCULAR DISORDERS	28 (25.7%)
Hypertension	22 (20.2%)
Haemorrhage	2 (1.8%)
Haematoma	1 (0.9%)
Hot Flush	1 (0.9%)
Hypotension	1 (0.9%)
Peripheral Venous Disease	1 (0.9%)

System Organ Class Preferred Term	Fostamatinib (N=109) n (%)
Phlebitis Superficial	1 (0.9%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	26 (23.9%)
Anaemia	7 (6.4%)
Thrombocytopenia	7 (6.4%)
Neutropenia	5 (4.6%)
Increased Tendency To Bruise	2 (1.8%)
Leukopenia	2 (1.8%)
Lymphadenopathy	2 (1.8%)
Microcytic Anaemia	2 (1.8%)
Febrile Neutropenia	1 (0.9%)
Leukocytosis	1 (0.9%)
Polycythaemia	1 (0.9%)
Thrombocytosis	1 (0.9%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	26 (23.9%)
Myalgia	7 (6.4%)
Back Pain	6 (5.5%)
Arthralgia	5 (4.6%)
Muscle Spasms	4 (3.7%)
Pain In Extremity	3 (2.8%)
Joint Swelling	2 (1.8%)
Musculoskeletal Chest Pain	2 (1.8%)
Musculoskeletal Pain	2 (1.8%)
Neck Pain	2 (1.8%)
Ankylosing Spondylitis	1 (0.9%)
Bone Pain	1 (0.9%)
Muscular Weakness	1 (0.9%)
Osteoporosis	1 (0.9%)
Tendonitis	1 (0.9%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	17 (15.6%)
Contusion	12 (11.0%)
Animal Bite	2 (1.8%)
Anaphylactic Transfusion Reaction	1 (0.9%)
Limb Injury	1 (0.9%)
Procedural Pain	1 (0.9%)
Thoracic Vertebral Fracture	1 (0.9%)
METABOLISM AND NUTRITION DISORDERS	7 (6.4%)
Decreased Appetite	2 (1.8%)
Fluid Overload	1 (0.9%)
Gout	1 (0.9%)
Hyperglycaemia	1 (0.9%)
Iron Deficiency	1 (0.9%)
Vitamin D Deficiency	1 (0.9%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	7 (6.4%)
Vaginal Haemorrhage	3 (2.8%)
Menorrhagia	2 (1.8%)
Erectile Dysfunction	1 (0.9%)
Uterine Polyp	1 (0.9%)
Vulvovaginal Pain	1 (0.9%)
CARDIAC DISORDERS	5 (4.6%)
Tachycardia	3 (2.8%)
Cardiac Failure Congestive	1 (0.9%)
Ventricular Extrasystoles	1 (0.9%)
EYE DISORDERS	5 (4.6%)
Conjunctival Haemorrhage	1 (0.9%)
Eye Disorder	1 (0.9%)
Eye Haemorrhage	1 (0.9%)
Eye Pain	1 (0.9%)
Eyelid Oedema	1 (0.9%)
Vision Blurred	1 (0.9%)
RENAL AND URINARY DISORDERS	5 (4.6%)
Nephrolithiasis	3 (2.8%)
Haematuria	1 (0.9%)

System Organ Class Preferred Term	Fostamatinib (N=109) n (%)
Hypertonic Bladder	1 (0.9%)
Renal Cyst	1 (0.9%)
EAR AND LABYRINTH DISORDERS	4 (3.7%)
Ear Haemorrhage	1 (0.9%)
Excessive Cerumen Production	1 (0.9%)
Tinnitus	1 (0.9%)
Tympanic Membrane Disorder	1 (0.9%)
PSYCHIATRIC DISORDERS	4 (3.7%)
Insomnia	2 (1.8%)
Anxiety	1 (0.9%)
Depressed Mood	1 (0.9%)
Depression	1 (0.9%)
HEPATOBILIARY DISORDERS	3 (2.8%)
Cholecystitis	1 (0.9%)
Hepatic Cyst	1 (0.9%)
Hyperbilirubinaemia	1 (0.9%)
IMMUNE SYSTEM DISORDERS	2 (1.8%)
Allergy To Chemicals	1 (0.9%)
Allergy To Metals	1 (0.9%)
Drug Hypersensitivity	1 (0.9%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	2 (1.8%)
Basal Cell Carcinoma	1 (0.9%)
Squamous Cell Carcinoma Of Skin	1 (0.9%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.9%)
Hydrocele	1 (0.9%)
ENDOCRINE DISORDERS	1 (0.9%)
Cushingoid	1 (0.9%)
SURGICAL AND MEDICAL PROCEDURES	1 (0.9%)
Tooth Extraction	1 (0.9%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the age and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.2.1.1)

Age >= 65 years

System Organ Class Preferred Term	Fostamatinib (N=37) n (%)
Any Adverse Events	35 (94.6%)
GASTROINTESTINAL DISORDERS	23 (62.2%)
Diarrhoea	16 (43.2%)
Nausea	6 (16.2%)
Constipation	2 (5.4%)
Gingival Bleeding	2 (5.4%)
Vomiting	2 (5.4%)
Abdominal Distension	1 (2.7%)
Ascites	1 (2.7%)
Cheilitis	1 (2.7%)
Dry Mouth	1 (2.7%)
Dyspepsia	1 (2.7%)
Dysphagia	1 (2.7%)
Flatulence	1 (2.7%)
Frequent Bowel Movements	1 (2.7%)
Gastric Antral Vascular Ectasia	1 (2.7%)
Gastrointestinal Disorder	1 (2.7%)
Gastrointestinal Haemorrhage	1 (2.7%)
Haemorrhoidal Haemorrhage	1 (2.7%)
Haemorrhoids	1 (2.7%)
Inguinal Hernia	1 (2.7%)
Irritable Bowel Syndrome	1 (2.7%)
Lip Oedema	1 (2.7%)
Melaena	1 (2.7%)

System Organ Class Preferred Term	Fostamatinib (N=37) n (%)
Mouth Haemorrhage	1 (2.7%)
Oral Mucosal Blistering	1 (2.7%)
Oral Pain	1 (2.7%)
Rectal Haemorrhage	1 (2.7%)
Toothache	1 (2.7%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	15 (40.5%)
Epistaxis	8 (21.6%)
Cough	3 (8.1%)
Nasal Congestion	3 (8.1%)
Dyspnoea	2 (5.4%)
Dyspnoea Exertional	2 (5.4%)
Dysphonia	1 (2.7%)
Nasal Inflammation	1 (2.7%)
Oropharyngeal Pain	1 (2.7%)
Pleural Effusion	1 (2.7%)
Rhinorrhoea	1 (2.7%)
INVESTIGATIONS	14 (37.8%)
Alanine Aminotransferase Increased	4 (10.8%)
Blood Pressure Increased	4 (10.8%)
Aspartate Aminotransferase Increased	2 (5.4%)
Blood Creatinine Increased	2 (5.4%)
Liver Function Test Abnormal	2 (5.4%)
Platelet Count Decreased	2 (5.4%)
Blood Bicarbonate Increased	1 (2.7%)
Blood Glucose Increased	1 (2.7%)
Blood Lactate Dehydrogenase Increased	1 (2.7%)
Blood Pressure Measurement	1 (2.7%)
Blood Urea Increased	1 (2.7%)
Globulins Increased	1 (2.7%)
Haemoglobin Decreased	1 (2.7%)
Neutrophil Count Decreased	1 (2.7%)
Transaminases Increased	1 (2.7%)
Troponin Increased	1 (2.7%)
Weight Decreased	1 (2.7%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	13 (35.1%)
Fatigue	6 (16.2%)
Oedema Peripheral	4 (10.8%)
Peripheral Swelling	3 (8.1%)
Asthenia	2 (5.4%)
Chest Pain	2 (5.4%)
Chest Discomfort	1 (2.7%)
Chills	1 (2.7%)
Gait Disturbance	1 (2.7%)
Glassy Eyes	1 (2.7%)
Pyrexia	1 (2.7%)
VASCULAR DISORDERS	12 (32.4%)
Hypertension	10 (27.0%)
Haematoma	3 (8.1%)
Aortic Stenosis	1 (2.7%)
Blood Pressure Inadequately Controlled	1 (2.7%)
Haemorrhage	1 (2.7%)
Hypertensive Crisis	1 (2.7%)
Hypotension	1 (2.7%)
INFECTIONS AND INFESTATIONS	11 (29.7%)
Bronchitis	2 (5.4%)
Nasopharyngitis	2 (5.4%)
Upper Respiratory Tract Infection	2 (5.4%)
Urinary Tract Infection	2 (5.4%)
Abscess	1 (2.7%)
Bacteriuria	1 (2.7%)
Cellulitis	1 (2.7%)
Cellulitis Staphylococcal	1 (2.7%)

System Organ Class Preferred Term	Fostamatinib (N=37) n (%)
Endocarditis Bacterial	1 (2.7%)
Escherichia Urinary Tract Infection	1 (2.7%)
Eye Infection	1 (2.7%)
Fungal Infection	1 (2.7%)
Fungal Skin Infection	1 (2.7%)
Gastroenteritis	1 (2.7%)
Lower Respiratory Tract Infection	1 (2.7%)
Mastoiditis	1 (2.7%)
Onychomycosis	1 (2.7%)
Otitis Media	1 (2.7%)
Pneumonia	1 (2.7%)
Sepsis	1 (2.7%)
Subacute Endocarditis	1 (2.7%)
Tinea Infection	1 (2.7%)
Urinary Tract Infection Bacterial	1 (2.7%)
Urosepsis	1 (2.7%)
Viral Infection	1 (2.7%)
NERVOUS SYSTEM DISORDERS	11 (29.7%)
Dizziness	8 (21.6%)
Headache	2 (5.4%)
Cerebral Haemorrhage	1 (2.7%)
Dysarthria	1 (2.7%)
Dysgeusia	1 (2.7%)
Haemorrhagic Stroke	1 (2.7%)
Hypoaesthesia	1 (2.7%)
Hypogeusia	1 (2.7%)
Memory Impairment	1 (2.7%)
Neuralgia	1 (2.7%)
Paraesthesia	1 (2.7%)
Peroneal Nerve Palsy	1 (2.7%)
Presyncope	1 (2.7%)
Sciatica	1 (2.7%)
Somnolence	1 (2.7%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	9 (24.3%)
Petechiae	4 (10.8%)
Ecchymosis	3 (8.1%)
Rash	3 (8.1%)
Skin Lesion	2 (5.4%)
Blister	1 (2.7%)
Blood Blister	1 (2.7%)
Dermatitis Allergic	1 (2.7%)
Papule	1 (2.7%)
Precancerous Skin Lesion	1 (2.7%)
Rash Macular	1 (2.7%)
Skin Ulcer	1 (2.7%)
Urticaria	1 (2.7%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	7 (18.9%)
Contusion	5 (13.5%)
Fall	3 (8.1%)
Joint Injury	2 (5.4%)
Graft Complication	1 (2.7%)
Head Injury	1 (2.7%)
Muscle Injury	1 (2.7%)
Scratch	1 (2.7%)
Skin Wound	1 (2.7%)
METABOLISM AND NUTRITION DISORDERS	7 (18.9%)
Hypokalaemia	5 (13.5%)
Decreased Appetite	1 (2.7%)
Dehydration	1 (2.7%)
Glucose Tolerance Impaired	1 (2.7%)
Hyperkalaemia	1 (2.7%)
Hypernatraemia	1 (2.7%)

System Organ Class Preferred Term	Fostamatinib (N=37) n (%)
Hyperuricaemia	1 (2.7%)
Hypomagnesaemia	1 (2.7%)
Hypophosphataemia	1 (2.7%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	6 (16.2%)
Thrombocytopenia	4 (10.8%)
Neutropenia	3 (8.1%)
Anaemia	1 (2.7%)
Aplastic Anaemia	1 (2.7%)
Immune Thrombocytopenic Purpura	1 (2.7%)
Leukopenia	1 (2.7%)
Thrombocytosis	1 (2.7%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	6 (16.2%)
Arthralgia	4 (10.8%)
Arthritis	2 (5.4%)
Chondrocalcinosis Pyrophosphate	2 (5.4%)
Joint Swelling	2 (5.4%)
Muscle Spasms	2 (5.4%)
Musculoskeletal Pain	2 (5.4%)
Neck Pain	2 (5.4%)
Bone Lesion	1 (2.7%)
Haemarthrosis	1 (2.7%)
Mobility Decreased	1 (2.7%)
Muscular Weakness	1 (2.7%)
Myalgia	1 (2.7%)
Osteoporosis	1 (2.7%)
Pain In Extremity	1 (2.7%)
Plantar Fasciitis	1 (2.7%)
Rotator Cuff Syndrome	1 (2.7%)
Spinal Column Stenosis	1 (2.7%)
Tendon Sheath Disorder	1 (2.7%)
Trigger Finger	1 (2.7%)
CARDIAC DISORDERS	5 (13.5%)
Atrial Fibrillation	2 (5.4%)
Angina Pectoris	1 (2.7%)
Aortic Valve Incompetence	1 (2.7%)
Cardiac Failure Chronic	1 (2.7%)
Cardiac Failure Congestive	1 (2.7%)
Cardio-Respiratory Arrest	1 (2.7%)
Mitral Valve Incompetence	1 (2.7%)
Palpitations	1 (2.7%)
Tricuspid Valve Incompetence	1 (2.7%)
EYE DISORDERS	4 (10.8%)
Blepharitis	1 (2.7%)
Conjunctival Haemorrhage	1 (2.7%)
Eyelid Oedema	1 (2.7%)
Retinal Tear	1 (2.7%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	4 (10.8%)
Squamous Cell Carcinoma Of Skin	2 (5.4%)
Basal Cell Carcinoma	1 (2.7%)
Basosquamous Carcinoma Of Skin	1 (2.7%)
Cholesteatoma	1 (2.7%)
Plasma Cell Myeloma	1 (2.7%)
PSYCHIATRIC DISORDERS	4 (10.8%)
Insomnia	2 (5.4%)
Anxiety	1 (2.7%)
Mental Status Changes	1 (2.7%)
Restlessness	1 (2.7%)
RENAL AND URINARY DISORDERS	4 (10.8%)
Pollakiuria	2 (5.4%)
Acute Kidney Injury	1 (2.7%)
Chronic Kidney Disease	1 (2.7%)

System Organ Class Preferred Term	Fostamatinib (N=37) n (%)
Leukocyturia	1 (2.7%)
Nephrolithiasis	1 (2.7%)
Renal Failure	1 (2.7%)
EAR AND LABYRINTH DISORDERS	2 (5.4%)
Otorrhoea	1 (2.7%)
Tympanic Membrane Perforation	1 (2.7%)
Vertigo	1 (2.7%)
SURGICAL AND MEDICAL PROCEDURES	2 (5.4%)
Micrographic Skin Surgery	1 (2.7%)
Rotator Cuff Repair	1 (2.7%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (2.7%)
Dacryostenosis Congenital	1 (2.7%)
HEPATOBILIARY DISORDERS	1 (2.7%)
Hepatic Cirrhosis	1 (2.7%)
Portal Hypertension	1 (2.7%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (2.7%)
Breast Mass	1 (2.7%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the age and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.2.1.1)

表 2.7.4.9-3 Adverse Events (AEs): Incidence by System Organ Class/Preferred Term and Gender (Subject Level) (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Males

System Organ Class Preferred Term	Fostamatinib (N=59) n (%)
Any Adverse Events	53 (89.8%)
GASTROINTESTINAL DISORDERS	29 (49.2%)
Diarrhoea	19 (32.2%)
Nausea	5 (8.5%)
Flatulence	4 (6.8%)
Vomiting	4 (6.8%)
Abdominal Pain Upper	3 (5.1%)
Gastrointestinal Haemorrhage	2 (3.4%)
Haematochezia	2 (3.4%)
Mouth Haemorrhage	2 (3.4%)
Abdominal Discomfort	1 (1.7%)
Abdominal Distension	1 (1.7%)
Abdominal Pain	1 (1.7%)
Ascites	1 (1.7%)
Constipation	1 (1.7%)
Eructation	1 (1.7%)
Gastritis	1 (1.7%)
Inguinal Hernia	1 (1.7%)
Oral Mucosal Blistering	1 (1.7%)
Oral Pain	1 (1.7%)
Toothache	1 (1.7%)
INFECTIONS AND INFESTATIONS	23 (39.0%)
Upper Respiratory Tract Infection	5 (8.5%)
Respiratory Tract Infection	4 (6.8%)
Nasopharyngitis	3 (5.1%)
Viral Infection	3 (5.1%)
Gastrointestinal Infection	2 (3.4%)
Pneumonia	2 (3.4%)
Bronchitis	1 (1.7%)
Cellulitis Staphylococcal	1 (1.7%)
Diverticulitis	1 (1.7%)
Fungal Skin Infection	1 (1.7%)
Gastroenteritis	1 (1.7%)
Laryngitis	1 (1.7%)
Lower Respiratory Tract Infection	1 (1.7%)
Oral Candidiasis	1 (1.7%)
Oral Herpes	1 (1.7%)
Pulpitis Dental	1 (1.7%)
Pyelonephritis Acute	1 (1.7%)
Tinea Infection	1 (1.7%)
Tooth Abscess	1 (1.7%)
Tooth Infection	1 (1.7%)
Urinary Tract Infection	1 (1.7%)
INVESTIGATIONS	17 (28.8%)
Alanine Aminotransferase Increased	5 (8.5%)
Aspartate Aminotransferase Increased	3 (5.1%)
Blood Pressure Increased	3 (5.1%)
Hepatic Enzyme Increased	3 (5.1%)
Platelet Count Decreased	2 (3.4%)
Blood Bilirubin Increased	1 (1.7%)
Blood Lactate Dehydrogenase Increased	1 (1.7%)
Blood Pressure Diastolic Abnormal	1 (1.7%)
Blood Pressure Measurement	1 (1.7%)
C-Reactive Protein Increased	1 (1.7%)
Gamma-Glutamyltransferase Increased	1 (1.7%)
Lymphocyte Count Decreased	1 (1.7%)
Neutrophil Count Decreased	1 (1.7%)

System Organ Class Preferred Term	Fostamatinib (N=59) n (%)
Weight Decreased	1 (1.7%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	17 (28.8%)
Epistaxis	10 (16.9%)
Oropharyngeal Pain	2 (3.4%)
Rhinorrhoea	2 (3.4%)
Cough	1 (1.7%)
Dry Throat	1 (1.7%)
Dyspnoea	1 (1.7%)
Nasal Congestion	1 (1.7%)
Pleural Effusion	1 (1.7%)
Sleep Apnoea Syndrome	1 (1.7%)
Upper Respiratory Tract Inflammation	1 (1.7%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	17 (28.8%)
Petechiae	9 (15.3%)
Rash	4 (6.8%)
Blood Blister	2 (3.4%)
Eczema	2 (3.4%)
Skin Lesion	2 (3.4%)
Dermatitis Allergic	1 (1.7%)
Haemorrhage Subcutaneous	1 (1.7%)
Pruritus	1 (1.7%)
Rash Macular	1 (1.7%)
Rash Papular	1 (1.7%)
NERVOUS SYSTEM DISORDERS	14 (23.7%)
Headache	6 (10.2%)
Dizziness	4 (6.8%)
Dysgeusia	1 (1.7%)
Loss Of Consciousness	1 (1.7%)
Memory Impairment	1 (1.7%)
Peroneal Nerve Palsy	1 (1.7%)
Syncope	1 (1.7%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	13 (22.0%)
Thrombocytopenia	4 (6.8%)
Anaemia	2 (3.4%)
Increased Tendency To Bruise	2 (3.4%)
Neutropenia	2 (3.4%)
Febrile Neutropenia	1 (1.7%)
Leukopenia	1 (1.7%)
Microcytic Anaemia	1 (1.7%)
Polycythaemia	1 (1.7%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	12 (20.3%)
Pyrexia	3 (5.1%)
Asthenia	2 (3.4%)
Chest Pain	2 (3.4%)
Fatigue	2 (3.4%)
Influenza Like Illness	2 (3.4%)
Oedema Peripheral	2 (3.4%)
Adverse Drug Reaction	1 (1.7%)
Pain	1 (1.7%)
Peripheral Swelling	1 (1.7%)
Polyp	1 (1.7%)
VASCULAR DISORDERS	12 (20.3%)
Hypertension	8 (13.6%)
Blood Pressure Inadequately Controlled	1 (1.7%)
Haematoma	1 (1.7%)
Haemorrhage	1 (1.7%)
Hypotension	1 (1.7%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	9 (15.3%)
Contusion	6 (10.2%)
Fall	1 (1.7%)
Joint Injury	1 (1.7%)
Limb Injury	1 (1.7%)

System Organ Class Preferred Term	Fostamatinib (N=59) n (%)
Muscle Injury	1 (1.7%)
Procedural Pain	1 (1.7%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	9 (15.3%)
Arthralgia	3 (5.1%)
Myalgia	3 (5.1%)
Ankylosing Spondylitis	1 (1.7%)
Back Pain	1 (1.7%)
Muscle Spasms	1 (1.7%)
Muscular Weakness	1 (1.7%)
Neck Pain	1 (1.7%)
Pain In Extremity	1 (1.7%)
RENAL AND URINARY DISORDERS	4 (6.8%)
Nephrolithiasis	3 (5.1%)
Haematuria	1 (1.7%)
CARDIAC DISORDERS	2 (3.4%)
Aortic Valve Incompetence	1 (1.7%)
Cardiac Failure Chronic	1 (1.7%)
Cardiac Failure Congestive	1 (1.7%)
Cardio-Respiratory Arrest	1 (1.7%)
Mitral Valve Incompetence	1 (1.7%)
Tricuspid Valve Incompetence	1 (1.7%)
HEPATOBILIARY DISORDERS	2 (3.4%)
Hepatic Cirrhosis	1 (1.7%)
Hyperbilirubinaemia	1 (1.7%)
Portal Hypertension	1 (1.7%)
METABOLISM AND NUTRITION DISORDERS	2 (3.4%)
Gout	1 (1.7%)
Hyperglycaemia	1 (1.7%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (1.7%)
Hydrocele	1 (1.7%)
EYE DISORDERS	1 (1.7%)
Retinal Tear	1 (1.7%)
PSYCHIATRIC DISORDERS	1 (1.7%)
Depressed Mood	1 (1.7%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (1.7%)
Erectile Dysfunction	1 (1.7%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the gender and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.2.1.2)

Females

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
Any Adverse Events	77 (88.5%)
GASTROINTESTINAL DISORDERS	56 (64.4%)
Diarrhoea	34 (39.1%)
Nausea	23 (26.4%)
Vomiting	9 (10.3%)
Abdominal Pain	8 (9.2%)
Constipation	7 (8.0%)
Dyspepsia	6 (6.9%)
Gingival Bleeding	6 (6.9%)
Abdominal Pain Upper	5 (5.7%)
Oral Mucosal Blistering	5 (5.7%)
Mouth Haemorrhage	4 (4.6%)
Abdominal Distension	3 (3.4%)
Dysphagia	3 (3.4%)
Haemorrhoidal Haemorrhage	3 (3.4%)
Rectal Haemorrhage	3 (3.4%)
Toothache	3 (3.4%)
Flatulence	2 (2.3%)

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
Frequent Bowel Movements	2 (2.3%)
Gastrointestinal Haemorrhage	2 (2.3%)
Gastrooesophageal Reflux Disease	2 (2.3%)
Haematochezia	2 (2.3%)
Haemorrhoids	2 (2.3%)
Stomatitis	2 (2.3%)
Abdominal Discomfort	1 (1.1%)
Abdominal Pain Lower	1 (1.1%)
Anal Fissure	1 (1.1%)
Bile Acid Malabsorption	1 (1.1%)
Cheilitis	1 (1.1%)
Dry Mouth	1 (1.1%)
Gastric Antral Vascular Ectasia	1 (1.1%)
Gastritis	1 (1.1%)
Gastritis Erosive	1 (1.1%)
Gastrointestinal Disorder	1 (1.1%)
Irritable Bowel Syndrome	1 (1.1%)
Lip Oedema	1 (1.1%)
Melaena	1 (1.1%)
Odynophagia	1 (1.1%)
Oesophageal Pain	1 (1.1%)
Palatal Disorder	1 (1.1%)
Retching	1 (1.1%)
INFECTIONS AND INFESTATIONS	41 (47.1%)
Upper Respiratory Tract Infection	13 (14.9%)
Urinary Tract Infection	8 (9.2%)
Nasopharyngitis	7 (8.0%)
Bronchitis	5 (5.7%)
Lower Respiratory Tract Infection	5 (5.7%)
Pharyngitis	4 (4.6%)
Gastroenteritis	3 (3.4%)
Pneumonia	3 (3.4%)
Sepsis	3 (3.4%)
Tooth Infection	3 (3.4%)
Viral Infection	3 (3.4%)
Cellulitis	2 (2.3%)
Ear Infection	2 (2.3%)
Eye Infection	2 (2.3%)
Post Procedural Infection	2 (2.3%)
Respiratory Tract Infection	2 (2.3%)
Sinusitis	2 (2.3%)
Abscess	1 (1.1%)
Arthritis Viral	1 (1.1%)
Bacteriuria	1 (1.1%)
Carbuncle	1 (1.1%)
Endocarditis Bacterial	1 (1.1%)
Erythema Induratum	1 (1.1%)
Escherichia Urinary Tract Infection	1 (1.1%)
Fungal Infection	1 (1.1%)
Gingivitis	1 (1.1%)
Herpes Simplex	1 (1.1%)
Herpes Zoster	1 (1.1%)
Infection	1 (1.1%)
Influenza	1 (1.1%)
Klebsiella Bacteraemia	1 (1.1%)
Mastoiditis	1 (1.1%)
Onychomycosis	1 (1.1%)
Oral Candidiasis	1 (1.1%)
Oral Herpes	1 (1.1%)
Otitis Media	1 (1.1%)
Rhinitis	1 (1.1%)
Subacute Endocarditis	1 (1.1%)

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
Tonsillitis	1 (1.1%)
Tuberculosis	1 (1.1%)
Urinary Tract Infection Bacterial	1 (1.1%)
Urosepsis	1 (1.1%)
Viral Pharyngitis	1 (1.1%)
Viral Upper Respiratory Tract Infection	1 (1.1%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	35 (40.2%)
Fatigue	12 (13.8%)
Chest Pain	7 (8.0%)
Pyrexia	7 (8.0%)
Oedema Peripheral	6 (6.9%)
Peripheral Swelling	6 (6.9%)
Asthenia	5 (5.7%)
Chills	5 (5.7%)
Influenza Like Illness	4 (4.6%)
Chest Discomfort	2 (2.3%)
Feeling Cold	2 (2.3%)
Pain	2 (2.3%)
Facial Pain	1 (1.1%)
Gait Disturbance	1 (1.1%)
General Physical Health Deterioration	1 (1.1%)
Glassy Eyes	1 (1.1%)
Mucosal Haemorrhage	1 (1.1%)
Vessel Puncture Site Bruise	1 (1.1%)
NERVOUS SYSTEM DISORDERS	33 (37.9%)
Headache	16 (18.4%)
Dizziness	14 (16.1%)
Dysgeusia	3 (3.4%)
Hypoaesthesia	3 (3.4%)
Sciatica	3 (3.4%)
Neuralgia	2 (2.3%)
Presyncope	2 (2.3%)
Cerebral Haemorrhage	1 (1.1%)
Disturbance In Attention	1 (1.1%)
Dysarthria	1 (1.1%)
Haemorrhagic Stroke	1 (1.1%)
Hypogeusia	1 (1.1%)
Lethargy	1 (1.1%)
Memory Impairment	1 (1.1%)
Migraine	1 (1.1%)
Neuropathy Peripheral	1 (1.1%)
Paraesthesia	1 (1.1%)
Restless Legs Syndrome	1 (1.1%)
Somnolence	1 (1.1%)
Transient Ischaemic Attack	1 (1.1%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	33 (37.9%)
Epistaxis	17 (19.5%)
Cough	10 (11.5%)
Dyspnoea	7 (8.0%)
Oropharyngeal Pain	4 (4.6%)
Dyspnoea Exertional	2 (2.3%)
Nasal Congestion	2 (2.3%)
Rhinorrhoea	2 (2.3%)
Chronic Obstructive Pulmonary Disease	1 (1.1%)
Dry Throat	1 (1.1%)
Dysphonia	1 (1.1%)
Haemoptysis	1 (1.1%)
Hypoxia	1 (1.1%)
Nasal Inflammation	1 (1.1%)
Pulmonary Mass	1 (1.1%)
Sleep Apnoea Syndrome	1 (1.1%)
INVESTIGATIONS	29 (33.3%)

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
Alanine Aminotransferase Increased	9 (10.3%)
Aspartate Aminotransferase Increased	7 (8.0%)
Blood Pressure Increased	4 (4.6%)
Liver Function Test Abnormal	4 (4.6%)
Platelet Count Decreased	4 (4.6%)
Blood Bilirubin Increased	2 (2.3%)
Blood Creatinine Increased	2 (2.3%)
Blood Lactate Dehydrogenase Increased	2 (2.3%)
Blood Pressure Diastolic Increased	2 (2.3%)
Hepatic Enzyme Increased	2 (2.3%)
Transaminases Increased	2 (2.3%)
Weight Increased	2 (2.3%)
Angiogram	1 (1.1%)
Blood Alkaline Phosphatase Increased	1 (1.1%)
Blood Bicarbonate Increased	1 (1.1%)
Blood Glucose Increased	1 (1.1%)
Blood Potassium Decreased	1 (1.1%)
Blood Pressure Systolic Increased	1 (1.1%)
Blood Urea Increased	1 (1.1%)
Cardiac Murmur	1 (1.1%)
Globulins Increased	1 (1.1%)
Haemoglobin Decreased	1 (1.1%)
Heart Rate Increased	1 (1.1%)
Neutrophil Count Decreased	1 (1.1%)
Platelet Count Increased	1 (1.1%)
Troponin Increased	1 (1.1%)
Vitamin B12 Increased	1 (1.1%)
Weight Decreased	1 (1.1%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	28 (32.2%)
Petechiae	13 (14.9%)
Rash	6 (6.9%)
Ecchymosis	4 (4.6%)
Dry Skin	2 (2.3%)
Erythema	2 (2.3%)
Hair Colour Changes	2 (2.3%)
Hyperhidrosis	2 (2.3%)
Pruritus	2 (2.3%)
Purpura	2 (2.3%)
Swelling Face	2 (2.3%)
Actinic Keratosis	1 (1.1%)
Alopecia	1 (1.1%)
Blister	1 (1.1%)
Blood Blister	1 (1.1%)
Dermatitis Allergic	1 (1.1%)
Hypertrichosis	1 (1.1%)
Nail Discolouration	1 (1.1%)
Nail Disorder	1 (1.1%)
Papule	1 (1.1%)
Photosensitivity Reaction	1 (1.1%)
Precancerous Skin Lesion	1 (1.1%)
Rash Erythematous	1 (1.1%)
Skin Hypopigmentation	1 (1.1%)
Skin Lesion	1 (1.1%)
Skin Ulcer	1 (1.1%)
Urticaria	1 (1.1%)
VASCULAR DISORDERS	28 (32.2%)
Hypertension	24 (27.6%)
Haematoma	3 (3.4%)
Haemorrhage	2 (2.3%)
Aortic Stenosis	1 (1.1%)
Hot Flush	1 (1.1%)
Hypertensive Crisis	1 (1.1%)

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
Hypotension	1 (1.1%)
Peripheral Venous Disease	1 (1.1%)
Phlebitis Superficial	1 (1.1%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	23 (26.4%)
Arthralgia	6 (6.9%)
Back Pain	5 (5.7%)
Muscle Spasms	5 (5.7%)
Myalgia	5 (5.7%)
Joint Swelling	4 (4.6%)
Musculoskeletal Pain	4 (4.6%)
Neck Pain	3 (3.4%)
Pain In Extremity	3 (3.4%)
Arthritis	2 (2.3%)
Chondrocalcinosis Pyrophosphate	2 (2.3%)
Musculoskeletal Chest Pain	2 (2.3%)
Osteoporosis	2 (2.3%)
Bone Lesion	1 (1.1%)
Bone Pain	1 (1.1%)
Haemarthrosis	1 (1.1%)
Mobility Decreased	1 (1.1%)
Muscular Weakness	1 (1.1%)
Plantar Fasciitis	1 (1.1%)
Rotator Cuff Syndrome	1 (1.1%)
Spinal Column Stenosis	1 (1.1%)
Tendon Sheath Disorder	1 (1.1%)
Tendonitis	1 (1.1%)
Trigger Finger	1 (1.1%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	19 (21.8%)
Thrombocytopenia	7 (8.0%)
Anaemia	6 (6.9%)
Neutropenia	6 (6.9%)
Leukopenia	2 (2.3%)
Lymphadenopathy	2 (2.3%)
Thrombocytosis	2 (2.3%)
Aplastic Anaemia	1 (1.1%)
Immune Thrombocytopenic Purpura	1 (1.1%)
Leukocytosis	1 (1.1%)
Microcytic Anaemia	1 (1.1%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	15 (17.2%)
Contusion	11 (12.6%)
Animal Bite	2 (2.3%)
Fall	2 (2.3%)
Anaphylactic Transfusion Reaction	1 (1.1%)
Graft Complication	1 (1.1%)
Head Injury	1 (1.1%)
Joint Injury	1 (1.1%)
Scratch	1 (1.1%)
Skin Wound	1 (1.1%)
Thoracic Vertebral Fracture	1 (1.1%)
METABOLISM AND NUTRITION DISORDERS	12 (13.8%)
Hypokalaemia	5 (5.7%)
Decreased Appetite	3 (3.4%)
Dehydration	1 (1.1%)
Fluid Overload	1 (1.1%)
Glucose Tolerance Impaired	1 (1.1%)
Hyperkalaemia	1 (1.1%)
Hypernatraemia	1 (1.1%)
Hyperuricaemia	1 (1.1%)
Hypomagnesaemia	1 (1.1%)
Hypophosphataemia	1 (1.1%)
Iron Deficiency	1 (1.1%)
Vitamin D Deficiency	1 (1.1%)

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
CARDIAC DISORDERS	8 (9.2%)
Tachycardia	3 (3.4%)
Atrial Fibrillation	2 (2.3%)
Angina Pectoris	1 (1.1%)
Cardiac Failure Congestive	1 (1.1%)
Palpitations	1 (1.1%)
Ventricular Extrasystoles	1 (1.1%)
EYE DISORDERS	8 (9.2%)
Conjunctival Haemorrhage	2 (2.3%)
Eyelid Oedema	2 (2.3%)
Blepharitis	1 (1.1%)
Eye Disorder	1 (1.1%)
Eye Haemorrhage	1 (1.1%)
Eye Pain	1 (1.1%)
Vision Blurred	1 (1.1%)
PSYCHIATRIC DISORDERS	7 (8.0%)
Insomnia	4 (4.6%)
Anxiety	2 (2.3%)
Depression	1 (1.1%)
Mental Status Changes	1 (1.1%)
Restlessness	1 (1.1%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	7 (8.0%)
Vaginal Haemorrhage	3 (3.4%)
Menorrhagia	2 (2.3%)
Breast Mass	1 (1.1%)
Uterine Polyp	1 (1.1%)
Vulvovaginal Pain	1 (1.1%)
EAR AND LABYRINTH DISORDERS	6 (6.9%)
Ear Haemorrhage	1 (1.1%)
Excessive Cerumen Production	1 (1.1%)
Otorrhoea	1 (1.1%)
Tinnitus	1 (1.1%)
Tympanic Membrane Disorder	1 (1.1%)
Tympanic Membrane Perforation	1 (1.1%)
Vertigo	1 (1.1%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	6 (6.9%)
Squamous Cell Carcinoma Of Skin	3 (3.4%)
Basal Cell Carcinoma	2 (2.3%)
Basosquamous Carcinoma Of Skin	1 (1.1%)
Cholesteatoma	1 (1.1%)
Plasma Cell Myeloma	1 (1.1%)
RENAL AND URINARY DISORDERS	5 (5.7%)
Pollakiuria	2 (2.3%)
Acute Kidney Injury	1 (1.1%)
Chronic Kidney Disease	1 (1.1%)
Hypertonic Bladder	1 (1.1%)
Leukocyturia	1 (1.1%)
Nephrolithiasis	1 (1.1%)
Renal Cyst	1 (1.1%)
Renal Failure	1 (1.1%)
SURGICAL AND MEDICAL PROCEDURES	3 (3.4%)
Micrographic Skin Surgery	1 (1.1%)
Rotator Cuff Repair	1 (1.1%)
Tooth Extraction	1 (1.1%)
HEPATOBILIARY DISORDERS	2 (2.3%)
Cholecystitis	1 (1.1%)
Hepatic Cyst	1 (1.1%)
IMMUNE SYSTEM DISORDERS	2 (2.3%)
Allergy To Chemicals	1 (1.1%)
Allergy To Metals	1 (1.1%)
Drug Hypersensitivity	1 (1.1%)

System Organ Class Preferred Term	Fostamatinib (N=87) n (%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (1.1%)
Dacryostenosis Congenital	1 (1.1%)
ENDOCRINE DISORDERS	1 (1.1%)
Cushingoid	1 (1.1%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the gender and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.2.1.2)

表 2.7.4.9-4 Treatment-Related Adverse Events (AEs): Incidence by System Organ Class and Preferred Term (Subject Level) (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Any Treatment-Related Adverse Events	96 (65.8%)
GASTROINTESTINAL DISORDERS	58 (39.7%)
Diarrhoea	46 (31.5%)
Nausea	18 (12.3%)
Abdominal Pain	5 (3.4%)
Constipation	5 (3.4%)
Abdominal Pain Upper	4 (2.7%)
Flatulence	4 (2.7%)
Abdominal Distension	3 (2.1%)
Dyspepsia	3 (2.1%)
Vomiting	3 (2.1%)
Abdominal Discomfort	1 (0.7%)
Eructation	1 (0.7%)
Frequent Bowel Movements	1 (0.7%)
Gastritis	1 (0.7%)
Gastrointestinal Disorder	1 (0.7%)
Gastrooesophageal Reflux Disease	1 (0.7%)
Haemorrhoidal Haemorrhage	1 (0.7%)
Haemorrhoids	1 (0.7%)
Oesophageal Pain	1 (0.7%)
Palatal Disorder	1 (0.7%)
Retching	1 (0.7%)
INVESTIGATIONS	30 (20.5%)
Alanine Aminotransferase Increased	13 (8.9%)
Aspartate Aminotransferase Increased	8 (5.5%)
Blood Pressure Increased	5 (3.4%)
Blood Bilirubin Increased	3 (2.1%)
Hepatic Enzyme Increased	3 (2.1%)
Blood Lactate Dehydrogenase Increased	2 (1.4%)
Liver Function Test Abnormal	2 (1.4%)
Neutrophil Count Decreased	2 (1.4%)
Blood Alkaline Phosphatase Increased	1 (0.7%)
Blood Pressure Systolic Increased	1 (0.7%)
Platelet Count Decreased	1 (0.7%)
Platelet Count Increased	1 (0.7%)
Transaminases Increased	1 (0.7%)
Weight Decreased	1 (0.7%)
VASCULAR DISORDERS	23 (15.8%)
Hypertension	21 (14.4%)
Blood Pressure Inadequately Controlled	1 (0.7%)
Hypertensive Crisis	1 (0.7%)
NERVOUS SYSTEM DISORDERS	18 (12.3%)
Dizziness	9 (6.2%)
Headache	7 (4.8%)
Dysgeusia	3 (2.1%)
Disturbance In Attention	1 (0.7%)
Hypogeusia	1 (0.7%)
Lethargy	1 (0.7%)
Memory Impairment	1 (0.7%)
Peroneal Nerve Palsy	1 (0.7%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	15 (10.3%)
Fatigue	6 (4.1%)
Chest Pain	5 (3.4%)
Chills	2 (1.4%)
Pyrexia	2 (1.4%)
Facial Pain	1 (0.7%)
Influenza Like Illness	1 (0.7%)
Oedema Peripheral	1 (0.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Pain	1 (0.7%)
Peripheral Swelling	1 (0.7%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	14 (9.6%)
Epistaxis	5 (3.4%)
Cough	3 (2.1%)
Dyspnoea	3 (2.1%)
Dry Throat	2 (1.4%)
Rhinorrhoea	2 (1.4%)
Dysphonia	1 (0.7%)
Dyspnoea Exertional	1 (0.7%)
Hypoxia	1 (0.7%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	13 (8.9%)
Rash	6 (4.1%)
Petechiae	3 (2.1%)
Hair Colour Changes	2 (1.4%)
Pruritus	2 (1.4%)
Actinic Keratosis	1 (0.7%)
Alopecia	1 (0.7%)
Blood Blister	1 (0.7%)
Dry Skin	1 (0.7%)
Erythema	1 (0.7%)
Nail Disorder	1 (0.7%)
Photosensitivity Reaction	1 (0.7%)
Skin Hypopigmentation	1 (0.7%)
Skin Lesion	1 (0.7%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	11 (7.5%)
Neutropenia	5 (3.4%)
Thrombocytosis	2 (1.4%)
Anaemia	1 (0.7%)
Aplastic Anaemia	1 (0.7%)
Febrile Neutropenia	1 (0.7%)
Leukocytosis	1 (0.7%)
Leukopenia	1 (0.7%)
INFECTIONS AND INFESTATIONS	11 (7.5%)
Pneumonia	2 (1.4%)
Arthritis Viral	1 (0.7%)
Bacteriuria	1 (0.7%)
Erythema Induratum	1 (0.7%)
Herpes Zoster	1 (0.7%)
Lower Respiratory Tract Infection	1 (0.7%)
Nasopharyngitis	1 (0.7%)
Oral Candidiasis	1 (0.7%)
Post Procedural Infection	1 (0.7%)
Respiratory Tract Infection	1 (0.7%)
Sepsis	1 (0.7%)
Tuberculosis	1 (0.7%)
Upper Respiratory Tract Infection	1 (0.7%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	11 (7.5%)
Arthralgia	3 (2.1%)
Myalgia	3 (2.1%)
Joint Swelling	2 (1.4%)
Muscle Spasms	2 (1.4%)
Ankylosing Spondylitis	1 (0.7%)
Back Pain	1 (0.7%)
Muscular Weakness	1 (0.7%)
PSYCHIATRIC DISORDERS	4 (2.7%)
Insomnia	2 (1.4%)
Depressed Mood	1 (0.7%)
Restlessness	1 (0.7%)
EAR AND LABYRINTH DISORDERS	3 (2.1%)
Excessive Cerumen Production	1 (0.7%)
Tinnitus	1 (0.7%)

System Organ Class Preferred Term	Fostamatinib (N=146) n (%)
Vertigo	1 (0.7%)
EYE DISORDERS	3 (2.1%)
Blepharitis	1 (0.7%)
Eye Pain	1 (0.7%)
Eyelid Oedema	1 (0.7%)
METABOLISM AND NUTRITION DISORDERS	3 (2.1%)
Decreased Appetite	2 (1.4%)
Gout	1 (0.7%)
CARDIAC DISORDERS	2 (1.4%)
Atrial Fibrillation	1 (0.7%)
Tachycardia	1 (0.7%)
HEPATOBILIARY DISORDERS	1 (0.7%)
Hyperbilirubinaemia	1 (0.7%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (0.7%)
Contusion	1 (0.7%)
RENAL AND URINARY DISORDERS	1 (0.7%)
Leukocyturia	1 (0.7%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one treatment-related AE in that system organ class or with that preferred term.
Treatment-related AEs are AEs with a possible, probable, or missing causal relationship to study drug.
(Source: 5.3.5.3.2, Table 4.2.1.2.2)

表 2.7.4.9-5 Adverse Events (AEs): Incidence by System Organ Class and Preferred Term (Subject Level) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

System Organ Class Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Any Adverse Events	85 (83.3%)	36 (75.0%)
GASTROINTESTINAL DISORDERS	49 (48.0%)	16 (33.3%)
Diarrhoea	30 (29.4%)	7 (14.6%)
Nausea	19 (18.6%)	4 (8.3%)
Flatulence	5 (4.9%)	1 (2.1%)
Vomiting	3 (2.9%)	3 (6.3%)
Gingival Bleeding	4 (3.9%)	1 (2.1%)
Abdominal Pain Upper	3 (2.9%)	1 (2.1%)
Constipation	3 (2.9%)	1 (2.1%)
Dyspepsia	3 (2.9%)	1 (2.1%)
Abdominal Pain	3 (2.9%)	0 (0.0%)
Toothache	2 (2.0%)	1 (2.1%)
Abdominal Discomfort	1 (1.0%)	1 (2.1%)
Abdominal Distension	2 (2.0%)	0 (0.0%)
Frequent Bowel Movements	2 (2.0%)	0 (0.0%)
Rectal Haemorrhage	0 (0.0%)	2 (4.2%)
Anal Haemorrhage	0 (0.0%)	1 (2.1%)
Eructation	1 (1.0%)	0 (0.0%)
Faeces Discoloured	0 (0.0%)	1 (2.1%)
Gastric Haemorrhage	0 (0.0%)	1 (2.1%)
Gastritis	1 (1.0%)	0 (0.0%)
Gastrointestinal Disorder	1 (1.0%)	0 (0.0%)
Gastrointestinal Haemorrhage	0 (0.0%)	1 (2.1%)
Gastrooesophageal Reflux Disease	1 (1.0%)	0 (0.0%)
Haematochezia	1 (1.0%)	0 (0.0%)
Haemorrhoids	1 (1.0%)	0 (0.0%)
Melaena	0 (0.0%)	1 (2.1%)
Oesophageal Pain	1 (1.0%)	0 (0.0%)
Oral Mucosal Blistering	0 (0.0%)	1 (2.1%)
Retching	1 (1.0%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	26 (25.5%)	13 (27.1%)
Headache	11 (10.8%)	9 (18.8%)
Dizziness	11 (10.8%)	4 (8.3%)
Dysgeusia	4 (3.9%)	0 (0.0%)
Memory Impairment	2 (2.0%)	0 (0.0%)
Neuralgia	2 (2.0%)	0 (0.0%)
Disturbance In Attention	1 (1.0%)	0 (0.0%)
Hypoaesthesia	0 (0.0%)	1 (2.1%)
Hypogeusia	1 (1.0%)	0 (0.0%)
Lethargy	1 (1.0%)	0 (0.0%)
Migraine	1 (1.0%)	0 (0.0%)
Neuropathy Peripheral	1 (1.0%)	0 (0.0%)
Paraesthesia	0 (0.0%)	1 (2.1%)
Somnolence	0 (0.0%)	1 (2.1%)
Syncope	1 (1.0%)	0 (0.0%)
Transient Ischaemic Attack	1 (1.0%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	27 (26.5%)	10 (20.8%)
Upper Respiratory Tract Infection	6 (5.9%)	2 (4.2%)
Respiratory Tract Infection	3 (2.9%)	1 (2.1%)
Bronchitis	3 (2.9%)	0 (0.0%)
Gastroenteritis	2 (2.0%)	1 (2.1%)
Nasopharyngitis	2 (2.0%)	1 (2.1%)
Urinary Tract Infection	3 (2.9%)	0 (0.0%)
Viral Infection	2 (2.0%)	1 (2.1%)
Abscess	1 (1.0%)	0 (0.0%)
Bacteriuria	1 (1.0%)	0 (0.0%)
Eye Infection	0 (0.0%)	1 (2.1%)
Gingivitis	1 (1.0%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Infection	0 (0.0%)	1 (2.1%)
Influenza	0 (0.0%)	1 (2.1%)
Laryngitis	1 (1.0%)	0 (0.0%)
Lower Respiratory Tract Infection	1 (1.0%)	0 (0.0%)
Oral Candidiasis	1 (1.0%)	0 (0.0%)
Oral Herpes	1 (1.0%)	0 (0.0%)
Pneumonia	1 (1.0%)	0 (0.0%)
Pulpitis Dental	1 (1.0%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (2.1%)
Viral Upper Respiratory Tract Infection	1 (1.0%)	0 (0.0%)
INVESTIGATIONS	28 (27.5%)	5 (10.4%)
Alanine Aminotransferase Increased	11 (10.8%)	0 (0.0%)
Aspartate Aminotransferase Increased	9 (8.8%)	0 (0.0%)
Blood Pressure Increased	5 (4.9%)	2 (4.2%)
Blood Bilirubin Increased	2 (2.0%)	0 (0.0%)
Blood Lactate Dehydrogenase Increased	2 (2.0%)	0 (0.0%)
C-Reactive Protein Increased	1 (1.0%)	1 (2.1%)
Neutrophil Count Decreased	2 (2.0%)	0 (0.0%)
Platelet Count Decreased	2 (2.0%)	0 (0.0%)
Blood Alkaline Phosphatase Increased	1 (1.0%)	0 (0.0%)
Blood Glucose Increased	1 (1.0%)	0 (0.0%)
Blood Potassium Decreased	0 (0.0%)	1 (2.1%)
Blood Pressure Diastolic Abnormal	1 (1.0%)	0 (0.0%)
Blood Pressure Diastolic Increased	1 (1.0%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.0%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (1.0%)	0 (0.0%)
Heart Rate Increased	1 (1.0%)	0 (0.0%)
Hepatic Enzyme Increased	1 (1.0%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.0%)	0 (0.0%)
Lymphocyte Count Decreased	1 (1.0%)	0 (0.0%)
Platelet Count Increased	0 (0.0%)	1 (2.1%)
Weight Decreased	1 (1.0%)	0 (0.0%)
Weight Increased	1 (1.0%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	23 (22.5%)	10 (20.8%)
Epistaxis	16 (15.7%)	5 (10.4%)
Dyspnoea	4 (3.9%)	2 (4.2%)
Oropharyngeal Pain	1 (1.0%)	2 (4.2%)
Cough	1 (1.0%)	1 (2.1%)
Chronic Obstructive Pulmonary Disease	0 (0.0%)	1 (2.1%)
Dry Throat	1 (1.0%)	0 (0.0%)
Dysphonia	1 (1.0%)	0 (0.0%)
Hypoxia	1 (1.0%)	0 (0.0%)
Nasal Congestion	1 (1.0%)	0 (0.0%)
Rhinorrhoea	1 (1.0%)	0 (0.0%)
Sleep Apnoea Syndrome	1 (1.0%)	0 (0.0%)
Upper Respiratory Tract Inflammation	1 (1.0%)	0 (0.0%)
VASCULAR DISORDERS	24 (23.5%)	9 (18.8%)
Hypertension	20 (19.6%)	4 (8.3%)
Haemorrhage	2 (2.0%)	2 (4.2%)
Haematoma	1 (1.0%)	2 (4.2%)
Hot Flush	1 (1.0%)	0 (0.0%)
Hypertensive Crisis	1 (1.0%)	0 (0.0%)
Peripheral Coldness	0 (0.0%)	1 (2.1%)
Peripheral Venous Disease	1 (1.0%)	0 (0.0%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	18 (17.6%)	5 (10.4%)
Rash	8 (7.8%)	1 (2.1%)
Petechiae	4 (3.9%)	3 (6.3%)
Blood Blister	2 (2.0%)	0 (0.0%)
Hair Colour Changes	2 (2.0%)	0 (0.0%)
Hyperhidrosis	2 (2.0%)	0 (0.0%)
Swelling Face	2 (2.0%)	0 (0.0%)
Actinic Keratosis	1 (1.0%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Alopecia	1 (1.0%)	0 (0.0%)
Dermatitis Allergic	1 (1.0%)	0 (0.0%)
Dry Skin	1 (1.0%)	0 (0.0%)
Ecchymosis	1 (1.0%)	0 (0.0%)
Erythema	1 (1.0%)	0 (0.0%)
Hypertrichosis	1 (1.0%)	0 (0.0%)
Nail Disorder	1 (1.0%)	0 (0.0%)
Photosensitivity Reaction	1 (1.0%)	0 (0.0%)
Pruritus	1 (1.0%)	0 (0.0%)
Rash Erythematous	1 (1.0%)	0 (0.0%)
Rash Macular	1 (1.0%)	0 (0.0%)
Skin Haemorrhage	0 (0.0%)	1 (2.1%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	17 (16.7%)	5 (10.4%)
Chest Pain	6 (5.9%)	1 (2.1%)
Fatigue	6 (5.9%)	1 (2.1%)
Pyrexia	3 (2.9%)	2 (4.2%)
Influenza Like Illness	3 (2.9%)	0 (0.0%)
Oedema Peripheral	3 (2.9%)	0 (0.0%)
Asthenia	1 (1.0%)	1 (2.1%)
Chills	2 (2.0%)	0 (0.0%)
Peripheral Swelling	2 (2.0%)	0 (0.0%)
Oedema	0 (0.0%)	1 (2.1%)
Vessel Puncture Site Bruise	1 (1.0%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	15 (14.7%)	4 (8.3%)
Anaemia	3 (2.9%)	2 (4.2%)
Neutropenia	5 (4.9%)	0 (0.0%)
Leukopenia	3 (2.9%)	0 (0.0%)
Thrombocytopenia	1 (1.0%)	2 (4.2%)
Febrile Neutropenia	1 (1.0%)	0 (0.0%)
Immune Thrombocytopenic Purpura	1 (1.0%)	0 (0.0%)
Leukocytosis	1 (1.0%)	0 (0.0%)
Lymphadenopathy	1 (1.0%)	0 (0.0%)
Thrombocytosis	1 (1.0%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	10 (9.8%)	4 (8.3%)
Arthralgia	2 (2.0%)	1 (2.1%)
Back Pain	2 (2.0%)	0 (0.0%)
Muscle Spasms	1 (1.0%)	1 (2.1%)
Musculoskeletal Pain	0 (0.0%)	2 (4.2%)
Myalgia	2 (2.0%)	0 (0.0%)
Ankylosing Spondylitis	1 (1.0%)	0 (0.0%)
Bone Lesion	1 (1.0%)	0 (0.0%)
Chondrocalcinosis Pyrophosphate	1 (1.0%)	0 (0.0%)
Joint Swelling	1 (1.0%)	0 (0.0%)
Musculoskeletal Chest Pain	0 (0.0%)	1 (2.1%)
Osteoporosis	1 (1.0%)	0 (0.0%)
Pain In Extremity	1 (1.0%)	0 (0.0%)
METABOLISM AND NUTRITION DISORDERS	8 (7.8%)	2 (4.2%)
Hypokalaemia	3 (2.9%)	0 (0.0%)
Decreased Appetite	2 (2.0%)	0 (0.0%)
Iron Deficiency	1 (1.0%)	1 (2.1%)
Glucose Tolerance Impaired	1 (1.0%)	0 (0.0%)
Hyperglycaemia	1 (1.0%)	0 (0.0%)
Hypomagnesaemia	0 (0.0%)	1 (2.1%)
Hypophosphataemia	0 (0.0%)	1 (2.1%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6 (5.9%)	2 (4.2%)
Contusion	6 (5.9%)	0 (0.0%)
Muscle Rupture	0 (0.0%)	1 (2.1%)
Tooth Fracture	0 (0.0%)	1 (2.1%)
EYE DISORDERS	5 (4.9%)	2 (4.2%)
Eye Pain	1 (1.0%)	1 (2.1%)
Blepharitis	1 (1.0%)	0 (0.0%)
Conjunctival Pallor	0 (0.0%)	1 (2.1%)

System Organ Class Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Eye Disorder	1 (1.0%)	0 (0.0%)
Eyelid Oedema	1 (1.0%)	0 (0.0%)
Ocular Icterus	0 (0.0%)	1 (2.1%)
Retinal Tear	1 (1.0%)	0 (0.0%)
Visual Impairment	0 (0.0%)	1 (2.1%)
PSYCHIATRIC DISORDERS	5 (4.9%)	0 (0.0%)
Insomnia	3 (2.9%)	0 (0.0%)
Anxiety	1 (1.0%)	0 (0.0%)
Depression	1 (1.0%)	0 (0.0%)
Restlessness	1 (1.0%)	0 (0.0%)
RENAL AND URINARY DISORDERS	4 (3.9%)	1 (2.1%)
Haematuria	1 (1.0%)	1 (2.1%)
Leukocyturia	1 (1.0%)	0 (0.0%)
Nephrolithiasis	1 (1.0%)	0 (0.0%)
Pollakiuria	1 (1.0%)	0 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	3 (2.9%)	2 (4.2%)
Menorrhagia	1 (1.0%)	2 (4.2%)
Erectile Dysfunction	1 (1.0%)	0 (0.0%)
Uterine Polyp	1 (1.0%)	0 (0.0%)
Vaginal Haemorrhage	1 (1.0%)	0 (0.0%)
CARDIAC DISORDERS	3 (2.9%)	1 (2.1%)
Tachycardia	3 (2.9%)	0 (0.0%)
Cardiac Failure Congestive	0 (0.0%)	1 (2.1%)
EAR AND LABYRINTH DISORDERS	2 (2.0%)	1 (2.1%)
Excessive Cerumen Production	1 (1.0%)	0 (0.0%)
Tinnitus	0 (0.0%)	1 (2.1%)
Vertigo	1 (1.0%)	0 (0.0%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (1.0%)	0 (0.0%)
Hydrocele	1 (1.0%)	0 (0.0%)
ENDOCRINE DISORDERS	1 (1.0%)	0 (0.0%)
Cushingoid	1 (1.0%)	0 (0.0%)
HEPATOBILIARY DISORDERS	1 (1.0%)	0 (0.0%)
Hepatic Cyst	1 (1.0%)	0 (0.0%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (1.0%)	0 (0.0%)
Plasma Cell Myeloma	1 (1.0%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.1.1)

表 2.7.4.9-6 Adverse Events (AEs): Incidence by System Organ Class/Preferred Term and Age Group (Subject Level) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Age < 65 years

System Organ Class Preferred Term	Fostamatinib (N=74) n (%)	Placebo (N=37) n (%)
Any Adverse Events	59 (79.7%)	30 (81.1%)
GASTROINTESTINAL DISORDERS	34 (45.9%)	14 (37.8%)
Diarrhoea	19 (25.7%)	7 (18.9%)
Nausea	14 (18.9%)	4 (10.8%)
Vomiting	3 (4.1%)	3 (8.1%)
Flatulence	4 (5.4%)	1 (2.7%)
Abdominal Pain Upper	3 (4.1%)	1 (2.7%)
Abdominal Pain	3 (4.1%)	0 (0.0%)
Dyspepsia	2 (2.7%)	1 (2.7%)
Gingival Bleeding	2 (2.7%)	1 (2.7%)
Abdominal Distension	2 (2.7%)	0 (0.0%)
Toothache	1 (1.4%)	1 (2.7%)
Abdominal Discomfort	1 (1.4%)	0 (0.0%)
Anal Haemorrhage	0 (0.0%)	1 (2.7%)
Constipation	1 (1.4%)	0 (0.0%)
Eructation	1 (1.4%)	0 (0.0%)
Faeces Discoloured	0 (0.0%)	1 (2.7%)
Frequent Bowel Movements	1 (1.4%)	0 (0.0%)
Gastric Haemorrhage	0 (0.0%)	1 (2.7%)
Gastritis	1 (1.4%)	0 (0.0%)
Gastrointestinal Haemorrhage	0 (0.0%)	1 (2.7%)
Gastrooesophageal Reflux Disease	1 (1.4%)	0 (0.0%)
Haematochezia	1 (1.4%)	0 (0.0%)
Melaena	0 (0.0%)	1 (2.7%)
Oesophageal Pain	1 (1.4%)	0 (0.0%)
Oral Mucosal Blistering	0 (0.0%)	1 (2.7%)
Rectal Haemorrhage	0 (0.0%)	1 (2.7%)
Retching	1 (1.4%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	20 (27.0%)	13 (35.1%)
Headache	11 (14.9%)	9 (24.3%)
Dizziness	6 (8.1%)	4 (10.8%)
Dysgeusia	3 (4.1%)	0 (0.0%)
Disturbance In Attention	1 (1.4%)	0 (0.0%)
Hypoaesthesia	0 (0.0%)	1 (2.7%)
Lethargy	1 (1.4%)	0 (0.0%)
Memory Impairment	1 (1.4%)	0 (0.0%)
Migraine	1 (1.4%)	0 (0.0%)
Neuralgia	1 (1.4%)	0 (0.0%)
Neuropathy Peripheral	1 (1.4%)	0 (0.0%)
Paraesthesia	0 (0.0%)	1 (2.7%)
Somnolence	0 (0.0%)	1 (2.7%)
Syncope	1 (1.4%)	0 (0.0%)
Transient Ischaemic Attack	1 (1.4%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	20 (27.0%)	9 (24.3%)
Upper Respiratory Tract Infection	5 (6.8%)	2 (5.4%)
Respiratory Tract Infection	3 (4.1%)	1 (2.7%)
Gastroenteritis	2 (2.7%)	1 (2.7%)
Urinary Tract Infection	3 (4.1%)	0 (0.0%)
Bronchitis	2 (2.7%)	0 (0.0%)
Nasopharyngitis	1 (1.4%)	1 (2.7%)
Viral Infection	1 (1.4%)	1 (2.7%)
Eye Infection	0 (0.0%)	1 (2.7%)
Gingivitis	1 (1.4%)	0 (0.0%)
Infection	0 (0.0%)	1 (2.7%)
Influenza	0 (0.0%)	1 (2.7%)
Laryngitis	1 (1.4%)	0 (0.0%)
Oral Candidiasis	1 (1.4%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=74) n (%)	Placebo (N=37) n (%)
Oral Herpes	1 (1.4%)	0 (0.0%)
Pneumonia	1 (1.4%)	0 (0.0%)
Pulpitis Dental	1 (1.4%)	0 (0.0%)
Viral Upper Respiratory Tract Infection	1 (1.4%)	0 (0.0%)
INVESTIGATIONS	19 (25.7%)	4 (10.8%)
Alanine Aminotransferase Increased	9 (12.2%)	0 (0.0%)
Aspartate Aminotransferase Increased	8 (10.8%)	0 (0.0%)
Blood Bilirubin Increased	2 (2.7%)	0 (0.0%)
Blood Lactate Dehydrogenase Increased	2 (2.7%)	0 (0.0%)
Blood Pressure Increased	1 (1.4%)	1 (2.7%)
C-Reactive Protein Increased	1 (1.4%)	1 (2.7%)
Platelet Count Decreased	2 (2.7%)	0 (0.0%)
Blood Alkaline Phosphatase Increased	1 (1.4%)	0 (0.0%)
Blood Potassium Decreased	0 (0.0%)	1 (2.7%)
Blood Pressure Diastolic Abnormal	1 (1.4%)	0 (0.0%)
Blood Pressure Diastolic Increased	1 (1.4%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.4%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (1.4%)	0 (0.0%)
Heart Rate Increased	1 (1.4%)	0 (0.0%)
Hepatic Enzyme Increased	1 (1.4%)	0 (0.0%)
Lymphocyte Count Decreased	1 (1.4%)	0 (0.0%)
Neutrophil Count Decreased	1 (1.4%)	0 (0.0%)
Platelet Count Increased	0 (0.0%)	1 (2.7%)
Weight Increased	1 (1.4%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	14 (18.9%)	9 (24.3%)
Epistaxis	9 (12.2%)	4 (10.8%)
Dyspnoea	3 (4.1%)	2 (5.4%)
Oropharyngeal Pain	1 (1.4%)	2 (5.4%)
Cough	1 (1.4%)	1 (2.7%)
Chronic Obstructive Pulmonary Disease	0 (0.0%)	1 (2.7%)
Dry Throat	1 (1.4%)	0 (0.0%)
Hypoxia	1 (1.4%)	0 (0.0%)
Rhinorrhoea	1 (1.4%)	0 (0.0%)
Sleep Apnoea Syndrome	1 (1.4%)	0 (0.0%)
Upper Respiratory Tract Inflammation	1 (1.4%)	0 (0.0%)
VASCULAR DISORDERS	16 (21.6%)	7 (18.9%)
Hypertension	14 (18.9%)	3 (8.1%)
Haemorrhage	1 (1.4%)	2 (5.4%)
Haematoma	0 (0.0%)	1 (2.7%)
Hot Flush	1 (1.4%)	0 (0.0%)
Peripheral Coldness	0 (0.0%)	1 (2.7%)
Peripheral Venous Disease	1 (1.4%)	0 (0.0%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	14 (18.9%)	5 (13.5%)
Petechiae	3 (4.1%)	3 (8.1%)
Rash	5 (6.8%)	1 (2.7%)
Blood Blister	2 (2.7%)	0 (0.0%)
Hair Colour Changes	2 (2.7%)	0 (0.0%)
Hyperhidrosis	2 (2.7%)	0 (0.0%)
Swelling Face	2 (2.7%)	0 (0.0%)
Actinic Keratosis	1 (1.4%)	0 (0.0%)
Alopecia	1 (1.4%)	0 (0.0%)
Dry Skin	1 (1.4%)	0 (0.0%)
Ecchymosis	1 (1.4%)	0 (0.0%)
Erythema	1 (1.4%)	0 (0.0%)
Hypertrichosis	1 (1.4%)	0 (0.0%)
Nail Disorder	1 (1.4%)	0 (0.0%)
Photosensitivity Reaction	1 (1.4%)	0 (0.0%)
Pruritus	1 (1.4%)	0 (0.0%)
Rash Erythematous	1 (1.4%)	0 (0.0%)
Skin Haemorrhage	0 (0.0%)	1 (2.7%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	12 (16.2%)	3 (8.1%)
Chest Pain	4 (5.4%)	1 (2.7%)

System Organ Class Preferred Term	Fostamatinib (N=74) n (%)	Placebo (N=37) n (%)
Fatigue	3 (4.1%)	1 (2.7%)
Pyrexia	3 (4.1%)	1 (2.7%)
Influenza Like Illness	3 (4.1%)	0 (0.0%)
Asthenia	1 (1.4%)	1 (2.7%)
Chills	2 (2.7%)	0 (0.0%)
Oedema Peripheral	1 (1.4%)	0 (0.0%)
Peripheral Swelling	1 (1.4%)	0 (0.0%)
Vessel Puncture Site Bruise	1 (1.4%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	10 (13.5%)	4 (10.8%)
Anaemia	3 (4.1%)	2 (5.4%)
Neutropenia	3 (4.1%)	0 (0.0%)
Leukopenia	2 (2.7%)	0 (0.0%)
Thrombocytopenia	0 (0.0%)	2 (5.4%)
Febrile Neutropenia	1 (1.4%)	0 (0.0%)
Leukocytosis	1 (1.4%)	0 (0.0%)
Lymphadenopathy	1 (1.4%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	7 (9.5%)	4 (10.8%)
Arthralgia	2 (2.7%)	1 (2.7%)
Back Pain	2 (2.7%)	0 (0.0%)
Muscle Spasms	1 (1.4%)	1 (2.7%)
Musculoskeletal Pain	0 (0.0%)	2 (5.4%)
Myalgia	2 (2.7%)	0 (0.0%)
Ankylosing Spondylitis	1 (1.4%)	0 (0.0%)
Musculoskeletal Chest Pain	0 (0.0%)	1 (2.7%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	4 (5.4%)	2 (5.4%)
Contusion	4 (5.4%)	0 (0.0%)
Muscle Rupture	0 (0.0%)	1 (2.7%)
Tooth Fracture	0 (0.0%)	1 (2.7%)
METABOLISM AND NUTRITION DISORDERS	4 (5.4%)	2 (5.4%)
Decreased Appetite	2 (2.7%)	0 (0.0%)
Iron Deficiency	1 (1.4%)	1 (2.7%)
Hyperglycaemia	1 (1.4%)	0 (0.0%)
Hypomagnesaemia	0 (0.0%)	1 (2.7%)
Hypophosphataemia	0 (0.0%)	1 (2.7%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	3 (4.1%)	2 (5.4%)
Menorrhagia	1 (1.4%)	2 (5.4%)
Erectile Dysfunction	1 (1.4%)	0 (0.0%)
Uterine Polyp	1 (1.4%)	0 (0.0%)
Vaginal Haemorrhage	1 (1.4%)	0 (0.0%)
CARDIAC DISORDERS	3 (4.1%)	1 (2.7%)
Tachycardia	3 (4.1%)	0 (0.0%)
Cardiac Failure Congestive	0 (0.0%)	1 (2.7%)
EYE DISORDERS	2 (2.7%)	2 (5.4%)
Eye Pain	1 (1.4%)	1 (2.7%)
Conjunctival Pallor	0 (0.0%)	1 (2.7%)
Eye Disorder	1 (1.4%)	0 (0.0%)
Ocular Icterus	0 (0.0%)	1 (2.7%)
Visual Impairment	0 (0.0%)	1 (2.7%)
PSYCHIATRIC DISORDERS	3 (4.1%)	0 (0.0%)
Insomnia	2 (2.7%)	0 (0.0%)
Anxiety	1 (1.4%)	0 (0.0%)
Depression	1 (1.4%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	1 (1.4%)	1 (2.7%)
Excessive Cerumen Production	1 (1.4%)	0 (0.0%)
Tinnitus	0 (0.0%)	1 (2.7%)
RENAL AND URINARY DISORDERS	1 (1.4%)	1 (2.7%)
Haematuria	1 (1.4%)	1 (2.7%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (1.4%)	0 (0.0%)
Hydrocele	1 (1.4%)	0 (0.0%)
ENDOCRINE DISORDERS	1 (1.4%)	0 (0.0%)
Cushingoid	1 (1.4%)	0 (0.0%)
HEPATOBILIARY DISORDERS	1 (1.4%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=74) n (%)	Placebo (N=37) n (%)
Hepatic Cyst	1 (1.4%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the age and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.1.1.1)

Age >= 65 years

System Organ Class Preferred Term	Fostamatinib (N=28) n (%)	Placebo (N=11) n (%)
Any Adverse Events	26 (92.9%)	6 (54.5%)
GASTROINTESTINAL DISORDERS	15 (53.6%)	2 (18.2%)
Diarrhoea	11 (39.3%)	0 (0.0%)
Nausea	5 (17.9%)	0 (0.0%)
Constipation	2 (7.1%)	1 (9.1%)
Gingival Bleeding	2 (7.1%)	0 (0.0%)
Abdominal Discomfort	0 (0.0%)	1 (9.1%)
Dyspepsia	1 (3.6%)	0 (0.0%)
Flatulence	1 (3.6%)	0 (0.0%)
Frequent Bowel Movements	1 (3.6%)	0 (0.0%)
Gastrointestinal Disorder	1 (3.6%)	0 (0.0%)
Haemorrhoids	1 (3.6%)	0 (0.0%)
Rectal Haemorrhage	0 (0.0%)	1 (9.1%)
Toothache	1 (3.6%)	0 (0.0%)
INVESTIGATIONS	9 (32.1%)	1 (9.1%)
Blood Pressure Increased	4 (14.3%)	1 (9.1%)
Alanine Aminotransferase Increased	2 (7.1%)	0 (0.0%)
Aspartate Aminotransferase Increased	1 (3.6%)	0 (0.0%)
Blood Glucose Increased	1 (3.6%)	0 (0.0%)
Liver Function Test Abnormal	1 (3.6%)	0 (0.0%)
Neutrophil Count Decreased	1 (3.6%)	0 (0.0%)
Weight Decreased	1 (3.6%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	9 (32.1%)	1 (9.1%)
Epistaxis	7 (25.0%)	1 (9.1%)
Dysphonia	1 (3.6%)	0 (0.0%)
Dyspnoea	1 (3.6%)	0 (0.0%)
Nasal Congestion	1 (3.6%)	0 (0.0%)
VASCULAR DISORDERS	8 (28.6%)	2 (18.2%)
Hypertension	6 (21.4%)	1 (9.1%)
Haematoma	1 (3.6%)	1 (9.1%)
Haemorrhage	1 (3.6%)	0 (0.0%)
Hypertensive Crisis	1 (3.6%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	7 (25.0%)	1 (9.1%)
Abscess	1 (3.6%)	0 (0.0%)
Bacteriuria	1 (3.6%)	0 (0.0%)
Bronchitis	1 (3.6%)	0 (0.0%)
Lower Respiratory Tract Infection	1 (3.6%)	0 (0.0%)
Nasopharyngitis	1 (3.6%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (9.1%)
Upper Respiratory Tract Infection	1 (3.6%)	0 (0.0%)
Viral Infection	1 (3.6%)	0 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	5 (17.9%)	2 (18.2%)
Fatigue	3 (10.7%)	0 (0.0%)
Chest Pain	2 (7.1%)	0 (0.0%)
Oedema Peripheral	2 (7.1%)	0 (0.0%)
Oedema	0 (0.0%)	1 (9.1%)
Peripheral Swelling	1 (3.6%)	0 (0.0%)
Pyrexia	0 (0.0%)	1 (9.1%)
NERVOUS SYSTEM DISORDERS	6 (21.4%)	0 (0.0%)
Dizziness	5 (17.9%)	0 (0.0%)
Dysgeusia	1 (3.6%)	0 (0.0%)
Hypogeusia	1 (3.6%)	0 (0.0%)
Memory Impairment	1 (3.6%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=28) n (%)	Placebo (N=11) n (%)
Neuralgia	1 (3.6%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	5 (17.9%)	0 (0.0%)
Neutropenia	2 (7.1%)	0 (0.0%)
Immune Thrombocytopenic Purpura	1 (3.6%)	0 (0.0%)
Leukopenia	1 (3.6%)	0 (0.0%)
Thrombocytopenia	1 (3.6%)	0 (0.0%)
Thrombocytosis	1 (3.6%)	0 (0.0%)
METABOLISM AND NUTRITION DISORDERS	4 (14.3%)	0 (0.0%)
Hypokalaemia	3 (10.7%)	0 (0.0%)
Glucose Tolerance Impaired	1 (3.6%)	0 (0.0%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	4 (14.3%)	0 (0.0%)
Rash	3 (10.7%)	0 (0.0%)
Dermatitis Allergic	1 (3.6%)	0 (0.0%)
Petechiae	1 (3.6%)	0 (0.0%)
Rash Macular	1 (3.6%)	0 (0.0%)
EYE DISORDERS	3 (10.7%)	0 (0.0%)
Blepharitis	1 (3.6%)	0 (0.0%)
Eyelid Oedema	1 (3.6%)	0 (0.0%)
Retinal Tear	1 (3.6%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	3 (10.7%)	0 (0.0%)
Bone Lesion	1 (3.6%)	0 (0.0%)
Chondrocalcinosis Pyrophosphate	1 (3.6%)	0 (0.0%)
Joint Swelling	1 (3.6%)	0 (0.0%)
Osteoporosis	1 (3.6%)	0 (0.0%)
Pain In Extremity	1 (3.6%)	0 (0.0%)
RENAL AND URINARY DISORDERS	3 (10.7%)	0 (0.0%)
Leukocyturia	1 (3.6%)	0 (0.0%)
Nephrolithiasis	1 (3.6%)	0 (0.0%)
Pollakiuria	1 (3.6%)	0 (0.0%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	2 (7.1%)	0 (0.0%)
Contusion	2 (7.1%)	0 (0.0%)
PSYCHIATRIC DISORDERS	2 (7.1%)	0 (0.0%)
Insomnia	1 (3.6%)	0 (0.0%)
Restlessness	1 (3.6%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	1 (3.6%)	0 (0.0%)
Vertigo	1 (3.6%)	0 (0.0%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (3.6%)	0 (0.0%)
Plasma Cell Myeloma	1 (3.6%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the age and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.1.1.1)

表 2.7.4.9-7 Adverse Events (AEs): Incidence by System Organ Class/Preferred Term and Gender (Subject Level) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047and C788-048 study

Males

System Organ Class Preferred Term	Fostamatinib (N=41) n (%)	Placebo (N=18) n (%)
Any Adverse Events	33 (80.5%)	12 (66.7%)
GASTROINTESTINAL DISORDERS	17 (41.5%)	4 (22.2%)
Diarrhoea	12 (29.3%)	2 (11.1%)
Flatulence	3 (7.3%)	0 (0.0%)
Nausea	3 (7.3%)	0 (0.0%)
Vomiting	2 (4.9%)	1 (5.6%)
Abdominal Distension	1 (2.4%)	0 (0.0%)
Abdominal Pain	1 (2.4%)	0 (0.0%)
Abdominal Pain Upper	1 (2.4%)	0 (0.0%)
Anal Haemorrhage	0 (0.0%)	1 (5.6%)
Eructation	1 (2.4%)	0 (0.0%)
Faeces Discoloured	0 (0.0%)	1 (5.6%)
Gastric Haemorrhage	0 (0.0%)	1 (5.6%)
Gastrointestinal Haemorrhage	0 (0.0%)	1 (5.6%)
Haematochezia	1 (2.4%)	0 (0.0%)
Melaena	0 (0.0%)	1 (5.6%)
Rectal Haemorrhage	0 (0.0%)	1 (5.6%)
Toothache	1 (2.4%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	12 (29.3%)	2 (11.1%)
Respiratory Tract Infection	2 (4.9%)	1 (5.6%)
Upper Respiratory Tract Infection	3 (7.3%)	0 (0.0%)
Nasopharyngitis	1 (2.4%)	1 (5.6%)
Bronchitis	1 (2.4%)	0 (0.0%)
Laryngitis	1 (2.4%)	0 (0.0%)
Lower Respiratory Tract Infection	1 (2.4%)	0 (0.0%)
Oral Candidiasis	1 (2.4%)	0 (0.0%)
Oral Herpes	1 (2.4%)	0 (0.0%)
Pulpitis Dental	1 (2.4%)	0 (0.0%)
Urinary Tract Infection	1 (2.4%)	0 (0.0%)
Viral Infection	1 (2.4%)	0 (0.0%)
INVESTIGATIONS	11 (26.8%)	0 (0.0%)
Alanine Aminotransferase Increased	4 (9.8%)	0 (0.0%)
Aspartate Aminotransferase Increased	3 (7.3%)	0 (0.0%)
Blood Pressure Increased	2 (4.9%)	0 (0.0%)
Blood Bilirubin Increased	1 (2.4%)	0 (0.0%)
Blood Lactate Dehydrogenase Increased	1 (2.4%)	0 (0.0%)
Blood Pressure Diastolic Abnormal	1 (2.4%)	0 (0.0%)
C-Reactive Protein Increased	1 (2.4%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (2.4%)	0 (0.0%)
Hepatic Enzyme Increased	1 (2.4%)	0 (0.0%)
Lymphocyte Count Decreased	1 (2.4%)	0 (0.0%)
Neutrophil Count Decreased	1 (2.4%)	0 (0.0%)
Platelet Count Decreased	1 (2.4%)	0 (0.0%)
Weight Decreased	1 (2.4%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	7 (17.1%)	3 (16.7%)
Dizziness	2 (4.9%)	2 (11.1%)
Headache	3 (7.3%)	1 (5.6%)
Dysgeusia	1 (2.4%)	0 (0.0%)
Hypoaesthesia	0 (0.0%)	1 (5.6%)
Memory Impairment	1 (2.4%)	0 (0.0%)
Syncope	1 (2.4%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	8 (19.5%)	2 (11.1%)
Epistaxis	6 (14.6%)	0 (0.0%)
Dyspnoea	0 (0.0%)	1 (5.6%)
Nasal Congestion	1 (2.4%)	0 (0.0%)
Oropharyngeal Pain	0 (0.0%)	1 (5.6%)
Sleep Apnoea Syndrome	1 (2.4%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=41) n (%)	Placebo (N=18) n (%)
Upper Respiratory Tract Inflammation	1 (2.4%)	0 (0.0%)
VASCULAR DISORDERS	5 (12.2%)	4 (22.2%)
Hypertension	5 (12.2%)	2 (11.1%)
Haematoma	0 (0.0%)	2 (11.1%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	5 (12.2%)	3 (16.7%)
Petechiae	1 (2.4%)	2 (11.1%)
Rash	3 (7.3%)	0 (0.0%)
Blood Blister	2 (4.9%)	0 (0.0%)
Rash Macular	1 (2.4%)	0 (0.0%)
Skin Haemorrhage	0 (0.0%)	1 (5.6%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	5 (12.2%)	1 (5.6%)
Anaemia	1 (2.4%)	1 (5.6%)
Febrile Neutropenia	1 (2.4%)	0 (0.0%)
Leukopenia	1 (2.4%)	0 (0.0%)
Neutropenia	1 (2.4%)	0 (0.0%)
Thrombocytopenia	1 (2.4%)	0 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (9.8%)	1 (5.6%)
Fatigue	1 (2.4%)	1 (5.6%)
Asthenia	0 (0.0%)	1 (5.6%)
Chest Pain	1 (2.4%)	0 (0.0%)
Influenza Like Illness	1 (2.4%)	0 (0.0%)
Oedema Peripheral	1 (2.4%)	0 (0.0%)
Peripheral Swelling	1 (2.4%)	0 (0.0%)
Pyrexia	1 (2.4%)	0 (0.0%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	3 (7.3%)	1 (5.6%)
Contusion	3 (7.3%)	0 (0.0%)
Muscle Rupture	0 (0.0%)	1 (5.6%)
RENAL AND URINARY DISORDERS	2 (4.9%)	1 (5.6%)
Haematuria	1 (2.4%)	1 (5.6%)
Nephrolithiasis	1 (2.4%)	0 (0.0%)
EYE DISORDERS	1 (2.4%)	1 (5.6%)
Conjunctival Pallor	0 (0.0%)	1 (5.6%)
Ocular Icterus	0 (0.0%)	1 (5.6%)
Retinal Tear	1 (2.4%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	2 (4.9%)	0 (0.0%)
Ankylosing Spondylitis	1 (2.4%)	0 (0.0%)
Arthralgia	1 (2.4%)	0 (0.0%)
Myalgia	1 (2.4%)	0 (0.0%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (2.4%)	0 (0.0%)
Hydrocele	1 (2.4%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	0 (0.0%)	1 (5.6%)
Tinnitus	0 (0.0%)	1 (5.6%)
METABOLISM AND NUTRITION DISORDERS	1 (2.4%)	0 (0.0%)
Hyperglycaemia	1 (2.4%)	0 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	1 (2.4%)	0 (0.0%)
Erectile Dysfunction	1 (2.4%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the gender and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.1.1.2)

Females

System Organ Class Preferred Term	Fostamatinib (N=61) n (%)	Placebo (N=30) n (%)
Any Adverse Events	52 (85.2%)	24 (80.0%)
GASTROINTESTINAL DISORDERS	32 (52.5%)	12 (40.0%)
Diarrhoea	18 (29.5%)	5 (16.7%)
Nausea	16 (26.2%)	4 (13.3%)
Gingival Bleeding	4 (6.6%)	1 (3.3%)
Constipation	3 (4.9%)	1 (3.3%)
Dyspepsia	3 (4.9%)	1 (3.3%)
Abdominal Pain Upper	2 (3.3%)	1 (3.3%)

System Organ Class Preferred Term	Fostamatinib (N=61) n (%)	Placebo (N=30) n (%)
Flatulence	2 (3.3%)	1 (3.3%)
Vomiting	1 (1.6%)	2 (6.7%)
Abdominal Discomfort	1 (1.6%)	1 (3.3%)
Abdominal Pain	2 (3.3%)	0 (0.0%)
Frequent Bowel Movements	2 (3.3%)	0 (0.0%)
Toothache	1 (1.6%)	1 (3.3%)
Abdominal Distension	1 (1.6%)	0 (0.0%)
Gastritis	1 (1.6%)	0 (0.0%)
Gastrointestinal Disorder	1 (1.6%)	0 (0.0%)
Gastrooesophageal Reflux Disease	1 (1.6%)	0 (0.0%)
Haemorrhoids	1 (1.6%)	0 (0.0%)
Oesophageal Pain	1 (1.6%)	0 (0.0%)
Oral Mucosal Blistering	0 (0.0%)	1 (3.3%)
Rectal Haemorrhage	0 (0.0%)	1 (3.3%)
Retching	1 (1.6%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	19 (31.1%)	10 (33.3%)
Headache	8 (13.1%)	8 (26.7%)
Dizziness	9 (14.8%)	2 (6.7%)
Dysgeusia	3 (4.9%)	0 (0.0%)
Neuralgia	2 (3.3%)	0 (0.0%)
Disturbance In Attention	1 (1.6%)	0 (0.0%)
Hypogeusia	1 (1.6%)	0 (0.0%)
Lethargy	1 (1.6%)	0 (0.0%)
Memory Impairment	1 (1.6%)	0 (0.0%)
Migraine	1 (1.6%)	0 (0.0%)
Neuropathy Peripheral	1 (1.6%)	0 (0.0%)
Paraesthesia	0 (0.0%)	1 (3.3%)
Somnolence	0 (0.0%)	1 (3.3%)
Transient Ischaemic Attack	1 (1.6%)	0 (0.0%)
VASCULAR DISORDERS	19 (31.1%)	5 (16.7%)
Hypertension	15 (24.6%)	2 (6.7%)
Haemorrhage	2 (3.3%)	2 (6.7%)
Haematoma	1 (1.6%)	0 (0.0%)
Hot Flush	1 (1.6%)	0 (0.0%)
Hypertensive Crisis	1 (1.6%)	0 (0.0%)
Peripheral Coldness	0 (0.0%)	1 (3.3%)
Peripheral Venous Disease	1 (1.6%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	15 (24.6%)	8 (26.7%)
Upper Respiratory Tract Infection	3 (4.9%)	2 (6.7%)
Gastroenteritis	2 (3.3%)	1 (3.3%)
Bronchitis	2 (3.3%)	0 (0.0%)
Urinary Tract Infection	2 (3.3%)	0 (0.0%)
Viral Infection	1 (1.6%)	1 (3.3%)
Abscess	1 (1.6%)	0 (0.0%)
Bacteriuria	1 (1.6%)	0 (0.0%)
Eye Infection	0 (0.0%)	1 (3.3%)
Gingivitis	1 (1.6%)	0 (0.0%)
Infection	0 (0.0%)	1 (3.3%)
Influenza	0 (0.0%)	1 (3.3%)
Nasopharyngitis	1 (1.6%)	0 (0.0%)
Pneumonia	1 (1.6%)	0 (0.0%)
Respiratory Tract Infection	1 (1.6%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (3.3%)
Viral Upper Respiratory Tract Infection	1 (1.6%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	15 (24.6%)	8 (26.7%)
Epistaxis	10 (16.4%)	5 (16.7%)
Dyspnoea	4 (6.6%)	1 (3.3%)
Cough	1 (1.6%)	1 (3.3%)
Oropharyngeal Pain	1 (1.6%)	1 (3.3%)
Chronic Obstructive Pulmonary Disease	0 (0.0%)	1 (3.3%)
Dry Throat	1 (1.6%)	0 (0.0%)
Dysphonia	1 (1.6%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=61) n (%)	Placebo (N=30) n (%)
Hypoxia	1 (1.6%)	0 (0.0%)
Rhinorrhoea	1 (1.6%)	0 (0.0%)
INVESTIGATIONS	17 (27.9%)	5 (16.7%)
Alanine Aminotransferase Increased	7 (11.5%)	0 (0.0%)
Aspartate Aminotransferase Increased	6 (9.8%)	0 (0.0%)
Blood Pressure Increased	3 (4.9%)	2 (6.7%)
Blood Alkaline Phosphatase Increased	1 (1.6%)	0 (0.0%)
Blood Bilirubin Increased	1 (1.6%)	0 (0.0%)
Blood Glucose Increased	1 (1.6%)	0 (0.0%)
Blood Lactate Dehydrogenase Increased	1 (1.6%)	0 (0.0%)
Blood Potassium Decreased	0 (0.0%)	1 (3.3%)
Blood Pressure Diastolic Increased	1 (1.6%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.6%)	0 (0.0%)
C-Reactive Protein Increased	0 (0.0%)	1 (3.3%)
Heart Rate Increased	1 (1.6%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.6%)	0 (0.0%)
Neutrophil Count Decreased	1 (1.6%)	0 (0.0%)
Platelet Count Decreased	1 (1.6%)	0 (0.0%)
Platelet Count Increased	0 (0.0%)	1 (3.3%)
Weight Increased	1 (1.6%)	0 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	13 (21.3%)	4 (13.3%)
Chest Pain	5 (8.2%)	1 (3.3%)
Fatigue	5 (8.2%)	0 (0.0%)
Pyrexia	2 (3.3%)	2 (6.7%)
Chills	2 (3.3%)	0 (0.0%)
Influenza Like Illness	2 (3.3%)	0 (0.0%)
Oedema Peripheral	2 (3.3%)	0 (0.0%)
Asthenia	1 (1.6%)	0 (0.0%)
Oedema	0 (0.0%)	1 (3.3%)
Peripheral Swelling	1 (1.6%)	0 (0.0%)
Vessel Puncture Site Bruise	1 (1.6%)	0 (0.0%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	13 (21.3%)	2 (6.7%)
Rash	5 (8.2%)	1 (3.3%)
Petechiae	3 (4.9%)	1 (3.3%)
Hair Colour Changes	2 (3.3%)	0 (0.0%)
Hyperhidrosis	2 (3.3%)	0 (0.0%)
Swelling Face	2 (3.3%)	0 (0.0%)
Actinic Keratosis	1 (1.6%)	0 (0.0%)
Alopecia	1 (1.6%)	0 (0.0%)
Dermatitis Allergic	1 (1.6%)	0 (0.0%)
Dry Skin	1 (1.6%)	0 (0.0%)
Ecchymosis	1 (1.6%)	0 (0.0%)
Erythema	1 (1.6%)	0 (0.0%)
Hypertrichosis	1 (1.6%)	0 (0.0%)
Nail Disorder	1 (1.6%)	0 (0.0%)
Photosensitivity Reaction	1 (1.6%)	0 (0.0%)
Pruritus	1 (1.6%)	0 (0.0%)
Rash Erythematous	1 (1.6%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	10 (16.4%)	3 (10.0%)
Neutropenia	4 (6.6%)	0 (0.0%)
Anaemia	2 (3.3%)	1 (3.3%)
Leukopenia	2 (3.3%)	0 (0.0%)
Thrombocytopenia	0 (0.0%)	2 (6.7%)
Immune Thrombocytopenic Purpura	1 (1.6%)	0 (0.0%)
Leukocytosis	1 (1.6%)	0 (0.0%)
Lymphadenopathy	1 (1.6%)	0 (0.0%)
Thrombocytosis	1 (1.6%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	8 (13.1%)	4 (13.3%)
Arthralgia	1 (1.6%)	1 (3.3%)
Back Pain	2 (3.3%)	0 (0.0%)
Muscle Spasms	1 (1.6%)	1 (3.3%)
Musculoskeletal Pain	0 (0.0%)	2 (6.7%)

System Organ Class Preferred Term	Fostamatinib (N=61) n (%)	Placebo (N=30) n (%)
Bone Lesion	1 (1.6%)	0 (0.0%)
Chondrocalcinosis Pyrophosphate	1 (1.6%)	0 (0.0%)
Joint Swelling	1 (1.6%)	0 (0.0%)
Musculoskeletal Chest Pain	0 (0.0%)	1 (3.3%)
Myalgia	1 (1.6%)	0 (0.0%)
Osteoporosis	1 (1.6%)	0 (0.0%)
Pain In Extremity	1 (1.6%)	0 (0.0%)
METABOLISM AND NUTRITION DISORDERS	7 (11.5%)	2 (6.7%)
Hypokalaemia	3 (4.9%)	0 (0.0%)
Decreased Appetite	2 (3.3%)	0 (0.0%)
Iron Deficiency	1 (1.6%)	1 (3.3%)
Glucose Tolerance Impaired	1 (1.6%)	0 (0.0%)
Hypomagnesaemia	0 (0.0%)	1 (3.3%)
Hypophosphataemia	0 (0.0%)	1 (3.3%)
EYE DISORDERS	4 (6.6%)	1 (3.3%)
Eye Pain	1 (1.6%)	1 (3.3%)
Blepharitis	1 (1.6%)	0 (0.0%)
Eye Disorder	1 (1.6%)	0 (0.0%)
Eyelid Oedema	1 (1.6%)	0 (0.0%)
Visual Impairment	0 (0.0%)	1 (3.3%)
PSYCHIATRIC DISORDERS	5 (8.2%)	0 (0.0%)
Insomnia	3 (4.9%)	0 (0.0%)
Anxiety	1 (1.6%)	0 (0.0%)
Depression	1 (1.6%)	0 (0.0%)
Restlessness	1 (1.6%)	0 (0.0%)
CARDIAC DISORDERS	3 (4.9%)	1 (3.3%)
Tachycardia	3 (4.9%)	0 (0.0%)
Cardiac Failure Congestive	0 (0.0%)	1 (3.3%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	3 (4.9%)	1 (3.3%)
Contusion	3 (4.9%)	0 (0.0%)
Tooth Fracture	0 (0.0%)	1 (3.3%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	2 (3.3%)	2 (6.7%)
Menorrhagia	1 (1.6%)	2 (6.7%)
Uterine Polyp	1 (1.6%)	0 (0.0%)
Vaginal Haemorrhage	1 (1.6%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	2 (3.3%)	0 (0.0%)
Excessive Cerumen Production	1 (1.6%)	0 (0.0%)
Vertigo	1 (1.6%)	0 (0.0%)
RENAL AND URINARY DISORDERS	2 (3.3%)	0 (0.0%)
Leukocyturia	1 (1.6%)	0 (0.0%)
Pollakiuria	1 (1.6%)	0 (0.0%)
ENDOCRINE DISORDERS	1 (1.6%)	0 (0.0%)
Cushingoid	1 (1.6%)	0 (0.0%)
HEPATOBILIARY DISORDERS	1 (1.6%)	0 (0.0%)
Hepatic Cyst	1 (1.6%)	0 (0.0%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1 (1.6%)	0 (0.0%)
Plasma Cell Myeloma	1 (1.6%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the gender and treatment group, and the numerator is the number of such subjects with at least one AE in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.2.1.1.1.2)

表 2.7.4.9-8 Treatment-Related Adverse Events (AEs): Incidence by System Organ Class and Preferred Term (Subject Level) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

System Organ Class Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Any Treatment-Related Adverse Events	60 (58.8%)	13 (27.1%)
GASTROINTESTINAL DISORDERS	38 (37.3%)	9 (18.8%)
Diarrhoea	27 (26.5%)	6 (12.5%)
Nausea	15 (14.7%)	3 (6.3%)
Constipation	3 (2.9%)	1 (2.1%)
Flatulence	3 (2.9%)	1 (2.1%)
Abdominal Pain	3 (2.9%)	0 (0.0%)
Abdominal Discomfort	1 (1.0%)	1 (2.1%)
Abdominal Distension	2 (2.0%)	0 (0.0%)
Abdominal Pain Upper	1 (1.0%)	1 (2.1%)
Dyspepsia	1 (1.0%)	1 (2.1%)
Vomiting	1 (1.0%)	1 (2.1%)
Eructation	1 (1.0%)	0 (0.0%)
Frequent Bowel Movements	1 (1.0%)	0 (0.0%)
Gastritis	1 (1.0%)	0 (0.0%)
Gastrointestinal Disorder	1 (1.0%)	0 (0.0%)
Gastrooesophageal Reflux Disease	1 (1.0%)	0 (0.0%)
Gingival Bleeding	0 (0.0%)	1 (2.1%)
Haemorrhoids	1 (1.0%)	0 (0.0%)
Oesophageal Pain	1 (1.0%)	0 (0.0%)
Retching	1 (1.0%)	0 (0.0%)
INVESTIGATIONS	19 (18.6%)	1 (2.1%)
Alanine Aminotransferase Increased	10 (9.8%)	0 (0.0%)
Aspartate Aminotransferase Increased	7 (6.9%)	0 (0.0%)
Blood Pressure Increased	4 (3.9%)	0 (0.0%)
Blood Bilirubin Increased	2 (2.0%)	0 (0.0%)
Neutrophil Count Decreased	2 (2.0%)	0 (0.0%)
Blood Alkaline Phosphatase Increased	1 (1.0%)	0 (0.0%)
Blood Lactate Dehydrogenase Increased	1 (1.0%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.0%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.0%)	0 (0.0%)
Platelet Count Increased	0 (0.0%)	1 (2.1%)
Weight Decreased	1 (1.0%)	0 (0.0%)
VASCULAR DISORDERS	17 (16.7%)	2 (4.2%)
Hypertension	16 (15.7%)	2 (4.2%)
Hypertensive Crisis	1 (1.0%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	14 (13.7%)	2 (4.2%)
Dizziness	9 (8.8%)	2 (4.2%)
Headache	4 (3.9%)	0 (0.0%)
Dysgeusia	3 (2.9%)	0 (0.0%)
Disturbance In Attention	1 (1.0%)	0 (0.0%)
Hypogeusia	1 (1.0%)	0 (0.0%)
Lethargy	1 (1.0%)	0 (0.0%)
Memory Impairment	1 (1.0%)	0 (0.0%)
Somnolence	0 (0.0%)	1 (2.1%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	9 (8.8%)	0 (0.0%)
Epistaxis	4 (3.9%)	0 (0.0%)
Dyspnoea	3 (2.9%)	0 (0.0%)
Cough	1 (1.0%)	0 (0.0%)
Dry Throat	1 (1.0%)	0 (0.0%)
Dysphonia	1 (1.0%)	0 (0.0%)
Hypoxia	1 (1.0%)	0 (0.0%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	8 (7.8%)	1 (2.1%)
Rash	5 (4.9%)	0 (0.0%)
Hair Colour Changes	2 (2.0%)	0 (0.0%)
Actinic Keratosis	1 (1.0%)	0 (0.0%)
Alopecia	1 (1.0%)	0 (0.0%)
Blood Blister	1 (1.0%)	0 (0.0%)

System Organ Class Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Dry Skin	1 (1.0%)	0 (0.0%)
Erythema	1 (1.0%)	0 (0.0%)
Nail Disorder	1 (1.0%)	0 (0.0%)
Petechiae	0 (0.0%)	1 (2.1%)
Photosensitivity Reaction	1 (1.0%)	0 (0.0%)
Pruritus	1 (1.0%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	8 (7.8%)	0 (0.0%)
Neutropenia	4 (3.9%)	0 (0.0%)
Febrile Neutropenia	1 (1.0%)	0 (0.0%)
Leukocytosis	1 (1.0%)	0 (0.0%)
Leukopenia	1 (1.0%)	0 (0.0%)
Thrombocytosis	1 (1.0%)	0 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	8 (7.8%)	0 (0.0%)
Chest Pain	5 (4.9%)	0 (0.0%)
Fatigue	3 (2.9%)	0 (0.0%)
Chills	1 (1.0%)	0 (0.0%)
Influenza Like Illness	1 (1.0%)	0 (0.0%)
Oedema Peripheral	1 (1.0%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	6 (5.9%)	0 (0.0%)
Arthralgia	2 (2.0%)	0 (0.0%)
Myalgia	2 (2.0%)	0 (0.0%)
Ankylosing Spondylitis	1 (1.0%)	0 (0.0%)
Joint Swelling	1 (1.0%)	0 (0.0%)
Muscle Spasms	1 (1.0%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	3 (2.9%)	0 (0.0%)
Bacteriuria	1 (1.0%)	0 (0.0%)
Oral Candidiasis	1 (1.0%)	0 (0.0%)
Pneumonia	1 (1.0%)	0 (0.0%)
PSYCHIATRIC DISORDERS	3 (2.9%)	0 (0.0%)
Insomnia	2 (2.0%)	0 (0.0%)
Restlessness	1 (1.0%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	2 (2.0%)	0 (0.0%)
Excessive Cerumen Production	1 (1.0%)	0 (0.0%)
Vertigo	1 (1.0%)	0 (0.0%)
EYE DISORDERS	2 (2.0%)	0 (0.0%)
Blepharitis	1 (1.0%)	0 (0.0%)
Eye Pain	1 (1.0%)	0 (0.0%)
METABOLISM AND NUTRITION DISORDERS	2 (2.0%)	0 (0.0%)
Decreased Appetite	2 (2.0%)	0 (0.0%)
CARDIAC DISORDERS	1 (1.0%)	0 (0.0%)
Tachycardia	1 (1.0%)	0 (0.0%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	1 (1.0%)	0 (0.0%)
Contusion	1 (1.0%)	0 (0.0%)
RENAL AND URINARY DISORDERS	1 (1.0%)	0 (0.0%)
Leukocyturia	1 (1.0%)	0 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	0 (0.0%)	1 (2.1%)
Menorrhagia	0 (0.0%)	1 (2.1%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one treatment-related AE in that system organ class or with that preferred term. Treatment-related AEs are AEs with a possible, probable, or missing causal relationship to study drug.
(Source: 5.3.5.3.2, Table 4.2.1.1.2)

表 2.7.4.9-9 Occurrence of Adverse Events by Onset Time – R788-1301 study

R788 Treatment Period

	<= Week 12			Week 12< <=24			Week 24< <=36			Week 36< <=48			Week 48< <=72			> Week 72			Follow-up		
SOC, PT	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e
N	33	---	---	31	---	---	26	---	---	23	---	---	18	---	---	7	---	---	12	---	---
Total	25	75.8	80	18	58.1	37	16	61.5	28	8	34.8	14	8	44.4	16	3	42.9	6	3	25.0	3
Infections and infestations	2	6.1	2	7	22.6	8	5	19.2	6	1	4.3	1	1	5.6	1	1	14.3	1	0	0.0	0
COVID-19	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	14.3	1	0	0.0	0
Cellulitis	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Cystitis	0	0.0	0	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Diverticulitis	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Gastroenteritis	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Gingivitis	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Herpes zoster	0	0.0	0	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Nasopharyngitis	0	0.0	0	0	0.0	0	1	3.8	1	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Paronychia	0	0.0	0	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Periodontitis	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Pulpitis dental	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Tinea infection	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Urinary tract infection	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Viral infection	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	8.3	1
Lipoma	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	8.3	1
Blood and lymphatic system disorders	2	6.1	2	1	3.2	1	0	0.0	0	1	4.3	1	1	5.6	1	1	14.3	1	0	0.0	0
Leukopenia	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Neutropenia	1	3.0	1	0	0.0	0	0	0.0	0	1	4.3	1	1	5.6	1	1	14.3	1	0	0.0	0
Thrombocytopenia	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Endocrine disorders	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hypothyroidism	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Metabolism and nutrition disorders	2	6.1	2	1	3.2	1	1	3.8	1	1	4.3	2	0	0.0	0	0	0.0	0	0	0.0	0
Decreased appetite	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Dehydration	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hyperglycaemia	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hypoalbuminaemia	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Hypoglycaemia	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hypoproteinaemia	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Psychiatric disorders	1	3.0	1	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Affect lability	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Insomnia	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Nervous system disorders	1	3.0	1	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0

SOC, PT	<= Week 12			Week 12< <=24			Week 24< <=36			Week 36< <=48			Week 48< <=72			> Week 72			Follow-up		
	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e
Cervicobrachial syndrome	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Dizziness	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Eye disorders	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	2	11.1	2	0	0.0	0	0	0.0	0
Asthenopia	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Conjunctival haemorrhage	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Punctate keratitis	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Ear and labyrinth disorders	1	3.0	1	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	1	14.3	1	0	0.0	0
Auricular swelling	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Eustachian tube patulous	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Meniere's disease	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Sudden hearing loss	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	14.3	1	0	0.0	0
Cardiac disorders	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Atrial fibrillation	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Vascular disorders	9	27.3	10	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hypertension	9	27.3	10	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Respiratory, thoracic and mediastinal disorders	2	6.1	2	0	0.0	0	0	0.0	0	1	4.3	2	0	0.0	0	0	0.0	0	0	0.0	0
Cough	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Epistaxis	2	6.1	2	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Gastrointestinal disorders	15	45.5	25	7	22.6	9	3	11.5	3	3	13.0	3	2	11.1	2	0	0.0	0	0	0.0	0
Abdominal discomfort	2	6.1	2	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Abdominal pain	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Abdominal pain upper	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Constipation	3	9.1	3	1	3.2	1	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Diarrhoea	11	33.3	18	4	12.9	4	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Faeces soft	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Large intestine polyp	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Mouth haemorrhage	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Nausea	1	3.0	1	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Stomatitis	0	0.0	0	1	3.2	1	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Toothache	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Vomiting	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hepatobiliary disorders	3	9.1	3	1	3.2	1	1	3.8	2	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Autoimmune hepatitis	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hepatic cyst	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hepatic function abnormal	2	6.1	2	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hepatic steatosis	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Skin and subcutaneous tissue disorders	4	12.1	7	2	6.5	3	2	7.7	2	1	4.3	1	3	16.7	3	1	14.3	1	2	16.7	2
Dry skin	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Eczema	2	6.1	2	2	6.5	2	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Erythema	1	3.0	1	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0

SOC, PT	<= Week 12			Week 12< <=24			Week 24< <=36			Week 36< <=48			Week 48< <=72			> Week 72			Follow-up		
	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e
Haemorrhage subcutaneous	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	1	14.3	1	0	0.0	0
Pruritus	2	6.1	2	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Purpura	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Rash	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	2	16.7	2
Rash erythematous	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Rosacea	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Seborrhoeic dermatitis	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	0	0.0	0	0	0.0	0
Musculoskeletal and connective tissue disorders	0	0.0	0	1	3.2	1	3	11.5	3	2	8.7	2	1	5.6	4	1	14.3	1	0	0.0	0
Arthralgia	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	1	5.6	2	0	0.0	0	0	0.0	0
Back pain	0	0.0	0	0	0.0	0	0	0.0	0	1	4.3	1	0	0.0	0	1	14.3	1	0	0.0	0
Joint contracture	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Lumbar spinal stenosis	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Muscle spasms	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Neck pain	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Pain in extremity	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Reproductive system and breast disorders	1	3.0	1	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Menopausal symptoms	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Menorrhagia	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
General disorders and administration site conditions	2	6.1	4	2	6.5	3	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Face oedema	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Incarcerated hernia	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Malaise	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Oedema	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Oedema peripheral	0	0.0	0	1	3.2	2	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Pyrexia	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Investigations	10	30.3	16	5	16.1	8	3	11.5	4	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Alanine aminotransferase increased	2	6.1	2	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Aspartate aminotransferase increased	2	6.1	2	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Blood bilirubin increased	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Blood creatine phosphokinase increased	2	6.1	2	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Blood pressure increased	1	3.0	2	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Hepatic enzyme increased	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Liver function test abnormal	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Liver function test increased	2	6.1	2	1	3.2	1	1	3.8	1	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0
Lymphocyte count increased	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Neutrophil count decreased	2	6.1	2	2	6.5	2	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Platelet count decreased	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Weight increased	0	0.0	0	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
White blood cell count decreased	1	3.0	1	1	3.2	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Injury, poisoning and procedural complications	3	9.1	3	0	0.0	0	1	3.8	1	0	0.0	0	1	5.6	1	1	14.3	1	0	0.0	0

SOC, PT	<= Week 12			Week 12< <=24			Week 24< <=36			Week 36< <=48			Week 48< <=72			> Week 72			Follow-up		
	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e	n	%	e
Allergic transfusion reaction	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Contusion	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	14.3	1	0	0.0	0
Limb injury	1	3.0	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Radius fracture	0	0.0	0	0	0.0	0	1	3.8	1	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0
Vaccination complication	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0	0	1	5.6	1	0	0.0	0	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.3.4.1.8.1)

表 2.7.4.9-10 Adverse Events (AEs): Incidence by System Organ Class/Preferred Term and Onset Time (Subject Level) Fostamatinib Treated Population: Fostamatinib Exposure Period – C788-047, C788-048 and C788-049 study

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N	146	146	128	101	65	58	50	47	45	40	38	23
Adverse Events	130 (89.0%)	112 (76.7%)	62 (48.4%)	44 (43.6%)	29 (44.6%)	33 (56.9%)	25 (50.0%)	17 (36.2%)	19 (42.2%)	13 (32.5%)	13 (34.2%)	7 (30.4%)
Adverse Events Leading to Death	5 (3.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (4.3%)
Other Serious Adverse Events	42 (28.8%)	19 (13.0%)	12 (9.4%)	4 (4.0%)	4 (6.2%)	2 (3.4%)	3 (6.0%)	1 (2.1%)	3 (6.7%)	4 (10.0%)	4 (10.5%)	3 (13.0%)
Adverse Events Leading to Study Drug Withdrawal	28 (19.2%)	13 (8.9%)	5 (3.9%)	2 (2.0%)	1 (1.5%)	3 (5.2%)	1 (2.0%)	1 (2.1%)	2 (4.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GASTROINTESTINAL DISORDERS	85 (58.2%)	65 (44.5%)	29 (22.7%)	17 (16.8%)	7 (10.8%)	13 (22.4%)	7 (14.0%)	4 (8.5%)	5 (11.1%)	4 (10.0%)	5 (13.2%)	6 (26.1%)
Diarrhoea	53 (36.3%)	31 (21.2%)	19 (14.8%)	10 (9.9%)	2 (3.1%)	9 (15.5%)	3 (6.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	2 (5.3%)	2 (8.7%)
Nausea	28 (19.2%)	23 (15.8%)	4 (3.1%)	3 (3.0%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vomiting	13 (8.9%)	4 (2.7%)	3 (2.3%)	3 (3.0%)	1 (1.5%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Abdominal Pain	9 (6.2%)	4 (2.7%)	3 (2.3%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (4.3%)
Abdominal Pain Upper	8 (5.5%)	4 (2.7%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation	8 (5.5%)	4 (2.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dyspepsia	6 (4.1%)	5 (3.4%)	0 (0.0%)	2 (2.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Flatulence	6 (4.1%)	6 (4.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gingival Bleeding	6 (4.1%)	4 (2.7%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Mouth Haemorrhage	6 (4.1%)	0 (0.0%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Mucosal Blistering	6 (4.1%)	0 (0.0%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	2 (5.3%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Abdominal Distension	4 (2.7%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrointestinal Haemorrhage	4 (2.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haematochezia	4 (2.7%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Toothache	4 (2.7%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dysphagia	3 (2.1%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Haemorrhoidal Haemorrhage	3 (2.1%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rectal Haemorrhage	3 (2.1%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abdominal Discomfort	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Frequent Bowel Movements	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastritis	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrooesophageal Reflux Disease	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemorrhoids	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Stomatitis	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abdominal Pain Lower	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anal Fissure	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ascites	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Bile Acid Malabsorption	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cheilitis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dry Mouth	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Eructation	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastric Antral Vascular Ectasia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastritis Erosive	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrointestinal Disorder	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Inguinal Hernia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Irritable Bowel Syndrome	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Lip Oedema	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Melaena	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Odynophagia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oesophageal Pain	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Pain	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Palatal Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retching	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	64 (43.8%)	27 (18.5%)	16 (12.5%)	13 (12.9%)	8 (12.3%)	14 (24.1%)	10 (20.0%)	10 (21.3%)	12 (26.7%)	8 (20.0%)	4 (10.5%)	3 (13.0%)
Upper Respiratory Tract Infection	18 (12.3%)	6 (4.1%)	2 (1.6%)	5 (5.0%)	1 (1.5%)	1 (1.7%)	4 (8.0%)	1 (2.1%)	1 (2.2%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
Nasopharyngitis	10 (6.8%)	2 (1.4%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	3 (5.2%)	2 (4.0%)	4 (8.5%)	1 (2.2%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Urinary Tract Infection	9 (6.2%)	2 (1.4%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	3 (5.2%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	2 (5.0%)	2 (5.3%)	0 (0.0%)
Bronchitis	6 (4.1%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	2 (4.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lower Respiratory Tract Infection	6 (4.1%)	3 (2.1%)	1 (0.8%)	3 (3.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Respiratory Tract Infection	6 (4.1%)	2 (1.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Viral Infection	6 (4.1%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pneumonia	5 (3.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastroenteritis	4 (2.7%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pharyngitis	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	2 (4.4%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tooth Infection	4 (2.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Sepsis	3 (2.1%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cellulitis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Ear Infection	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Infection	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Gastrointestinal Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Candidiasis	2 (1.4%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Herpes	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post Procedural Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Sinusitis	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abscess	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Arthritis Viral	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Bacteriuria	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Carbuncle	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cellulitis Staphylococcal	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diverticulitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Endocarditis Bacterial	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Erythema Induratum	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Escherichia Urinary Tract Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Fungal Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fungal Skin Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gingivitis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Herpes Simplex	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Herpes Zoster	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infection	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Influenza	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Klebsiella Bacteraemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Laryngitis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mastoiditis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Onychomycosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Otitis Media	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pulpitis Dental	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pyelonephritis Acute	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rhinitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subacute Endocarditis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Tinea Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tonsillitis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Tooth Abscess	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tuberculosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Urinary Tract Infection Bacterial	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Urosepsis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Viral Pharyngitis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Viral Upper Respiratory Tract Infection	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	50 (34.2%)	29 (19.9%)	13 (10.2%)	7 (6.9%)	7 (10.8%)	6 (10.3%)	2 (4.0%)	2 (4.3%)	3 (6.7%)	3 (7.5%)	2 (5.3%)	1 (4.3%)
Epistaxis	27 (18.5%)	17 (11.6%)	9 (7.0%)	3 (3.0%)	2 (3.1%)	3 (5.2%)	0 (0.0%)	2 (4.3%)	2 (4.4%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Cough	11 (7.5%)	2 (1.4%)	0 (0.0%)	2 (2.0%)	2 (3.1%)	0 (0.0%)	2 (4.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Dyspnoea	8 (5.5%)	6 (4.1%)	1 (0.8%)	2 (2.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Oropharyngeal Pain	6 (4.1%)	1 (0.7%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Rhinorrhoea	4 (2.7%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nasal Congestion	3 (2.1%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dry Throat	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyspnoea Exertional	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Sleep Apnoea Syndrome	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Obstructive Pulmonary Disease	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dysphonia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Haemoptysis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypoxia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nasal Inflammation	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pleural Effusion	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Pulmonary Mass	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Upper Respiratory Tract Inflammation	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	47 (32.2%)	22 (15.1%)	14 (10.9%)	4 (4.0%)	1 (1.5%)	6 (10.3%)	6 (12.0%)	3 (6.4%)	6 (13.3%)	1 (2.5%)	3 (7.9%)	2 (8.7%)
Fatigue	14 (9.6%)	6 (4.1%)	3 (2.3%)	1 (1.0%)	1 (1.5%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Pyrexia	10 (6.8%)	5 (3.4%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	1 (2.6%)	1 (4.3%)
Chest Pain	9 (6.2%)	5 (3.4%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oedema Peripheral	8 (5.5%)	2 (1.4%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Asthenia	7 (4.8%)	3 (2.1%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peripheral Swelling	7 (4.8%)	3 (2.1%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Influenza Like Illness	6 (4.1%)	2 (1.4%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chills	5 (3.4%)	3 (2.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Pain	3 (2.1%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chest Discomfort	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Feeling Cold	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adverse Drug Reaction	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Facial Pain	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gait Disturbance	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
General Physical Health Deterioration	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glassy Eyes	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Mucosal Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Polyp	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vessel Puncture Site Bruise	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	47 (32.2%)	29 (19.9%)	12 (9.4%)	2 (2.0%)	3 (4.6%)	9 (15.5%)	1 (2.0%)	2 (4.3%)	2 (4.4%)	2 (5.0%)	3 (7.9%)	3 (13.0%)
Headache	22 (15.1%)	12 (8.2%)	5 (3.9%)	2 (2.0%)	1 (1.5%)	4 (6.9%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	2 (5.0%)	2 (5.3%)	2 (8.7%)
Dizziness	18 (12.3%)	13 (8.9%)	5 (3.9%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dysgeusia	4 (2.7%)	3 (2.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypoaesthesia	3 (2.1%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Sciatica	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Memory Impairment	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Neuralgia	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Presyncope	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cerebral Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Disturbance In Attention	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dysarthria	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Haemorrhagic Stroke	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hypogeusia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lethargy	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Loss Of Consciousness	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Migraine	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Neuropathy Peripheral	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Paraesthesia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Peroneal Nerve Palsy	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Restless Legs Syndrome	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Somnolence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Syncope	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Transient Ischaemic Attack	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INVESTIGATIONS	46 (31.5%)	24 (16.4%)	13 (10.2%)	5 (5.0%)	7 (10.8%)	4 (6.9%)	2 (4.0%)	3 (6.4%)	4 (8.9%)	4 (10.0%)	0 (0.0%)	4 (17.4%)
Alanine Aminotransferase Increased	14 (9.6%)	9 (6.2%)	5 (3.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspartate Aminotransferase Increased	10 (6.8%)	7 (4.8%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Increased	7 (4.8%)	4 (2.7%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet Count Decreased	6 (4.1%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hepatic Enzyme Increased	5 (3.4%)	1 (0.7%)	1 (0.8%)	1 (1.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Function Test Abnormal	4 (2.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Bilirubin Increased	3 (2.1%)	1 (0.7%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Blood Lactate Dehydrogenase Increased	3 (2.1%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Blood Creatinine Increased	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Pressure Diastolic Increased	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Neutrophil Count Decreased	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Transaminases Increased	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Weight Decreased	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Weight Increased	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Angiogram	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Alkaline Phosphatase Increased	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Bicarbonate Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Glucose Increased	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Potassium Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Blood Pressure Diastolic Abnormal	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Measurement	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Blood Urea Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
C-Reactive Protein Increased	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac Murmur	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gamma-Glutamyltransferase Increased	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Globulins Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Haemoglobin Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Heart Rate Increased	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lymphocyte Count Decreased	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet Count Increased	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Troponin Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Vitamin B12 Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	45 (30.8%)	23 (15.8%)	13 (10.2%)	10 (9.9%)	3 (4.6%)	7 (12.1%)	4 (8.0%)	4 (8.5%)	3 (6.7%)	2 (5.0%)	3 (7.9%)	1 (4.3%)
Petechiae	22 (15.1%)	7 (4.8%)	7 (5.5%)	5 (5.0%)	2 (3.1%)	3 (5.2%)	2 (4.0%)	2 (4.3%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Rash	10 (6.8%)	6 (4.1%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ecchymosis	4 (2.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Blister	3 (2.1%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Pruritus	3 (2.1%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Lesion	3 (2.1%)	1 (0.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Dermatitis Allergic	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dry Skin	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eczema	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erythema	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)

Time to Onset System Organ Class Preferred Term	Overall n (%)	<=Week 12 n (%)	Week 12< <=24 n (%)	Week 24< <=36 n (%)	Week 36< <=48 n (%)	Week 48< <=Month 18 n (%)	Month 18< <=24 n (%)	Month 24< <=30 n (%)	Month 30< <=36 n (%)	Month 36< <=42 n (%)	Month 42< <=48 n (%)	Month 48< n (%)
Hair Colour Changes	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperhidrosis	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Purpura	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Swelling Face	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Actinic Keratosis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Alopecia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blister	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemorrhage Subcutaneous	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertrichosis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nail Discolouration	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nail Disorder	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Papule	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Photosensitivity Reaction	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Precancerous Skin Lesion	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash Erythematous	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash Macular	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash Papular	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Hypopigmentation	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Ulcer	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Urticaria	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
VASCULAR DISORDERS	40 (27.4%)	29 (19.9%)	5 (3.9%)	3 (3.0%)	5 (7.7%)	3 (5.2%)	5 (10.0%)	2 (4.3%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	1 (4.3%)
Hypertension	32 (21.9%)	22 (15.1%)	4 (3.1%)	2 (2.0%)	4 (6.2%)	3 (5.2%)	4 (8.0%)	2 (4.3%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
Haematoma	4 (2.7%)	1 (0.7%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Haemorrhage	3 (2.1%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypotension	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Aortic Stenosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Inadequately Controlled	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hot Flush	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertensive Crisis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peripheral Venous Disease	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Phlebitis Superficial	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	32 (21.9%)	17 (11.6%)	11 (8.6%)	3 (3.0%)	2 (3.1%)	1 (1.7%)	2 (4.0%)	2 (4.3%)	2 (4.4%)	0 (0.0%)	5 (13.2%)	1 (4.3%)
Thrombocytopenia	11 (7.5%)	5 (3.4%)	3 (2.3%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	4 (10.5%)	0 (0.0%)
Anaemia	8 (5.5%)	3 (2.1%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	2 (4.3%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Neutropenia	8 (5.5%)	3 (2.1%)	4 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Leukopenia	3 (2.1%)	2 (1.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Increased Tendency To Bruise	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lymphadenopathy	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Microcytic Anaemia	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Thrombocytosis	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aplastic Anaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Febrile Neutropenia	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune Thrombocytopenic Purpura	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leukocytosis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Polycythaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	32 (21.9%)	9 (6.2%)	11 (8.6%)	7 (6.9%)	5 (7.7%)	7 (12.1%)	4 (8.0%)	3 (6.4%)	3 (6.7%)	2 (5.0%)	4 (10.5%)	1 (4.3%)
Arthralgia	9 (6.2%)	2 (1.4%)	2 (1.6%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Myalgia	8 (5.5%)	1 (0.7%)	2 (1.6%)	4 (4.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Back Pain	6 (4.1%)	3 (2.1%)	2 (1.6%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Muscle Spasms	6 (4.1%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	3 (5.2%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Joint Swelling	4 (2.7%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Musculoskeletal Pain	4 (2.7%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Neck Pain	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Pain In Extremity	4 (2.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	2 (3.4%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Arthritis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
Chondrocalcinosis Pyrophosphate	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Muscular Weakness	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Musculoskeletal Chest Pain	2 (1.4%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Osteoporosis	2 (1.4%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ankylosing Spondylitis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Bone Lesion	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Bone Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemarthrosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mobility Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Plantar Fasciitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Rotator Cuff Syndrome	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Spinal Column Stenosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tendon Sheath Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tendonitis	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trigger Finger	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	24 (16.4%)	8 (5.5%)	2 (1.6%)	4 (4.0%)	4 (6.2%)	4 (6.9%)	2 (4.0%)	0 (0.0%)	2 (4.4%)	2 (5.0%)	3 (7.9%)	2 (8.7%)
Contusion	17 (11.6%)	8 (5.5%)	1 (0.8%)	2 (2.0%)	0 (0.0%)	2 (3.4%)	2 (4.0%)	0 (0.0%)	2 (4.4%)	2 (5.0%)	1 (2.6%)	1 (4.3%)
Fall	3 (2.1%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Animal Bite	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Joint Injury	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Anaphylactic Transfusion Reaction	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Graft Complication	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Head Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Limb Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Muscle Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Procedural Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Scratch	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Wound	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Thoracic Vertebral Fracture	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
METABOLISM AND NUTRITION DISORDERS	14 (9.6%)	6 (4.1%)	3 (2.3%)	1 (1.0%)	2 (3.1%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	2 (5.0%)	0 (0.0%)	2 (8.7%)
Hypokalaemia	5 (3.4%)	2 (1.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Decreased Appetite	3 (2.1%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dehydration	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fluid Overload	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glucose Tolerance Impaired	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gout	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperglycaemia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperkalaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Hypernatraemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Hyperuricaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hypomagnesaemia	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hypophosphataemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Iron Deficiency	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vitamin D Deficiency	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
CARDIAC DISORDERS	10 (6.8%)	2 (1.4%)	2 (1.6%)	2 (2.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	2 (8.7%)
Tachycardia	3 (2.1%)	2 (1.4%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Atrial Fibrillation	2 (1.4%)	0 (0.0%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Cardiac Failure Congestive	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Angina Pectoris	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aortic Valve Incompetence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Cardiac Failure Chronic	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Cardio-Respiratory Arrest	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Mitral Valve Incompetence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Palpitations	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Tricuspid Valve Incompetence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Ventricular Extrasystoles	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EYE DISORDERS	9 (6.2%)	3 (2.1%)	1 (0.8%)	3 (3.0%)	1 (1.5%)	0 (0.0%)	2 (4.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Conjunctival Haemorrhage	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Eyelid Oedema	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blepharitis	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Disorder	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Eye Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Pain	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retinal Tear	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vision Blurred	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RENAL AND URINARY DISORDERS	9 (6.2%)	3 (2.1%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	1 (2.2%)	2 (5.0%)	1 (2.6%)	2 (8.7%)
Nephrolithiasis	4 (2.7%)	1 (0.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Pollakiuria	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Acute Kidney Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Chronic Kidney Disease	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haematuria	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertonic Bladder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Leukocyturia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Renal Cyst	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Renal Failure	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
PSYCHIATRIC DISORDERS	8 (5.5%)	5 (3.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	2 (8.7%)
Insomnia	4 (2.7%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Anxiety	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Depressed Mood	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Depression	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Mental Status Changes	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Restlessness	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	8 (5.5%)	1 (0.7%)	3 (2.3%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	2 (4.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Vaginal Haemorrhage	3 (2.1%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Menorrhagia	2 (1.4%)	0 (0.0%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Breast Mass	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erectile Dysfunction	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Uterine Polyp	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vulvovaginal Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	6 (4.1%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	2 (4.4%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Ear Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Excessive Cerumen Production	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Otorrhoea	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tinnitus	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tympanic Membrane Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tympanic Membrane Perforation	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vertigo	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	6 (4.1%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	2 (5.3%)	1 (4.3%)
Squamous Cell Carcinoma Of Skin	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Basal Cell Carcinoma	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Basosquamous Carcinoma Of Skin	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesteatoma	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Plasma Cell Myeloma	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEPATOBILIARY DISORDERS	4 (2.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Cholecystitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hepatic Cirrhosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hepatic Cyst	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperbilirubinaemia	1 (0.7%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Portal Hypertension	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
SURGICAL AND MEDICAL PROCEDURES	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Micrographic Skin Surgery	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Rotator Cuff Repair	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tooth Extraction	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dacryostenosis Congenital	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hydrocele	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
IMMUNE SYSTEM DISORDERS	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Allergy To Chemicals	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Allergy To Metals	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Drug Hypersensitivity	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
ENDOCRINE DISORDERS	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cushingoid	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. Subjects are counted only once in each preferred term category and only once in each system organ class category and in each term.
(Source: 5.3.5.3.2, Table 4.5.1.1)

表 2.7.4.9-11 Occurrence of Adverse Events and Adverse Drug Reactions with Interest – R788-1301 study

R788 Treatment Period

Category, PT	Adverse Events			Adverse Drug Reactions		
	n	%	e	n	%	e
N	33	---	---	33	---	---
Total	28	84.8	104	24	72.7	57
Bleeding Events	6	18.2	11	1	3.0	2
Conjunctival haemorrhage	1	3.0	1	0	0.0	0
Contusion	1	3.0	2	0	0.0	0
Epistaxis	2	6.1	3	0	0.0	0
Haemorrhage subcutaneous	2	6.1	2	0	0.0	0
Menorrhagia	1	3.0	1	0	0.0	0
Mouth haemorrhage	1	3.0	1	1	3.0	1
Purpura	1	3.0	1	1	3.0	1
Gastrointestinal Complaints	16	48.5	31	11	33.3	20
Nausea	1	3.0	2	1	3.0	1
Nausea	1	3.0	2	1	3.0	1
Vomiting	1	3.0	1	0	0.0	0
Vomiting	1	3.0	1	0	0.0	0
Non-Infectious Diarrhea SMQ	13	39.4	23	10	30.3	18
Diarrhoea	13	39.4	23	10	30.3	18
Abdominal Pain	5	15.2	5	1	3.0	1
Abdominal discomfort	3	9.1	3	1	3.0	1
Abdominal pain	1	3.0	1	0	0.0	0
Abdominal pain upper	1	3.0	1	0	0.0	0
Infection	10	30.3	19	0	0.0	0
COVID-19	1	3.0	1	0	0.0	0
Cellulitis	1	3.0	1	0	0.0	0
Cystitis	2	6.1	2	0	0.0	0
Diverticulitis	1	3.0	1	0	0.0	0
Gastroenteritis	1	3.0	1	0	0.0	0
Gingivitis	1	3.0	1	0	0.0	0
Herpes zoster	2	6.1	2	0	0.0	0
Nasopharyngitis	2	6.1	2	0	0.0	0
Paronychia	1	3.0	2	0	0.0	0
Periodontitis	1	3.0	1	0	0.0	0
Pulpitis dental	1	3.0	1	0	0.0	0
Tinea infection	1	3.0	1	0	0.0	0
Urinary tract infection	1	3.0	1	0	0.0	0
Viral infection	2	6.1	2	0	0.0	0
Hypertension SMQ	12	36.4	15	11	33.3	14
Blood pressure increased	2	6.1	3	2	6.1	3
Hypertension	10	30.3	12	9	27.3	11
Neutropenia	5	15.2	8	4	12.1	6
Neutropenia	2	6.1	4	1	3.0	2
Neutrophil count decreased	3	9.1	4	3	9.1	4
Drug Related Hepatic Disorders SMQ	11	33.3	20	10	30.3	15
Alanine aminotransferase increased	2	6.1	3	2	6.1	3
Aspartate aminotransferase increased	2	6.1	3	2	6.1	3
Autoimmune hepatitis	1	3.0	1	0	0.0	0
Blood bilirubin increased	1	3.0	1	1	3.0	1
Hepatic cyst	1	3.0	1	0	0.0	0
Hepatic enzyme increased	1	3.0	1	1	3.0	1
Hepatic function abnormal	2	6.1	3	2	6.1	3
Hepatic steatosis	1	3.0	1	0	0.0	0
Liver function test abnormal	1	3.0	1	1	3.0	1
Liver function test increased	4	12.1	5	3	9.1	3

e: The Nunber of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.3.4.1.3.2)

表 2.7.4.9-12 Occurrence of Adverse Events and Adverse Drug Reactions with Interest by Severity (R788 Treatment Period) – R788-1301 study

R788 Treatment Period

	Adverse Events						Adverse Drug Reactions					
	Mild		Moderate		Severe		Mild		Moderate		Severe	
Category, PT	n	%	n	%	n	%	n	%	n	%	n	%
N	33	---	---	---	---	---	33	---	---	---	---	---
Total	20	60.6	7	21.2	1	3.0	20	60.6	3	9.1	1	3.0
Bleeding Events	4	12.1	2	6.1	0	0.0	1	3.0	0	0.0	0	0.0
Conjunctival haemorrhage	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Contusion	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Epistaxis	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Haemorrhage subcutaneous	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Menorrhagia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Mouth haemorrhage	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Purpura	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Gastrointestinal Complaints	13	39.4	2	6.1	1	3.0	8	24.2	2	6.1	1	3.0
Nausea	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Nausea	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Vomiting	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Vomiting	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Non-Infectious Diarrhea SMQ	10	30.3	2	6.1	1	3.0	7	21.2	2	6.1	1	3.0
Diarrhoea	10	30.3	2	6.1	1	3.0	7	21.2	2	6.1	1	3.0
Abdominal Pain	5	15.2	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Abdominal discomfort	3	9.1	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Abdominal pain	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Abdominal pain upper	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Infection	7	21.2	3	9.1	0	0.0	0	0.0	0	0.0	0	0.0
COVID-19	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cellulitis	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Cystitis	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Diverticulitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Gastroenteritis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Gingivitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Herpes zoster	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Nasopharyngitis	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Paronychia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Periodontitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pulpitis dental	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Tinea infection	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Urinary tract infection	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Viral infection	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Hypertension SMQ	11	33.3	1	3.0	0	0.0	10	30.3	1	3.0	0	0.0
Blood pressure increased	2	6.1	0	0.0	0	0.0	2	6.1	0	0.0	0	0.0
Hypertension	9	27.3	1	3.0	0	0.0	8	24.2	1	3.0	0	0.0
Neutropenia	5	15.2	0	0.0	0	0.0	4	12.1	0	0.0	0	0.0
Neutropenia	2	6.1	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Neutrophil count decreased	3	9.1	0	0.0	0	0.0	3	9.1	0	0.0	0	0.0
Drug Related Hepatic Disorders SMQ	9	27.3	2	6.1	0	0.0	9	27.3	1	3.0	0	0.0
Alanine aminotransferase increased	2	6.1	0	0.0	0	0.0	2	6.1	0	0.0	0	0.0
Aspartate aminotransferase increased	2	6.1	0	0.0	0	0.0	2	6.1	0	0.0	0	0.0
Autoimmune hepatitis	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0
Blood bilirubin increased	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Hepatic cyst	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic enzyme increased	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Hepatic function abnormal	1	3.0	1	3.0	0	0.0	1	3.0	1	3.0	0	0.0
Hepatic steatosis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Liver function test abnormal	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0
Liver function test increased	4	12.1	0	0.0	0	0.0	3	9.1	0	0.0	0	0.0

MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.3.4.1.5.2)

表 2.7.4.9-13 Occurrence of Serious Adverse Events and Adverse Drug Reactions with Interest – R788-1301 study

R788 Treatment Period

Category, PT	Adverse Events			Adverse Drug Reactions		
	n	%	e	n	%	e
N	33	---	---	33	---	---
Total	3	9.1	4	1	3.0	1
Gastrointestinal Complaints	1	3.0	1	1	3.0	1
Non-Infectious Diarrhea SMQ	1	3.0	1	1	3.0	1
Diarrhoea	1	3.0	1	1	3.0	1
Infection	2	6.1	2	0	0.0	0
Cellulitis	1	3.0	1	0	0.0	0
Herpes zoster	1	3.0	1	0	0.0	0
Drug Related Hepatic Disorders SMQ	1	3.0	1	0	0.0	0
Autoimmune hepatitis	1	3.0	1	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.3.4.1.3.4)

表 2.7.4.9-14 Occurrence of Adverse Events and Adverse Drug Reactions with Interest Leading to Study Drug Withdrawal – R788-1301 study

R788 Treatment Period

Category, PT	Adverse Events			Adverse Drug Reactions		
	n	%	e	n	%	e
N	33	---	---	33	---	---
Total	3	9.1	4	3	9.1	4
Gastrointestinal Complaints	1	3.0	1	1	3.0	1
Non-Infectious Diarrhea SMQ	1	3.0	1	1	3.0	1
Diarrhoea	1	3.0	1	1	3.0	1
Hypertension SMQ	1	3.0	1	1	3.0	1
Hypertension	1	3.0	1	1	3.0	1
Drug Related Hepatic Disorders SMQ	2	6.1	2	2	6.1	2
Hepatic function abnormal	2	6.1	2	2	6.1	2

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.3.4.1.3.6)

表 2.7.4.9-15 Occurrence of Adverse Events and Adverse Drug Reactions with Interest Leading to Dose Reduction – R788-1301 study

R788 Treatment Period

Category, PT	Adverse Events			Adverse Drug Reactions		
	n	%	e	n	%	e
N	33	---	---	33	---	---
Total	18	54.5	26	15	45.5	21
Gastrointestinal Complaints	5	15.2	6	5	15.2	6
Non-Infectious Diarrhea SMQ	4	12.1	5	4	12.1	5
Diarrhoea	4	12.1	5	4	12.1	5
Abdominal Pain	1	3.0	1	1	3.0	1
Abdominal discomfort	1	3.0	1	1	3.0	1
Infection	1	3.0	1	0	0.0	0
Viral infection	1	3.0	1	0	0.0	0
Hypertension SMQ	6	18.2	6	5	15.2	5
Blood pressure increased	2	6.1	2	2	6.1	2
Hypertension	4	12.1	4	3	9.1	3
Neutropenia	4	12.1	7	3	9.1	5
Neutropenia	2	6.1	4	1	3.0	2
Neutrophil count decreased	2	6.1	3	2	6.1	3
Drug Related Hepatic Disorders SMQ	5	15.2	6	4	12.1	5
Alanine aminotransferase increased	1	3.0	1	1	3.0	1
Aspartate aminotransferase increased	1	3.0	1	1	3.0	1
Autoimmune hepatitis	1	3.0	1	0	0.0	0
Hepatic function abnormal	1	3.0	1	1	3.0	1
Liver function test abnormal	1	3.0	1	1	3.0	1
Liver function test increased	1	3.0	1	1	3.0	1

e: The Number of Events, MedDRA version 23.0

(Source: 5.3.5.1.1, Table 14.3.4.1.3.8)

表 2.7.4.9-16 Occurrence of Adverse Events and Adverse Drug Reactions with Interest Leading to Dose Interrupt – R788-1301 study

R788 Treatment Period

Category, PT	Adverse Events			Adverse Drug Reactions		
	n	%	e	n	%	e
N	33	---	---	33	---	---
Total	1	3.0	1	0	0.0	0
Gastrointestinal Complaints	1	3.0	1	0	0.0	0
Nausea	1	3.0	1	0	0.0	0
Nausea	1	3.0	1	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.3.4.1.3.10)

表 2.7.4.9-17 Occurrence of Adverse Events and Adverse Drug Reactions with Interest – R788-1301 study

Period I

Category, PT	Adverse Events						Adverse Drug Reactions					
	R788			Placebo			R788			Placebo		
	n	%	e	n	%	e	n	%	e	n	%	e
N	22	---	---	12	---	---	22	---	---	12	---	---
Total	18	81.8	51	7	58.3	8	16	72.7	37	1	8.3	1
Bleeding Events	3	13.6	5	2	16.7	2	1	4.5	2	0	0.0	0
Epistaxis	2	9.1	2	0	0.0	0	0	0.0	0	0	0.0	0
Haemorrhage subcutaneous	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Menorrhagia	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Mouth haemorrhage	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Procedural haemorrhage	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Purpura	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Gastrointestinal Complaints	11	50.0	20	0	0.0	0	9	40.9	15	0	0.0	0
Nausea	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Nausea	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Non-Infectious Diarrhea SMQ	9	40.9	17	0	0.0	0	7	31.8	13	0	0.0	0
Diarrhoea	9	40.9	17	0	0.0	0	7	31.8	13	0	0.0	0
Abdominal Pain	2	9.1	2	0	0.0	0	1	4.5	1	0	0.0	0
Abdominal discomfort	2	9.1	2	0	0.0	0	1	4.5	1	0	0.0	0
Infection	2	9.1	3	3	25.0	3	0	0.0	0	0	0.0	0
Diarrhoea infectious	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Gingivitis	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Herpes zoster	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Nasopharyngitis	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Otitis media	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Paronychia	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Hypertension SMQ	8	36.4	10	1	8.3	1	7	31.8	9	1	8.3	1
Blood pressure increased	1	4.5	2	0	0.0	0	1	4.5	2	0	0.0	0
Hypertension	7	31.8	8	1	8.3	1	6	27.3	7	1	8.3	1
Neutropenia	4	18.2	4	0	0.0	0	3	13.6	3	0	0.0	0
Neutropenia	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Neutrophil count decreased	3	13.6	3	0	0.0	0	3	13.6	3	0	0.0	0
Drug Related Hepatic Disorders SMQ	6	27.3	9	1	8.3	2	6	27.3	8	0	0.0	0
Alanine aminotransferase increased	1	4.5	1	1	8.3	1	1	4.5	1	0	0.0	0
Aspartate aminotransferase increased	1	4.5	1	1	8.3	1	1	4.5	1	0	0.0	0
Hepatic enzyme increased	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Hepatic function abnormal	2	9.1	3	0	0.0	0	2	9.1	3	0	0.0	0
Hepatic steatosis	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Liver function test abnormal	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Liver function test increased	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.1.4.1.3.2)

表 2.7.4.9-18 Occurrence of Adverse Events and Adverse Drug Reactions with Interest by Severity – R788-1301 study

Period I

	Adverse Events												Adverse Drug Reactions											
	R788						Placebo						R788						Placebo					
	Mild		Moderate		Severe		Mild		Moderate		Severe		Mild		Moderate		Severe		Mild		Moderate		Severe	
Category, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	22	---	---	---	---	---	12	---	---	---	---	---	22	---	---	---	---	---	12	---	---	---	---	---
Total	15	68.2	2	9.1	1	4.5	6	50.0	1	8.3	0	0.0	13	59.1	2	9.1	1	4.5	1	8.3	0	0.0	0	0.0
Bleeding Events	2	9.1	1	4.5	0	0.0	1	8.3	1	8.3	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Epistaxis	1	4.5	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Haemorrhage subcutaneous	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Menorrhagia	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Mouth haemorrhage	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Procedural haemorrhage	0	0.0	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Purpura	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Gastrointestinal Complaints	8	36.4	2	9.1	1	4.5	0	0.0	0	0.0	0	0.0	6	27.3	2	9.1	1	4.5	0	0.0	0	0.0	0	0.0
Nausea	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Nausea	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Non-Infectious Diarrhea SMQ	6	27.3	2	9.1	1	4.5	0	0.0	0	0.0	0	0.0	4	18.2	2	9.1	1	4.5	0	0.0	0	0.0	0	0.0
Diarrhoea	6	27.3	2	9.1	1	4.5	0	0.0	0	0.0	0	0.0	4	18.2	2	9.1	1	4.5	0	0.0	0	0.0	0	0.0
Abdominal Pain	2	9.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Abdominal discomfort	2	9.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Infection	2	9.1	0	0.0	0	0.0	3	25.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Diarrhoea infectious	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Gingivitis	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Herpes zoster	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Nasopharyngitis	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Otitis media	0	0.0	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Paronychia	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hypertension SMQ	8	36.4	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	7	31.8	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0
Blood pressure increased	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hypertension	7	31.8	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	6	27.3	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0
Neutropenia	4	18.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	13.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Neutropenia	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Neutrophil count decreased	3	13.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	13.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Drug Related Hepatic Disorders SMQ	5	22.7	1	4.5	0	0.0	1	8.3	0	0.0	0	0.0	5	22.7	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0
Alanine aminotransferase increased	1	4.5	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

	Adverse Events												Adverse Drug Reactions									
	R788						Placebo						R788						Placebo			
	Mild		Moderate		Severe		Mild		Moderate		Severe		Mild		Moderate		Severe		Mild		Moderate		Severe	
Category, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Aspartate aminotransferase increased	1	4.5	0	0.0	0	0.0	1	8.3	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic enzyme increased	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic function abnormal	1	4.5	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic steatosis	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Liver function test abnormal	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Liver function test increased	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.1.4.1.5.2)

表 2.7.4.9-19 Occurrence of Serious Adverse Events and Adverse Drug Reactions with Interest – R788-1301 study

Period I

	Adverse Events						Adverse Drug Reactions					
	R788			Placebo			R788			Placebo		
Category, PT	n	%	e	n	%	e	n	%	e	n	%	e
N	22	---	---	12	---	---	22	---	---	12	---	---
Total	1	4.5	1	1	8.3	1	1	4.5	1	0	0.0	0
Bleeding Events	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Procedural haemorrhage	0	0.0	0	1	8.3	1	0	0.0	0	0	0.0	0
Gastrointestinal Complaints	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Non-Infectious Diarrhea SMQ	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Diarrhoea	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.1.4.1.3.4)

表 2.7.4.9-20 Occurrence of Adverse Events and Adverse Drug Reactions with Interest Leading to Study Drug Withdrawal – R788-1301 study

Period I

	Adverse Events						Adverse Drug Reactions					
	R788			Placebo			R788			Placebo		
Category, PT	n	%	e	n	%	e	n	%	e	n	%	e
N	22	---	---	12	---	---	22	---	---	12	---	---
Total	3	13.6	4	0	0.0	0	3	13.6	4	0	0.0	0
Gastrointestinal Complaints	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Non-Infectious Diarrhea SMQ	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Diarrhoea	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Hypertension SMQ	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Hypertension	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Drug Related Hepatic Disorders SMQ	2	9.1	2	0	0.0	0	2	9.1	2	0	0.0	0
Hepatic function abnormal	2	9.1	2	0	0.0	0	2	9.1	2	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.1.4.1.3.6)

表 2.7.4.9-21 Occurrence of Adverse Events and Adverse Drug Reactions with Interest Leading to Dose Reduction – R788-1301 study

Period I

	Adverse Events						Adverse Drug Reactions					
	R788			Placebo			R788			Placebo		
Category, PT	n	%	e	n	%	e	n	%	e	n	%	e
N	22	---	---	12	---	---	22	---	---	12	---	---
Total	9	40.9	11	0	0.0	0	8	36.4	10	0	0.0	0
Gastrointestinal Complaints	3	13.6	4	0	0.0	0	3	13.6	4	0	0.0	0
Non-Infectious Diarrhea SMQ	3	13.6	4	0	0.0	0	3	13.6	4	0	0.0	0
Diarrhoea	3	13.6	4	0	0.0	0	3	13.6	4	0	0.0	0
Hypertension SMQ	2	9.1	2	0	0.0	0	2	9.1	2	0	0.0	0
Blood pressure increased	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Hypertension	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Neutropenia	3	13.6	3	0	0.0	0	2	9.1	2	0	0.0	0
Neutropenia	1	4.5	1	0	0.0	0	0	0.0	0	0	0.0	0
Neutrophil count decreased	2	9.1	2	0	0.0	0	2	9.1	2	0	0.0	0
Drug Related Hepatic Disorders SMQ	2	9.1	2	0	0.0	0	2	9.1	2	0	0.0	0
Hepatic function abnormal	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0
Liver function test abnormal	1	4.5	1	0	0.0	0	1	4.5	1	0	0.0	0

e: The Number of Events, MedDRA version 23.0
(Source: 5.3.5.1.1, Table 14.1.4.1.3.8)

表 2.7.4.9-22 Occurrence of Adverse Events and Adverse Drug Reactions with Interest Leading to Dose Interrupt – R788-1301 study

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表 2.7.4.9-23 Adverse Events (AEs) of Interest (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Type of AE Preferred Term	Fostamatinib (N=146) n (%)
Number of Subjects with at Least One AE of Interest	112 (76.7%)
Gastrointestinal Complaints	70 (47.9%)
Nausea	28 (19.2%)
Nausea	28 (19.2%)
Vomiting	14 (9.6%)
Vomiting	13 (8.9%)
Retching	1 (0.7%)
Non-Infectious Diarrhea SMQ	53 (36.3%)
Diarrhoea	53 (36.3%)
Frequent Bowel Movements	2 (1.4%)
Abdominal Pain	19 (13.0%)
Abdominal Pain	9 (6.2%)
Abdominal Pain Upper	8 (5.5%)
Abdominal Discomfort	2 (1.4%)
Abdominal Pain Lower	1 (0.7%)
Infection	68 (46.6%)
Upper Respiratory Tract Infection	18 (12.3%)
Nasopharyngitis	10 (6.8%)
Urinary Tract Infection	9 (6.2%)
Bronchitis	6 (4.1%)
Influenza Like Illness	6 (4.1%)
Lower Respiratory Tract Infection	6 (4.1%)
Respiratory Tract Infection	6 (4.1%)
Viral Infection	6 (4.1%)
Pneumonia	5 (3.4%)
Gastroenteritis	4 (2.7%)
Pharyngitis	4 (2.7%)
Tooth Infection	4 (2.7%)
Sepsis	3 (2.1%)
Cellulitis	2 (1.4%)
Ear Infection	2 (1.4%)
Eye Infection	2 (1.4%)
Gastrointestinal Infection	2 (1.4%)
Oral Candidiasis	2 (1.4%)
Oral Herpes	2 (1.4%)
Post Procedural Infection	2 (1.4%)
Sinusitis	2 (1.4%)
Abscess	1 (0.7%)
Arthritis Viral	1 (0.7%)
Bacteriuria	1 (0.7%)
Carbuncle	1 (0.7%)
Cellulitis Staphylococcal	1 (0.7%)
Diverticulitis	1 (0.7%)
Endocarditis Bacterial	1 (0.7%)
Erythema Induratum	1 (0.7%)
Escherichia Urinary Tract Infection	1 (0.7%)
Fungal Infection	1 (0.7%)
Fungal Skin Infection	1 (0.7%)
Gingivitis	1 (0.7%)
Herpes Simplex	1 (0.7%)
Herpes Zoster	1 (0.7%)
Infection	1 (0.7%)
Influenza	1 (0.7%)
Klebsiella Bacteraemia	1 (0.7%)
Laryngitis	1 (0.7%)
Mastoiditis	1 (0.7%)
Onychomycosis	1 (0.7%)
Otitis Media	1 (0.7%)
Pulpitis Dental	1 (0.7%)

Type of AE Preferred Term	Fostamatinib (N=146) n (%)
Pyelonephritis Acute	1 (0.7%)
Rhinitis	1 (0.7%)
Subacute Endocarditis	1 (0.7%)
Tinea Infection	1 (0.7%)
Tonsillitis	1 (0.7%)
Tooth Abscess	1 (0.7%)
Tuberculosis	1 (0.7%)
Upper Respiratory Tract Inflammation	1 (0.7%)
Urinary Tract Infection Bacterial	1 (0.7%)
Urosepsis	1 (0.7%)
Viral Pharyngitis	1 (0.7%)
Viral Upper Respiratory Tract Infection	1 (0.7%)
Hypertension SMQ	43 (29.5%)
Hypertension	32 (21.9%)
Blood Pressure Increased	7 (4.8%)
Blood Pressure Diastolic Increased	2 (1.4%)
Blood Pressure Inadequately Controlled	1 (0.7%)
Blood Pressure Systolic Increased	1 (0.7%)
Hypertensive Crisis	1 (0.7%)
Neutropenia	10 (6.8%)
Neutropenia	8 (5.5%)
Neutrophil Count Decreased	2 (1.4%)
Febrile Neutropenia	1 (0.7%)
Drug Related Hepatic Disorders SMQ	28 (19.2%)
Alanine Aminotransferase Increased	14 (9.6%)
Aspartate Aminotransferase Increased	10 (6.8%)
Hepatic Enzyme Increased	5 (3.4%)
Liver Function Test Abnormal	4 (2.7%)
Blood Bilirubin Increased	3 (2.1%)
Transaminases Increased	2 (1.4%)
Ascites	1 (0.7%)
Gamma-Glutamyltransferase Increased	1 (0.7%)
Hepatic Cirrhosis	1 (0.7%)
Hepatic Cyst	1 (0.7%)
Hyperbilirubinaemia	1 (0.7%)
Portal Hypertension	1 (0.7%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.2.1)

表 2.7.4.9-24 Adverse Events (AEs) of Interest by Age Group (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Age < 65 years

Type of AE Preferred Term	Fostamatinib (N=109) n (%)
Number of Subjects with at Least One AE of Interest	82 (75.2%)
Gastrointestinal Complaints	52 (47.7%)
Nausea	22 (20.2%)
Nausea	22 (20.2%)
Vomiting	12 (11.0%)
Vomiting	11 (10.1%)
Retching	1 (0.9%)
Non-Infectious Diarrhea SMQ	37 (33.9%)
Diarrhoea	37 (33.9%)
Frequent Bowel Movements	1 (0.9%)
Abdominal Pain	19 (17.4%)
Abdominal Pain	9 (8.3%)
Abdominal Pain Upper	8 (7.3%)
Abdominal Discomfort	2 (1.8%)
Abdominal Pain Lower	1 (0.9%)
Infection	57 (52.3%)
Upper Respiratory Tract Infection	16 (14.7%)
Nasopharyngitis	8 (7.3%)
Urinary Tract Infection	7 (6.4%)
Influenza Like Illness	6 (5.5%)
Respiratory Tract Infection	6 (5.5%)
Lower Respiratory Tract Infection	5 (4.6%)
Viral Infection	5 (4.6%)
Bronchitis	4 (3.7%)
Pharyngitis	4 (3.7%)
Pneumonia	4 (3.7%)
Tooth Infection	4 (3.7%)
Gastroenteritis	3 (2.8%)
Ear Infection	2 (1.8%)
Gastrointestinal Infection	2 (1.8%)
Oral Candidiasis	2 (1.8%)
Oral Herpes	2 (1.8%)
Post Procedural Infection	2 (1.8%)
Sepsis	2 (1.8%)
Sinusitis	2 (1.8%)
Arthritis Viral	1 (0.9%)
Carbuncle	1 (0.9%)
Cellulitis	1 (0.9%)
Diverticulitis	1 (0.9%)
Erythema Induratum	1 (0.9%)
Eye Infection	1 (0.9%)
Gingivitis	1 (0.9%)
Herpes Simplex	1 (0.9%)
Herpes Zoster	1 (0.9%)
Infection	1 (0.9%)
Influenza	1 (0.9%)
Klebsiella Bacteraemia	1 (0.9%)
Laryngitis	1 (0.9%)
Pulpitis Dental	1 (0.9%)
Pyelonephritis Acute	1 (0.9%)
Rhinitis	1 (0.9%)
Tonsillitis	1 (0.9%)
Tooth Abscess	1 (0.9%)
Tuberculosis	1 (0.9%)
Upper Respiratory Tract Inflammation	1 (0.9%)
Viral Pharyngitis	1 (0.9%)
Viral Upper Respiratory Tract Infection	1 (0.9%)

Type of AE Preferred Term	Fostamatinib (N=109) n (%)
Hypertension SMQ	28 (25.7%)
Hypertension	22 (20.2%)
Blood Pressure Increased	3 (2.8%)
Blood Pressure Diastolic Increased	2 (1.8%)
Blood Pressure Systolic Increased	1 (0.9%)
Neutropenia	7 (6.4%)
Neutropenia	5 (4.6%)
Febrile Neutropenia	1 (0.9%)
Neutrophil Count Decreased	1 (0.9%)
Drug Related Hepatic Disorders SMQ	21 (19.3%)
Alanine Aminotransferase Increased	10 (9.2%)
Aspartate Aminotransferase Increased	8 (7.3%)
Hepatic Enzyme Increased	5 (4.6%)
Blood Bilirubin Increased	3 (2.8%)
Liver Function Test Abnormal	2 (1.8%)
Gamma-Glutamyltransferase Increased	1 (0.9%)
Hepatic Cyst	1 (0.9%)
Hyperbilirubinaemia	1 (0.9%)
Transaminases Increased	1 (0.9%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.2.1.1)

Age >= 65 years

Type of AE Preferred Term	Fostamatinib (N=37) n (%)
Number of Subjects with at Least One AE of Interest	30 (81.1%)
Gastrointestinal Complaints	18 (48.6%)
Nausea	6 (16.2%)
Nausea	6 (16.2%)
Vomiting	2 (5.4%)
Vomiting	2 (5.4%)
Non-Infectious Diarrhea SMQ	16 (43.2%)
Diarrhoea	16 (43.2%)
Frequent Bowel Movements	1 (2.7%)
Infection	11 (29.7%)
Bronchitis	2 (5.4%)
Nasopharyngitis	2 (5.4%)
Upper Respiratory Tract Infection	2 (5.4%)
Urinary Tract Infection	2 (5.4%)
Abscess	1 (2.7%)
Bacteriuria	1 (2.7%)
Cellulitis	1 (2.7%)
Cellulitis Staphylococcal	1 (2.7%)
Endocarditis Bacterial	1 (2.7%)
Escherichia Urinary Tract Infection	1 (2.7%)
Eye Infection	1 (2.7%)
Fungal Infection	1 (2.7%)
Fungal Skin Infection	1 (2.7%)
Gastroenteritis	1 (2.7%)
Lower Respiratory Tract Infection	1 (2.7%)
Mastoiditis	1 (2.7%)
Onychomycosis	1 (2.7%)
Otitis Media	1 (2.7%)
Pneumonia	1 (2.7%)
Sepsis	1 (2.7%)
Subacute Endocarditis	1 (2.7%)
Tinea Infection	1 (2.7%)
Urinary Tract Infection Bacterial	1 (2.7%)
Urosepsis	1 (2.7%)
Viral Infection	1 (2.7%)
Hypertension SMQ	15 (40.5%)

Type of AE Preferred Term	Fostamatinib (N=37) n (%)
Hypertension	10 (27.0%)
Blood Pressure Increased	4 (10.8%)
Blood Pressure Inadequately Controlled	1 (2.7%)
Hypertensive Crisis	1 (2.7%)
Neutropenia	3 (8.1%)
Neutropenia	3 (8.1%)
Neutrophil Count Decreased	1 (2.7%)
Drug Related Hepatic Disorders SMQ	7 (18.9%)
Alanine Aminotransferase Increased	4 (10.8%)
Aspartate Aminotransferase Increased	2 (5.4%)
Liver Function Test Abnormal	2 (5.4%)
Ascites	1 (2.7%)
Hepatic Cirrhosis	1 (2.7%)
Portal Hypertension	1 (2.7%)
Transaminases Increased	1 (2.7%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.2.1.1)

表 2.7.4.9-25 Adverse Events (AEs) of Interest by Gender (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Males

Type of AE Preferred Term	Fostamatinib (N=59) n (%)
Number of Subjects with at Least One AE of Interest	45 (76.3%)
Gastrointestinal Complaints	25 (42.4%)
Nausea	5 (8.5%)
Nausea	5 (8.5%)
Vomiting	4 (6.8%)
Vomiting	4 (6.8%)
Non-Infectious Diarrhea SMQ	19 (32.2%)
Diarrhoea	19 (32.2%)
Abdominal Pain	5 (8.5%)
Abdominal Pain Upper	3 (5.1%)
Abdominal Discomfort	1 (1.7%)
Abdominal Pain	1 (1.7%)
Infection	25 (42.4%)
Upper Respiratory Tract Infection	5 (8.5%)
Respiratory Tract Infection	4 (6.8%)
Nasopharyngitis	3 (5.1%)
Viral Infection	3 (5.1%)
Gastrointestinal Infection	2 (3.4%)
Influenza Like Illness	2 (3.4%)
Pneumonia	2 (3.4%)
Bronchitis	1 (1.7%)
Cellulitis Staphylococcal	1 (1.7%)
Diverticulitis	1 (1.7%)
Fungal Skin Infection	1 (1.7%)
Gastroenteritis	1 (1.7%)
Laryngitis	1 (1.7%)
Lower Respiratory Tract Infection	1 (1.7%)
Oral Candidiasis	1 (1.7%)
Oral Herpes	1 (1.7%)
Pulpitis Dental	1 (1.7%)
Pyelonephritis Acute	1 (1.7%)
Tinea Infection	1 (1.7%)
Tooth Abscess	1 (1.7%)
Tooth Infection	1 (1.7%)
Upper Respiratory Tract Inflammation	1 (1.7%)
Urinary Tract Infection	1 (1.7%)
Hypertension SMQ	12 (20.3%)
Hypertension	8 (13.6%)
Blood Pressure Increased	3 (5.1%)
Blood Pressure Inadequately Controlled	1 (1.7%)
Neutropenia	4 (6.8%)
Neutropenia	2 (3.4%)
Febrile Neutropenia	1 (1.7%)
Neutrophil Count Decreased	1 (1.7%)
Drug Related Hepatic Disorders SMQ	11 (18.6%)
Alanine Aminotransferase Increased	5 (8.5%)
Aspartate Aminotransferase Increased	3 (5.1%)
Hepatic Enzyme Increased	3 (5.1%)
Ascites	1 (1.7%)
Blood Bilirubin Increased	1 (1.7%)
Gamma-Glutamyltransferase Increased	1 (1.7%)
Hepatic Cirrhosis	1 (1.7%)
Hyperbilirubinaemia	1 (1.7%)
Portal Hypertension	1 (1.7%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.2.1.2)

Females

Type of AE Preferred Term	Fostamatinib (N=87) n (%)
Number of Subjects with at Least One AE of Interest	67 (77.0%)
Gastrointestinal Complaints	45 (51.7%)
Nausea	23 (26.4%)
Nausea	23 (26.4%)
Vomiting	10 (11.5%)
Vomiting	9 (10.3%)
Retching	1 (1.1%)
Non-Infectious Diarrhea SMQ	34 (39.1%)
Diarrhoea	34 (39.1%)
Frequent Bowel Movements	2 (2.3%)
Abdominal Pain	14 (16.1%)
Abdominal Pain	8 (9.2%)
Abdominal Pain Upper	5 (5.7%)
Abdominal Discomfort	1 (1.1%)
Abdominal Pain Lower	1 (1.1%)
Infection	43 (49.4%)
Upper Respiratory Tract Infection	13 (14.9%)
Urinary Tract Infection	8 (9.2%)
Nasopharyngitis	7 (8.0%)
Bronchitis	5 (5.7%)
Lower Respiratory Tract Infection	5 (5.7%)
Influenza Like Illness	4 (4.6%)
Pharyngitis	4 (4.6%)
Gastroenteritis	3 (3.4%)
Pneumonia	3 (3.4%)
Sepsis	3 (3.4%)
Tooth Infection	3 (3.4%)
Viral Infection	3 (3.4%)
Cellulitis	2 (2.3%)
Ear Infection	2 (2.3%)
Eye Infection	2 (2.3%)
Post Procedural Infection	2 (2.3%)
Respiratory Tract Infection	2 (2.3%)
Sinusitis	2 (2.3%)
Abscess	1 (1.1%)
Arthritis Viral	1 (1.1%)
Bacteriuria	1 (1.1%)
Carbuncle	1 (1.1%)
Endocarditis Bacterial	1 (1.1%)
Erythema Induratum	1 (1.1%)
Escherichia Urinary Tract Infection	1 (1.1%)
Fungal Infection	1 (1.1%)
Gingivitis	1 (1.1%)
Herpes Simplex	1 (1.1%)
Herpes Zoster	1 (1.1%)
Infection	1 (1.1%)
Influenza	1 (1.1%)
Klebsiella Bacteraemia	1 (1.1%)
Mastoiditis	1 (1.1%)
Onychomycosis	1 (1.1%)
Oral Candidiasis	1 (1.1%)
Oral Herpes	1 (1.1%)
Otitis Media	1 (1.1%)
Rhinitis	1 (1.1%)
Subacute Endocarditis	1 (1.1%)
Tonsillitis	1 (1.1%)
Tuberculosis	1 (1.1%)
Urinary Tract Infection Bacterial	1 (1.1%)
Urosepsis	1 (1.1%)
Viral Pharyngitis	1 (1.1%)
Viral Upper Respiratory Tract Infection	1 (1.1%)

Type of AE Preferred Term	Fostamatinib (N=87) n (%)
Hypertension SMQ	31 (35.6%)
Hypertension	24 (27.6%)
Blood Pressure Increased	4 (4.6%)
Blood Pressure Diastolic Increased	2 (2.3%)
Blood Pressure Systolic Increased	1 (1.1%)
Hypertensive Crisis	1 (1.1%)
Neutropenia	6 (6.9%)
Neutropenia	6 (6.9%)
Neutrophil Count Decreased	1 (1.1%)
Drug Related Hepatic Disorders SMQ	17 (19.5%)
Alanine Aminotransferase Increased	9 (10.3%)
Aspartate Aminotransferase Increased	7 (8.0%)
Liver Function Test Abnormal	4 (4.6%)
Blood Bilirubin Increased	2 (2.3%)
Hepatic Enzyme Increased	2 (2.3%)
Transaminases Increased	2 (2.3%)
Hepatic Cyst	1 (1.1%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.2.1.2)

表 2.7.4.9-26 Adverse Events (AEs) of Interest: Incidence by System Organ Class/Preferred Term and Severity (Subject Level) (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Type of AE Preferred Term	Fostamatinib (N=146)			
	Mild	Moderate	Severe	Total
	n (%)	n (%)	n (%)	n (%)
Number of Subjects with at Least One AE of Interest	38 (26.0%)	58 (39.7%)	16 (11.0%)	112 (76.7%)
Gastrointestinal Complaints	35 (24.0%)	32 (21.9%)	3 (2.1%)	70 (47.9%)
Nausea	25 (17.1%)	3 (2.1%)	0 (0.0%)	28 (19.2%)
Nausea	25 (17.1%)	3 (2.1%)	0 (0.0%)	28 (19.2%)
Vomiting	13 (8.9%)	1 (0.7%)	0 (0.0%)	14 (9.6%)
Vomiting	12 (8.2%)	1 (0.7%)	0 (0.0%)	13 (8.9%)
Retching	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Non-Infectious Diarrhea SMQ	25 (17.1%)	25 (17.1%)	3 (2.1%)	53 (36.3%)
Diarrhoea	25 (17.1%)	25 (17.1%)	3 (2.1%)	53 (36.3%)
Frequent Bowel Movements	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Abdominal Pain	16 (11.0%)	3 (2.1%)	0 (0.0%)	19 (13.0%)
Abdominal Pain	6 (4.1%)	3 (2.1%)	0 (0.0%)	9 (6.2%)
Abdominal Pain Upper	8 (5.5%)	0 (0.0%)	0 (0.0%)	8 (5.5%)
Abdominal Discomfort	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Abdominal Pain Lower	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Infection	37 (25.3%)	22 (15.1%)	9 (6.2%)	68 (46.6%)
Upper Respiratory Tract Infection	14 (9.6%)	4 (2.7%)	0 (0.0%)	18 (12.3%)
Nasopharyngitis	9 (6.2%)	1 (0.7%)	0 (0.0%)	10 (6.8%)
Urinary Tract Infection	5 (3.4%)	4 (2.7%)	0 (0.0%)	9 (6.2%)
Bronchitis	4 (2.7%)	2 (1.4%)	0 (0.0%)	6 (4.1%)
Influenza Like Illness	4 (2.7%)	1 (0.7%)	1 (0.7%)	6 (4.1%)
Lower Respiratory Tract Infection	2 (1.4%)	4 (2.7%)	0 (0.0%)	6 (4.1%)
Respiratory Tract Infection	4 (2.7%)	2 (1.4%)	0 (0.0%)	6 (4.1%)
Viral Infection	4 (2.7%)	1 (0.7%)	1 (0.7%)	6 (4.1%)
Pneumonia	0 (0.0%)	3 (2.1%)	2 (1.4%)	5 (3.4%)
Gastroenteritis	3 (2.1%)	1 (0.7%)	0 (0.0%)	4 (2.7%)
Pharyngitis	4 (2.7%)	0 (0.0%)	0 (0.0%)	4 (2.7%)
Tooth Infection	3 (2.1%)	1 (0.7%)	0 (0.0%)	4 (2.7%)
Sepsis	0 (0.0%)	1 (0.7%)	2 (1.4%)	3 (2.1%)
Cellulitis	1 (0.7%)	0 (0.0%)	1 (0.7%)	2 (1.4%)
Ear Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Eye Infection	0 (0.0%)	2 (1.4%)	0 (0.0%)	2 (1.4%)
Gastrointestinal Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Oral Candidiasis	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (1.4%)
Oral Herpes	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Post Procedural Infection	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (1.4%)
Sinusitis	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Abscess	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Arthritis Viral	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Bacteriuria	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Carbuncle	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Cellulitis Staphylococcal	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Diverticulitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Endocarditis Bacterial	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Erythema Induratum	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Escherichia Urinary Tract Infection	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Fungal Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Fungal Skin Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Gingivitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Herpes Simplex	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Herpes Zoster	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Influenza	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Klebsiella Bacteraemia	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Laryngitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Mastoiditis	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Onychomycosis	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)

Type of AE	Fostamatinib (N=146)			
	Mild	Moderate	Severe	Total
Preferred Term	n (%)	n (%)	n (%)	n (%)
Otitis Media	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Pulpitis Dental	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Pyelonephritis Acute	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Rhinitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Subacute Endocarditis	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Tinea Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Tonsillitis	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Tooth Abscess	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Tuberculosis	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Upper Respiratory Tract Inflammation	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Urinary Tract Infection Bacterial	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Urosepsis	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Viral Pharyngitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Viral Upper Respiratory Tract Infection	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Hypertension SMQ	26 (17.8%)	14 (9.6%)	3 (2.1%)	43 (29.5%)
Hypertension	17 (11.6%)	14 (9.6%)	1 (0.7%)	32 (21.9%)
Blood Pressure Increased	5 (3.4%)	1 (0.7%)	1 (0.7%)	7 (4.8%)
Blood Pressure Diastolic Increased	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Blood Pressure Inadequately Controlled	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Blood Pressure Systolic Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Hypertensive Crisis	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Neutropenia	4 (2.7%)	4 (2.7%)	2 (1.4%)	10 (6.8%)
Neutropenia	3 (2.1%)	4 (2.7%)	1 (0.7%)	8 (5.5%)
Neutrophil Count Decreased	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)
Febrile Neutropenia	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)
Drug Related Hepatic Disorders SMQ	15 (10.3%)	10 (6.8%)	3 (2.1%)	28 (19.2%)
Alanine Aminotransferase Increased	8 (5.5%)	6 (4.1%)	0 (0.0%)	14 (9.6%)
Aspartate Aminotransferase Increased	6 (4.1%)	4 (2.7%)	0 (0.0%)	10 (6.8%)
Hepatic Enzyme Increased	3 (2.1%)	1 (0.7%)	1 (0.7%)	5 (3.4%)
Liver Function Test Abnormal	4 (2.7%)	0 (0.0%)	0 (0.0%)	4 (2.7%)
Blood Bilirubin Increased	2 (1.4%)	1 (0.7%)	0 (0.0%)	3 (2.1%)
Transaminases Increased	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)
Ascites	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Gamma-Glutamyltransferase Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Hepatic Cirrhosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Hepatic Cyst	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Hyperbilirubinaemia	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)
Portal Hypertension	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review. Subjects are counted only once in each category, based upon their most severe AE in the category. AEs with missing severity were classified as severe. For diarrhea, severity was assigned based on the diarrhea severity grade as follows: 1=Mild; 2=Moderate; 3, 4, and 5=Severe.
(Source: 5.3.5.3.2, Table 4.3.2.2.1)

表 2.7.4.9-27 Treatment-Related Adverse Events (AEs) of Interest (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Type of AE Preferred Term	Fostamatinib (N=146) n (%)
Number of Subjects with at Least One AE of Interest	84 (57.5%)
Gastrointestinal Complaints	54 (37.0%)
Nausea	18 (12.3%)
Nausea	18 (12.3%)
Vomiting	4 (2.7%)
Vomiting	3 (2.1%)
Retching	1 (0.7%)
Non-Infectious Diarrhea SMQ	46 (31.5%)
Diarrhoea	46 (31.5%)
Frequent Bowel Movements	1 (0.7%)
Abdominal Pain	10 (6.8%)
Abdominal Pain	5 (3.4%)
Abdominal Pain Upper	4 (2.7%)
Abdominal Discomfort	1 (0.7%)
Infection	12 (8.2%)
Pneumonia	2 (1.4%)
Arthritis Viral	1 (0.7%)
Bacteriuria	1 (0.7%)
Erythema Induratum	1 (0.7%)
Herpes Zoster	1 (0.7%)
Influenza Like Illness	1 (0.7%)
Lower Respiratory Tract Infection	1 (0.7%)
Nasopharyngitis	1 (0.7%)
Oral Candidiasis	1 (0.7%)
Post Procedural Infection	1 (0.7%)
Respiratory Tract Infection	1 (0.7%)
Sepsis	1 (0.7%)
Tuberculosis	1 (0.7%)
Upper Respiratory Tract Infection	1 (0.7%)
Hypertension SMQ	28 (19.2%)
Hypertension	21 (14.4%)
Blood Pressure Increased	5 (3.4%)
Blood Pressure Inadequately Controlled	1 (0.7%)
Blood Pressure Systolic Increased	1 (0.7%)
Hypertensive Crisis	1 (0.7%)
Neutropenia	7 (4.8%)
Neutropenia	5 (3.4%)
Neutrophil Count Decreased	2 (1.4%)
Febrile Neutropenia	1 (0.7%)
Drug Related Hepatic Disorders SMQ	21 (14.4%)
Alanine Aminotransferase Increased	13 (8.9%)
Aspartate Aminotransferase Increased	8 (5.5%)
Blood Bilirubin Increased	3 (2.1%)
Hepatic Enzyme Increased	3 (2.1%)
Liver Function Test Abnormal	2 (1.4%)
Hyperbilirubinaemia	1 (0.7%)
Transaminases Increased	1 (0.7%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review. Treatment-related AEs are AEs with a possible, probable, or missing causal relationship to study drug.
(Source: 5.3.5.3.2, Table 4.2.3.2.2)

表 2.7.4.9-28 Occurrence of Serious Adverse Events with Interest (Fostamatinib Treated Population) –C788-047, C788-048 and C788-049 study

Category, PT	Fostamatinib n	Fostamatinib %
N	146	---
Bleeding Events	16	11.0
Contusion	1	0.7
Epistaxis	5	3.4
Gastrointestinal Haemorrhage	2	1.4
Haematochezia	1	0.7
Immune Thrombocytopenic Purpura	1	0.7
Melaena	1	0.7
Menorrhagia	1	0.7
Mouth Haemorrhage	1	0.7
Mucosal Haemorrhage	1	0.7
Petechiae	1	0.7
Purpura	1	0.7
Rectal Haemorrhage	1	0.7
Vaginal Haemorrhage	1	0.7
Gastrointestinal Complaints	2	1.4
Non-Infectious Diarrhea SMQ	2	1.4
Diarrhoea	2	1.4
Infection	12	8.2
Bronchitis	1	0.7
Cellulitis Staphylococcal	1	0.7
Endocarditis Bacterial	1	0.7
Erythema Induratum	1	0.7
Gastroenteritis	1	0.7
Mastoiditis	1	0.7
Oral Candidiasis	1	0.7
Pneumonia	2	1.4
Sepsis	2	1.4
Tuberculosis	1	0.7
Upper Respiratory Tract Infection	1	0.7
Urinary Tract Infection	1	0.7
Urosepsis	1	0.7
Viral Infection	1	0.7
Hypertension SMQ	1	0.7
Hypertensive Crisis	1	0.7
Neutropenia	1	0.7
Febrile Neutropenia	1	0.7
Drug Related Hepatic Disorders SMQ	3	2.1
Ascites	1	0.7
Transaminases Increased	2	1.4

(Source: 5.3.5.3.2, Table 7.1.2.1)

表 2.7.4.9-29 Occurrence of Adverse Events with Interest to Study Drug Withdrawal (Fostamatinib Treated Population) – C788-047, C788-048 and C788-049 study

	Fostamatinib	
Category, PT	n	%
N	146	---
Gastrointestinal Complaints	8	5.5
Non-Infectious Diarrhea SMQ	6	4.1
Diarrhoea	6	4.1
Abdominal Pain	2	1.4
Abdominal Pain	1	0.7
Abdominal Pain Upper	1	0.7
Infection	1	0.7
Pneumonia	1	0.7
Hypertension SMQ	1	0.7
Blood Pressure Increased	1	0.7
Neutropenia	3	2.1
Neutropenia	3	2.1
Drug Related Hepatic Disorders SMQ	5	3.4
Alanine Aminotransferase Increased	1	0.7
Blood Bilirubin Increased	1	0.7
Hepatic Enzyme Increased	2	1.4
Transaminases Increased	1	0.7

(Source: 5.3.5.3.2, Table 7.1.2.4)

表 2.7.4.9-30 Occurrence of Adverse Events with Interest to Dose Reduction (Fostamatinib Treated Population) – C788-047, C788-048 and C788-049 study

	Fostamatinib	
Category, PT	n	%
N	146	---
Gastrointestinal Complaints	4	2.7
Non-Infectious Diarrhea SMQ	4	2.7
Diarrhoea	4	2.7
Infection	2	1.4
Pneumonia	1	0.7
Respiratory Tract Infection	1	0.7
Hypertension SMQ	3	2.1
Blood Pressure Inadequately Controlled	1	0.7
Hypertension	2	1.4
Neutropenia	2	1.4
Febrile Neutropenia	1	0.7
Neutrophil Count Decreased	1	0.7
Drug Related Hepatic Disorders SMQ	4	2.7
Alanine Aminotransferase Increased	1	0.7
Aspartate Aminotransferase Increased	1	0.7
Hepatic Enzyme Increased	1	0.7
Liver Function Test Abnormal	1	0.7

(Source: 5.3.5.3.2, Table 7.1.2.2)

表 2.7.4.9-31 Occurrence of Adverse Events with Interest to Dose Interruption (Fostamatinib Treated Population) – C788-047, C788-048 and C788-049 study

Category, PT	Fostamatinib n	Fostamatinib %
N	146	---
Bleeding Events	1	0.7
Epistaxis	1	0.7
Gastrointestinal Complaints	8	5.5
Vomiting	1	0.7
Vomiting	1	0.7
Non-Infectious Diarrhea SMQ	5	3.4
Diarrhoea	5	3.4
Abdominal Pain	2	1.4
Abdominal Pain	2	1.4
Infection	9	6.2
Gastroenteritis	1	0.7
Influenza Like Illness	2	1.4
Lower Respiratory Tract Infection	1	0.7
Mastoiditis	1	0.7
Nasopharyngitis	1	0.7
Sepsis	2	1.4
Tooth Infection	1	0.7
Urosepsis	1	0.7
Hypertension SMQ	3	2.1
Hypertension	2	1.4
Hypertensive Crisis	1	0.7
Neutropenia	2	1.4
Febrile Neutropenia	1	0.7
Neutrophil Count Decreased	1	0.7
Drug Related Hepatic Disorders SMQ	9	6.2
Alanine Aminotransferase Increased	5	3.4
Aspartate Aminotransferase Increased	1	0.7
Blood Bilirubin Increased	1	0.7
Hepatic Enzyme Increased	2	1.4
Transaminases Increased	1	0.7

(Source: 5.3.5.3.2, Table 7.1.2.3)

表 2.7.4.9-32 Adverse Events (AEs) of Interest (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Type of AE Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Number of Subjects with at Least One AE of Interest	69 (67.6%)	21 (43.8%)
Gastrointestinal Complaints	42 (41.2%)	10 (20.8%)
Nausea	19 (18.6%)	4 (8.3%)
Nausea	19 (18.6%)	4 (8.3%)
Vomiting	4 (3.9%)	3 (6.3%)
Vomiting	3 (2.9%)	3 (6.3%)
Retching	1 (1.0%)	0 (0.0%)
Diarrhea	32 (31.4%)	7 (14.6%)
Diarrhoea	30 (29.4%)	7 (14.6%)
Frequent Bowel Movements	2 (2.0%)	0 (0.0%)
Abdominal Pain	7 (6.9%)	2 (4.2%)
Abdominal Pain Upper	3 (2.9%)	1 (2.1%)
Abdominal Pain	3 (2.9%)	0 (0.0%)
Abdominal Discomfort	1 (1.0%)	1 (2.1%)
Infection	31 (30.4%)	10 (20.8%)
Upper Respiratory Tract Infection	6 (5.9%)	2 (4.2%)
Respiratory Tract Infection	3 (2.9%)	1 (2.1%)
Bronchitis	3 (2.9%)	0 (0.0%)
Gastroenteritis	2 (2.0%)	1 (2.1%)
Influenza Like Illness	3 (2.9%)	0 (0.0%)
Nasopharyngitis	2 (2.0%)	1 (2.1%)
Urinary Tract Infection	3 (2.9%)	0 (0.0%)
Viral Infection	2 (2.0%)	1 (2.1%)
Abscess	1 (1.0%)	0 (0.0%)
Bacteriuria	1 (1.0%)	0 (0.0%)
Eye Infection	0 (0.0%)	1 (2.1%)
Gingivitis	1 (1.0%)	0 (0.0%)
Infection	0 (0.0%)	1 (2.1%)
Influenza	0 (0.0%)	1 (2.1%)
Laryngitis	1 (1.0%)	0 (0.0%)
Lower Respiratory Tract Infection	1 (1.0%)	0 (0.0%)
Oral Candidiasis	1 (1.0%)	0 (0.0%)
Oral Herpes	1 (1.0%)	0 (0.0%)
Pneumonia	1 (1.0%)	0 (0.0%)
Pulpitis Dental	1 (1.0%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (2.1%)
Upper Respiratory Tract Inflammation	1 (1.0%)	0 (0.0%)
Viral Upper Respiratory Tract Infection	1 (1.0%)	0 (0.0%)
Hypertension SMQ	28 (27.5%)	6 (12.5%)
Hypertension	20 (19.6%)	4 (8.3%)
Blood Pressure Increased	5 (4.9%)	2 (4.2%)
Blood Pressure Diastolic Increased	1 (1.0%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.0%)	0 (0.0%)
Hypertensive Crisis	1 (1.0%)	0 (0.0%)
Neutropenia	7 (6.9%)	0 (0.0%)
Neutropenia	5 (4.9%)	0 (0.0%)
Neutrophil Count Decreased	2 (2.0%)	0 (0.0%)
Febrile Neutropenia	1 (1.0%)	0 (0.0%)
Drug related hepatic disorders SMQ	16 (15.7%)	1 (2.1%)
Alanine Aminotransferase Increased	11 (10.8%)	0 (0.0%)
Aspartate Aminotransferase Increased	9 (8.8%)	0 (0.0%)
Blood Bilirubin Increased	2 (2.0%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (1.0%)	0 (0.0%)
Hepatic Cyst	1 (1.0%)	0 (0.0%)
Hepatic Enzyme Increased	1 (1.0%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.0%)	0 (0.0%)
Ocular Icterus	0 (0.0%)	1 (2.1%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.1.1)

表 2.7.4.9-33 Adverse Events (AEs) of Interest by Age Group (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047and C788-048 study

Age < 65 years

Type of AE Preferred Term	Fostamatinib (N=74) n (%)	Placebo (N=37) n (%)
Number of Subjects with at Least One AE of Interest	48 (64.9%)	17 (45.9%)
Gastrointestinal Complaints	29 (39.2%)	9 (24.3%)
Nausea	14 (18.9%)	4 (10.8%)
Nausea	14 (18.9%)	4 (10.8%)
Vomiting	4 (5.4%)	3 (8.1%)
Vomiting	3 (4.1%)	3 (8.1%)
Retching	1 (1.4%)	0 (0.0%)
Diarrhea	20 (27.0%)	7 (18.9%)
Diarrhoea	19 (25.7%)	7 (18.9%)
Frequent Bowel Movements	1 (1.4%)	0 (0.0%)
Abdominal Pain	7 (9.5%)	1 (2.7%)
Abdominal Pain Upper	3 (4.1%)	1 (2.7%)
Abdominal Pain	3 (4.1%)	0 (0.0%)
Abdominal Discomfort	1 (1.4%)	0 (0.0%)
Infection	24 (32.4%)	9 (24.3%)
Upper Respiratory Tract Infection	5 (6.8%)	2 (5.4%)
Respiratory Tract Infection	3 (4.1%)	1 (2.7%)
Gastroenteritis	2 (2.7%)	1 (2.7%)
Influenza Like Illness	3 (4.1%)	0 (0.0%)
Urinary Tract Infection	3 (4.1%)	0 (0.0%)
Bronchitis	2 (2.7%)	0 (0.0%)
Nasopharyngitis	1 (1.4%)	1 (2.7%)
Viral Infection	1 (1.4%)	1 (2.7%)
Eye Infection	0 (0.0%)	1 (2.7%)
Gingivitis	1 (1.4%)	0 (0.0%)
Infection	0 (0.0%)	1 (2.7%)
Influenza	0 (0.0%)	1 (2.7%)
Laryngitis	1 (1.4%)	0 (0.0%)
Oral Candidiasis	1 (1.4%)	0 (0.0%)
Oral Herpes	1 (1.4%)	0 (0.0%)
Pneumonia	1 (1.4%)	0 (0.0%)
Pulpitis Dental	1 (1.4%)	0 (0.0%)
Upper Respiratory Tract Inflammation	1 (1.4%)	0 (0.0%)
Viral Upper Respiratory Tract Infection	1 (1.4%)	0 (0.0%)
Hypertension SMQ	17 (23.0%)	4 (10.8%)
Hypertension	14 (18.9%)	3 (8.1%)
Blood Pressure Increased	1 (1.4%)	1 (2.7%)
Blood Pressure Diastolic Increased	1 (1.4%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.4%)	0 (0.0%)
Neutropenia	5 (6.8%)	0 (0.0%)
Neutropenia	3 (4.1%)	0 (0.0%)
Febrile Neutropenia	1 (1.4%)	0 (0.0%)
Neutrophil Count Decreased	1 (1.4%)	0 (0.0%)
Drug related hepatic disorders SMQ	13 (17.6%)	1 (2.7%)
Alanine Aminotransferase Increased	9 (12.2%)	0 (0.0%)
Aspartate Aminotransferase Increased	8 (10.8%)	0 (0.0%)
Blood Bilirubin Increased	2 (2.7%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (1.4%)	0 (0.0%)
Hepatic Cyst	1 (1.4%)	0 (0.0%)
Hepatic Enzyme Increased	1 (1.4%)	0 (0.0%)
Ocular Icterus	0 (0.0%)	1 (2.7%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.1.1.1)

Age >= 65 years

Type of AE Preferred Term	Fostamatinib (N=28) n (%)	Placebo (N=11) n (%)
Number of Subjects with at Least One AE of Interest	21 (75.0%)	4 (36.4%)
Gastrointestinal Complaints	13 (46.4%)	1 (9.1%)
Nausea	5 (17.9%)	0 (0.0%)
Nausea	5 (17.9%)	0 (0.0%)
Diarrhea	12 (42.9%)	0 (0.0%)
Diarrhoea	11 (39.3%)	0 (0.0%)
Frequent Bowel Movements	1 (3.6%)	0 (0.0%)
Abdominal Pain	0 (0.0%)	1 (9.1%)
Abdominal Discomfort	0 (0.0%)	1 (9.1%)
Infection	7 (25.0%)	1 (9.1%)
Abscess	1 (3.6%)	0 (0.0%)
Bacteriuria	1 (3.6%)	0 (0.0%)
Bronchitis	1 (3.6%)	0 (0.0%)
Lower Respiratory Tract Infection	1 (3.6%)	0 (0.0%)
Nasopharyngitis	1 (3.6%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (9.1%)
Upper Respiratory Tract Infection	1 (3.6%)	0 (0.0%)
Viral Infection	1 (3.6%)	0 (0.0%)
Hypertension SMQ	11 (39.3%)	2 (18.2%)
Hypertension	6 (21.4%)	1 (9.1%)
Blood Pressure Increased	4 (14.3%)	1 (9.1%)
Hypertensive Crisis	1 (3.6%)	0 (0.0%)
Neutropenia	2 (7.1%)	0 (0.0%)
Neutropenia	2 (7.1%)	0 (0.0%)
Neutrophil Count Decreased	1 (3.6%)	0 (0.0%)
Drug related hepatic disorders SMQ	3 (10.7%)	0 (0.0%)
Alanine Aminotransferase Increased	2 (7.1%)	0 (0.0%)
Aspartate Aminotransferase Increased	1 (3.6%)	0 (0.0%)
Liver Function Test Abnormal	1 (3.6%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.1.1.1)

表 2.7.4.9-34 Adverse Events (AEs) of Interest by Gender (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Males

Type of AE Preferred Term	Fostamatinib (N=41) n (%)	Placebo (N=18) n (%)
Number of Subjects with at Least One AE of Interest	26 (63.4%)	6 (33.3%)
Gastrointestinal Complaints	15 (36.6%)	2 (11.1%)
Nausea	3 (7.3%)	0 (0.0%)
Nausea	3 (7.3%)	0 (0.0%)
Vomiting	2 (4.9%)	1 (5.6%)
Vomiting	2 (4.9%)	1 (5.6%)
Diarrhea	12 (29.3%)	2 (11.1%)
Diarrhoea	12 (29.3%)	2 (11.1%)
Abdominal Pain	2 (4.9%)	0 (0.0%)
Abdominal Pain	1 (2.4%)	0 (0.0%)
Abdominal Pain Upper	1 (2.4%)	0 (0.0%)
Infection	14 (34.1%)	2 (11.1%)
Respiratory Tract Infection	2 (4.9%)	1 (5.6%)
Upper Respiratory Tract Infection	3 (7.3%)	0 (0.0%)
Nasopharyngitis	1 (2.4%)	1 (5.6%)
Bronchitis	1 (2.4%)	0 (0.0%)
Influenza Like Illness	1 (2.4%)	0 (0.0%)
Laryngitis	1 (2.4%)	0 (0.0%)
Lower Respiratory Tract Infection	1 (2.4%)	0 (0.0%)
Oral Candidiasis	1 (2.4%)	0 (0.0%)
Oral Herpes	1 (2.4%)	0 (0.0%)
Pulpitis Dental	1 (2.4%)	0 (0.0%)
Upper Respiratory Tract Inflammation	1 (2.4%)	0 (0.0%)
Urinary Tract Infection	1 (2.4%)	0 (0.0%)
Viral Infection	1 (2.4%)	0 (0.0%)
Hypertension SMQ	7 (17.1%)	2 (11.1%)
Hypertension	5 (12.2%)	2 (11.1%)
Blood Pressure Increased	2 (4.9%)	0 (0.0%)
Neutropenia	3 (7.3%)	0 (0.0%)
Febrile Neutropenia	1 (2.4%)	0 (0.0%)
Neutropenia	1 (2.4%)	0 (0.0%)
Neutrophil Count Decreased	1 (2.4%)	0 (0.0%)
Drug related hepatic disorders SMQ	6 (14.6%)	1 (5.6%)
Alanine Aminotransferase Increased	4 (9.8%)	0 (0.0%)
Aspartate Aminotransferase Increased	3 (7.3%)	0 (0.0%)
Blood Bilirubin Increased	1 (2.4%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (2.4%)	0 (0.0%)
Hepatic Enzyme Increased	1 (2.4%)	0 (0.0%)
Ocular Icterus	0 (0.0%)	1 (5.6%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.1.1.2)

Females

Type of AE Preferred Term	Fostamatinib (N=61) n (%)	Placebo (N=30) n (%)
Number of Subjects with at Least One AE of Interest	43 (70.5%)	15 (50.0%)
Gastrointestinal Complaints	27 (44.3%)	8 (26.7%)
Nausea	16 (26.2%)	4 (13.3%)
Nausea	16 (26.2%)	4 (13.3%)
Vomiting	2 (3.3%)	2 (6.7%)
Vomiting	1 (1.6%)	2 (6.7%)
Retching	1 (1.6%)	0 (0.0%)
Diarrhea	20 (32.8%)	5 (16.7%)
Diarrhoea	18 (29.5%)	5 (16.7%)
Frequent Bowel Movements	2 (3.3%)	0 (0.0%)
Abdominal Pain	5 (8.2%)	2 (6.7%)
Abdominal Pain Upper	2 (3.3%)	1 (3.3%)

Type of AE Preferred Term	Fostamatinib (N=61) n (%)	Placebo (N=30) n (%)
Abdominal Discomfort	1 (1.6%)	1 (3.3%)
Abdominal Pain	2 (3.3%)	0 (0.0%)
Infection	17 (27.9%)	8 (26.7%)
Upper Respiratory Tract Infection	3 (4.9%)	2 (6.7%)
Gastroenteritis	2 (3.3%)	1 (3.3%)
Bronchitis	2 (3.3%)	0 (0.0%)
Influenza Like Illness	2 (3.3%)	0 (0.0%)
Urinary Tract Infection	2 (3.3%)	0 (0.0%)
Viral Infection	1 (1.6%)	1 (3.3%)
Abscess	1 (1.6%)	0 (0.0%)
Bacteriuria	1 (1.6%)	0 (0.0%)
Eye Infection	0 (0.0%)	1 (3.3%)
Gingivitis	1 (1.6%)	0 (0.0%)
Infection	0 (0.0%)	1 (3.3%)
Influenza	0 (0.0%)	1 (3.3%)
Nasopharyngitis	1 (1.6%)	0 (0.0%)
Pneumonia	1 (1.6%)	0 (0.0%)
Respiratory Tract Infection	1 (1.6%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (3.3%)
Viral Upper Respiratory Tract Infection	1 (1.6%)	0 (0.0%)
Hypertension SMQ	21 (34.4%)	4 (13.3%)
Hypertension	15 (24.6%)	2 (6.7%)
Blood Pressure Increased	3 (4.9%)	2 (6.7%)
Blood Pressure Diastolic Increased	1 (1.6%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.6%)	0 (0.0%)
Hypertensive Crisis	1 (1.6%)	0 (0.0%)
Neutropenia	4 (6.6%)	0 (0.0%)
Neutropenia	4 (6.6%)	0 (0.0%)
Neutrophil Count Decreased	1 (1.6%)	0 (0.0%)
Drug related hepatic disorders SMQ	10 (16.4%)	0 (0.0%)
Alanine Aminotransferase Increased	7 (11.5%)	0 (0.0%)
Aspartate Aminotransferase Increased	6 (9.8%)	0 (0.0%)
Blood Bilirubin Increased	1 (1.6%)	0 (0.0%)
Hepatic Cyst	1 (1.6%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.6%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review.
(Source: 5.3.5.3.2, Table 4.2.3.1.1.2)

表 2.7.4.9-35 Adverse Events (AEs) of Interest: Incidence by System Organ Class/Preferred Term and Severity (Subject Level) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Type of AE Preferred Term	Fostamatinib (N=102)			
	Mild	Moderate	Severe	Total
	n (%)	n (%)	n (%)	n (%)
Number of Subjects with at Least One AE of Interest	32 (31.4%)	30 (29.4%)	7 (6.9%)	69 (67.6%)
Gastrointestinal Complaints	27 (26.5%)	14 (13.7%)	1 (1.0%)	42 (41.2%)
Nausea	16 (15.7%)	3 (2.9%)	0 (0.0%)	19 (18.6%)
Nausea	16 (15.7%)	3 (2.9%)	0 (0.0%)	19 (18.6%)
Vomiting	4 (3.9%)	0 (0.0%)	0 (0.0%)	4 (3.9%)
Vomiting	3 (2.9%)	0 (0.0%)	0 (0.0%)	3 (2.9%)
Retching	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Diarrhea	21 (20.6%)	10 (9.8%)	1 (1.0%)	32 (31.4%)
Diarrhoea	19 (18.6%)	10 (9.8%)	1 (1.0%)	30 (29.4%)
Frequent Bowel Movements	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Abdominal Pain	6 (5.9%)	1 (1.0%)	0 (0.0%)	7 (6.9%)
Abdominal Pain	2 (2.0%)	1 (1.0%)	0 (0.0%)	3 (2.9%)
Abdominal Pain Upper	3 (2.9%)	0 (0.0%)	0 (0.0%)	3 (2.9%)
Abdominal Discomfort	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Infection	23 (22.5%)	6 (5.9%)	2 (2.0%)	31 (30.4%)
Upper Respiratory Tract Infection	5 (4.9%)	1 (1.0%)	0 (0.0%)	6 (5.9%)
Bronchitis	2 (2.0%)	1 (1.0%)	0 (0.0%)	3 (2.9%)
Influenza Like Illness	2 (2.0%)	0 (0.0%)	1 (1.0%)	3 (2.9%)
Respiratory Tract Infection	2 (2.0%)	1 (1.0%)	0 (0.0%)	3 (2.9%)
Urinary Tract Infection	2 (2.0%)	1 (1.0%)	0 (0.0%)	3 (2.9%)
Gastroenteritis	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Nasopharyngitis	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Viral Infection	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Abscess	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Bacteriuria	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Gingivitis	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Laryngitis	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Lower Respiratory Tract Infection	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)
Oral Candidiasis	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Oral Herpes	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Pneumonia	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)
Pulpitis Dental	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Upper Respiratory Tract Inflammation	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Viral Upper Respiratory Tract Infection	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.0%)
Hypertension SMQ	17 (16.7%)	9 (8.8%)	2 (2.0%)	28 (27.5%)
Hypertension	12 (11.8%)	8 (7.8%)	0 (0.0%)	20 (19.6%)
Blood Pressure Increased	3 (2.9%)	1 (1.0%)	1 (1.0%)	5 (4.9%)
Blood Pressure Diastolic Increased	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Blood Pressure Systolic Increased	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Hypertensive Crisis	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)
Neutropenia	3 (2.9%)	2 (2.0%)	2 (2.0%)	7 (6.9%)
Neutropenia	2 (2.0%)	2 (2.0%)	1 (1.0%)	5 (4.9%)
Neutrophil Count Decreased	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Febrile Neutropenia	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.0%)
Drug related hepatic disorders SMQ	10 (9.8%)	6 (5.9%)	0 (0.0%)	16 (15.7%)
Alanine Aminotransferase Increased	5 (4.9%)	6 (5.9%)	0 (0.0%)	11 (10.8%)
Aspartate Aminotransferase Increased	5 (4.9%)	4 (3.9%)	0 (0.0%)	9 (8.8%)
Blood Bilirubin Increased	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Gamma-Glutamyltransferase Increased	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Hepatic Cyst	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Hepatic Enzyme Increased	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)
Liver Function Test Abnormal	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review. Subjects are counted only once in each category, based upon their most severe AE in the category. AEs with missing severity were classified as severe. For diarrhea, severity was assigned based on the diarrhea severity grade as follows: 1=Mild; 2=Moderate; 3, 4, and 5=Severe.
(Source: 5.3.5.3.2, Table 4.3.2.1.1)

Type of AE Preferred Term	Placebo (N=48) Mild n (%)	 Moderate n (%)	 Severe n (%)	 Total n (%)
Number of Subjects with at Least One AE of Interest	16 (33.3%)	3 (6.3%)	2 (4.2%)	21 (43.8%)
Gastrointestinal Complaints	8 (16.7%)	2 (4.2%)	0 (0.0%)	10 (20.8%)
Nausea	4 (8.3%)	0 (0.0%)	0 (0.0%)	4 (8.3%)
Nausea	4 (8.3%)	0 (0.0%)	0 (0.0%)	4 (8.3%)
Vomiting	2 (4.2%)	1 (2.1%)	0 (0.0%)	3 (6.3%)
Vomiting	2 (4.2%)	1 (2.1%)	0 (0.0%)	3 (6.3%)
Diarrhea	6 (12.5%)	1 (2.1%)	0 (0.0%)	7 (14.6%)
Diarrhoea	6 (12.5%)	1 (2.1%)	0 (0.0%)	7 (14.6%)
Abdominal Pain	2 (4.2%)	0 (0.0%)	0 (0.0%)	2 (4.2%)
Abdominal Discomfort	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Abdominal Pain Upper	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Infection	7 (14.6%)	2 (4.2%)	1 (2.1%)	10 (20.8%)
Upper Respiratory Tract Infection	2 (4.2%)	0 (0.0%)	0 (0.0%)	2 (4.2%)
Eye Infection	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.1%)
Gastroenteritis	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Infection	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.1%)
Influenza	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Nasopharyngitis	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Respiratory Tract Infection	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Sepsis	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.1%)
Viral Infection	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Hypertension SMQ	5 (10.4%)	0 (0.0%)	1 (2.1%)	6 (12.5%)
Hypertension	3 (6.3%)	0 (0.0%)	1 (2.1%)	4 (8.3%)
Blood Pressure Increased	2 (4.2%)	0 (0.0%)	0 (0.0%)	2 (4.2%)
Drug related hepatic disorders SMQ	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)
Ocular Icterus	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.1%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review. Subjects are counted only once in each category, based upon their most severe AE in the category. AEs with missing severity were classified as severe. For diarrhea, severity was assigned based on the diarrhea severity grade as follows: 1=Mild; 2=Moderate; 3, 4, and 5=Severe.
(Source: 5.3.5.3.2, Table 4.3.2.1.1)

表 2.7.4.9-36 Treatment-Related Adverse Events (AEs) of Interest (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Type of AE Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Number of Subjects with at Least One Treatment-Related AE of Interest	51 (50.0%)	9 (18.8%)
Gastrointestinal Complaints	35 (34.3%)	8 (16.7%)
Nausea	15 (14.7%)	3 (6.3%)
Nausea	15 (14.7%)	3 (6.3%)
Vomiting	2 (2.0%)	1 (2.1%)
Vomiting	1 (1.0%)	1 (2.1%)
Retching	1 (1.0%)	0 (0.0%)
Non-Infectious Diarrhea SMQ	28 (27.5%)	6 (12.5%)
Diarrhoea	27 (26.5%)	6 (12.5%)
Frequent Bowel Movements	1 (1.0%)	0 (0.0%)
Abdominal Pain	5 (4.9%)	2 (4.2%)
Abdominal Pain	3 (2.9%)	0 (0.0%)
Abdominal Discomfort	1 (1.0%)	1 (2.1%)
Abdominal Pain Upper	1 (1.0%)	1 (2.1%)
Infection	4 (3.9%)	0 (0.0%)
Bacteriuria	1 (1.0%)	0 (0.0%)
Influenza Like Illness	1 (1.0%)	0 (0.0%)
Oral Candidiasis	1 (1.0%)	0 (0.0%)
Pneumonia	1 (1.0%)	0 (0.0%)
Hypertension SMQ	22 (21.6%)	2 (4.2%)
Hypertension	16 (15.7%)	2 (4.2%)
Blood Pressure Increased	4 (3.9%)	0 (0.0%)
Blood Pressure Systolic Increased	1 (1.0%)	0 (0.0%)
Hypertensive Crisis	1 (1.0%)	0 (0.0%)
Neutropenia	6 (5.9%)	0 (0.0%)
Neutropenia	4 (3.9%)	0 (0.0%)
Neutrophil Count Decreased	2 (2.0%)	0 (0.0%)
Febrile Neutropenia	1 (1.0%)	0 (0.0%)
Drug Related Hepatic Disorders SMQ	12 (11.8%)	0 (0.0%)
Alanine Aminotransferase Increased	10 (9.8%)	0 (0.0%)
Aspartate Aminotransferase Increased	7 (6.9%)	0 (0.0%)
Blood Bilirubin Increased	2 (2.0%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.0%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. Narrow scope was used for SMQs from MedDRA dictionary. Categories that are not SMQ based were identified by medical review. Treatment-related AEs are AEs with a possible, probable, or missing causal relationship to study drug.
(Source: 5.3.5.3.2, Table 4.2.3.1.2)

表 2.7.4.9-37 Occurrence of Serious Adverse Events with Interest (Placebo-Controlled Safety Population) – C788-047 and C788-048 study

	Fostamatinib		Placebo	
Category, PT	n	%	n	%
N	102	---	48	---
Bleeding Events	5	4.9	5	10.4
Contusion	1	1.0	0	0.0
Epistaxis	2	2.0	1	2.1
Gastrointestinal Haemorrhage	0	0.0	1	2.1
Immune Thrombocytopenic Purpura	1	1.0	0	0.0
Menorrhagia	0	0.0	2	4.2
Petechiae	0	0.0	1	2.1
Vaginal Haemorrhage	1	1.0	0	0.0
Gastrointestinal Complaints	1	1.0	0	0.0
Non-Infectious Diarrhea SMQ	1	1.0	0	0.0
Diarrhoea	1	1.0	0	0.0
Infection	2	2.0	2	4.2
Bronchitis	1	1.0	0	0.0
Infection	0	0.0	1	2.1
Pneumonia	1	1.0	0	0.0
Sepsis	0	0.0	1	2.1
Hypertension SMQ	1	1.0	0	0.0
Hypertensive Crisis	1	1.0	0	0.0
Neutropenia	1	1.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0

(Source: 5.3.5.3.2, Table 7.1.1.1)

表 2.7.4.9-38 Occurrence of Adverse Events with Interest to Study Drug Withdrawal (Placebo-Controlled Safety Population) – C788-047 and C788-048 study

	Fostamatinib		Placebo	
Category, PT	n	%	n	%
N	102	---	48	---
Bleeding Events	0	0.0	1	2.1
Epistaxis	0	0.0	1	2.1
Gastrointestinal Complaints	2	2.0	2	4.2
Non-Infectious Diarrhea SMQ	1	1.0	1	2.1
Diarrhoea	1	1.0	1	2.1
Abdominal Pain	1	1.0	1	2.1
Abdominal Discomfort	0	0.0	1	2.1
Abdominal Pain	1	1.0	0	0.0
Infection	1	1.0	0	0.0
Pneumonia	1	1.0	0	0.0
Hypertension SMQ	0	0.0	1	2.1
Hypertension	0	0.0	1	2.1
Neutropenia	2	2.0	0	0.0
Neutropenia	2	2.0	0	0.0
Drug Related Hepatic Disorders SMQ	1	1.0	0	0.0
Alanine Aminotransferase Increased	1	1.0	0	0.0

(Source: 5.3.5.3.2, Table 7.1.1.4)

表 2.7.4.9-39 Occurrence of Adverse Events with Interest to Dose Reduction (Placebo-Controlled Safety Population) – C788-047 and C788-048 study

	Fostamatinib		Placebo	
Category, PT	n	%	n	%
N	102	---	48	---
Gastrointestinal Complaints	2	2.0	0	0.0
Non-Infectious Diarrhea SMQ	2	2.0	0	0.0
Diarrhoea	2	2.0	0	0.0
Hypertension SMQ	2	2.0	0	0.0
Hypertension	2	2.0	0	0.0
Neutropenia	2	2.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0
Neutrophil Count Decreased	1	1.0	0	0.0
Drug Related Hepatic Disorders SMQ	2	2.0	0	0.0
Alanine Aminotransferase Increased	1	1.0	0	0.0
Aspartate Aminotransferase Increased	1	1.0	0	0.0

(Source: 5.3.5.3.2, Table 7.1.1.2)

表 2.7.4.9-40 Occurrence of Adverse Events with Interest to Dose Interruption (Placebo-Controlled Safety Population) – C788-047 and C788-048 study

	Fostamatinib		Placebo	
Category, PT	n	%	n	%
N	102	---	48	---
Bleeding Events	1	1.0	1	2.1
Epistaxis	1	1.0	0	0.0
Gastrointestinal Haemorrhage	0	0.0	1	2.1
Gastrointestinal Complaints	3	2.9	0	0.0
Non-Infectious Diarrhea SMQ	3	2.9	0	0.0
Diarrhoea	3	2.9	0	0.0
Infection	2	2.0	0	0.0
Influenza Like Illness	2	2.0	0	0.0
Hypertension SMQ	1	1.0	0	0.0
Hypertensive Crisis	1	1.0	0	0.0
Neutropenia	2	2.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0
Neutrophil Count Decreased	1	1.0	0	0.0
Drug Related Hepatic Disorders SMQ	6	5.9	0	0.0
Alanine Aminotransferase Increased	5	4.9	0	0.0
Aspartate Aminotransferase Increased	1	1.0	0	0.0
Blood Bilirubin Increased	1	1.0	0	0.0

(Source: 5.3.5.3.2, Table 7.1.1.3)

表 2.7.4.9-41 Adverse Events (AEs) of Interest: Incidence with Onset Date ≤12 Weeks from First Dose by Type of AE and Preferred Term (Subject Level) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Type of AE Preferred Term	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
Number of Subjects with at Least One AE of Interest	64 (62.7%)	19 (39.6%)
Gastrointestinal Complaints	39 (38.2%)	10 (20.8%)
Nausea	19 (18.6%)	4 (8.3%)
Nausea	19 (18.6%)	4 (8.3%)
Vomiting	4 (3.9%)	3 (6.3%)
Vomiting	3 (2.9%)	3 (6.3%)
Retching	1 (1.0%)	0 (0.0%)
Diarrhea	27 (26.5%)	7 (14.6%)
Diarrhoea	25 (24.5%)	7 (14.6%)
Frequent Bowel Movements	2 (2.0%)	0 (0.0%)
Abdominal Pain	6 (5.9%)	2 (4.2%)
Abdominal Pain Upper	3 (2.9%)	1 (2.1%)
Abdominal Discomfort	1 (1.0%)	1 (2.1%)
Abdominal Pain	2 (2.0%)	0 (0.0%)
Infection	23 (22.5%)	8 (16.7%)
Upper Respiratory Tract Infection	4 (3.9%)	2 (4.2%)
Bronchitis	3 (2.9%)	0 (0.0%)
Gastroenteritis	2 (2.0%)	1 (2.1%)
Viral Infection	2 (2.0%)	1 (2.1%)
Influenza Like Illness	2 (2.0%)	0 (0.0%)
Nasopharyngitis	1 (1.0%)	1 (2.1%)
Respiratory Tract Infection	2 (2.0%)	0 (0.0%)
Urinary Tract Infection	2 (2.0%)	0 (0.0%)
Bacteriuria	1 (1.0%)	0 (0.0%)
Gingivitis	1 (1.0%)	0 (0.0%)
Infection	0 (0.0%)	1 (2.1%)
Influenza	0 (0.0%)	1 (2.1%)
Lower Respiratory Tract Infection	1 (1.0%)	0 (0.0%)
Pneumonia	1 (1.0%)	0 (0.0%)
Pulpitis Dental	1 (1.0%)	0 (0.0%)
Sepsis	0 (0.0%)	1 (2.1%)
Upper Respiratory Tract Inflammation	1 (1.0%)	0 (0.0%)
Viral Upper Respiratory Tract Infection	1 (1.0%)	0 (0.0%)
Hypertension SMQ	26 (25.5%)	6 (12.5%)
Hypertension	20 (19.6%)	4 (8.3%)
Blood Pressure Increased	4 (3.9%)	2 (4.2%)
Blood Pressure Diastolic Increased	1 (1.0%)	0 (0.0%)
Hypertensive Crisis	1 (1.0%)	0 (0.0%)
Neutropenia	4 (3.9%)	0 (0.0%)
Neutropenia	3 (2.9%)	0 (0.0%)
Neutrophil Count Decreased	2 (2.0%)	0 (0.0%)
Drug Related Hepatic Disorders SMQ	12 (11.8%)	1 (2.1%)
Alanine Aminotransferase Increased	7 (6.9%)	0 (0.0%)
Aspartate Aminotransferase Increased	7 (6.9%)	0 (0.0%)
Blood Bilirubin Increased	1 (1.0%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (1.0%)	0 (0.0%)
Hepatic Cyst	1 (1.0%)	0 (0.0%)
Hepatic Enzyme Increased	1 (1.0%)	0 (0.0%)
Liver Function Test Abnormal	1 (1.0%)	0 (0.0%)
Ocular Icterus	0 (0.0%)	1 (2.1%)

Note: Adverse events were coded using MedDRA version 18.1. The denominator for the calculation of the percentage is N, the number of subjects in the treatment group, and the numerator is the number of such subjects with at least one moderate or severe bleeding event in that system organ class or with that preferred term.
(Source: 5.3.5.3.2, Table 4.4.2.1.1)

表 2.7.4.9-42 Hypertension Management – Post-Baseline (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Type of Hypertension Intervention	Fostamatinib (N=146) n (%)
No hypertension interventions	104 (71.2%)
At least one hypertension intervention (1)	42 (28.8%)
Increased dose of current anti-hypertensive medication (2)	18 (12.3%)
Started new anti-hypertensive medication (2)	37 (25.3%)
Dose reduction of study drug (3)	3 (2.1%)
Discontinuation of study drug (3)	1 (0.7%)

(1) The types of hypertension intervention are not mutually exclusive. Therefore the percentages may sum to more than 100%.
(2) Anti-hypertensive medications are medications with the following ATC codes: C02 (anti-hypertensives), C03 (diuretics), C04 (peripheral vasodilators), C07 (beta blocking agents), C08 (calcium channel blockers), and C09 (agents acting on the rennin-angiotensin system).
(3) Due to hypertension (SMQ) events. Narrow scope was used for the SMQ from MedDRA dictionary.
(Source: 5.3.5.3.2, Table 6.5.2)

表 2.7.4.9-43 Hypertension Management – Post-Baseline (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Type of Hypertension Intervention	Fostamatinib (N=102) n (%)	Placebo (N=48) n (%)
No hypertension interventions	81 (79.4%)	40 (83.3%)
At least one hypertension intervention (1)	21 (20.6%)	8 (16.7%)
Increased dose of current anti-hypertensive medication (2)	11 (10.8%)	3 (6.3%)
Started new anti-hypertensive medication (2)	18 (17.6%)	7 (14.6%)
Dose reduction of study drug (3)	2 (2.0%)	0 (0.0%)
Discontinuation of study drug (3)	0 (0.0%)	1 (2.1%)

(1) The types of hypertension intervention are not mutually exclusive. Therefore the percentages may sum to more than 100%.
(2) Anti-hypertensive medications are medications with the following ATC codes: C02 (anti-hypertensives), C03 (diuretics), C04 (peripheral vasodilators), C07 (beta blocking agents), C08 (calcium channel blockers), and C09 (agents acting on the rennin-angiotensin system).
(3) Due to hypertension (SMQ) events. Narrow scope was used for the SMQ from MedDRA dictionary.
(Source: 5.3.5.3.2, Table 6.5.1)

表 2.7.4.9-44 Laboratory Tests – R788-1301 study

Period I
Parameter: Neutrophils (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	4.590	2.455	1.89	2.76	3.50	5.90	11.82
	Screening B	22	4.266	2.149	1.91	2.50	3.34	5.87	8.88
	Day 1	22	4.475	2.386	1.67	2.92	3.60	6.33	10.96
	Week 2	22	3.310	1.837	0.87	2.24	2.90	4.19	8.39
	Week 4	22	2.855	1.572	0.45	1.29	2.56	3.96	5.59
	Week 6	22	2.898	1.501	1.00	1.75	2.72	3.96	6.60
	Week 8	21	2.573	1.406	0.70	1.64	2.10	2.90	6.64
	Week 10	20	2.465	1.306	0.70	1.50	2.30	3.16	6.27
	Week 12	20	2.700	1.337	0.97	1.92	2.23	3.50	5.35
	Week 14	16	2.185	1.332	0.99	1.46	1.82	2.46	6.40
	Week 16	10	3.217	2.505	0.89	1.74	2.51	3.27	9.05
	Week 18	10	2.287	1.327	0.78	1.11	2.15	2.80	5.29
	Week 20	10	2.452	1.118	1.01	1.42	2.60	2.77	4.83
	Week 22	10	2.567	1.281	1.16	1.65	2.18	3.40	4.84
	Week 24	10	2.574	1.335	1.04	1.89	2.53	2.75	5.95
	LOV	22	3.339	2.929	1.04	1.89	2.42	3.86	14.76
Placebo	Screening A	12	5.356	2.318	2.70	3.35	4.75	7.41	9.61
	Screening B	12	4.867	2.056	2.38	3.05	4.56	6.54	7.99
	Day 1	12	5.589	2.787	2.63	3.64	4.94	7.17	11.86
	Week 2	12	4.677	2.447	2.10	2.94	3.93	6.04	10.32
	Week 4	10	5.070	2.134	3.08	3.25	4.29	6.77	9.51
	Week 6	10	4.937	1.752	2.23	3.54	5.33	6.68	6.92
	Week 8	11	4.376	1.858	2.16	2.92	3.53	6.18	7.12
	Week 10	11	4.299	2.153	2.20	2.86	3.40	5.66	9.22
	Week 12	10	4.867	2.823	1.95	2.84	4.04	5.59	10.98
	Week 14	4	2.917	0.953	1.68	2.32	2.99	3.51	4.00
	Week 16	4	3.082	1.089	2.11	2.40	2.79	3.77	4.64
	Week 18	4	2.824	0.653	2.05	2.34	2.82	3.31	3.60
	Week 20	3	3.169	1.100	2.16	2.16	3.00	4.34	4.34
	Week 22	4	3.328	1.390	2.01	2.24	3.10	4.42	5.10
	Week 24	4	2.753	0.609	1.89	2.33	2.97	3.18	3.19
	LOV	12	5.020	2.904	1.89	3.02	4.04	6.37	10.98

Period I
Parameter: Hemoglobin (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	134.0	17.7	107	119	133	152	160
	Screening B	22	132.9	16.8	100	118	134	141	167
	Day 1	22	132.2	16.8	107	117	133	145	169
	Week 2	22	136.2	14.6	112	127	135	146	166
	Week 4	22	132.3	15.8	108	119	132	148	165
	Week 6	22	132.5	17.0	99	123	130	147	168
	Week 8	21	130.1	12.9	109	118	130	137	153
	Week 10	20	126.1	12.9	92	118	127	135	145
	Week 12	20	124.5	13.5	98	117	123	136	147
	Week 14	16	124.3	12.7	104	116	124	134	152
	Week 16	10	124.2	8.4	109	120	125	128	141
	Week 18	10	123.8	10.3	102	120	123	129	141
	Week 20	10	122.8	9.9	101	120	124	126	140
	Week 22	10	123.4	11.6	103	121	125	128	146
	Week 24	10	126.1	13.2	99	125	129	131	148
	LOV	22	126.9	15.7	99	113	129	134	168
Placebo	Screening A	12	144.3	15.4	113	134	147	155	165
	Screening B	12	142.9	14.5	114	134	143	153	167
	Day 1	12	142.8	15.8	114	131	143	156	169

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 2	12	142.7	16.3	111	131	145	158	166
	Week 4	10	142.8	17.2	110	130	142	156	169
	Week 6	10	138.9	19.5	100	127	139	156	165
	Week 8	11	137.9	19.2	98	127	137	157	165
	Week 10	11	138.9	19.3	104	124	139	161	167
	Week 12	10	141.9	17.8	119	126	142	152	171
	Week 14	4	129.5	18.4	114	118	124	142	156
	Week 16	4	133.3	16.1	122	124	127	143	157
	Week 18	4	132.5	14.1	121	125	128	141	153
	Week 20	3	135.0	17.3	120	120	131	154	154
	Week 22	4	129.0	22.3	105	116	126	143	159
	Week 24	4	132.5	20.1	109	120	132	146	158
	LOV	12	141.0	19.4	109	128	139	155	172

Period I
Parameter: Alanine Aminotransferase (U/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	17.0	5.8	10	12	15	20	31
	Day 1	22	17.0	7.0	10	13	15	19	38
	Week 2	22	22.8	8.0	11	17	23	28	40
	Week 4	22	30.2	31.4	10	16	23	36	164
	Week 6	22	55.9	128.4	11	19	26	34	626
	Week 8	21	38.3	33.4	15	21	26	33	155
	Week 10	20	38.7	28.4	16	21	33	43	143
	Week 12	20	35.1	18.9	14	19	28	54	73
	Week 14	16	40.2	38.6	16	20	25	46	173
	Week 16	10	32.1	11.5	17	24	29	42	54
	Week 18	10	29.9	10.3	15	23	29	35	50
	Week 20	10	30.9	11.7	18	19	29	39	49
	Week 22	10	33.4	17.3	17	23	29	36	71
	Week 24	10	34.4	24.2	12	24	29	35	99
	LOV	22	37.7	35.6	11	19	28	41	173
Placebo	Screening A	12	24.8	9.7	15	17	23	28	49
	Day 1	12	23.6	9.4	13	17	21	27	42
	Week 2	12	23.4	9.5	11	16	24	32	38
	Week 4	10	22.8	7.6	14	17	22	26	38
	Week 6	10	20.2	9.2	10	13	18	25	37
	Week 8	11	21.9	9.5	13	13	18	29	40
	Week 10	11	21.0	7.7	12	15	17	24	36
	Week 12	10	24.4	9.6	11	17	23	30	44
	Week 14	4	27.0	23.7	10	13	18	41	62
	Week 16	4	16.0	7.4	11	12	13	21	27
	Week 18	4	14.5	7.8	9	10	12	19	26
	Week 20	3	18.3	9.2	13	13	13	29	29
	Week 22	4	17.3	8.3	9	11	16	24	28
	Week 24	4	15.8	3.8	11	13	16	19	20
	LOV	12	22.8	9.7	11	17	20	29	47

Period I
Parameter: Aspartate Aminotransferase (U/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	20.0	5.8	11	17	19	24	36
	Day 1	22	20.5	7.3	14	16	18	22	45
	Week 2	22	26.8	7.5	14	20	28	32	40
	Week 4	22	30.9	22.8	15	19	26	32	125
	Week 6	22	44.8	69.9	14	19	25	39	350
	Week 8	21	33.1	18.5	17	22	25	44	84
	Week 10	20	33.3	15.6	19	23	29	38	85
	Week 12	20	32.6	13.2	17	22	30	44	65

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 14	16	38.3	33.5	17	23	27	41	158
	Week 16	10	29.2	9.7	18	20	28	34	50
	Week 18	10	28.4	9.0	18	22	26	34	44
	Week 20	10	30.1	8.6	19	22	31	36	46
	Week 22	10	32.1	12.0	21	23	28	36	57
	Week 24	10	30.6	12.4	19	22	29	33	60
	LOV	22	35.3	29.2	14	23	29	38	158
Placebo	Screening A	12	24.1	7.0	14	19	24	28	36
	Day 1	12	23.0	6.0	13	19	23	28	32
	Week 2	12	23.8	7.4	13	19	23	29	37
	Week 4	10	24.1	5.0	16	22	24	28	30
	Week 6	10	22.7	7.1	12	17	22	29	35
	Week 8	11	23.6	7.3	15	16	24	30	35
	Week 10	11	23.2	5.9	16	19	22	28	34
	Week 12	10	25.8	7.6	12	21	26	32	37
	Week 14	4	29.8	23.6	16	17	19	43	65
	Week 16	4	18.0	6.8	11	13	17	23	27
	Week 18	4	17.8	5.6	14	15	16	21	26
	Week 20	3	18.7	7.2	14	14	15	27	27
	Week 22	4	18.3	5.2	15	16	16	21	26
	Week 24	4	17.5	3.1	15	16	17	20	22
	LOV	12	23.3	7.8	13	17	22	30	37

Period I
Parameter: Bilirubin (umol/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	9.640	3.640	5.13	6.84	9.41	11.97	22.24
	Day 1	22	9.174	3.191	3.42	8.55	8.55	10.26	15.39
	Week 2	22	10.962	4.211	3.42	8.55	10.26	13.68	18.81
	Week 4	22	11.273	4.857	5.13	8.55	10.26	11.97	23.95
	Week 6	22	11.273	5.578	5.13	6.84	10.26	11.97	27.37
	Week 8	21	11.240	3.529	6.84	8.55	10.26	11.97	18.81
	Week 10	20	11.802	3.677	6.84	8.55	11.97	13.68	20.52
	Week 12	20	11.716	4.272	5.13	8.55	11.12	12.83	23.95
	Week 14	16	11.652	3.810	6.84	8.55	11.97	13.68	18.81
	Week 16	10	12.315	4.824	6.84	8.55	11.97	13.68	23.95
	Week 18	10	12.144	6.957	6.84	8.55	9.41	11.97	27.37
	Week 20	10	10.947	2.929	6.84	8.55	10.26	11.97	17.10
	Week 22	10	10.776	3.610	6.84	8.55	10.26	10.26	18.81
	Week 24	10	10.947	3.884	6.84	8.55	10.26	11.97	20.52
	LOV	22	11.662	3.643	6.84	8.55	11.12	13.68	20.52
Placebo	Screening A	12	11.118	4.221	6.84	7.70	10.26	13.68	20.52
	Day 1	12	12.685	7.088	6.84	6.84	11.12	16.25	29.08
	Week 2	12	11.973	8.219	3.42	8.55	9.41	13.68	35.92
	Week 4	10	12.144	6.473	6.84	8.55	9.41	13.68	27.37
	Week 6	10	12.144	7.711	5.13	8.55	10.26	11.97	32.50
	Week 8	11	11.817	7.355	6.84	6.84	10.26	10.26	30.79
	Week 10	11	10.262	3.825	3.42	8.55	10.26	11.97	18.81
	Week 12	10	11.460	6.938	3.42	8.55	8.55	13.68	27.37
	Week 14	4	6.414	0.855	5.13	5.99	6.84	6.84	6.84
	Week 16	4	6.842	3.123	3.42	4.28	6.84	9.41	10.26
	Week 18	4	8.552	2.793	5.13	6.84	8.55	10.26	11.97
	Week 20	3	9.122	2.613	6.84	6.84	8.55	11.97	11.97
	Week 22	4	7.697	2.208	5.13	5.99	7.70	9.41	10.26
	Week 24	4	9.407	4.072	5.13	5.99	9.41	12.83	13.68
	LOV	12	11.830	5.718	5.13	7.70	11.97	13.68	27.37

Period I
Parameter: Alkaline Phosphatase (U/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	218.7	103.8	75	161	188	251	564
	Day 1	22	207.8	85.8	76	160	188	250	489
	Week 2	22	255.2	96.1	117	197	244	306	519
	Week 4	22	244.6	89.0	132	186	226	276	551
	Week 6	22	258.1	128.4	114	189	234	295	729
	Week 8	21	251.0	80.6	125	204	241	297	466
	Week 10	20	248.2	89.4	121	188	240	271	524
	Week 12	20	264.4	142.0	122	171	237	297	769
	Week 14	16	252.1	79.5	136	185	252	298	420
	Week 16	10	229.5	74.4	117	171	237	272	343
	Week 18	10	235.6	79.4	120	179	230	261	374
	Week 20	10	245.1	95.5	111	177	236	281	417
	Week 22	10	233.3	85.1	111	177	237	282	390
	Week 24	10	231.6	70.2	115	209	230	295	351
	LOV	22	245.9	77.4	115	199	231	296	420
Placebo	Screening A	12	242.5	71.3	135	197	236	283	382
	Day 1	12	245.0	69.1	134	199	238	293	357
	Week 2	12	245.2	73.2	119	195	241	318	344
	Week 4	10	250.7	64.6	165	176	250	321	331
	Week 6	10	240.1	77.8	141	173	232	301	360
	Week 8	11	237.5	71.9	127	179	232	313	363
	Week 10	11	252.9	93.8	131	177	243	336	456
	Week 12	10	244.2	74.5	162	189	231	311	370
	Week 14	4	244.0	80.8	186	195	214	294	363
	Week 16	4	227.3	29.9	191	208	227	247	264
	Week 18	4	217.0	39.4	159	194	232	241	246
	Week 20	3	210.0	34.6	170	170	230	230	230
	Week 22	4	206.5	38.4	150	183	223	231	231
	Week 24	4	217.8	51.8	141	187	239	249	253
	LOV	12	242.8	70.9	141	195	239	286	368

Period I
Parameter: Lactate Dehydrogenase (U/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	191.9	31.5	143	173	188	200	295
	Day 1	22	187.4	24.6	149	164	188	203	237
	Week 2	22	230.0	44.4	149	196	229	260	325
	Week 4	22	229.5	41.9	163	195	221	255	323
	Week 6	22	241.3	82.9	138	200	225	272	539
	Week 8	21	241.4	48.3	163	218	232	258	355
	Week 10	20	240.5	35.6	198	215	236	256	321
	Week 12	20	247.0	49.7	164	215	231	285	368
	Week 14	16	256.6	76.9	174	217	233	277	447
	Week 16	10	244.8	65.4	200	204	230	237	419
	Week 18	10	239.6	45.2	195	209	223	247	330
	Week 20	10	242.8	45.6	175	228	232	250	324
	Week 22	10	244.9	44.1	172	212	249	254	324
	Week 24	10	248.3	54.8	162	220	249	269	366
	LOV	22	260.5	59.3	162	220	255	293	422
Placebo	Screening A	12	207.1	71.1	122	157	187	255	357
	Day 1	12	201.9	74.7	135	153	170	223	361
	Week 2	12	212.4	68.4	152	158	193	232	358
	Week 4	10	215.6	77.1	139	160	184	245	348
	Week 6	10	203.8	63.1	136	162	180	270	321
	Week 8	11	205.7	73.6	129	169	181	236	389
	Week 10	11	202.1	73.6	122	148	182	233	376
	Week 12	10	194.3	61.6	125	147	180	225	304

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 14	4	176.8	37.0	135	154	174	200	225
	Week 16	4	173.5	36.4	134	150	169	198	222
	Week 18	4	162.5	23.9	131	145	166	180	187
	Week 20	3	170.0	39.7	140	140	155	215	215
	Week 22	4	167.3	21.2	142	152	167	183	193
	Week 24	4	162.3	22.6	137	149	160	176	192
	LOV	12	193.1	59.8	125	154	180	213	308

(Source: 5.3.5.1.1, Table 14.1.4.4.1)

表 2.7.4.9-45 Laboratory Tests: Selected Hematology Parameters (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Lab Test: Basophils (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	0.024		0.025		
	Median	0.020		0.020		
	Q1, Q3	0.000, 0.030		0.000, 0.030		
	SD	0.027		0.036		
	Min, Max	0.00, 0.17		0.00, 0.21		
Week 2	n	98	97	43	43	
	Mean	0.022	−0.001	0.030	0.003	−0.004
	Median	0.020	0.000	0.020	0.000	
	Q1, Q3	0.010, 0.030	−0.010, 0.010	0.010, 0.040	−0.010, 0.010	
	SD	0.021	0.030	0.032	0.036	
	Min, Max	0.00, 0.11	−0.16, 0.10	0.00, 0.12	−0.09, 0.09	
Week 4	n	96	94	46	46	
	Mean	0.016	−0.008	0.024	−0.002	−0.006
	Median	0.015	0.000	0.020	0.000	
	Q1, Q3	0.005, 0.020	−0.020, 0.010	0.000, 0.030	−0.010, 0.010	
	SD	0.015	0.028	0.026	0.037	
	Min, Max	0.00, 0.06	−0.12, 0.05	0.00, 0.10	−0.15, 0.10	
Week 8	n	94	92	42	42	
	Mean	0.015	−0.008	0.025	0.000	−0.007
	Median	0.010	0.000	0.020	0.000	
	Q1, Q3	0.000, 0.020	−0.020, 0.000	0.000, 0.030	−0.010, 0.010	
	SD	0.019	0.025	0.032	0.036	
	Min, Max	0.00, 0.13	−0.08, 0.08	0.00, 0.14	−0.09, 0.10	
Week 12	n	87	87	40	40	
	Mean	0.016	−0.009	0.024	−0.003	−0.006
	Median	0.010	−0.010	0.020	0.000	
	Q1, Q3	0.000, 0.020	−0.020, 0.000	0.000, 0.030	−0.010, 0.010	
	SD	0.020	0.027	0.042	0.029	
	Min, Max	0.00, 0.12	−0.10, 0.10	0.00, 0.25	−0.07, 0.10	
Week 16	n	35	35	9	9	
	Mean	0.013	−0.009	0.009	−0.001	−0.007
	Median	0.010	0.000	0.010	0.000	
	Q1, Q3	0.000, 0.020	−0.020, 0.010	0.000, 0.010	0.000, 0.010	
	SD	0.010	0.035	0.008	0.015	
	Min, Max	0.00, 0.04	−0.17, 0.02	0.00, 0.02	−0.04, 0.01	
Week 20	n	26	26	5	5	
	Mean	0.019	−0.003	0.018	0.010	−0.013
	Median	0.010	0.000	0.020	0.010	
	Q1, Q3	0.000, 0.020	−0.020, 0.010	0.010, 0.020	0.000, 0.010	
	SD	0.035	0.049	0.015	0.019	
	Min, Max	0.00, 0.18	−0.15, 0.16	0.00, 0.04	−0.01, 0.04	
Week 24	n	25	25	2	2	
	Mean	0.014	−0.006	0.025	0.010	−0.016
	Median	0.010	0.000	0.025	0.010	
	Q1, Q3	0.000, 0.020	−0.010, 0.010	0.010, 0.040	−0.010, 0.030	
	SD	0.016	0.042	0.021	0.028	
	Min, Max	0.00, 0.07	−0.16, 0.05	0.01, 0.04	−0.01, 0.03	
Week 26	n	9	9	0	0	
	Mean	0.007	−0.004			
	Median	0.000	0.000			
	Q1, Q3	0.000, 0.010	−0.010, 0.000			
	SD	0.010	0.010			
	Min, Max	0.00, 0.03	−0.02, 0.01			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Eosinophils (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	0.154		0.161		
	Median	0.110		0.105		
	Q1, Q3	0.050, 0.200		0.075, 0.220		
	SD	0.164		0.166		
	Min, Max	0.00, 1.20		0.00, 1.02		
Week 2	n	98	97	43	43	
	Mean	0.109	−0.043	0.195	0.029	−0.071
	Median	0.090	−0.010	0.130	0.010	
	Q1, Q3	0.040, 0.120	−0.090, 0.010	0.090, 0.280	−0.020, 0.070	
	SD	0.112	0.144	0.203	0.087	
	Min, Max	0.00, 0.70	−0.92, 0.40	0.00, 1.20	−0.20, 0.22	
Week 4	n	96	94	46	46	
	Mean	0.120	−0.038	0.179	0.021	−0.059
	Median	0.090	−0.005	0.135	0.020	
	Q1, Q3	0.050, 0.170	−0.060, 0.030	0.060, 0.250	−0.050, 0.090	
	SD	0.107	0.160	0.160	0.183	
	Min, Max	0.00, 0.70	−0.93, 0.60	0.00, 0.65	−0.90, 0.40	
Week 8	n	94	92	42	42	
	Mean	0.085	−0.067	0.217	0.058	−0.126
	Median	0.050	−0.045	0.175	0.015	
	Q1, Q3	0.030, 0.120	−0.090, 0.000	0.090, 0.310	−0.020, 0.090	
	SD	0.077	0.161	0.211	0.223	
	Min, Max	0.00, 0.32	−1.17, 0.30	0.00, 1.26	−0.52, 1.21	
Week 12	n	87	87	40	40	
	Mean	0.090	−0.074	0.179	0.022	−0.096
	Median	0.060	−0.050	0.120	0.015	
	Q1, Q3	0.030, 0.110	−0.100, 0.000	0.075, 0.225	−0.030, 0.080	
	SD	0.083	0.148	0.171	0.110	
	Min, Max	0.00, 0.40	−0.95, 0.13	0.00, 0.85	−0.20, 0.37	
Week 16	n	35	35	9	9	
	Mean	0.081	−0.091	0.233	0.121	−0.212
	Median	0.050	−0.070	0.100	0.000	
	Q1, Q3	0.020, 0.120	−0.110, 0.000	0.050, 0.110	−0.010, 0.050	
	SD	0.079	0.187	0.403	0.355	
	Min, Max	0.00, 0.30	−0.94, 0.20	0.00, 1.26	−0.10, 1.06	
Week 20	n	26	26	5	5	
	Mean	0.095	−0.080	0.128	−0.008	−0.072
	Median	0.070	−0.040	0.100	−0.020	
	Q1, Q3	0.030, 0.130	−0.090, 0.000	0.050, 0.120	−0.030, 0.040	
	SD	0.087	0.209	0.124	0.066	
	Min, Max	0.00, 0.30	−1.04, 0.11	0.03, 0.34	−0.10, 0.07	
Week 24	n	25	25	2	2	
	Mean	0.090	−0.092	0.235	0.180	−0.272
	Median	0.060	−0.040	0.235	0.180	
	Q1, Q3	0.030, 0.120	−0.100, 0.000	0.060, 0.410	0.000, 0.360	
	SD	0.084	0.217	0.247	0.255	
	Min, Max	0.00, 0.36	−1.00, 0.20	0.06, 0.41	0.00, 0.36	
Week 26	n	9	9	0	0	
	Mean	0.077	0.023			
	Median	0.050	0.000			
	Q1, Q3	0.030, 0.100	0.000, 0.050			
	SD	0.092	0.039			
	Min, Max	0.00, 0.30	−0.01, 0.09			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Hematocrit (RATIO)

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib − Placebo)
Baseline	n	100		48		
	Mean	0.4200		0.4118		
	Median	0.4195		0.4125		
	Q1, Q3	0.3905, 0.4500		0.3740, 0.4370		
	SD	0.0420		0.0528		
	Min, Max	0.319, 0.507		0.278, 0.535		
Week 2	n	99	98	44	44	
	Mean	0.4291	0.0089	0.4135	0.0025	0.0064
	Median	0.4260	0.0100	0.4135	0.0030	
	Q1, Q3	0.4020, 0.4700	−0.0040, 0.0220	0.3745, 0.4535	−0.0070, 0.0165	
	SD	0.0463	0.0221	0.0557	0.0208	
	Min, Max	0.294, 0.533	−0.041, 0.120	0.297, 0.549	−0.058, 0.044	
Week 4	n	98	96	46	46	
	Mean	0.4229	0.0034	0.4125	0.0008	0.0025
	Median	0.4205	0.0055	0.4135	−0.0010	
	Q1, Q3	0.3920, 0.4540	−0.0080, 0.0145	0.3680, 0.4540	−0.0150, 0.0210	
	SD	0.0439	0.0227	0.0636	0.0334	
	Min, Max	0.308, 0.518	−0.054, 0.098	0.230, 0.550	−0.125, 0.060	
Week 8	n	94	92	42	42	
	Mean	0.4195	0.0007	0.4190	0.0052	−0.0045
	Median	0.4175	−0.0010	0.4260	0.0055	
	Q1, Q3	0.3890, 0.4520	−0.0175, 0.0165	0.3950, 0.4540	−0.0200, 0.0260	
	SD	0.0433	0.0275	0.0567	0.0309	
	Min, Max	0.298, 0.520	−0.065, 0.111	0.273, 0.515	−0.054, 0.073	
Week 12	n	88	88	41	41	
	Mean	0.4166	−0.0056	0.4160	0.0044	−0.0100
	Median	0.4160	−0.0095	0.4250	0.0020	
	Q1, Q3	0.3895, 0.4460	−0.0255, 0.0135	0.3950, 0.4470	−0.0130, 0.0190	
	SD	0.0429	0.0292	0.0505	0.0376	
	Min, Max	0.316, 0.526	−0.057, 0.082	0.241, 0.498	−0.114, 0.088	
Week 16	n	35	35	9	9	
	Mean	0.4145	−0.0067	0.4127	0.0078	−0.0145
	Median	0.4260	−0.0060	0.4230	0.0110	
	Q1, Q3	0.3760, 0.4460	−0.0280, 0.0130	0.4140, 0.4700	−0.0150, 0.0490	
	SD	0.0422	0.0346	0.0821	0.0661	
	Min, Max	0.312, 0.490	−0.073, 0.081	0.222, 0.485	−0.133, 0.087	
Week 20	n	26	26	5	5	
	Mean	0.4103	−0.0131	0.4394	0.0262	−0.0393
	Median	0.4095	−0.0115	0.4630	0.0350	
	Q1, Q3	0.3800, 0.4370	−0.0390, 0.0140	0.4170, 0.4780	0.0280, 0.0420	
	SD	0.0447	0.0335	0.0638	0.0318	
	Min, Max	0.339, 0.499	−0.069, 0.080	0.339, 0.500	−0.028, 0.054	
Week 24	n	25	25	2	2	
	Mean	0.4114	−0.0100	0.4525	0.0530	−0.0630
	Median	0.4050	−0.0070	0.4525	0.0530	
	Q1, Q3	0.3840, 0.4450	−0.0370, 0.0070	0.4160, 0.4890	0.0530, 0.0530	
	SD	0.0431	0.0373	0.0516	0.0000	
	Min, Max	0.344, 0.510	−0.093, 0.092	0.416, 0.489	0.053, 0.053	
Week 26	n	9	9	0	0	
	Mean	0.3921	−0.0092			
	Median	0.4280	−0.0100			
	Q1, Q3	0.3800, 0.4280	−0.0260, 0.0130			
	SD	0.0590	0.0306			
	Min, Max	0.287, 0.459	−0.060, 0.039			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Hemoglobin (g/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	136.4		132.2		
	Median	137.0		133.0		
	Q1, Q3	126.0, 148.0		118.5, 144.5		
	SD	14.8		19.5		
	Min, Max	97, 170		79, 174		
Week 2	n	99	98	44	44	
	Mean	139.5	2.9	132.7	0.6	2.4
	Median	139.0	3.0	131.5	1.0	
	Q1, Q3	128.0, 151.0	−1.0, 7.0	118.0, 148.0	−4.0, 5.0	
	SD	16.0	6.7	19.2	6.6	
	Min, Max	94, 171	−12, 38	86, 173	−19, 13	
Week 4	n	98	96	46	46	
	Mean	137.7	1.5	131.9	−0.2	1.7
	Median	137.5	2.0	130.5	0.0	
	Q1, Q3	126.0, 150.0	−4.0, 5.5	118.0, 148.0	−5.0, 5.0	
	SD	15.4	7.3	22.3	10.6	
	Min, Max	100, 174	−13, 30	66, 174	−39, 21	
Week 8	n	94	92	42	42	
	Mean	136.4	0.5	134.2	1.2	−0.7
	Median	136.0	0.0	135.5	1.0	
	Q1, Q3	126.0, 148.0	−6.0, 5.0	123.0, 152.0	−5.0, 5.0	
	SD	15.0	8.3	20.5	10.7	
	Min, Max	101, 168	−19, 31	83, 170	−20, 29	
Week 12	n	88	88	41	41	
	Mean	136.1	−1.1	133.6	1.6	−2.7
	Median	136.0	−3.0	134.0	1.0	
	Q1, Q3	125.5, 147.0	−6.5, 3.0	122.0, 148.0	−5.0, 6.0	
	SD	14.5	9.2	18.2	13.2	
	Min, Max	101, 174	−19, 26	72, 167	−33, 38	
Week 16	n	35	35	9	9	
	Mean	134.9	−1.8	132.4	2.9	−4.7
	Median	137.0	−2.0	141.0	6.0	
	Q1, Q3	121.0, 146.0	−10.0, 4.0	132.0, 150.0	−9.0, 12.0	
	SD	14.6	11.4	28.3	21.0	
	Min, Max	105, 165	−28, 30	66, 156	−39, 28	
Week 20	n	26	26	5	5	
	Mean	132.9	−4.4	140.4	6.8	−11.2
	Median	130.5	−6.0	146.0	11.0	
	Q1, Q3	124.0, 143.0	−10.0, 0.0	135.0, 153.0	2.0, 11.0	
	SD	14.7	10.7	19.7	12.7	
	Min, Max	110, 171	−19, 29	109, 159	−12, 22	
Week 24	n	25	25	2	2	
	Mean	133.2	−2.9	140.0	11.5	−14.4
	Median	131.0	−4.0	140.0	11.5	
	Q1, Q3	126.0, 146.0	−9.0, 2.0	130.0, 150.0	6.0, 17.0	
	SD	15.2	12.1	14.1	7.8	
	Min, Max	111, 170	−23, 31	130, 150	6, 17	
Week 26	n	9	9	0	0	
	Mean	128.1	−2.0			
	Median	139.0	−2.0			
	Q1, Q3	124.0, 141.0	−6.0, 1.0			
	SD	19.8	7.7			
	Min, Max	92, 146	−15, 12			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Lymphocytes (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	1.873		1.980		
	Median	1.700		1.765		
	Q1, Q3	1.220, 2.355		1.295, 2.510		
	SD	0.928		1.055		
	Min, Max	0.29, 4.93		0.46, 5.30		
Week 2	n	98	97	43	43	
	Mean	2.145	0.282	2.162	0.221	0.061
	Median	1.880	0.280	1.930	0.140	
	Q1, Q3	1.550, 2.720	−0.130, 0.670	1.520, 2.540	−0.300, 0.540	
	SD	1.041	0.669	1.101	0.669	
	Min, Max	0.30, 5.60	−1.40, 2.77	0.45, 5.70	−0.79, 2.60	
Week 4	n	96	94	46	46	
	Mean	1.913	0.099	2.117	0.136	−0.038
	Median	1.645	0.145	1.820	0.055	
	Q1, Q3	1.245, 2.495	−0.220, 0.480	1.400, 2.600	−0.150, 0.500	
	SD	0.911	0.698	1.118	0.575	
	Min, Max	0.20, 4.76	−2.81, 2.73	0.44, 5.20	−1.53, 1.76	
Week 8	n	94	92	42	42	
	Mean	1.860	0.069	2.121	0.096	−0.027
	Median	1.665	0.045	1.915	0.115	
	Q1, Q3	1.130, 2.320	−0.300, 0.460	1.200, 2.760	−0.300, 0.500	
	SD	0.952	0.731	1.261	0.855	
	Min, Max	0.50, 4.49	−2.78, 2.59	0.47, 5.92	−2.41, 2.82	
Week 12	n	87	87	40	40	
	Mean	1.887	0.076	2.106	0.057	0.019
	Median	1.700	0.080	1.870	−0.040	
	Q1, Q3	1.230, 2.410	−0.330, 0.430	1.420, 2.800	−0.340, 0.350	
	SD	0.961	0.779	1.075	0.736	
	Min, Max	0.25, 5.10	−1.85, 3.20	0.54, 4.67	−1.47, 2.30	
Week 16	n	35	35	9	9	
	Mean	1.835	0.089	1.742	0.263	−0.174
	Median	1.400	−0.030	1.200	0.300	
	Q1, Q3	1.290, 2.300	−0.320, 0.460	1.120, 1.940	−0.040, 0.500	
	SD	0.952	0.814	0.983	0.553	
	Min, Max	0.52, 5.18	−1.37, 3.28	0.71, 3.80	−0.60, 1.22	
Week 20	n	26	26	5	5	
	Mean	1.864	0.118	1.412	−0.056	0.174
	Median	1.495	0.025	1.500	−0.020	
	Q1, Q3	1.290, 1.880	−0.230, 0.410	1.090, 1.680	−0.300, 0.110	
	SD	0.957	0.670	0.369	0.329	
	Min, Max	0.63, 4.11	−1.07, 1.87	0.97, 1.82	−0.45, 0.38	
Week 24	n	25	25	2	2	
	Mean	1.777	0.040	1.335	−0.160	0.200
	Median	1.410	0.000	1.335	−0.160	
	Q1, Q3	1.200, 2.480	−0.490, 0.170	1.140, 1.530	−0.280, −0.040	
	SD	0.878	0.827	0.276	0.170	
	Min, Max	0.65, 4.10	−1.22, 2.20	1.14, 1.53	−0.28, −0.04	
Week 26	n	9	9	0	0	
	Mean	1.310	−0.074			
	Median	1.040	−0.040			
	Q1, Q3	1.000, 1.450	−0.180, 0.100			
	SD	0.706	0.327			
	Min, Max	0.30, 2.62	−0.75, 0.30			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Erythrocytes Mean Corpuscular Hemoglobin (pg)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	29.12		28.35		
	Median	29.35		28.95		
	Q1, Q3	27.80, 30.60		27.10, 29.90		
	SD	2.53		2.50		
	Min, Max	19.0, 38.6		20.7, 33.4		
Week 2	n	99	98	44	44	
	Mean	29.11	−0.05	28.25	−0.18	0.13
	Median	29.30	−0.10	28.55	−0.20	
	Q1, Q3	27.70, 30.70	−0.20, 0.20	27.05, 29.65	−0.55, 0.00	
	SD	2.47	0.54	2.19	0.60	
	Min, Max	18.6, 37.2	−3.1, 2.5	23.5, 32.5	−2.0, 1.3	
Week 4	n	98	96	46	46	
	Mean	29.18	0.06	28.00	−0.30	0.36
	Median	29.30	0.10	28.60	−0.35	
	Q1, Q3	27.90, 30.50	−0.20, 0.35	26.20, 29.90	−0.80, 0.20	
	SD	2.47	0.78	2.31	1.24	
	Min, Max	18.6, 36.4	−4.2, 3.3	22.3, 31.4	−4.7, 4.1	
Week 8	n	94	92	42	42	
	Mean	29.53	0.38	28.10	−0.28	0.66
	Median	29.65	0.40	28.70	−0.30	
	Q1, Q3	28.40, 30.80	0.00, 0.80	26.20, 29.70	−1.00, 0.20	
	SD	2.35	1.00	2.23	1.46	
	Min, Max	19.1, 35.3	−4.3, 4.2	22.4, 32.1	−3.4, 4.7	
Week 12	n	88	88	41	41	
	Mean	30.03	0.88	28.17	−0.19	1.07
	Median	30.20	0.85	28.70	−0.40	
	Q1, Q3	29.00, 31.30	0.40, 1.40	26.20, 29.50	−1.10, 0.50	
	SD	2.18	1.10	2.32	1.96	
	Min, Max	19.1, 34.7	−3.9, 5.3	22.7, 33.6	−3.7, 6.7	
Week 16	n	35	35	9	9	
	Mean	30.45	1.31	27.89	−1.23	2.54
	Median	30.50	1.40	28.40	−0.60	
	Q1, Q3	29.60, 31.30	0.80, 1.80	26.60, 29.90	−1.60, 0.00	
	SD	1.59	1.15	2.98	1.89	
	Min, Max	26.9, 33.5	−2.0, 5.0	21.3, 31.6	−5.7, 0.5	
Week 20	n	26	26	5	5	
	Mean	30.75	1.70	29.08	−0.76	2.46
	Median	30.70	2.00	29.50	−0.40	
	Q1, Q3	29.70, 31.90	1.00, 2.50	27.70, 30.10	−1.30, −0.10	
	SD	1.79	1.28	1.94	0.92	
	Min, Max	26.4, 34.2	−1.7, 3.8	26.6, 31.5	−2.1, 0.1	
Week 24	n	25	25	2	2	
	Mean	30.60	1.96	27.60	−1.85	3.81
	Median	30.70	2.00	27.60	−1.85	
	Q1, Q3	29.60, 31.80	1.20, 2.80	27.10, 28.10	−1.90, −1.80	
	SD	1.90	1.57	0.71	0.07	
	Min, Max	26.5, 34.0	−1.3, 6.1	27.1, 28.1	−1.9, −1.8	
Week 26	n	9	9	0	0	
	Mean	30.94	0.67			
	Median	30.70	0.50			
	Q1, Q3	30.10, 30.80	0.20, 0.70			
	SD	2.04	2.39			
	Min, Max	27.7, 34.8	−3.8, 5.5			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Erythrocytes Mean Corpuscular HGB Concentration (g/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	353.2		320.4		
	Median	325.5		320.0		
	Q1, Q3	318.0, 332.0		312.0, 330.0		
	SD	286.7		12.8		
	Min, Max	292, 3190		284, 343		
Week 2	n	99	98	43	43	
	Mean	325.1	−28.9	319.8	−1.2	−27.7
	Median	326.0	0.0	319.0	−3.0	
	Q1, Q3	320.0, 332.0	−3.0, 4.0	311.0, 329.0	−6.0, 3.0	
	SD	9.2	290.4	11.3	6.9	
	Min, Max	291, 342	−2874, 18	289, 338	−12, 24	
Week 4	n	98	96	46	46	
	Mean	325.5	−28.8	319.0	−1.1	−27.8
	Median	325.0	0.0	320.0	−1.5	
	Q1, Q3	320.0, 331.0	−3.5, 5.0	312.0, 327.0	−5.0, 3.0	
	SD	8.4	293.5	11.0	7.1	
	Min, Max	300, 347	−2874, 22	287, 338	−17, 17	
Week 8	n	94	92	42	42	
	Mean	325.2	−30.2	319.5	−1.2	−28.9
	Median	326.0	0.0	322.0	−2.0	
	Q1, Q3	320.0, 330.0	−4.5, 5.0	310.0, 328.0	−9.0, 5.0	
	SD	8.6	298.9	11.2	9.2	
	Min, Max	303, 344	−2865, 26	296, 340	−18, 19	
Week 12	n	88	88	41	41	
	Mean	326.7	−30.5	319.8	−0.2	−30.3
	Median	327.5	2.5	320.0	−2.0	
	Q1, Q3	322.0, 331.5	−6.0, 7.5	314.0, 328.0	−6.0, 5.0	
	SD	9.3	306.4	10.8	12.7	
	Min, Max	284, 354	−2871, 31	299, 344	−44, 35	
Week 16	n	35	35	8	8	
	Mean	325.4	1.3	315.9	−2.4	3.7
	Median	325.0	1.0	318.0	−1.0	
	Q1, Q3	321.0, 330.0	−6.0, 8.0	315.0, 320.5	−10.5, 4.0	
	SD	8.2	9.8	8.6	7.8	
	Min, Max	307, 348	−21, 22	296, 324	−12, 8	
Week 20	n	26	26	5	5	
	Mean	324.2	0.4	320.4	−2.8	3.2
	Median	325.5	−0.5	321.0	1.0	
	Q1, Q3	320.0, 329.0	−8.0, 8.0	319.0, 325.0	−8.0, 3.0	
	SD	11.0	9.0	8.6	14.2	
	Min, Max	282, 343	−15, 19	307, 330	−24, 14	
Week 24	n	25	25	2	2	
	Mean	323.6	1.0	310.5	−10.5	11.5
	Median	326.0	0.0	310.5	−10.5	
	Q1, Q3	318.0, 329.0	−4.0, 6.0	308.0, 313.0	−23.0, 2.0	
	SD	10.7	9.8	3.5	17.7	
	Min, Max	288, 345	−15, 22	308, 313	−23, 2	
Week 26	n	9	9	0	0	
	Mean	325.9	2.9			
	Median	325.0	4.0			
	Q1, Q3	323.0, 328.0	−2.0, 7.0			
	SD	7.4	10.0			
	Min, Max	315, 342	−15, 22			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Erythrocytes Mean Corpuscular Volume (fL)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	89.8		88.4		
	Median	90.0		90.0		
	Q1, Q3	86.0, 94.0		85.0, 92.0		
	SD	6.8		5.9		
	Min, Max	59, 117		73, 104		
Week 2	n	99	98	44	44	
	Mean	89.5	−0.3	88.2	−0.3	0.0
	Median	90.0	0.0	89.0	0.0	
	Q1, Q3	85.0, 94.0	−1.0, 1.0	84.0, 92.0	−1.0, 1.0	
	SD	6.7	1.6	5.5	1.9	
	Min, Max	59, 115	−10, 4	77, 103	−6, 3	
Week 4	n	98	96	46	46	
	Mean	89.6	−0.1	87.7	−0.7	0.5
	Median	89.0	0.0	88.0	−1.0	
	Q1, Q3	86.0, 93.0	−1.0, 1.0	84.0, 92.0	−2.0, 1.0	
	SD	6.9	2.3	5.7	3.6	
	Min, Max	59, 114	−16, 5	75, 101	−13, 10	
Week 8	n	94	92	42	42	
	Mean	90.8	0.9	88.0	−0.4	1.3
	Median	91.0	1.0	88.5	0.0	
	Q1, Q3	88.0, 94.0	0.0, 2.0	86.0, 91.0	−3.0, 1.0	
	SD	6.6	3.1	5.4	3.9	
	Min, Max	59, 110	−18, 8	74, 99	−9, 13	
Week 12	n	88	88	41	41	
	Mean	91.9	2.1	87.6	−0.9	3.1
	Median	92.5	2.0	89.0	−1.0	
	Q1, Q3	89.0, 96.0	1.0, 4.0	83.0, 91.0	−4.0, 2.0	
	SD	6.0	3.0	5.5	4.6	
	Min, Max	60, 105	−12, 9	74, 98	−10, 13	
Week 16	n	35	35	9	9	
	Mean	93.6	3.6	87.4	−3.8	7.4
	Median	94.0	4.0	89.0	−2.0	
	Q1, Q3	91.0, 97.0	3.0, 6.0	84.0, 91.0	−5.0, 0.0	
	SD	4.3	3.7	7.5	6.3	
	Min, Max	84, 101	−9, 10	72, 98	−19, 2	
Week 20	n	26	26	5	5	
	Mean	95.0	5.2	90.8	−1.6	6.8
	Median	95.0	6.0	91.0	−1.0	
	Q1, Q3	92.0, 98.0	3.0, 7.0	90.0, 91.0	−4.0, 0.0	
	SD	4.6	3.7	5.7	2.9	
	Min, Max	84, 104	−7, 11	83, 99	−5, 2	
Week 24	n	25	25	2	2	
	Mean	94.6	5.8	89.0	−3.0	8.8
	Median	95.0	7.0	89.0	−3.0	
	Q1, Q3	93.0, 97.0	4.0, 8.0	88.0, 90.0	−6.0, 0.0	
	SD	4.3	3.7	1.4	4.2	
	Min, Max	86, 103	−3, 13	88, 90	−6, 0	
Week 26	n	9	9	0	0	
	Mean	95.0	1.4			
	Median	94.0	2.0			
	Q1, Q3	94.0, 96.0	−1.0, 5.0			
	SD	5.2	6.3			
	Min, Max	86, 106	−11, 12			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Mean Platelet Volume (fL)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	99		47		
	Mean	10.15		10.50		
	Median	10.20		10.70		
	Q1, Q3	8.80, 11.40		9.40, 11.30		
	SD	1.67		1.56		
	Min, Max	7.0, 13.9		7.4, 13.9		
Week 2	n	91	90	40	39	
	Mean	10.54	0.46	10.05	−0.35	0.81
	Median	10.90	0.20	10.50	−0.30	
	Q1, Q3	9.10, 11.90	−0.70, 1.10	8.65, 11.05	−1.00, 0.60	
	SD	1.83	1.84	1.53	2.30	
	Min, Max	6.8, 15.5	−4.4, 5.7	6.9, 13.9	−5.8, 5.9	
Week 4	n	92	89	45	44	
	Mean	10.39	0.21	9.89	−0.63	0.83
	Median	10.65	0.20	10.30	−0.45	
	Q1, Q3	9.30, 11.40	−0.90, 0.90	8.70, 11.00	−1.80, 0.45	
	SD	1.71	1.78	1.72	1.88	
	Min, Max	6.9, 15.8	−4.6, 5.0	6.4, 12.8	−5.8, 4.0	
Week 8	n	89	87	41	40	
	Mean	10.49	0.31	9.91	−0.70	1.01
	Median	10.50	0.10	10.30	−0.40	
	Q1, Q3	9.50, 11.40	−0.80, 1.40	8.00, 11.00	−1.35, 0.40	
	SD	1.68	1.83	1.71	1.88	
	Min, Max	6.9, 15.5	−4.9, 5.0	6.3, 13.4	−5.7, 3.1	
Week 12	n	80	80	40	39	
	Mean	10.71	0.51	10.04	−0.55	1.06
	Median	10.80	0.40	10.10	−0.50	
	Q1, Q3	9.80, 11.60	−0.75, 1.30	8.70, 11.40	−1.50, 0.30	
	SD	1.61	1.83	1.78	1.59	
	Min, Max	7.2, 15.2	−2.6, 7.3	6.9, 14.6	−4.8, 2.6	
Week 16	n	34	33	7	7	
	Mean	11.04	0.24	9.14	−0.30	0.54
	Median	10.75	−0.50	9.30	−0.10	
	Q1, Q3	10.10, 11.90	−1.30, 0.60	7.70, 11.00	−1.10, 0.30	
	SD	1.80	2.46	1.83	1.29	
	Min, Max	7.8, 15.7	−2.1, 8.0	6.4, 11.5	−2.3, 1.8	
Week 20	n	26	26	5	5	
	Mean	11.17	0.24	9.36	−0.78	1.02
	Median	11.00	−0.30	10.00	−0.30	
	Q1, Q3	10.30, 12.00	−1.50, 0.80	7.70, 10.90	−1.40, −0.30	
	SD	1.84	2.40	1.74	0.82	
	Min, Max	7.0, 15.0	−2.3, 8.0	7.3, 10.9	−1.9, 0.0	
Week 24	n	24	23	2	2	
	Mean	11.21	0.37	12.55	2.60	−2.23
	Median	10.90	−0.60	12.55	2.60	
	Q1, Q3	10.05, 12.20	−1.50, 1.10	9.60, 15.50	−2.30, 7.50	
	SD	1.87	2.87	4.17	6.93	
	Min, Max	7.9, 16.2	−2.5, 8.5	9.6, 15.5	−2.3, 7.5	
Week 26	n	9	9	0	0	
	Mean	11.60	1.40			
	Median	11.30	0.60			
	Q1, Q3	10.70, 12.40	0.10, 2.80			
	SD	1.41	1.96			
	Min, Max	9.9, 13.7	−0.8, 4.5			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Neutrophils (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	6.007		6.254		
	Median	5.115		5.605		
	Q1, Q3	4.075, 6.760		4.245, 7.695		
	SD	3.177		3.019		
	Min, Max	1.52, 17.49		1.63, 16.88		
Week 2	n	98	97	43	43	
	Mean	5.142	−0.889	6.372	−0.017	−0.872
	Median	4.155	−1.010	5.820	0.140	
	Q1, Q3	3.050, 6.400	−2.050, 0.190	4.100, 7.370	−0.730, 1.000	
	SD	3.137	2.368	3.502	1.588	
	Min, Max	1.09, 14.14	−7.23, 10.32	1.83, 19.62	−5.00, 2.74	
Week 4	n	96	94	46	46	
	Mean	3.903	−2.021	6.212	−0.010	−2.011
	Median	3.180	−1.550	4.990	−0.095	
	Q1, Q3	2.420, 4.870	−2.870, −0.680	4.090, 8.310	−1.000, 0.530	
	SD	2.148	2.182	3.376	2.397	
	Min, Max	1.10, 13.01	−9.69, 3.91	2.01, 14.64	−8.30, 8.34	
Week 8	n	94	92	42	42	
	Mean	3.854	−2.245	6.172	0.036	−2.281
	Median	3.135	−1.810	5.400	0.165	
	Q1, Q3	2.330, 4.650	−2.845, −1.080	4.030, 6.980	−1.190, 0.960	
	SD	2.079	2.199	2.997	2.250	
	Min, Max	1.10, 10.15	−8.74, 3.29	1.27, 15.00	−5.87, 5.80	
Week 12	n	87	87	40	40	
	Mean	3.926	−2.074	5.824	−0.308	−1.767
	Median	3.500	−1.790	5.560	−0.250	
	Q1, Q3	2.450, 5.100	−2.760, −0.840	3.290, 7.625	−1.145, 1.025	
	SD	2.128	2.162	2.830	2.598	
	Min, Max	0.58, 13.04	−8.90, 1.89	2.09, 13.51	−8.10, 5.76	
Week 16	n	35	35	9	9	
	Mean	3.925	−2.408	5.521	−0.074	−2.334
	Median	3.280	−1.800	4.060	−0.640	
	Q1, Q3	2.380, 4.550	−2.790, −0.920	2.600, 6.500	−2.460, 0.800	
	SD	2.513	2.718	4.300	4.947	
	Min, Max	1.15, 11.53	−11.12, 1.54	1.60, 15.09	−8.40, 9.75	
Week 20	n	26	26	5	5	
	Mean	4.317	−2.385	5.948	1.454	−3.839
	Median	3.040	−1.580	5.150	0.330	
	Q1, Q3	2.520, 4.610	−3.820, −0.820	4.970, 6.300	0.110, 2.000	
	SD	3.033	2.910	2.556	1.990	
	Min, Max	1.50, 15.50	−8.85, 2.07	3.24, 10.08	0.11, 4.72	
Week 24	n	25	25	2	2	
	Mean	3.785	−2.490	6.410	1.300	−3.790
	Median	3.060	−1.750	6.410	1.300	
	Q1, Q3	2.680, 4.410	−3.530, −0.530	3.580, 9.240	−1.280, 3.880	
	SD	1.711	2.706	4.002	3.649	
	Min, Max	1.60, 9.10	−8.39, 0.74	3.58, 9.24	−1.28, 3.88	
Week 26	n	9	9	0	0	
	Mean	4.516	−1.402			
	Median	3.760	−1.000			
	Q1, Q3	3.550, 5.200	−1.500, −0.210			
	SD	1.526	2.586			
	Min, Max	3.00, 7.32	−7.70, 1.32			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Erythrocytes (10^12/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	4.708		4.672		
	Median	4.675		4.700		
	Q1, Q3	4.325, 5.070		4.310, 5.135		
	SD	0.551		0.597		
	Min, Max	3.13, 5.95		2.95, 5.91		
Week 2	n	99	98	44	44	
	Mean	4.816	0.108	4.703	0.041	0.068
	Median	4.750	0.100	4.755	0.015	
	Q1, Q3	4.470, 5.200	−0.010, 0.230	4.285, 5.175	−0.105, 0.215	
	SD	0.582	0.228	0.635	0.218	
	Min, Max	3.10, 6.12	−0.32, 1.36	3.25, 5.92	−0.57, 0.41	
Week 4	n	98	96	46	46	
	Mean	4.742	0.036	4.705	0.032	0.005
	Median	4.675	0.060	4.800	0.000	
	Q1, Q3	4.400, 5.160	−0.160, 0.160	4.260, 5.130	−0.130, 0.240	
	SD	0.553	0.245	0.679	0.317	
	Min, Max	2.77, 6.19	−0.44, 1.12	2.96, 5.85	−0.94, 0.64	
Week 8	n	94	92	42	42	
	Mean	4.639	−0.048	4.785	0.088	−0.136
	Median	4.610	−0.090	4.940	0.110	
	Q1, Q3	4.320, 5.000	−0.260, 0.085	4.380, 5.320	−0.190, 0.260	
	SD	0.528	0.319	0.669	0.291	
	Min, Max	2.95, 5.76	−0.72, 1.09	2.76, 5.67	−0.39, 0.88	
Week 12	n	88	88	41	41	
	Mean	4.547	−0.183	4.760	0.100	−0.284
	Median	4.515	−0.200	4.880	0.100	
	Q1, Q3	4.250, 4.860	−0.380, −0.015	4.430, 5.100	−0.140, 0.280	
	SD	0.494	0.380	0.573	0.438	
	Min, Max	3.56, 6.01	−1.02, 1.19	2.96, 5.91	−0.94, 1.11	
Week 16	n	35	35	9	9	
	Mean	4.436	−0.261	4.687	0.241	−0.502
	Median	4.460	−0.360	4.880	0.190	
	Q1, Q3	4.050, 4.860	−0.510, −0.150	4.400, 5.050	0.060, 0.500	
	SD	0.479	0.439	0.711	0.616	
	Min, Max	3.42, 5.48	−1.02, 1.27	3.08, 5.48	−0.82, 1.19	
Week 20	n	26	26	5	5	
	Mean	4.332	−0.397	4.820	0.340	−0.737
	Median	4.270	−0.480	5.050	0.350	
	Q1, Q3	3.950, 4.710	−0.700, −0.160	4.580, 5.090	0.300, 0.360	
	SD	0.504	0.479	0.478	0.323	
	Min, Max	3.50, 5.49	−1.17, 1.19	4.10, 5.28	−0.11, 0.80	
Week 24	n	25	25	2	2	
	Mean	4.356	−0.403	5.100	0.720	−1.123
	Median	4.390	−0.430	5.100	0.720	
	Q1, Q3	4.170, 4.630	−0.630, −0.210	4.640, 5.560	0.580, 0.860	
	SD	0.449	0.470	0.651	0.198	
	Min, Max	3.54, 5.38	−1.33, 1.11	4.64, 5.56	0.58, 0.86	
Week 26	n	9	9	0	0	
	Mean	4.144	−0.181			
	Median	4.400	−0.120			
	Q1, Q3	3.610, 4.580	−0.490, −0.020			
	SD	0.688	0.435			
	Min, Max	3.07, 5.00	−0.89, 0.48			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Erythrocytes Distribution Width (RATIO)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	0.1506		0.1558		
	Median	0.1430		0.1460		
	Q1, Q3	0.1350, 0.1570		0.1365, 0.1605		
	SD	0.0266		0.0326		
	Min, Max	0.121, 0.290		0.109, 0.291		
Week 2	n	99	98	43	43	
	Mean	0.1500	0.0010	0.1558	0.0003	0.0007
	Median	0.1440	0.0010	0.1460	0.0010	
	Q1, Q3	0.1350, 0.1570	−0.0030, 0.0050	0.1360, 0.1580	−0.0040, 0.0050	
	SD	0.0256	0.0083	0.0326	0.0103	
	Min, Max	0.122, 0.301	−0.030, 0.039	0.111, 0.296	−0.027, 0.032	
Week 4	n	98	96	46	46	
	Mean	0.1549	0.0045	0.1598	0.0035	0.0010
	Median	0.1485	0.0040	0.1480	0.0010	
	Q1, Q3	0.1380, 0.1610	0.0000, 0.0095	0.1370, 0.1660	−0.0040, 0.0060	
	SD	0.0278	0.0107	0.0384	0.0180	
	Min, Max	0.127, 0.286	−0.041, 0.051	0.114, 0.296	−0.024, 0.074	
Week 8	n	94	92	42	42	
	Mean	0.1667	0.0155	0.1619	0.0064	0.0092
	Median	0.1580	0.0150	0.1505	0.0060	
	Q1, Q3	0.1490, 0.1780	0.0065, 0.0260	0.1370, 0.1710	−0.0040, 0.0160	
	SD	0.0256	0.0211	0.0361	0.0214	
	Min, Max	0.133, 0.246	−0.070, 0.082	0.123, 0.262	−0.058, 0.067	
Week 12	n	88	88	41	41	
	Mean	0.1734	0.0239	0.1595	0.0054	0.0185
	Median	0.1700	0.0235	0.1510	0.0030	
	Q1, Q3	0.1560, 0.1815	0.0155, 0.0370	0.1370, 0.1710	−0.0060, 0.0110	
	SD	0.0281	0.0311	0.0284	0.0185	
	Min, Max	0.133, 0.318	−0.119, 0.155	0.128, 0.237	−0.034, 0.054	
Week 16	n	35	35	8	8	
	Mean	0.1699	0.0179	0.1694	−0.0011	0.0191
	Median	0.1710	0.0220	0.1530	0.0015	
	Q1, Q3	0.1550, 0.1830	0.0130, 0.0310	0.1440, 0.1900	−0.0080, 0.0095	
	SD	0.0206	0.0301	0.0393	0.0348	
	Min, Max	0.134, 0.226	−0.128, 0.064	0.139, 0.242	−0.071, 0.056	
Week 20	n	26	26	5	5	
	Mean	0.1607	0.0104	0.1474	−0.0138	0.0242
	Median	0.1660	0.0100	0.1440	0.0000	
	Q1, Q3	0.1430, 0.1720	0.0050, 0.0180	0.1410, 0.1520	−0.0030, 0.0030	
	SD	0.0200	0.0127	0.0122	0.0411	
	Min, Max	0.124, 0.197	−0.013, 0.039	0.134, 0.166	−0.086, 0.017	
Week 24	n	25	25	2	2	
	Mean	0.1551	−0.0007	0.1565	−0.0330	0.0323
	Median	0.1530	0.0060	0.1565	−0.0330	
	Q1, Q3	0.1360, 0.1640	−0.0060, 0.0110	0.1410, 0.1720	−0.0890, 0.0230	
	SD	0.0219	0.0307	0.0219	0.0792	
	Min, Max	0.121, 0.204	−0.134, 0.041	0.141, 0.172	−0.089, 0.023	
Week 26	n	9	9	0	0	
	Mean	0.1622	−0.0009			
	Median	0.1600	−0.0030			
	Q1, Q3	0.1500, 0.1750	−0.0110, 0.0160			
	SD	0.0240	0.0281			
	Min, Max	0.123, 0.207	−0.058, 0.036			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Reticulocyte Count (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	99		48		
	Mean	71.6		82.9		
	Median	70.0		70.0		
	Q1, Q3	50.0, 80.0		45.0, 100.0		
	SD	32.6		70.1		
	Min, Max	20, 180		20, 490		
Week 2	n	99	97	44	44	
	Mean	58.8	−12.4	70.0	−5.5	−6.9
	Median	50.0	−10.0	60.0	0.0	
	Q1, Q3	30.0, 70.0	−30.0, 0.0	50.0, 90.0	−20.0, 10.0	
	SD	49.4	51.8	32.0	23.7	
	Min, Max	10, 450	−90, 420	30, 200	−60, 50	
Week 4	n	98	95	46	46	
	Mean	58.1	−14.7	67.0	−16.3	1.6
	Median	50.0	−10.0	65.0	−5.0	
	Q1, Q3	40.0, 70.0	−30.0, 0.0	40.0, 80.0	−20.0, 10.0	
	SD	28.4	27.2	28.4	73.6	
	Min, Max	10, 150	−90, 60	20, 140	−460, 50	
Week 8	n	94	92	42	42	
	Mean	65.5	−7.1	78.6	−1.4	−5.6
	Median	60.0	−10.0	75.0	10.0	
	Q1, Q3	40.0, 80.0	−30.0, 15.0	50.0, 100.0	−10.0, 30.0	
	SD	29.2	34.9	36.7	82.7	
	Min, Max	10, 160	−140, 80	10, 190	−460, 150	
Week 12	n	87	86	40	40	
	Mean	67.2	−3.8	71.8	−12.0	8.2
	Median	60.0	0.0	70.0	0.0	
	Q1, Q3	40.0, 90.0	−30.0, 20.0	40.0, 90.0	−20.0, 20.0	
	SD	30.1	36.4	36.9	78.1	
	Min, Max	20, 150	−160, 70	20, 200	−450, 80	
Week 16	n	35	35	9	9	
	Mean	76.3	−2.0	72.1	−51.2	49.2
	Median	70.0	0.0	49.0	−20.0	
	Q1, Q3	50.0, 90.0	−20.0, 30.0	40.0, 70.0	−30.0, 30.0	
	SD	37.6	44.4	55.7	149.0	
	Min, Max	20, 200	−130, 90	20, 180	−441, 40	
Week 20	n	26	26	5	5	
	Mean	67.7	−6.9	64.0	−74.0	67.1
	Median	60.0	0.0	60.0	0.0	
	Q1, Q3	50.0, 90.0	−30.0, 20.0	60.0, 60.0	−20.0, 20.0	
	SD	27.8	34.5	21.9	201.2	
	Min, Max	20, 120	−110, 50	40, 100	−430, 60	
Week 24	n	25	25	2	2	
	Mean	61.2	−11.6	75.0	25.0	−36.6
	Median	60.0	−10.0	75.0	25.0	
	Q1, Q3	50.0, 80.0	−30.0, 10.0	30.0, 120.0	−30.0, 80.0	
	SD	24.4	32.1	63.6	77.8	
	Min, Max	20, 110	−120, 40	30, 120	−30, 80	
Week 26	n	9	9	0	0	
	Mean	68.9	3.3			
	Median	70.0	10.0			
	Q1, Q3	50.0, 70.0	−20.0, 10.0			
	SD	33.0	26.9			
	Min, Max	30, 120	−40, 40			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

Lab Test: Leukocytes (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	8.600		8.922		
	Median	7.850		8.000		
	Q1, Q3	5.800, 10.425		6.835, 10.650		
	SD	3.683		3.516		
	Min, Max	3.40, 19.80		2.60, 21.10		
Week 2	n	99	98	44	44	
	Mean	7.702	−0.886	9.291	0.296	−1.182
	Median	6.700	−0.805	8.900	0.250	
	Q1, Q3	5.200, 10.000	−1.960, 0.500	6.350, 10.250	−0.300, 1.000	
	SD	3.397	2.546	4.141	1.622	
	Min, Max	1.60, 16.40	−7.70, 10.10	3.50, 25.80	−4.86, 4.70	
Week 4	n	98	96	46	46	
	Mean	6.235	−2.214	9.088	0.191	−2.405
	Median	5.600	−2.000	7.800	−0.100	
	Q1, Q3	4.400, 8.160	−3.100, −0.600	6.480, 12.020	−0.890, 1.000	
	SD	2.446	2.391	3.997	2.579	
	Min, Max	2.20, 14.90	−11.59, 1.90	3.11, 18.50	−9.27, 8.50	
Week 8	n	94	92	42	42	
	Mean	6.117	−2.477	9.204	0.397	−2.874
	Median	5.400	−2.235	7.850	0.150	
	Q1, Q3	4.200, 7.700	−3.470, −0.930	6.800, 11.300	−0.800, 1.400	
	SD	2.445	2.446	3.773	2.171	
	Min, Max	2.40, 13.95	−9.40, 3.70	2.12, 18.50	−4.50, 5.50	
Week 12	n	88	88	41	41	
	Mean	6.192	−2.347	8.602	−0.206	−2.141
	Median	5.600	−1.750	7.900	0.000	
	Q1, Q3	4.350, 7.750	−3.200, −0.755	6.100, 10.400	−1.330, 1.100	
	SD	2.404	2.388	3.360	2.418	
	Min, Max	1.80, 14.50	−9.90, 1.80	3.00, 15.50	−7.19, 6.40	
Week 16	n	35	35	9	9	
	Mean	6.233	−2.644	7.898	0.169	−2.813
	Median	5.100	−2.290	5.700	−0.700	
	Q1, Q3	4.200, 8.100	−3.400, −0.900	4.080, 9.500	−2.400, 1.500	
	SD	3.018	2.992	5.490	5.815	
	Min, Max	2.30, 15.43	−12.85, 2.80	3.60, 20.40	−9.48, 11.90	
Week 20	n	26	26	5	5	
	Mean	6.628	−2.693	7.940	1.420	−4.113
	Median	5.450	−1.650	8.100	0.700	
	Q1, Q3	4.500, 8.110	−4.400, −0.400	6.300, 8.400	0.200, 1.500	
	SD	3.350	3.200	2.943	2.235	
	Min, Max	3.04, 16.89	−9.00, 2.77	4.50, 12.40	−0.50, 5.20	
Week 24	n	25	25	2	2	
	Mean	6.038	−2.768	8.400	1.400	−4.168
	Median	5.800	−1.700	8.400	1.400	
	Q1, Q3	4.400, 7.200	−4.370, −0.900	5.200, 11.600	−1.600, 4.400	
	SD	2.130	3.149	4.525	4.243	
	Min, Max	3.10, 11.40	−8.77, 2.00	5.20, 11.60	−1.60, 4.40	
Week 26	n	9	9	0	0	
	Mean	6.474	−1.292			
	Median	6.270	−0.900			
	Q1, Q3	5.200, 7.800	−1.200, −0.300			
	SD	1.687	2.250			
	Min, Max	3.90, 9.00	−7.00, 0.87			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.

(Source: 5.3.5.3.2, Table 5.1.1.1)

表 2.7.4.9-46 Extremum Post-Baseline Observation in Laboratory Tests – R788-1301 study

Period I
Parameter: Alanine Aminotransferase (U/L)

		Maximum Post Day 1					
		>3*ULN		>5*ULN		>10*ULN	
Group	N	n	%	n	%	n	%
R788	22	4	18.2	2	9.1	1	4.5
Placebo	12	0	0.0	0	0.0	0	0.0

Period I
Parameter: Aspartate Aminotransferase (U/L)

		Maximum Post Day 1					
		>3*ULN		>5*ULN		>10*ULN	
Group	N	n	%	n	%	n	%
R788	22	2	9.1	1	4.5	0	0.0
Placebo	12	0	0.0	0	0.0	0	0.0

Period I
Parameter: Alkaline Phosphatase (U/L)

		Maximum Post Day 1	
		>1.5*ULN	
Group	N	n	%
R788	22	1	4.5
Placebo	12	0	0.0

Period I
Parameter: Bilirubin (umol/L)

		Maximum Post Day 1	
		>2*ULN	
Group	N	n	%
R788	22	0	0.0
Placebo	12	0	0.0

Period I
Parameter: Neutrophils (10^9/L)

		Minimum Post Day 1							
		<0.5		0.5<= <1		1<= <1.5		>=1.5	
Group	N	n	%	n	%	n	%	n	%
R788	22	1	4.5	3	13.6	7	31.8	11	50.0
Placebo	12	0	0.0	0	0.0	0	0.0	12	100.0

(Source: 5.3.5.1.1, Table 14.1.4.4.5)

表 2.7.4.9-47 Extremum Post-Baseline Observation in Laboratory Tests – R788-1301 study

Long-Term Treatment of R788
Parameter: Alanine Aminotransferase (U/L)

		Maximum Post Day 1					
		>3*ULN		>5*ULN		>10*ULN	
Group	N	n	%	n	%	n	%
R788	22	3	13.6	2	9.1	1	4.5

ULN: Upper Limit of Normal

Long-Term Treatment of R788
Parameter: Aspartate Aminotransferase (U/L)

		Maximum Post Day 1					
		>3*ULN		>5*ULN		>10*ULN	
Group	N	n	%	n	%	n	%
R788	22	2	9.1	1	4.5	0	0.0

ULN: Upper Limit of Normal

Long-Term Treatment of R788
Parameter: Alkaline Phosphatase (U/L)

		Maximum Post Day 1 >1.5*ULN	
Group	N	n	%
R788	22	2	9.1

ULN: Upper Limit of Normal

Long-Term Treatment of R788
Parameter: Bilirubin (umol/L)

		Maximum Post Day 1 >2*ULN	
Group	N	n	%
R788	22	0	0.0

ULN: Upper Limit of Normal

Long-Term Treatment of R788
Parameter: Neutrophils (10^9/L)

		Minimum Post Day 1							
		<0.5		0.5<= <1		1<= <1.5		>=1.5	
Group	N	n	%	n	%	n	%	n	%
R788	22	1	4.5	5	22.7	6	27.3	10	45.5

(Source: 5.3.5.1.1, Table 14.2.4.4.5)

表 2.7.4.9-48 Laboratory Tests: Liver Function Tests (LFTs) (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Lab Test: Alkaline Phosphatase (U/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	70.5		72.0		
	Median	67.0		68.5		
	Q1, Q3	55.0, 84.0		53.5, 88.0		
	SD	19.8		20.4		
	Min, Max	32, 140		43, 123		
Week 2	n	99	99	48	48	
	Mean	81.4	11.1	71.4	-0.6	11.7
	Median	78.0	8.0	68.0	0.0	
	Q1, Q3	62.0, 100.0	2.0, 17.0	54.0, 86.5	-5.0, 4.0	
	SD	26.7	14.7	20.9	7.9	
	Min, Max	38, 189	-11, 87	39, 127	-31, 14	
Week 4	n	97	97	47	47	
	Mean	83.4	12.8	71.9	-0.5	13.3
	Median	80.0	12.0	68.0	0.0	
	Q1, Q3	61.0, 99.0	3.0, 18.0	51.0, 90.0	-5.0, 5.0	
	SD	26.6	13.8	23.1	9.3	
	Min, Max	38, 160	-12, 60	41, 122	-25, 28	
Week 6	n	96	96	45	45	
	Mean	85.1	14.2	69.4	-1.7	15.9
	Median	79.0	13.0	69.0	-1.0	
	Q1, Q3	66.0, 103.0	3.0, 22.0	51.0, 83.0	-5.0, 4.0	
	SD	27.6	16.4	21.7	8.3	
	Min, Max	39, 187	-23, 85	38, 125	-27, 13	
Week 8	n	96	96	42	42	
	Mean	85.4	14.6	71.4	-0.8	15.4
	Median	82.0	12.5	71.0	0.0	
	Q1, Q3	64.0, 99.0	2.5, 24.5	51.0, 88.0	-7.0, 6.0	
	SD	27.4	17.4	22.9	10.6	
	Min, Max	42, 158	-27, 93	38, 139	-26, 23	
Week 10	n	92	92	44	44	
	Mean	83.1	11.6	71.6	-0.1	11.7
	Median	79.5	9.0	68.0	0.0	
	Q1, Q3	61.0, 101.0	0.0, 18.5	52.5, 86.0	-6.0, 4.0	
	SD	27.5	18.1	23.1	10.5	
	Min, Max	37, 147	-23, 65	41, 141	-20, 25	
Week 12	n	89	89	41	41	
	Mean	80.2	9.7	71.3	-1.9	11.6
	Median	75.0	8.0	69.0	0.0	
	Q1, Q3	61.0, 95.0	-1.0, 18.0	54.0, 88.0	-8.0, 4.0	
	SD	25.7	15.5	21.1	10.7	
	Min, Max	42, 159	-20, 59	42, 139	-22, 23	
Week 14	n	39	39	12	12	
	Mean	79.8	8.9	78.5	0.2	8.8
	Median	75.0	7.0	80.0	1.0	
	Q1, Q3	61.0, 90.0	-2.0, 17.0	67.0, 88.5	-4.0, 7.5	
	SD	26.2	15.4	13.1	9.9	
	Min, Max	35, 159	-18, 59	58, 100	-24, 13	
Week 16	n	35	35	9	9	
	Mean	79.0	7.9	77.1	-3.4	11.3

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
	Median	76.0	9.0	74.0	-5.0	
	Q1, Q3	64.0, 88.0	-3.0, 16.0	67.0, 76.0	-10.0, -2.0	
	SD	24.9	14.4	20.1	17.7	
	Min, Max	34, 148	-20, 48	55, 125	-24, 35	
Week 18	n	34	34	4	4	
	Mean	79.3	8.9	82.5	-1.8	10.6
	Median	73.0	6.0	74.5	-5.0	
	Q1, Q3	60.0, 86.0	-1.0, 15.0	67.5, 97.5	-23.0, 19.5	
	SD	26.8	15.7	25.1	25.9	
	Min, Max	37, 153	-16, 53	62, 119	-26, 29	
Week 20	n	25	25	5	5	
	Mean	81.6	9.1	88.2	5.8	3.3
	Median	75.0	7.0	90.0	9.0	
	Q1, Q3	59.0, 92.0	-4.0, 17.0	82.0, 93.0	6.0, 16.0	
	SD	30.0	17.1	15.4	15.9	
	Min, Max	37, 148	-19, 48	67, 109	-21, 19	
Week 22	n	26	26	4	4	
	Mean	83.4	9.8	80.3	-1.8	11.5
	Median	78.0	6.5	78.5	3.5	
	Q1, Q3	59.0, 99.0	-1.0, 17.0	69.0, 91.5	-13.5, 10.0	
	SD	32.1	21.0	15.9	16.5	
	Min, Max	35, 163	-26, 63	63, 101	-25, 11	
Week 24	n	25	25	2	2	
	Mean	84.1	9.3	91.5	2.5	6.8
	Median	79.0	3.0	91.5	2.5	
	Q1, Q3	66.0, 94.0	0.0, 19.0	62.0, 121.0	-26.0, 31.0	
	SD	28.1	17.2	41.7	40.3	
	Min, Max	38, 143	-22, 43	62, 121	-26, 31	
Week 26	n	8	8	0	0	
	Mean	73.5	1.1			
	Median	69.0	-4.0			
	Q1, Q3	56.5, 77.0	-5.5, 6.5			
	SD	27.0	12.2			
	Min, Max	48, 135	-12, 27			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If bothcentral and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

Lab Test: Alanine Aminotransferase (U/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	21.2		18.4		
	Median	18.5		16.0		
	Q1, Q3	14.0, 25.0		12.5, 23.5		
	SD	10.8		8.3		
	Min, Max	7, 69		7, 46		
Week 2	n	99	99	48	48	
	Mean	23.7	2.2	19.5	1.1	1.1
	Median	21.0	1.0	17.0	1.0	
	Q1, Q3	14.0, 28.0	-2.0, 5.0	13.0, 24.5	-1.0, 3.0	
	SD	14.1	10.8	9.2	4.8	
	Min, Max	6, 87	-36, 56	7, 59	-14, 17	
Week 4	n	97	97	47	47	
	Mean	24.1	3.0	20.1	1.6	1.4
	Median	21.0	2.0	17.0	1.0	
	Q1, Q3	17.0, 28.0	-1.0, 7.0	13.0, 24.0	-2.0, 5.0	
	SD	12.0	9.9	10.2	5.8	
	Min, Max	5, 68	-40, 38	7, 50	-9, 21	
Week 6	n	96	96	45	45	
	Mean	31.6	10.7	21.7	2.9	7.8
	Median	23.5	4.0	18.0	1.0	
	Q1, Q3	18.0, 33.0	-1.0, 11.5	14.0, 29.0	-1.0, 7.0	
	SD	30.9	31.7	11.5	6.8	
	Min, Max	9, 194	-37, 185	7, 70	-9, 25	
Week 8	n	96	96	42	42	
	Mean	31.4	10.3	20.8	1.9	8.4
	Median	26.0	6.0	18.5	0.0	
	Q1, Q3	18.5, 37.5	1.0, 13.5	13.0, 24.0	-3.0, 4.0	
	SD	20.6	20.4	11.1	6.7	
	Min, Max	7, 145	-26, 135	6, 64	-8, 18	
Week 10	n	92	92	44	44	
	Mean	31.3	10.4	21.5	2.8	7.7
	Median	26.5	6.0	18.5	2.0	
	Q1, Q3	19.5, 34.5	0.0, 15.0	13.0, 28.5	-2.0, 6.5	
	SD	22.8	21.0	10.4	7.3	
	Min, Max	7, 160	-29, 118	7, 50	-10, 28	
Week 12	n	89	89	41	41	
	Mean	32.8	11.6	19.2	0.3	11.3
	Median	26.0	6.0	18.0	-1.0	
	Q1, Q3	19.0, 37.0	2.0, 14.0	11.0, 24.0	-3.0, 3.0	
	SD	31.2	30.7	8.5	7.0	
	Min, Max	9, 280	-29, 263	9, 40	-17, 26	
Week 14	n	39	39	12	12	
	Mean	36.0	13.6	15.8	0.0	13.6
	Median	25.0	7.0	15.0	-1.0	
	Q1, Q3	20.0, 46.0	3.0, 22.0	11.5, 18.0	-3.0, 1.5	
	SD	22.5	21.4	5.4	5.2	
	Min, Max	13, 101	-45, 84	10, 26	-7, 13	

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Week 16	n	35	35	9	9	
	Mean	31.6	9.3	18.1	1.8	7.5
	Median	24.0	4.0	17.0	2.0	
	Q1, Q3	18.0, 40.0	0.0, 13.0	14.0, 19.0	2.0, 3.0	
	SD	18.6	16.4	8.7	4.4	
	Min, Max	12, 84	-16, 66	8, 37	-5, 10	
Week 18	n	34	34	4	4	
	Mean	31.0	8.8	19.3	2.0	6.8
	Median	24.0	5.0	19.0	3.0	
	Q1, Q3	16.0, 37.0	-1.0, 11.0	16.0, 22.5	-1.5, 5.5	
	SD	20.0	19.5	4.6	5.1	
	Min, Max	11, 103	-32, 89	14, 25	-5, 7	
Week 20	n	25	25	5	5	
	Mean	27.4	4.6	15.4	-0.6	5.2
	Median	23.0	2.0	14.0	3.0	
	Q1, Q3	17.0, 32.0	-1.0, 7.0	13.0, 19.0	0.0, 3.0	
	SD	14.4	14.5	4.5	7.7	
	Min, Max	12, 68	-44, 36	10, 21	-14, 5	
Week 22	n	26	26	4	4	
	Mean	30.7	7.7	17.5	1.0	6.7
	Median	28.0	5.5	19.0	2.5	
	Q1, Q3	18.0, 36.0	1.0, 9.0	14.0, 21.0	-2.5, 4.5	
	SD	15.4	9.7	5.3	5.6	
	Min, Max	13, 63	-6, 33	10, 22	-7, 6	
Week 24	n	25	25	3	3	
	Mean	28.4	5.0	19.7	2.0	3.0
	Median	26.0	4.0	21.0	7.0	
	Q1, Q3	20.0, 31.0	-1.0, 9.0	14.0, 24.0	-9.0, 8.0	
	SD	15.4	11.7	5.1	9.5	
	Min, Max	9, 82	-19, 44	14, 24	-9, 8	
Week 26	n	8	8	0	0	
	Mean	28.0	6.5			
	Median	21.5	5.0			
	Q1, Q3	14.0, 41.5	-0.5, 12.0			
	SD	18.4	8.0			
	Min, Max	11, 59	-2, 21			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

Lab Test: Aspartate Aminotransferase (U/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	22.1		20.1		
	Median	19.5		19.0		
	Q1, Q3	17.0, 24.0		15.0, 23.0		
	SD	12.2		6.9		
	Min, Max	10, 126		8, 42		
Week 2	n	99	99	48	48	
	Mean	24.1	1.9	20.3	0.3	1.7
	Median	22.0	2.0	19.0	0.0	
	Q1, Q3	18.0, 27.0	-1.0, 5.0	16.0, 23.0	-1.5, 2.0	
	SD	9.4	12.8	8.0	6.7	
	Min, Max	14, 77	-105, 40	8, 57	-27, 26	
Week 4	n	97	97	47	47	
	Mean	24.2	2.1	20.9	0.7	1.5
	Median	22.0	3.0	18.0	1.0	
	Q1, Q3	19.0, 27.0	0.0, 5.0	16.0, 24.0	-2.0, 4.0	
	SD	8.8	13.2	7.5	6.4	
	Min, Max	12, 65	-109, 34	8, 44	-27, 15	
Week 6	n	96	96	45	45	
	Mean	27.6	5.8	22.9	2.4	3.3
	Median	24.0	4.0	19.0	1.0	
	Q1, Q3	20.0, 30.0	0.0, 8.0	16.0, 25.0	-2.0, 4.0	
	SD	15.5	19.7	10.8	9.3	
	Min, Max	12, 114	-112, 95	5, 54	-26, 37	
Week 8	n	96	96	42	42	
	Mean	27.2	5.3	20.6	0.1	5.2
	Median	25.0	5.0	18.5	-0.5	
	Q1, Q3	21.0, 30.0	1.0, 9.0	16.0, 23.0	-3.0, 2.0	
	SD	10.7	15.1	7.6	6.6	
	Min, Max	13, 80	-103, 68	10, 52	-27, 16	
Week 10	n	92	92	44	44	
	Mean	26.6	4.7	21.8	1.3	3.4
	Median	25.0	4.0	20.0	1.0	
	Q1, Q3	20.0, 29.5	1.0, 9.0	15.5, 26.0	-2.0, 5.0	
	SD	11.2	14.6	8.6	7.7	
	Min, Max	13, 88	-103, 51	6, 48	-25, 23	
Week 12	n	89	89	41	41	
	Mean	28.6	6.6	20.3	-0.5	7.2
	Median	25.0	5.0	19.0	-1.0	
	Q1, Q3	21.0, 30.0	2.0, 10.0	17.0, 22.0	-3.0, 4.0	
	SD	16.3	19.3	6.7	7.5	
	Min, Max	16, 151	-98, 135	11, 41	-25, 23	
Week 14	n	39	39	12	12	
	Mean	29.8	8.3	18.3	-0.9	9.2
	Median	27.0	7.0	17.5	0.0	
	Q1, Q3	22.0, 36.0	0.0, 14.0	15.0, 20.5	-1.0, 2.5	
	SD	11.3	10.6	6.5	6.9	
	Min, Max	15, 56	-13, 35	9, 35	-22, 5	

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Week 16	n	35	35	9	9	
	Mean	28.8	7.3	21.7	3.1	4.2
	Median	25.0	3.0	19.0	3.0	
	Q1, Q3	21.0, 32.0	1.0, 10.0	16.0, 27.0	2.0, 4.0	
	SD	12.9	11.6	7.0	3.7	
	Min, Max	16, 67	-3, 52	14, 34	-2, 10	
Week 18	n	34	34	4	4	
	Mean	30.4	8.8	23.0	1.8	7.0
	Median	25.0	5.0	23.0	1.5	
	Q1, Q3	22.0, 35.0	1.0, 11.0	16.5, 29.5	-2.5, 6.0	
	SD	14.2	13.0	8.5	5.0	
	Min, Max	13, 76	-11, 61	13, 33	-3, 7	
Week 20	n	25	25	5	5	
	Mean	26.4	4.3	22.0	4.6	-0.3
	Median	23.0	3.0	21.0	2.0	
	Q1, Q3	20.0, 26.0	0.0, 8.0	17.0, 29.0	0.0, 8.0	
	SD	11.4	8.5	7.4	6.9	
	Min, Max	15, 67	-15, 28	13, 30	-2, 15	
Week 22	n	26	26	4	4	
	Mean	28.7	6.7	18.5	1.5	5.2
	Median	24.5	4.5	18.0	1.5	
	Q1, Q3	21.0, 32.0	1.0, 10.0	17.5, 19.5	-0.5, 3.5	
	SD	11.8	7.7	1.7	2.4	
	Min, Max	15, 61	-3, 24	17, 21	-1, 4	
Week 24	n	25	25	3	3	
	Mean	26.4	4.2	24.0	0.7	3.5
	Median	24.0	3.0	26.0	4.0	
	Q1, Q3	22.0, 29.0	0.0, 7.0	17.0, 29.0	-7.0, 5.0	
	SD	9.0	5.5	6.2	6.7	
	Min, Max	15, 53	-5, 15	17, 29	-7, 5	
Week 26	n	8	8	0	0	
	Mean	24.4	3.3			
	Median	22.5	3.0			
	Q1, Q3	15.5, 31.5	-1.0, 8.0			
	SD	11.6	4.7			
	Min, Max	11, 45	-3, 9			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

Lab Test: Direct Bilirubin (umol/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	3		1		
	Mean	3.4200		3.2490		
	Median	3.4200		3.2490		
	Q1, Q3	3.4200, 3.4200		3.2490, 3.2490		
	SD	0.0000				
	Min, Max	3.420, 3.420		3.249, 3.249		
Week 2	n	98	3	47	1	
	Mean	4.1108	0.1933	3.4570	0.1710	0.0223
	Median	3.4200	0.0000	3.4200	0.1710	
	Q1, Q3	3.4200, 4.0000	0.0000, 0.5800	3.4200, 3.4200	0.1710, 0.1710	
	SD	1.2673	0.3349	0.1433		
	Min, Max	3.000, 9.000	0.000, 0.580	3.420, 4.000	0.171, 0.171	
Week 6	n	95	3	45	1	
	Mean	4.2226	1.9033	3.5447	0.1710	1.7323
	Median	3.4200	0.5800	3.4200	0.1710	
	Q1, Q3	3.4200, 5.0000	0.0000, 5.1300	3.4200, 3.4200	0.1710, 0.1710	
	SD	1.4083	2.8094	0.4282		
	Min, Max	3.000, 10.260	0.000, 5.130	3.000, 5.130	0.171, 0.171	
Week 8	n	1	0	0	0	
	Mean	3.4200				
	Median	3.4200				
	Q1, Q3	3.4200, 3.4200				
	SD					
	Min, Max	3.420, 3.420				
Week 10	n	89	3	43	1	
	Mean	3.8998	0.1933	3.4874	0.1710	0.0223
	Median	3.4200	0.0000	3.4200	0.1710	
	Q1, Q3	3.4200, 4.0000	0.0000, 0.5800	3.4200, 3.4200	0.1710, 0.1710	
	SD	1.1430	0.3349	0.1881		
	Min, Max	3.000, 9.000	0.000, 0.580	3.420, 4.000	0.171, 0.171	
Week 12	n	1	0	0	0	
	Mean	6.8400				
	Median	6.8400				
	Q1, Q3	6.8400, 6.8400				
	SD					
	Min, Max	6.840, 6.840				
Week 14	n	33	1	9	0	
	Mean	4.1452	0.0000	3.4844		
	Median	3.4200	0.0000	3.4200		
	Q1, Q3	3.4200, 5.0000	0.0000, 0.0000	3.4200, 3.4200		
	SD	1.2513		0.1933		
	Min, Max	3.000, 7.000	0.000, 0.000	3.420, 4.000		
Week 18	n	29	0	4	0	
	Mean	4.3476		3.5650		
	Median	3.4200		3.4200		
	Q1, Q3	3.4200, 4.0000		3.4200, 3.7100		
	SD	1.7712		0.2900		

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
	Min, Max	3.000, 10.000		3.420, 4.000		
Week 20	n	1	0	0	0	
	Mean	5.0000				
	Median	5.0000				
	Q1, Q3	5.0000, 5.0000				
	SD					
	Min, Max	5.000, 5.000				
Week 22	n	25	0	2	0	
	Mean	4.0560		3.7100		
	Median	3.4200		3.7100		
	Q1, Q3	3.4200, 4.0000		3.4200, 4.0000		
	SD	1.3630		0.4101		
	Min, Max	3.000, 9.000		3.420, 4.000		

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

Lab Test: Total Bilirubin (umol/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	8.476		6.938		
	Median	7.000		6.840		
	Q1, Q3	5.130, 10.260		5.000, 8.550		
	SD	4.938		2.917		
	Min, Max	1.71, 29.07		3.00, 15.39		
Week 2	n	99	99	48	48	
	Mean	11.133	2.625	6.739	-0.200	2.825
	Median	10.000	2.000	6.840	0.000	
	Q1, Q3	6.840, 14.000	0.000, 5.130	5.130, 8.000	-1.855, 1.710	
	SD	6.438	3.990	2.535	2.596	
	Min, Max	3.42, 37.62	-12.00, 13.68	1.71, 13.00	-5.29, 6.84	
Week 4	n	97	97	47	47	
	Mean	11.052	2.506	7.218	0.303	2.203
	Median	9.000	2.000	6.840	0.000	
	Q1, Q3	6.840, 13.680	0.000, 5.000	5.000, 8.550	0.000, 1.710	
	SD	7.276	4.273	3.388	2.214	
	Min, Max	2.00, 53.01	-10.00, 23.94	1.71, 17.10	-5.00, 5.13	
Week 6	n	96	96	45	45	
	Mean	11.107	2.671	7.198	0.267	2.404
	Median	10.000	3.000	6.840	0.000	
	Q1, Q3	6.840, 13.680	0.000, 5.065	5.130, 9.000	-1.710, 1.710	
	SD	6.625	4.190	3.241	2.888	
	Min, Max	1.71, 39.33	-5.13, 15.00	3.00, 17.10	-6.84, 8.00	
Week 8	n	96	96	42	42	
	Mean	10.854	2.579	7.429	0.525	2.053
	Median	10.000	2.000	6.920	0.000	
	Q1, Q3	6.840, 12.000	0.000, 5.000	5.130, 10.000	-1.000, 1.710	
	SD	6.713	4.560	3.590	2.353	
	Min, Max	3.00, 35.91	-8.00, 18.81	1.71, 20.52	-5.00, 6.84	
Week 10	n	92	92	44	44	
	Mean	10.299	2.136	6.564	-0.370	2.506
	Median	8.775	1.710	5.565	0.000	
	Q1, Q3	6.000, 11.970	0.000, 3.420	4.500, 8.550	-2.000, 0.500	
	SD	7.299	4.859	3.056	2.466	
	Min, Max	3.42, 59.85	-13.00, 30.78	1.71, 15.39	-5.13, 5.13	
Week 12	n	89	89	41	41	
	Mean	10.751	2.515	7.280	0.292	2.223
	Median	9.000	2.000	6.840	0.000	
	Q1, Q3	6.840, 12.000	0.000, 5.000	5.000, 9.000	-1.710, 1.710	
	SD	7.242	4.564	3.799	3.143	
	Min, Max	1.71, 56.43	-7.00, 27.36	1.71, 16.00	-6.00, 12.00	
Week 14	n	39	39	12	12	
	Mean	12.846	3.708	7.380	0.557	3.151
	Median	9.000	3.000	6.500	0.000	
	Q1, Q3	6.840, 14.000	0.000, 5.000	5.065, 9.630	-1.710, 1.710	
	SD	12.269	8.887	3.490	3.717	
	Min, Max	4.00, 78.66	-5.13, 49.59	3.42, 15.39	-4.00, 10.26	

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Week 16	n	35	35	9	9	
	Mean	11.530	2.339	9.083	1.602	0.736
	Median	11.000	1.710	7.000	0.000	
	Q1, Q3	7.000, 13.680	-1.000, 5.000	6.000, 13.000	0.000, 3.580	
	SD	6.326	5.102	4.901	2.701	
	Min, Max	3.00, 30.78	-9.00, 20.52	3.42, 18.81	-1.71, 6.84	
Week 18	n	34	34	4	4	
	Mean	12.600	3.461	9.993	0.000	3.461
	Median	11.130	3.000	11.485	-0.500	
	Q1, Q3	7.000, 14.000	0.000, 6.000	8.000, 11.985	-1.500, 1.500	
	SD	7.809	5.463	3.361	2.160	
	Min, Max	3.42, 37.62	-12.00, 17.10	5.00, 12.00	-2.00, 3.00	
Week 20	n	25	25	5	5	
	Mean	10.993	3.280	10.214	1.026	2.254
	Median	10.000	3.000	11.000	0.000	
	Q1, Q3	7.000, 11.970	0.000, 5.130	8.550, 11.000	0.000, 2.000	
	SD	5.821	3.612	4.939	2.695	
	Min, Max	4.00, 29.00	-4.00, 10.26	3.42, 17.10	-2.00, 5.13	
Week 22	n	26	26	4	4	
	Mean	10.432	2.638	8.243	-1.105	3.743
	Median	9.500	1.500	8.420	-0.500	
	Q1, Q3	6.000, 13.000	0.000, 5.000	5.985, 10.500	-3.565, 1.355	
	SD	5.972	4.347	2.729	3.128	
	Min, Max	3.42, 27.00	-5.00, 11.97	5.13, 11.00	-5.13, 1.71	
Week 24	n	25	25	3	3	
	Mean	9.091	1.260	8.420	-1.903	3.163
	Median	8.000	1.710	10.000	-1.710	
	Q1, Q3	6.840, 10.260	0.000, 3.000	5.000, 10.260	-3.000, -1.000	
	SD	5.069	2.929	2.965	1.014	
	Min, Max	4.00, 29.00	-5.00, 8.55	5.00, 10.26	-3.00, -1.00	
Week 26	n	8	8	0	0	
	Mean	8.251	-1.069			
	Median	7.695	-0.855			
	Q1, Q3	5.130, 11.630	-4.275, 1.710			
	SD	3.798	3.288			
	Min, Max	3.42, 13.68	-5.13, 3.42			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

Lab Test: Indirect Bilirubin (umol/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	1		1		
	Mean	5.1300		5.8140		
	Median	5.1300		5.8140		
	Q1, Q3	5.1300, 5.1300		5.8140, 5.8140		
	SD					
	Min, Max	5.130, 5.130		5.814, 5.814		
Week 2	n	51	1	7	0	
	Mean	10.6747	0.0000	7.0514		
	Median	10.0000	0.0000	6.8400		
	Q1, Q3	8.0000, 12.0000	0.0000, 0.0000	5.1300, 8.5500		
	SD	4.8666		1.5776		
	Min, Max	3.420, 30.780	0.000, 0.000	5.000, 9.000		
Week 6	n	48	1	9	0	
	Mean	10.4513	10.2600	7.9433		
	Median	8.5500	10.2600	6.8400		
	Q1, Q3	6.8400, 13.0000	10.2600, 10.2600	6.8400, 10.0000		
	SD	5.3497		2.1439		
	Min, Max	3.420, 32.490	10.260, 10.260	6.000, 11.970		
Week 10	n	43	0	9	0	
	Mean	9.8233		6.5956		
	Median	8.0000		6.8400		
	Q1, Q3	6.0000, 10.2600		5.1300, 7.0000		
	SD	8.1981		2.3603		
	Min, Max	3.420, 54.720		3.420, 11.970		
Week 12	n	1	0	0	0	
	Mean	49.5900				
	Median	49.5900				
	Q1, Q3	49.5900, 49.5900				
	SD					
	Min, Max	49.590, 49.590				
Week 14	n	18	0	2	0	
	Mean	13.1483		6.4200		
	Median	8.5500		6.4200		
	Q1, Q3	7.0000, 13.6800		6.0000, 6.8400		
	SD	15.6435		0.5940		
	Min, Max	5.000, 73.530		6.000, 6.840		
Week 18	n	17	0	1	0	
	Mean	10.1888		8.0000		
	Median	9.0000		8.0000		
	Q1, Q3	6.8400, 11.0000		8.0000, 8.0000		
	SD	5.1956				
	Min, Max	3.420, 22.000		8.000, 8.000		
Week 20	n	1	0	0	0	
	Mean	13.0000				
	Median	13.0000				
	Q1, Q3	13.0000, 13.0000				

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
	SD					
	Min, Max	13.000, 13.000				
Week 22	n	14	0	1	0	
	Mean	9.2129		7.0000		
	Median	7.5000		7.0000		
	Q1, Q3	6.8400, 10.2600		7.0000, 7.0000		
	SD	4.1948				
	Min, Max	5.130, 18.000		7.000, 7.000		

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

Lab Test: Lactate Dehydrogenase (U/L)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	195.3		202.1		
	Median	187.0		196.0		
	Q1, Q3	162.0, 227.0		161.5, 218.0		
	SD	45.3		75.6		
	Min, Max	112, 340		68, 595		
Week 2	n	99	99	47	47	
	Mean	199.8	4.4	196.4	-5.7	10.1
	Median	194.0	7.0	200.0	0.0	
	Q1, Q3	166.0, 229.0	-13.0, 20.0	155.0, 226.0	-14.0, 17.0	
	SD	46.2	29.6	48.4	65.5	
	Min, Max	118, 361	-73, 88	68, 324	-418, 53	
Week 4	n	97	97	47	47	
	Mean	198.0	3.8	199.7	-3.0	6.8
	Median	192.0	7.0	194.0	0.0	
	Q1, Q3	165.0, 215.0	-13.0, 23.0	170.0, 235.0	-12.0, 18.0	
	SD	46.3	31.6	52.7	67.6	
	Min, Max	111, 349	-82, 98	70, 328	-424, 75	
Week 6	n	96	96	45	45	
	Mean	206.5	11.9	199.5	-3.8	15.7
	Median	203.0	13.0	190.0	-2.0	
	Q1, Q3	170.5, 230.5	-16.0, 37.0	166.0, 232.0	-12.0, 21.0	
	SD	51.9	38.4	49.6	74.7	
	Min, Max	94, 392	-87, 105	77, 302	-423, 114	
Week 8	n	96	96	42	42	
	Mean	216.5	20.5	191.9	-5.1	25.6
	Median	207.5	10.0	191.5	-3.5	
	Q1, Q3	178.5, 243.5	-7.0, 59.5	149.0, 225.0	-16.0, 11.0	
	SD	55.5	42.6	49.4	75.0	
	Min, Max	104, 444	-70, 121	68, 323	-417, 155	
Week 10	n	92	92	44	44	
	Mean	217.0	20.8	194.5	-9.6	30.4
	Median	209.5	17.5	186.0	-4.0	
	Q1, Q3	176.0, 255.0	-5.0, 46.0	153.5, 233.5	-25.5, 14.5	
	SD	54.8	41.8	44.0	72.5	
	Min, Max	97, 414	-73, 113	121, 291	-410, 103	
Week 12	n	89	89	41	41	
	Mean	224.3	26.9	197.8	-8.3	35.2
	Median	212.0	19.0	185.0	-1.0	
	Q1, Q3	184.0, 253.0	-1.0, 58.0	156.0, 226.0	-18.0, 18.0	
	SD	63.8	51.4	59.6	76.1	
	Min, Max	111, 547	-59, 319	65, 346	-409, 129	
Week 14	n	39	39	12	12	
	Mean	240.5	29.8	191.6	-33.4	63.2
	Median	221.0	20.0	194.5	-1.5	
	Q1, Q3	183.0, 281.0	-11.0, 56.0	159.0, 208.5	-22.0, 14.0	
	SD	75.5	61.7	40.9	115.3	
	Min, Max	151, 509	-68, 241	123, 282	-394, 30	

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Week 16	n	35	35	9	9	
	Mean	240.5	27.3	205.8	4.3	23.0
	Median	224.0	22.0	200.0	-3.0	
	Q1, Q3	190.0, 285.0	-3.0, 59.0	186.0, 214.0	-11.0, 17.0	
	SD	65.4	48.0	47.6	18.6	
	Min, Max	139, 443	-81, 124	145, 306	-15, 36	
Week 18	n	33	33	4	4	
	Mean	249.3	33.3	201.8	-2.0	35.3
	Median	241.0	25.0	190.0	-3.5	
	Q1, Q3	197.0, 293.0	3.0, 67.0	185.0, 218.5	-28.5, 24.5	
	SD	72.7	53.2	29.8	30.7	
	Min, Max	151, 443	-71, 170	181, 246	-29, 28	
Week 20	n	25	25	5	5	
	Mean	232.8	10.8	193.6	7.2	3.6
	Median	220.0	5.0	187.0	11.0	
	Q1, Q3	204.0, 256.0	-17.0, 39.0	183.0, 209.0	-20.0, 22.0	
	SD	61.9	46.6	38.4	29.1	
	Min, Max	131, 430	-90, 92	142, 247	-23, 46	
Week 22	n	26	26	4	4	
	Mean	235.6	18.5	211.5	11.3	7.2
	Median	229.0	21.0	195.0	1.5	
	Q1, Q3	196.0, 259.0	-12.0, 56.0	177.0, 246.0	-11.5, 34.0	
	SD	63.4	53.0	51.8	34.8	
	Min, Max	134, 444	-93, 112	170, 286	-19, 61	
Week 24	n	25	25	3	3	
	Mean	234.4	18.4	217.7	16.0	2.4
	Median	223.0	17.0	229.0	20.0	
	Q1, Q3	203.0, 263.0	-7.0, 56.0	179.0, 245.0	-38.0, 66.0	
	SD	60.8	48.4	34.4	52.1	
	Min, Max	136, 445	-81, 105	179, 245	-38, 66	
Week 26	n	8	8	0	0	
	Mean	205.5	18.6			
	Median	199.0	12.0			
	Q1, Q3	168.5, 242.5	1.5, 47.5			
	SD	42.7	29.6			
	Min, Max	154, 270	-29, 56			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.3.1)

表 2.7.4.9-49 Incidences of Elevations in Liver Function Tests (LFTs) for Post-Baseline Period (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

LFT Abnormality	Fostamatinib n/N (%)	Placebo n/N (%)
ALT> 3xULN	9/102 (8.8%)	0/48 (0.0%)
ALT> 5xULN	6/102 (5.9%)	0/48 (0.0%)
ALT> 10xULN	1/102 (1.0%)	0/48 (0.0%)
ALT> 20xULN	0/102 (0.0%)	0/48 (0.0%)
AST> 3xULN	2/102 (2.0%)	0/48 (0.0%)
AST> 5xULN	1/102 (1.0%)	0/48 (0.0%)
AST> 10xULN	0/102 (0.0%)	0/48 (0.0%)
AST> 20xULN	0/102 (0.0%)	0/48 (0.0%)
ALT and/or AST > 3xULN	9/102 (8.8%)	0/48 (0.0%)
ALT and/or AST > 5xULN	6/102 (5.9%)	0/48 (0.0%)
ALT and/or AST > 10xULN	1/102 (1.0%)	0/48 (0.0%)
ALT and/or AST > 20xULN	0/102 (0.0%)	0/48 (0.0%)
Total Bilirubin > 2xULN	1/102 (1.0%)	0/48 (0.0%)
Alkaline Phosphatase > 1.5xULN	4/102 (3.9%)	0/48 (0.0%)
ALT and/or AST > 3xULN and Total Bilirubin > 2xULN	0/102 (0.0%)	0/48 (0.0%)
ALT and/or AST > 3xULN in temporal association with specific adverse events (1)	1/102 (1.0%)	0/48 (0.0%)
ALT and/or AST > 3xULN and Total Bilirubin > 2xULN and Alkaline Phosphatase < 2xULN	0/102 (0.0%)	0/48 (0.0%)

Note: ULN = Upper limit of normal of the laboratory reference Min, Max. For each treatment group, percentages are based on the number of subjects in the Placebo-Controlled Safety Population: Placebo-Controlled Period with at least 1 post-baseline measurement for the given LFT/LFTs. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(1) ALT and/or AST > 3xULN within 14 days before or after adverse event onset date for one or more of the following adverse events: nausea, vomiting, fatigue, abdominal pain, upper quadrant pain or tenderness, fever, rash, and eosinophilia.
(Source: 5.3.5.3.2, Table 5.3.1)

表 2.7.4.9-50 Incidences of Elevations in Liver Function Tests (LFTs) for Post-Baseline Period (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

LFT Abnormality	Fostamatinib n/N (%)
ALT> 3xULN	17/144 (11.8%)
ALT> 5xULN	10/144 (6.9%)
ALT> 10xULN	2/144 (1.4%)
ALT> 20xULN	1/144 (0.7%)
AST> 3xULN	6/144 (4.2%)
AST> 5xULN	2/144 (1.4%)
AST> 10xULN	1/144 (0.7%)
AST> 20xULN	1/144 (0.7%)
ALT and/or AST > 3xULN	18/144 (12.5%)
ALT and/or AST > 5xULN	10/144 (6.9%)
ALT and/or AST > 10xULN	2/144 (1.4%)
ALT and/or AST > 20xULN	1/144 (0.7%)
Total Bilirubin > 2xULN	3/144 (2.1%)
Alkaline Phosphatase > 1.5xULN	11/144 (7.6%)
ALT and/or AST > 3xULN and Total Bilirubin > 2xULN	1/144 (0.7%)
ALT and/or AST > 3xULN in temporal association with specific adverse events (1)	1/144 (0.7%)
ALT and/or AST > 3xULN and Total Bilirubin > 2xULN and Alkaline Phosphatase < 2xULN	1/144 (0.7%)

Note: ULN = Upper limit of normal of the laboratory reference Min, Max. Percentages are based on the number of subjects in the Fostamatinib Treated Population: Fostamatinib Exposure Period with at least 1 post-baseline measurement for the given LFT/LFTs. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(1) ALT and/or AST > 3xULN within 14 days before or after adverse event onset date for one or more of the following adverse events: nausea, vomiting, fatigue, abdominal pain, upper quadrant pain or tenderness, fever, rash, and eosinophilia.
(Source: 5.3.5.3.2, Table 5.3.2)

表 2.7.4.9-51　　Vital Sign – R788-1301 study

Long-Term Treatment of R788
Parameter: Systolic Blood Pressure (mmHg)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	125.8	10.3	102	122	128	134	139
	Screening B	22	123.7	10.4	104	117	126	133	139
	Day 1	22	121.2	11.1	93	115	121	126	139
	Week 2	22	131.8	13.7	108	124	129	143	155
	Week 4	22	135.3	15.8	105	123	136	148	169
	Week 6	22	130.9	14.0	110	122	129	138	164
	Week 8	21	130.7	10.5	108	126	134	137	149
	Week 10	20	130.4	12.9	110	119	133	141	151
	Week 12	20	128.7	12.4	98	125	128	136	156
	Week 14	16	125.0	11.5	106	115	126	136	139
	Week 16	10	126.6	11.3	109	116	129	136	144
	Week 18	10	126.4	12.9	98	117	130	134	141
	Week 20	10	123.7	8.7	113	116	122	129	141
	Week 22	10	128.3	8.2	117	123	128	131	145
	Week 24	10	134.0	10.8	114	126	136	138	155
	Week 28	10	126.5	14.5	102	116	128	135	156
	Week 32	10	129.8	8.1	120	121	131	138	141
	Week 36	9	128.5	13.1	104	120	129	135	149
	Week 40	9	130.2	7.3	120	124	133	137	139
	Week 44	9	123.9	9.8	107	121	122	126	144
	Week 48	9	127.7	10.1	112	122	126	136	143
	Week 52	9	127.3	12.5	116	119	120	134	151
	LOV	22	125.4	11.3	106	116	124	134	151

LOV: Last Observed Visit

Long-Term Treatment of R788
Parameter: Diastolic Blood Pressure (mmHg)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	73.2	7.8	61	66	74	78	88
	Screening B	22	71.4	8.0	58	66	71	76	89
	Day 1	22	70.9	7.5	56	66	73	77	83
	Week 2	22	78.7	8.6	58	75	79	84	96
	Week 4	22	80.5	7.2	71	74	80	86	93
	Week 6	22	77.9	6.6	66	74	77	81	93
	Week 8	21	79.1	8.4	61	74	78	85	95
	Week 10	20	77.2	10.1	51	73	76	83	99
	Week 12	20	76.9	9.3	58	72	76	85	94
	Week 14	16	75.7	9.6	60	69	76	82	92
	Week 16	10	72.8	11.8	48	68	73	80	91
	Week 18	10	74.7	7.6	66	69	73	81	88
	Week 20	10	72.0	7.7	65	67	70	73	89
	Week 22	10	76.0	4.8	67	72	78	79	81
	Week 24	10	79.5	5.1	73	74	79	86	86
	Week 28	10	74.2	11.7	53	67	75	78	97
	Week 32	10	76.0	8.0	63	69	77	84	85
	Week 36	9	74.1	9.6	58	69	74	83	86
	Week 40	9	74.8	8.7	59	71	75	79	88
	Week 44	9	75.0	11.9	61	64	74	79	94
	Week 48	9	74.6	8.9	61	68	76	82	85
	Week 52	9	73.0	9.6	63	66	69	79	91
	LOV	22	75.9	8.5	63	68	76	84	91

LOV: Last Observed Visit

Long-Term Treatment of R788
Parameter: Pulse Rate (beats/min)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	74.3	11.5	53	67	72	83	94
	Screening B	22	78.3	13.6	53	74	79	84	116
	Day 1	22	76.5	13.0	52	68	73	86	101
	Week 2	22	74.2	10.8	49	66	76	78	98
	Week 4	22	75.8	14.4	51	69	74	81	117
	Week 6	22	74.3	13.5	55	65	73	86	99
	Week 8	21	72.9	11.3	47	65	71	80	94
	Week 10	20	76.7	12.0	57	68	76	85	101
	Week 12	20	76.2	13.8	51	68	74	88	103
	Week 14	16	74.1	12.3	46	66	74	82	96
	Week 16	10	72.6	13.8	51	63	72	81	100
	Week 18	10	75.3	14.7	52	67	73	84	99
	Week 20	10	74.2	12.5	55	65	74	87	91
	Week 22	10	75.0	14.2	51	67	74	84	99
	Week 24	10	71.0	11.5	53	64	69	81	93
	Week 28	10	78.0	11.8	60	69	80	87	92
	Week 32	10	77.3	14.4	54	69	76	84	107
	Week 36	9	76.7	14.2	55	65	77	85	97
	Week 40	9	76.1	14.5	55	62	77	85	100
	Week 44	9	80.8	17.5	48	77	83	89	107
	Week 48	9	74.1	12.1	57	65	79	85	89
	Week 52	9	74.4	12.1	56	66	72	84	92
	LOV	22	75.5	10.8	56	67	74	84	97

LOV: Last Observed Visit

Long-Term Treatment of R788
Parameter: Temperature (C)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	36.29	0.43	35.4	36.2	36.3	36.6	36.9
	Screening B	22	36.33	0.35	35.8	36.1	36.3	36.6	37.2
	Day 1	22	36.33	0.35	35.6	36.1	36.4	36.6	36.8
	Week 2	22	36.39	0.33	35.7	36.2	36.4	36.6	36.9
	Week 4	22	36.30	0.30	35.7	36.2	36.3	36.4	36.9
	Week 6	22	36.25	0.37	35.1	36.1	36.3	36.5	36.8
	Week 8	21	36.24	0.40	35.5	36.1	36.2	36.4	37.0
	Week 10	20	36.24	0.45	35.1	35.9	36.4	36.6	36.9
	Week 12	20	36.22	0.45	35.0	35.9	36.3	36.6	36.8
	Week 14	16	36.26	0.38	35.6	36.0	36.2	36.6	37.1
	Week 16	10	36.15	0.38	35.4	35.9	36.3	36.4	36.6
	Week 18	10	36.25	0.50	35.2	36.0	36.2	36.7	36.9
	Week 20	10	36.24	0.36	35.7	36.0	36.2	36.5	36.8
	Week 22	10	36.27	0.37	35.7	36.0	36.3	36.5	36.9
	Week 24	10	36.24	0.34	35.7	36.0	36.3	36.6	36.6
	Week 28	10	36.35	0.31	35.8	36.2	36.3	36.5	36.8
	Week 32	10	36.20	0.49	35.4	35.8	36.1	36.7	36.9
	Week 36	9	36.18	0.43	35.2	36.2	36.2	36.3	36.7
	Week 40	9	36.24	0.49	35.6	36.0	36.1	36.6	37.0
	Week 44	9	36.32	0.65	35.2	36.1	36.4	36.9	37.1
	Week 48	9	36.04	0.47	35.5	35.7	35.9	36.2	36.8
	Week 52	9	36.28	0.72	34.5	36.3	36.4	36.6	37.0
	LOV	22	36.37	0.53	34.5	36.3	36.4	36.7	37.1

LOV: Last Observed Visit
(Source: 5.3.5.1.1, Table 14.2.4.6.1)

表 2.7.4.9-52 Vital Sign – R788-1301 study

Period I
Parameter: Systolic Blood Pressure (mmHg)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	125.8	10.3	102	122	128	134	139
	Screening B	22	123.7	10.4	104	117	126	133	139
	Day 1	22	121.2	11.1	93	115	121	126	139
	Week 2	22	131.8	13.7	108	124	129	143	155
	Week 4	22	135.3	15.8	105	123	136	148	169
	Week 6	22	130.9	14.0	110	122	129	138	164
	Week 8	21	130.7	10.5	108	126	134	137	149
	Week 10	20	130.4	12.9	110	119	133	141	151
	Week 12	20	128.7	12.4	98	125	128	136	156
	Week 14	16	125.0	11.5	106	115	126	136	139
	Week 16	10	126.6	11.3	109	116	129	136	144
	Week 18	10	126.4	12.9	98	117	130	134	141
	Week 20	10	123.7	8.7	113	116	122	129	141
	Week 22	10	128.3	8.2	117	123	128	131	145
	Week 24	10	134.0	10.8	114	126	136	138	155
	LOV	22	128.1	11.8	106	120	129	137	155
Placebo	Screening A	12	124.5	8.9	111	118	124	131	139
	Screening B	12	122.8	8.6	111	116	122	130	136
	Day 1	12	121.6	8.7	103	116	123	128	133
	Week 2	12	122.4	12.3	97	114	124	133	141
	Week 4	10	119.1	11.2	97	114	119	128	134
	Week 6	10	122.4	16.3	95	118	124	129	144
	Week 8	11	124.3	13.4	101	113	124	137	143
	Week 10	11	122.8	7.8	108	118	122	130	133
	Week 12	10	117.1	4.7	108	115	118	120	122
	Week 14	4	119.0	4.3	113	116	120	122	123
	Week 16	4	115.4	4.8	110	112	116	119	121
	Week 18	4	115.7	16.3	94	105	118	127	133
	Week 20	3	113.2	7.6	107	107	111	122	122
	Week 22	4	109.4	9.9	96	102	112	117	117
	Week 24	4	117.8	7.1	112	112	117	124	126
	LOV	12	120.6	5.9	112	117	121	124	133

Period I
Parameter: Diastolic Blood Pressure (mmHg)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	73.2	7.8	61	66	74	78	88
	Screening B	22	71.4	8.0	58	66	71	76	89
	Day 1	22	70.9	7.5	56	66	73	77	83
	Week 2	22	78.7	8.6	58	75	79	84	96
	Week 4	22	80.5	7.2	71	74	80	86	93
	Week 6	22	77.9	6.6	66	74	77	81	93
	Week 8	21	79.1	8.4	61	74	78	85	95
	Week 10	20	77.2	10.1	51	73	76	83	99
	Week 12	20	76.9	9.3	58	72	76	85	94
	Week 14	16	75.7	9.6	60	69	76	82	92
	Week 16	10	72.8	11.8	48	68	73	80	91
	Week 18	10	74.7	7.6	66	69	73	81	88
	Week 20	10	72.0	7.7	65	67	70	73	89
	Week 22	10	76.0	4.8	67	72	78	79	81
	Week 24	10	79.5	5.1	73	74	79	86	86
	LOV	22	78.3	6.4	68	74	78	84	89
Placebo	Screening A	12	73.9	8.6	55	74	77	79	86
	Screening B	12	74.4	5.1	66	69	76	79	80
	Day 1	12	77.6	6.9	66	73	78	83	88

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 2	12	76.1	9.8	64	69	74	82	95
	Week 4	10	76.9	11.7	63	67	75	89	95
	Week 6	10	78.3	9.5	61	73	78	86	94
	Week 8	11	77.9	10.4	65	68	77	87	95
	Week 10	11	76.7	9.6	63	69	74	84	95
	Week 12	10	73.9	7.7	66	68	71	80	87
	Week 14	4	75.8	9.4	67	70	74	82	89
	Week 16	4	71.2	10.7	62	65	68	77	87
	Week 18	4	73.5	12.9	59	64	73	84	89
	Week 20	3	73.0	8.7	67	67	69	83	83
	Week 22	4	69.9	12.8	56	60	69	80	86
	Week 24	4	77.3	12.1	60	70	81	85	88
	LOV	12	75.6	8.6	60	68	78	82	88

Period I
Parameter: Pulse Rate (beats/min)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	74.3	11.5	53	67	72	83	94
	Screening B	22	78.3	13.6	53	74	79	84	116
	Day 1	22	76.5	13.0	52	68	73	86	101
	Week 2	22	74.2	10.8	49	66	76	78	98
	Week 4	22	75.8	14.4	51	69	74	81	117
	Week 6	22	74.3	13.5	55	65	73	86	99
	Week 8	21	72.9	11.3	47	65	71	80	94
	Week 10	20	76.7	12.0	57	68	76	85	101
	Week 12	20	76.2	13.8	51	68	74	88	103
	Week 14	16	74.1	12.3	46	66	74	82	96
	Week 16	10	72.6	13.8	51	63	72	81	100
	Week 18	10	75.3	14.7	52	67	73	84	99
	Week 20	10	74.2	12.5	55	65	74	87	91
	Week 22	10	75.0	14.2	51	67	74	84	99
	Week 24	10	71.0	11.5	53	64	69	81	93
	LOV	22	74.1	11.1	53	65	73	81	97
Placebo	Screening A	12	76.7	11.5	59	67	78	87	92
	Screening B	12	74.3	10.1	56	67	78	82	86
	Day 1	12	77.3	14.1	59	69	76	81	105
	Week 2	12	73.8	10.7	61	62	74	81	95
	Week 4	10	73.3	8.9	61	65	74	78	86
	Week 6	10	72.6	9.1	58	65	74	81	82
	Week 8	11	72.2	9.8	60	63	72	82	86
	Week 10	11	71.5	7.5	59	64	71	78	82
	Week 12	10	75.6	12.0	60	62	76	85	94
	Week 14	4	72.0	4.1	68	69	72	76	76
	Week 16	4	73.3	8.4	62	67	75	80	81
	Week 18	4	72.8	8.7	65	66	72	80	83
	Week 20	3	75.7	8.5	67	67	76	84	84
	Week 22	4	70.8	11.3	60	61	71	81	81
	Week 24	4	70.5	11.6	60	63	68	78	87
	LOV	12	75.2	11.8	60	65	75	84	94

Period I
Parameter: Temperature (C)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	36.29	0.43	35.4	36.2	36.3	36.6	36.9
	Screening B	22	36.33	0.35	35.8	36.1	36.3	36.6	37.2
	Day 1	22	36.33	0.35	35.6	36.1	36.4	36.6	36.8
	Week 2	22	36.39	0.33	35.7	36.2	36.4	36.6	36.9
	Week 4	22	36.30	0.30	35.7	36.2	36.3	36.4	36.9
	Week 6	22	36.25	0.37	35.1	36.1	36.3	36.5	36.8

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 8	21	36.24	0.40	35.5	36.1	36.2	36.4	37.0
	Week 10	20	36.24	0.45	35.1	35.9	36.4	36.6	36.9
	Week 12	20	36.22	0.45	35.0	35.9	36.3	36.6	36.8
	Week 14	16	36.26	0.38	35.6	36.0	36.2	36.6	37.1
	Week 16	10	36.15	0.38	35.4	35.9	36.3	36.4	36.6
	Week 18	10	36.25	0.50	35.2	36.0	36.2	36.7	36.9
	Week 20	10	36.24	0.36	35.7	36.0	36.2	36.5	36.8
	Week 22	10	36.27	0.37	35.7	36.0	36.3	36.5	36.9
	Week 24	10	36.24	0.34	35.7	36.0	36.3	36.6	36.6
	LOV	22	36.33	0.36	35.6	36.1	36.4	36.6	37.1
Placebo	Screening A	12	36.43	0.26	36.0	36.3	36.5	36.7	36.7
	Screening B	12	36.19	0.41	35.5	36.0	36.3	36.5	36.8
	Day 1	12	36.24	0.61	34.9	35.8	36.4	36.8	36.9
	Week 2	12	36.05	0.44	35.2	35.8	36.1	36.4	36.7
	Week 4	10	36.13	0.47	35.2	35.9	36.1	36.6	36.7
	Week 6	10	36.25	0.48	35.3	36.1	36.4	36.6	36.8
	Week 8	11	36.35	0.47	35.4	36.2	36.3	36.5	37.3
	Week 10	11	36.46	0.44	35.7	36.2	36.4	36.8	37.4
	Week 12	10	36.19	0.45	35.3	35.9	36.3	36.4	36.9
	Week 14	4	36.50	0.34	36.3	36.3	36.4	36.7	37.0
	Week 16	4	36.53	0.51	35.9	36.2	36.6	36.9	37.1
	Week 18	4	36.48	0.29	36.1	36.3	36.5	36.7	36.8
	Week 20	3	36.40	0.60	35.8	35.8	36.4	37.0	37.0
	Week 22	4	36.33	0.60	35.5	35.9	36.5	36.8	36.9
	Week 24	4	36.45	0.31	36.1	36.2	36.5	36.7	36.8
	LOV	12	36.20	0.31	35.8	35.9	36.2	36.4	36.8

LOV: Last Observed Visit
(Source: 5.3.5.1.1, Table 14.1.4.6.1)

表 2.7.4.9-53 Occurrences of Elevated Blood Pressure at Scheduled Visits – R788-1301 study

Long-Term Treatment of R788
Parameter:Number of Scheduled Visits for SBP>=140 or DBP>=90 (mmHg)

Number	N	%
N	22	---
0	8	36.4
1	4	18.2
2	1	4.5
3	3	13.6
4	1	4.5
5	3	13.6
6	0	0.0
7	0	0.0
8	1	4.5
9	1	4.5

Long-Term Treatment of R788
Parameter:Number of Scheduled Visits for SBP>=160 or DBP>=100 (mmHg)

Number	N	%
N	22	---
0	20	90.9
1	2	9.1

(Source: 5.3.5.1.1, Table 14.2.4.6.4)

表 2.7.4.9-54 Occurrences of Elevated Blood Pressure at Scheduled Visits – R788-1301 study

Period I
Parameter:Number of Scheduled Visits for SBP>=140 or DBP>=90 (mmHg)

	R788		Placebo	
Number	N	%	N	%
N	22	---	12	---
0	8	36.4	8	66.7
1	4	18.2	1	8.3
2	2	9.1	1	8.3
3	2	9.1	1	8.3
4	3	13.6	1	8.3
5	2	9.1	0	0.0
6	0	0.0	0	0.0
7	1	4.5	0	0.0

Period I
Parameter:Number of Scheduled Visits for SBP>=160 or DBP>=100 (mmHg)

	R788		Placebo	
Number	N	%	N	%
N	22	---	12	---
0	20	90.9	12	100.0
1	2	9.1	0	0.0

(Source: 5.3.5.1.1, Table 14.1.4.6.4)

表 2.7.4.9-55 Vital Signs (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Vital Sign: Systolic BP (mmHg)

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Baseline	n	146	
	Mean	122.3	
	Median	123.0	
	Q1, Q3	117.0, 129.0	
	SD	9.45	
	Min, Max	97, 160	
Week 4	n	144	144
	Mean	124.1	1.8
	Median	124.0	1.0
	Q1, Q3	118.0, 130.0	-5.0, 8.0
	SD	10.19	9.49
	Min, Max	95, 151	-37, 28
Week 8	n	138	138
	Mean	125.5	3.3
	Median	125.0	3.0
	Q1, Q3	120.0, 130.0	-3.0, 10.0
	SD	10.24	10.02
	Min, Max	100, 160	-23, 36
Week 12	n	131	131
	Mean	124.0	2.1
	Median	125.0	0.0
	Q1, Q3	118.0, 129.0	-4.0, 8.0
	SD	10.24	10.94
	Min, Max	100, 154	-37, 41
Week 16	n	116	116
	Mean	122.7	0.7
	Median	122.0	0.0
	Q1, Q3	118.0, 128.0	-5.0, 6.0
	SD	7.88	8.90
	Min, Max	101, 145	-24, 25
Week 20	n	101	101
	Mean	125.2	2.3
	Median	125.0	2.0
	Q1, Q3	120.0, 130.0	-3.0, 9.0
	SD	9.04	9.09
	Min, Max	91, 152	-25, 28
Week 24	n	101	101
	Mean	125.0	2.3
	Median	125.0	2.0
	Q1, Q3	120.0, 130.0	-5.0, 8.0
	SD	9.20	9.53
	Min, Max	90, 161	-18, 32
Week 28	n	90	90
	Mean	124.5	1.4
	Median	124.0	0.5

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Q1, Q3	120.0, 128.0	-5.0, 7.0
	SD	8.19	9.51
	Min, Max	106, 149	-19, 29
Week 32	n	65	65
	Mean	123.3	-0.1
	Median	124.0	0.0
	Q1, Q3	119.0, 129.0	-7.0, 7.0
	SD	8.70	8.96
	Min, Max	100, 154	-19, 22
Week 36	n	58	58
	Mean	123.1	0.1
	Median	122.0	-1.0
	Q1, Q3	117.0, 129.0	-7.0, 5.0
	SD	9.48	11.18
	Min, Max	93, 151	-23, 34
Week 40	n	62	62
	Mean	125.1	1.7
	Median	126.0	0.0
	Q1, Q3	120.0, 129.0	-4.0, 7.0
	SD	8.57	9.21
	Min, Max	96, 146	-17, 26
Week 44	n	54	54
	Mean	122.6	-0.5
	Median	124.0	-1.5
	Q1, Q3	116.0, 128.0	-7.0, 5.0
	SD	9.70	8.60
	Min, Max	96, 148	-16, 28
Week 48	n	54	54
	Mean	124.4	1.3
	Median	124.0	0.0
	Q1, Q3	119.0, 130.0	-5.0, 5.0
	SD	9.59	9.87
	Min, Max	95, 146	-20, 26
Week 52	n	56	56
	Mean	124.0	0.7
	Median	125.0	0.0
	Q1, Q3	118.5, 130.0	-5.0, 4.5
	SD	9.35	11.58
	Min, Max	103, 150	-25, 43
Week 56	n	49	49
	Mean	123.9	0.8
	Median	125.0	0.0
	Q1, Q3	120.0, 128.0	-3.0, 7.0
	SD	8.52	8.39
	Min, Max	91, 138	-19, 19
Week 60	n	54	54
	Mean	123.7	0.2
	Median	124.0	0.5

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Q1, Q3	120.0, 129.0	-5.0, 6.0
	SD	8.20	8.48
	Min, Max	97, 140	-17, 18
Week 64	n	53	53
	Mean	122.4	-0.7
	Median	123.0	-2.0
	Q1, Q3	119.0, 127.0	-5.0, 6.0
	SD	8.66	8.82
	Min, Max	91, 140	-21, 15
Week 68	n	50	50
	Mean	123.1	0.3
	Median	124.0	0.0
	Q1, Q3	120.0, 128.0	-5.0, 7.0
	SD	7.37	9.84
	Min, Max	100, 140	-22, 24
Week 72	n	49	49
	Mean	123.8	0.7
	Median	124.0	0.0
	Q1, Q3	120.0, 128.0	-3.0, 7.0
	SD	8.65	9.00
	Min, Max	100, 147	-25, 17
Week 76	n	50	50
	Mean	124.6	1.3
	Median	125.0	0.0
	Q1, Q3	120.0, 129.0	-5.0, 6.0
	SD	8.29	9.79
	Min, Max	100, 156	-25, 25
Week 80	n	37	37
	Mean	121.0	-2.6
	Median	123.0	-2.0
	Q1, Q3	118.0, 125.0	-9.0, 3.0
	SD	7.14	8.12
	Min, Max	103, 136	-17, 19
Week 84	n	46	46
	Mean	123.7	0.2
	Median	123.0	-1.5
	Q1, Q3	120.0, 128.0	-5.0, 7.0
	SD	8.35	11.05
	Min, Max	100, 145	-32, 27
Week 88	n	36	36
	Mean	122.2	-0.3
	Median	124.5	0.0
	Q1, Q3	120.0, 127.0	-6.0, 5.0
	SD	9.52	8.81
	Min, Max	97, 147	-19, 27
Week 92	n	31	31
	Mean	125.1	1.5
	Median	124.0	0.0

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Q1, Q3	120.0, 129.0	-6.0, 8.0
	SD	7.90	10.52
	Min, Max	114, 151	-17, 31
Week 96	n	37	37
	Mean	123.9	0.5
	Median	123.0	0.0
	Q1, Q3	120.0, 128.0	-5.0, 5.0
	SD	8.37	8.36
	Min, Max	105, 142	-20, 17
Week 100	n	29	29
	Mean	122.3	-1.3
	Median	121.0	-2.0
	Q1, Q3	117.0, 127.0	-8.0, 5.0
	SD	7.06	7.10
	Min, Max	110, 141	-13, 15
Week 104	n	25	25
	Mean	125.6	1.8
	Median	123.0	-2.0
	Q1, Q3	120.0, 130.0	-7.0, 4.0
	SD	9.72	11.31
	Min, Max	105, 150	-10, 30
Week 108	n	24	24
	Mean	124.1	1.5
	Median	123.5	-0.5
	Q1, Q3	120.0, 128.0	-5.0, 8.5
	SD	10.59	8.21
	Min, Max	104, 161	-9, 22
Week 112	n	26	26
	Mean	124.8	0.7
	Median	122.5	-0.5
	Q1, Q3	119.0, 128.0	-5.0, 5.0
	SD	11.29	10.52
	Min, Max	110, 171	-15, 32
Week 116	n	19	19
	Mean	122.2	-1.4
	Median	123.0	0.0
	Q1, Q3	118.0, 125.0	-7.0, 3.0
	SD	6.26	6.86
	Min, Max	111, 140	-15, 12
Week 120	n	38	38
	Mean	122.4	-0.9
	Median	122.5	0.0
	Q1, Q3	120.0, 128.0	-5.0, 4.0
	SD	9.06	8.86
	Min, Max	94, 139	-31, 22
Week 128	n	44	44
	Mean	122.7	-0.7
	Median	125.0	-1.0

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Q1, Q3	120.0, 128.0	-6.5, 6.0
	SD	8.30	9.48
	Min, Max	96, 137	-20, 22
Week 136	n	43	43
	Mean	120.6	-2.1
	Median	122.0	0.0
	Q1, Q3	119.0, 126.0	-6.0, 4.0
	SD	9.70	9.45
	Min, Max	90, 135	-40, 14
Week 144	n	38	38
	Mean	123.5	1.4
	Median	124.0	0.5
	Q1, Q3	120.0, 128.0	-4.0, 7.0
	SD	7.62	8.16
	Min, Max	99, 143	-15, 21
Week 152	n	42	42
	Mean	122.7	0.4
	Median	124.0	1.0
	Q1, Q3	120.0, 128.0	-6.0, 5.0
	SD	6.83	8.09
	Min, Max	99, 131	-15, 19
Week 160	n	39	39
	Mean	123.1	1.0
	Median	123.0	-1.0
	Q1, Q3	119.0, 128.0	-5.0, 6.0
	SD	8.94	8.61
	Min, Max	100, 150	-11, 28
Week 168	n	39	39
	Mean	123.2	0.9
	Median	125.0	0.0
	Q1, Q3	119.0, 128.0	-4.0, 8.0
	SD	8.43	8.89
	Min, Max	98, 147	-20, 32
Week 176	n	30	30
	Mean	125.2	3.2
	Median	124.0	1.0
	Q1, Q3	120.0, 127.0	-4.0, 6.0
	SD	10.81	11.90
	Min, Max	111, 173	-15, 53
Week 184	n	32	32
	Mean	124.2	1.9
	Median	124.5	1.5
	Q1, Q3	120.0, 128.5	-2.0, 5.0
	SD	8.78	8.80
	Min, Max	107, 147	-20, 30
Week 192	n	27	27
	Mean	123.2	1.6
	Median	124.0	3.0

Time Point	Statistic	Fostamatinib (N=146) Value	Change from Baseline
	Q1, Q3	120.0, 128.0	-7.0, 7.0
	SD	8.55	10.59
	Min, Max	104, 142	-15, 27
Week 200	n	30	30
	Mean	123.1	1.2
	Median	124.0	2.5
	Q1, Q3	120.0, 128.0	-6.0, 6.0
	SD	5.88	8.01
	Min, Max	108, 132	-12, 21
Week 208	n	19	19
	Mean	124.8	1.6
	Median	125.0	3.0
	Q1, Q3	120.0, 128.0	-5.0, 7.0
	SD	6.07	6.86
	Min, Max	115, 136	-11, 14
Week 216	n	20	20
	Mean	123.3	2.1
	Median	124.0	2.0
	Q1, Q3	119.5, 129.0	-5.5, 9.5
	SD	7.77	8.98
	Min, Max	110, 136	-11, 16
Week 224	n	17	17
	Mean	126.5	3.9
	Median	128.0	5.0
	Q1, Q3	124.0, 130.0	-1.0, 8.0
	SD	5.78	7.34
	Min, Max	113, 137	-9, 21

Note: The baseline value is the last measurement for the given lab test prior to the first dose of fostamatinib. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.2)

Vital Sign: Diastolic BP (mmHg)

Time Point	Statistic	Fostamatinib (N=146) Value	Change from Baseline
Baseline	n	146	
	Mean	74.5	
	Median	75.0	
	Q1, Q3	70.0, 80.0	
	SD	6.03	
	Min, Max	56, 86	
Week 4	n	144	144
	Mean	76.3	1.7
	Median	77.0	1.0
	Q1, Q3	71.0, 80.0	-3.0, 7.0
	SD	7.52	7.23
	Min, Max	55, 94	-15, 18
Week 8	n	138	138
	Mean	76.9	2.3

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	77.5	2.0
	Q1, Q3	72.0, 80.0	-2.0, 6.0
	SD	7.56	8.28
	Min, Max	58, 99	-22, 26
Week 12	n	131	131
	Mean	76.1	1.6
	Median	76.0	0.0
	Q1, Q3	70.0, 80.0	-4.0, 8.0
	SD	7.98	8.37
	Min, Max	58, 97	-20, 24
Week 16	n	116	116
	Mean	75.2	0.5
	Median	77.0	0.0
	Q1, Q3	70.0, 80.0	-3.0, 5.0
	SD	6.73	7.64
	Min, Max	54, 96	-21, 22
Week 20	n	101	101
	Mean	76.7	1.8
	Median	78.0	0.0
	Q1, Q3	72.0, 80.0	-2.0, 7.0
	SD	6.88	7.62
	Min, Max	52, 94	-20, 26
Week 24	n	101	101
	Mean	76.7	2.0
	Median	78.0	1.0
	Q1, Q3	73.0, 81.0	-3.0, 8.0
	SD	7.35	8.90
	Min, Max	53, 92	-21, 22
Week 28	n	90	90
	Mean	75.9	0.9
	Median	77.0	0.5
	Q1, Q3	72.0, 80.0	-3.0, 7.0
	SD	7.27	8.37
	Min, Max	56, 99	-18, 24
Week 32	n	65	65
	Mean	76.4	2.2
	Median	78.0	2.0
	Q1, Q3	73.0, 80.0	-4.0, 8.0
	SD	7.30	8.37
	Min, Max	50, 95	-20, 20
Week 36	n	58	58
	Mean	75.2	1.2
	Median	75.0	0.0
	Q1, Q3	71.0, 80.0	-4.0, 8.0
	SD	7.09	8.87
	Min, Max	51, 87	-22, 23
Week 40	n	62	62
	Mean	75.6	1.0

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	75.5	1.0
	Q1, Q3	72.0, 78.0	-3.0, 6.0
	SD	5.67	6.79
	Min, Max	56, 87	-16, 17
Week 44	n	54	54
	Mean	75.9	1.5
	Median	78.0	1.5
	Q1, Q3	73.0, 80.0	-2.0, 8.0
	SD	7.88	8.36
	Min, Max	48, 93	-20, 16
Week 48	n	54	54
	Mean	77.5	3.2
	Median	78.0	2.5
	Q1, Q3	73.0, 80.0	-2.0, 8.0
	SD	8.40	8.24
	Min, Max	60, 104	-12, 29
Week 52	n	56	56
	Mean	76.6	2.2
	Median	78.0	0.5
	Q1, Q3	71.0, 80.0	-4.0, 8.5
	SD	7.32	8.22
	Min, Max	60, 95	-19, 19
Week 56	n	49	49
	Mean	75.6	1.1
	Median	76.0	1.0
	Q1, Q3	72.0, 80.0	-4.0, 8.0
	SD	6.45	7.83
	Min, Max	56, 88	-16, 17
Week 60	n	54	54
	Mean	75.1	0.7
	Median	76.0	0.0
	Q1, Q3	73.0, 79.0	-4.0, 6.0
	SD	6.31	7.46
	Min, Max	60, 87	-15, 18
Week 64	n	53	53
	Mean	73.8	-0.4
	Median	75.0	0.0
	Q1, Q3	70.0, 80.0	-6.0, 6.0
	SD	7.59	8.18
	Min, Max	56, 92	-16, 17
Week 68	n	50	50
	Mean	76.2	1.8
	Median	76.0	1.0
	Q1, Q3	74.0, 80.0	-5.0, 10.0
	SD	7.41	8.37
	Min, Max	51, 91	-19, 16
Week 72	n	49	49
	Mean	77.2	2.8

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	77.0	3.0
	Q1, Q3	74.0, 80.0	-2.0, 8.0
	SD	7.42	8.66
	Min, Max	55, 96	-19, 18
Week 76	n	50	50
	Mean	75.7	1.1
	Median	75.0	0.0
	Q1, Q3	70.0, 80.0	-5.0, 7.0
	SD	6.99	7.94
	Min, Max	52, 87	-18, 16
Week 80	n	37	37
	Mean	73.4	-0.8
	Median	75.0	0.0
	Q1, Q3	72.0, 78.0	-5.0, 5.0
	SD	7.49	8.35
	Min, Max	51, 87	-23, 15
Week 84	n	46	46
	Mean	75.9	1.4
	Median	77.5	1.0
	Q1, Q3	72.0, 80.0	-5.0, 5.0
	SD	7.12	8.72
	Min, Max	55, 93	-20, 21
Week 88	n	36	36
	Mean	74.2	0.3
	Median	78.0	1.0
	Q1, Q3	70.0, 80.0	-4.0, 6.5
	SD	8.03	9.18
	Min, Max	50, 83	-23, 18
Week 92	n	31	31
	Mean	75.6	1.8
	Median	76.0	3.0
	Q1, Q3	70.0, 80.0	-3.0, 8.0
	SD	8.29	8.95
	Min, Max	55, 92	-16, 21
Week 96	n	37	37
	Mean	75.2	0.2
	Median	75.0	0.0
	Q1, Q3	74.0, 80.0	-5.0, 5.0
	SD	7.43	8.90
	Min, Max	60, 92	-19, 17
Week 100	n	29	29
	Mean	74.8	0.9
	Median	76.0	1.0
	Q1, Q3	70.0, 80.0	-2.0, 6.0
	SD	6.00	7.63
	Min, Max	62, 84	-15, 18
Week 104	n	25	25
	Mean	73.6	-2.5

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	75.0	-2.0
	Q1, Q3	70.0, 80.0	-8.0, 2.0
	SD	8.52	8.89
	Min, Max	54, 85	-20, 15
Week 108	n	24	24
	Mean	76.9	4.3
	Median	80.0	5.5
	Q1, Q3	73.0, 80.5	-1.0, 11.0
	SD	7.11	8.81
	Min, Max	60, 92	-17, 18
Week 112	n	26	26
	Mean	74.3	-1.1
	Median	75.0	-1.0
	Q1, Q3	70.0, 79.0	-10.0, 5.0
	SD	8.15	9.76
	Min, Max	58, 91	-19, 16
Week 116	n	19	19
	Mean	73.6	0.6
	Median	75.0	1.0
	Q1, Q3	68.0, 78.0	-8.0, 8.0
	SD	8.77	9.31
	Min, Max	57, 90	-15, 16
Week 120	n	38	38
	Mean	74.3	-0.7
	Median	75.0	0.0
	Q1, Q3	70.0, 79.0	-7.0, 4.0
	SD	7.56	8.66
	Min, Max	53, 91	-18, 19
Week 128	n	44	44
	Mean	74.2	-0.4
	Median	73.0	0.0
	Q1, Q3	70.0, 78.5	-8.5, 5.5
	SD	7.69	9.29
	Min, Max	52, 92	-18, 22
Week 136	n	43	43
	Mean	73.3	-1.0
	Median	75.0	0.0
	Q1, Q3	68.0, 80.0	-6.0, 4.0
	SD	7.64	9.10
	Min, Max	54, 86	-23, 17
Week 144	n	38	38
	Mean	74.3	0.5
	Median	75.0	-0.5
	Q1, Q3	70.0, 80.0	-6.0, 9.0
	SD	7.62	9.30
	Min, Max	55, 88	-16, 18
Week 152	n	42	42
	Mean	73.2	-1.0

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	74.0	-0.5
	Q1, Q3	70.0, 79.0	-7.0, 5.0
	SD	7.31	9.18
	Min, Max	52, 87	-20, 17
Week 160	n	39	39
	Mean	74.7	0.7
	Median	76.0	0.0
	Q1, Q3	70.0, 80.0	-8.0, 8.0
	SD	7.80	9.32
	Min, Max	58, 91	-16, 17
Week 168	n	39	39
	Mean	73.8	-0.1
	Median	75.0	0.0
	Q1, Q3	70.0, 80.0	-7.0, 7.0
	SD	8.24	8.69
	Min, Max	50, 87	-23, 16
Week 176	n	30	30
	Mean	75.8	1.9
	Median	76.0	0.0
	Q1, Q3	71.0, 80.0	-4.0, 9.0
	SD	5.77	8.81
	Min, Max	62, 85	-16, 20
Week 184	n	32	32
	Mean	74.4	0.9
	Median	76.5	0.0
	Q1, Q3	69.5, 80.0	-5.0, 6.5
	SD	7.43	8.45
	Min, Max	60, 91	-13, 21
Week 192	n	27	27
	Mean	75.0	1.7
	Median	75.0	2.0
	Q1, Q3	70.0, 80.0	-4.0, 8.0
	SD	6.52	8.29
	Min, Max	57, 88	-13, 21
Week 200	n	30	30
	Mean	73.4	-0.3
	Median	73.0	-1.5
	Q1, Q3	70.0, 79.0	-6.0, 8.0
	SD	5.94	8.03
	Min, Max	60, 81	-12, 18
Week 208	n	19	19
	Mean	73.6	-1.3
	Median	76.0	-1.0
	Q1, Q3	70.0, 77.0	-5.0, 5.0
	SD	7.30	7.37
	Min, Max	54, 85	-16, 13
Week 216	n	20	20
	Mean	74.7	2.1

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	74.0	0.5
	Q1, Q3	70.0, 78.0	-3.0, 5.0
	SD	5.40	8.39
	Min, Max	68, 88	-10, 21
Week 224	n	17	17
	Mean	73.7	2.0
	Median	74.0	1.0
	Q1, Q3	70.0, 80.0	-4.0, 10.0
	SD	7.25	8.68
	Min, Max	61, 83	-13, 15

Note: The baseline value is the last measurement for the given lab test prior to the first dose of fostamatinib. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.2)

Vital Sign: Pulse (bpm)

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
Baseline	n	146	
	Mean	75.4	
	Median	76.0	
	Q1, Q3	70.0, 80.0	
	SD	9.83	
	Min, Max	52, 106	
Week 4	n	144	144
	Mean	73.5	-2.0
	Median	72.0	-2.0
	Q1, Q3	68.0, 79.0	-7.0, 2.0
	SD	10.18	9.27
	Min, Max	51, 113	-32, 34
Week 8	n	139	139
	Mean	74.5	-0.9
	Median	74.0	-1.0
	Q1, Q3	68.0, 81.0	-7.0, 3.0
	SD	10.43	9.16
	Min, Max	52, 111	-22, 32
Week 12	n	131	131
	Mean	74.1	-1.4
	Median	72.0	-2.0
	Q1, Q3	68.0, 80.0	-6.0, 3.0
	SD	11.47	9.45
	Min, Max	51, 115	-22, 53
Week 16	n	117	117
	Mean	74.5	-1.3
	Median	72.0	-2.0
	Q1, Q3	68.0, 80.0	-8.0, 4.0
	SD	11.49	8.57
	Min, Max	50, 122	-29, 19
Week 20	n	104	104

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Mean	74.5	-1.3
	Median	74.0	-0.5
	Q1, Q3	68.0, 80.0	-7.0, 3.0
	SD	11.19	8.48
	Min, Max	50, 110	-20, 25
Week 24	n	100	100
	Mean	74.2	-1.5
	Median	74.0	-2.0
	Q1, Q3	69.0, 80.0	-6.0, 3.5
	SD	11.07	8.60
	Min, Max	52, 106	-29, 20
Week 28	n	88	88
	Mean	75.8	-0.3
	Median	76.0	0.0
	Q1, Q3	70.0, 80.5	-6.0, 6.0
	SD	10.42	8.68
	Min, Max	50, 102	-20, 20
Week 32	n	65	65
	Mean	76.0	-0.8
	Median	76.0	-2.0
	Q1, Q3	68.0, 82.0	-6.0, 4.0
	SD	11.34	8.65
	Min, Max	52, 111	-15, 21
Week 36	n	57	57
	Mean	75.2	-0.2
	Median	75.0	0.0
	Q1, Q3	70.0, 82.0	-7.0, 4.0
	SD	11.48	9.95
	Min, Max	51, 123	-22, 38
Week 40	n	60	60
	Mean	75.3	-1.2
	Median	75.0	-1.0
	Q1, Q3	70.0, 81.0	-5.5, 4.5
	SD	10.05	8.83
	Min, Max	50, 105	-30, 15
Week 44	n	53	53
	Mean	75.4	-1.2
	Median	76.0	-2.0
	Q1, Q3	70.0, 80.0	-6.0, 6.0
	SD	9.35	9.22
	Min, Max	56, 100	-27, 21
Week 48	n	53	53
	Mean	76.1	-0.9
	Median	75.0	-2.0
	Q1, Q3	70.0, 82.0	-7.0, 5.0
	SD	11.10	8.57
	Min, Max	54, 102	-18, 24
Week 52	n	56	56

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Mean	75.0	-1.3
	Median	74.0	-1.5
	Q1, Q3	69.0, 80.0	-5.5, 5.5
	SD	9.27	8.55
	Min, Max	54, 95	-21, 17
Week 56	n	50	50
	Mean	74.3	-1.3
	Median	76.0	-1.0
	Q1, Q3	70.0, 80.0	-8.0, 4.0
	SD	9.29	7.48
	Min, Max	50, 90	-18, 11
Week 60	n	54	54
	Mean	75.2	-0.9
	Median	75.0	0.0
	Q1, Q3	68.0, 82.0	-8.0, 6.0
	SD	10.02	9.06
	Min, Max	54, 101	-20, 18
Week 64	n	53	53
	Mean	74.2	-1.4
	Median	74.0	-4.0
	Q1, Q3	68.0, 80.0	-8.0, 6.0
	SD	9.44	8.70
	Min, Max	50, 93	-16, 17
Week 68	n	51	51
	Mean	74.4	-1.8
	Median	72.0	-3.0
	Q1, Q3	66.0, 82.0	-10.0, 6.0
	SD	10.89	10.96
	Min, Max	51, 106	-34, 28
Week 72	n	49	49
	Mean	75.4	-1.4
	Median	75.0	-4.0
	Q1, Q3	69.0, 80.0	-10.0, 7.0
	SD	11.44	10.91
	Min, Max	52, 120	-23, 40
Week 76	n	49	49
	Mean	74.1	-2.7
	Median	73.0	-4.0
	Q1, Q3	69.0, 80.0	-8.0, 2.0
	SD	10.68	10.17
	Min, Max	53, 113	-29, 33
Week 80	n	37	37
	Mean	76.1	-0.3
	Median	76.0	0.0
	Q1, Q3	70.0, 80.0	-8.0, 8.0
	SD	8.80	9.78
	Min, Max	63, 100	-27, 20
Week 84	n	47	47

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Mean	75.2	-2.1
	Median	74.0	-3.0
	Q1, Q3	68.0, 81.0	-8.0, 4.0
	SD	8.56	8.21
	Min, Max	53, 97	-20, 17
Week 88	n	36	36
	Mean	73.4	-3.3
	Median	73.5	-5.0
	Q1, Q3	68.0, 79.5	-10.0, 4.0
	SD	7.99	7.75
	Min, Max	60, 90	-17, 12
Week 92	n	33	33
	Mean	73.6	-4.1
	Median	73.0	-5.0
	Q1, Q3	70.0, 80.0	-12.0, 3.0
	SD	8.26	9.52
	Min, Max	54, 88	-20, 14
Week 96	n	35	35
	Mean	75.2	-2.5
	Median	76.0	-4.0
	Q1, Q3	68.0, 82.0	-8.0, 4.0
	SD	10.46	9.87
	Min, Max	60, 100	-25, 20
Week 100	n	28	28
	Mean	73.0	-3.5
	Median	75.0	-2.5
	Q1, Q3	66.0, 78.0	-9.5, 3.0
	SD	9.42	9.34
	Min, Max	52, 91	-34, 12
Week 104	n	25	25
	Mean	73.0	-5.0
	Median	70.0	-8.0
	Q1, Q3	68.0, 78.0	-10.0, -1.0
	SD	9.85	8.83
	Min, Max	56, 100	-17, 20
Week 108	n	24	24
	Mean	72.7	-2.6
	Median	72.0	-2.0
	Q1, Q3	68.0, 78.0	-9.0, 4.0
	SD	9.01	7.53
	Min, Max	53, 92	-16, 12
Week 112	n	26	26
	Mean	71.7	-6.7
	Median	72.0	-8.0
	Q1, Q3	68.0, 77.0	-14.0, 0.0
	SD	9.05	11.42
	Min, Max	55, 93	-25, 15
Week 116	n	19	19

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Mean	72.1	-2.9
	Median	72.0	-3.0
	Q1, Q3	68.0, 76.0	-8.0, 3.0
	SD	6.51	6.50
	Min, Max	61, 88	-16, 9
Week 120	n	38	38
	Mean	73.6	-3.6
	Median	73.5	-4.0
	Q1, Q3	68.0, 77.0	-7.0, 0.0
	SD	9.29	6.49
	Min, Max	57, 101	-16, 13
Week 128	n	44	44
	Mean	74.4	-3.0
	Median	73.5	-3.5
	Q1, Q3	70.0, 82.0	-9.0, 3.0
	SD	8.87	7.69
	Min, Max	55, 99	-16, 14
Week 136	n	44	44
	Mean	74.4	-2.9
	Median	72.5	-3.5
	Q1, Q3	66.0, 78.5	-10.0, 3.0
	SD	11.70	9.65
	Min, Max	57, 104	-21, 23
Week 144	n	39	39
	Mean	73.8	-2.9
	Median	73.0	-4.0
	Q1, Q3	66.0, 78.0	-10.0, 5.0
	SD	9.00	9.61
	Min, Max	57, 98	-20, 18
Week 152	n	42	42
	Mean	72.9	-4.8
	Median	73.5	-4.5
	Q1, Q3	65.0, 78.0	-11.0, 0.0
	SD	8.72	7.77
	Min, Max	55, 95	-16, 24
Week 160	n	39	39
	Mean	71.3	-5.9
	Median	72.0	-4.0
	Q1, Q3	67.0, 76.0	-11.0, -1.0
	SD	7.26	6.77
	Min, Max	55, 83	-22, 8
Week 168	n	39	39
	Mean	71.1	-6.1
	Median	70.0	-6.0
	Q1, Q3	66.0, 77.0	-10.0, 0.0
	SD	8.11	9.44
	Min, Max	54, 97	-28, 17
Week 176	n	29	29

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
	Mean	71.6	-5.7
	Median	72.0	-5.0
	Q1, Q3	70.0, 76.0	-10.0, 0.0
	SD	6.03	7.22
	Min, Max	60, 82	-20, 6
Week 184	n	32	32
	Mean	72.5	-4.6
	Median	74.0	-4.0
	Q1, Q3	69.0, 76.5	-10.0, 0.5
	SD	7.83	7.89
	Min, Max	55, 89	-19, 10
Week 192	n	29	29
	Mean	73.6	-4.0
	Median	74.0	-4.0
	Q1, Q3	68.0, 80.0	-10.0, 1.0
	SD	9.67	7.88
	Min, Max	53, 89	-20, 9
Week 200	n	30	30
	Mean	73.2	-4.2
	Median	73.5	-6.0
	Q1, Q3	70.0, 77.0	-12.0, 4.0
	SD	7.50	9.65
	Min, Max	56, 87	-20, 16
Week 208	n	18	18
	Mean	71.0	-6.7
	Median	70.5	-7.0
	Q1, Q3	65.0, 75.0	-14.0, -4.0
	SD	9.04	9.66
	Min, Max	56, 96	-19, 22
Week 216	n	20	20
	Mean	74.7	-2.6
	Median	73.0	-3.5
	Q1, Q3	69.0, 80.5	-9.5, 3.0
	SD	8.23	8.04
	Min, Max	58, 90	-14, 16
Week 224	n	17	17
	Mean	72.0	-4.5
	Median	71.0	-5.0
	Q1, Q3	67.0, 78.0	-13.0, 1.0
	SD	7.54	8.40
	Min, Max	58, 89	-15, 10

Note: The baseline value is the last measurement for the given lab test prior to the first dose of fostamatinib. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.2)

Vital Sign: Temperature (°C)

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Baseline	n	146	
	Mean	36.52	
	Median	36.50	
	Q1, Q3	36.30, 36.70	
	SD	0.344	
	Min, Max	35.3, 37.6	
Week 4	n	144	144
	Mean	36.48	-0.04
	Median	36.50	0.00
	Q1, Q3	36.40, 36.70	-0.15, 0.15
	SD	0.353	0.355
	Min, Max	35.0, 37.4	-1.4, 0.8
Week 8	n	139	139
	Mean	36.90	0.38
	Median	36.50	0.00
	Q1, Q3	36.30, 36.70	-0.20, 0.10
	SD	5.230	5.225
	Min, Max	35.6, 98.0	-1.3, 61.4
Week 12	n	130	130
	Mean	36.43	-0.09
	Median	36.50	0.00
	Q1, Q3	36.30, 36.60	-0.20, 0.10
	SD	0.395	0.400
	Min, Max	35.0, 37.5	-1.4, 1.2
Week 16	n	117	117
	Mean	36.48	-0.04
	Median	36.50	0.00
	Q1, Q3	36.30, 36.70	-0.10, 0.10
	SD	0.394	0.347
	Min, Max	35.0, 37.3	-1.3, 0.8
Week 20	n	104	104
	Mean	36.50	-0.03
	Median	36.50	0.00
	Q1, Q3	36.40, 36.65	-0.15, 0.20
	SD	0.358	0.342
	Min, Max	35.2, 37.5	-1.1, 0.9
Week 24	n	100	100
	Mean	36.50	-0.02
	Median	36.50	0.00
	Q1, Q3	36.40, 36.70	-0.15, 0.15
	SD	0.344	0.361
	Min, Max	34.5, 37.4	-1.6, 1.0
Week 28	n	88	88
	Mean	36.49	-0.03
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.10
	SD	0.343	0.426
	Min, Max	35.1, 37.9	-2.2, 1.1

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Week 32	n	64	64
	Mean	36.45	-0.06
	Median	36.50	0.00
	Q1, Q3	36.35, 36.60	-0.20, 0.20
	SD	0.303	0.404
	Min, Max	35.1, 37.1	-1.8, 0.5
Week 36	n	57	57
	Mean	36.46	-0.02
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.10
	SD	0.313	0.340
	Min, Max	35.2, 37.3	-1.3, 0.9
Week 40	n	60	60
	Mean	36.51	0.02
	Median	36.50	0.05
	Q1, Q3	36.40, 36.60	0.00, 0.15
	SD	0.231	0.304
	Min, Max	35.9, 37.1	-1.6, 0.7
Week 44	n	53	53
	Mean	36.49	0.00
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.20
	SD	0.273	0.390
	Min, Max	35.7, 37.1	-1.6, 0.8
Week 48	n	53	53
	Mean	36.53	0.04
	Median	36.50	0.00
	Q1, Q3	36.40, 36.70	-0.10, 0.20
	SD	0.368	0.381
	Min, Max	35.8, 37.9	-1.6, 1.0
Week 52	n	56	56
	Mean	36.47	-0.04
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.10
	SD	0.270	0.349
	Min, Max	35.9, 37.1	-1.1, 1.1
Week 56	n	50	50
	Mean	36.46	-0.06
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.10
	SD	0.331	0.324
	Min, Max	35.3, 37.3	-1.1, 0.5
Week 60	n	54	54
	Mean	36.47	-0.04
	Median	36.45	0.00
	Q1, Q3	36.30, 36.60	-0.30, 0.10
	SD	0.452	0.428
	Min, Max	35.4, 38.8	-1.6, 1.9

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Week 64	n	53	53
	Mean	36.53	0.02
	Median	36.50	0.10
	Q1, Q3	36.30, 36.70	-0.10, 0.10
	SD	0.345	0.425
	Min, Max	35.9, 37.4	-1.6, 1.4
Week 68	n	51	51
	Mean	36.52	0.02
	Median	36.50	0.00
	Q1, Q3	36.30, 36.70	-0.10, 0.20
	SD	0.367	0.425
	Min, Max	35.6, 37.4	-1.2, 0.9
Week 72	n	49	49
	Mean	36.38	-0.09
	Median	36.40	-0.10
	Q1, Q3	36.20, 36.60	-0.20, 0.10
	SD	0.328	0.334
	Min, Max	35.2, 37.1	-1.0, 1.1
Week 76	n	49	49
	Mean	36.40	-0.10
	Median	36.40	0.00
	Q1, Q3	36.40, 36.50	-0.20, 0.10
	SD	0.342	0.468
	Min, Max	35.0, 37.3	-1.4, 1.3
Week 80	n	37	37
	Mean	36.49	-0.02
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.10
	SD	0.272	0.380
	Min, Max	35.8, 37.0	-1.1, 0.8
Week 84	n	47	47
	Mean	36.46	-0.05
	Median	36.40	0.00
	Q1, Q3	36.30, 36.60	-0.10, 0.10
	SD	0.253	0.349
	Min, Max	35.9, 37.2	-1.1, 1.2
Week 88	n	36	36
	Mean	36.43	-0.07
	Median	36.45	0.00
	Q1, Q3	36.30, 36.65	-0.10, 0.10
	SD	0.351	0.409
	Min, Max	35.1, 37.0	-1.6, 0.9
Week 92	n	33	33
	Mean	36.44	-0.08
	Median	36.40	0.00
	Q1, Q3	36.30, 36.70	-0.20, 0.10
	SD	0.459	0.525
	Min, Max	35.0, 37.6	-1.6, 1.6

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Week 96	n	35	35
	Mean	36.48	0.03
	Median	36.50	0.00
	Q1, Q3	36.30, 36.60	-0.10, 0.10
	SD	0.278	0.301
	Min, Max	35.8, 37.3	-0.5, 1.3
Week 100	n	28	28
	Mean	36.48	0.00
	Median	36.50	0.00
	Q1, Q3	36.35, 36.60	-0.15, 0.10
	SD	0.297	0.346
	Min, Max	35.8, 37.1	-0.8, 0.7
Week 104	n	25	25
	Mean	36.44	-0.06
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.10
	SD	0.220	0.281
	Min, Max	36.0, 36.9	-0.9, 0.5
Week 108	n	24	24
	Mean	36.49	0.04
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.05, 0.10
	SD	0.273	0.219
	Min, Max	36.0, 37.4	-0.3, 0.7
Week 112	n	26	26
	Mean	36.46	-0.05
	Median	36.55	0.00
	Q1, Q3	36.30, 36.70	-0.30, 0.20
	SD	0.351	0.346
	Min, Max	35.6, 37.0	-0.9, 0.6
Week 116	n	19	19
	Mean	36.45	-0.01
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.10, 0.20
	SD	0.257	0.301
	Min, Max	35.5, 36.7	-0.8, 0.6
Week 120	n	38	38
	Mean	36.43	-0.06
	Median	36.50	0.00
	Q1, Q3	36.30, 36.60	-0.10, 0.20
	SD	0.370	0.402
	Min, Max	35.1, 37.2	-1.2, 0.7
Week 128	n	44	44
	Mean	36.54	0.06
	Median	36.55	0.10
	Q1, Q3	36.40, 36.70	0.00, 0.20
	SD	0.300	0.288
	Min, Max	35.6, 37.3	-0.5, 0.9

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Week 136	n	44	44
	Mean	36.45	-0.02
	Median	36.50	0.00
	Q1, Q3	36.35, 36.60	-0.05, 0.10
	SD	0.359	0.346
	Min, Max	35.0, 37.4	-1.3, 0.9
Week 144	n	39	39
	Mean	36.42	-0.05
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	-0.20, 0.20
	SD	0.388	0.336
	Min, Max	35.1, 37.0	-1.1, 0.5
Week 152	n	42	42
	Mean	36.44	-0.02
	Median	36.50	0.00
	Q1, Q3	36.20, 36.60	-0.20, 0.10
	SD	0.351	0.301
	Min, Max	35.2, 37.0	-1.1, 1.0
Week 160	n	39	39
	Mean	36.45	0.00
	Median	36.50	0.00
	Q1, Q3	36.30, 36.60	-0.10, 0.10
	SD	0.232	0.195
	Min, Max	35.9, 36.9	-0.4, 0.5
Week 168	n	39	39
	Mean	36.47	0.02
	Median	36.50	0.00
	Q1, Q3	36.30, 36.60	-0.10, 0.10
	SD	0.388	0.428
	Min, Max	35.3, 38.1	-0.9, 2.1
Week 176	n	30	30
	Mean	36.48	0.04
	Median	36.50	0.00
	Q1, Q3	36.40, 36.60	0.00, 0.20
	SD	0.227	0.205
	Min, Max	35.9, 37.1	-0.5, 0.5
Week 184	n	32	32
	Mean	36.48	0.01
	Median	36.50	0.00
	Q1, Q3	36.35, 36.65	-0.15, 0.20
	SD	0.328	0.345
	Min, Max	35.7, 37.1	-1.0, 0.9
Week 192	n	29	29
	Mean	36.42	-0.01
	Median	36.50	0.10
	Q1, Q3	36.40, 36.60	0.00, 0.20
	SD	0.297	0.379
	Min, Max	35.5, 36.9	-1.5, 0.7

		Fostamatinib (N=146)	
Time Point	Statistic	Value	Change from Baseline
Week 200	n	30	30
	Mean	36.44	0.00
	Median	36.45	0.00
	Q1, Q3	36.30, 36.60	-0.10, 0.10
	SD	0.253	0.338
	Min, Max	35.8, 37.1	-1.0, 1.1
Week 208	n	18	18
	Mean	36.56	0.12
	Median	36.60	0.10
	Q1, Q3	36.50, 36.70	-0.10, 0.30
	SD	0.397	0.471
	Min, Max	35.5, 37.3	-1.0, 1.3
Week 216	n	20	20
	Mean	36.43	-0.01
	Median	36.50	0.00
	Q1, Q3	36.25, 36.65	-0.10, 0.20
	SD	0.311	0.373
	Min, Max	35.6, 36.8	-0.9, 0.8
Week 224	n	17	17
	Mean	36.53	0.10
	Median	36.50	0.10
	Q1, Q3	36.30, 36.70	-0.10, 0.20
	SD	0.293	0.322
	Min, Max	36.0, 37.0	-0.5, 1.0

Note: The baseline value is the last measurement for the given lab test prior to the first dose of fostamatinib. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.2)

表 2.7.4.9-56 Vital Signs (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Vital Sign: Systolic BP (mmHg)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	122.8		120.8		
	Median	123.0		120.0		
	Q1, Q3	117.0, 129.0		116.5, 128.5		
	SD	9.11		8.63		
	Min, Max	97, 143		100, 136		
Week 2	n	102	102	48	48	
	Mean	125.7	3.0	121.9	1.1	1.89
	Median	125.0	2.0	120.0	0.0	
	Q1, Q3	120.0, 130.0	-2.0, 8.0	115.5, 130.0	-5.5, 6.5	
	SD	11.28	8.91	10.31	10.74	
	Min, Max	90, 163	-22, 31	100, 148	-23, 32	
Week 4	n	97	97	47	47	
	Mean	125.4	2.8	120.1	-0.5	3.30
	Median	126.0	3.0	121.0	0.0	
	Q1, Q3	118.0, 132.0	-5.0, 9.0	114.0, 128.0	-5.0, 5.0	
	SD	10.37	9.57	10.32	8.80	
	Min, Max	95, 151	-15, 28	91, 137	-23, 17	
Week 6	n	96	96	45	45	
	Mean	125.4	2.8	120.0	-0.8	3.56
	Median	125.0	2.0	120.0	0.0	
	Q1, Q3	119.0, 130.0	-4.0, 9.5	117.0, 123.0	-5.0, 4.0	
	SD	10.95	10.95	8.53	9.87	
	Min, Max	90, 150	-28, 34	95, 141	-27, 20	
Week 8	n	96	96	44	44	
	Mean	126.4	3.9	120.3	-0.2	4.12
	Median	126.5	3.5	120.0	-1.0	
	Q1, Q3	120.0, 130.0	-3.0, 10.0	114.0, 128.0	-4.5, 1.5	
	SD	10.06	10.31	9.59	6.87	
	Min, Max	100, 160	-23, 36	100, 145	-14, 16	
Week 10	n	91	91	43	43	
	Mean	124.9	2.5	118.3	-2.3	4.88
	Median	125.0	0.0	120.0	-3.0	
	Q1, Q3	118.0, 130.0	-3.0, 8.0	112.0, 126.0	-6.0, 5.0	
	SD	10.12	9.58	10.06	10.47	
	Min, Max	100, 156	-19, 29	95, 135	-41, 17	
Week 12	n	89	89	44	44	
	Mean	124.3	1.2	119.5	-1.1	2.32
	Median	125.0	0.0	120.0	0.0	
	Q1, Q3	120.0, 130.0	-5.0, 8.0	112.5, 125.5	-7.5, 5.0	
	SD	10.04	9.84	7.89	9.09	
	Min, Max	101, 154	-23, 25	100, 135	-22, 20	
Week 14	n	41	41	12	12	
	Mean	125.1	1.7	123.3	2.1	-0.35
	Median	125.0	0.0	125.5	2.0	

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
	Q1, Q3	120.0, 130.0	-4.0, 8.0	120.0, 129.0	-6.5, 8.5	
	SD	8.95	8.58	9.57	9.96	
	Min, Max	110, 150	-18, 25	100, 136	-10, 22	
Week 16	n	36	36	9	9	
	Mean	123.9	-0.1	124.2	1.3	-1.42
	Median	125.0	-1.5	125.0	0.0	
	Q1, Q3	120.0, 128.5	-5.0, 5.0	121.0, 128.0	-5.0, 10.0	
	SD	7.48	8.81	5.49	11.92	
	Min, Max	111, 145	-20, 25	114, 132	-15, 23	
Week 18	n	34	34	4	4	
	Mean	124.8	0.6	128.0	8.5	-7.85
	Median	124.0	-0.5	127.5	6.0	
	Q1, Q3	120.0, 129.0	-5.0, 7.0	124.5, 131.5	0.0, 17.0	
	SD	10.27	9.14	4.24	13.40	
	Min, Max	105, 162	-19, 26	124, 133	-5, 27	
Week 20	n	29	29	5	5	
	Mean	124.6	-0.5	125.8	5.2	-5.68
	Median	123.0	1.0	125.0	5.0	
	Q1, Q3	120.0, 130.0	-5.0, 5.0	124.0, 129.0	0.0, 13.0	
	SD	7.86	7.47	4.32	10.99	
	Min, Max	112, 141	-19, 10	120, 131	-10, 18	
Week 22	n	27	27	4	4	
	Mean	124.4	0.4	125.5	5.8	-5.34
	Median	122.0	-2.0	125.0	4.5	
	Q1, Q3	118.0, 128.0	-8.0, 5.0	120.0, 131.0	-7.5, 19.0	
	SD	12.10	12.06	6.40	15.97	
	Min, Max	110, 176	-21, 37	120, 132	-10, 24	
Week 24	n	26	26	3	3	
	Mean	125.8	0.8	122.0	6.0	-5.19
	Median	125.5	2.0	121.0	4.0	
	Q1, Q3	118.0, 129.0	-8.0, 7.0	120.0, 125.0	0.0, 14.0	
	SD	10.64	9.54	2.65	7.21	
	Min, Max	110, 161	-14, 21	120, 125	0, 14	

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.1)

Vital Sign: Diastolic BP (mmHg)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	74.4		74.2		
	Median	75.0		75.0		
	Q1, Q3	70.0, 80.0		70.0, 79.5		
	SD	6.11		6.46		
	Min, Max	56, 86		56, 84		
Week 2	n	102	102	48	48	
	Mean	76.9	2.5	74.5	0.4	2.11
	Median	79.0	2.0	75.0	0.5	

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
	Q1, Q3	71.0, 80.0	-2.0, 8.0	70.0, 80.0	-5.0, 5.5	
	SD	6.90	7.09	7.35	7.88	
	Min, Max	57, 93	-20, 19	60, 95	-17, 17	
Week 4	n	97	97	47	47	
	Mean	77.3	2.8	73.9	-0.4	3.22
	Median	79.0	2.0	75.0	0.0	
	Q1, Q3	72.0, 80.0	-1.0, 9.0	70.0, 80.0	-5.0, 4.0	
	SD	7.60	7.43	6.75	7.98	
	Min, Max	55, 94	-15, 18	56, 86	-17, 24	
Week 6	n	96	96	45	45	
	Mean	77.6	3.2	73.1	-1.1	4.30
	Median	78.0	1.5	75.0	0.0	
	Q1, Q3	73.5, 80.0	-2.0, 9.0	68.0, 80.0	-7.0, 4.0	
	SD	7.69	8.39	8.17	8.12	
	Min, Max	60, 102	-18, 24	50, 88	-20, 13	
Week 8	n	96	96	44	44	
	Mean	77.3	2.7	73.5	-0.8	3.47
	Median	78.0	2.5	74.0	0.0	
	Q1, Q3	72.0, 80.0	-2.0, 6.0	70.0, 80.0	-4.0, 2.0	
	SD	7.39	8.43	7.10	6.92	
	Min, Max	58, 99	-22, 26	60, 85	-17, 21	
Week 10	n	91	91	43	43	
	Mean	76.7	2.1	73.4	-0.8	2.89
	Median	77.0	0.0	75.0	0.0	
	Q1, Q3	72.0, 80.0	-3.0, 6.0	68.0, 80.0	-5.0, 5.0	
	SD	6.98	7.46	8.08	7.86	
	Min, Max	62, 102	-15, 23	54, 90	-25, 17	
Week 12	n	89	89	44	44	
	Mean	75.7	1.0	74.6	0.3	0.65
	Median	77.0	0.0	74.5	0.0	
	Q1, Q3	70.0, 80.0	-4.0, 5.0	70.5, 79.5	-5.0, 5.0	
	SD	7.41	7.65	5.82	6.98	
	Min, Max	60, 91	-20, 19	54, 83	-17, 14	
Week 14	n	41	41	12	12	
	Mean	77.3	2.7	73.9	1.4	1.24
	Median	78.0	2.0	75.0	0.5	
	Q1, Q3	72.0, 80.0	-2.0, 7.0	70.0, 80.0	-5.0, 9.0	
	SD	6.80	7.22	9.23	10.01	
	Min, Max	60, 95	-10, 22	57, 87	-14, 20	
Week 16	n	36	36	9	9	
	Mean	75.7	0.9	74.3	0.0	0.92
	Median	78.0	0.0	75.0	0.0	
	Q1, Q3	70.0, 80.0	-2.0, 6.0	70.0, 80.0	-7.0, 2.0	
	SD	7.13	7.70	9.03	10.56	
	Min, Max	54, 85	-21, 15	57, 87	-14, 17	
Week 18	n	34	34	4	4	
	Mean	76.2	1.6	78.0	0.8	0.90
	Median	75.5	0.5	78.5	-1.0	

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
	Q1, Q3	70.0, 80.0	-3.0, 6.0	76.0, 80.0	-3.5, 5.0	
	SD	7.57	7.96	2.45	6.50	
	Min, Max	62, 97	-15, 21	75, 80	-5, 10	
Week 20	n	29	29	5	5	
	Mean	77.3	3.0	79.0	6.6	-3.60
	Median	79.0	0.0	80.0	11.0	
	Q1, Q3	74.0, 80.0	0.0, 9.0	78.0, 81.0	0.0, 13.0	
	SD	6.03	5.31	2.55	8.56	
	Min, Max	66, 91	-8, 11	75, 81	-5, 14	
Week 22	n	27	27	4	4	
	Mean	75.8	1.9	79.0	4.8	-2.82
	Median	75.0	1.0	80.0	5.0	
	Q1, Q3	70.0, 80.0	-5.0, 9.0	75.0, 83.0	-5.0, 14.5	
	SD	8.42	8.99	6.63	12.53	
	Min, Max	60, 95	-15, 23	70, 86	-10, 19	
Week 24	n	26	26	3	3	
	Mean	77.2	3.0	77.0	0.7	2.37
	Median	78.0	3.0	76.0	0.0	
	Q1, Q3	75.0, 82.0	-2.0, 10.0	75.0, 80.0	-3.0, 5.0	
	SD	7.28	8.67	2.65	4.04	
	Min, Max	60, 87	-21, 17	75, 80	-3, 5	

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.1)

Vital Sign: Pulse (bpm)

		Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Time Point	Statistic	Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	102		48		
	Mean	75.4		75.5		
	Median	76.0		76.0		
	Q1, Q3	70.0, 80.0		68.5, 82.0		
	SD	9.91		10.97		
	Min, Max	52, 106		53, 101		
Week 2	n	101	101	48	48	
	Mean	73.8	-1.6	75.6	0.1	-1.64
	Median	72.0	-2.0	74.5	0.0	
	Q1, Q3	68.0, 80.0	-6.0, 2.0	68.5, 80.0	-5.0, 4.0	
	SD	10.56	10.18	10.45	8.77	
	Min, Max	52, 102	-27, 39	56, 104	-18, 19	
Week 4	n	97	97	47	47	
	Mean	73.2	-2.3	77.3	1.6	-3.87
	Median	73.0	-2.0	76.0	3.0	
	Q1, Q3	68.0, 79.0	-6.0, 3.0	70.0, 86.0	-5.0, 7.0	
	SD	10.01	8.64	10.83	10.05	
	Min, Max	51, 100	-26, 22	55, 99	-25, 31	
Week 6	n	96	96	45	45	
	Mean	72.4	-3.0	74.2	-1.4	-1.64

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
	Median	72.0	-2.5	76.0	0.0	
	Q1, Q3	66.0, 78.0	-9.0, 2.0	68.0, 80.0	-4.0, 4.0	
	SD	10.46	9.74	11.20	8.41	
	Min, Max	50, 102	-28, 42	53, 100	-27, 12	
Week 8	n	96	96	43	43	
	Mean	74.4	-0.8	75.1	-0.7	-0.18
	Median	74.0	-2.0	76.0	0.0	
	Q1, Q3	68.0, 81.5	-7.0, 3.5	67.0, 80.0	-6.0, 7.0	
	SD	11.00	8.95	10.49	9.13	
	Min, Max	53, 111	-16, 32	54, 111	-18, 20	
Week 10	n	92	92	44	44	
	Mean	75.5	0.3	75.0	-0.7	1.04
	Median	75.0	0.0	74.5	-2.0	
	Q1, Q3	68.0, 82.0	-6.0, 5.0	70.0, 80.0	-7.5, 5.0	
	SD	12.10	10.92	9.68	8.76	
	Min, Max	52, 115	-27, 53	51, 102	-17, 20	
Week 12	n	89	89	44	44	
	Mean	73.9	-1.4	75.4	-0.4	-1.01
	Median	72.0	-1.0	76.5	-1.0	
	Q1, Q3	68.0, 80.0	-5.0, 3.0	69.0, 80.0	-8.0, 5.5	
	SD	11.47	8.33	8.95	10.36	
	Min, Max	51, 115	-22, 31	56, 99	-18, 24	
Week 14	n	41	41	12	12	
	Mean	75.6	-2.8	72.8	-1.2	-1.59
	Median	78.0	-3.0	71.5	-4.0	
	Q1, Q3	70.0, 82.0	-7.0, 2.0	66.0, 78.0	-8.0, 6.0	
	SD	8.98	6.53	9.32	7.93	
	Min, Max	49, 89	-17, 12	60, 90	-9, 12	
Week 16	n	36	36	9	9	
	Mean	77.9	-0.6	79.0	2.3	-2.89
	Median	77.5	0.0	77.0	1.0	
	Q1, Q3	71.0, 80.0	-7.0, 5.5	68.0, 90.0	-4.0, 10.0	
	SD	12.33	9.00	11.59	10.51	
	Min, Max	55, 122	-25, 19	67, 96	-13, 19	
Week 18	n	34	34	4	4	
	Mean	77.8	-0.8	79.5	2.3	-3.01
	Median	78.0	-2.0	76.5	5.5	
	Q1, Q3	75.0, 80.0	-6.0, 4.0	69.5, 89.5	-3.5, 8.0	
	SD	10.63	7.11	13.13	9.74	
	Min, Max	53, 114	-13, 17	68, 97	-12, 10	
Week 20	n	30	30	5	5	
	Mean	77.1	-1.3	80.0	1.6	-2.87
	Median	77.5	-0.5	78.0	4.0	
	Q1, Q3	70.0, 83.0	-8.0, 4.0	78.0, 84.0	1.0, 6.0	
	SD	11.70	8.69	8.83	8.14	
	Min, Max	53, 109	-18, 18	68, 92	-12, 9	
Week 22	n	26	26	4	4	
	Mean	75.2	-3.3	75.3	-5.5	2.15

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
	Median	76.5	-4.5	71.0	-5.0	
	Q1, Q3	69.0, 80.0	-9.0, 1.0	69.0, 81.5	-10.0, -1.0	
	SD	9.20	6.98	10.63	5.51	
	Min, Max	60, 101	-15, 12	68, 91	-12, 0	
Week 24	n	25	25	3	3	
	Mean	75.2	-3.2	77.7	1.3	-4.53
	Median	73.0	-4.0	72.0	2.0	
	Q1, Q3	69.0, 82.0	-9.0, 2.0	68.0, 93.0	0.0, 2.0	
	SD	13.67	8.77	13.43	1.15	
	Min, Max	52, 106	-18, 20	68, 93	0, 2	

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.1)

Vital Sign: Temperature (°C)

Time Point	Statistic	Fostamatinib (N=102) Value	Fostamatinib (N=102) Change from Baseline	Placebo (N=48) Value	Placebo (N=48) Change from Baseline	Difference in Mean Change from Baseline (Fostamatinib - Placebo)
Baseline	n	102		48		
	Mean	36.51		36.53		
	Median	36.50		36.55		
	Q1, Q3	36.30, 36.70		36.40, 36.70		
	SD	0.329		0.343		
	Min, Max	35.8, 37.4		35.2, 37.5		
Week 2	n	101	101	48	48	
	Mean	36.46	-0.05	36.50	-0.03	-0.02
	Median	36.50	0.00	36.50	0.00	
	Q1, Q3	36.40, 36.60	-0.20, 0.10	36.30, 36.70	-0.20, 0.10	
	SD	0.295	0.306	0.334	0.277	
	Min, Max	35.0, 37.2	-1.1, 0.9	35.4, 37.1	-0.7, 0.6	
Week 4	n	95	95	47	47	
	Mean	36.48	-0.02	36.47	-0.06	0.04
	Median	36.50	0.00	36.50	0.00	
	Q1, Q3	36.40, 36.60	-0.20, 0.20	36.30, 36.70	-0.20, 0.10	
	SD	0.346	0.324	0.355	0.291	
	Min, Max	35.3, 37.4	-1.2, 0.8	35.4, 37.1	-0.9, 0.5	
Week 6	n	95	95	45	45	
	Mean	36.48	-0.03	36.48	-0.04	0.02
	Median	36.50	0.00	36.50	-0.10	
	Q1, Q3	36.30, 36.70	-0.20, 0.20	36.30, 36.70	-0.30, 0.10	
	SD	0.371	0.373	0.425	0.335	
	Min, Max	35.1, 37.8	-2.0, 0.9	35.1, 37.3	-0.7, 0.8	
Week 8	n	96	96	43	43	
	Mean	37.09	0.57	36.45	-0.07	0.65
	Median	36.50	0.00	36.50	-0.10	
	Q1, Q3	36.30, 36.60	-0.30, 0.10	36.30, 36.70	-0.20, 0.10	
	SD	6.290	6.282	0.374	0.281	
	Min, Max	35.6, 98.0	-1.3, 61.4	35.2, 37.2	-0.7, 0.7	
Week 10	n	92	92	44	44	
	Mean	36.44	-0.06	36.46	-0.07	0.01

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib - Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
	Median	36.50	0.00	36.50	0.00	
	Q1, Q3	36.35, 36.60	-0.20, 0.10	36.20, 36.70	-0.25, 0.10	
	SD	0.406	0.366	0.390	0.325	
	Min, Max	34.3, 37.3	-1.8, 1.0	35.3, 37.4	-0.9, 0.6	
Week 12	n	90	90	44	44	
	Mean	36.42	-0.09	36.53	0.00	-0.09
	Median	36.45	-0.10	36.50	0.00	
	Q1, Q3	36.30, 36.60	-0.20, 0.00	36.40, 36.70	-0.20, 0.20	
	SD	0.387	0.362	0.398	0.368	
	Min, Max	35.0, 37.4	-1.4, 1.0	35.3, 37.6	-0.8, 0.9	
Week 14	n	39	39	12	12	
	Mean	36.47	0.02	36.47	0.02	0.00
	Median	36.50	0.00	36.55	0.00	
	Q1, Q3	36.40, 36.70	-0.10, 0.20	36.35, 36.65	-0.20, 0.25	
	SD	0.386	0.378	0.380	0.298	
	Min, Max	35.0, 37.5	-1.2, 0.9	35.6, 37.0	-0.5, 0.5	
Week 16	n	36	36	9	9	
	Mean	36.48	-0.02	36.46	-0.01	-0.01
	Median	36.45	0.00	36.40	0.00	
	Q1, Q3	36.40, 36.60	-0.10, 0.10	36.40, 36.80	-0.10, 0.10	
	SD	0.326	0.288	0.500	0.190	
	Min, Max	35.0, 37.2	-1.1, 0.6	35.3, 37.1	-0.3, 0.3	
Week 18	n	34	34	4	4	
	Mean	36.46	-0.04	36.35	0.00	-0.04
	Median	36.45	0.00	36.30	-0.15	
	Q1, Q3	36.30, 36.60	-0.10, 0.10	36.20, 36.50	-0.45, 0.45	
	SD	0.219	0.263	0.252	0.648	
	Min, Max	36.0, 37.0	-0.7, 0.3	36.1, 36.7	-0.6, 0.9	
Week 20	n	30	30	5	5	
	Mean	36.41	-0.06	36.62	-0.02	-0.04
	Median	36.40	0.00	36.60	-0.10	
	Q1, Q3	36.40, 36.60	-0.10, 0.10	36.40, 36.80	-0.10, -0.10	
	SD	0.336	0.390	0.228	0.239	
	Min, Max	35.2, 36.9	-1.1, 0.9	36.4, 36.9	-0.2, 0.4	
Week 22	n	26	26	4	4	
	Mean	36.44	-0.04	36.60	-0.08	0.03
	Median	36.50	0.00	36.60	-0.05	
	Q1, Q3	36.40, 36.60	-0.10, 0.20	36.40, 36.80	-0.40, 0.25	
	SD	0.416	0.380	0.327	0.492	
	Min, Max	35.0, 37.1	-1.1, 0.8	36.2, 37.0	-0.7, 0.5	
Week 24	n	25	25	3	3	
	Mean	36.53	0.04	36.33	0.10	-0.06
	Median	36.50	0.00	36.40	0.10	
	Q1, Q3	36.40, 36.70	-0.10, 0.10	35.60, 37.00	-0.20, 0.40	
	SD	0.256	0.304	0.702	0.300	
	Min, Max	36.0, 37.0	-0.6, 1.0	35.6, 37.0	-0.2, 0.4	

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 6.1.1)

表 2.7.4.9-57 Occurrences of Elevated Blood Pressure at Consecutive Scheduled Visits – Post-Baseline (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Elevated Blood Pressure Category (mmHg)	Number of Consecutive Scheduled Visits	Fostamatinib (N=146) n/N (%)
SBP >= 140 and/or DBP >= 90	>= 2	19/135 (14.1%)
	>= 3	7/129 (5.4%)
SBP >= 160 and/or DBP >= 100	>= 2	1/137 (0.7%)
	>= 3	0/131 (0.0%)
SBP >= 180 and/or DBP >= 110	>= 2	0/138 (0.0%)
	>= 3	0/132 (0.0%)

Note: Subjects falling into one of the elevated blood pressure categories at baseline will be excluded from the results for the given category and any lower categories. For each elevated blood pressure category, percentages are based on the number of such subjects in the Fostamatinib Treated Population: Fostamatinib Exposure Period with at least 2 scheduled post-baseline blood pressure measurements or at least 3 scheduled post-baseline blood pressure measurements, as appropriate, who were not excluded. Each blood pressure assessment was categorized into one category according to the higher of the levels reached by systolic blood pressure and diastolic blood pressure.
(Source: 5.3.5.3.2, Table 6.4.2)

表 2.7.4.9-58 Occurrences of Elevated Blood Pressure at Consecutive Scheduled Visits – Post-Baseline (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Elevated Blood Pressure Category (mmHg)	Number of Consecutive Scheduled Visits	Fostamatinib (N=102) n/N (%)	Placebo (N=48) n/N (%)
SBP >= 140 and/or DBP >= 90	>= 2	15/100 (15.0%)	0/48 (0.0%)
	>= 3	7/99 (7.1%)	0/45 (0.0%)
SBP >= 160 and/or DBP >= 100	>= 2	0/100 (0.0%)	0/48 (0.0%)
	>= 3	0/99 (0.0%)	0/45 (0.0%)
SBP >= 180 and/or DBP >= 110	>= 2	0/100 (0.0%)	0/48 (0.0%)
	>= 3	0/99 (0.0%)	0/45 (0.0%)

Note: Subjects falling into one of the elevated blood pressure categories at baseline will be excluded from the results for the given category and any lower categories. For each elevated blood pressure category and treatment group, percentages are based on the number of such subjects in the Placebo-Controlled Safety Population: Placebo-Controlled Period with at least 2 scheduled post-baseline blood pressure measurements or at least 3 scheduled post-baseline blood pressure measurements, as appropriate. Each blood pressure assessment was categorized into one category according to the higher of the levels reached by systolic blood pressure and diastolic blood pressure.
(Source: 5.3.5.3.2, Table 6.4.1)

表 2.7.4.9-59 Study Drug Exposure by Sex (Placebo-Controlled Safety Population) – C788-047 and C788-048 study

Parameter: Duration of Exposure (weeks)

Sex	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
Female	Fostamatinib	61	15.34	6.26	1.1	12.0	12.1	23.7	24.6
	Placebo	30	12.43	4.63	2.3	11.7	12.1	12.7	24.7
Male	Fostamatinib	41	14.52	6.33	2.4	11.9	12.3	19.9	26.1
	Placebo	18	14.41	4.21	11.9	12.0	12.1	14.6	24.1

(Source: 5.3.5.3.2, Table 6.1.1.1)

Parameter: Mean Total Daily Dose (mg)

Sex	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
Female	Fostamatinib	61	239.98	39.61	140.0	211.0	260.7	266.7	283.3
	Placebo	30	246.21	26.22	187.5	235.5	258.8	265.9	270.2
Male	Fostamatinib	41	242.92	52.91	40.0	223.3	258.2	264.1	389.7
	Placebo	18	246.07	33.87	131.3	231.3	263.0	266.9	267.6

(Source: 5.3.5.3.2, Table 6.1.1.1)

表 2.7.4.9-60 Study Drug Exposure by Sex (Fostamatinib Treated Population) – C788-047, C788-048 and C788-049 study

Parameter: Duration of Exposure (weeks)

Sex	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
Female	Fostamatinib	87	95.91	93.23	1.1	20.9	30.3	197.0	268.1
Male	Fostamatinib	59	62.83	73.57	2.4	13.1	25.9	100.0	247.1

(Source: 5.3.5.3.2, Table 6.1.2.1)

Parameter: Mean Total Daily Dose (mg)

Sex	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
Female	Fostamatinib	87	309.94	122.89	99.1	233.5	265.9	397.1	648.8
Male	Fostamatinib	59	287.17	119.19	40.0	223.8	257.1	309.6	665.7

(Source: 5.3.5.3.2, Table 6.1.2.1)

表 2.7.4.9-61 Study Drug Exposure by Age (Placebo-Controlled Safety Population) – C788-047 and C788-048 study

Parameter: Duration of Exposure (weeks)

Age	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
<65	Fostamatinib	74	15.64	5.93	3.3	12.0	12.6	23.7	26.1
	Placebo	37	13.38	4.44	2.3	12.0	12.1	13.0	24.7
>=65	Fostamatinib	28	13.35	6.94	1.1	10.3	12.1	17.1	24.6
	Placebo	11	12.47	4.99	2.9	12.0	12.4	14.1	23.9

(Source: 5.3.5.3.2, Table 6.1.1.2)

Parameter: Mean Total Daily Dose (mg)

Age	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
<65	Fostamatinib	74	244.98	45.90	40.0	230.3	260.0	266.7	389.7
	Placebo	37	245.81	30.39	131.3	235.5	259.0	265.9	267.6
>=65	Fostamatinib	28	231.06	42.43	141.8	196.1	244.1	263.9	297.9
	Placebo	11	247.31	24.88	190.0	231.3	246.0	268.2	270.2

(Source: 5.3.5.3.2, Table 6.1.1.2)

表 2.7.4.9-62 Study Drug Exposure by Age (Fostamatinib Treated Population) – C788-047, C788-048 and C788-049 study

Parameter: Duration of Exposure (weeks)

Age	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
<65	Fostamatinib	109	91.42	89.71	3.3	17.9	31.3	192.6	256.0
>=65	Fostamatinib	37	56.41	73.95	1.1	10.4	24.3	63.3	268.1

(Source: 5.3.5.3.2, Table 6.1.2.2)

Parameter: Mean Total Daily Dose (mg)

Age	Treatment Group	N	Mean	SD	Min	Q1	Median	Q3	Max
<65	Fostamatinib	109	308.29	124.57	40.0	230.6	266.3	373.5	665.7
>=65	Fostamatinib	37	278.49	110.63	141.8	219.1	249.3	275.2	565.1

(Source: 5.3.5.3.2, Table 6.1.2.2)

表 2.7.4.9-63 Occurrence of Adverse Events and Adverse Drug Reactions with Interest – R788-1301 study

Non-Dosing Period

	Adverse Events			Adverse Drug Reactions		
Category, PT	n	%	e	n	%	e
N	12	---	---	12	---	---
Total	4	33.3	5	0	0.0	0
Gastrointestinal Complaints	2	16.7	2	0	0.0	0
Abdominal Pain	2	16.7	2	0	0.0	0
Abdominal discomfort	1	8.3	1	0	0.0	0
Abdominal pain upper	1	8.3	1	0	0.0	0
Infection	2	16.7	2	0	0.0	0
Tinea infection	1	8.3	1	0	0.0	0
Viral infection	1	8.3	1	0	0.0	0
Drug Related Hepatic Disorders SMQ	1	8.3	1	0	0.0	0
Hepatic cyst	1	8.3	1	0	0.0	0

(Source: 5.3.5.1.1, Table 14.6.4.1.3.2)

表 2.7.4.9-64 Occurrence of Adverse Events with Interest - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	22	66.7	14	42.4
Gastrointestinal Disorders	19	57.6	11	33.3
Abdominal discomfort	3	9.1	1	3.0
Abdominal pain	1	3.0	0	0.0
Abdominal pain upper	1	3.0	0	0.0
Constipation	5	15.2	0	0.0
Diarrhoea	13	39.4	10	30.3
Faeces soft	1	3.0	0	0.0
Mouth haemorrhage	1	3.0	1	3.0
Nausea	1	3.0	1	3.0
Stomatitis	2	6.1	1	3.0
Vomiting	1	3.0	0	0.0
Leukopenia	5	15.2	4	12.1
Leukopenia	1	3.0	1	3.0
Neutropenia	2	6.1	1	3.0
Neutrophil count decreased	3	9.1	3	9.1
White blood cell count decreased	1	3.0	1	3.0

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-65 Occurrence of Adverse Events with Interest Leading to Dose Interruption - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	1	3.0	0	0.0
Gastrointestinal Disorders	1	3.0	0	0.0
Nausea	1	3.0	0	0.0

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-66 Occurrence of Adverse Events with Interest Leading to Dose Reduction - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	9	27.3	8	24.2
Gastrointestinal Disorders	5	15.2	5	15.2
Abdominal discomfort	1	3.0	1	3.0
Diarrhoea	4	12.1	4	12.1
Leukopenia	4	12.1	3	9.1
Neutropenia	2	6.1	1	3.0
Neutrophil count decreased	2	6.1	2	6.1

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-67 Occurrence of Adverse Events with Interest Leading to Study Drug Withdrawal - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	1	3.0	1	3.0
Gastrointestinal Disorders	1	3.0	1	3.0
Diarrhoea	1	3.0	1	3.0

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-68 Occurrence of Mild Adverse Events with Interest - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	22	66.7	14	42.4
Gastrointestinal Disorders	19	57.6	11	33.3
Abdominal discomfort	3	9.1	1	3.0
Abdominal pain	1	3.0	0	0.0
Abdominal pain upper	1	3.0	0	0.0
Constipation	5	15.2	0	0.0
Diarrhoea	13	39.4	10	30.3
Faeces soft	1	3.0	0	0.0
Mouth haemorrhage	1	3.0	1	3.0
Nausea	1	3.0	1	3.0
Stomatitis	2	6.1	1	3.0
Vomiting	1	3.0	0	0.0
Leukopenia	5	15.2	4	12.1
Leukopenia	1	3.0	1	3.0
Neutropenia	2	6.1	1	3.0
Neutrophil count decreased	3	9.1	3	9.1
White blood cell count decreased	1	3.0	1	3.0

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-69 Occurrence of Moderate Adverse Events with Interest - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	2	6.1	2	6.1
Gastrointestinal Disorders	2	6.1	2	6.1
Diarrhoea	2	6.1	2	6.1

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-70 Occurrence of Severe Adverse Events with Interest - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	1	3.0	1	3.0
Gastrointestinal Disorders	1	3.0	1	3.0
Diarrhoea	1	3.0	1	3.0

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-71 Occurrence of Serious Adverse Events with Interest - R788-1301

R788 Treatment Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	33	---	33	---
Total	1	3.0	1	3.0
Gastrointestinal Disorders	1	3.0	1	3.0
Diarrhoea	1	3.0	1	3.0

MedDRA version 23.0
（Source: 1.13.3-5, C-07 付録 220823-C-07）

表 2.7.4.9-72 Occurrence of Adverse Events with Interest - R788-1301

Placebo-Controlled Period

Category, PT	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	15	68.2	0	0.0	12	54.5	0	0.0
Gastrointestinal Disorders	11	50.0	0	0.0	9	40.9	0	0.0
Abdominal discomfort	2	9.1	0	0.0	1	4.5	0	0.0
Constipation	2	9.1	0	0.0	0	0.0	0	0.0
Diarrhoea	9	40.9	0	0.0	7	31.8	0	0.0
Mouth haemorrhage	1	4.5	0	0.0	1	4.5	0	0.0
Nausea	1	4.5	0	0.0	1	4.5	0	0.0
Stomatitis	1	4.5	0	0.0	1	4.5	0	0.0
Leukopenia	5	22.7	0	0.0	4	18.2	0	0.0
Leukopenia	1	4.5	0	0.0	1	4.5	0	0.0
Neutropenia	1	4.5	0	0.0	0	0.0	0	0.0
Neutrophil count decreased	3	13.6	0	0.0	3	13.6	0	0.0
White blood cell count decreased	1	4.5	0	0.0	1	4.5	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-73 Occurrence of Adverse Events with Interest Leading to Dose Interruption - R788-1301

Placebo-Controlled Period

Category, PT	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	0	0.0	0	0.0	0	0.0	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-74 Occurrence of Adverse Events with Interest Leading to Dose Reduction - R788-1301

Placebo-Controlled Period

Category, PT	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	6	27.3	0	0.0	5	22.7	0	0.0
Gastrointestinal Disorders	3	13.6	0	0.0	3	13.6	0	0.0
Diarrhoea	3	13.6	0	0.0	3	13.6	0	0.0
Leukopenia	3	13.6	0	0.0	2	9.1	0	0.0
Neutropenia	1	4.5	0	0.0	0	0.0	0	0.0
Neutrophil count decreased	2	9.1	0	0.0	2	9.1	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-75 Occurrence of Adverse Events with Interest Leading to Study Drug Withdrawal - R788-1301

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	1	4.5	0	0.0	1	4.5	0	0.0
Gastrointestinal Disorders	1	4.5	0	0.0	1	4.5	0	0.0
Diarrhoea	1	4.5	0	0.0	1	4.5	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-76 Occurrence of Mild Adverse Events with Interest - R788-1301

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	15	68.2	0	0.0	12	54.5	0	0.0
Gastrointestinal Disorders	11	50.0	0	0.0	9	40.9	0	0.0
Abdominal discomfort	2	9.1	0	0.0	1	4.5	0	0.0
Constipation	2	9.1	0	0.0	0	0.0	0	0.0
Diarrhoea	9	40.9	0	0.0	7	31.8	0	0.0
Mouth haemorrhage	1	4.5	0	0.0	1	4.5	0	0.0
Nausea	1	4.5	0	0.0	1	4.5	0	0.0
Stomatitis	1	4.5	0	0.0	1	4.5	0	0.0
Leukopenia	5	22.7	0	0.0	4	18.2	0	0.0
Leukopenia	1	4.5	0	0.0	1	4.5	0	0.0
Neutropenia	1	4.5	0	0.0	0	0.0	0	0.0
Neutrophil count decreased	3	13.6	0	0.0	3	13.6	0	0.0
White blood cell count decreased	1	4.5	0	0.0	1	4.5	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-77 Occurrence of Moderate Adverse Events with Interest - R788-1301

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	2	9.1	0	0.0	2	9.1	0	0.0
Gastrointestinal Disorders	2	9.1	0	0.0	2	9.1	0	0.0
Diarrhoea	2	9.1	0	0.0	2	9.1	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-78 Occurrence of Severe Adverse Events with Interest - R788-1301

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	1	4.5	0	0.0	1	4.5	0	0.0
Gastrointestinal Disorders	1	4.5	0	0.0	1	4.5	0	0.0
Diarrhoea	1	4.5	0	0.0	1	4.5	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-79 Occurrence of Serious Adverse Events with Interest - R788-1301

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	22	---	12	---	22	---	12	---
Total	1	4.5	0	0.0	1	4.5	0	0.0
Gastrointestinal Disorders	1	4.5	0	0.0	1	4.5	0	0.0
Diarrhoea	1	4.5	0	0.0	1	4.5	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-80 Occurrence of Adverse Events with Interest - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

	Adverse Events		Adverse Drug Reactions	
Category, PT	n	%	n	%
N	146	---	146	---
Total	84	57.5	61	41.8
Gastrointestinal Disorders	81	55.5	57	39.0
Abdominal Discomfort	2	1.4	1	0.7
Abdominal Distension	4	2.7	3	2.1
Abdominal Pain	9	6.2	5	3.4
Abdominal Pain Lower	1	0.7	0	0.0
Abdominal Pain Upper	8	5.5	4	2.7
Constipation	8	5.5	5	3.4
Diarrhoea	53	36.3	46	31.5
Dyspepsia	6	4.1	3	2.1
Eructation	1	0.7	1	0.7
Flatulence	6	4.1	4	2.7
Frequent Bowel Movements	2	1.4	1	0.7
Gastric Antral Vascular Ectasia	1	0.7	0	0.0
Gastritis	2	1.4	1	0.7
Gastritis Erosive	1	0.7	0	0.0
Gastrointestinal Haemorrhage	4	2.7	0	0.0
Gastrooesophageal Reflux Disease	2	1.4	1	0.7
Haematochezia	4	2.7	0	0.0
Haemorrhoidal Haemorrhage	3	2.1	1	0.7
Melaena	1	0.7	0	0.0
Mouth Haemorrhage	6	4.1	0	0.0
Mucosal Haemorrhage	1	0.7	0	0.0
Nausea	28	19.2	18	12.3
Oesophageal Pain	1	0.7	1	0.7
Rectal Haemorrhage	3	2.1	0	0.0
Stomatitis	2	1.4	0	0.0
Vomiting	13	8.9	3	2.1
Leukopenia	12	8.2	8	5.5
Febrile Neutropenia	1	0.7	1	0.7
Leukopenia	3	2.1	1	0.7
Lymphocyte Count Decreased	1	0.7	0	0.0
Neutropenia	8	5.5	5	3.4
Neutrophil Count Decreased	2	1.4	2	1.4

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-81 Occurrence of Adverse Events with Interest Leading to Dose Interruption - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	10	6.8	7	4.8
Gastrointestinal Disorders	8	5.5	5	3.4
Abdominal Pain	2	1.4	1	0.7
Diarrhoea	5	3.4	4	2.7
Vomiting	1	0.7	0	0.0
Leukopenia	2	1.4	2	1.4
Febrile Neutropenia	1	0.7	1	0.7
Neutrophil Count Decreased	1	0.7	1	0.7

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-82 Occurrence of Adverse Events with Interest Leading to Dose Reduction - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	5	3.4	5	3.4
Gastrointestinal Disorders	4	2.7	4	2.7
Diarrhoea	4	2.7	4	2.7
Leukopenia	2	1.4	2	1.4
Febrile Neutropenia	1	0.7	1	0.7
Neutrophil Count Decreased	1	0.7	1	0.7

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-83 Occurrence of Adverse Events with Interest Leading to Study Drug Withdrawal - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	11	7.5	11	7.5
Gastrointestinal Disorders	8	5.5	8	5.5
Abdominal Pain	1	0.7	1	0.7
Abdominal Pain Upper	1	0.7	1	0.7
Diarrhoea	6	4.1	6	4.1
Leukopenia	3	2.1	3	2.1
Neutropenia	3	2.1	3	2.1

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-84 Occurrence of Mild Adverse Events with Interest - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	70	47.9	50	34.2
Gastrointestinal Disorders	68	46.6	47	32.2
Abdominal Discomfort	2	1.4	1	0.7
Abdominal Distension	4	2.7	3	2.1
Abdominal Pain	7	4.8	4	2.7
Abdominal Pain Lower	1	0.7	0	0.0
Abdominal Pain Upper	8	5.5	4	2.7
Constipation	8	5.5	5	3.4
Diarrhoea	41	28.1	34	23.3
Dyspepsia	6	4.1	3	2.1
Eructation	1	0.7	1	0.7
Flatulence	4	2.7	3	2.1
Frequent Bowel Movements	2	1.4	1	0.7
Gastritis	2	1.4	1	0.7
Gastritis Erosive	1	0.7	0	0.0
Gastrointestinal Haemorrhage	2	1.4	0	0.0
Gastrooesophageal Reflux Disease	2	1.4	1	0.7
Haematochezia	3	2.1	0	0.0
Haemorrhoidal Haemorrhage	3	2.1	1	0.7
Mouth Haemorrhage	4	2.7	0	0.0
Mucosal Haemorrhage	1	0.7	0	0.0
Nausea	25	17.1	16	11.0
Oesophageal Pain	1	0.7	1	0.7
Rectal Haemorrhage	1	0.7	0	0.0
Stomatitis	2	1.4	0	0.0
Vomiting	12	8.2	3	2.1
Leukopenia	9	6.2	6	4.1
Leukopenia	3	2.1	1	0.7
Neutropenia	5	3.4	3	2.1
Neutrophil Count Decreased	2	1.4	2	1.4

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-85 Occurrence of Moderate Adverse Events with Interest - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	41	28.1	33	22.6
Gastrointestinal Disorders	37	25.3	29	19.9
Abdominal Pain	3	2.1	2	1.4
Diarrhoea	27	18.5	25	17.1
Flatulence	3	2.1	1	0.7
Gastrointestinal Haemorrhage	3	2.1	0	0.0
Melaena	1	0.7	0	0.0
Mouth Haemorrhage	2	1.4	0	0.0
Mucosal Haemorrhage	1	0.7	0	0.0
Nausea	3	2.1	2	1.4
Rectal Haemorrhage	1	0.7	0	0.0
Vomiting	1	0.7	0	0.0
Leukopenia	6	4.1	4	2.7
Febrile Neutropenia	1	0.7	1	0.7
Lymphocyte Count Decreased	1	0.7	0	0.0
Neutropenia	4	2.7	3	2.1

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-86 Occurrence of Severe Adverse Events with Interest - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	9	6.2	4	2.7
Gastrointestinal Disorders	7	4.8	2	1.4
Diarrhoea	3	2.1	2	1.4
Gastric Antral Vascular Ectasia	1	0.7	0	0.0
Gastrointestinal Haemorrhage	1	0.7	0	0.0
Haematochezia	1	0.7	0	0.0
Melaena	1	0.7	0	0.0
Mucosal Haemorrhage	1	0.7	0	0.0
Rectal Haemorrhage	1	0.7	0	0.0
Leukopenia	2	1.4	2	1.4
Febrile Neutropenia	1	0.7	1	0.7
Neutropenia	1	0.7	1	0.7

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-87 Occurrence of Serious Adverse Events with Interest - C788-047, C788-048 and C788-049

Fostamatinib Exposure Period

Category, PT	Adverse Events		Adverse Drug Reactions	
	n	%	n	%
N	146	---	146	---
Total	9	6.2	3	2.1
Gastrointestinal Disorders	8	5.5	2	1.4
Diarrhoea	2	1.4	2	1.4
Gastric Antral Vascular Ectasia	1	0.7	0	0.0
Gastrointestinal Haemorrhage	2	1.4	0	0.0
Haematochezia	1	0.7	0	0.0
Melaena	1	0.7	0	0.0
Mouth Haemorrhage	1	0.7	0	0.0
Mucosal Haemorrhage	1	0.7	0	0.0
Rectal Haemorrhage	1	0.7	0	0.0
Leukopenia	1	0.7	1	0.7
Febrile Neutropenia	1	0.7	1	0.7

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-88 Occurrence of Adverse Events with Interest - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	51	50.0	14	29.2	41	40.2	9	18.8
Gastrointestinal Disorders	47	46.1	14	29.2	38	37.3	9	18.8
Abdominal Discomfort	1	1.0	1	2.1	1	1.0	1	2.1
Abdominal Distension	2	2.0	0	0.0	2	2.0	0	0.0
Abdominal Pain	3	2.9	0	0.0	3	2.9	0	0.0
Abdominal Pain Upper	3	2.9	1	2.1	1	1.0	1	2.1
Anal Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Constipation	3	2.9	1	2.1	3	2.9	1	2.1
Diarrhoea	30	29.4	7	14.6	27	26.5	6	12.5
Dyspepsia	3	2.9	1	2.1	1	1.0	1	2.1
Eructation	1	1.0	0	0.0	1	1.0	0	0.0
Flatulence	5	4.9	1	2.1	3	2.9	1	2.1
Frequent Bowel Movements	2	2.0	0	0.0	1	1.0	0	0.0
Gastric Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Gastritis	1	1.0	0	0.0	1	1.0	0	0.0
Gastrointestinal Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Gastrooesophageal Reflux Disease	1	1.0	0	0.0	1	1.0	0	0.0
Haematochezia	1	1.0	0	0.0	0	0.0	0	0.0
Melaena	0	0.0	1	2.1	0	0.0	0	0.0
Nausea	19	18.6	4	8.3	15	14.7	3	6.3
Oesophageal Pain	1	1.0	0	0.0	1	1.0	0	0.0
Rectal Haemorrhage	0	0.0	2	4.2	0	0.0	0	0.0
Vomiting	3	2.9	3	6.3	1	1.0	1	2.1
Leukopenia	10	9.8	0	0.0	7	6.9	0	0.0
Febrile Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0
Leukopenia	3	2.9	0	0.0	1	1.0	0	0.0
Lymphocyte Count Decreased	1	1.0	0	0.0	0	0.0	0	0.0
Neutropenia	5	4.9	0	0.0	4	3.9	0	0.0
Neutrophil Count Decreased	2	2.0	0	0.0	2	2.0	0	0.0

MedDRA version 18.1

（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-89 Occurrence of Adverse Events with Interest Leading to Dose Interruption - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	5	4.9	2	4.2	4	3.9	1	2.1
Gastrointestinal Disorders	3	2.9	2	4.2	2	2.0	1	2.1
Diarrhoea	3	2.9	0	0.0	2	2.0	0	0.0
Dyspepsia	0	0.0	1	2.1	0	0.0	1	2.1
Gastrointestinal Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Leukopenia	2	2.0	0	0.0	2	2.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0
Neutrophil Count Decreased	1	1.0	0	0.0	1	1.0	0	0.0

MedDRA version 18.1

（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-90 Occurrence of Adverse Events with Interest Leading to Dose Reduction - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	3	2.9	0	0.0	3	2.9	0	0.0
Gastrointestinal Disorders	2	2.0	0	0.0	2	2.0	0	0.0
Diarrhoea	2	2.0	0	0.0	2	2.0	0	0.0
Leukopenia	2	2.0	0	0.0	2	2.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0
Neutrophil Count Decreased	1	1.0	0	0.0	1	1.0	0	0.0

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-91 Occurrence of Adverse Events with Interest Leading to Study Drug Withdrawal - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	4	3.9	2	4.2	4	3.9	2	4.2
Gastrointestinal Disorders	2	2.0	2	4.2	2	2.0	2	4.2
Abdominal Discomfort	0	0.0	1	2.1	0	0.0	1	2.1
Abdominal Pain	1	1.0	0	0.0	1	1.0	0	0.0
Diarrhoea	1	1.0	1	2.1	1	1.0	1	2.1
Leukopenia	2	2.0	0	0.0	2	2.0	0	0.0
Neutropenia	2	2.0	0	0.0	2	2.0	0	0.0

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-92 Occurrence of Mild Adverse Events with Interest - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	43	42.2	13	27.1	37	36.3	8	16.7
Gastrointestinal Disorders	40	39.2	13	27.1	34	33.3	8	16.7
Abdominal Discomfort	1	1.0	1	2.1	1	1.0	1	2.1
Abdominal Distension	2	2.0	0	0.0	2	2.0	0	0.0
Abdominal Pain	2	2.0	0	0.0	2	2.0	0	0.0
Abdominal Pain Upper	3	2.9	1	2.1	1	1.0	1	2.1
Anal Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Constipation	3	2.9	1	2.1	3	2.9	1	2.1
Diarrhoea	26	25.5	6	12.5	23	22.5	5	10.4
Dyspepsia	3	2.9	0	0.0	1	1.0	0	0.0
Eructation	1	1.0	0	0.0	1	1.0	0	0.0
Flatulence	2	2.0	1	2.1	2	2.0	1	2.1
Frequent Bowel Movements	2	2.0	0	0.0	1	1.0	0	0.0
Gastric Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Gastritis	1	1.0	0	0.0	1	1.0	0	0.0
Gastrooesophageal Reflux Disease	1	1.0	0	0.0	1	1.0	0	0.0
Haematochezia	1	1.0	0	0.0	0	0.0	0	0.0
Nausea	16	15.7	4	8.3	13	12.7	3	6.3
Oesophageal Pain	1	1.0	0	0.0	1	1.0	0	0.0
Rectal Haemorrhage	0	0.0	2	4.2	0	0.0	0	0.0
Vomiting	3	2.9	3	6.3	1	1.0	1	2.1
Leukopenia	8	7.8	0	0.0	6	5.9	0	0.0
Leukopenia	3	2.9	0	0.0	1	1.0	0	0.0
Neutropenia	4	3.9	0	0.0	3	2.9	0	0.0
Neutrophil Count Decreased	2	2.0	0	0.0	2	2.0	0	0.0

MedDRA version 18.1

（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-93 Occurrence of Moderate Adverse Events with Interest - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	20	19.6	3	6.3	15	14.7	1	2.1
Gastrointestinal Disorders	16	15.7	3	6.3	12	11.8	1	2.1
Abdominal Pain	1	1.0	0	0.0	1	1.0	0	0.0
Diarrhoea	10	9.8	1	2.1	9	8.8	1	2.1
Dyspepsia	0	0.0	1	2.1	0	0.0	1	2.1
Flatulence	3	2.9	0	0.0	1	1.0	0	0.0
Melaena	0	0.0	1	2.1	0	0.0	0	0.0
Nausea	3	2.9	0	0.0	2	2.0	0	0.0
Vomiting	0	0.0	1	2.1	0	0.0	0	0.0
Leukopenia	4	3.9	0	0.0	3	2.9	0	0.0
Febrile Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0
Lymphocyte Count Decreased	1	1.0	0	0.0	0	0.0	0	0.0
Neutropenia	2	2.0	0	0.0	2	2.0	0	0.0

MedDRA version 18.1

（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-94 Occurrence of Severe Adverse Events with Interest - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	3	2.9	1	2.1	3	2.9	0	0.0
Gastrointestinal Disorders	1	1.0	1	2.1	1	1.0	0	0.0
Diarrhoea	1	1.0	0	0.0	1	1.0	0	0.0
Gastrointestinal Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Leukopenia	2	2.0	0	0.0	2	2.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0
Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-95 Occurrence of Serious Adverse Events with Interest - C788-047 and C788-048

Placebo-Controlled Period

	Adverse Events				Adverse Drug Reactions			
	R788		Placebo		R788		Placebo	
Category, PT	n	%	n	%	n	%	n	%
N	102	---	48	---	102	---	48	---
Total	2	2.0	1	2.1	2	2.0	0	0.0
Gastrointestinal Disorders	1	1.0	1	2.1	1	1.0	0	0.0
Diarrhoea	1	1.0	0	0.0	1	1.0	0	0.0
Gastrointestinal Haemorrhage	0	0.0	1	2.1	0	0.0	0	0.0
Leukopenia	1	1.0	0	0.0	1	1.0	0	0.0
Febrile Neutropenia	1	1.0	0	0.0	1	1.0	0	0.0

MedDRA version 18.1
（Source: 1.13.3-4, C-07 付録 C-07-1）

表 2.7.4.9-96　収縮期血圧 140 mmHg 以上又は拡張期血圧 90 mmHg 以上の上昇に該当した被験者の血圧の一覧表（R788-1301 試験）

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	134	114	127	95	82	87
		SCREEN B	20[redacted]	130	136	133	90	90	88
		DAY 1	20[redacted]	133	127	129	81	82	85
		WEEK 2	20[redacted]	144	140	134	90	94	90
		WEEK 4	20[redacted]	144	133	136	95	82	81
		WEEK 6	20[redacted]	142	141	142	93	95	92
		WEEK 8	20[redacted]	141	145	137	103	91	91
		WEEK 10	20[redacted]	141	142	136	90	91	89
		WEEK 12	20[redacted]	135	135	142	95	92	95
		WEEK 14	20[redacted]	141	132	144	95	82	98
		WEEK 16	20[redacted]	147	146	138	87	99	87
		WEEK 18	20[redacted]	137	138	128	92	88	85
		WEEK 20	20[redacted]	130	129	128	81	78	85
		WEEK 22	20[redacted]	128	129	128	85	78	75
		WEEK 24	20[redacted]	138	140	129	84	87	86
		WEEK 28	20[redacted]	128			75		
		WEEK 32	20[redacted]	118	120	121	85	83	85
		WEEK 36	20[redacted]	133	135	131	88	85	85
		WEEK 40	20[redacted]	133	135	131	88	87	88
		WEEK 44	20[redacted]	127	131	133	93	95	93
		WEEK 48	20[redacted]	130	129	133	81	85	81
		WEEK 52	20[redacted]	149	135	137	84	85	82
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	128			68		
		SCREEN B	20[redacted]	126			66		
		DAY 1	20[redacted]	117			61		
		WEEK 2	20[redacted]	152	150	162	79	87	84
		WEEK 4	20[redacted]	165	158	185	88	87	91
		WEEK 6	20[redacted]	152	141	140	78	75	75
		WEEK 8	20[redacted]	142	133	136	83	72	73
		WEEK 10	20[redacted]	145	130	134	74	69	72
		WEEK 12	20[redacted]	139	163	166	69	88	87
		WEEK 14	20[redacted]	131	121	123	67	69	66
		WEEK 16	20[redacted]	116			62		
		WEEK 16 UNSCHEDULED 1	20[redacted]	107			55		
		WEEK 18	20[redacted]	98			67		
		WEEK 20	20[redacted]	135	135	118	71	71	58
		WEEK 22	20[redacted]	131	125	136	70	70	69
		WEEK 24	20[redacted]	135	128	146	72	69	78
		WEEK 28	20[redacted]	130			69		
		WEEK 32	20[redacted]	146	144	132	82	72	72
		WEEK 36	20[redacted]	132	136	148	71	72	81
		WEEK 40	20[redacted]	156	127	128	78	69	65
		WEEK 44	20[redacted]	121			64		
		WEEK 48	20[redacted]	126			61		
		WEEK 52	20[redacted]	130			64		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	129			73		
		SCREEN B	20[redacted]	122			71		
		DAY 1	20[redacted]	125			75		
		WEEK 2	20[redacted]	128			76		
		WEEK 2 UNSCHEDULED 1	20[redacted]	93			56		
		WEEK 4	20[redacted]	127			74		
		WEEK 4 UNSCHEDULED 2	20[redacted]	139			76		
		WEEK 6	20[redacted]	137			74		
		WEEK 6 UNSCHEDULED 1	20[redacted]	137			74		
		WEEK 8	20[redacted]	145	137	123	83	79	73

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		WEEK 10	20[redacted]	146	132	132	70	78	74
		WEEK 12	20[redacted]	128			74		
		WEEK 14	20[redacted]	145	135	125	81	81	72
		WEEK 16	20[redacted]	129			72		
		WEEK 18	20[redacted]	127			76		
		WEEK 20	20[redacted]	120			66		
		WEEK 22	20[redacted]	152	140	143	83	77	83
		WEEK 24	20[redacted]	150	131	132	78	80	80
		WEEK 28	20[redacted]	115			67		
		WEEK 32	20[redacted]	121			69		
		WEEK 36	20[redacted]	120			66		
		WEEK 40	20[redacted]	124			72		
		WEEK 44	20[redacted]	125			78		
		WEEK 48	20[redacted]	117			70		
		WEEK 52	20[redacted]	119			63		
R788-1301 [redacted]	R788	SCREEN A	20[redacted]	134	125	147	73	64	75
		SCREEN B	20[redacted]	145	127	122	69	74	73
		DAY 1	20[redacted]	116			59		
		DAY 1 UNSCHEDULED 1	20[redacted]	145	158	149	91	91	96
		WEEK 2	20[redacted]	132	129	131	74	79	76
		WEEK 4	20[redacted]	155	171	117	85	76	73
		WEEK 4 UNSCHEDULED 1	20[redacted]						
		WEEK 4 UNSCHEDULED 2	20[redacted]	118			70		
		WEEK 6	20[redacted]	120			66		
		WEEK 6 UNSCHEDULED 2	20[redacted]	114			62		
		WEEK 8	20[redacted]	139	133	124	82	73	70
		WEEK 10	20[redacted]	113			64		
		WEEK 12	20[redacted]	125			74		
		DBP DISCONTINUATION	20[redacted]	111			71		
		FOLLOW-UP	20[redacted]	139	131	112	81	73	69
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	127			74		
		SCREEN B	20[redacted]	125			76		
		DAY 1	20[redacted]	112			75		
		WEEK 2	20[redacted]	125	129	135	84	81	85
		WEEK 4	20[redacted]	139	141	134	86	94	87
		WEEK 6	20[redacted]	127	126	120	92	87	84
		WEEK 8	20[redacted]	139	128	135	95	83	96
		WEEK 10	20[redacted]	147	138	152	99	98	99
		WEEK 12	20[redacted]	128	146	142	90	89	92
		DBP DISCONTINUATION	20[redacted]	128	132	135	90	88	90
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	139	139	135	96	96	91
		EARLY SHIFT WEEK 4	20[redacted]	125	132	128	88	88	82
		EARLY SHIFT WEEK 8	20[redacted]	126	128	131	87	83	88
		EARLY SHIFT WEEK 12	20[redacted]	144	154	144	103	100	97
		EARLY SHIFT WEEK 16	20[redacted]	136	144	141	99	104	98
		EARLY SHIFT WEEK 20	20[redacted]	137	141	139	99	97	90
		EARLY SHIFT WEEK 24	20[redacted]	139	126	130	91	87	86
		EARLY SHIFT WEEK 28	20[redacted]	127	134	120	83	83	86
		EARLY SHIFT WEEK 28 UNSCHEDULED 1	20[redacted]	141	135	134	90	94	92
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	137	136	130	68	63	64
		SCREEN B	20[redacted]	129			58		
		DAY 1	20[redacted]	137	136	134	57	55	57
		DAY 1 UNSCHEDULED 1	20[redacted]	142	142	141	84	73	72
		WEEK 2	20[redacted]	142	142	144	70	71	74
		WEEK 4	20[redacted]	136	136	140	77	77	73
		WEEK 6	20[redacted]	146	153	144	78	87	71

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		WEEK 8	20[redacted]	132	131	138	78	64	64
		WEEK 10	20[redacted]	132	137	137	73	68	71
		WEEK 12	20[redacted]	146	133	123	65	73	63
		WEEK 14	20[redacted]	125			67		
		WEEK 16	20[redacted]	128			73		
		WEEK 16 UNSCHEDULED 1	20[redacted]	131	138	134	69	74	70
		WEEK 18	20[redacted]	134	126	136	69	69	69
		WEEK 20	20[redacted]	137	128	127	70	52	73
		WEEK 22	20[redacted]	133	138	139	76	74	79
		WEEK 24	20[redacted]	140	139	128	74	80	69
		WEEK 24 UNSCHEDULED 1	20[redacted]	140	121	122	67	63	62
		WEEK 28	20[redacted]	143	126	135	75	78	73
		WEEK 32	20[redacted]	133	121	131	54	62	73
		WEEK 32 UNSCHEDULED 1	20[redacted]	126			76		
		WEEK 36	20[redacted]	134	139	132	68	66	75
		WEEK 40	20[redacted]	138	127	141	70	68	66
		WEEK 44	20[redacted]	139	123	115	68	55	63
		WEEK 48	20[redacted]	147	138	145	84	78	67
		WEEK 48 UNSCHEDULED 1	20[redacted]	122			70		
		WEEK 52	20[redacted]	141	134	127	68	69	70
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	124			61		
		SCREEN B	20[redacted]	126			62		
		DAY 1	20[redacted]	110			58		
		WEEK 2	20[redacted]	128			69		
		WEEK 4	20[redacted]	126			72		
		WEEK 6	20[redacted]	127			71		
		WEEK 8	20[redacted]	126			73		
		WEEK 10	20[redacted]	126			73		
		WEEK 12	20[redacted]	147	144	141	75	76	76
		WEEK 12 UNSCHEDULED 1	20[redacted]	159	150	152	67	79	76
		WEEK 14	20[redacted]	116			60		
		WEEK 16	20[redacted]	125			73		
		WEEK 18	20[redacted]	129			66		
		WEEK 20	20[redacted]	120			73		
		WEEK 22	20[redacted]	117			72		
		WEEK 24	20[redacted]	125			78		
		WEEK 28	20[redacted]	102			53		
		WEEK 32	20[redacted]	123			66		
		WEEK 36	20[redacted]	129			69		
		WEEK 40	20[redacted]	123			59		
		WEEK 44	20[redacted]	107			61		
		WEEK 48	20[redacted]	122			68		
		WEEK 52	20[redacted]	120			66		
		FOLLOW-UP	20[redacted]	111			61		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	138	140	138	84	88	82
		SCREEN B	20[redacted]	138	140	138	86	88	86
		DAY 1	20[redacted]	150	138	128	82	78	70
		WEEK 2	20[redacted]	152	146	148	84	84	88
		WEEK 4	20[redacted]	162	148	158	90	76	88
		WEEK 6	20[redacted]	168	162	162	78	80	82
		WEEK 8	20[redacted]	148	148	150	78	80	78
		WEEK 10	20[redacted]	148	152	154	82	88	90
		DBP DISCONTINUATION	20[redacted]	128			78		
		EARLY SHIFT WEEK 4	20[redacted]	126			72		
		EARLY SHIFT WEEK 8	20[redacted]	120			76		
		EARLY SHIFT WEEK 12	20[redacted]	136	130	120	78	80	78
		EARLY SHIFT WEEK 16	20[redacted]	126			74		
		EARLY SHIFT WEEK 20	20[redacted]	128			76		

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		EARLY SHIFT WEEK 24	20[redacted]	114			74		
		EARLY SHIFT WEEK 28	20[redacted]	116			66		
		FOLLOW-UP	20[redacted]	124			66		
		FOLLOW-UP UNSCHEDULED 1	20[redacted]	138			76		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	133	133	139	89	93	81
		SCREEN B	20[redacted]	126			80		
		DAY 1	20[redacted]	126			77		
		WEEK 2	20[redacted]	147	151	147	97	98	93
		WEEK 4	20[redacted]	142	138	143	92	94	93
		WEEK 6	20[redacted]	139	137	137	82	89	82
		WEEK 8	20[redacted]	145	148	124	89	95	89
		WEEK 10	20[redacted]	126	133	134	86	91	88
		WEEK 12	20[redacted]	134	130	137	83	91	89
		WEEK 14	20[redacted]	141	140	136	91	91	85
		WEEK 16	20[redacted]	131	133	127	79	80	78
		WEEK 18	20[redacted]	142	138	142	83	89	80
		WEEK 20	20[redacted]	123			73		
		WEEK 22	20[redacted]	132	136	122	80	84	72
		WEEK 24	20[redacted]	136	139	136	87	87	85
		WEEK 28	20[redacted]	135	133	138	83	86	89
		OLP DISCONTINUATION	20[redacted]	141	135	130	86	86	84
		FOLLOW-UP	20[redacted]	132	132	132	81	79	78
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	136	136	121	66	66	67
		SCREEN B	20[redacted]	139	139	133	68	74	70
		DAY 1	20[redacted]	125			66		
		WEEK 2	20[redacted]	150	158	158	82	87	83
		WEEK 4	20[redacted]	142	146	144	81	79	81
		WEEK 6	20[redacted]	140	139	134	66	78	79
		WEEK 8	20[redacted]	139	137	130	78	74	78
		WEEK 10	20[redacted]	148	149	141	83	84	79
		DBP DISCONTINUATION	20[redacted]	138	140	140	76	82	82
		ES DISCONTINUATION	20[redacted]	141	140	140	74	77	72
		FOLLOW-UP	20[redacted]	141	137	141	67	68	70
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	119			76		
		SCREEN B	20[redacted]	114			69		
		DAY 1	20[redacted]	109			68		
		WEEK 2	20[redacted]	127	121	125	86	86	81
		WEEK 4	20[redacted]	117			80		
		WEEK 4 UNSCHEDULED 1	20[redacted]	128	125	135	82	78	79
		WEEK 6	20[redacted]	129			77		
		WEEK 8	20[redacted]	110			74		
		WEEK 10	20[redacted]	118			74		
		WEEK 12	20[redacted]	135	125	128	88	80	88
		DBP DISCONTINUATION	20[redacted]	129			80		
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	93			69		
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	112			79		
		EARLY SHIFT WEEK 4	20[redacted]	131	122	125	82	79	87
		EARLY SHIFT WEEK 8	20[redacted]	114			78		
		EARLY SHIFT WEEK 12	20[redacted]	116			79		
		EARLY SHIFT WEEK 16	20[redacted]	110			77		
		EARLY SHIFT WEEK 20	20[redacted]	131	123	120	83	82	81
		EARLY SHIFT WEEK 24	20[redacted]	127	136	122	88	84	86
		EARLY SHIFT WEEK 28	20[redacted]	109			77		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	135	130	140	65	62	65
		SCREEN B	20[redacted]	135	146	131	64	69	58
		DAY 1	20[redacted]	134	140	144	66	81	89

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		WEEK 2	20[redacted]	166	153	136	87	54	51
		WEEK 4	20[redacted]	135	154	157	74	77	82
		WEEK 6	20[redacted]	150	146	164	76	78	80
		WEEK 8	20[redacted]	152	130	138	97	72	86
		WEEK 10	20[redacted]	135	158	143	66	41	46
		WEEK 12	20[redacted]	128			58		
		DBP DISCONTINUATION	20[redacted]	132	147	135	69	65	76
		EARLY SHIFT WEEK 4	20[redacted]	138	145	141	71	86	60
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	133	147	136	72	69	72
		ES DISCONTINUATION	20[redacted]	145	132	146	77	79	73
		FOLLOW-UP	20[redacted]	147	138	138	56	74	80
		FOLLOW-UP UNSCHEDULED 1	20[redacted]	133	140	131	72	63	65
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	127	136	130	84	82	78
		SCREEN B	20[redacted]	134	130	136	76	78	79
		DAY 1	20[redacted]	125			68		
		WEEK 2	20[redacted]	138	136	119	77	70	78
		WEEK 4	20[redacted]	130	136	138	82	80	80
		WEEK 6	20[redacted]	133	129	127	77	85	80
		WEEK 8	20[redacted]	143	145	149	95	93	91
		WEEK 10	20[redacted]	137	135	152	85	83	83
		WEEK 12	20[redacted]	128			76		
		WEEK 14	20[redacted]	131	132	119	92	80	77
		WEEK 16	20[redacted]	136	133	138	82	78	80
		WEEK 18	20[redacted]	130			75		
		WEEK 20	20[redacted]	115			68		
		WEEK 22	20[redacted]	126			80		
		WEEK 24	20[redacted]	139	138	136	80	83	78
		WEEK 24 UNSCHEDULED 1	20[redacted]	124			79		
		WEEK 28	20[redacted]	120			75		
		WEEK 28 UNSCHEDULED 1	20[redacted]	117			76		
		WEEK 32	20[redacted]	136	121	143	79	72	87
		WEEK 32 UNSCHEDULED 1	20[redacted]	109			62		
		WEEK 36	20[redacted]	119			74		
		WEEK 40	20[redacted]	120			77		
		WEEK 44	20[redacted]	129	112	126	84	72	81
		WEEK 48	20[redacted]	150	138	121	84	94	75
		WEEK 52	20[redacted]	131	107	120	84	71	81
		WEEK 52 UNSCHEDULED 1	20[redacted]	112			76		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	125			68		
		SCREEN B	20[redacted]	124			59		
		DAY 1	20[redacted]	122			71		
		WEEK 2	20[redacted]	119			58		
		WEEK 4	20[redacted]	162	149	167	94	85	99
		WEEK 6	20[redacted]	126			73		
		WEEK 8	20[redacted]	121			73		
		WEEK 10	20[redacted]	123			73		
		DBP DISCONTINUATION	20[redacted]	137	108	127	75	60	68
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	124			78		
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	128			71		
		EARLY SHIFT WEEK 4	20[redacted]	125			71		
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	127			79		
		EARLY SHIFT WEEK 8	20[redacted]	147	156	145	91	87	95
		EARLY SHIFT WEEK 8 UNSCHEDULED 1	20[redacted]	117			74		

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		ES DISCONTINUATION	20[redacted]	151	155	158	88	89	88
		FOLLOW-UP	20[redacted]	116			76		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	143	136	138	76	86	81
		SCREEN B	20[redacted]	135	133	137	85	70	71
		DAY 1	20[redacted]	136	136	135	83	75	76
		WEEK 2	20[redacted]	135	133	128	82	84	81
		WEEK 4	20[redacted]	155	146	148	91	87	89
		WEEK 6	20[redacted]	136	132	134	82	82	82
		WEEK 8	20[redacted]	143	135	131	74	76	71
		WEEK 10	20[redacted]	147	137	133	80	75	82
		WEEK 12	20[redacted]	129			71		
		WEEK 14	20[redacted]	147	131	134	86	76	76
		WEEK 16	20[redacted]	147	137	128	85	82	78
		WEEK 18	20[redacted]	147	138	135	86	80	77
		WEEK 20	20[redacted]	141	143	138	89	88	90
		WEEK 22	20[redacted]	127			79		
		WEEK 24	20[redacted]	156	154	156	89	82	87
		WEEK 24 UNSCHEDULED 1	20[redacted]	172	173	171	103	100	99
		WEEK 24 UNSCHEDULED 2	20[redacted]	162	154	155	88	90	97
		WEEK 28	20[redacted]	142	158	167	98	93	99
		WEEK 28 UNSCHEDULED 1	20[redacted]	134	138	144	91	76	82
		WEEK 32	20[redacted]	133	140	140	86	86	82
		WEEK 36	20[redacted]	164	135	149	72	94	92
		WEEK 36 UNSCHEDULED 1	20[redacted]	149	140	129	83	86	80
		WEEK 40	20[redacted]	147	130	139	80	85	89
		WEEK 44	20[redacted]	145	145	141	95	91	87
		WEEK 44 UNSCHEDULED 1	20[redacted]	136	132	129	81	80	79
		WEEK 48	20[redacted]	146	136	129	83	85	87
		WEEK 52	20[redacted]	155	156	143	87	95	90
		WEEK 52 UNSCHEDULED 1	20[redacted]	137			89		
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	122			78		
		SCREEN B	20[redacted]	119			70		
		DAY 1	20[redacted]	126			78		
		WEEK 2	20[redacted]	128	129	128	88	80	88
		WEEK 4	20[redacted]	137	125	129	76	72	78
		WEEK 6	20[redacted]	139	129	132	90	79	73
		WEEK 8	20[redacted]	137	125	117	85	75	75
		WEEK 10	20[redacted]	112			77		
		WEEK 12	20[redacted]	128	126	128	82	86	88
		DBP DISCONTINUATION	20[redacted]	120			77		
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	112			77		
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	116			79		
		EARLY SHIFT WEEK 4	20[redacted]	118			76		
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	118			72		
		EARLY SHIFT WEEK 8	20[redacted]	130	130	129	85	88	78
		EARLY SHIFT WEEK 8 UNSCHEDULED 1	20[redacted]	130			79		
		EARLY SHIFT WEEK 8 UNSCHEDULED 2	20[redacted]	121			93		
		EARLY SHIFT WEEK 8 UNSCHEDULED 3	20[redacted]	115			72		
		EARLY SHIFT WEEK 12	20[redacted]	136	135	130	88	94	82
		EARLY SHIFT WEEK 12 UNSCHEDULED 1	20[redacted]	115			80		
		EARLY SHIFT WEEK 12	20[redacted]	129	123	126	94	83	80

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		UNSCHEDULED 2							
		EARLY SHIFT WEEK 16	20[redacted]	131	127	116	92	82	84
		EARLY SHIFT WEEK 20	20[redacted]	135	128	129	95	72	75
		EARLY SHIFT WEEK 24	20[redacted]	157	146	128	85	91	80
		EARLY SHIFT WEEK 28	20[redacted]	124			80		
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	132	133	131	75	75	78
		SCREEN B	20[redacted]	125			79		
		DAY 1	20[redacted]	129	131	127	84	68	63
		WEEK 2	20[redacted]	137	135	131	72	75	72
		WEEK 8	20[redacted]	128			70		
		WEEK 10	20[redacted]	128	145	124	88	67	82
		WEEK 12	20[redacted]	139	118	123	79	63	64
		WEEK 14	20[redacted]	123			74		
		WEEK 16	20[redacted]	118			62		
		WEEK 18	20[redacted]	136	129	134	71	67	66
		WEEK 20	20[redacted]	126			65		
		WEEK 22	20[redacted]	117			56		
		WEEK 24	20[redacted]	121			60		
		WEEK 28	20[redacted]	149	159	152	90	83	85
		WEEK 32	20[redacted]	119			66		
		WEEK 36	20[redacted]	128			76		
		WEEK 40	20[redacted]	147	148	133	79	74	67
		WEEK 44	20[redacted]	134	146	130	73	75	78
		WEEK 48	20[redacted]	145	120	128	79	71	70
		WEEK 52	20[redacted]	140	141	131	80	85	75
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	129			77		
		SCREEN B	20[redacted]	119			68		
		DAY 1	20[redacted]	121			70		
		WEEK 2	20[redacted]	112			64		
		WEEK 4	20[redacted]	122			64		
		WEEK 6	20[redacted]	129			73		
		WEEK 8	20[redacted]	123			68		
		WEEK 10	20[redacted]	118			63		
		DBP DISCONTINUATION	20[redacted]	122			67		
		EARLY SHIFT WEEK 4	20[redacted]	120			75		
		EARLY SHIFT WEEK 8	20[redacted]	125			73		
		EARLY SHIFT WEEK 12	20[redacted]	123			69		
		EARLY SHIFT WEEK 16	20[redacted]	116			71		
		EARLY SHIFT WEEK 20	20[redacted]	126			72		
		EARLY SHIFT WEEK 24	20[redacted]	112			68		
		EARLY SHIFT WEEK 28	20[redacted]	185	174	176	104	95	100
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	132	137	147	80	76	81
		SCREEN B	20[redacted]	136	134	139	80	80	79
		DAY 1	20[redacted]	125	139	134	81	81	80
		WEEK 2	20[redacted]	124	137	131	84	77	81
		WEEK 4	20[redacted]	125	118	116	81	73	71
		WEEK 6	20[redacted]	148	135	150	70	82	87
		WEEK 8	20[redacted]	155	132	141	92	87	82
		WEEK 10	20[redacted]	133	119	133	71	64	72
		DBP DISCONTINUATION	20[redacted]	120			74		
		EARLY SHIFT WEEK 4	20[redacted]	159	148	145	98	93	97
		EARLY SHIFT WEEK 8	20[redacted]	155	158	152	107	104	94
		EARLY SHIFT WEEK 12	20[redacted]	162	147	158	97	92	93
		EARLY SHIFT WEEK 16	20[redacted]	148	129	145	35	89	94
		EARLY SHIFT WEEK 20	20[redacted]	162	144	141	94	88	88
		EARLY SHIFT WEEK 24	20[redacted]	145	144	140	95	97	95
		EARLY SHIFT WEEK 28	20[redacted]	155	138	156	94	90	84
R788-1301	Placebo/R788	SCREEN A	20[redacted]	112	108	112	83	75	80

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
[redacted]		SCREEN B	20[redacted]	112			78		
		DAY 1	20[redacted]	121	127	111	91	91	82
		WEEK 2	20[redacted]	146	134	142	89	87	89
		WEEK 4	20[redacted]	132	141	125	91	97	91
		WEEK 6	20[redacted]	127	126	129	90	85	83
		WEEK 8	20[redacted]	137	141	133	84	96	79
		WEEK 10	20[redacted]	134	122	143	95	91	98
		WEEK 10 UNSCHEDULED 1	20[redacted]	118	119	108	88	88	77
		DBP DISCONTINUATION	20[redacted]	118	117	121	85	85	86
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	185			113		
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	118			95		
		DBP DISCONTINUATION UNSCHEDULED 3	20[redacted]	140	128	128	86	84	85
		EARLY SHIFT WEEK 4	20[redacted]	142	125	112	93	94	92
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	130	120	126	93	89	88
		EARLY SHIFT WEEK 8	20[redacted]	131	124	123	90	90	89
		EARLY SHIFT WEEK 12	20[redacted]	124			72		
		EARLY SHIFT WEEK 16	20[redacted]	123	116	118	91	85	92
		EARLY SHIFT WEEK 16 UNSCHEDULED 1	20[redacted]	137	127	127	96	84	89
		EARLY SHIFT WEEK 20	20[redacted]	134	123	115	96	87	69
		EARLY SHIFT WEEK 24	20[redacted]	120			75		
		EARLY SHIFT WEEK 28	20[redacted]	106			74		
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	138	138	138	87	66	69
		SCREEN B	20[redacted]	136	132	133	63	75	61
		DAY 1	20[redacted]	126	137	128	89	86	84
		DAY 1 UNSCHEDULED 1	20[redacted]	139	137	139	87	81	88
		DAY 1 UNSCHEDULED 2	20[redacted]	136	137	126	88	88	89
		WEEK 2	20[redacted]	130	138	136	95	93	98
		WEEK 2 UNSCHEDULED 1	20[redacted]	128	138	134	90	86	84
		WEEK 4	20[redacted]	136	136	131	93	95	96
		WEEK 4 UNSCHEDULED 1	20[redacted]	130	128	121	81	95	85
		WEEK 6	20[redacted]	144	140	148	89	97	97
		WEEK 6 UNSCHEDULED 1	20[redacted]	132	134	134	84	84	86
		WEEK 8	20[redacted]	137	140	146	92	96	97
		WEEK 8 UNSCHEDULED 1	20[redacted]	125	137	142	95	86	86
		WEEK 10	20[redacted]	121	124	117	85	82	86
		WEEK 10 UNSCHEDULED 1	20[redacted]	122			76		
		WEEK 12	20[redacted]	120			80		
		DBP DISCONTINUATION	20[redacted]	138	130	130	70	86	81
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	147	139	141	89	88	91
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	144	131	131	98	86	81
		EARLY SHIFT WEEK 4	20[redacted]	137	134	133	93	93	82
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	143	126	139	93	92	95
		EARLY SHIFT WEEK 8	20[redacted]	113	131	119	84	91	86
		EARLY SHIFT WEEK 8 UNSCHEDULED 1	20[redacted]	127			80		
		EARLY SHIFT WEEK 12	20[redacted]	130			80		
		EARLY SHIFT WEEK 12 UNSCHEDULED 1	20[redacted]	134	130	127	86	81	86
		EARLY SHIFT WEEK 16	20[redacted]	144	134	129	94	90	93
		EARLY SHIFT WEEK 16	20[redacted]	136	141	136	96	88	96

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	Visit	Date	Systolic Blood Pressure (mmHg)			Diastolic Blood Pressure (mmHg)		
				1st	2nd	3rd	1st	2nd	3rd
		UNSCHEDULED 1							
		EARLY SHIFT WEEK 20	20[redacted]	144	136	133	86	81	85
		EARLY SHIFT WEEK 24	20[redacted]	140	140	131	85	84	79
		EARLY SHIFT WEEK 28	20[redacted]	125	130	130	88	81	81
		EARLY SHIFT WEEK 28 UNSCHEDULED 1	20[redacted]	126			79		

*グレーの網掛け部分はプラセボ投与時のデータ
（Source: 1.13.3-4, C-15 付録 1）

表 2.7.4.9-97　　好中球数 1000/uL 未満の減少に該当した患者の好中球数の一覧表（R788-1301 試験）

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Neutrophils			
				Result		Unit	Range
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	3.20		10^9/L	1.32-6.02
		SCREEN B	20[redacted]	3.50		10^9/L	1.32-6.02
		DAY 1	20[redacted]	4.46		10^9/L	1.32-6.02
		WEEK 2	20[redacted]	2.90		10^9/L	1.32-6.02
		WEEK 4	20[redacted]	2.88		10^9/L	1.32-6.02
		WEEK 6	20[redacted]	4.18		10^9/L	1.32-6.02
		WEEK 8	20[redacted]	2.10		10^9/L	1.32-6.02
		WEEK 10	20[redacted]	2.73		10^9/L	1.32-6.02
		WEEK 12	20[redacted]	1.67		10^9/L	1.32-6.02
		WEEK 14	20[redacted]	1.13	L	10^9/L	1.32-6.02
		WEEK 16	20[redacted]	2.71		10^9/L	1.32-6.02
		WEEK 18	20[redacted]	3.07		10^9/L	1.32-6.02
		WEEK 20	20[redacted]	2.77		10^9/L	1.32-6.02
		WEEK 22	20[redacted]	2.43		10^9/L	1.32-6.02
		WEEK 24	20[redacted]	2.10		10^9/L	1.32-6.02
		WEEK 28	20[redacted]	1.79		10^9/L	1.32-6.02
		WEEK 32	20[redacted]	1.74		10^9/L	1.32-6.02
		WEEK 36	20[redacted]	1.45		10^9/L	1.32-6.02
		WEEK 40	20[redacted]	0.88	L	10^9/L	1.32-6.02
		WEEK 40 UNSCHEDULED 1	20[redacted]	1.18	L	10^9/L	1.32-6.02
		WEEK 44	20[redacted]	0.86	L	10^9/L	1.32-6.02
		WEEK 48	20[redacted]	0.95	L	10^9/L	1.32-6.02
		WEEK 52	20[redacted]	0.92	L	10^9/L	1.32-6.02
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	3.50		10^9/L	0.99-6.02
		SCREEN B	20[redacted]	3.31		10^9/L	0.99-6.02
		DAY 1	20[redacted]	3.24		10^9/L	0.99-6.02
		DAY 1 UNSCHEDULED 1	20[redacted]	4.49		10^9/L	0.99-6.02
		WEEK 2	20[redacted]	4.25		10^9/L	0.99-6.02
		WEEK 4	20[redacted]	2.62		10^9/L	0.99-6.02
		WEEK 6	20[redacted]	1.37		10^9/L	0.99-6.02
		WEEK 8	20[redacted]	1.87		10^9/L	0.99-6.02
		WEEK 10	20[redacted]	2.36		10^9/L	0.99-6.02
		WEEK 12	20[redacted]	2.10		10^9/L	0.99-6.02
		WEEK 14	20[redacted]	1.79		10^9/L	0.99-6.02
		WEEK 16	20[redacted]	1.06		10^9/L	0.99-6.02
		WEEK 16 UNSCHEDULED 1	20[redacted]	2.81		10^9/L	0.99-6.02
		WEEK 18	20[redacted]	1.80		10^9/L	0.99-6.02
		WEEK 20	20[redacted]	2.54		10^9/L	0.99-6.02
		WEEK 22	20[redacted]	1.65		10^9/L	0.99-6.02
		WEEK 24	20[redacted]	2.75		10^9/L	0.99-6.02
		WEEK 24 UNSCHEDULED 1	20[redacted]	1.31		10^9/L	0.99-6.02
		WEEK 28	20[redacted]	1.83		10^9/L	0.99-6.02
		WEEK 32	20[redacted]	1.23		10^9/L	0.99-6.02
		WEEK 32 UNSCHEDULED 1	20[redacted]	0.85	L	10^9/L	0.99-6.02
		WEEK 36	20[redacted]	1.36		10^9/L	0.99-6.02
		WEEK 40	20[redacted]	1.11		10^9/L	0.99-6.02
		WEEK 44	20[redacted]	1.08		10^9/L	0.99-6.02
		WEEK 48	20[redacted]	1.42		10^9/L	0.99-6.02
		WEEK 48 UNSCHEDULED 1	20[redacted]	0.96	L	10^9/L	0.99-6.02
		WEEK 52	20[redacted]	1.33		10^9/L	0.99-6.02
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	3407		/uL	1271-6923
		SCREEN B	20[redacted]	2860		/uL	1271-6923
		DAY 1	20[redacted]	2238		/uL	1271-6923
		WEEK 2	20[redacted]	3307		/uL	1271-6923
		WEEK 4	20[redacted]	1292		/uL	1271-6923

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Neutrophils			
				Result		Unit	Range
		WEEK 6	20[redacted]	1263	L	/uL	1271-6923
		WEEK 8	20[redacted]	1641		/uL	1271-6923
		WEEK 10	20[redacted]	1464		/uL	1271-6923
		WEEK 12	20[redacted]	970	L	/uL	1271-6923
		WEEK 12 UNSCHEDULED 1	20[redacted]	1419		/uL	1271-6923
		WEEK 14	20[redacted]	1149	L	/uL	1271-6923
		WEEK 16	20[redacted]	1740		/uL	1271-6923
		WEEK 18	20[redacted]	1091	L	/uL	1271-6923
		WEEK 20	20[redacted]	1423		/uL	1271-6923
		WEEK 22	20[redacted]	1607		/uL	1271-6923
		WEEK 24	20[redacted]	1382		/uL	1271-6923
		WEEK 24 UNSCHEDULED 1	20[redacted]	1580		/uL	1271-6923
		WEEK 28	20[redacted]	2060		/uL	1271-6923
		WEEK 32	20[redacted]	1658		/uL	1271-6923
		WEEK 36	20[redacted]	2138		/uL	1271-6923
		WEEK 40	20[redacted]	1870		/uL	1271-6923
		WEEK 44	20[redacted]	2050		/uL	1271-6923
		WEEK 48	20[redacted]	1791		/uL	1271-6923
		WEEK 52	20[redacted]	1699		/uL	1271-6923
		FOLLOW-UP	20[redacted]	2491		/uL	1271-6923
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	1886.5		/uL	1600-5600
		SCREEN B	20[redacted]	2361.6		/uL	1600-5600
		DAY 1	20[redacted]	1673.1		/uL	1600-5600
		WEEK 2	20[redacted]	865.2	L	/uL	1600-5600
		WEEK 4	20[redacted]	1008.0	L	/uL	1600-5600
		WEEK 6	20[redacted]	3213		/uL	1600-5600
		WEEK 8	20[redacted]	1231.2	L	/uL	1600-5600
		WEEK 10	20[redacted]	1360.1	L	/uL	1600-5600
		WEEK 12	20[redacted]	1217.7	L	/uL	1600-5600
		WEEK 14	20[redacted]	992.5	L	/uL	1600-5600
		WEEK 16	20[redacted]	885.0	L	/uL	1600-5600
		WEEK 18	20[redacted]	777.4	L	/uL	1600-5600
		WEEK 20	20[redacted]	1062.0	L	/uL	1600-5600
		WEEK 22	20[redacted]	1656.0		/uL	1600-5600
		WEEK 24	20[redacted]	1044.0	L	/uL	1600-5600
		WEEK 24 UNSCHEDULED 1	20[redacted]	1334.4	L	/uL	1600-5600
		WEEK 28	20[redacted]	937.5	L	/uL	1600-5600
		OLP DISCONTINUATION	20[redacted]	895.0	L	/uL	1600-5600
		FOLLOW-UP	20[redacted]	3169.1		/uL	1600-5600
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	3018		/uL	1320-6450
		SCREEN B	20[redacted]	1905		/uL	1320-6450
		DAY 1	20[redacted]	2009		/uL	1320-6450
		WEEK 2	20[redacted]	1516		/uL	1320-6450
		WEEK 4	20[redacted]	452	L	/uL	1320-6450
		WEEK 4 UNSCHEDULED 1	20[redacted]	3899		/uL	1320-6450
		WEEK 6	20[redacted]	1744		/uL	1320-6450
		WEEK 8	20[redacted]	1428		/uL	1320-6450
		WEEK 10	20[redacted]	1683		/uL	1320-6450
		WEEK 12	20[redacted]	1053	L	/uL	1320-6450
		DBP DISCONTINUATION	20[redacted]	1530		/uL	1320-6450
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	480	L	/uL	1320-6450
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	1740		/uL	1320-6450
		EARLY SHIFT WEEK 4	20[redacted]	1767		/uL	1320-6450
		EARLY SHIFT WEEK 8	20[redacted]	2132		/uL	1320-6450
		EARLY SHIFT WEEK 12	20[redacted]	1444		/uL	1320-6450
		EARLY SHIFT WEEK 16	20[redacted]	1848		/uL	1320-6450

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Neutrophils			
				Result		Unit	Range
		EARLY SHIFT WEEK 20	20[redacted]	1113	L	/uL	1320-6450
		EARLY SHIFT WEEK 24	20[redacted]	1302	L	/uL	1320-6450
		EARLY SHIFT WEEK 28	20[redacted]	2099		/uL	1320-6450
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	2.4		10^9/L	1.3-6.4
		SCREEN B	20[redacted]	2.5		10^9/L	1.3-6.4
		DAY 1	20[redacted]	3.1		10^9/L	1.3-6.4
		WEEK 2	20[redacted]	1.3		10^9/L	1.3-6.4
		WEEK 4	20[redacted]	1.1	L	10^9/L	1.3-6.4
		WEEK 6	20[redacted]	1.0	L	10^9/L	1.3-6.4
		WEEK 8	20[redacted]	0.7	L	10^9/L	1.3-6.4
		WEEK 8 UNSCHEDULED 1	20[redacted]	0.7	L	10^9/L	1.3-6.4
		WEEK 10	20[redacted]	0.7	L	10^9/L	1.3-6.4
		WEEK 10 UNSCHEDULED 1	20[redacted]	1.5		10^9/L	1.3-6.4
		WEEK 12	20[redacted]	2.1		10^9/L	1.3-6.4
		DBP DISCONTINUATION	20[redacted]	1.9		10^9/L	1.3-6.4
		EARLY SHIFT WEEK 4	20[redacted]	0.9	L	10^9/L	1.3-6.4
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	0.7	L	10^9/L	1.3-6.4
		ES DISCONTINUATION	20[redacted]	0.8	L	10^9/L	1.3-6.4
		FOLLOW-UP	20[redacted]	2.8		10^9/L	1.3-6.4
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	3.66		10^9/L	1.32-6.02
		SCREEN B	20[redacted]	2.43		10^9/L	1.32-6.02
		DAY 1	20[redacted]	3.56		10^9/L	1.32-6.02
		WEEK 2	20[redacted]	2.45		10^9/L	1.32-6.02
		WEEK 8	20[redacted]	3.06		10^9/L	1.32-6.02
		WEEK 10	20[redacted]	3.09		10^9/L	1.32-6.02
		WEEK 12	20[redacted]	1.82		10^9/L	1.32-6.02
		WEEK 14	20[redacted]	1.68		10^9/L	1.32-6.02
		WEEK 16	20[redacted]	2.11		10^9/L	1.32-6.02
		WEEK 18	20[redacted]	3.01		10^9/L	1.32-6.02
		WEEK 20	20[redacted]	2.20		10^9/L	1.32-6.02
		WEEK 22	20[redacted]	2.46		10^9/L	1.32-6.02
		WEEK 24	20[redacted]	2.76		10^9/L	1.32-6.02
		WEEK 28	20[redacted]	1.67		10^9/L	1.32-6.02
		WEEK 32	20[redacted]	1.81		10^9/L	1.32-6.02
		WEEK 36	20[redacted]	2.64		10^9/L	1.32-6.02
		WEEK 40	20[redacted]	2.17		10^9/L	1.32-6.02
		WEEK 44	20[redacted]	2.46		10^9/L	1.32-6.02
		WEEK 48	20[redacted]	1.66		10^9/L	1.32-6.02
		WEEK 52	20[redacted]	0.86	L	10^9/L	1.32-6.02
		WEEK 52 UNSCHEDULED 1	20[redacted]	1.52		10^9/L	1.32-6.02

（Source: 1.13.3-4, C-15 付録 2）

表 2.7.4.9-98　　肝機能障害の投与量調節の基準に該当した被験者の肝機能検査値の一覧表（R788-1301 試験）

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase (U/L) Reference Range 5-45		Aspartate Aminotransferase (U/L) Reference Range 10-40		Alkaline Phosphatase (U/L) Reference Range 115-359		Bilirubin (mg/dL) Reference Range 0.3-1.2		Direct Bilirubin (mg/dL) Reference Range <=0.4		Indirect Bilirubin (mg/dL) Reference Range <=0.8	
R788-1301 [redacted]	R788	SCREEN A	20[redacted]	21		19		75	L	0.4		0.1		0.3	
		DAY 1	20[redacted]	19		17		76	L	0.5		0.2		0.3	
		WEEK 2	20[redacted]	40		31		133		0.4		0.2		0.2	
		WEEK 4	20[redacted]	164	H	125	H	185		0.6		0.2		0.4	
		WEEK 6	20[redacted]	68	H	55	H	114	L	0.4		0.2		0.2	
		WEEK 8	20[redacted]	32		29		125		0.4		0.2		0.2	
		WEEK 10	20[redacted]	40		38		143		0.5		0.2		0.3	
		WEEK 12	20[redacted]	64	H	49	H	158		0.7		0.2		0.5	
		DBP DISCONTINUATION	20[redacted]	173	H	158	H	240		0.5		0.2		0.3	
		FOLLOW-UP	20[redacted]	52	H	48	H	146		0.4		0.2		0.2	
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	27		27		341		0.5		0.2		0.3	
		DAY 1	20[redacted]	23		30		272		0.5		0.2		0.3	
		WEEK 2	20[redacted]	30		36		286		0.5		0.2		0.3	
		WEEK 4	20[redacted]	43	H	43	H	324		0.6		0.2		0.4	
		WEEK 6	20[redacted]	80	H	77	H	395	H	0.6		0.2		0.4	
		WEEK 8	20[redacted]	66	H	73	H	385	H	0.5		0.2		0.3	
		WEEK 10	20[redacted]	59	H	53	H	371	H	0.5		0.2		0.3	
		WEEK 12	20[redacted]	73	H	65	H	417	H	0.5		0.2		0.3	
		WEEK 14	20[redacted]	40		41	H	352		0.4		0.1		0.3	
		WEEK 16	20[redacted]	44	H	38		343		0.5		0.1		0.4	
		WEEK 18	20[redacted]	50	H	44	H	374	H	0.5		0.1		0.4	
		WEEK 20	20[redacted]	47	H	46	H	417	H	0.4		0.1		0.3	
		WEEK 22	20[redacted]	56	H	57	H	390	H	0.5		0.2		0.3	
		WEEK 24	20[redacted]	41	H	42	H	351		0.5		0.2		0.3	
		WEEK 28	20[redacted]	45	H	54	H	470	H	0.5		0.2		0.3	
		WEEK 32	20[redacted]	88	H	103	H	514	H	0.5		0.2		0.3	
		WEEK 32 UNSCHEDULED 1	20[redacted]	50	H	46	H	432	H	0.6					
		WEEK 36	20[redacted]	47	H	47	H	445	H	0.6		0.2		0.4	
		WEEK 40	20[redacted]	58	H	55	H	496	H	0.4		0.2		0.2	
		WEEK 44	20[redacted]	46	H	46	H	395	H	0.4		0.1		0.3	
		WEEK 48	20[redacted]	78	H	87	H	547	H	0.6		0.2		0.4	
		WEEK 48 UNSCHEDULED 1	20[redacted]	61	H	71	H	498	H	0.6					
		WEEK 52	20[redacted]	36		38		439	H	0.5		0.2		0.3	
R788-1301 [redacted]	R788	SCREEN A	20[redacted]	20		24		207		0.5		0.2		0.3	
		DAY 1	20[redacted]	18		22		191		0.5		0.2		0.3	
		WEEK 2	20[redacted]	26		33		242		0.9		0.2		0.7	
		WEEK 4	20[redacted]	22		26		226		0.8		0.3		0.5	
		WEEK 6	20[redacted]	626	H	350	H	250		0.6		0.2		0.4	

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase (U/L) Reference Range 5-45		Aspartate Aminotransferase (U/L) Reference Range 10-40		Alkaline Phosphatase (U/L) Reference Range 115-359		Bilirubin (mg/dL) Reference Range 0.3-1.2		Direct Bilirubin (mg/dL) Reference Range <=0.4		Indirect Bilirubin (mg/dL) Reference Range <=0.8	
		WEEK 8	20[redacted]	155	H	55	H	246		0.4		0.1		0.3	
		DBP DISCONTINUATION	20[redacted]	53	H	24		211		0.5		0.2		0.3	
		FOLLOW-UP	20[redacted]	36		32		222		0.5		0.2		0.3	
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	14		17		152		0.3		0.1		0.2	
		DAY 1	20[redacted]	13		16		171		0.3		0.1		0.2	
		WEEK 2	20[redacted]	12		20		190		0.4		0.2		0.2	
		WEEK 4	20[redacted]	17		22		211		0.4		0.1		0.3	
		WEEK 6	20[redacted]	19		23		229		0.4		0.1		0.3	
		WEEK 8	20[redacted]	24		23		230		0.4		0.2		0.2	
		WEEK 10	20[redacted]	143	H	85	H	214		0.5		0.2		0.3	
		WEEK 12	20[redacted]	53	H	30		177		0.3		0.1		0.2	
		WEEK 14	20[redacted]	28		27		167		0.4		0.2		0.2	
		WEEK 16	20[redacted]	31		30		184		0.7		0.3		0.4	
		WEEK 18	20[redacted]	23		25		236		0.4		0.1		0.3	
		WEEK 20	20[redacted]	19		22		238		0.5		0.2		0.3	
		WEEK 22	20[redacted]	18		24		177		0.6		0.2		0.4	
		WEEK 24	20[redacted]	12		19		209		0.4		0.2		0.2	
		WEEK 28	20[redacted]	15		22		168		0.5		0.2		0.3	
		WEEK 32	20[redacted]	17		24		191		0.5		0.2		0.3	
		WEEK 36	20[redacted]	15		19		203		0.5		0.1		0.4	
		WEEK 40	20[redacted]	17		23		208		0.5		0.2		0.3	
		WEEK 44	20[redacted]	15		24		196		0.6		0.2		0.4	
		WEEK 48	20[redacted]	14		22		233		0.4		0.1		0.3	
		WEEK 52	20[redacted]	14		20		141		0.5		0.2		0.3	
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	27		24		277		0.3		0.1		0.2	
		DAY 1	20[redacted]	19		20		277		0.2	L	0.1		0.1	
		WEEK 2	20[redacted]	26		28		356		0.4		0.2		0.2	
		WEEK 4	20[redacted]	27		29		342		0.3		0.1		0.2	
		WEEK 6	20[redacted]	19		21		264		0.3		0.1		0.2	
		WEEK 8	20[redacted]	25		24		220		0.6		0.2		0.4	
		WEEK 10	20[redacted]	25		22		245		0.4		0.2		0.2	
		WEEK 12	20[redacted]	55	H	43	H	308		0.7		0.3		0.4	
		DBP DISCONTINUATION	20[redacted]	46	H	27		316		0.7		0.2		0.5	
		EARLY SHIFT WEEK 4	20[redacted]	46	H	41	H	286		0.4		0.2		0.2	
		EARLY SHIFT WEEK 8	20[redacted]	43	H	28		247		0.8		0.3		0.5	
		EARLY SHIFT WEEK 12	20[redacted]	93	H	46	H	337		0.6		0.2		0.4	
		EARLY SHIFT WEEK 16	20[redacted]	82	H	34		341		0.5		0.2		0.3	
		EARLY SHIFT WEEK 20	20[redacted]	44	H	28		294		0.9		0.3		0.6	
		EARLY SHIFT WEEK 24	20[redacted]	73	H	39		284		0.8		0.3		0.5	
		EARLY SHIFT WEEK 28	20[redacted]	49	H	33		279		0.6		0.2		0.4	

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase (U/L) Reference Range 5-45		Aspartate Aminotransferase (U/L) Reference Range 10-40		Alkaline Phosphatase (U/L) Reference Range 115-359		Bilirubin (mg/dL) Reference Range 0.3-1.2		Direct Bilirubin (mg/dL) Reference Range <=0.4		Indirect Bilirubin (mg/dL) Reference Range <=0.8	
R788-1301 [redacted]	R788/R788	SCREEN A	20[redacted]	22		27		378	H	0.7		0.3		0.4	
		DAY 1	20[redacted]	38		45	H	489	H	0.9		0.3		0.6	
		WEEK 2	20[redacted]	31		39		519	H	1.0		0.4		0.6	
		WEEK 4	20[redacted]	36		38		551	H	1.0		0.3		0.7	
		WEEK 6	20[redacted]	40		53	H	729	H	0.8		0.3		0.5	
		WEEK 8	20[redacted]	59	H	46	H	466	H	1.1		0.3		0.8	
		WEEK 10	20[redacted]	36		38		524	H	1.0		0.3		0.7	
		WEEK 12	20[redacted]	40		47	H	769	H	0.9		0.3		0.6	
		DBP DISCONTINUATION	20[redacted]	35		40		420	H	1.0		0.3		0.7	
		EARLY SHIFT WEEK 4	20[redacted]	32		40		369	H	1.0		0.4		0.6	
		EARLY SHIFT WEEK 8	20[redacted]	28		38		622	H	1.0		0.3		0.7	
		EARLY SHIFT WEEK 12	20[redacted]	33		54	H	486	H	0.7		0.3		0.4	
		EARLY SHIFT WEEK 16	20[redacted]	41	H	61	H	536	H	0.9		0.3		0.6	
		EARLY SHIFT WEEK 20	20[redacted]	38		50	H	488	H	0.8		0.3		0.5	
		EARLY SHIFT WEEK 24	20[redacted]	33		43	H	465	H	0.9		0.3		0.6	
		EARLY SHIFT WEEK 28	20[redacted]	36		52	H	454	H	0.7		0.2		0.5	
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	28		25		229		0.7		0.3		0.4	
		DAY 1	20[redacted]	40		28		251		0.7		0.3		0.4	
		WEEK 2	20[redacted]	23		21		246		0.6		0.2		0.4	
		WEEK 4	20[redacted]	26		22		251		0.7		0.2		0.5	
		WEEK 6	20[redacted]	19		21		240		0.7		0.3		0.4	
		WEEK 8	20[redacted]	26		25		239		0.6		0.2		0.4	
		WEEK 10	20[redacted]	21		19		212		0.6		0.2		0.4	
		WEEK 12	20[redacted]	23		21		235		0.5		0.2		0.3	
		DBP DISCONTINUATION	20[redacted]	28		21		200		0.7		0.2		0.5	
		EARLY SHIFT WEEK 4	20[redacted]	33		27		210		0.7		0.3		0.4	
		EARLY SHIFT WEEK 8	20[redacted]	30		31		236		0.6		0.2		0.4	
		EARLY SHIFT WEEK 12	20[redacted]	41	H	34		274		0.6		0.2		0.4	
		EARLY SHIFT WEEK 16	20[redacted]	37		31		262		0.6		0.2		0.4	
		EARLY SHIFT WEEK 20	20[redacted]	27		27		248		0.7		0.2		0.5	
		EARLY SHIFT WEEK 24	20[redacted]	39		37		443	H	0.3		0.2		0.1	
		EARLY SHIFT WEEK 28	20[redacted]	296	H	146	H	486	H	0.8		0.3		0.5	
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	24		35		382	H	0.5		0.2		0.3	
		DAY 1	20[redacted]	21		28		357		0.4		0.2		0.2	
		WEEK 2	20[redacted]	24		29		338		0.5		0.2		0.3	
		WEEK 4	20[redacted]	20		29		331		0.5		0.2		0.3	
		WEEK 6	20[redacted]	20		26		356		0.6		0.2		0.4	
		WEEK 8	20[redacted]	29		35		363	H	0.4		0.2		0.2	
		WEEK 10	20[redacted]	24		31		350		0.4		0.2		0.2	
		DBP DISCONTINUATION	20[redacted]	23		26		349		0.5		0.2		0.3	

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase (U/L) Reference Range 5-45		Aspartate Aminotransferase (U/L) Reference Range 10-40		Alkaline Phosphatase (U/L) Reference Range 115-359		Bilirubin (mg/dL) Reference Range 0.3-1.2		Direct Bilirubin (mg/dL) Reference Range <=0.4		Indirect Bilirubin (mg/dL) Reference Range <=0.8	
		EARLY SHIFT WEEK 4	20[redacted]	65	H	72	H	526	H	0.8		0.2		0.6	
		EARLY SHIFT WEEK 8	20[redacted]	96	H	84	H	521	H	0.7		0.2		0.5	
		EARLY SHIFT WEEK 12	20[redacted]	74	H	72	H	623	H	0.7		0.2		0.5	
		EARLY SHIFT WEEK 16	20[redacted]	52	H	68	H	652	H	0.7		0.2		0.5	
		EARLY SHIFT WEEK 20	20[redacted]	68	H	66	H	656	H	0.6		0.2		0.4	
		EARLY SHIFT WEEK 24	20[redacted]	36		46	H	582	H	0.7		0.2		0.5	
		EARLY SHIFT WEEK 28	20[redacted]	34		45	H	539	H	0.5		0.2		0.3	
R788-1301 [redacted]	Placebo/R788	SCREEN A	20[redacted]	49	H	36		297		0.9		0.3		0.6	
		DAY 1	20[redacted]	42	H	32		316		1.2		0.4		0.8	
		WEEK 2	20[redacted]	38		29		302		0.8		0.3		0.5	
		WEEK 4	20[redacted]	38		30		321		1.1		0.4		0.7	
		WEEK 6	20[redacted]	34		29		301		0.9		0.3		0.6	
		WEEK 8	20[redacted]	40		30		316		1.2		0.5	H	0.7	
		WEEK 10	20[redacted]	33		24		336		0.7		0.3		0.4	
		WEEK 12	20[redacted]	44	H	31		370	H	1.1		0.4		0.7	
		DBP DISCONTINUATION	20[redacted]	47	H	33		368	H	0.8		0.3		0.5	
		EARLY SHIFT WEEK 4	20[redacted]	41	H	30		445	H	1.4	H	0.6	H	0.8	
		EARLY SHIFT WEEK 8	20[redacted]	32		23		468	H	1.4	H	0.6	H	0.8	
		EARLY SHIFT WEEK 12	20[redacted]	42	H	28		479	H	2.1	H	0.8	H	1.3	H
		EARLY SHIFT WEEK 16	20[redacted]	54	H	37		480	H	2.6	H	0.9	H	1.7	H
		EARLY SHIFT WEEK 20	20[redacted]	38		30		445	H	1.9	H	0.8	H	1.1	H
		EARLY SHIFT WEEK 24	20[redacted]	30		24		429	H	1.3	H	0.5	H	0.8	
		EARLY SHIFT WEEK 28	20[redacted]	36		27		442	H	1.8	H	0.7	H	1.1	H

（Source: 1.13.3-4, C-15 付録 3）

表 2.7.4.9-99　肝機能障害の投与量調節の基準に該当した被験者の肝機能検査値の一覧表（規定外来院）（R788-1301 試験）

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase				Aspartate Aminotransferase				Alkaline Phosphatase				Bilirubin				Direct Bilirubin				Indirect Bilirubin			
				Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range
R788-1301 [redacted]	R788	WEEK 4 UNSCHEDULED 1	20[redacted]	183	H	U/L	5-35	162	H	U/L	13-35	64		U/L	38-113	0.7		mg/dL	0.2-1.2				0-0.2				0.2-1
		WEEK 4 UNSCHEDULED 2	20[redacted]	84	H	U/L	5-35	53	H	U/L	13-35	43		U/L	38-113				0.2-1.2				0-0.2				0.2-1
		WEEK 6 UNSCHEDULED 1	20[redacted]	69	H	U/L	5-35	53	H	U/L	13-35	37	L	U/L	38-113	0.6		mg/dL	0.2-1.2				0-0.2				0.2-1
		WEEK 6 UNSCHEDULED 2	20[redacted]	33		U/L	5-35	28		U/L	13-35	37	L	U/L	38-113	0.7		mg/dL	0.2-1.2				0-0.2				0.2-1
		WEEK 8 UNSCHEDULED 1	20[redacted]	33		U/L	5-35	30		U/L	13-35	40		U/L	38-113	0.6		mg/dL	0.2-1.2				0-0.2				0.2-1
		WEEK 10 UNSCHEDULED 1	20[redacted]	41	H	U/L	5-35	38	H	U/L	13-35	48		U/L	38-113	0.7		mg/dL	0.2-1.2				0-0.2				0.2-1
		WEEK 12 UNSCHEDULED 1	20[redacted]	65	H	U/L	5-35	49	H	U/L	13-35	53		U/L	38-113	0.9		mg/dL	0.2-1.2				0-0.2				0.2-1
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	175	H	U/L	5-35	156	H	U/L	13-35	228	H	U/L	38-113	0.8		mg/dL	0.2-1.2				0-0.2				0.2-1
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	111	H	U/L	5-35	75	H	U/L	13-35	79		U/L	38-113	0.8		mg/dL	0.2-1.2				0-0.2				0.2-1
		DBP DISCONTINUATION UNSCHEDULED 3	20[redacted]	72	H	U/L	5-35	68	H	U/L	13-35	57		U/L	38-113	0.7		mg/dL	0.2-1.2				0-0.2				0.2-1
		FOLLOW-UP UNSCHEDULED 1	20[redacted]	48	H	U/L	5-35	47	H	U/L	13-35	49		U/L	38-113	0.5		mg/dL	0.2-1.2				0-0.2				0.2-1
R788-1301 [redacted]	R788/R788	WEEK 6 UNSCHEDULED 1	20[redacted]	80	H	U/L	7-23	77	H	U/L	13-30	127	H	U/L	38-113	0.6		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.5		mg/dL	0.1-0.8
		WEEK 8 UNSCHEDULED 1	20[redacted]	65	H	U/L	7-23	71	H	U/L	13-30	126	H	U/L	38-113	0.6		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.5		mg/dL	0.1-0.8
		WEEK 12 UNSCHEDULED 1	20[redacted]	72	H	U/L	7-23	66	H	U/L	13-30	138	H	U/L	38-113	0.5		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.4		mg/dL	0.1-0.8
		WEEK 14 UNSCHEDULED 1	20[redacted]	39	H	U/L	7-23	41	H	U/L	13-30	108		U/L	38-113	0.4		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.3		mg/dL	0.1-0.8
		WEEK 16 UNSCHEDULED 1	20[redacted]	45	H	U/L	7-23	36	H	U/L	13-30	122	H	U/L	38-113	0.5		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.4		mg/dL	0.1-0.8
		WEEK 18 UNSCHEDULED 1	20[redacted]	50	H	U/L	7-23	43	H	U/L	13-30	121	H	U/L	38-113	0.5		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.4		mg/dL	0.1-0.8
R788-1301 [redacted]	R788	WEEK 6 UNSCHEDULED 1	20[redacted]	641	H	U/L	7-23	281	H	U/L	13-30	324	H	U/L	106-322	1.0		mg/dL	0.4-1.5	0.3		mg/dL	0-0.4	NA		mg/dL	0.4-1.1
		WEEK 8 UNSCHEDULED 1	20[redacted]	155	H	U/L	7-23	54	H	U/L	13-30	254		U/L	106-322	0.5		mg/dL	0.4-1.5	0.1		mg/dL	0-0.4	NA		mg/dL	0.4-1.1
		WEEK 8 UNSCHEDULED 2	20[redacted]	81	H	U/L	7-23	41	H	U/L	13-30	NA		U/L	106-322	0.5		mg/dL	0.4-1.5	NA		mg/dL	0-0.4	NA		mg/dL	0.4-1.1
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	33	H	U/L	7-23	22		U/L	13-30				106-322	0.6		mg/dL	0.4-1.5				0-0.4				0.4-1.1
		FOLLOW-UP UNSCHEDULED 1	20[redacted]	34	H	U/L	7-23	31	H	U/L	13-30	NA		U/L	106-322	0.6		mg/dL	0.4-1.5	NA		mg/dL	0-0.4	NA		mg/dL	0.4-1.1
		FOLLOW-UP UNSCHEDULED 2	20[redacted]	26	H	U/L	7-23	25		U/L	13-30	NA		U/L	106-322	0.7		mg/dL	0.4-1.5	NA		mg/dL	0-0.4	NA		mg/dL	0.4-1.1
R788-1301 [redacted]	R788/R788	WEEK 10 UNSCHEDULED 1	20[redacted]	142	H	U/L	7-23	84	H	U/L	13-30	60		U/L	38-113	0.6		mg/dL	0.4-1.5				0.05-0.3				-
		WEEK 10 UNSCHEDULED 2	20[redacted]	120	H	U/L	7-23	72	H	U/L	13-30	50		U/L	38-113	0.5		mg/dL	0.4-1.5	0.1		mg/dL	0.05-0.3				-
		WEEK 12 UNSCHEDULED 1	20[redacted]	51	H	U/L	7-23	30		U/L	13-30	52		U/L	38-113	0.4		mg/dL	0.4-1.5				0.05-0.3				-
		WEEK 14 UNSCHEDULED 1	20[redacted]	31	H	U/L	7-23	29		U/L	13-30	50		U/L	38-113	0.5		mg/dL	0.4-1.5				0.05-0.3				-

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase				Aspartate Aminotransferase				Alkaline Phosphatase				Bilirubin				Direct Bilirubin				Indirect Bilirubin			
				Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range
R788-1301 [redacted]	R788/R788	DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	87	H	U/L	7-23	133	H	U/L	13-30	83		U/L	38-113	0.56		mg/dL	0.4-1.5				0.1-0.4				0.1-0.8
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	57	H	U/L	7-23	34	H	U/L	13-30	72		U/L	38-113	0.64		mg/dL	0.4-1.5	0.05	L	mg/dL	0.1-0.4	0.59		mg/dL	0.1-0.8
R788-1301 [redacted]	R788/R788	WEEK 2 UNSCHEDULED 1	20[redacted]	34	H	U/L	7-23	45	H	U/L	13-30				38-113				0.4-1.5				0-0.4				0-1.1
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	25	H	U/L	7-23	33	H	U/L	13-30				38-113				0.4-1.5				0-0.4				0-1.1
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]				-				-				-				-				-				-
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	24	H	U/L	7-23	31	H	U/L	13-30				38-113				0.4-1.5				0-0.4				0-1.1
		EARLY SHIFT WEEK 8 UNSCHEDULED 1	20[redacted]	32	H	U/L	7-23	43	H	U/L	13-30				38-113				0.4-1.5				0-0.4				0-1.1
		EARLY SHIFT WEEK 8 UNSCHEDULED 2	20[redacted]	23		U/L	7-23	38	H	U/L	13-30	93		U/L	38-113	1.5		mg/dL	0.4-1.5				0-0.4				0-1.1
		EARLY SHIFT WEEK 8 UNSCHEDULED 3	20[redacted]	27	H	U/L	7-23	45	H	U/L	13-30	96		U/L	38-113	0.9		mg/dL	0.4-1.5				0-0.4				0-1.1
		EARLY SHIFT WEEK 12 UNSCHEDULED 2	20[redacted]	28	H	U/L	7-23	41	H	U/L	13-30	156	H	U/L	38-113	0.9		mg/dL	0.4-1.5				0-0.4				0-1.1
R788-1301 [redacted]	Placebo/R788	EARLY SHIFT WEEK 24 UNSCHEDULED 1	20[redacted]	102	H	U/L	7-23	100	H	U/L	13-30	157	H	U/L	38-113	0.4		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.3		mg/dL	0.1-0.8
		EARLY SHIFT WEEK 24 UNSCHEDULED 2	20[redacted]	157	H	U/L	7-23	134	H	U/L	13-30	171	H	U/L	38-113	0.5		mg/dL	0.4-1.5	0.1		mg/dL	0.1-0.4	0.4		mg/dL	0.1-0.8
		EARLY SHIFT WEEK 24 UNSCHEDULED 3	20[redacted]	418	H	U/L	7-23	315	H	U/L	13-30	246	H	U/L	38-113	0.7		mg/dL	0.4-1.5	0.2		mg/dL	0.1-0.4	0.5		mg/dL	0.1-0.8
		EARLY SHIFT WEEK 24 UNSCHEDULED 4	20[redacted]	453	H	U/L	7-23	250	H	U/L	13-30	176	H	U/L	38-113	0.8		mg/dL	0.4-1.5	0.2		mg/dL	0.1-0.4	0.6		mg/dL	0.1-0.8
		EARLY SHIFT WEEK 28 UNSCHEDULED 1	20[redacted]	307	H	U/L	7-23	150	H	U/L	13-30	167	H	U/L	38-113	0.9		mg/dL	0.4-1.5	0.2		mg/dL	0.1-0.4	0.7		mg/dL	0.1-0.8
		EARLY SHIFT WEEK 28 UNSCHEDULED 2	20[redacted]	225	H	U/L	7-23	115	H	U/L	13-30	167	H	U/L	38-113	0.9		mg/dL	0.4-1.5	0.2		mg/dL	0.1-0.4	0.7		mg/dL	0.1-0.8
R788-1301 [redacted]	Placebo/R788	EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	85	H	U/L	7-23	80	H	U/L	13-30	157	H	U/L	38-113	1.1		mg/dL	0.4-1.5				0-0.4				-
R788-1301 [redacted]	Placebo/R788	DAY 1 UNSCHEDULED 1	20[redacted]	46	H	U/L	4-44	33		U/L	8-38	109		U/L	38-113	1.7	H	mg/dL	0.2-1.2				0-0.4				-
		DAY 1 UNSCHEDULED 2	20[redacted]	41		U/L	4-44	31		U/L	8-38	108		U/L	38-113	1.3	H	mg/dL	0.2-1.2	0.3		mg/dL	0-0.4	1.0		mg/dL	-
		WEEK 2 UNSCHEDULED 1	20[redacted]	33		U/L	4-44	27		U/L	8-38	101		U/L	38-113	1.4	H	mg/dL	0.2-1.2	0.4		mg/dL	0-0.4	1.0		mg/dL	-
		WEEK 4 UNSCHEDULED 1	20[redacted]	35		U/L	4-44	29		U/L	8-38	110		U/L	38-113	1.3	H	mg/dL	0.2-1.2	0.4		mg/dL	0-0.4	0.9		mg/dL	-
		WEEK 6 UNSCHEDULED 1	20[redacted]	34		U/L	4-44	29		U/L	8-38	100		U/L	38-113	1.5	H	mg/dL	0.2-1.2	0.4		mg/dL	0-0.4	1.1		mg/dL	-
		WEEK 8 UNSCHEDULED 1	20[redacted]	34		U/L	4-44	26		U/L	8-38	106		U/L	38-113	1.0		mg/dL	0.2-1.2	0.3		mg/dL	0-0.4	0.7		mg/dL	-
		WEEK 10 UNSCHEDULED 1	20[redacted]	43		U/L	4-44	34		U/L	8-38	121	H	U/L	38-113	0.9		mg/dL	0.2-1.2	0.2		mg/dL	0-0.4	0.7		mg/dL	-
		DBP DISCONTINUATION UNSCHEDULED 1	20[redacted]	36		U/L	4-44	44	H	U/L	8-38	140	H	U/L	38-113	2.3	H	mg/dL	0.2-1.2	0.6	H	mg/dL	0-0.4	1.7		mg/dL	-
		DBP DISCONTINUATION UNSCHEDULED 2	20[redacted]	31		U/L	4-44	26		U/L	8-38	145	H	U/L	38-113	1.6	H	mg/dL	0.2-1.2	0.4		mg/dL	0-0.4	1.2		mg/dL	-
		EARLY SHIFT WEEK 4 UNSCHEDULED 1	20[redacted]	35		U/L	4-44	29		U/L	8-38	163	H	U/L	38-113	1.9	H	mg/dL	0.2-1.2	0.5	H	mg/dL	0-0.4	1.4		mg/dL	-
		EARLY SHIFT WEEK 8 UNSCHEDULED 1	20[redacted]	45	H	U/L	4-44	31		U/L	8-38	176	H	U/L	38-113	2.3	H	mg/dL	0.2-1.2	0.6	H	mg/dL	0-0.4	1.7		mg/dL	-
		EARLY SHIFT WEEK 12 UNSCHEDULED 1	20[redacted]	48	H	U/L	4-44	36		U/L	8-38	173	H	U/L	38-113	2.6	H	mg/dL	0.2-1.2	0.6	H	mg/dL	0-0.4	2.0		mg/dL	-
		EARLY SHIFT WEEK 16 UNSCHEDULED 1	20[redacted]	48	H	U/L	4-44	34		U/L	8-38	161	H	U/L	38-113	1.4	H	mg/dL	0.2-1.2	0.4		mg/dL	0-0.4	1.0		mg/dL	-

Protocol No. Site ID Subject ID	Group (Period I /Period II and after)	VISIT	Date	Alanine Aminotransferase				Aspartate Aminotransferase				Alkaline Phosphatase				Bilirubin				Direct Bilirubin				Indirect Bilirubin			
				Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range	Result		Unit	Range
		EARLY SHIFT WEEK 28 UNSCHEDULED 1	20[redacted]	33		U/L	4-44	28		U/L	8-38	143	H	U/L	38-113	2.0	H	mg/dL	0.2-1.2	0.5	H	mg/dL	0-0.4	1.5		mg/dL	-

（Source: 1.13.3-4, C-15 付録 3）

表 2.7.4.9-100　国内第 III 相臨床試験（R788-1301）における重篤又は重症度が中等度以上の消化管障害、高血圧 SMQ、薬物関連肝障害 SMQ 及び白血球減少の一覧表

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	No.	事象名(PT)	発現時治験薬投与量	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表			
																	R788投与後日数	持続期間（日）	処置の経過	治験薬投与中止の有無
R788-1301	[redacted]	R788	ITP	6[redacted]	F	ITP, diabetes mellitus, hypertension, hyperlipidemia, bronchial asthma, lupus miliaris disseminatus facial, Leg cramps, right optic neuropathy	1	Diarrhoea	100 MG BID	N		MODERATE	TREATMENT I	DOSE REDUCED	RECOVERED/ RESOLVED	RELATED	78	42	発現35日目に休薬し、発現42日目に症状が回復したため、治験薬を150mgQDに減量し再開した。	無
R788-1301	[redacted]	R788	ITP	6[redacted]	F	ITP, Hypertension, Hyperlipidaemia, Functionaldyspepsia, Numbness of limbs, Headaches, Legpain, Bilateral kidney stones	1	Diarrhoea	100 MG BID	Y	Requires or Prolongs Hospitalization	SEVERE	TREATMENT I	DOSE REDUCED	RECOVERED/ RESOLVED	RELATED	19	8	発現3日目に休薬し、発現8日目に症状が回復したため、治験薬を100mgQDに減量し再開した。	無
R788-1301	[redacted]	R788	ITP	6[redacted]	F	ITP, Uterine myoma, Pollinosis, Periodontitis	1	Diarrhoea	100 MG BID	N		MODERATE	TREATMENT I	DOSE REDUCED	RECOVERED/ RESOLVED	RELATED	29	3	有害事象のため、増量基準に該当する来院時点で増量できなかった。発現3日目、100mgBID投与継続中に回復した。	無
							2	Diarrhoea	100 MG BID	N		MODERATE	TREATMENT I	DOSE NOT CHANGED	RECOVERED/ RESOLVED	RELATED	35	1	治験薬に対する処置を実施せず、発現3日目に回復した。	無
							3	Diarrhoea	100 MG BID	N		MODERATE	TREATMENT I	DOSE REDUCED	RECOVERED/ RESOLVED	RELATED	39	12	有害事象のため、増量基準に該当する来院時点で増量できなかった。発現4日目に休薬し、発現12日後に回復した。	無

（Source: 1.13.3-4, C-07 付録 C-07-2）

表 2.7.4.9-101　海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）における重篤又は重症度が中等度以上の消化管障害、高血圧 SMQ、薬物関連肝障害 SMQ 及び白血球減少の一覧表

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名(PT)	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表		
															R788投与後日数	持続期間（日）	治験薬中止の有無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, COLONSCOPY, CESAREAN, EAR SURGERY, HYPERTENSION, THYROID PROBLEMS, ANXIETY, ALLERGIES, DENTAL/TOOTH INFECTION, DIZZINESS, KNEE SURGERY, BLEEDING, SCIATICA, RIGHT KNEE ARTHRITIS, HIATAL HERNIA, INTRACRANIAL HEMORRHAGE, ENDOSCOPY, HYSTERECTOMY, COLONOSCOPY, UPPER GI [redacted]	Diarrhoea	N		SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	1449	31	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, BREAST CANCER, BASAL CELL CARCINOMA/RESECTION, BILATERAL PATELLAR FRACTURE, CATARACT EXTRACTION OF BOTH EYES, GASTRITIS W/ HELICOBACTER PYLORI, BLEEDING, SLEEP DEPRIVATION/PROBLEMS, LOWER EXTREMITY EDEMA, PERSISTENT TOE PAIN, ENDOMETRIAL CANCER/HYSTERECTOMY, FUNCTIONAL HEART MURMUR, ACOUSTIC NEUROMA/RESECTION, BREAST BIOPSY FOR BENIGN PARENCHYMAL HEMATOMA/DRAINAGE, COLONOSCOPY - INTERNAL HEMORRHOIDS, ENDOSCOPY, ARTERIOVENOUS MALFORMATION/ARGON PLASMA COAGULATION, BASAL CELL RESECTION, RIGHT PATELLAR FRACTURE	Lymphopenia	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERING /RESOLVING	UNLIKELY RELATED	-1549		無
							Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	210	3	無
							Gastrointestinal Haemorrhage	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	263	8	無
							Melaena	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	263	8	無
							Gastric Antral Vascular Ectasia	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	267	4	無
							Gastrointestinal Haemorrhage	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	490	6	無
							Neutropenia	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERING /RESOLVING	UNLIKELY RELATED	698		無
							Melaena	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	839	8	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, URINARY RETENTION, HEARTBURN, SEASONAL ALLERGIES, BLEEDING, TINGLING/NUMBNESS TO LEFT FOREARM, PAIN TO RIGHT EAR/RIGHT SIDE OF HEAD (PAIN GOING TO NECK AND BACK), COLON POLYP, DIVERTICULITIS, MILD LIVER DYSFUNCTION - 2CM LIKER NODULE. NO CLINICAL SIGNIFICANCE, COLONOSCOPY - POLY REMOVED. DIVERTICULITIS, L. INGUINAL HERNIA REPAIR, COLONOSCOPY, AORTIC ANEURYSM. NO INTERVENTION REQUIRED, TINNITUS - LONG STANDING, ANXIETY/DEPRESSION, ANAPHYLACTIC REACTION TO RITUXIMAB	Nausea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	4	26	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, APPENDECTOMY, LUMPECTOMY, PLASTIC SURGERY POST PLANE CRASH, FRONTAL ARTERITIS -POST PLANE CRASH, HYPOTHYROIDISM, AORTIC ANEURYSM OF UNSPECIFIED SITE WITHOUT MENTION OF RUPTURE, BLEEDING, GALL BLADDER REMOVED, R BREAST TUMOR EXCISION, BREAST IMPLANTATION AND REMOVAL, HYPERCHOLESTEREMIAS, BREAST CANCER, HYSTERECTOMY, TRIGGER FINGER" RELEASE SURGERY	Rectal Haemorrhage	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	37	1	無

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名(PT)	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表		
															R788投与後日数	持続期間(日)	治験薬中止の有無
C_935788_048	[redacted]	Fostamatinib	ITP	4[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, CRAMPS OF LEG, ELEVATION OF WHITE BLOOD CELLS, METABOLIC SYNDROME, DIABETTES MELLITUS, HYPERURICEMIA, TINNITUS, TONSILLITIS CHRONICAL, POLYARTRALGIC SYNDROME, STATUS POST ARTROSCOPY	Flatulence	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	12	31	無
C_935788_049	[redacted]	Fostamatinib	ITP	4[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, CRAMPS OF LEG, ELEVATION OF WHITE BLOOD CELLS, METABOLIC SYNDROME, DIABETTES MELLITUS, HYPERURICEMIA, TINNITUS, TONSILLITIS CHRONICAL, POLYARTRALGIC SYNDROME, STATUS POST ARTROSCOPY	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED WITH SEQUELA E	POSSIBLY RELATED	138	2	無
C_935788_048	[redacted]	Fostamatinib	ITP	6[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ARTERIAL HYPERTENSION, DIABETES MELLITUS, HYPERTRIGLICERYDEMIA, ADRENAL ADENOMA	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	PROBABLY RELATED	71	2	無
C_935788_049	[redacted]	Fostamatinib	ITP	4[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, FRACTURE OF RIGHT CLAVICULAR BONE, CARIES	Diarrhoea	N		MODERATE	Open Label Extension Study	DRUG INTERRUP TED	RECOVERED /RESOLVED	PROBABLY RELATED	233	243	無
C_935788_047	[redacted]	Fostamatinib	ITP	7[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, PAROXYSMAL ATRIAL FIBRILLATION, TIA, RETINAL DETACHMENT, DIVERTICULAR DISEASE, HEARING LOSS IN LEFT EAR	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	6	1	無
							Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	7	32	無
							Diarrhoea	N		MODERATE	Double- Blind	DRUG INTERRUP TED	RECOVERED/ RESOLVED	POSSIBLY RELATED	41	21	無
							Diarrhoea	Y	Requires or Prolongs Hospitalization	MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	61	3	無
C_935788_049	[redacted]	Placebo	ITP	4[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HASHIMOTO'S THYROIDITIS, ASTHMA BRONCHIAL, MONOCLONAL GAMMOPHATHY	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	PROBABLY RELATED	212		無
							Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	UNLIKELY RELATED	345		無
C_935788_047	[redacted]	Fostamatinib	ITP	8[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, APOPLEXIA CEREBRI	Diarrhoea	N		MODERATE	Double- Blind	DRUG WITHDRA WN	RECOVERED/ RESOLVED	POSSIBLY RELATED	5	39	有
C_935788_049	[redacted]	Placebo	ITP	2[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, MULTIPLE LEG FRACTURES, WISDOM TEETH EXTRACTION	Haematochezia	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED	90	2	無
C_935788_049	[redacted]	Fostamatinib	ITP	7[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, HERNIA, HYPERCHOLESTEROL	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED	101	117	無
C_935788_049	[redacted]	Placebo	ITP	6[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, SPLENECTOMY, HYPERTENSION, GI BLEEDING (PRE-EXISTING CONDITION, HISTORY OF GI BLEEDING), ANEMIA	Gastrointestinal Haemorrhage	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED	-4	13	無
							Gastrointestinal Haemorrhage	Y	Requires or Prolongs Hospitalization	MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED	30	6	無
C_935788_049	[redacted]	Placebo	ITP	6[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HYSTERECTOMY, MENINGIOMA, LEFT NEPHRECTOMY, LEFT ADRENALECTOMY, TONSILLECTOMY WITH ADENOIDECTOMY, EPISTAXIS, HYPERLIPIDEMIA, LEUKOCYTOSIS, GI BLEED, HIGH BLOOD PRESSURE, HERPES SIMPLEX, ENDOMETRIAL CARCINOMA, SUBCLINICAL HYPERTHYROIDISM, SQUAMOUS CELL CARCINOMA OF LEFT LOWER LEG, VITAMIN B12 DEFICIENCY, VITAMIN D DEFICIENCY	Diarrhoea	N		MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED/ RESOLVED	PROBABLY RELATED	27	41	有

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名(PT)	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表		
															R788投与後日数	持続期間(日)	治験薬中止の有無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HYSTERECTOMY, BREAST REDUCTION, LOW POTASSIUM, DEPRESSION, INCREASED URINARY FREQUENCEY, HYPERTENSION, CHOLECYSTECTOMY, NAUSEA, PANCYTOPENIA, PETECHIAE, HYPOTHYROIDISM, MIGRAINES, SPINAL FUSION	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED	4	11	無
							Flatulence	N		MODERATE	Double- Blind	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	POSSIBLY RELATED	49		無
							Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVER ED/RESOL VED	POSSIBLY RELATED	50	1	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, ACUTE GASTRITIS HP NEGATIVE, HEMORRHOIDS	Neutropenia	N		MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED/ RESOLVED	PROBABLY RELATED	91	22	有
C_935788_048	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED	44	13	無
							Diarrhoea	N		MODERATE	Double- Blind	DOSE REDUCED	RECOVERED /RESOLVED	POSSIBLY RELATED	59	32	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ACUTE PANCREATITIS, APPENDIX REMOVAL, CONTINUES HEADACHES, INFECTION OF MIDDLE EAR	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	216	67	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION	Gastrointestinal Haemorrhage	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	826	77	無
							Vomiting	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	1022	1	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTHYREOSIS, LIPOMA SURGERY, CARDIOVASCULAR	Febrile Neutropenia	N		MODERATE	Double- Blind	DOSE REDUCED	RECOVERED/ RESOLVED	PROBABLY RELATED	100	6	無
							Febrile Neutropenia	Y	Requires or Prolongs Hospitalization	SEVERE	Double- Blind	DRUG INTERRUP TED	RECOVERED/ RESOLVED	POSSIBLY RELATED	103	6	無
C_935788_048	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ARTERIAL HYPERTENSION GRADE 1, DIABETES MELLITUS, OPEN-ANGLE GLAUCOMA, PAIN	Flatulence	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	12	16	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ARTERIAL HYPERTENSION GRADE 1, DIABETES MELLITUS, OPEN-ANGLE GLAUCOMA, PAIN MUSCLE	Mouth Haemorrhage	Y	Requires or Prolongs Hospitalization	MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	128	3	無
							Mouth Haemorrhage	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	128	3	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DIABETES, HYPERTENSION, CHOLECYSTECTOMY, HYPOTHYROIDISM, THROMBOCYTOPENIA, HEMANGIOMAS OF LIVER	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	159	3	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ROSACEA, HYPERTENSION, HYPOTHYROIDISM, INCREASED OCULAR PRESSURE SECONDARY TO CHRONIC STEROID USE, OSTEOPOROSIS, GALL BLADDER SURGERY, POSITIVE H. PYLORI SEROLOGY	Diarrhoea	N		SEVERE	Double- Blind	DRUG INTERRUP TED	RECOVERED /RESOLVED	PROBABLY RELATED	103	17	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ROSACEA, HYPERTENSION, HYPOTHYROIDISM, INCREASED OCULAR PRESSURE SECONDARY TO CHRONIC STEROID USE, OSTEOPOROSIS, GALL BLADDER SURGERY, POSITIVE H. PYLORI SEROLOGY	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE REDUCED	RECOVERED /RESOLVED	PROBABLY RELATED	352	42	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, EVANS SYNDROME, HAIR LOSS, FATIGUE, CONSTIPATION, IVIG ASSOCIATED HEADACHE, VISUAL FIELD DEFICITS, GASTROESOPHAGEAL REFLUX DISEASE, POSITIVE ANTIPHOSPHOLIPID AND ANTICARDIOLIPIN ANTIBODIES, REMOVAL OF THYMUS MASS, LEFT ELBOW INJURY, DEPRESSION	Nausea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	27	18	無

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名(PT)	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表		
															R788投与後日数	持続期間(日)	治験薬中止の有無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, FATIGUE, SUBCUTANEOUS CYST (RIGHT LOWER POSTERIOR CERVICAL AREA)	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	POSSIBLY RELATED	57		無
C_935788_049	[redacted]						Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	57	89	無
							Diarrhoea	N		SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	PROBABLY RELATED	146	1	無
							Diarrhoea	N		MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED /RESOLVED	PROBABLY RELATED	147	16	有
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, AUTOIMMUNE HEMOLYTIC ANEMIA, INTERMITTENT HEADACHE, TRAUMATIC BRAIN INJURY, OCCASIONAL SMALL BRUISES AND PETECHIAE, RASH, INTERMITTENT FATIGUE, INTERMITTENT HEARTBURN, INTERMITTENT ACNE	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED WITH SEQUELA E	PROBABLY RELATED	61	27	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, CUTANEOUS LUPUS ERYTHEMATOSUS OF THE SCALP, SPONTANEOUS SUBDURAL HEAMATOMA, BILATERAL AVASCULAR NECROSIS OF HIP JOINTS, TONSILLECTOMY, SLEEP DISTURBANCES, MENORRHAGIA, BACTERIAL LYMPHADENITIS, OCCASIONAL HEADACHE	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	139	14	無
							Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	PROBABLY RELATED	428		無
							Mouth Haemorrhage	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	695	18	無
							Rectal Haemorrhage	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	695	18	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION	Lymphocyte Count Decreased	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	99	29	無
							Diarrhoea	N		MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED /RESOLVED	PROBABLY RELATED	257	35	有
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DIVERTICULAR DISEASE, HASHIMOTO'S THYROIDITIS, MILD AGINA, PYELOPLASTY, AMNESIA, CICLOSPORIN TOXICITY	Neutropenia	N		MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED /RESOLVED	POSSIBLY RELATED	71	101	有
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, SKIN BLEEDING, FATIGUE, APPENDECTOMY, OVARIAN CYST NOS	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	167	6	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, SKULL FRACTURE, TIREDNESS, IRRITABILITY	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	PROBABLY RELATED	104	77	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, COLONIC RESECTION FOR COLORECTAL CANCER STAGE 2, IRON DEFICIENCY, WHITE COAT HYPERTENSION, SUBDURAL HEMATOMA (IN CONTEXT OF SEVERE THROMBOCYTOPENIA, OSTEOPOROSIS, MYELOFIBROSIS, TOTAL ABDOMINAL HYSTERECTOMY, MONOCLONAL GAMMOPATHY OF UNKNOWN SIGNIFICANCE, COLON CANCER, HEMORRHOIDAL BLEEDING	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	25	2	無
C_935788_049	[redacted]						Diarrhoea	Y	Requires or Prolongs Hospitalization	MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED /RESOLVED	PROBABLY RELATED	516	8	有

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名(PT)	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表		
															R788投与後日数	持続期間(日)	治験薬中止の有無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, LEFT FOREARM FRACTURE, ABDOMINAL CRAMPS, IRON DEFICIENCY, CONSTIPATION, PACEMAKER, RECTAL BLEEDING, DIZZINESS, CELLULITIS, LOW THYROID, BREAST CANCER, TREATED WITH LEFT LUMPECTOMY, RADIOTHERAPY AND CHEMOTHERAPY, THYROIDECTOMY, APPENDECTOMY, BILATERAL CATARACT SURGERY, CHRONIC LUNG DISEASE, SLEEP APNEA, DYSLIPIDEMIA, COLONOSCOPY	Nausea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	2	14	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, SPLENECTOMY, GLANDULAR FEVER, PERFORATED DUODENAL ULCER, DEPRESSION, ALCOHOLIC DEPENDANCY, APPENDICECTOMY	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOL VED	UNLIKELY RELATED	96	3	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA	Mucosal Haemorrhage	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	611	6	無
							Mucosal Haemorrhage	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	634	3	無
							Mucosal Haemorrhage	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	1017	2	無
							Mucosal Haemorrhage	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	UNLIKELY RELATED	1290	6	無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, H PYLORI GASTRITIS, BACK ACHE CERVICAL SPINE, ANAEMIA, POLYARTHRALGIA, GASTRIC	Abdominal Pain	N		MODERATE	Open Label Extension Study	DRUG INTERRUP TED	RECOVERED /RESOLVED	UNLIKELY RELATED	25	6	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HIGH CHOLESTEROL, HYPERTENSION, COLONOSCOPIC POLYPECTOMY, GLAUCOMA, TRABECULECTOMY	Diarrhoea	N		MODERATE	Double- Blind	DRUG INTERRUP TED	RECOVERED/ RESOLVED	UNLIKELY RELATED	60	6	無
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, BETA THALASSEMIA TRAIT, OVARIAN CYSTS, ENDOMETRIOSIS, ANXIETY, OSTEOPENIA, HYSTERECTOMY, BIOSY OF RESIDUAL UTERINE CERVIX	Abdominal Pain	N		MODERATE	Open Label Extension Study	DRUG INTERRUP TED	RECOVERED /RESOLVED	PROBABLY RELATED	182	16	無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, COELIAC DISEASE, CHRONIC IRON DEFICIENCY, OSTEOPOROSIS, ENDOMETRIAL ABLATION, ARTHRITIS, UPPER RESPIRATORY TRACT INFECTION	Abdominal Pain	N		MODERATE	Double- Blind	DRUG WITHDRA WN	RECOVERED /RESOLVED	PROBABLY RELATED	90	5	有
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, ASTHMA, ECZEMA, OESOPHAGEAL ULCERATION	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	POSSIBLY RELATED	681		無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, EPS/ABALATION, FATIGUE, IRON DEFICIENCY, OBESITY, IMPAIRED GLUCOSE TOLERANCE, OSTEOARTHRITIS ANMD LUMBER SPONDYLOSIS, SEVERE SLEEP APNOEA, CHOLELITHIASIS, ANXIETY AND DEPRESSION, HYPERTENSION, MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE	Diarrhoea	N		MODERATE	Double- Blind	DOSE NOT CHANGED	RECOVERED /RESOLVED	POSSIBLY RELATED	57	70	無
							Neutropenia	N		SEVERE	Double- Blind	DRUG WITHDRA WN	RECOVERED /RESOLVED	PROBABLY RELATED	83	21	有
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, IRON DEFICIENCY, HYPOTHYROIDISM, GASTRO-OESOPHAGEAL REFLUX DISEASE, FUNGAL INFECTION TO SKIN AROUND MOUTH, VITAMIN D DEFICIENCY, HYPOCALCEMIA, MUSCLE ACHES	Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE REDUCED	RECOVERED /RESOLVED	POSSIBLY RELATED	874	73	無
							Diarrhoea	N		MODERATE	Open Label Extension Study	DOSE NOT CHANGED	RECOVERED /RESOLVED	PROBABLY RELATED	1021	32	無

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名(PT)	重篤性		重症度	発現時期	治験薬に対する処置	転帰	因果関係	臨床経過表		
															R788投与後日数	持続期間(日)	治験薬中止の有無
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, HYPERLIPIDEMIA, NON INSULIN DEPENDETN DIABETIC	Neutropenia	N		MODERATE	Double- Blind	DOSE NOT CHANGED	NOT RECOVERED /NOT RESOLVED	POSSIBLY RELATED	87		無
C_935788_049	[redacted]	Placebo	ITP	[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, INFARCTION, ATHEROSCLEROSIS, STENTED, HYPOTHYREOSIS, LYME DISEASE, VITAMIN B12 DEFICIENCY, AUTOIMMUNE?, NUMBNESS IN HIS LEGS	Diarrhoea	N		MODERATE	Open Label Extension Study	DRUG WITHDRA WN	RECOVERED /RESOLVED	PROBABLY RELATED	41	18	有

灰色網掛けは、C788-049 試験で発現した有害事象としてデータセットに格納されているものの、発現日が R788 の投与前であった有害事象
（Source: 1.13.3-4, C-07 付録 C-07-3）

表 2.7.4.9-102　　国内第 III 相臨床試験（R788-1301）における重篤又は重症度が中等度以上の高血圧 SMQ の一覧表

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名（PT）	発現時治験薬投与量	重篤性		重症度	発現時期	R788投与後日数	持続期間（日）	治験薬に対する処置	転帰	因果関係
R788-1301	[redacted]	PLACEBO	ITP	[redacted]	F	IDIOPATHIC TROMBOCYTOPENIC PURPURA, Dyslipidemia, Constipation, Chronic kidney disease, Right knee pain	Hypertension	100 MG BID	N		MODERATE	EARLY SHIFT TREATMENT II	4	12	DOSE REDUCED	RECOVERED/RESOLVED	RELATED

（Source: 1.13.3-6, C-03 付録 220907-C-03-1-1）

表 2.7.4.9-103　　海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）における重篤又は重症度が中等度以上の高血圧 SMQ の一覧表

StudyID	SubjectID	ARM	Primary Disease	AGE	SEX	Medical History	AETERM (PT)	Serious Event		Severity/ Intensity	Period	Start of adverse event relative to the first R788 administrati on.	Duration of Adverse Event	Action Taken with Study Treatment	Outcome	Causality
C_935788_047	[redacted]	Fostamatinib	ITP	6[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, COLONSCOPY, CESAREAN, EAR SURGERY, HYPERTENSION, THYROID PROBLEMS, ANXIETY, ALLERGIES, DENTAL/TOOTH INFECTION, DIZZINESS, KNEE SURGERY, BLEEDING, SCIATICA, RIGHT KNEE ARTHRITIS, HIATAL HERNIA, INTRACRANIAL HEMORRHAGE, ENDOSCOPY, HYSTERECTOMY, COLONOSCOPY, UPPER GI ENDOSCOPY	Blood Pressure Increased	N		SEVERE	Double-Blind	158	14	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_049							Hypertension	N		MODERATE	Open Label Extension Study	527		DOSE NOT CHANGED	NOT RECOVERED/ NOT RESOLVED	POSSIBLY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	8[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, BREAST CANCER, BASAL CELL CARCINOMA/RESECTION, BILATERAL PATELLAR FRACTURE, CATARACT EXTRACTION OF BOTH EYES, GASTRITIS W/ HELICOBACTER PYLORI, BLEEDING, SLEEP DEPRIVATION/PROBLEMS, LOWER EXTREMITY EDEMA, PERSISTENT TOE PAIN, ENDOMETRIAL CANCER/HYSTERECTOMY, FUNCTIONAL HEART MURMUR, ACOUSTIC NEUROMA/RESECTION, BREAST BIOPSY FOR BENIGN PARENCHYMAL HEMATOMA/DRAINAGE, COLONOSCOPY - INTERNAL HEMORRHOIDS, ENDOSCOPY, ARTERIOVENOUS MALFORMATION/ARGON PLASMA COAGULATION, BASAL CELL RESECTION, RIGHT PATELLAR FRACTURE	Hypertension	N		MODERATE	Open Label Extension Study	625		DOSE NOT CHANGED	NOT RECOVERED/ NOT RESOLVED	UNLIKELY RELATED
							Hypertension	N		SEVERE	Open Label Extension Study	831	17	DRUG INTERRUP TED	RECOVERED/ RESOLVED	UNLIKELY RELATED
							Hypertension	N		SEVERE	Open Label Extension Study	891	1	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
							Hypertension	N		SEVERE	Open Label Extension Study	1226	22	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_048	[redacted]	Fostamatinib	ITP	7[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, COPD STADIUM 1, DEPRESSION, HEARTBURN	Hypertensive Crisis	Y	Requires or Prolongs Hospitalization	SEVERE	Double-Blind	21	5	DRUG INTERRUP TED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	5[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, ARTERIAL HYPERTENSION	Hypertension	N		MODERATE	Open Label Extension Study	382	1	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_048	[redacted]	Fostamatinib	ITP	6[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, ARTERIAL HYPERTENSION, ASYMPTOMATIC MYOCARDIAL INFARCTION	Hypertension	N		MODERATE	Double-Blind	29	43	DOSE REDUCED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_048	[redacted]	Fostamatinib	ITP	6[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ARTERIAL HYPERTENSION GRADE 1, DIABETES MELLITUS, OPEN- ANGLE GLAUCOMA, PAIN MUSCLE	Hypertension	N		MODERATE	Double-Blind	41	1	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	6[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, ARTHROPLASTY OF LEFT KNEE, DEPRESSION, HIPERTENSION, APPENDECTOMY, ARTHRITIS	Hypertension	N		MODERATE	Open Label Extension Study	351	358	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED

StudyID	SubjectID	ARM	Primary Disease	AGE	SEX	Medical History	AETERM (PT)	Serious Event		Severity/ Intensity	Period	Start of adverse event relative to the first R788 administrati on.	Duration of Adverse Event	Action Taken with Study Treatment	Outcome	Causality
C_935788_049	[redacted]	Placebo	ITP	4[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DIABETES, HYPERTENSION, CHOLECYSTECTOMY, HYPOTHYROIDISM, THROMBOCYTOPENIA, HEMANGIOMAS OF LIVER	Hypertension	N		MODERATE	Open Label Extension Study	231	40	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	5[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HEART MURMUR, TINNITUS, INTERMITTENT PETECHIAE, GENERAL ARTHRITIS, OSTEOARTHRITIS LEFT HAND, ALOPECIA-AGE RELATED MALE PATTERN, ALLERGIC TO BEE STINGS, RECURRENT BOIL TO LEFT BUTTOX, NEAR SYNCOPE WITH BLOOD DRAWS, GENERALIZED PAIN	Hypertension	N		MODERATE	Open Label Extension Study	127	17	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	5[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION	Hypertension	N		MODERATE	Double-Blind	30	158	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_049							Hypertension	N		MODERATE	Open Label Extension Study	30	158	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	7[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DIVERTICULAR DISEASE, HASHIMOTO'S THYROIDITIS, MILD AGINA, PYELOPLASTY, AMNESIA, CICLOSPORIN TOXICITY	Hypertension	N		MODERATE	Double-Blind	2	14	DRUG INTERRUP TED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_049							Hypertension	N		MODERATE	Open Label Extension Study	2	14	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	8[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, COLONIC RESECTION FOR COLORECTAL CANCER STAGE 2, IRON DEFICIENCY, WHITE COAT HYPERTENSION, SUBDURAL HEMATOMA (IN CONTEXT OF SEVERE THROMBOCYTOPENIA, OSTEOPOROSIS, MYELOFIBROSIS, TOTAL ABDOMINAL HYSTERECTOMY, MONOCLONAL GAMMOPATHY OF UNKNOWN SIGNIFICANCE, COLON CANCER, HEMORRHOIDAL BLEEDING	Hypertension	N		MODERATE	Double-Blind	128		DRUG INTERRUP TED	NOT RECOVERED/ NOT RESOLVED	POSSIBLY RELATED
C_935788_049							Hypertension	N		MODERATE	Open Label Extension Study	128		DOSE NOT CHANGED	NOT RECOVERED/ NOT RESOLVED	POSSIBLY RELATED
C_935788_049	[redacted]	Placebo	ITP	5[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DISCOID LUPUS, GALL BLADDER REMOVED, VARICOSE VEINS	Hypertension	N		MODERATE	Open Label Extension Study	64	43	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	5[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DEPRESSION, GRAND MALSEIZURES, OSTEOARTHRITIS, HYPERLIPIDAEMIA	Hypertension	N		MODERATE	Double-Blind	22	16	DRUG INTERRUPTED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_049							Hypertension	N		MODERATE	Open Label Extension Study	22		DOSE NOT CHANGED	RECOVERING/ RESOLVING	UNLIKELY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	6[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HISTORY OF HYPERTENSION, HISTORY OF HIGH CHOLESTEROL, HYPERTROPHY (BENIGN) OF PROSTATE WITHOUT URINARY OBSTRUCTION, MALAISE AND FATIQUE, DIABETES MELLITUS (TYPE II), COLONIC POLYPS, VINTILIGO, ARTHRITIS	Blood Pressure Increased	N		MODERATE	Double-Blind	43	15	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_048	[redacted]	Fostamatinib	ITP	2[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA	Hypertension	N		MODERATE	Double-Blind	30	43	DOSE REDUCED	RECOVERED/ RESOLVED	PROBABLY RELATED

StudyID	SubjectID	ARM	Primary Disease	AGE	SEX	Medical History	AETERM (PT)	Serious Event		Severity/ Intensity	Period	Start of adverse event relative to the first R788 administrati on.	Duration of Adverse Event	Action Taken with Study Treatment	Outcome	Causality
C_935788_048	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, HYPOTHYRIODISM, ERYTHEMA MIGRANS. LOWER EXTREMITY SYMPTOMS. SEROLOGY CONFIRMED BORRHELIA INFECTION.	Hypertension	N		MODERATE	Double-Blind	68		DOSE NOT CHANGED	NOT RECOVERED/ NOT RESOLVED	PROBABLY RELATED
C_935788_049							Hypertension	N		MODERATE	Open Label Extension Study	68	371	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED

灰色網掛けは、C788-049 試験で発現した有害事象としてデータセットに格納されているものの、発現日が R788 の投与前であった有害事象
（Source: 1.13.3-6, C-03 付録 220907-C-03-1-2）

表 2.7.4.9-104　　国内第 III 相臨床試験（R788-1301）における重篤又は重症度が中等度以上の薬物関連肝障害 SMQ の一覧表

試験番号	被験者番号	投与群	対象疾患	年齢	性別	既往/合併	事象名（PT）	発現時治験薬投与量	重篤性		重症度	発現時期	R788投与後日数	持続期間（日）	治験薬に対する処置	転帰	因果関係
R788-1301	[redacted]	PLACEBO	ITP	[redacted]	F	IDIOPATHIC THROMBOCYTOPENIC PURPURA, Hypertension, Constipation, Headache, Complete Right Bundle Branch Block, Hand eczema	Autoimmune hepatitis	150 MG BID	Y	Requires or Prolongs Hospitalization	MODERAT E	EARLY SHIFT TREATMENT II	173	116	DOSE REDUCED	RECOVERED/ RESOLVED	NOT RELATED
R788-1301	[redacted]	R788	ITP	[redacted]	F	IDIOPATHIC THROMBOCYTOPENIC PURPURA, Uterine myoma, Pollinosis, Periodontitis	Hepatic function abnormal	100 MG BID	N		MODERAT E	TREATMENT I	43		DRUG WITHDRAWN	RECOVERING/RES OLVING	RELATED

（Source: 1.13.3-6, C-03 付録 220907-C-03-1-3）

表 2.7.4.9-105　海外第 III 相臨床試験（C788-047、C788-048 及び C788-049）における重篤又は重症度が中等度以上の薬物関連肝障害 SMQ の一覧表

StudyID	SubjectID	ARM	Primary Disease	AGE	SEX	Medical History	AETERM（PT）	Serious Event		Severity/ Intensity	Period	Start of adverse event relative to the first R788 administrati on.	Duration of Adverse Event	Action Taken with Study Treatment	Outcome	Causality
C_935788_049	[redacted]	Fostamatinib	ITP	8[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, BREAST CANCER, BASAL CELL CARCINOMA/RESECTION, BILATERAL PATELLAR FRACTURE, CATARACT EXTRACTION OF BOTH EYES, GASTRITIS W/ HELICOBACTER PYLORI, BLEEDING, SLEEP DEPRIVATION/PROBLEMS, LOWER EXTREMITY EDEMA, PERSISTENT TOE PAIN, ENDOMETRIAL CANCER/HYSTERECTOMY, FUNCTIONAL HEART MURMUR, ACOUSTIC NEUROMA/RESECTION, BREAST BIOPSY FOR BENIGN PARENCHYMAL HEMATOMA/DRAINAGE, COLONOSCOPY - INTERNAL HEMORRHOIDS, ENDOSCOPY, ARTERIOVENOUS MALFORMATION/ARGON PLASMA COAGULATION, BASAL CELL RESECTION, RIGHT PATELLAR FRACTURE	Transaminases Increased	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	890	12	DRUG INTERRUPTED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	4[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, APPENDECTOMY, SPINE ALGESIA, INTESTINAL POLYPOSIS	Hepatic Enzyme Increased	N		MODERATE	Open Label Extension Study	1016	25	DRUG WITHDRAWN	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	4[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, HYPERTENSION, CRAMPS OF LEG, ELEVATION OF WHITE BLOOD CELLS, METABOLIC SYNDROME, DIABETTES MELLITUS, HYPERURICEMIA, TINNITUS, TONSILLITIS CHRONICAL, POLYARTRALGIC SYNDROME, STATUS POST ARTROSCOPY	Hyperbilirubinaemia	N		MODERATE	Open Label Extension Study	155	85	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	5[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, MYOMA.	Transaminases Increased	Y	Requires or Prolongs Hospitalization	SEVERE	Open Label Extension Study	156	13	DRUG WITHDRAWN	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	2[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA	Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	100		DOSE NOT CHANGED	NOT RECOVERED/ NOT RESOLVED	POSSIBLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	7[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, MILD AORTIC REGURGITATION, VARICOSE VEINS, FACIAL ODEMA, HYPOTHYROIDISM, ECZEMA, ACUTE SUBDURAL HAEMATOMA, VIRAL PNEUMONIA, UTERINE PROLAPSE AND HYSTERECTOMY, MILD ARTHRITIS, HYPERTENSION, HAEMORRHOIDS	Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	44	49	DRUG WITHDRAWN	RECOVERED/ RESOLVED	POSSIBLY RELATED
							Aspartate Aminotransferase Increased	N		MODERATE	Double-Blind	44	15	DOSE NOT CHANGED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_049	[redacted]	Placebo	ITP	7[redacted]	M	IMMUNE THROMBOCYTOPENIC PURPURA, CHRONIC ATRIAL FIBHRILATION;, INTRACEREBRAL BLEEDING IN THE LEFT	Ascites	N		MODERATE	Open Label Extension Study	1253	18	DOSE NOT CHANGED	NOT RECOVERED/ NOT RESOLVED	UNLIKELY RELATED

StudyID	SubjectID	ARM	Primary Disease	AGE	SEX	Medical History	AETERM（PT）	Serious Event		Severity/ Intensity	Period	Start of adverse event relative to the first R788 administrati on.	Duration of Adverse Event	Action Taken with Study Treatment	Outcome	Causality
						BRAIN HEMISPHERE, HYDROCELE RIGHT TESTICLE, POLYPOSIS COLON, HYPERTENSION	Ascites	Y	Requires or Prolongs Hospitalization	MODERATE	Open Label Extension Study	1271	6	DOSE NOT CHANGED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, INTERMITTENT LOWER EXTREMITY EDEMA, HYSTERECTOMY, LEFT OOPHORECTOMY, APPENDECTOMY, HYPERTENSION, INTERMITTENT CONSTIPATION, INTERMITTENT TINGLING FINGERS, ANEMIA, BRUISING, THYROIDECTOMY, ARTHRITIS, MYELOFIBROSIS	Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	127	18	DRUG INTERRUPTED	RECOVERED/ RESOLVED	POSSIBLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DYSMENORRHOEA, ANXIETY	Aspartate Aminotransferase Increased	N		MODERATE	Double-Blind	86	28	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED
							Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	86	28	DRUG INTERRUPTED	RECOVERED/ RESOLVED	PROBABLY RELATED
							Aspartate Aminotransferase Increased	N		MODERATE	Double-Blind	92	22	DRUG INTERRUPTED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DYSMENORRHOEA, ANXIETY	Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	92	22	DRUG INTERRUPTED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_049	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, BETA THALASSEMIA TRAIT, OVARIAN CYSTS, ENDOMETRIOSIS, ANXIETY, OSTEOPENIA, HYSTERECTOMY, BIOSY OF RESIDUAL UTERINE CERVIX	Blood Bilirubin Increased	N		MODERATE	Open Label Extension Study	171	9	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, COELIAC DISEASE, CHRONIC IRON DEFICIENCY, OSTEOPOROSIS, ENDOMETRIAL ABLATION, ARTHRITIS, UPPER RESPIRATORY TRACT INFECTION	Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	43	29	DRUG INTERRUPTED	RECOVERED/ RESOLVED	PROBABLY RELATED
							Aspartate Aminotransferase Increased	N		MODERATE	Double-Blind	43	19	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED
C_935788_049	[redacted]	Placebo	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, CHOLECYSTECTOMY, DEPRESSION, SLEEP APNOEA	Hepatic Enzyme Increased	N		SEVERE	Open Label Extension Study	120	34	DRUG INTERRUPTED	RECOVERED/ RESOLVED	UNLIKELY RELATED
C_935788_047	[redacted]	Fostamatinib	ITP	[redacted]	F	IMMUNE THROMBOCYTOPENIC PURPURA, DEPRESSION, GRAND MAL SEIZURES, OSTEOARTHRITIS, HYPERLIPIDAEMIA	Alanine Aminotransferase Increased	N		MODERATE	Double-Blind	44	18	DRUG INTERRUPTED	RECOVERED/ RESOLVED	PROBABLY RELATED
							Aspartate Aminotransferase Increased	N		MODERATE	Double-Blind	44	18	DOSE NOT CHANGED	RECOVERED/ RESOLVED	PROBABLY RELATED

（Source: 1.13.3-6, C-03 付録 220907-C-03-1-4）

表 2.7.4.9-106　海外第 III 相臨床試験（C788-048）で認められた血栓症、塞栓症及び血栓塞栓症に関する有害事象の臨床経過

患者背景

被験者番号	[redacted]
投与群	R788
年齢	6[redacted]歳
性別	女性
人種	白人
合併症	高血圧、慢性閉塞性肺疾患、変形性股関節症、脊椎間すべり症
既往歴	なし
ITP の罹病期間	10 年（[redacted]/[redacted] 診断）
ITP に対する治療歴	脾摘（[redacted]年）、メチルプレドニゾロン
一過性脳虚血性発作の発現前 15 日以内に使用した併用薬	Nebivolol（β 遮断薬）、アトルバスタチン、イルベサルタン、Teotard®（テオフィリン）

一過性脳虚血性発作の概要

発現日	20[redacted]/[redacted]（Day 80）
回復日	Day 83*
程度	軽度
重篤の判定	重篤
治験薬に対する処置	変更なし
転帰	回復
治験薬との因果関係	おそらく関連なし

本剤の投与量

Day 1*	R788 100 mg 1 日 2 回で投与開始
Day 15*	Week 2 の血小板数が 250000/μL を超えたため R788 150 mg 1 日 1 回に減量
Day 165*	Week 22 後の規定外来院で血小板数増加のため R788 100 mg 1 日 1 回に減量
Day 170*	C788-049 試験に移行し、R788 100 mg 1 日 1 回で投与開始
Day 323*	Month 5 の血小板数が 100000/μL を下回ったため R788 100 mg 1 日 2 回に増量
Day 351*	Month 6 の血小板数が 250000/μL を超えたため R788 100 mg 1 日 1 回に減量 以降、R788 100 mg 1 日 1 回で継続

血小板数の推移
C788-048 study

Visit	Date	Platelet Count (/μL)
SCREEN A (VISIT 1)	20[redacted]	30000
SCREEN B (VISIT 2)	20[redacted]	34000
DAY 1 (VISIT 3)	20[redacted]	26000
WEEK 2 (VISIT 4)	20[redacted]	254000
UNSCHEDULED VISIT 4.01	20[redacted]	255000
UNSCHEDULED VISIT 4.02	20[redacted]	223000
UNSCHEDULED VISIT 4.03	20[redacted]	164000
WEEK 4 (VISIT 5)	20[redacted]	166000
UNSCHEDULED VISIT 5.01	20[redacted]	228000
WEEK 6 (VISIT 6)	20[redacted]	191000
WEEK 8 (VISIT 7)	20[redacted]	234000
WEEK 10 (VISIT 8)	20[redacted]	186000
WEEK 12 (VISIT 9)	20[redacted]	246000
WEEK 14 (VISIT 10)	20[redacted]	255000
WEEK 16 (VISIT 11)	20[redacted]	289000
UNSCHEDULED VISIT 11.01	20[redacted]	226000
WEEK 18 (VISIT 12)	20[redacted]	291000
WEEK 20 (VISIT 13)	20[redacted]	314000
UNSCHEDULED VISIT 13.01	20[redacted]	301000
WEEK 22 (VISIT 14)	20[redacted]	337000
UNSCHEDULED VISIT 14.01	20[redacted]	478000
UNSCHEDULED VISIT 14.02	20[redacted]	391000
WEEK 24/ET (VISIT 15)	20[redacted]	367000

C788-049 study

Visit	Date	Platelet Count (/μL)
MONTH 1	20[redacted]	330000
MONTH 2	20[redacted]	308000
MONTH 3	20[redacted]	277000
MONTH 4	20[redacted]	231000
MONTH 5	20[redacted]	81000
MONTH 6	20[redacted]	339000
MONTH 7	20[redacted]	304000
MONTH 8	20[redacted]	272000
MONTH 9	20[redacted]	294000
MONTH 10	20[redacted]	292000
MONTH 11	20[redacted]	283000
MONTH 12	20[redacted]	333000
MONTH 13	20[redacted]	317000
MONTH 14	20[redacted]	307000
MONTH 15	20[redacted]	298000
MONTH 16	20[redacted]	272000
MONTH 17	20[redacted]	288000
MONTH 18	20[redacted]	327000
UNSCHEDULED VISIT 19.01	20[redacted]	278000
MONTH 20	20[redacted]	351000
MONTH 22	20[redacted]	366000
MONTH 24/ET	20[redacted]	219000
MONTH 26	20[redacted]	228000
MONTH 28	20[redacted]	181000
MONTH 30	20[redacted]	161000
MONTH 32	20[redacted]	213000
MONTH 34	20[redacted]	396000
MONTH 36	20[redacted]	177000
MONTH 38	20[redacted]	140000
MONTH 40	20[redacted]	57000
UNSCHEDULED VISIT 34.01	20[redacted]	40000
UNSCHEDULED VISIT 34.02	20[redacted]	217000
MONTH 42	20[redacted]	262000
MONTH 44	20[redacted]	346000
FOLLOW-UP	20[redacted]	189000

測定された凝固系マーカーの検査値及び推移

治験実施計画書で規定されている Screening A 及び Day 1 のみ INR、aPTT 及び PT を評価している。

Visit	Date	INR	aPTT (sec)	PT (sec)
SCREEN A (VISIT 1)	20[redacted]	1	42.9	12.9
DAY 1 (VISIT 3)	20[redacted]	1	42.2	12.3

基準値の範囲：INR 0.8～1.3、aPTT 0～40 sec、PT 8.8～14.1 sec

臨床経過

20[redacted] 年[redacted] 月[redacted] 日（Day 80）、昼頃に浮動性めまい、悪心、下肢の脱力感を認めたため、神経内科に入院し、一過性脳虚血発作と診断された。神経学的検査は、神経根髄膜の刺激を示さず、左右の瞳孔は等しく光線に反応し、水平性眼振、口唇角は対称、言語は正中、腱反射は鋭敏で両側性であり、病的バビンスキーなし、並びに潜在性麻痺、感覚障害、静的運動失調及び歩行運動失調の所見はなかった。 Day 80* 、血小板数 245×10^9/L（基準値 130～360×10^9/L）、Hb 124 g/L（基準値 120～160 g/L）、赤血球数 4.25×10^{12}/L（基準値 3.7～5.3×10^{12}/L）、白血球数 9.14×10^9/L（基準値 3.5～10.5×10^9/L）、血圧 140/80 mmHg、脈拍 87 回/分であった。20[redacted] 年[redacted] 月[redacted] 日のベースラインの血圧は 125/80 mmHg であり、 Day 72* の血圧は 125/80 mmHg であった。本事象発現前の Day 72* の血小板数は 186000/μL であった。 Day 80* 、脳 CT により、脳実質の巣状変化はなく、慢性高血圧性脳症、大脳鎌髄膜腫、及び両側頭シルビウス裂による軽度の皮質萎縮が確認された。肺及び心臓の X 線は正常であった。生理食塩水 0.9%溶液、リンゲル液、降圧薬ネビボロールを 5 mg/日から 2×5 mg/日に増量し治療した。 Day 83* に退院し、本事象は回復したと判断された。 Day 88* 、血小板数 246000/μL、血圧 110/65 mmHg であった。

本事象に対して治験薬の変更は行わず、治験を継続した。その後、C788-048 試験の完了後に C788-049 試験に移行しており、C788-049 試験が終了するまで治験を継続した。一過性脳虚血発作以外に認めた有害事象は、C788-049 試験の実施中に発現した鼻咽頭炎のみであった。

治験担当医師は、一過性脳虚血発作の重症度は軽度であり、治験薬との因果関係はおそらく関連なしと判定し、

＊新薬承認情報提供時に置き換え

R788 以外の要因として合併していたアテローム性動脈硬化症を挙げた。治験依頼者は、本事象を予測できる治験薬との関連のない重篤な有害事象と判断した。

（Source: 1.13.3-4, C-08-2）

表 2.7.4.9-107　海外第 II 相臨床試験（D4300-022）で認められた血栓症、塞栓症及び血栓塞栓症に関する有害事象の臨床経過

1) 深部静脈血栓症：被験者番号[redacted]

患者背景

被験者番号	[redacted]
開始用量	R788 125 mg 1 日 2 回
年齢	8[redacted] 歳
性別	女性
人種	白人
病歴 [1)]	関節痛、糖尿病、不眠症、消化性潰瘍、結腸内視鏡検査、甲状腺機能低下症、高血圧、薬物過敏症、鼻出血、結膜出血、頭痛、挫傷、斑状出血、歯肉出血
ITP の罹病期間 [2)]	—
ITP に対する治療歴	脾摘（[redacted] 年）、DANAZOL、AZATHIOPRINE、RITUXIMAB、VINCRISTINE、IMMUNOGLOBULINS
深部静脈血栓症の発現前 15 日以内に使用した併用薬	RISEDRONATE SODIUM、CALCIUM CARBONATE、CENTRUM SILVER、METOPROLOL TARTRATE、METHYLPREDNISOLONE、OMEPRAZOLE、LEVOTHYROXINE SODIUM、DIPHENHYDRAMINE+PARACETAMOL、RANITIDINE HYDROCHLORIDE

1) 既往歴、合併症は分けずに病歴として収集している。
2) ITP の罹病期間は収集していない。

深部静脈血栓症の概要

発現日	20[redacted]（Day 21）
回復日	Day 46*
程度	高度
重篤の判定	重篤
治験薬に対する処置	中止
転帰	回復
治験薬との因果関係	おそらく関連あり

本薬の投与量

投与量	開始日	終了日	備考
125 mg 1 日 2 回	Day 1*	Day 28*	
150 mg 1 日 2 回	Day 28*	Day 46*	

血小板数の推移

Visit	Date	Platelet Count (/mm^3)
SCREENING	20[redacted]	28000
SCREENING	20[redacted]	30000
SCREENING	20[redacted]	22000
SCREENING	20[redacted]	14000
SCREENING	20[redacted]	27000
SCREENING	20[redacted]	22000
SCREENING	20[redacted]	80000
BASELINE	20[redacted]	25000
WEEK 1	20[redacted]	159000
WEEK 2	20[redacted]	106000
WEEK 4	20[redacted]	97000
FOLLOW-UP	20[redacted]	96000

測定された凝固系マーカー検査値の推移
　凝固系マーカーの検査は実施していない。

臨床経過

Day 1* 、ベースラインの血小板数は 25000/mm^3 であった。被験者は、治験実施計画書に従い、Day 1* から Day 27* まで、4 週間にわたり 125 mg 1 日 2 回の治験薬投与を受け、その後 Day 28* に 150 mg 1 日 2 回に変更された。125 mg 1 日 2 回、4 週間の投与により、血小板数は 100000～160000/mm^3 へと増加した。尿路感染症（R788 との関連性が否定された事象）で入院加療中（入院日： Day 17* ）、陳旧性の血栓と重なるものの、左下肢に新たな DVT を認めた。ヘパリンによる治療を受け、 Day 23* に退院した際、治験担当医師及び Rigel 社のモニターは、R788 とは無関係であると判定した。しかし、 Day 30* 、被験者は悪寒、発熱、疲労、悪心及び嘔吐を訴えたことから救急救命室に収容された。被験者は膝窩動脈血栓症と診断され、ヘパリンによる治療を受けた後退院した。

退院日は不明であるが、被験者は Day 227* に回復した。治験担当医師及び治験依頼者による再考の結果、当該有害事象を R788 とおそらく関連ありと判定した。

2) 血栓症：被験者番号[redacted]

患者背景

被験者番号	[redacted]
開始用量	R788 75 mg 1 日 2 回
年齢	5[redacted] 歳
性別	女性
人種	白人
病歴 [1)]	抗リン脂質抗体症候群、深部静脈血栓症、薬物過敏症、消化不良、血中コレステロール増加、糖尿病、血圧上昇、骨粗鬆症、胆嚢切除
ITP の罹病期間 [2)]	—
ITP に対する治療歴	脾摘（[redacted] 年）、IMMUNOGLOBULINS
血栓症の発現前 15 日以内に使用した併用薬	WARFARIN SODIUM、ESOMEPRAZOLE MAGNESIUM、GLIBENCLAMIDE、VITAMINS NOS、ASCORBIC ACID

1) 既往歴、合併症は分けずに病歴として収集している。
2) ITP の罹病期間は収集していない。

血栓症の概要

発現日	20[redacted]（Day 265）
回復日	Day 281*
程度	高度
重篤の判定	非重篤
治験薬に対する処置	休薬
転帰	回復
治験薬との因果関係	関連あるかもしれない

本薬の投与量

投与量	開始日	終了日	備考
75 mg 1 日 2 回	Day 1*	Day 29*	
100 mg 1 日 2 回	Day 29*	Day 50*	
125 mg 1 日 2 回	Day 50*	Day 92*	
150 mg 1 日 2 回	Day 92*	Day 127*	
175 mg 1 日 2 回	Day 127*	Day 701*	
100 mg 1 日 2 回	Day 701*	Day 722*	血小板数の増加により減量
50 mg 1 日 2 回	Day 722*	Day 729*	血小板数の増加により減量
25 mg 1 日 2 回	Day 729*	Day 757*	血小板数の増加により減量

血小板数の推移

Visit	Date	Platelet Count (/mm^3)
SCREENING	20[redacted]	16000
SCREENING	20[redacted]	8000
SCREENING	20[redacted]	5000
SCREENING	20[redacted]	32000
SCREENING	20[redacted]	26000
SCREENING	20[redacted]	36000
SCREENING	20[redacted]	36000
BASELINE	20[redacted]	24000

＊新薬承認情報提供時に置き換え

WEEK 1	20[redacted]		37000
WEEK 2	20[redacted]		53000
WEEK 3	20[redacted]		24000
WEEK 4	20[redacted]		6000
WEEK 5	20[redacted]		24000
WEEK 6	20[redacted]		20000
WEEK 7	20[redacted]		14000
WEEK 8	20[redacted]		36000
WEEK 9	20[redacted]		45000
WEEK 9/UNSCH	20[redacted]		14000
WEEK 10	20[redacted]		13000
WEEK 11	20[redacted]		33000
WEEK 12	20[redacted]		27000
WEEK 12/UNSCH	20[redacted]		19000
WEEK 14	20[redacted]		36000
WEEK 16	20[redacted]		10000
WEEK 18	20[redacted]		17000
WEEK 20	20[redacted]		22000
WEEK 22	20[redacted]		22000
WEEK 24	20[redacted]		13000
WEEK 24/UNSCH	20[redacted]		103000
WEEK 24/UNSCH	20[redacted]		222000
MONTH 7	20[redacted]		18000
MONTH 7/UNSCH	20[redacted]		49000
MONTH 7/UNSCH	20[redacted]		39000
MONTH 8	20[redacted]		35000
MONTH 8/UNSCH	20[redacted]		24000
MONTH 9	20[redacted]		13000
MONTH 9/UNSCH	20[redacted]		31000
MONTH 9/UNSCH	20[redacted]		120000
MONTH 10	20[redacted]		38000
MONTH 10/UNSCH	20[redacted]		40000
MONTH 10/UNSCH	20[redacted]		65000
MONTH 11	20[redacted]		22000
MONTH 11/UNSCH	20[redacted]		22000
MONTH 12	20[redacted]		11000
MONTH 13	20[redacted]		25000
MONTH 14	20[redacted]		26000
MONTH 14/UNSCH	20[redacted]		16000
MONTH 15	20[redacted]		16000
MONTH 16	20[redacted]		12000
MONTH 16/UNSCH	20[redacted]		15000
MONTH 16/UNSCH	20[redacted]		22000
MONTH 16/UNSCH	20[redacted]		25000
MONTH 17	20[redacted]		14000
MONTH 17/UNSCH	20[redacted]		24000
MONTH 17/UNSCH	20[redacted]		72000
MONTH 18	20[redacted]		28000
MONTH 18/UNSCH	20[redacted]		26000
MONTH 19	20[redacted]		17000
MONTH 19/UNSCH	20[redacted]		5000
MONTH 19/UNSCH	20[redacted]		33000
MONTH 20	20[redacted]		13000
MONTH 20/UNSCH	20[redacted]		18000
MONTH 21	20[redacted]		31000
MONTH 21/UNSCH	20[redacted]		27000
MONTH 22	20[redacted]		20000
MONTH 22/UNSCH	20[redacted]		31000
MONTH 23	20[redacted]		37000
MONTH 23/UNSCH	20[redacted]		44000
MONTH 24	20[redacted]		13000
MONTH 24/UNSCH	20[redacted]		68000
MONTH 24/UNSCH	20[redacted]		44000
MONTH 24/UNSCH	20[redacted]		20000
MONTH 25	20[redacted]		63000

MONTH 25/UNSCH	20[redacted]	105000
MONTH 25/UNSCH	20[redacted]	90000
MONTH 26	20[redacted]	90000
FOLLOW-UP	20[redacted]	131000

UNSCH = Unscheduled Visit

測定された凝固系マーカー検査値の推移

Visit	Date	aPTT (sec)	PT (sec)
SCREENING	20[redacted]	35.2	16.3
WEEK 9/UNSCH	20[redacted]		35.2
WEEK 12/UNSCH	20[redacted]		28.8
WEEK 24/UNSCH	20[redacted]		30.8
WEEK 24/UNSCH	20[redacted]		33.6
MONTH 9/UNSCH	20[redacted]	33.6	15.6
MONTH 9/UNSCH	20[redacted]	36.9	22.7
MONTH 10/UNSCH	20[redacted]	49.7	31.8
MONTH 10/UNSCH	20[redacted]	48.3	
MONTH 11/UNSCH	20[redacted]	47.7	47.7
MONTH 14/UNSCH	20[redacted]		14.2
MONTH 16/UNSCH	20[redacted]		16.3
MONTH 16/UNSCH	20[redacted]		16.7
MONTH 16/UNSCH	20[redacted]	47.4	31.8
MONTH 17/UNSCH	20[redacted]		16.1
MONTH 17/UNSCH	20[redacted]		21.7
MONTH 18/UNSCH	20[redacted]		19.1
MONTH 19/UNSCH	20[redacted]		15.4
MONTH 19/UNSCH	20[redacted]		17.2
MONTH 20/UNSCH	20[redacted]		21.4
MONTH 21/UNSCH	20[redacted]		16.3
MONTH 22/UNSCH	20[redacted]		17.2
MONTH 23/UNSCH	20[redacted]		27.2
MONTH 24/UNSCH	20[redacted]		22.7
MONTH 24/UNSCH	20[redacted]		24.1
MONTH 24/UNSCH	20[redacted]		29.9
MONTH 25/UNSCH	20[redacted]		31.6
MONTH 25/UNSCH	20[redacted]		29.3

基準値の範囲：aPTT 24.4～31.7 sec、PT 9～13 sec
UNSCH = Unscheduled Visit

臨床経過

被験者[redacted]は、Day 1* に R788 75 mg 1 日 2 回で投与を開始した。Day 29* に 100 mg 1 日 2 回、Day 50* に 125 mg 1 日 2 回、Day 92* に 150 mg 1 日 2 回、Day 120* に 175 mg 1 日 2 回と R788 の投与を漸増した。175 mg 1 日 2 回の投与中であった 20[redacted] 年[redacted] 月[redacted] 日（Day 265）に血栓症が発現した。血栓症の程度は高度であり、治験薬との因果関係は関連あるかもしれないと判定された。治験薬の休薬により回復しており、その後、175 mg 1 日 2 回で R788 の投与を再開した。以降、血栓症の再発は認めていない。血栓症の発現日から直前の血小板数は、20[redacted] 年[redacted] 月[redacted] 日（Month 9）の 13000/mm^3 であった。

3) 血栓症：被験者番号[redacted]

患者背景

被験者番号	[redacted]
開始用量	R788 150 mg 1 日 2 回
年齢	8[redacted] 歳
性別	男性
人種	白人
病歴 [1)]	挫傷、冠動脈ステント挿入、肺塞栓症、心房細動、高脂血症
ITP の罹病期間 [2)]	—
ITP に対する治療歴	脾摘（時期不明）、IMMUNOGLOBULINS、RITUXIMAB、STEROID ANTIBACTERIALS /OLD CODE/、IMMUNOGLOBULIN HUMAN ANTI-RH
血栓症の発現前 15 日以内に使用した併用薬	ACETYLSALICYLIC ACID、PENICILLIN NOS、GLIMEPIRIDE、LOSARTAN POTASSIUM、TERAZOSIN HYDROCHLORIDE、SIMVASTATIN、ATENOLOL、FUROSEMIDE

1) 既往歴、合併症は分けずに病歴として収集している。

＊新薬承認情報提供時に置き換え

2) ITP の罹病期間は収集していない。

血栓症の概要

発現日	20[redacted] (Day 129)
回復日	Day 146*
程度	中等度
重篤の判定	非重篤
治験薬に対する処置	変更なし
転帰	回復
治験薬との因果関係	おそらく関連なし

本薬の投与量

投与量	開始日	終了日	備考
150 mg 1 日 2 回	Day 1*	Day 349*	
175 mg 1 日 2 回	Day 349*	Day 386*	
125 mg 1 日 2 回	Day 386*	Day 456*	血小板数の増加により減量

血小板数の推移

Visit	Date	Platelet Count (/mm^3)
SCREENING	20[redacted]	11000
SCREENING	20[redacted]	16000
SCREENING	20[redacted]	18000
SCREENING	20[redacted]	14000
SCREENING	20[redacted]	35000
BASELINE	20[redacted]	36000
WEEK 1	20[redacted]	100000
WEEK 2	20[redacted]	144000
WEEK 4	20[redacted]	154000
WEEK 6	20[redacted]	55000
WEEK 9	20[redacted]	68000
WEEK 18	20[redacted]	141000
MONTH 7	20[redacted]	50000
MONTH 8	20[redacted]	78000
MONTH 9	20[redacted]	72000
MONTH 9/UNSCH	20[redacted]	54000
MONTH 10	20[redacted]	72000
MONTH 11	20[redacted]	44000
MONTH 12	20[redacted]	37000
MONTH 13	20[redacted]	44000
MONTH 14	20[redacted]	36000
MONTH 15	20[redacted]	35000
MONTH 15/UNSCH	20[redacted]	33000
MONTH 15/UNSCH	20[redacted]	201000

UNSCH = Unscheduled Visit

測定された凝固系マーカー検査値の推移

凝固系マーカーの検査は実施していない。

臨床経過

被験者[redacted]は、Day 1* に R788 150 mg 1 日 2 回で投与を開始した。150 mg 1 日 2 回の投与中であった 20[redacted] 年[redacted] 月[redacted] 日（Day 129）に血栓症が発現した。血栓症の程度は中等度であり、治験薬との因果関係はおそらく関連なしと判定された。治験薬の投与は変更せずに回復しており、その後、最大で 175 mg 1 日 2 回まで R788 の投与を増量したが、血栓症の再発は認めていない。血栓症の発現日から直前の血小板数は、20[redacted] 年[redacted] 月[redacted] 日（Week 9）の 68000/mm^3 であった。

4) 血小板数のオーバーシュート：被験者番号[redacted]

患者背景

被験者番号	[redacted]
開始用量	R788 125 mg 1 日 2 回
年齢	5[redacted] 歳
性別	女性

＊新薬承認情報提供時に置き換え

人種	白人
病歴 [1)]	高コレステロール血症、不眠症、出血
ITP の罹病期間 [2)]	—
ITP に対する治療歴	脾摘（[redacted]）、RITUXIMAB、IMMUNOGLOBULINS

1) 既往歴、合併症は分けずに病歴として収集している。
2) ITP の罹病期間は収集していない。

本薬の投与量

投与量	開始日	終了日	備考
125 mg 1 日 2 回	Day 1*	Day 15*	
225 mg 1 日 1 回	Day 15*	Day 22*	血小板数の増加により減量
100 mg 1 日 2 回	Day 22*	Day 38*	血小板数の増加により減量
175 mg 1 日 1 回	Day 38*	Day 57*	血小板数の増加により減量
50 mg 1 日 2 回	Day 57*	Day 71*	血小板数の増加により減量
50 mg 1 日 1 回	Day 71*	Day 105*	血小板数の増加により減量
100 mg 1 日 2 回	Day 105*	Day 136*	
75 mg 1 日 2 回	Day 136*	Day 155*	血小板数の増加により減量
125 mg 1 日 1 回	Day 155*	Day 219*	血小板数の増加により減量
50 mg 1 日 2 回	Day 219*	投与継続しているが、Day 444*以降の投与データなし	血小板数の増加により減量

血小板数の推移

Visit	Date	Platelet Count (/mm^3)
SCREENING	20[redacted]	4000
SCREENING	20[redacted]	12000
SCREENING	20[redacted]	5000
SCREENING	20[redacted]	13000
SCREENING	20[redacted]	24000
SCREENING	20[redacted]	7000
SCREENING	20[redacted]	46000
BASELINE	20[redacted]	155000
WEEK 1	20[redacted]	179000
WEEK 2	20[redacted]	272000
WEEK 3	20[redacted]	329000
WEEK 4	20[redacted]	305000
WEEK 5	20[redacted]	280000
WEEK 6	20[redacted]	338000
WEEK 7	20[redacted]	308000
WEEK 8	20[redacted]	310000
WEEK 9	20[redacted]	327000
WEEK 10	20[redacted]	317000
WEEK 12	20[redacted]	310000
WEEK 14	20[redacted]	8000
WEEK 14/UNSCH	20[redacted]	133000
WEEK 16	20[redacted]	329000
WEEK 16/UNSCH	20[redacted]	329000
WEEK 18	20[redacted]	318000
WEEK 20	20[redacted]	373000
WEEK 22	20[redacted]	371000
WEEK 24	20[redacted]	294000
MONTH 7	20[redacted]	331000
MONTH 7/UNSCH	20[redacted]	291000
MONTH 8	20[redacted]	310000
MONTH 8/UNSCH	20[redacted]	394000
MONTH 9	20[redacted]	337000
MONTH 10	20[redacted]	369000
MONTH 11	20[redacted]	394000
MONTH 12	20[redacted]	357000
MONTH 13	20[redacted]	428000
MONTH 14	20[redacted]	348000
MONTH 14/UNSCH	20[redacted]	32000
MONTH 15	20[redacted]	351000

＊新薬承認情報提供時に置き換え

MONTH 15/UNSCH	20[redacted]	257000
MONTH 17	20[redacted]	344000
MONTH 17/UNSCH	20[redacted]	336000
MONTH 18	20[redacted]	335000
MONTH 19	20[redacted]	364000
MONTH 20	20[redacted]	355000
MONTH 21	20[redacted]	315000
MONTH 21/UNSCH	20[redacted]	378000
MONTH 22	20[redacted]	401000
MONTH 23	20[redacted]	332000
MONTH 24	20[redacted]	348000
MONTH 25	20[redacted]	351000
MONTH 26	20[redacted]	363000
MONTH 27	20[redacted]	264000
MONTH 28	20[redacted]	308000
MONTH 29	20[redacted]	312000
MONTH 30	20[redacted]	310000
MONTH 30/UNSCH	20[redacted]	8000
MONTH 31	20[redacted]	27000
MONTH 32	20[redacted]	386000
MONTH 33	20[redacted]	343000
MONTH 34	20[redacted]	353000
MONTH 35	20[redacted]	363000
MONTH 36	20[redacted]	355000
MONTH 37	20[redacted]	324000

黄色網掛け：血小板数のオーバーシュートを認めた時点
UNSCH = Unscheduled Visit

測定された凝固系マーカーの検査値の推移

Visit	Date	aPTT (sec)	PT (sec)
WEEK 16/UNSCH	20[redacted]	29.8	9.8
MONTH 8/UNSCH	20[redacted]	28.0	10.1

基準値の範囲：aPTT 24.4～31.7 sec、PT 9～13 sec
UNSCH = Unscheduled Visit

臨床経過

被験者[redacted]は、Day 1* に R788 125 mg 1 日 2 回で投与を開始した。20[redacted] 年[redacted] 月[redacted] 日（Week 2）に血小板数が 272000/mm^3 まで増加し 225 mg 1 日 1 回に減量した。以降、血小板数の増加により投与量を漸減しており、Day 219* 以降は 50 mg 1 日 2 回の投与量で継続していた。20[redacted] 年[redacted] 月[redacted] 日（Month 13）に血小板数が 428000/mm^3 となり、血小板数のオーバーシュートを認めた。Day 444* 以降の R788 の投与データが収集されていないため、R788 の投与状況については不明であるが、20[redacted] 年[redacted] 月[redacted] 日（Month 22）に血小板数が 401000/mm^3 となり、再度、血小板数のオーバーシュートを認めた。

5) 血小板数のオーバーシュート：被験者番号[redacted]

患者背景

被験者番号	[redacted]
開始用量	R788 150 mg 1 日 2 回
年齢	7[redacted] 歳
性別	女性
人種	その他（白人、黒人、アジア人、ヒスパニック以外）
病歴 [1)]	高脂血症、甲状腺機能低下症、子宮摘出、骨粗鬆症、冠動脈バイパス、高血圧
ITP の罹病期間 [2)]	—
ITP に対する治療歴	脾摘（時期不明）、PREDNISONE、IMMUNOGLOBULINS

1) 既往歴、合併症は分けずに病歴として収集している。
2) ITP の罹病期間は収集していない。

本薬の投与量

投与量	開始日	終了日	備考
150 mg 1 日 2 回	Day 1*	Day 42*	
100 mg 1 日 2 回	Day 42*	Day 78*	血小板数の増加により減量
75 mg 1 日 1 回	Day 78*	Day 90*	血小板数の増加により減量

100 mg 1 日 1 回	Day 78*	Day 90*	
75 mg 1 日 2 回	Day 90*	Day 131*	
150 mg 1 日 2 回	Day 131*	Day 146*	
75 mg 1 日 2 回	Day 146*	Day 163*	血小板数の増加により減量
100 mg 1 日 2 回	Day 163*	Day 218*	
150 mg 1 日 2 回	Day 218*	Day 258*	
125 mg 1 日 2 回	Day 258*	投与継続しているが、Day 289* 以降の投与データなし	血小板数の増加により減量

血小板数の推移

Visit	Date	Platelet Count (/mm^3)
SCREENING	20[redacted]	25000
SCREENING	20[redacted]	9000
SCREENING	20[redacted]	24000
SCREENING	20[redacted]	17000
BASELINE	20[redacted]	17000
WEEK 1	20[redacted]	181000
WEEK 2	20[redacted]	146000
WEEK 3	20[redacted]	90000
WEEK 4	20[redacted]	151000
WEEK 6	20[redacted]	252000
WEEK 8	20[redacted]	304000
WEEK 11	20[redacted]	458000
WEEK 12	20[redacted]	251000
WEEK 14	20[redacted]	103000
WEEK 14/UNSCH	20[redacted]	185000
WEEK 20	20[redacted]	60000
WEEK 22	20[redacted]	42000
WEEK 24	20[redacted]	66000
MONTH 7	20[redacted]	44000
MONTH 7/UNSCH	20[redacted]	36000
MONTH 8	20[redacted]	119000
MONTH 9	20[redacted]	206000
MONTH 10	20[redacted]	220000
MONTH 11	20[redacted]	293000
MONTH 12	20[redacted]	290000
MONTH 13	20[redacted]	301000
MONTH 14	20[redacted]	349000
MONTH 15	20[redacted]	282000
MONTH 16	20[redacted]	392000
MONTH 17	20[redacted]	372000
MONTH 18	20[redacted]	346000
MONTH 19	20[redacted]	341000
MONTH 20	20[redacted]	329000
MONTH 21	20[redacted]	309000
MONTH 22	20[redacted]	271000
MONTH 23	20[redacted]	302000
MONTH 24	20[redacted]	294000
MONTH 25	20[redacted]	342000
MONTH 26	20[redacted]	288000
MONTH 27	20[redacted]	328000
MONTH 28	20[redacted]	299000
MONTH 29	20[redacted]	314000
MONTH 30	20[redacted]	318000

黄色網掛け：血小板数のオーバーシュートを認めた時点
UNSCH = Unscheduled Visit

測定された凝固系マーカーの検査値の推移

Visit	Date	aPTT (sec)	PT (sec)
SCREENING	20[redacted]	24.7	9.4
WEEK 14/UNSCH	20[redacted]	25.9	9.8

基準値の範囲：aPTT 24.4～31.7 sec、PT 9～13 sec
UNSCH = Unscheduled Visit

＊新薬承認情報提供時に置き換え

臨床経過
被験者[redacted]は、 Day 1* に R788 150 mg 1 日 2 回で投与を開始した。20[redacted] 年[redacted] 月[redacted] 日（Week 6）に血小板数が 252000/mm^3 まで増加し 100 mg 1 日 2 回に減量した。100 mg 1 日 2 回の投与中であった 20[redacted] 年[redacted] 月[redacted] 日（Week 11）に血小板数が 458000/mm^3 となり、血小板数のオーバーシュートを認めた。血小板数のオーバーシュートにより、75 mg 1 日 1 回に減量したものの、R788 の再増量は可能であり、投与量を調節することにより以降は血小板数のオーバーシュートは認められなかった。

（Source: 1.13.3-8, C-01）

＊新薬承認情報提供時に置き換え

表 2.7.4.9-108　国内及び海外第 III 相臨床試験（R788-1301、C788-047 及び C788-048）のプラセボ対照期における注目すべき有害事象の年齢別の発現状況

カテゴリー PT	海外第 III 相試験（C788-047, 048 試験）				R788-1301 試験（第 I 期）			
	65 歳未満		65 歳以上		65 歳未満		65 歳以上	
	R788 (N=74) n (%)	Placebo (N=37) n (%)	R788 (N=28) n (%)	Placebo (N=11) n (%)	R788 (N=12) n (%)	Placebo (N=7) n (%)	R788 (N=10) n (%)	Placebo (N=5) n (%)
消化管障害	33 (44.6)	12 (32.4)	14 (50.0)	2 (18.2)	6 (50.0)	0 (0.0)	5 (50.0)	0 (0.0)
Abdominal Discomfort	1 (1.4)	0 (0.0)	0 (0.0)	1 (9.1)	2 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal Distension	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal Pain	3 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal Pain Upper	3 (4.1)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anal Haemorrhage	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	1 (1.4)	0 (0.0)	2 (7.1)	1 (9.1)	2 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhoea	19 (25.7)	7 (18.9)	11 (39.3)	0 (0.0)	5 (41.7)	0 (0.0)	4 (40.0)	0 (0.0)
Dyspepsia	2 (2.7)	1 (2.7)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eructation	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Flatulence	4 (5.4)	1 (2.7)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Frequent Bowel Movements	1 (1.4)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastric Haemorrhage	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal Haemorrhage	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrooesophageal Reflux Disease	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haematochezia	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Melaena	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mouth Haemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	14 (18.9)	4 (10.8)	5 (17.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Oesophageal Pain	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rectal Haemorrhage	0 (0.0)	1 (2.7)	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stomatitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Vomiting	3 (4.1)	3 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非感染性下痢 SMQ	20 (27.0)	7 (18.9)	12 (42.9)	0 (0.0)	5 (41.7)	0 (0.0)	4 (40.0)	0 (0.0)
Diarrhoea	19 (25.7)	7 (18.9)	11 (39.3)	0 (0.0)	5 (41.7)	0 (0.0)	4 (40.0)	0 (0.0)
Frequent Bowel Movements	1 (1.4)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少	7 (9.5)	0 (0.0)	3 (10.7)	0 (0.0)	2 (16.7)	0 (0.0)	3 (30.0)	0 (0.0)
Febrile Neutropenia	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	2 (2.7)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Lymphocyte Count Decreased	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia	3 (4.1)	0 (0.0)	2 (7.1)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil Count Decreased	1 (1.4)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	2 (20.0)	0 (0.0)
White Blood Cell Count Decreased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
好中球減少症	5 (6.8)	0 (0.0)	2 (7.1)	0 (0.0)	2 (16.7)	0 (0.0)	2 (20.0)	0 (0.0)
Febrile Neutropenia	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia	3 (4.1)	0 (0.0)	2 (7.1)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil Count Decreased	1 (1.4)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	2 (20.0)	0 (0.0)
高血圧 SMQ	17 (23.0)	4 (10.8)	11 (39.3)	2 (18.2)	4 (33.3)	1 (14.3)	4 (40.0)	0 (0.0)
Blood Pressure Diastolic Increased	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood Pressure Increased	1 (1.4)	1 (2.7)	4 (14.3)	1 (9.1)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Blood Pressure Systolic Increased	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	14 (18.9)	3 (8.1)	6 (21.4)	1 (9.1)	4 (33.3)	1 (14.3)	3 (30.0)	0 (0.0)
Hypertensive Crisis	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物関連肝障害 SMQ	13 (17.6)	1 (2.7)	3 (10.7)	0 (0.0)	4 (33.3)	1 (14.3)	2 (20.0)	0 (0.0)
Alanine Aminotransferase Increased	9 (12.2)	0 (0.0)	2 (7.1)	0 (0.0)	1 (8.3)	1 (14.3)	0 (0.0)	0 (0.0)
Aspartate Aminotransferase Increased	8 (10.8)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	1 (14.3)	0 (0.0)	0 (0.0)
Blood Bilirubin Increased	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gamma-Glutamyltransferase Increased	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic Cyst	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic Enzyme Increased	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic Function Abnormal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	1 (10.0)	0 (0.0)
Hepatic steatosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular Icterus	0 (0.0)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver Function Test Abnormal	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Liver Function Test Increased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)

（Source: 1.13.3-6, C-04 表 18）

表 2.7.4.9-109　国内及び海外第 III 相臨床試験（R788-1301、C788-047 及び C788-048）のプラセボ対照期における治験薬との因果関係が否定できない注目すべき有害事象の年齢別の発現状況

カテゴリー PT	海外第 III 相試験（C788-047, 048 試験）				R788-1301 試験（第 I 期）			
	65 歳未満		65 歳以上		65 歳未満		65 歳以上	
	R788 (N=74) n (%)	Placebo (N=37) n (%)	R788 (N=28) n (%)	Placebo (N=11) n (%)	R788 (N=12) n (%)	Placebo (N=7) n (%)	R788 (N=10) n (%)	Placebo (N=5) n (%)
消化管障害	26 (35.1)	8 (21.6)	12 (42.9)	1 (9.1)	5 (41.7)	0 (0.0)	4 (40.0)	0 (0.0)
Abdominal Discomfort	1 (1.4)	0 (0.0)	0 (0.0)	1 (9.1)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal Distension	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal Pain	3 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal Pain Upper	1 (1.4)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	1 (1.4)	0 (0.0)	2 (7.1)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhoea	18 (24.3)	6 (16.2)	9 (32.1)	0 (0.0)	4 (33.3)	0 (0.0)	3 (30.0)	0 (0.0)
Dyspepsia	1 (1.4)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eructation	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Flatulence	3 (4.1)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Frequent Bowel Movements	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrooesophageal Reflux Disease	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mouth Haemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	11 (14.9)	3 (8.1)	4 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Oesophageal Pain	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stomatitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Vomiting	1 (1.4)	1 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非感染性下痢 SMQ	18 (24.3)	6 (16.2)	10 (35.7)	0 (0.0)	4 (33.3)	0 (0.0)	3 (30.0)	0 (0.0)
Diarrhoea	18 (24.3)	6 (16.2)	9 (32.1)	0 (0.0)	4 (33.3)	0 (0.0)	3 (30.0)	0 (0.0)
Frequent Bowel Movements	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球減少	5 (6.8)	0 (0.0)	2 (7.1)	0 (0.0)	1 (8.3)	0 (0.0)	3 (30.0)	0 (0.0)
Febrile Neutropenia	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Neutropenia	2 (2.7)	0 (0.0)	2 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil Count Decreased	1 (1.4)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	2 (20.0)	0 (0.0)
White Blood Cell Count Decreased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
好中球減少症	4 (5.4)	0 (0.0)	2 (7.1)	0 (0.0)	1 (8.3)	0 (0.0)	2 (20.0)	0 (0.0)
Febrile Neutropenia	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia	2 (2.7)	0 (0.0)	2 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil Count Decreased	1 (1.4)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	2 (20.0)	0 (0.0)
高血圧 SMQ	14 (18.9)	2 (5.4)	8 (28.6)	0 (0.0)	4 (33.3)	1 (14.3)	3 (30.0)	0 (0.0)
Blood Pressure Increased	1 (1.4)	0 (0.0)	3 (10.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Blood Pressure Systolic Increased	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	12 (16.2)	2 (5.4)	4 (14.3)	0 (0.0)	4 (33.3)	1 (14.3)	2 (20.0)	0 (0.0)
Hypertensive Crisis	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物関連肝障害 SMQ	9 (12.2)	0 (0.0)	3 (10.7)	0 (0.0)	4 (33.3)	0 (0.0)	2 (20.0)	0 (0.0)
Alanine Aminotransferase Increased	8 (10.8)	0 (0.0)	2 (7.1)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Aspartate Aminotransferase Increased	6 (8.1)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic Enzyme Increased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic Function Abnormal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	0 (0.0)	1 (10.0)	0 (0.0)
Liver Function Test Abnormal	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	0 (0.0)
Liver Function Test Increased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)
Blood Bilirubin Increased	2 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

（Source: 1.13.3-6, C-04 表 19）

表 2.7.4.9-110　海外第 III 相臨床試験（C788-047 及び C788-048）における年齢別の重篤な有害事象の一覧表

	事象名	因果関係	重症度	治験薬の処置	加療	転帰	被験者 ID
65 歳以上 (N=28) n=6	鼻出血	おそらく関連なし	中等度	—	有	回復	[redacted]
	鼻出血	おそらく関連なし	中等度	—	有	回復	
	鼻出血	おそらく関連なし	中等度	—	有	回復	
	血小板減少症	おそらく関連なし	高度	中止	有	回復	
	血小板減少症	おそらく関連なし	中等度	—	有	回復	
	形質細胞性骨髄腫	おそらく関連なし	中等度	中止	有	死亡	
	高血圧クリーゼ	おそらく関連あり	高度	休薬	有	回復	
	下痢	関連があるかもしれない	中等度	—	有	回復	
	免疫性血小板減少性紫斑病	おそらく関連なし	軽度	—	有	回復	
	網膜裂孔	おそらく関連なし	中等度	—	無	回復	
65 歳未満 (N=74) n=7	失神	おそらく関連なし	高度	中止	有	回復	
	肺炎	おそらく関連あり	高度	中止	有	回復	
	発熱性好中球減少症	関連があるかもしれない	高度	休薬	有	回復	
	膣出血	おそらく関連なし	中等度	—	無	回復	
	挫傷	おそらく関連なし	高度	—	無	回復したが残存症状あり	
	気管支炎	おそらく関連なし	中等度	—	有	回復	
	血小板数減少	おそらく関連なし	中等度	—	有	回復	
	一過性脳虚血発作	おそらく関連なし	軽度	—	有	回復	

（Source: 1.13.3-5, C-04 表 4）

表 2.7.4.9-111　海外第 III 相臨床試験（C788-047 及び C788-048）における年齢別の治験薬の投与中止に至った有害事象の一覧表

	事象名	因果関係	重篤性	重症度	加療	転帰	被験者 ID
65 歳以上 (N=28) n=6	好中球減少症	関連があるかもしれない	非重篤	中等度	—	回復	[redacted]
	血小板減少症	おそらく関連なし	重篤	高度	有	回復	
	形質細胞性骨髄腫	おそらく関連なし	重篤	中等度	有	死亡	
	アラニンアミノトランスフェラーゼ増加	関連があるかもしれない	非重篤	中等度	無	回復	
	下痢	関連があるかもしれない	非重篤	中等度	無	回復	
	胸痛	関連があるかもしれない	非重篤	高度	無	回復	
65 歳未満 (N=74) n=5	好中球減少症	おそらく関連あり	非重篤	高度	無	回復	
	失神	おそらく関連なし	重篤	高度	有	回復	
	肺炎	おそらく関連あり	重篤	高度	有	回復	
	腹痛	おそらく関連あり	非重篤	中等度	有	回復	
	頭痛	おそらく関連なし	非重篤	軽度	無	未回復	

（Source: 1.13.3-5, C-04 表 5）

表 2.7.4.9-112　海外第 III 相臨床試験（C788-047 及び C788-048）における年齢別の治験薬の休薬に至った有害事象の一覧表

	事象銘	因果関係	重篤性	重症度	加療	転帰	被験者 ID
65 歳以上 (N=28) n=6	アラニンアミノトランスフェラーゼ増加	関連があるかもしれない	非重篤	中等度	無	回復	[redacted]
	下痢	関連があるかもしれない	非重篤	中等度	有	回復	[redacted]
	下痢	おそらく関連なし	非重篤	中等度	有	回復	[redacted]
	高血圧クリーゼ	おそらく関連あり	重篤	高度	有	回復	[redacted]
	好中球数減少	関連があるかもしれない	非重篤	軽度	無	回復	[redacted]
	鼻出血	おそらく関連なし	非重篤	軽度	無	回復	[redacted]
65 歳未満 (N=74) n=12	アラニンアミノトランスフェラーゼ増加	おそらく関連あり	非重篤	軽度	無	回復	[redacted]
	アラニンアミノトランスフェラーゼ増加	おそらく関連あり	非重篤	中等度	無	回復	[redacted]
	アラニンアミノトランスフェラーゼ増加	おそらく関連あり	非重篤	中等度	無	回復	[redacted]
	アラニンアミノトランスフェラーゼ増加	おそらく関連あり	非重篤	中等度	無	回復	[redacted]
	アラニンアミノトランスフェラーゼ増加	おそらく関連あり	非重篤	軽度	無	回復	[redacted]
	アラニンアミノトランスフェラーゼ増加	おそらく関連あり	非重篤	中等度	無	回復	[redacted]
	下痢	おそらく関連あり	非重篤	高度	無	回復	[redacted]
	インフルエンザ様疾患	—	非重篤	—	—	未回復	[redacted]
	インフルエンザ様疾患	おそらく関連なし	非重篤	軽度	無	回復	[redacted]
	発熱性好中球減少症	関連があるかもしれない	重篤	高度	有	回復	[redacted]
	血中ビリルビン増加	関連があるかもしれない	非重篤	軽度	無	回復	[redacted]
	呼吸困難	おそらく関連あり	非重篤	高度	有	改善	[redacted]
	アスパラギン酸アミノトランスフェラーゼ増加	おそらく関連あり	非重篤	中等度	無	回復	[redacted]
	関節痛	おそらく関連あり	非重篤	高度	無	回復	[redacted]
	末梢静脈疾患	おそらく関連なし	非重篤	軽度	無	回復したが残存症状あり	[redacted]

（Source: 1.13.3-5, C-04 表 6）

表 2.7.4.9-113　国内第 III 相臨床試験（R788-1301）の第 I 期における年齢別の治験薬の減量に至った有害事象の一覧表

	事象名	因果関係	重篤性	重症度	加療	転帰	被験者 ID
65 歳以上 (N=10) n=6	下痢	有	非重篤	中等度	併用薬	回復	[redacted]
	好中球数減少	有	非重篤	軽度	—	回復	[redacted]
	好中球数減少	有	非重篤	軽度	—	回復	[redacted]
	高血圧	有	非重篤	軽度	併用薬	改善	[redacted]
	肝機能異常	有	非重篤	軽度	—	回復	[redacted]
	血圧上昇	有	非重篤	軽度	併用薬	回復	[redacted]
	血中クレアチンホスホキナーゼ増加	無	非重篤	軽度	—	回復	[redacted]
65 歳未満 (N=12) n=4	下痢	有	重篤	高度	併用薬	回復	[redacted]
	下痢	有	非重篤	中等度	併用薬	回復	[redacted]
	下痢	有	非重篤	中等度	併用薬	回復	[redacted]
	肝機能検査異常	有	非重篤	軽度	併用薬	回復	[redacted]
	好中球減少症	無	非重篤	軽度	—	回復	[redacted]

（Source: 1.13.3-5, C-04 表 7）

表 2.7.4.9-114 Occurrence of Adverse Events by Onset Time – R788-1301 study

R788 Treatment Period

SOC, PT	Overall		<=Week 2		Week 2< <=4		Week 4< <=12		Week 12< <=24		Week 24< <=36		Week 36< <=48		Week 48< <=72		> Week 72		Follow-up	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	33	---	33	---			33	---	31	---	26	---	23	---	18	---	7	---	12	---
Total	32	97.0	12	36.4	12	36.4	19	57.6	18	58.1	16	61.5	8	34.8	8	44.4	3	42.9	3	25.0
Infections and infestations	10	30.3	0	0.0	0	0.0	2	6.1	7	22.6	5	19.2	1	4.3	1	5.6	1	14.3	0	0.0
COVID-19	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	14.3	0	0.0
Cellulitis	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Cystitis	2	6.1	0	0.0	0	0.0	0	0.0	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Diverticulitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Gastroenteritis	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Gingivitis	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Herpes zoster	2	6.1	0	0.0	0	0.0	0	0.0	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Nasopharyngitis	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	1	4.3	0	0.0	0	0.0	0	0.0
Paronychia	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Periodontitis	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pulpitis dental	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Tinea infection	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Urinary tract infection	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Viral infection	2	6.1	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	8.3
Lipoma	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	8.3
Blood and lymphatic system disorders	3	9.1	0	0.0	1	3.0	1	3.0	1	3.2	0	0.0	1	4.3	1	5.6	1	14.3	0	0.0
Leukopenia	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Neutropenia	2	6.1	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	1	4.3	1	5.6	1	14.3	0	0.0
Thrombocytopenia	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Endocrine disorders	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Hypothyroidism	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Metabolism and nutrition disorders	4	12.1	1	3.0	0	0.0	1	3.0	1	3.2	1	3.8	1	4.3	0	0.0	0	0.0	0	0.0
Decreased appetite	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Dehydration	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hyperglycaemia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Hypoalbuminaemia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Hypoglycaemia	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hypoproteinaemia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Psychiatric disorders	2	6.1	1	3.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Affect lability	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Insomnia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Nervous system disorders	2	6.1	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0

SOC, PT	Overall		<=Week 2		Week 2< <=4		Week 4< <=12		Week 12< <=24		Week 24< <=36		Week 36< <=48		Week 48< <=72		> Week 72		Follow-up	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Cervicobrachial syndrome	1	3.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Dizziness	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Eye disorders	3	9.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	2	11.1	0	0.0	0	0.0
Asthenopia	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Conjunctival haemorrhage	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Punctate keratitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Ear and labyrinth disorders	3	9.1	0	0.0	0	0.0	1	3.0	1	3.2	1	3.8	0	0.0	0	0.0	1	14.3	0	0.0
Auricular swelling	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Eustachian tube patulous	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Meniere's disease	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Sudden hearing loss	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	14.3	0	0.0
Cardiac disorders	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Atrial fibrillation	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Vascular disorders	10	30.3	4	12.1	3	9.1	3	9.1	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Hypertension	10	30.3	4	12.1	3	9.1	3	9.1	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Respiratory, thoracic and mediastinal disorders	2	6.1	1	3.0	0	0.0	1	3.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Cough	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Epistaxis	2	6.1	1	3.0	0	0.0	1	3.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Gastrointestinal disorders	20	60.6	6	18.2	5	15.2	10	30.3	7	22.6	3	11.5	3	13.0	2	11.1	0	0.0	0	0.0
Abdominal discomfort	3	9.1	0	0.0	1	3.0	1	3.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Abdominal pain	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Abdominal pain upper	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Constipation	5	15.2	0	0.0	1	3.0	2	6.1	1	3.2	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Diarrhoea	13	39.4	5	15.2	4	12.1	8	24.2	4	12.9	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Faeces soft	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Large intestine polyp	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Mouth haemorrhage	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Nausea	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Stomatitis	2	6.1	0	0.0	0	0.0	0	0.0	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Toothache	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Vomiting	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hepatobiliary disorders	4	12.1	0	0.0	1	3.0	2	6.1	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Autoimmune hepatitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic cyst	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic function abnormal	2	6.1	0	0.0	1	3.0	1	3.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic steatosis	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Skin and subcutaneous tissue disorders	14	42.4	0	0.0	2	6.1	4	12.1	2	6.5	2	7.7	1	4.3	3	16.7	1	14.3	2	16.7
Dry skin	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Eczema	5	15.2	0	0.0	1	3.0	1	3.0	2	6.5	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0

SOC, PT	Overall		<=Week 2		Week 2< <=4		Week 4< <=12		Week 12< <=24		Week 24< <=36		Week 36< <=48		Week 48< <=72		> Week 72		Follow-up	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Erythema	2	6.1	0	0.0	1	3.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Haemorrhage subcutaneous	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	1	14.3	0	0.0
Pruritus	2	6.1	0	0.0	0	0.0	2	6.1	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Purpura	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Rash	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	16.7
Rash erythematous	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Rosacea	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Seborrhoeic dermatitis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
Musculoskeletal and connective tissue disorders	6	18.2	0	0.0	0	0.0	0	0.0	1	3.2	3	11.5	2	8.7	1	5.6	1	14.3	0	0.0
Arthralgia	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	1	5.6	0	0.0	0	0.0
Back pain	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	1	14.3	0	0.0
Joint contracture	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Lumbar spinal stenosis	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Muscle spasms	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
Neck pain	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Pain in extremity	2	6.1	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	1	5.6	0	0.0	0	0.0
Reproductive system and breast disorders	2	6.1	1	3.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Menopausal symptoms	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Menorrhagia	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
General disorders and administration site conditions	5	15.2	0	0.0	1	3.0	2	6.1	2	6.5	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Face oedema	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Incarcerated hernia	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Malaise	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Oedema	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Oedema peripheral	2	6.1	0	0.0	0	0.0	0	0.0	1	3.2	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Pyrexia	1	3.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Investigations	15	45.5	2	6.1	3	9.1	7	21.2	5	16.1	3	11.5	0	0.0	1	5.6	0	0.0	0	0.0
Alanine aminotransferase increased	2	6.1	0	0.0	1	3.0	1	3.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Aspartate aminotransferase increased	2	6.1	0	0.0	1	3.0	1	3.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Blood bilirubin increased	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Blood creatine phosphokinase increased	2	6.1	2	6.1	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Blood pressure increased	2	6.1	0	0.0	1	3.0	1	3.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Hepatic enzyme increased	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Liver function test abnormal	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Liver function test increased	4	12.1	0	0.0	0	0.0	2	6.1	1	3.2	1	3.8	0	0.0	1	5.6	0	0.0	0	0.0
Lymphocyte count increased	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Neutrophil count decreased	3	9.1	0	0.0	1	3.0	1	3.0	2	6.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Platelet count decreased	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0

SOC, PT	Overall		<=Week 2		Week 2< <=4		Week 4< <=12		Week 12< <=24		Week 24< <=36		Week 36< <=48		Week 48< <=72		> Week 72		Follow-up	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Weight increased	1	3.0	0	0.0	0	0.0	0	0.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
White blood cell count decreased	1	3.0	0	0.0	0	0.0	1	3.0	1	3.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Injury, poisoning and procedural complications	5	15.2	1	3.0	0	0.0	2	6.1	0	0.0	1	3.8	0	0.0	1	5.6	1	14.3	0	0.0
Allergic transfusion reaction	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Contusion	1	3.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	14.3	0	0.0
Limb injury	1	3.0	0	0.0	0	0.0	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Radius fracture	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	1	3.8	0	0.0	0	0.0	0	0.0	0	0.0
Vaccination complication	1	3.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0

MedDRA version 23.0
（Source: 1.13.3-4, C-10 表 45）

表 2.7.4.9-115 Adverse Events (AEs): Incidence by System Organ Class/Preferred Term and Onset Time (Subject Level) Fostamatinib Treated Population: Fostamatinib Exposure Period – C788-047, C788-048 and C788-049 study

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N	146	146	146	143	146	128	101	65	58	50	47	45	40	38	23
Adverse Events	130 (89.0%)	55 (37.7%)	40 (27.4%)	93 (65.0%)	112 (76.7%)	62 (48.4%)	44 (43.6%)	29 (44.6%)	33 (56.9%)	25 (50.0%)	17 (36.2%)	19 (42.2%)	13 (32.5%)	13 (34.2%)	7 (30.4%)
GASTROINTESTINAL DISORDERS	85 (58.2%)	30 (20.5%)	18 (12.3%)	40 (28.0%)	65 (44.5%)	29 (22.7%)	17 (16.8%)	7 (10.8%)	13 (22.4%)	7 (14.0%)	4 (8.5%)	5 (11.1%)	4 (10.0%)	5 (13.2%)	6 (26.1%)
Diarrhoea	53 (36.3%)	12 (8.2%)	6 (4.1%)	20 (14.0%)	31 (21.2%)	19 (14.8%)	10 (9.9%)	2 (3.1%)	9 (15.5%)	3 (6.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	2 (5.3%)	2 (8.7%)
Nausea	28 (19.2%)	11 (7.5%)	5 (3.4%)	9 (6.3%)	23 (15.8%)	4 (3.1%)	3 (3.0%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vomiting	13 (8.9%)	0 (0.0%)	1 (0.7%)	3 (2.1%)	4 (2.7%)	3 (2.3%)	3 (3.0%)	1 (1.5%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Abdominal Pain	9 (6.2%)	1 (0.7%)	2 (1.4%)	1 (0.7%)	4 (2.7%)	3 (2.3%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	1 (4.3%)
Abdominal Pain Upper	8 (5.5%)	0 (0.0%)	0 (0.0%)	4 (2.8%)	4 (2.7%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Constipation	8 (5.5%)	2 (1.4%)	0 (0.0%)	2 (1.4%)	4 (2.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dyspepsia	6 (4.1%)	2 (1.4%)	2 (1.4%)	1 (0.7%)	5 (3.4%)	0 (0.0%)	2 (2.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Flatulence	6 (4.1%)	4 (2.7%)	1 (0.7%)	1 (0.7%)	6 (4.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gingival Bleeding	6 (4.1%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	4 (2.7%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Mouth Haemorrhage	6 (4.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Mucosal Blistering	6 (4.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	2 (5.3%)	0 (0.0%)
Abdominal Distension	4 (2.7%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrointestinal Haemorrhage	4 (2.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haematochezia	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Toothache	4 (2.7%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dysphagia	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Haemorrhoidal Haemorrhage	3 (2.1%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rectal Haemorrhage	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abdominal Discomfort	2 (1.4%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Frequent Bowel Movements	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastritis	2 (1.4%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrooesophageal Reflux Disease	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemorrhoids	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Stomatitis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abdominal Pain Lower	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Anal Fissure	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ascites	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Bile Acid Malabsorption	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cheilitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dry Mouth	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Eructation	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastric Antral Vascular Ectasia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastritis Erosive	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastrointestinal Disorder	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Inguinal Hernia	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Irritable Bowel Syndrome	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Lip Oedema	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Melaena	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Odynophagia	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oesophageal Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Palatal Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retching	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INFECTIONS AND INFESTATIONS	64 (43.8%)	5 (3.4%)	5 (3.4%)	18 (12.6%)	27 (18.5%)	16 (12.5%)	13 (12.9%)	8 (12.3%)	14 (24.1%)	10 (20.0%)	10 (21.3%)	12 (26.7%)	8 (20.0%)	4 (10.5%)	3 (13.0%)
Upper Respiratory Tract Infection	18 (12.3%)	2 (1.4%)	2 (1.4%)	3 (2.1%)	6 (4.1%)	2 (1.6%)	5 (5.0%)	1 (1.5%)	1 (1.7%)	4 (8.0%)	1 (2.1%)	1 (2.2%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
Nasopharyngitis	10 (6.8%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	3 (5.2%)	2 (4.0%)	4 (8.5%)	1 (2.2%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Urinary Tract Infection	9 (6.2%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	3 (5.2%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	2 (5.0%)	2 (5.3%)	0 (0.0%)
Bronchitis	6 (4.1%)	0 (0.0%)	0 (0.0%)	3 (2.1%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	2 (4.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lower Respiratory Tract Infection	6 (4.1%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	3 (2.1%)	1 (0.8%)	3 (3.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Respiratory Tract Infection	6 (4.1%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Viral Infection	6 (4.1%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Pneumonia	5 (3.4%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gastroenteritis	4 (2.7%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pharyngitis	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	2 (4.4%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tooth Infection	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Sepsis	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cellulitis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Ear Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Gastrointestinal Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Candidiasis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oral Herpes	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post Procedural Infection	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Sinusitis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Abscess	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Arthritis Viral	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Bacteriuria	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Carbuncle	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cellulitis Staphylococcal	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diverticulitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Endocarditis Bacterial	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Erythema Induratum	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Escherichia Urinary Tract Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Fungal Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fungal Skin Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gingivitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Herpes Simplex	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Herpes Zoster	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Influenza	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Klebsiella Bacteraemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Laryngitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mastoiditis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Onychomycosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Otitis Media	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pulpitis Dental	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pyelonephritis Acute	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rhinitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subacute Endocarditis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Tinea Infection	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tonsillitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tooth Abscess	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tuberculosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Urinary Tract Infection Bacterial	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Urosepsis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Viral Pharyngitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Viral Upper Respiratory Tract Infection	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	50 (34.2%)	7 (4.8%)	6 (4.1%)	17 (11.9%)	29 (19.9%)	13 (10.2%)	7 (6.9%)	7 (10.8%)	6 (10.3%)	2 (4.0%)	2 (4.3%)	3 (6.7%)	3 (7.5%)	2 (5.3%)	1 (4.3%)
Epistaxis	27 (18.5%)	3 (2.1%)	3 (2.1%)	11 (7.7%)	17 (11.6%)	9 (7.0%)	3 (3.0%)	2 (3.1%)	3 (5.2%)	0 (0.0%)	2 (4.3%)	2 (4.4%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Cough	11 (7.5%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	2 (2.0%)	2 (3.1%)	0 (0.0%)	2 (4.0%)	1 (2.1%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Dyspnoea	8 (5.5%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	6 (4.1%)	1 (0.8%)	2 (2.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Oropharyngeal Pain	6 (4.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Rhinorrhoea	4 (2.7%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nasal Congestion	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dry Throat	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dyspnoea Exertional	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Sleep Apnoea Syndrome	2 (1.4%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chronic Obstructive Pulmonary Disease	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Dysphonia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemoptysis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypoxia	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nasal Inflammation	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Pleural Effusion	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Pulmonary Mass	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Upper Respiratory Tract Inflammation	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	47 (32.2%)	8 (5.5%)	3 (2.1%)	13 (9.1%)	22 (15.1%)	14 (10.9%)	4 (4.0%)	1 (1.5%)	6 (10.3%)	6 (12.0%)	3 (6.4%)	6 (13.3%)	1 (2.5%)	3 (7.9%)	2 (8.7%)
Fatigue	14 (9.6%)	3 (2.1%)	2 (1.4%)	3 (2.1%)	6 (4.1%)	3 (2.3%)	1 (1.0%)	1 (1.5%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Pyrexia	10 (6.8%)	1 (0.7%)	1 (0.7%)	3 (2.1%)	5 (3.4%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	1 (2.6%)	1 (4.3%)
Chest Pain	9 (6.2%)	1 (0.7%)	1 (0.7%)	3 (2.1%)	5 (3.4%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Oedema Peripheral	8 (5.5%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Asthenia	7 (4.8%)	0 (0.0%)	2 (1.4%)	1 (0.7%)	3 (2.1%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peripheral Swelling	7 (4.8%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	3 (2.1%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Influenza Like Illness	6 (4.1%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	2 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chills	5 (3.4%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	3 (2.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Pain	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Chest Discomfort	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Feeling Cold	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Adverse Drug Reaction	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Facial Pain	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gait Disturbance	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
General Physical Health Deterioration	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Glassy Eyes	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Mucosal Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Polyp	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vessel Puncture Site Bruise	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NERVOUS SYSTEM DISORDERS	47 (32.2%)	12 (8.2%)	4 (2.7%)	20 (14.0%)	29 (19.9%)	12 (9.4%)	2 (2.0%)	3 (4.6%)	9 (15.5%)	1 (2.0%)	2 (4.3%)	2 (4.4%)	2 (5.0%)	3 (7.9%)	3 (13.0%)
Headache	22 (15.1%)	4 (2.7%)	2 (1.4%)	7 (4.9%)	12 (8.2%)	5 (3.9%)	2 (2.0%)	1 (1.5%)	4 (6.9%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	2 (5.0%)	2 (5.3%)	2 (8.7%)
Dizziness	18 (12.3%)	6 (4.1%)	2 (1.4%)	6 (4.2%)	13 (8.9%)	5 (3.9%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dysgeusia	4 (2.7%)	1 (0.7%)	0 (0.0%)	3 (2.1%)	3 (2.1%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypoaesthesia	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Sciatica	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Memory Impairment	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Neuralgia	2 (1.4%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Presyncope	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cerebral Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Disturbance In Attention	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dysarthria	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Haemorrhagic Stroke	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Hypogeusia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lethargy	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Loss Of Consciousness	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Migraine	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Neuropathy Peripheral	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Paraesthesia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Peroneal Nerve Palsy	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Restless Legs Syndrome	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Somnolence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Syncope	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Transient Ischaemic Attack	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
INVESTIGATIONS	46 (31.5%)	5 (3.4%)	1 (0.7%)	19 (13.3%)	24 (16.4%)	13 (10.2%)	5 (5.0%)	7 (10.8%)	4 (6.9%)	2 (4.0%)	3 (6.4%)	4 (8.9%)	4 (10.0%)	0 (0.0%)	4 (17.4%)
Alanine Aminotransferase Increased	14 (9.6%)	0 (0.0%)	0 (0.0%)	9 (6.3%)	9 (6.2%)	5 (3.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aspartate Aminotransferase Increased	10 (6.8%)	1 (0.7%)	0 (0.0%)	6 (4.2%)	7 (4.8%)	3 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Increased	7 (4.8%)	1 (0.7%)	0 (0.0%)	3 (2.1%)	4 (2.7%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet Count Decreased	6 (4.1%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hepatic Enzyme Increased	5 (3.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	1 (1.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Liver Function Test Abnormal	4 (2.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Bilirubin Increased	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Lactate Dehydrogenase Increased	3 (2.1%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Blood Creatinine Increased	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Pressure Diastolic Increased	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Neutrophil Count Decreased	2 (1.4%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Transaminases Increased	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Weight Decreased	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Weight Increased	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Angiogram	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Alkaline Phosphatase Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Bicarbonate Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Glucose Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Potassium Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Blood Pressure Diastolic Abnormal	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Measurement	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Blood Pressure Systolic Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Blood Urea Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
C-Reactive Protein Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac Murmur	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gamma-Glutamyltransferase Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Globulins Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Haemoglobin Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Heart Rate Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lymphocyte Count Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Platelet Count Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Troponin Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Vitamin B12 Increased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	45 (30.8%)	3 (2.1%)	7 (4.8%)	16 (11.2%)	23 (15.8%)	13 (10.2%)	10 (9.9%)	3 (4.6%)	7 (12.1%)	4 (8.0%)	4 (8.5%)	3 (6.7%)	2 (5.0%)	3 (7.9%)	1 (4.3%)
Petechiae	22 (15.1%)	1 (0.7%)	3 (2.1%)	4 (2.8%)	7 (4.8%)	7 (5.5%)	5 (5.0%)	2 (3.1%)	3 (5.2%)	2 (4.0%)	2 (4.3%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Rash	10 (6.8%)	1 (0.7%)	1 (0.7%)	4 (2.8%)	6 (4.1%)	2 (1.6%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ecchymosis	4 (2.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Blood Blister	3 (2.1%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Pruritus	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Lesion	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Dermatitis Allergic	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Dry Skin	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eczema	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	2 (3.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erythema	2 (1.4%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Hair Colour Changes	2 (1.4%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperhidrosis	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Purpura	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Swelling Face	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Actinic Keratosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Alopecia	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blister	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemorrhage Subcutaneous	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertrichosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nail Discolouration	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Nail Disorder	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Papule	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Photosensitivity Reaction	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Precancerous Skin Lesion	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash Erythematous	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash Macular	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Rash Papular	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Hypopigmentation	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Ulcer	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Urticaria	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
VASCULAR DISORDERS	40 (27.4%)	6 (4.1%)	7 (4.8%)	17 (11.9%)	29 (19.9%)	5 (3.9%)	3 (3.0%)	5 (7.7%)	3 (5.2%)	5 (10.0%)	2 (4.3%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	1 (4.3%)
Hypertension	32 (21.9%)	4 (2.7%)	5 (3.4%)	14 (9.8%)	22 (15.1%)	4 (3.1%)	2 (2.0%)	4 (6.2%)	3 (5.2%)	4 (8.0%)	2 (4.3%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
Haematoma	4 (2.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Haemorrhage	3 (2.1%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypotension	2 (1.4%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	1 (4.3%)
Aortic Stenosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blood Pressure Inadequately Controlled	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hot Flush	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertensive Crisis	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Peripheral Venous Disease	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Phlebitis Superficial	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	32 (21.9%)	6 (4.1%)	5 (3.4%)	7 (4.9%)	17 (11.6%)	11 (8.6%)	3 (3.0%)	2 (3.1%)	1 (1.7%)	2 (4.0%)	2 (4.3%)	2 (4.4%)	0 (0.0%)	5 (13.2%)	1 (4.3%)
Thrombocytopenia	11 (7.5%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	5 (3.4%)	3 (2.3%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	4 (10.5%)	0 (0.0%)
Anaemia	8 (5.5%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	3 (2.1%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	2 (4.3%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Neutropenia	8 (5.5%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	3 (2.1%)	4 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Leukopenia	3 (2.1%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Increased Tendency To Bruise	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Lymphadenopathy	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Microcytic Anaemia	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Thrombocytosis	2 (1.4%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aplastic Anaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Febrile Neutropenia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune Thrombocytopenic Purpura	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Leukocytosis	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Polycythaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	32 (21.9%)	2 (1.4%)	1 (0.7%)	6 (4.2%)	9 (6.2%)	11 (8.6%)	7 (6.9%)	5 (7.7%)	7 (12.1%)	4 (8.0%)	3 (6.4%)	3 (6.7%)	2 (5.0%)	4 (10.5%)	1 (4.3%)
Arthralgia	9 (6.2%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	2 (1.4%)	2 (1.6%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Myalgia	8 (5.5%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	2 (1.6%)	4 (4.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Back Pain	6 (4.1%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	3 (2.1%)	2 (1.6%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Muscle Spasms	6 (4.1%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	2 (1.4%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	3 (5.2%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Joint Swelling	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.6%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal Pain	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Neck Pain	4 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	1 (1.7%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Pain In Extremity	4 (2.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	2 (3.4%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Arthritis	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (5.0%)	0 (0.0%)	0 (0.0%)
Chondrocalcinosis Pyrophosphate	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Muscular Weakness	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Musculoskeletal Chest Pain	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Osteoporosis	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ankylosing Spondylitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Bone Lesion	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Bone Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haemarthrosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mobility Decreased	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Plantar Fasciitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Rotator Cuff Syndrome	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Spinal Column Stenosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tendon Sheath Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tendonitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Trigger Finger	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	24 (16.4%)	2 (1.4%)	1 (0.7%)	6 (4.2%)	8 (5.5%)	2 (1.6%)	4 (4.0%)	4 (6.2%)	4 (6.9%)	2 (4.0%)	0 (0.0%)	2 (4.4%)	2 (5.0%)	3 (7.9%)	2 (8.7%)
Contusion	17 (11.6%)	2 (1.4%)	1 (0.7%)	6 (4.2%)	8 (5.5%)	1 (0.8%)	2 (2.0%)	0 (0.0%)	2 (3.4%)	2 (4.0%)	0 (0.0%)	2 (4.4%)	2 (5.0%)	1 (2.6%)	1 (4.3%)
Fall	3 (2.1%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Animal Bite	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Joint Injury	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Anaphylactic Transfusion Reaction	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Graft Complication	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Head Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Limb Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Muscle Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Procedural Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Scratch	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Skin Wound	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Thoracic Vertebral Fracture	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
METABOLISM AND NUTRITION DISORDERS	14 (9.6%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	6 (4.1%)	3 (2.3%)	1 (1.0%)	2 (3.1%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	2 (5.0%)	0 (0.0%)	2 (8.7%)
Hypokalaemia	5 (3.4%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	2 (1.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Decreased Appetite	3 (2.1%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Dehydration	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Fluid Overload	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Glucose Tolerance Impaired	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Gout	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperglycaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperkalaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Hypernatraemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Hyperuricaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hypomagnesaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypophosphataemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Iron Deficiency	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vitamin D Deficiency	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
CARDIAC DISORDERS	10 (6.8%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	2 (1.6%)	2 (2.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	2 (8.7%)
Tachycardia	3 (2.1%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Atrial Fibrillation	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Cardiac Failure Congestive	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Angina Pectoris	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Aortic Valve Incompetence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Cardiac Failure Chronic	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Cardio-Respiratory Arrest	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Mitral Valve Incompetence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Palpitations	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Tricuspid Valve Incompetence	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Ventricular Extrasystoles	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
EYE DISORDERS	9 (6.2%)	0 (0.0%)	0 (0.0%)	3 (2.1%)	3 (2.1%)	1 (0.8%)	3 (3.0%)	1 (1.5%)	0 (0.0%)	2 (4.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Conjunctival Haemorrhage	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Eyelid Oedema	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Blepharitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Eye Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Retinal Tear	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vision Blurred	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
RENAL AND URINARY DISORDERS	9 (6.2%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	3 (2.1%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (4.3%)	1 (2.2%)	2 (5.0%)	1 (2.6%)	2 (8.7%)
Nephrolithiasis	4 (2.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Pollakiuria	2 (1.4%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Acute Kidney Injury	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Chronic Kidney Disease	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Haematuria	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hypertonic Bladder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Leukocyturia	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Renal Cyst	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Renal Failure	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
PSYCHIATRIC DISORDERS	8 (5.5%)	1 (0.7%)	0 (0.0%)	4 (2.8%)	5 (3.4%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	2 (8.7%)
Insomnia	4 (2.7%)	1 (0.7%)	0 (0.0%)	2 (1.4%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Anxiety	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Depressed Mood	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Depression	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mental Status Changes	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Restlessness	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	8 (5.5%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	3 (2.3%)	1 (1.0%)	0 (0.0%)	1 (1.7%)	2 (4.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Vaginal Haemorrhage	3 (2.1%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Menorrhagia	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Breast Mass	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Erectile Dysfunction	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Uterine Polyp	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vulvovaginal Pain	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
EAR AND LABYRINTH DISORDERS	6 (4.1%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	2 (4.4%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Ear Haemorrhage	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Excessive Cerumen Production	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Otorrhoea	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tinnitus	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tympanic Membrane Disorder	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Tympanic Membrane Perforation	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Vertigo	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	6 (4.1%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.4%)	1 (2.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	2 (5.3%)	1 (4.3%)
Squamous Cell Carcinoma Of Skin	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)
Basal Cell Carcinoma	2 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.2%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Basosquamous Carcinoma Of Skin	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cholesteatoma	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Plasma Cell Myeloma	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
HEPATOBILIARY DISORDERS	4 (2.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	1 (0.8%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Cholecystitis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hepatic Cirrhosis	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)

Time to Onset	Overall	<=Week 2	Week 2< <=4	Week 4< <=12	<=Week 12	Week 12< <=24	Week 24< <=36	Week 36< <=48	Week 48< <=Month 18	Month 18< <=24	Month 24< <=30	Month 30< <=36	Month 36< <=42	Month 42< <=48	Month 48<
System Organ Class Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hepatic Cyst	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperbilirubinaemia	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Portal Hypertension	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
SURGICAL AND MEDICAL PROCEDURES	3 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	1 (2.6%)	0 (0.0%)
Micrographic Skin Surgery	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.6%)	0 (0.0%)
Rotator Cuff Repair	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Tooth Extraction	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Dacryostenosis Congenital	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Hydrocele	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
IMMUNE SYSTEM DISORDERS	2 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
Allergy To Chemicals	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Allergy To Metals	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Drug Hypersensitivity	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	1 (2.5%)	0 (0.0%)	0 (0.0%)
ENDOCRINE DISORDERS	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cushingoid	1 (0.7%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Note: Adverse events were coded using MedDRA version 18.1. Subjects are counted only once in each preferred term category and only once in each system organ class category and in each term.
（Source: 1.13.3-4, C-10 表 46）

表 2.7.4.9-116　眼関連の有害事象（R788-1301 試験、プラセボ対照期）

SOC	R788（N=22）								プラセボ（N=12）							
	合計		軽度		中等度		重度		合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
眼障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 2）

表 2.7.4.9-117　眼関連の有害事象（R788-1301 試験、R788 投与期）

SOC	R788（N=33）							
	合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%
眼障害	3	9.1	3	9.1	0	0.0	0	0.0
眼精疲労	1	3.0	1	3.0	0	0.0	0	0.0
結膜出血	1	3.0	1	3.0	0	0.0	0	0.0
点状角膜炎	1	3.0	1	3.0	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 3）

表 2.7.4.9-118　眼関連の副作用（R788-1301 試験、R788 投与期）

SOC	R788（N=33）							
	合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%
眼障害	0	0.0	0	0.0	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 5）

表 2.7.4.9-119　眼関連の有害事象（C788-047 及び C788-048 試験、プラセボ対照期）

SOC	R788（N=102）								プラセボ（N=48）							
	合計		軽度		中等度		重度		合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
眼障害	5	4.9	3	2.9	2	2.0	0	0.0	2	4.2	1	2.1	1	2.1	0	0.0
眼痛	1	1.0	0	0.0	1	1.0	0	0.0	1	2.1	1	2.1	0	0.0	0	0.0
眼瞼炎	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼の障害	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼浮腫	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
網膜裂孔	1	1.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
結膜蒼白	0	0.0	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	1	2.1	0	0.0
黄疸眼	0	0.0	0	0.0	0	0.0	0	0.0	1	2.1	1	2.1	0	0.0	0	0.0
視力障害	0	0.0	0	0.0	0	0.0	0	0.0	1	2.1	1	2.1	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 6）

表 2.7.4.9-120　眼関連の有害事象（C788-047、C788-048 及び C788-049 試験、R788 投与期）

SOC	R788（N=146）							
	合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%
眼障害	9	6.2	4	2.7	4	2.7	1	0.7
結膜出血	2	1.4	0	0.0	1	0.7	1	0.7
眼瞼浮腫	2	1.4	2	1.4	0	0.0	0	0.0
眼瞼炎	1	0.7	1	0.7	0	0.0	0	0.0
眼の障害	1	0.7	1	0.7	0	0.0	0	0.0
眼出血	1	0.7	1	0.7	0	0.0	0	0.0
眼痛	1	0.7	0	0.0	1	0.7	0	0.0
網膜裂孔	1	0.7	0	0.0	1	0.7	0	0.0
霧視	1	0.7	0	0.0	1	0.7	0	0.0

（Source: 1.13.3-5, A-01 表 7）

表 2.7.4.9-121　　眼関連の副作用（C788-047 及び C788-048 試験、プラセボ対照期）

SOC	R788（N=102）								プラセボ（N=48）							
	合計		軽度		中等度		重度		合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
眼障害	2	2.0	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼炎	1	1.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼痛	1	1.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 8）

表 2.7.4.9-122　　眼関連の副作用（C788-047、C788-048 及び C788-049 試験、R788 投与期）

SOC	R788（N=146）							
	合計		軽度		中等度		重度	
PT	n	%	n	%	n	%	n	%
眼障害	3	2.1	2	1.4	1	0.7	0	0.0
眼瞼炎	1	0.7	1	0.7	0	0.0	0	0.0
眼痛	1	0.7	0	0.0	1	0.7	0	0.0
眼瞼浮腫	1	0.7	1	0.7	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 9）

表 2.7.4.9-123　　眼関連の有害事象（R788-1301 試験、R788 投与期、発現時期別）

	≤Week 2		Week 2< ≤4		Week 4< ≤12		Week 12< ≤24		Week 24< ≤36		Week 36< ≤48		Week 48< ≤72		> Week 72		Follow-up	
SOC	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
PT	33	---	33	---	33	---	31	---	26	---	23	---	18	---	7	---	12	---
眼障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	2	11.1	0	0.0	0	0.0
眼精疲労	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0
結膜出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	4.3	0	0.0	0	0.0	0	0.0
点状角膜炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 11）

表 2.7.4.9-124　　眼関連の有害事象（C788-047、C788-048 及び C788-049 試験、R788 投与期、発現時期別）

	≤Week 2		Week 2< ≤4		Week 4< ≤12		Week 12< ≤24		Week 24< ≤36		Week 36< ≤48		Week 48< ≤Month 18		Month 18< ≤24		Month 24< ≤30		Month 30< ≤36		Month 36< ≤42		Month 42< ≤48		Month 48<	
SOC	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
PT	146	---	146	---	143	---	128	---	101	---	65	---	58	---	50	---	47	---	45	---	40	---	38	---	23	---
眼障害	0	0.0	0	0.0	3	2.1	1	0.8	3	3.0	1	1.5	0	0.0	2	4.0	1	2.1	1	2.2	0	0.0	1	2.6	0	0.0
結膜出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	1.5	0	0.0	0	0.0	1	2.1	1	2.2	0	0.0	1	2.6	0	0.0
眼瞼浮腫	0	0.0	0	0.0	0	0.0	0	0.0	2	2.0	0	0.0	0	0.0	1	2.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼炎	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼の障害	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼出血	0	0.0	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼痛	0	0.0	0	0.0	0	0.0	1	0.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
網膜裂孔	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
霧視	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	2.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

（Source: 1.13.3-5, A-01 表 12）

表 2.7.4.9-125　　高血圧の管理（R788-1301 試験、プラセボ対照期）

Type of Hypertension Intervention	R788 (N=22) n(%)	Placebo (N=12) n(%)
No hypertension interventions	15(68.2%)	11(91.7%)
At least one hypertension intervention	7(31,8%)	1(8.3%)
Concomitant medication	5(22.7%)	1(8.3%)
Dose reduction of study drug	2(9.1%)	0(0.0%)
Discontinuation of study drug	1(4.5%)	0(0.0%)

（Source: 1.13.3-6, C-03-2 表 15）

表 2.7.4.9-126　　高血圧の管理（R788-1301 試験、R788 投与期）

Type of Hypertension Intervention	R788 (N=33) n(%)
No hypertension interventions	21(63.6%)
At least one hypertension intervention	12(36.4%)
Concomitant medication	9(27.3%)
Dose reduction of study drug	6(18.2%)
Discontinuation of study drug	1(3.0%)

（Source: 1.13.3-5, C-03-2 表 16）

表 2.7.4.9-127 Extremum Post-Baseline Observation in Laboratory Tests – R788-1301 study

R788 Treatment Period
Parameter: Alanine Aminotransferase (U/L)

		Maximum Post Day 1					
		>3*ULN		>5*ULN		>10*ULN	
Group	N	n	%	n	%	n	%
R788	33	4	12.1	3	9.1	2	6.1

ULN: Upper Limit of Normal

R788 Treatment Period
Parameter: Aspartate Aminotransferase (U/L)

		Maximum Post Day 1					
		>3*ULN		>5*ULN		>10*ULN	
Group	N	n	%	n	%	n	%
R788	33	4	12.1	2	6.1	1	3.0

ULN: Upper Limit of Normal

R788 Treatment Period
Parameter: Alkaline Phosphatase (U/L)

		Maximum Post Day 1 >1.5*ULN	
Group	N	n	%
R788	33	3	9.1

ULN: Upper Limit of Normal

R788 Treatment Period
Parameter: Bilirubin (umol/L)

		Maximum Post Day 1 >2*ULN	
Group	N	n	%
R788	33	2	6.1

ULN: Upper Limit of Normal
（Source: 1.13.3-6, C-03-3 付録 220907-C-03-3）

表 2.7.4.9-128　　海外市販後における重篤な肝機能障害関連有害事象の一覧

性別	年齢	ホスタマチニブ投与量（投与期間）	有害事象名（PT）	発現日	ホスタマチニブの処置	転帰	担当医意見		企業意見		肝機能検査値	他の有害事象
							重篤度	因果関係	重篤度	因果関係		
女	7[redacted]歳	200 mg/day (20[redacted]～)	肝酵素上昇	20[redacted]	中止	不明	重篤	関連あり	重篤	関連あり	ALT 56、AST 42、総ビリルビン 2.1、ALP 618	血小板数減少
男	3[redacted]歳	200 mg/day (20[redacted]～20[redacted])	アラニンアミノトランスフェラーゼ増加	Day 17*	中止	不明	重篤	関連あり	重篤	関連あり	20[redacted]:ALT 185、AST 正常、総ビリルビン 正常 20[redacted]: ALT 84、総ビリルビン 1.448	
			血中ビリルビン増加		中止	回復	重篤	関連あり	重篤	関連あり		
			γ-グルタミルトランスフェラーゼ増加		中止	回復	重篤	関連あり	重篤	関連あり		
男	7[redacted]歳	300 mg/day	肝硬変	20[redacted]	継続	不明	重篤	記載なし	重篤	関連なし		腎障害、皮膚創傷
女	8[redacted]歳	300 mg/day	肝毒性		継続	不明	重篤	記載なし	重篤	関連なし		
女	7[redacted]歳	200 mg/day (20[redacted]～20[redacted])	肝酵素上昇	20[redacted]	中止	不明	重篤	記載なし	重篤	関連あり		
男	8[redacted]歳	200 mg/day (20[redacted]～20[redacted]) 300 mg/day (20[redacted]～20[redacted])	肝毒性	20[redacted]	中止	不明	重篤	記載なし	重篤	関連あり		好中球減少症、高血圧、下痢
女	不明	300 mg/day (20[redacted]～20[redacted])	肝細胞融解	20[redacted]	中止	軽快	重篤	関連あり	重篤	関連あり		発熱、感染、低血圧
男	7[redacted]歳	200 mg/day (20[redacted]～)	肝障害	20[redacted]	継続	不明	重篤	記載なし	重篤	関連なし		出血
女	6[redacted]歳	200 mg/day (20[redacted]～)	肝腫大		継続	不明	重篤	記載なし	重篤	関連なし		うっ血性心不全、呼吸障害、ドレナージ、嘔吐、血清フェリチン増加、赤血球数減少、ヘモグロビン減少、挫傷、平均赤血球容積増加、平均赤血球ヘモグロビン増加、臨床検査異常、血小板数減少、乳房痛、脾腫、齲歯、舌嚢胞、評価不能の事象、無力症、下痢、悪心、疲労、血小板数

（Source: 1.13.3-6, C-03-3 表 17）

＊新薬承認情報提供時に置き換え

表 2.7.4.9-129　投与開始後 4 週間以内に発現した高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ に関する有害事象のうち治療介入した事象（R788-1301 試験）

被験者 ID	投与群 I 期/II 期以降	発現時投与量	有害事象名（PT）	発現日 （R788 投与後日数）	程度	重篤度	治験薬の処置	その他の処置	因果関係	転帰
[redacted]	R788/R788	100 mg BID	Hypertension	15	MILD	N	DOSE REDUCED	CONCOMITANT MEDICATION	RELATED	RECOVERING/ RESOLVING
[redacted]	R788/ -	100 mg BID	Hepatic function abnormal	29	MILD	N	DOSE REDUCED		RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	100 mg BID	Hypertension	8	MILD	N	DOSE NOT CHANGED	CONCOMITANT MEDICATION	RELATED	RECOVERING/ RESOLVING
[redacted]	P/R788	100 mg BID	Hypertension	15	MILD	N	DOSE REDUCED		RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	100 mg BID	Hypertension	29	MILD	N	DOSE NOT CHANGED	CONCOMITANT MEDICATION	RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	100 mg BID	Blood pressure increased	29	MILD	N	DOSE REDUCED	CONCOMITANT MEDICATION	RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	100 mg BID	Neutropenia	29	MILD	N	DOSE REDUCED		NOT RELATED	RECOVERED/ RESOLVED
[redacted]	P/R788	100 mg BID	Hypertension	4	MODERATE	N	DOSE REDUCED	CONCOMITANT MEDICATION	RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	100 mg BID	Hypertension	16	MILD	N	DOSE REDUCED		NOT RELATED	NOT RECOVERED/ NOT RESOLVED
[redacted]	P/R788	100 mg BID	Alanine aminotransferase increased	29	MILD	N	DOSE REDUCED		RELATED	RECOVERED/ RESOLVED
		100 mg BID	Aspartate aminotransferase increased	29	MILD	N	DOSE REDUCED		RELATED	RECOVERED/ RESOLVED

（Source: 1.13.3-8, C-02-2 表 1）

表 2.7.4.9-130　用量変更後 4 週間以内に発現した高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ に関する有害事象のうち治療介入した事象（R788-1301 試験）

被験者 ID	投与群 I 期/II 期以降	発現時投与量	有害事象名（PT）	発現日 （R788 投与後日数）	R788 増量後日数	程度	重篤度	治験薬の処置	その他の処置	因果関係	転帰
[redacted]	R788/ -	100 mg BID	Hepatic function abnormal	99	27	MILD	N	DRUG WITHDRAWN		RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	150 mg BID	Hypertension	57	28	MILD	N	DOSE NOT CHANGED	CONCOMITANT MEDICATION	RELATED	RECOVERING/ RESOLVING
[redacted]	R788	150 mg BID	Hypertension	38	9	MILD	N	DRUG WITHDRAWN		RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	150 mg BID	Liver function test abnormal	71	28	MILD	N	DOSE REDUCED	CONCOMITANT MEDICATION	RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	150 mg BID	Blood pressure increased	71	28	MILD	N	DOSE NOT CHANGED	CONCOMITANT MEDICATION	RELATED	RECOVERED/ RESOLVED
[redacted]	P/R788	150 mg BID	Liver function test increased	43	14	MILD	N	DOSE REDUCED		RELATED	NOT RECOVERED/ NOT RESOLVED
[redacted]	R788/R788	150 mg BID	Neutrophil count decreased	58	28	MILD	N	DOSE REDUCED		RELATED	RECOVERED/ RESOLVED

（Source: 1.13.3-8, C-02-2 表 2）

表 2.7.4.9-131　投与開始後 4 週間以内に発現した高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ に関する有害事象のうち治療介入した事象（C788-047、C788-048 及び C788-049 試験）

被験者 ID	投与群 047,048/049 試験	有害事象名（PT）	発現日 （R788 投与後日数）	程度	重篤度	治験薬の処置	その他の処置	因果関係	転帰
[redacted]	R788	Hypertension	3	MILD	N	DOSE NOT CHANGED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Hypertension	23	MILD	N	DOSE NOT CHANGED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Hypertension	2	MODERATE	N	DRUG INTERRUPTED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
		Neutrophil Count Decreased	29	MILD	N	DRUG INTERRUPTED	N	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Hypertension	15	MILD	N	DOSE NOT CHANGED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Hypertension	22	MODERATE	N	DRUG INTERRUPTED	Y	UNLIKELY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Neutropenia	29	MILD	N	DOSE NOT CHANGED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	R788	Hypertensive Crisis	21	SEVERE	Y	DRUG INTERRUPTED	Y	PROBABLY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Hypertension	29	MODERATE	N	DOSE REDUCED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	R788/R788	Hypertension	27	MILD	N	DOSE NOT CHANGED	Y	POSSIBLY RELATED	RECOVERED/RESOLVED
[redacted]	P/R788	Blood Pressure Inadequately Controlled	14	MILD	N	DOSE REDUCED		PROBABLY RELATED	RECOVERED/RESOLVED

（Source: 1.13.3-8, C-02-2 表 3）

表 2.7.4.9-132　用量変更後 4 週間以内に発現した高血圧 SMQ、好中球減少症及び薬物関連肝障害 SMQ に関する有害事象のうち治療介入した事象（C788-047、C788-048 及び C788-049 試験）

被験者 ID	投与群 047,048/049 試験	有害事象名（PT）	発現日（R788 投与後日数）	R788 増量後日数	程度	重篤度	治験薬の処置	その他の処置	因果関係	転帰
[redacted]	R788/R788	Transaminases Increased	890	25	SEVERE	Y	DRUG INTERRUPTED		UNLIKELY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Hypertension	57	14	MILD	N	DOSE NOT CHANGED	Y	PROBABLY RELATED	NOT RECOVERED/ NOT RESOLVED
[redacted]	R788/R788	Hypertension	36	7	MILD	N	DOSE NOT CHANGED	Y	POSSIBLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Febrile Neutropenia	103	3	SEVERE	Y	DRUG INTERRUPTED	Y	POSSIBLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Alanine Aminotransferase Increased	127	14	MODERATE	N	DRUG INTERRUPTED	N	POSSIBLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Hypertension	44	14	MILD	N	DOSE NOT CHANGED	Y	PROBABLY RELATED	NOT RECOVERED/ NOT RESOLVED
		Alanine Aminotransferase Increased	58	28	MILD	N	DRUG INTERRUPTED	N	PROBABLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Neutropenia	71	14	MODERATE	N	DRUG WITHDRAWN		POSSIBLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788	Alanine Aminotransferase Increased	85	14	MILD	N	DRUG INTERRUPTED	N	PROBABLY RELATED	RECOVERED/ RESOLVED
		Aspartate Aminotransferase Increased	85	14	MILD	N	DOSE REDUCED	N	PROBABLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Alanine Aminotransferase Increased	44	7	MODERATE	N	DRUG INTERRUPTED	N	PROBABLY RELATED	RECOVERED/ RESOLVED
[redacted]	R788/R788	Hypertension	57	28	MILD	N	DOSE NOT CHANGED	Y	PROBABLY RELATED	RECOVERING/ RESOLVING
[redacted]	R788/R788	Alanine Aminotransferase Increased	43	15	MILD	N	DOSE REDUCED	N	PROBABLY RELATED	RECOVERED/ RESOLVED

（Source: 1.13.3-8, C-02-2 表 4）

表 2.7.4.9-133 Laboratory Tests‑– R788-1301 study

Period I
Parameter: Leukocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	6.744	2.805	3.40	4.79	6.58	7.40	13.60
	Screening B	22	6.424	2.606	3.54	4.50	5.76	7.67	14.50
	Day 1	22	6.780	3.022	3.30	4.57	5.75	8.20	14.50
	Week 2	22	5.837	2.142	2.80	4.33	5.30	6.90	10.60
	Week 4	22	5.036	2.296	2.00	2.99	4.60	6.60	10.40
	Week 6	22	4.725	1.800	2.00	3.70	4.53	5.20	9.00
	Week 8	21	4.663	1.997	1.80	3.23	4.51	5.20	9.70
	Week 10	20	4.361	2.083	1.00	3.03	4.10	4.71	10.50
	Week 12	20	4.720	2.100	2.39	3.35	4.22	5.35	11.50
	Week 14	16	3.866	1.366	2.37	2.90	3.60	4.20	7.80
	Week 16	10	4.790	2.230	2.50	3.00	4.37	5.50	9.90
	Week 18	10	3.910	1.375	2.13	2.41	3.98	5.00	6.40
	Week 20	10	4.216	1.228	2.56	3.00	4.27	4.90	6.10
	Week 22	10	4.242	1.426	2.41	3.20	3.82	5.50	7.00
	Week 24	10	4.161	1.423	2.49	3.07	4.10	4.65	7.20
	LOV	22	5.361	3.319	2.49	3.23	4.50	5.50	16.58
Placebo	Screening A	12	7.528	2.538	4.35	5.29	7.40	9.02	12.02
	Screening B	12	7.138	2.507	3.91	5.12	6.67	8.69	12.89
	Day 1	12	7.858	3.453	4.39	5.33	6.92	8.74	15.60
	Week 2	12	6.780	2.839	3.59	4.74	6.25	7.41	12.53
	Week 4	10	7.208	2.479	4.66	5.16	6.53	8.26	11.60
	Week 6	10	7.156	2.490	3.61	5.40	7.06	8.80	12.01
	Week 8	11	6.596	2.580	3.64	4.81	5.10	8.70	12.13
	Week 10	11	6.491	2.407	3.76	4.77	5.80	7.80	11.03
	Week 12	10	6.929	3.136	3.20	4.87	6.10	7.74	12.33
	Week 14	4	4.878	0.900	3.80	4.14	5.04	5.62	5.64
	Week 16	4	5.095	1.081	4.20	4.22	4.87	5.97	6.44
	Week 18	4	4.733	0.909	3.39	4.22	5.07	5.25	5.40
	Week 20	3	5.203	1.584	3.43	3.43	5.70	6.48	6.48
	Week 22	4	5.453	1.831	3.22	4.01	5.60	6.90	7.39
	Week 24	4	4.798	1.175	3.20	3.95	5.05	5.65	5.90
	LOV	12	7.073	3.042	3.20	4.91	6.07	9.22	12.20

Parameter: Lymphocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	1.635	0.955	0.79	0.90	1.28	2.26	4.26
	Screening B	22	1.629	0.841	0.79	1.17	1.33	1.86	4.50
	Day 1	22	1.750	1.037	0.83	1.16	1.38	2.18	5.51
	Week 2	22	2.200	1.298	0.69	1.29	1.85	2.64	5.48
	Week 4	22	1.817	1.192	0.47	0.94	1.37	2.47	4.59
	Week 6	22	1.543	0.859	0.72	1.00	1.19	1.80	4.23
	Week 8	21	1.793	0.979	0.63	1.18	1.53	2.19	4.05

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 10	20	1.631	1.069	0.30	0.99	1.33	2.01	5.15
	Week 12	20	1.728	1.206	0.37	1.03	1.34	2.40	5.87
	Week 14	16	1.413	0.474	0.75	1.03	1.37	1.80	2.26
	Week 16	10	1.330	0.776	0.59	0.71	1.09	1.98	2.88
	Week 18	10	1.407	0.576	0.69	0.98	1.18	2.04	2.20
	Week 20	10	1.458	0.608	0.85	1.06	1.27	1.65	2.89
	Week 22	10	1.392	0.453	0.93	0.99	1.28	1.72	2.22
	Week 24	10	1.295	0.415	0.84	0.95	1.20	1.58	2.00
	LOV	22	1.702	1.069	0.84	1.07	1.51	1.77	5.87
Placebo	Screening A	12	1.506	0.515	0.90	1.01	1.47	1.88	2.40
	Screening B	12	1.546	0.629	0.95	1.11	1.32	1.85	3.00
	Day 1	12	1.533	0.575	0.92	1.12	1.38	1.77	2.58
	Week 2	12	1.456	0.629	0.68	1.05	1.27	1.78	3.02
	Week 4	10	1.549	0.462	1.02	1.21	1.51	1.81	2.56
	Week 6	10	1.508	0.686	0.93	1.13	1.28	1.66	3.31
	Week 8	11	1.583	0.751	0.92	1.11	1.49	1.77	3.65
	Week 10	11	1.569	0.568	0.84	1.24	1.50	2.04	2.78
	Week 12	10	1.447	0.505	0.95	1.01	1.33	1.71	2.60
	Week 14	4	1.453	0.329	1.16	1.17	1.45	1.74	1.75
	Week 16	4	1.483	0.290	1.22	1.23	1.48	1.73	1.75
	Week 18	4	1.349	0.409	0.96	1.00	1.34	1.70	1.77
	Week 20	3	1.413	0.461	0.98	0.98	1.36	1.90	1.90
	Week 22	4	1.572	0.460	0.93	1.24	1.70	1.90	1.95
	Week 24	4	1.494	0.632	0.87	0.97	1.45	2.02	2.21
	LOV	12	1.468	0.524	0.87	1.02	1.31	1.82	2.45

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.1.4.4.1）

表 2.7.4.9-134 Change from Baseline in Laboratory Tests – R788-1301 study

Period I
Parameter: Leukocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Week 2	22	-0.943	1.609	-4.90	-1.70	-0.60	0.00	2.07
	Week 4	22	-1.744	1.804	-6.10	-2.40	-1.61	-0.70	2.00
	Week 6	22	-2.055	1.853	-5.80	-3.20	-1.57	-0.70	1.20
	Week 8	21	-1.878	1.783	-6.30	-2.50	-1.34	-0.90	0.70
	Week 10	20	-2.046	1.743	-8.00	-2.60	-1.64	-1.02	-0.40
	Week 12	20	-1.687	2.016	-7.60	-2.75	-1.14	-0.64	1.10
	Week 14	16	-2.168	1.452	-4.90	-3.60	-1.56	-1.05	-0.80
	Week 16	10	-1.277	2.885	-5.90	-2.30	-1.33	-0.73	5.47
	Week 18	10	-2.157	1.594	-6.30	-2.02	-1.82	-1.10	-0.80
	Week 20	10	-1.851	1.918	-6.60	-2.10	-1.28	-0.70	-0.01
	Week 22	10	-1.825	1.973	-7.00	-2.02	-1.23	-1.02	0.30
	Week 24	10	-1.906	1.615	-5.50	-2.90	-1.32	-0.70	-0.40
	LOV	22	-1.419	2.526	-5.50	-3.00	-1.31	-0.70	7.35
Placebo	Week 2	12	-1.078	2.679	-8.79	-1.24	-0.65	-0.07	2.10
	Week 4	10	-0.122	1.034	-2.09	-0.60	0.00	0.34	1.70
	Week 6	10	-0.174	1.772	-2.00	-1.31	-0.92	0.60	3.00
	Week 8	11	-0.558	1.278	-2.80	-1.19	-0.49	0.04	1.90
	Week 10	11	-0.664	1.015	-2.29	-1.50	-0.63	0.20	0.80
	Week 12	10	-0.401	1.360	-2.30	-1.19	-0.14	0.17	2.30
	Week 14	4	-1.130	0.844	-1.80	-1.70	-1.40	-0.56	0.08
	Week 16	4	-0.913	0.796	-1.90	-1.55	-0.80	-0.28	-0.15
	Week 18	4	-1.275	0.780	-2.00	-1.90	-1.40	-0.65	-0.30
	Week 20	3	-1.007	0.671	-1.70	-1.70	-0.96	-0.36	-0.36
	Week 22	4	-0.555	0.774	-1.17	-1.09	-0.80	-0.03	0.55
	Week 24	4	-1.210	0.900	-2.15	-1.83	-1.35	-0.60	0.00
	LOV	12	-0.786	3.262	-9.36	-1.79	-0.16	0.25	4.32

Parameter: Lymphocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Week 2	22	0.450	0.896	-0.64	0.02	0.23	0.54	3.35
	Week 4	22	0.067	0.703	-1.13	-0.30	0.06	0.19	2.46
	Week 6	22	-0.207	0.584	-1.47	-0.51	-0.10	0.21	0.68
	Week 8	21	0.111	0.714	-1.46	-0.13	0.04	0.34	1.59
	Week 10	20	-0.058	0.494	-1.15	-0.33	-0.07	0.29	0.81
	Week 12	20	0.038	0.305	-0.73	-0.12	0.14	0.19	0.54
	Week 14	16	0.063	0.369	-0.77	-0.13	0.00	0.30	0.68
	Week 16	10	0.016	0.461	-0.76	-0.33	0.01	0.40	0.63
	Week 18	10	0.092	0.393	-0.39	-0.20	0.04	0.20	0.78
	Week 20	10	0.144	0.338	-0.29	-0.20	0.08	0.39	0.64
	Week 22	10	0.077	0.276	-0.41	-0.03	0.07	0.28	0.46
	Week 24	10	-0.019	0.345	-0.67	-0.30	0.06	0.30	0.40
	LOV	22	-0.048	0.468	-1.47	-0.30	0.12	0.30	0.54

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
Placebo	Week 2	12	-0.077	0.522	-1.35	-0.25	0.09	0.21	0.52
	Week 4	10	0.063	0.415	-0.90	-0.06	0.10	0.36	0.57
	Week 6	10	0.022	0.451	-0.92	-0.13	0.14	0.24	0.73
	Week 8	11	0.095	0.583	-1.24	-0.26	0.21	0.33	1.07
	Week 10	11	0.081	0.356	-0.54	-0.12	0.14	0.32	0.57
	Week 12	10	-0.039	0.451	-1.04	-0.31	0.01	0.31	0.49
	Week 14	4	-0.153	0.509	-0.86	-0.52	0.00	0.22	0.24
	Week 16	4	-0.123	0.528	-0.87	-0.50	0.06	0.25	0.27
	Week 18	4	-0.257	0.419	-0.82	-0.57	-0.17	0.06	0.12
	Week 20	3	-0.224	0.563	-0.69	-0.69	-0.39	0.40	0.40
	Week 22	4	-0.033	0.649	-0.73	-0.58	0.00	0.52	0.59
	Week 24	4	-0.111	0.608	-0.75	-0.53	-0.20	0.31	0.70
	LOV	12	-0.065	0.474	-0.91	-0.31	-0.10	0.34	0.70

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.1.4.4.2）

表 2.7.4.9-135 Immunoglobulin Tests – R788-1301 study

Period I
Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	13.187	3.127	7.38	10.71	13.21	15.23	18.95
	Day 1	22	13.057	3.379	6.56	10.37	12.73	15.32	20.15
	Week 24	10	10.771	2.373	7.97	8.95	10.57	12.00	15.46
	LOV	21	11.377	2.920	6.27	8.95	11.18	13.33	16.79
Placebo	Screening A	12	12.156	4.233	7.34	9.16	11.33	13.49	23.10
	Day 1	12	11.913	3.983	7.03	9.54	11.35	13.53	22.64
	Week 24	4	12.285	1.776	10.68	10.82	12.04	13.76	14.38
	LOV	12	12.978	5.019	6.82	10.15	11.63	13.76	23.43

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.1.4.5.1）

表 2.7.4.9-136 Change from Baseline in Immunoglobulin Tests – R788-1301 study

Period I
Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Week 24	10	-1.804	0.985	-3.28	-2.70	-1.86	-0.85	-0.48
	LOV	21	-1.342	1.591	-4.14	-2.31	-1.47	-0.73	2.74
Placebo	Week 24	4	0.065	0.615	-0.59	-0.43	0.03	0.56	0.80
	LOV	12	1.064	2.421	-0.59	-0.07	0.63	0.82	8.56

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.1.4.5.2）

表 2.7.4.9-137 Laboratory Tests – R788-1301 study

Long-Term Treatment of R788
Parameter: Leukocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	6.744	2.805	3.40	4.79	6.58	7.40	13.60
	Screening B	22	6.424	2.606	3.54	4.50	5.76	7.67	14.50
	Day 1	22	6.780	3.022	3.30	4.57	5.75	8.20	14.50
	Week 2	22	5.837	2.142	2.80	4.33	5.30	6.90	10.60
	Week 4	22	5.036	2.296	2.00	2.99	4.60	6.60	10.40
	Week 6	22	4.725	1.800	2.00	3.70	4.53	5.20	9.00
	Week 8	21	4.663	1.997	1.80	3.23	4.51	5.20	9.70
	Week 10	20	4.361	2.083	1.00	3.03	4.10	4.71	10.50
	Week 12	20	4.720	2.100	2.39	3.35	4.22	5.35	11.50
	Week 14	16	3.866	1.366	2.37	2.90	3.60	4.20	7.80
	Week 16	10	4.790	2.230	2.50	3.00	4.37	5.50	9.90
	Week 18	10	3.910	1.375	2.13	2.41	3.98	5.00	6.40
	Week 20	10	4.216	1.228	2.56	3.00	4.27	4.90	6.10
	Week 22	10	4.242	1.426	2.41	3.20	3.82	5.50	7.00
	Week 24	10	4.161	1.423	2.49	3.07	4.10	4.65	7.20
	Week 28	10	4.240	1.549	2.49	3.40	3.70	5.10	6.80
	Week 32	10	3.893	1.397	2.13	2.82	3.80	4.79	6.20
	Week 36	9	4.114	0.872	3.20	3.55	3.60	5.00	5.60
	Week 40	9	4.920	2.532	3.08	3.50	3.93	5.30	11.10
	Week 44	9	4.697	1.894	2.70	3.60	4.00	5.40	9.00
	Week 48	9	4.742	2.643	2.29	2.90	4.44	5.60	10.90
	Week 52	9	4.552	2.431	2.39	2.85	3.70	5.10	10.10
	LOV	22	5.446	3.518	2.39	3.23	4.10	6.43	16.58

Parameter: Lymphocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	1.635	0.955	0.79	0.90	1.28	2.26	4.26
	Screening B	22	1.629	0.841	0.79	1.17	1.33	1.86	4.50
	Day 1	22	1.750	1.037	0.83	1.16	1.38	2.18	5.51
	Week 2	22	2.200	1.298	0.69	1.29	1.85	2.64	5.48
	Week 4	22	1.817	1.192	0.47	0.94	1.37	2.47	4.59
	Week 6	22	1.543	0.859	0.72	1.00	1.19	1.80	4.23
	Week 8	21	1.793	0.979	0.63	1.18	1.53	2.19	4.05
	Week 10	20	1.631	1.069	0.30	0.99	1.33	2.01	5.15
	Week 12	20	1.728	1.206	0.37	1.03	1.34	2.40	5.87
	Week 14	16	1.413	0.474	0.75	1.03	1.37	1.80	2.26
	Week 16	10	1.330	0.776	0.59	0.71	1.09	1.98	2.88
	Week 18	10	1.407	0.576	0.69	0.98	1.18	2.04	2.20
	Week 20	10	1.458	0.608	0.85	1.06	1.27	1.65	2.89
	Week 22	10	1.392	0.453	0.93	0.99	1.28	1.72	2.22
	Week 24	10	1.295	0.415	0.84	0.95	1.20	1.58	2.00
	Week 28	10	1.386	0.481	0.69	1.01	1.40	1.50	2.41

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	Week 32	10	1.262	0.616	0.65	0.90	1.07	1.34	2.66
	Week 36	9	1.224	0.520	0.66	0.94	1.04	1.53	2.29
	Week 40	9	1.526	0.758	0.79	0.85	1.45	1.80	2.98
	Week 44	9	1.366	0.622	0.67	0.92	1.36	1.62	2.68
	Week 48	9	1.413	0.657	0.82	0.91	1.12	1.74	2.84
	Week 52	9	1.254	0.447	0.63	0.90	1.19	1.60	1.93
	LOV	22	1.680	1.079	0.63	1.11	1.47	1.72	5.87

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.2.4.4.1）

表 2.7.4.9-138 Change from Baseline in Laboratory Tests – R788-1301 study

Long-Term Treatment of R788
Parameter: Leukocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Week 2	22	-0.943	1.609	-4.90	-1.70	-0.60	0.00	2.07
	Week 4	22	-1.744	1.804	-6.10	-2.40	-1.61	-0.70	2.00
	Week 6	22	-2.055	1.853	-5.80	-3.20	-1.57	-0.70	1.20
	Week 8	21	-1.878	1.783	-6.30	-2.50	-1.34	-0.90	0.70
	Week 10	20	-2.046	1.743	-8.00	-2.60	-1.64	-1.02	-0.40
	Week 12	20	-1.687	2.016	-7.60	-2.75	-1.14	-0.64	1.10
	Week 14	16	-2.168	1.452	-4.90	-3.60	-1.56	-1.05	-0.80
	Week 16	10	-1.277	2.885	-5.90	-2.30	-1.33	-0.73	5.47
	Week 18	10	-2.157	1.594	-6.30	-2.02	-1.82	-1.10	-0.80
	Week 20	10	-1.851	1.918	-6.60	-2.10	-1.28	-0.70	-0.01
	Week 22	10	-1.825	1.973	-7.00	-2.02	-1.23	-1.02	0.30
	Week 24	10	-1.906	1.615	-5.50	-2.90	-1.32	-0.70	-0.40
	Week 28	10	-1.827	2.008	-5.90	-2.50	-1.16	-0.80	1.03
	Week 32	10	-2.174	1.926	-6.50	-3.10	-1.46	-0.90	-0.20
	Week 36	9	-2.260	2.269	-7.10	-2.80	-1.10	-0.80	-0.44
	Week 40	9	-1.454	1.568	-5.00	-1.60	-0.96	-0.70	0.50
	Week 44	9	-1.678	1.281	-3.70	-2.80	-1.00	-0.80	-0.17
	Week 48	9	-1.632	1.804	-5.40	-2.14	-1.34	-0.50	0.60
	Week 52	9	-1.822	1.445	-4.10	-2.60	-2.04	-1.00	0.71
	LOV	22	-1.335	2.454	-4.50	-3.00	-1.27	-0.80	7.35

Parameter: Lymphocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Week 2	22	0.450	0.896	-0.64	0.02	0.23	0.54	3.35
	Week 4	22	0.067	0.703	-1.13	-0.30	0.06	0.19	2.46
	Week 6	22	-0.207	0.584	-1.47	-0.51	-0.10	0.21	0.68
	Week 8	21	0.111	0.714	-1.46	-0.13	0.04	0.34	1.59
	Week 10	20	-0.058	0.494	-1.15	-0.33	-0.07	0.29	0.81
	Week 12	20	0.038	0.305	-0.73	-0.12	0.14	0.19	0.54
	Week 14	16	0.063	0.369	-0.77	-0.13	0.00	0.30	0.68
	Week 16	10	0.016	0.461	-0.76	-0.33	0.01	0.40	0.63
	Week 18	10	0.092	0.393	-0.39	-0.20	0.04	0.20	0.78
	Week 20	10	0.144	0.338	-0.29	-0.20	0.08	0.39	0.64
	Week 22	10	0.077	0.276	-0.41	-0.03	0.07	0.28	0.46
	Week 24	10	-0.019	0.345	-0.67	-0.30	0.06	0.30	0.40
	Week 28	10	0.072	0.131	-0.17	0.04	0.09	0.13	0.32
	Week 32	10	-0.053	0.259	-0.41	-0.23	-0.11	0.08	0.41
	Week 36	9	-0.107	0.301	-0.74	-0.19	-0.02	0.02	0.35
	Week 40	9	0.195	0.478	-0.26	-0.14	0.06	0.36	1.17
	Week 44	9	0.035	0.305	-0.48	-0.19	0.10	0.16	0.44
	Week 48	9	0.082	0.307	-0.25	-0.14	-0.02	0.20	0.59
	Week 52	9	-0.077	0.258	-0.32	-0.26	-0.10	-0.03	0.50

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
	LOV	22	-0.071	0.439	-1.47	-0.26	-0.05	0.20	0.54

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.2.4.4.2）

表 2.7.4.9-139 Immunoglobulin Tests – R788-1301 study

Long-Term Treatment of R788
Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Screening A	22	13.187	3.127	7.38	10.71	13.21	15.23	18.95
	Day 1	22	13.057	3.379	6.56	10.37	12.73	15.32	20.15
	Week 24	10	10.771	2.373	7.97	8.95	10.57	12.00	15.46
	Week 52	9	10.687	2.202	7.71	9.56	10.18	11.87	15.25
	LOV	21	11.465	2.856	6.27	9.56	11.18	13.38	16.79

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.2.4.5.1）

表 2.7.4.9-140 Change from Baseline in Immunoglobulin Tests – R788-1301 study

Long-Term Treatment of R788
Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Week 24	10	-1.804	0.985	-3.28	-2.70	-1.86	-0.85	-0.48
	Week 52	9	-1.710	1.014	-3.41	-2.08	-1.69	-0.85	-0.32
	LOV	21	-1.254	1.571	-4.14	-2.08	-1.30	-0.73	2.74

LOV: Last Observed Visit
（Source: 5.3.5.1.1, Table 14.2.4.5.2）

表 2.7.4.9-141　　Laboratory Tests – R788-1301 study

Period III
Parameter: Leukocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Day 1	22	4.721	2.511	1.79	3.20	3.77	5.10	13.10
	Week 8	17	4.344	1.648	2.46	3.61	3.82	4.71	8.19
	Week 16	13	4.495	2.272	2.27	2.80	3.60	6.30	8.30
	Week 24	9	4.296	1.861	2.64	3.20	3.80	3.90	8.00
	Week 32	8	4.050	2.255	2.32	2.67	3.22	4.75	8.80
	Week 40	7	4.300	2.112	2.14	2.69	3.37	7.00	7.40
	Week 48	6	4.725	1.939	3.23	3.40	4.16	5.00	8.40
	Week 56	3	4.877	2.890	2.95	2.95	3.48	8.20	8.20
	Week 64	1	4.200	---	4.20	4.20	4.20	4.20	4.20

Parameter: Lymphocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Day 1	22	1.144	0.330	0.52	0.88	1.12	1.48	1.75
	Week 8	17	1.358	0.542	0.59	0.96	1.17	1.62	2.44
	Week 16	13	1.478	0.300	0.93	1.38	1.53	1.67	1.94
	Week 24	9	1.212	0.254	0.84	1.03	1.13	1.45	1.58
	Week 32	8	1.336	0.379	0.79	1.01	1.39	1.61	1.89
	Week 40	7	1.210	0.441	0.76	0.88	1.17	1.58	2.00
	Week 48	6	1.262	0.248	0.90	1.12	1.29	1.47	1.51
	Week 56	3	1.061	0.355	0.74	0.74	1.00	1.44	1.44
	Week 64	1	1.058	---	1.06	1.06	1.06	1.06	1.06

（Source: 5.3.5.1.1, Table 14.7.4.4.1）

表 2.7.4.9-142　　Change from Baseline in Laboratory Tests – R788-1301 study

Period III
Parameter: Leukocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Day 1	22	-1.933	1.706	-5.51	-2.80	-1.77	-0.90	2.43
	Week 8	17	-2.651	1.421	-5.13	-3.90	-2.20	-1.50	-0.87
	Week 16	13	-2.809	1.480	-5.20	-3.60	-2.63	-1.63	-0.70
	Week 24	9	-2.918	1.329	-4.93	-3.50	-3.00	-1.50	-1.39
	Week 32	8	-3.215	1.232	-5.23	-3.95	-3.40	-2.09	-1.62
	Week 40	7	-3.376	1.571	-5.70	-5.43	-2.90	-2.50	-1.53
	Week 48	6	-3.353	1.382	-4.90	-4.34	-3.50	-2.60	-1.28
	Week 56	3	-3.513	1.814	-4.62	-4.62	-4.50	-1.42	-1.42
	Week 64	1	-0.700	---	-0.70	-0.70	-0.70	-0.70	-0.70

Parameter: Lymphocytes (10^9/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Day 1	22	-0.322	0.465	-1.42	-0.42	-0.22	-0.03	0.39
	Week 8	17	-0.203	0.534	-1.59	-0.41	-0.19	0.11	0.66
	Week 16	13	-0.078	0.535	-1.21	-0.12	0.06	0.13	0.54
	Week 24	9	-0.175	0.414	-1.12	-0.22	-0.07	0.11	0.16
	Week 32	8	-0.044	0.593	-1.28	-0.30	0.14	0.32	0.60
	Week 40	7	-0.171	0.483	-1.01	-0.40	-0.18	0.02	0.60
	Week 48	6	-0.190	0.504	-1.07	-0.39	-0.09	0.21	0.29
	Week 56	3	-0.160	0.387	-0.61	-0.61	0.05	0.08	0.08
	Week 64	1	-0.290	---	-0.29	-0.29	-0.29	-0.29	-0.29

（Source: 5.3.5.1.1, Table 14.7.4.4.2）

表 2.7.4.9-143　　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（R788-1301 試験）

被験者番号	該当した異常低値	第 I 期 投 与 群	年齢（歳）	性　別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	治験薬に対する処置	その他の処置	転帰	発現日	転帰日
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 3*	Day 4*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Hypertension	MILD	N	RELATED	DOSE REDUCED	CONCOMITANT MEDICATION(Period II or Later)	RECOVERING/RESOLVING	Day 15*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MODERATE	N	RELATED	DOSE REDUCED	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 78*	Day 119*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Stomatitis	MILD	N	RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 117*	Day 141*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II or Later)	RECOVERED/RESOLVED	Day 128*	Day 365*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Oedema peripheral	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)/[elastic stocking(Period II)]	RECOVERING/RESOLVING	Day 246*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Seborrhoeic dermatitis	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERING/RESOLVING	Day 297*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Asthenopia	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	RECOVERING/RESOLVING	Day 413*	
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Diarrhoea	MILD	N	RELATED	DOSE NOT CHANGED	[Discontinue of laxative(Period I)]	RECOVERED/RESOLVED	Day 6*	Day 26*
	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Hepatic function abnormal	MILD	N	RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 29*	Day 50*
	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Pyrexia	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 29*	Day 35*
	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Malaise	MODERATE	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 82*	Day 113*
	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Decreased appetite	MODERATE	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 82*	Day 113*
	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Hepatic function abnormal	MILD	N	RELATED	DRUG WITHDRAWN		RECOVERED/RESOLVED	Day 99*	Day 141*
	Lymphocytes (10^9/L)	R788	[redacted]	M	ASIAN	Dehydration	MODERATE	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 99*	Day 113*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Menorrhagia	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 11*	Day 17*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Epistaxis	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 12*	Day 165*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Affect lability	MILD	N	NOT RELATED	DRUG WITHDRAWN		RECOVERED/RESOLVED	Day 13*	Day 194*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Eczema	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 85*	Day 124*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Weight increased	MILD	N	NOT RELATED	DOSE NOT CHANGED	[Steroid discontinuation(Period II)]	RECOVERED/RESOLVED	Day 98*	Day 187*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Vomiting	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 166*	Day 166*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Liver function test increased	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 166*	Day 180*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Lipoma	MILD	N	NOT RELATED	NOT APPLICABLE	[Loxonin tape was used after the end of the follow up peiriod.(Follow-up)]	NOT RECOVERED/NOT RESOLVED	Day 171*	
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Hypertension	MILD	N	RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II or Later)	RECOVERING/RESOLVING	Day 57*	
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Neck pain	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	NOT RECOVERED/NOT RESOLVED	Day 107*	
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Large intestine polyp	MILD	Y	NOT RELATED	DOSE NOT CHANGED	[colonoscopy,EMS(Period II)]	RECOVERED/RESOLVED	Day 246*	Day 351*
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Constipation	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	NOT RECOVERED/NOT RESOLVED	Day 295*	
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Back pain	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	RECOVERED/RESOLVED	Day 617*	Day 631*
[redacted]	Lymphocytes (10^9/L)	R788	[redacted]	F	ASIAN	Sudden hearing loss	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	NOT RECOVERED/NOT RESOLVED	Day 655*	
[redacted]	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Hypertension	MILD	N	RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II or Later)	RECOVERING/RESOLVING	Day 8*	
[redacted]	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II or Later)	RECOVERED/RESOLVED	Day 15*	Day 366*
[redacted]	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Liver function test increased	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 43*	Day 379*
	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Cystitis	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 190*	Day 198*
	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Stomatitis	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 197*	Day 379*
	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Hypoalbuminaemia	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERING/RESOLVING	Day 306*	
	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Hypoproteinaemia	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 306*	Day 379*

被験者番号	該当した異常低値	第I期投与群	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	治験薬に対する処置	その他の処置	転帰	発現日	転帰日
[redacted]	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Vaccination complication	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 356*	Day 357*
	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Viral infection	MODERATE	N	NOT RELATED	DOSE REDUCED	CONCOMITANT MEDICATION(Rest)	RECOVERED/RESOLVED	Day 366*	Day 379*
[redacted]	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	NOT RECOVERED/NOT RESOLVED	Day 420*	
[redacted]	Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Liver function test increased	MILD	N	NOT RELATED	DOSE NOT CHANGED		NOT RECOVERED/NOT RESOLVED	Day 428*	
[redacted]	Lymphocytes (10^9/L)	PLACEBO	[redacted]	M	ASIAN	Contusion	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 89*	Day 170*
	Lymphocytes (10^9/L)	PLACEBO	[redacted]	M	ASIAN	Faeces soft	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	RECOVERING/RESOLVING	Day 348*	
[redacted]	Lymphocytes (10^9/L)	PLACEBO	[redacted]	M	ASIAN	Atrial fibrillation	SEVERE	Y	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)	NOT RECOVERED/NOT RESOLVED	Day 549*	
[redacted]	Lymphocytes (10^9/L)	PLACEBO	[redacted]	M	ASIAN	Contusion	MODERATE	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period III)/[Wound treatment(attaching Micropore)(Period III)]	NOT RECOVERED/NOT RESOLVED	Day 599*	
[redacted]	Lymphocytes (10^9/L)	PLACEBO	[redacted]	M	ASIAN	Haemorrhage subcutaneous	MODERATE	N	NOT RELATED	DOSE NOT CHANGED	[fine-needle aspiration(Period III)]	NOT RECOVERED/NOT RESOLVED	Day 599*	
[redacted]	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 2*	Day 5*
	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 18*	Day 18*
	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Cervicobrachial syndrome	MILD	N	NOT RELATED	DOSE NOT CHANGED	[chiropractic(Period II or Later)]	RECOVERING/RESOLVING	Day 21*	
	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Diarrhoea	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 40*	Day 71*
	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Rash	MILD	N	NOT RELATED	NOT APPLICABLE	CONCOMITANT MEDICATION(Follow-up)	RECOVERING/RESOLVING	Day 232*	
	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Neutropenia	MILD	N	NOT RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 29*	Day 34*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Viral infection	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 109*	Day 113*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	F	ASIAN	Neutropenia	MILD	N	NOT RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 414*	Day 419*
[redacted]	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Hypertension	MODERATE	N	RELATED	DOSE REDUCED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 88*	Day 99*
	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Diarrhoea	MILD	N	NOT RELATED	DOSE NOT CHANGED	[Magnesium Oxide reduced(Period II)]	RECOVERED/RESOLVED	Day 102*	Day 103*
	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Pain in extremity	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 255*	Day 260*
	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Abdominal discomfort	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Rest)	RECOVERING/RESOLVING	Day 284*	
	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Erythema	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Rest)	RECOVERED/RESOLVED	Day 285*	Day 295*
	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Hypertension	MILD	N	NOT RELATED	DOSE REDUCED		NOT RECOVERED/NOT RESOLVED	Day 16*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Incarcerated hernia	MODERATE	N	NOT RELATED	DOSE NOT CHANGED	[Manual reduction of incarcerated inguinal hernia.(Period I)]	RECOVERED/RESOLVED	Day 44*	Day 44*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	White blood cell count decreased	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 58*	Day 84*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Lymphocyte count increased	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 58*	Day 70*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Neutrophil count decreased	MILD	N	RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 58*	Day 78*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Face oedema	MILD	N	NOT RELATED	NOT APPLICABLE		RECOVERED/RESOLVED	Day 70*	Day 84*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Allergic transfusion reaction	MODERATE	N	NOT RELATED	NOT APPLICABLE	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 71*	Day 71*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Pruritus	MILD	N	NOT RELATED	NOT APPLICABLE	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 71*	Day 78*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Auricular swelling	MILD	N	NOT RELATED	NOT APPLICABLE		RECOVERED/RESOLVED	Day 71*	Day 75*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Dry skin	MILD	N	NOT RELATED	NOT APPLICABLE	CONCOMITANT MEDICATION(Period I)	RECOVERED/RESOLVED	Day 73*	Day 79*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Neutrophil count decreased	MILD	N	RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 141*	Day 169*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Abdominal pain	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 141*	Day 142*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Pruritus	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)/[(FU)Betamethasone valerate(Period II)]	RECOVERED/RESOLVED	Day 145*	Day 194*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	Eczema	MILD	N	NOT RELATED	DOSE NOT CHANGED	[(FU)Betamethasone Valerate(Period II)]	RECOVERED/RESOLVED	Day 145*	Day 194*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	R788	[redacted]	M	ASIAN	White blood cell count decreased	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 155*	Day 169*
[redacted]	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Alanine aminotransferase increased	MILD	N	RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 197*	Day 257*

被験者番号	該当した異常低値	第I期投与群	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	治験薬に対する処置	その他の処置	転帰	発現日	転帰日
[redacted]	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Aspartate aminotransferase increased	MILD	N	RELATED	DOSE REDUCED		RECOVERED/RESOLVED	Day 197*	Day 257*
[redacted]	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Alanine aminotransferase increased	MILD	N	RELATED	DOSE NOT CHANGED		NOT RECOVERED/NOT RESOLVED	Day 313*	
[redacted]	Immunoglobulin G (g/L)	PLACEBO	[redacted]	F	ASIAN	Aspartate aminotransferase increased	MILD	N	RELATED	DOSE NOT CHANGED		NOT RECOVERED/NOT RESOLVED	Day 313*	
[redacted]	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Hypoglycaemia	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 15*	Day 15*
[redacted]	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Urinary tract infection	MILD	N	NOT RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 113*	Day 176*
[redacted]	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Oedema	MILD	N	NOT RELATED	DOSE NOT CHANGED	CONCOMITANT MEDICATION(Period II)	RECOVERED/RESOLVED	Day 126*	Day 183*
[redacted]	Immunoglobulin G (g/L)	R788	[redacted]	F	ASIAN	Hypertension	MILD	N	RELATED	DOSE NOT CHANGED		RECOVERED/RESOLVED	Day 141*	Day 176*

（Source: 1.13.3-10, 付録 C-02-①-15）

＊新薬承認情報提供時に置き換え

表 2.7.4.9-144　　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（R788-1301 試験）

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間（Y: R788 投与中）
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Montelukast sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Sitagliptin Phosphate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Olmesartan medoxomil	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Pitavastatin calcium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fluticasone Furoate;Vilanterol trifenatate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Repaglinide	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Metformin hydrochloride	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Tranilast	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Adapalene	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Ozenoxacin	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Alendronate sodium	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Glycyrrhiza spp. root;Paeonia lactiflora root	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	10	mg	QD	ORAL	SCREENING		20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Immunoglobulin human normal	PRIOR MEDICATIONS						SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間（Y: R788投与中）
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Loperamide hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Trichlormethiazide	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Sodium gualenate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Loperamide hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	7.5	mg	QD	ORAL	TREATMENT II	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Furosemide	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Hydrocortisone butyrate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT II	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Benidipine hydrochloride	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Alfacalcidol	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Atenolol	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Famotidine	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Pravastatin sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Enalapril maleate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Sennoside a+b	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING		20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Magnesium oxide	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Achyranthes bidentata root;Aconitum spp. processed root;Alisma plantago- aquatica var. orientale tuber;Cinnamomum cassia bark;Cornus officinalis fruit;Dioscorea spp. rhizome;	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Azilsartan	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間(Y: R788投与中)
[redacted]	Lymphocytes (10^9/L)	Brimonidine tartrate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Brinzolamide	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Latanoprost	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	5	mg	QD	ORAL	SCREENING			Y
[redacted]	Lymphocytes (10^9/L)	Romiplostim	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	750	ug	1 TIME PER WEEK	PARENTERAL	SCREENING		20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Azathioprine	PRIOR MEDICATIONS						SCREENING	19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	Immunoglobulin human normal	PRIOR MEDICATIONS						SCREENING	19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	Romiplostim	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Romiplostim	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Eltrombopag olamine	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Ciclosporin	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Immunoglobulin human normal	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Amoxicillin trihydrate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Paracetamol	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Sennoside a+b	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Paracetamol	CONCOMITANT MEDICATIONS	ADVERSE EVENT				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Levofloxacin hemihydrate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Paracetamol	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Calcium gluconate monohydrate;Glucose;Magnesium chloride hexahydrate;Potassium chloride;Sodium acetate;Sodium chloride;Sodium citrate dihydrate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				PARENTERAL	FOLLOW-UP	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Romiplostim	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	750	ug	QD	PARENTERAL	FOLLOW-UP	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Romiplostim	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	750	ug	1 TIME PER WEEK	PARENTERAL	FOLLOW-UP	20[redacted]		

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Drospirenone;Ethinylestradiol betadex clathrate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Rebamipide	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Ascorbic acid	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Magnesium oxide	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING		20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	5	mg	QD	ORAL	SCREENING		20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	White soft paraffin	CONCOMITANT MEDICATIONS	OTHER				TOPICAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Prednisolone valeroacetate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Bilastine	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	CALCIUM CHLORIDE DIHYDRATE;POTASSIUM CHLORIDE;SODIUM CHLORIDE;SODIUM LACTATE	CONCOMITANT MEDICATIONS	OTHER				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Eltrombopag olamine	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	12.5	mg	QD	ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	Paracetamol	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Rabeprazole sodium	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Eltrombopag olamine	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	4	TABLET	QD	ORAL	SCREENING		20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	2	mg	QD	ORAL	SCREENING		20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	19[redacted]		
[redacted]	Lymphocytes (10^9/L)	Immunoglobulin human normal	PRIOR MEDICATIONS						SCREENING	19[redacted]		

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[redacted]	Lymphocytes (10^9/L)	Over-the-counter	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	TREATMENT I	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Over-the-counter	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Diclofenac sodium	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	EARLY SHIFT TREATMENT II	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Magnesium oxide	CONCOMITANT MEDICATIONS	PRETREATMENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Sennoside a+b calcium	CONCOMITANT MEDICATIONS	PRETREATMENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Magnesium citrate	CONCOMITANT MEDICATIONS	PRETREATMENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Platelets, concentrated	ITP CONCOMITANT MEDICATIONS	RESCUE	20	IU	OTHER	PARENTERAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS/OTHER	30	mg	QD	ORAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS/OTHER	20	mg	QD	ORAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS/OTHER	10	mg	QD	ORAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	2	mg	QD	ORAL	TREATMENT III	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	Platelets, concentrated	ITP CONCOMITANT MEDICATIONS	RESCUE	20	IU	OTHER	PARENTERAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	Levothyroxine sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Leukocytes (10^9/L)	Raloxifene hydrochloride	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING		20[redacted]	
[redacted]	Leukocytes (10^9/L)	Eldecalcitol	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Leukocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	2.5	mg	QD	ORAL	SCREENING		20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Eltrombopag olamine	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	

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[redacted]	Leukocytes (10^9/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		
[redacted]	Leukocytes (10^9/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Clostridium butyricum	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Loperamide hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Levofloxacin hemihydrate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Polaprezinc	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Polaprezinc	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Polaprezinc	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Triamcinolone acetonide	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Influenza vaccine	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Miconazole	CONCOMITANT MEDICATIONS	PROPHYLAXIS				TOPICAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Clostridium butyricum	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Paracetamol	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Paracetamol	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	REST	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	Immunoglobulin human normal	ITP CONCOMITANT MEDICATIONS	RESCUE	10	g	QD	PARENTERAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	Betamethasone	ITP CONCOMITANT MEDICATIONS	OTHER	0.75	mg	QD	ORAL	TREATMENT III	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Thiamazole	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Risedronate sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Rebamipide	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Coix spp. seed	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			

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[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	5	mg	QD	ORAL	SCREENING			Y
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	COVID-19 VACCINE MRNA (MRNA 1273)	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Candesartan cilexetil	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Ketoprofen	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Lymphocytes (10^9/L)	Dexamethasone sodium phosphate	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Influenza vaccine	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Indometacin	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Ketoprofen	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Teprenone	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	EARLY SHIFT TREATMENT II	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Triamcinolone acetonide	CONCOMITANT MEDICATIONS	ADVERSE EVENT				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Lidocaine	CONCOMITANT MEDICATIONS	ADVERSE EVENT				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Epinephrine bitartrate;Lidocaine hydrochloride	CONCOMITANT MEDICATIONS	PRETREATMENT				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Pneumococcal vaccine	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	Hyaluronate sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]		

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[redacted]	Lymphocytes (10^9/L)	Indometacin	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	EARLY SHIFT TREATMENT II	20[redacted]		
[redacted]	Lymphocytes (10^9/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	EARLY SHIFT TREATMENT II	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Angelica archangelica root;Astragalus spp. root;Atractylodes lancea rhizome;Bupleurum falcatum root;Dimocarpus longan aril;Gardenia jasminoides fruit;Glycyrrhiza spp. root;Panax ginseng root;	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING		20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Cinnamomum cassia bark;Paeonia lactiflora root;Paeonia x suffruticosa root bark;Poria cocos sclerotium;Prunus spp. seed	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING		20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Zolpidem tartrate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Rituximab	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Rituximab	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Romiplostim	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Angelica acutiloba root;Astragalus spp. root;Atractylodes spp. rhizome;Bupleurum falcatum root;Cimicifuga spp. rhizome;Citrus reticulata peel;Glycyrrhiza spp. root;Panax ginseng root;	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Alisma plantago-aquatica var. orientale tuber;Angelica acutiloba root;Atractylodes spp. rhizome;Cnidium officinale rhizome;Paeonia lactiflora root;Poria cocos sclerotium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Paracetamol	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		

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[redacted]	Immunoglobulin G (g/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Cinnamomum cassia bark;Paeonia lactiflora root;Paeonia x suffruticosa root bark;Poria cocos sclerotium;Prunus spp. seed	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Epinastine hydrochloride	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Fluorometholone	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Fluticasone Furoate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	White soft paraffin	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	FOLLOW-UP	20[redacted]		
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Carbazochrome sodium sulfonate	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Risedronate sodium	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Levothyroxine sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Saccharated iron oxide	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				PARENTERAL	SCREENING			
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	10	mg	QD	ORAL	SCREENING			Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING		20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Eltrombopag olamine	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Romiplostim	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Eltrombopag olamine	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Barium sulfate	CONCOMITANT MEDICATIONS	PRETREATMENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Sennoside a+b calcium	CONCOMITANT MEDICATIONS	OTHER				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Calcium chloride dihydrate;Potassium chloride;Sodium chloride;Sodium lactate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Magnesium oxide	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Rebamipide	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間（Y: R788投与中）
[redacted]	Immunoglobulin G (g/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Cepharanthine	CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Eltrombopag olamine	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	37.5	mg	QD	ORAL	SCREENING		20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Dexamethasone sodium phosphate	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Dexamethasone sodium phosphate	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Azilsartan	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Trichlormethiazide	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Carbazochrome sodium sulfonate	CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS				ORAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Nicardipine hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Difluprednate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Influenza vaccine	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Caffeine;Chlorphenamine maleate;Paracetamol;Salicylamide	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Paracetamol	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Difluprednate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	REST	20[redacted]		
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Donepezil hydrochloride	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Eltrombopag olamine	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	12	mg	QD	ORAL	SCREENING		20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Amlodipine besilate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Olopatadine hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Platelets, concentrated	ITP CONCOMITANT MEDICATIONS	RESCUE	10	IU	QD	PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Hydrocortisone sodium succinate	ITP CONCOMITANT MEDICATIONS	OTHER	100	mg	QD	PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Rupatadine fumarate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Mequitazine	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Hydrocortisone butyrate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Betamethasone valerate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Over-the-counter	CONCOMITANT MEDICATIONS	ADVERSE EVENT				TOPICAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Olopatadine hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Rupatadine fumarate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Olopatadine hydrochloride	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Sulfamethoxazole;Trimethoprim	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	2	mg	QD	ORAL	SCREENING		20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Immunoglobulin human normal	PRIOR						SCREENING	20[redacted]	20[redacted]	

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間（Y: R788投与中）
			MEDICATIONS									
[redacted]	Immunoglobulin G (g/L)	Immunoglobulin human normal	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Prednisolone	PRIOR MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Ferrous sodium citrate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Ferrous sodium citrate	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	TREATMENT II	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	1	mg	QD	ORAL	TREATMENT II	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	Esomeprazole magnesium	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Sulfamethoxazole;Trimethoprim	CONCOMITANT MEDICATIONS	PROPHYLAXIS				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Pregabalin	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Mecobalamin	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Eldecalcitol	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Denosumab	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				PARENTERAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Loxoprofen sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Glycyrrhiza spp. root;Rheum spp. rhizome	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				ORAL	SCREENING			
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	PRIMARY DIAGNOSIS	6	mg	QD	ORAL	SCREENING			Y
[redacted]	Immunoglobulin G (g/L)	Sitagliptin phosphate monohydrate	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Mitiglinide calcium	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Dexamethasone sodium phosphate	ITP CONCOMITANT MEDICATIONS	RESCUE	6.6	mg	PRN	PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	TREATMENT I	20[redacted]	20[redacted]	Y

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間（Y: R788投与中）
[redacted]	Immunoglobulin G (g/L)	Pirenoxine	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Hyaluronate sodium	CONCOMITANT MEDICATIONS	COMPLICATION DISEASE				TOPICAL	TREATMENT I	20[redacted]		
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	TREATMENT I	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	TREATMENT I	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	TOZINAMERAN	CONCOMITANT MEDICATIONS	PROPHYLAXIS				PARENTERAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	Furosemide	CONCOMITANT MEDICATIONS	ADVERSE EVENT				ORAL	EARLY SHIFT TREATMENT II	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	Prednisolone	ITP CONCOMITANT MEDICATIONS	RESCUE	20	mg	QD	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	

（Source: 1.13.3-10, 付録 C-02-①-16）

表 2.7.4.9-145　　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（R788-1301 試験）

被験者番号	該当した異常低値	区分	病歴名（PT）
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Diabetes mellitus
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Hypertension
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Hyperlipidaemia
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Asthma
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Lupus miliaris disseminatus faciei
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Muscle spasms
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AUTOIMMUNE DISEASE	Optic neuropathy
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Hypertension
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Hyperlipidaemia
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Intervertebral disc protrusion
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Lumbar spinal stenosis
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Glaucoma
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Tinea pedis
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Constipation
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Osteoporosis
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Normal pressure hydrocephalus
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Chronic kidney disease
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Gastritis
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Periodontitis
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Seasonal allergy
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Constipation
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Headache
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Breast mass
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Endometriosis

被験者番号	該当した異常低値	区分	病歴名（PT）
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	COMPLICATION DISEASE	Anal polyp
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Headache
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Musculoskeletal stiffness
	Leukocytes (10^9/L)	COMPLICATION DISEASE	Goitre
	Leukocytes (10^9/L)	COMPLICATION DISEASE	Liver disorder
	Leukocytes (10^9/L)	COMPLICATION DISEASE	Constipation
	Leukocytes (10^9/L)	COMPLICATION DISEASE	Diverticulitis
	Leukocytes (10^9/L)	COMPLICATION DISEASE	Osteoporosis
	Leukocytes (10^9/L)	COMPLICATION DISEASE	Diabetes mellitus
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Basedow's disease
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Osteoporosis
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Gastric polyps
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Large intestine polyp
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Skin papilloma
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Iron deficiency anaemia
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Hypertension
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Hepatic steatosis
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Musculoskeletal pain
	Lymphocytes (10^9/L)	COMPLICATION DISEASE	Osteoarthritis
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Menopausal symptoms
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Cervicobrachial syndrome
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Seasonal allergy
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	COMPLICATION DISEASE	Iron deficiency anaemia
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	COMPLICATION DISEASE	Constipation
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	COMPLICATION DISEASE	Hypothyroidism
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Dyslipidaemia
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Constipation
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Chronic kidney disease
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Arthralgia
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Iron deficiency anaemia
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Gamma-glutamyltransferase increased
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Back pain
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Headache

被験者番号	該当した異常低値	区分	病歴名（PT）
[redacted]	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Stomatitis
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Lumbar spinal stenosis
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Spinal compression fracture
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Osteoporosis
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Cataract
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Dry eye
	Immunoglobulin G (g/L)	COMPLICATION DISEASE	Constipation

（Source: 1.13.3-10, 付録 C-02-①-17）

表 2.7.4.9-146 Laboratory Tests: Selected Hematology Parameters (Placebo-Controlled Safety Population: Placebo-Controlled Period) – C788-047 and C788-048 study

Lab Test: Leukocytes (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	8.600		8.922		
	Median	7.850		8.000		
	Q1, Q3	5.800, 10.425		6.835, 10.650		
	SD	3.683		3.516		
	Min, Max	3.40, 19.80		2.60, 21.10		
Week 2	n	99	98	44	44	
	Mean	7.702	-0.886	9.291	0.296	-1.182
	Median	6.700	-0.805	8.900	0.250	
	Q1, Q3	5.200, 10.000	-1.960, 0.500	6.350, 10.250	-0.300, 1.000	
	SD	3.397	2.546	4.141	1.622	
	Min, Max	1.60, 16.40	-7.70, 10.10	3.50, 25.80	-4.86, 4.70	
Week 4	n	98	96	46	46	
	Mean	6.235	-2.214	9.088	0.191	-2.405
	Median	5.600	-2.000	7.800	-0.100	
	Q1, Q3	4.400, 8.160	-3.100, -0.600	6.480, 12.020	-0.890, 1.000	
	SD	2.446	2.391	3.997	2.579	
	Min, Max	2.20, 14.90	-11.59, 1.90	3.11, 18.50	-9.27, 8.50	
Week 8	n	94	92	42	42	
	Mean	6.117	-2.477	9.204	0.397	-2.874
	Median	5.400	-2.235	7.850	0.150	
	Q1, Q3	4.200, 7.700	-3.470, -0.930	6.800, 11.300	-0.800, 1.400	
	SD	2.445	2.446	3.773	2.171	
	Min, Max	2.40, 13.95	-9.40, 3.70	2.12, 18.50	-4.50, 5.50	
Week 12	n	88	88	41	41	
	Mean	6.192	-2.347	8.602	-0.206	-2.141
	Median	5.600	-1.750	7.900	0.000	
	Q1, Q3	4.350, 7.750	-3.200, -0.755	6.100, 10.400	-1.330, 1.100	
	SD	2.404	2.388	3.360	2.418	
	Min, Max	1.80, 14.50	-9.90, 1.80	3.00, 15.50	-7.19, 6.40	
Week 16	n	35	35	9	9	
	Mean	6.233	-2.644	7.898	0.169	-2.813
	Median	5.100	-2.290	5.700	-0.700	
	Q1, Q3	4.200, 8.100	-3.400, -0.900	4.080, 9.500	-2.400, 1.500	
	SD	3.018	2.992	5.490	5.815	
	Min, Max	2.30, 15.43	-12.85, 2.80	3.60, 20.40	-9.48, 11.90	
Week 20	n	26	26	5	5	
	Mean	6.628	-2.693	7.940	1.420	-4.113
	Median	5.450	-1.650	8.100	0.700	
	Q1, Q3	4.500, 8.110	-4.400, -0.400	6.300, 8.400	0.200, 1.500	
	SD	3.350	3.200	2.943	2.235	
	Min, Max	3.04, 16.89	-9.00, 2.77	4.50, 12.40	-0.50, 5.20	
Week 24	n	25	25	2	2	
	Mean	6.038	-2.768	8.400	1.400	-4.168
	Median	5.800	-1.700	8.400	1.400	
	Q1, Q3	4.400, 7.200	-4.370, -0.900	5.200, 11.600	-1.600, 4.400	
	SD	2.130	3.149	4.525	4.243	
	Min, Max	3.10, 11.40	-8.77, 2.00	5.20, 11.60	-1.60, 4.40	
Week 26	n	9	9	0	0	
	Mean	6.474	-1.292			
	Median	6.270	-0.900			
	Q1, Q3	5.200, 7.800	-1.200, -0.300			
	SD	1.687	2.250			
	Min, Max	3.90, 9.00	-7.00, 0.87			

Lab Test: Lymphocytes (10^9/L)

Time Point	Statistic	Fostamatinib (N=102)		Placebo (N=48)		Difference in Mean Change from Baseline (Fostamatinib − Placebo)
		Value	Change from Baseline	Value	Change from Baseline	
Baseline	n	100		48		
	Mean	1.873		1.980		
	Median	1.700		1.765		
	Q1, Q3	1.220, 2.355		1.295, 2.510		
	SD	0.928		1.055		
	Min, Max	0.29, 4.93		0.46, 5.30		
Week 2	n	98	97	43	43	
	Mean	2.145	0.282	2.162	0.221	0.061
	Median	1.880	0.280	1.930	0.140	
	Q1, Q3	1.550, 2.720	-0.130, 0.670	1.520, 2.540	-0.300, 0.540	
	SD	1.041	0.669	1.101	0.669	
	Min, Max	0.30, 5.60	-1.40, 2.77	0.45, 5.70	-0.79, 2.60	
Week 4	n	96	94	46	46	
	Mean	1.913	0.099	2.117	0.136	-0.038
	Median	1.645	0.145	1.820	0.055	
	Q1, Q3	1.245, 2.495	-0.220, 0.480	1.400, 2.600	-0.150, 0.500	
	SD	0.911	0.698	1.118	0.575	
	Min, Max	0.20, 4.76	-2.81, 2.73	0.44, 5.20	-1.53, 1.76	
Week 8	n	94	92	42	42	
	Mean	1.860	0.069	2.121	0.096	-0.027
	Median	1.665	0.045	1.915	0.115	
	Q1, Q3	1.130, 2.320	-0.300, 0.460	1.200, 2.760	-0.300, 0.500	
	SD	0.952	0.731	1.261	0.855	
	Min, Max	0.50, 4.49	-2.78, 2.59	0.47, 5.92	-2.41, 2.82	
Week 12	n	87	87	40	40	
	Mean	1.887	0.076	2.106	0.057	0.019
	Median	1.700	0.080	1.870	-0.040	
	Q1, Q3	1.230, 2.410	-0.330, 0.430	1.420, 2.800	-0.340, 0.350	
	SD	0.961	0.779	1.075	0.736	
	Min, Max	0.25, 5.10	-1.85, 3.20	0.54, 4.67	-1.47, 2.30	
Week 16	n	35	35	9	9	
	Mean	1.835	0.089	1.742	0.263	-0.174
	Median	1.400	-0.030	1.200	0.300	
	Q1, Q3	1.290, 2.300	-0.320, 0.460	1.120, 1.940	-0.040, 0.500	
	SD	0.952	0.814	0.983	0.553	
	Min, Max	0.52, 5.18	-1.37, 3.28	0.71, 3.80	-0.60, 1.22	
Week 20	n	26	26	5	5	
	Mean	1.864	0.118	1.412	-0.056	0.174
	Median	1.495	0.025	1.500	-0.020	
	Q1, Q3	1.290, 1.880	-0.230, 0.410	1.090, 1.680	-0.300, 0.110	
	SD	0.957	0.670	0.369	0.329	
	Min, Max	0.63, 4.11	-1.07, 1.87	0.97, 1.82	-0.45, 0.38	
Week 24	n	25	25	2	2	
	Mean	1.777	0.040	1.335	-0.160	0.200
	Median	1.410	0.000	1.335	-0.160	
	Q1, Q3	1.200, 2.480	-0.490, 0.170	1.140, 1.530	-0.280, -0.040	
	SD	0.878	0.827	0.276	0.170	
	Min, Max	0.65, 4.10	-1.22, 2.20	1.14, 1.53	-0.28, -0.04	
Week 26	n	9	9	0	0	
	Mean	1.310	-0.074			
	Median	1.040	-0.040			
	Q1, Q3	1.000, 1.450	-0.180, 0.100			
	SD	0.706	0.327			
	Min, Max	0.30, 2.62	-0.75, 0.30			

Note: The baseline value is the last measurement for the given lab test prior to the first randomized dose. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.1.1)

表 2.7.4.9-147 Immunoglobulin Tests – C788-047 and C788-048 study

Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Baseline	100	11.92	6.35	2.7	8.8	10.6	12.8	49.1
	Week 24	24	10.01	4.39	3.0	8.1	9.5	10.6	27.5
Placebo	Baseline	48	11.15	4.17	4.4	8.3	10.3	12.5	24.2
	Week 24	3	11.13	2.83	8.5	8.5	10.9	14.1	14.1

（Source: 1.13.3-10, 付録 C-02-①-6）

表 2.7.4.9-148 Change from Baseline in Immunoglobulin Tests – C788-047 and C788-048 study

Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Baseline	0	---	---	---	---	---	---	---
	Week 24	24	-1.77	3.72	-13.5	-2.7	-1.2	0.3	6.4
Placebo	Baseline	0	---	---	---	---	---	---	---
	Week 24	3	-0.47	0.92	-1.3	-1.3	-0.6	0.5	0.5

（Source: 1.13.3-10, 付録 C-02-①-6）

表 2.7.4.9-149 Laboratory Tests: Selected Hematology Parameters (Fostamatinib Treated Population: Fostamatinib Exposure Period) – C788-047, C788-048 and C788-049 study

Lab Test: Leukocytes (10^9/L)

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
Baseline	n	144	
	Mean	8.653	
	Median	7.900	
	Q1, Q3	5.890, 10.700	
	SD	3.697	
	Min, Max	3.40, 20.40	
Week 4	n	100	98
	Mean	6.309	-2.143
	Median	5.700	-1.950
	Q1, Q3	4.400, 8.230	-3.100, -0.500
	SD	2.515	2.408
	Min, Max	2.20, 14.90	-11.59, 1.90
Week 8	n	136	134
	Mean	6.175	-2.471
	Median	5.745	-2.280
	Q1, Q3	4.300, 7.750	-3.500, -0.900
	SD	2.406	2.637
	Min, Max	2.40, 13.95	-11.90, 5.36
Week 12	n	127	125
	Mean	6.435	-2.219
	Median	5.900	-1.800
	Q1, Q3	4.500, 8.000	-3.200, -0.600
	SD	2.488	2.463
	Min, Max	2.60, 14.50	-11.80, 5.80
Week 16	n	77	77
	Mean	6.327	-2.517
	Median	5.300	-2.300
	Q1, Q3	4.400, 8.100	-3.400, -0.870
	SD	2.681	2.920
	Min, Max	1.80, 15.43	-12.85, 2.90
Week 20	n	93	93
	Mean	6.875	-2.261
	Median	6.000	-2.000
	Q1, Q3	4.600, 8.830	-3.300, -0.500
	SD	2.928	2.851
	Min, Max	3.04, 17.10	-10.20, 5.84
Week 24	n	91	91
	Mean	6.715	-1.976
	Median	6.200	-1.600
	Q1, Q3	4.830, 7.900	-3.300, -0.300
	SD	2.414	2.567
	Min, Max	2.40, 13.00	-9.50, 4.60
Week 28	n	70	70
	Mean	73.796	64.750
	Median	7.050	-1.350
	Q1, Q3	5.300, 9.000	-2.900, -0.100
	SD	556.108	556.635
	Min, Max	3.40, 4660.00	-13.40, 4655.30
Week 32	n	63	63
	Mean	6.891	-2.005
	Median	6.600	-1.500
	Q1, Q3	4.800, 7.960	-2.940, -0.500
	SD	2.930	3.191
	Min, Max	2.58, 18.30	-11.70, 4.90
Week 36	n	56	56
	Mean	6.586	-2.361
	Median	5.900	-1.900

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Q1, Q3	4.600, 7.900	-3.830, -0.510
	SD	3.031	2.773
	Min, Max	2.66, 17.70	-11.60, 3.10
Week 40	n	55	55
	Mean	6.509	-2.503
	Median	5.800	-1.700
	Q1, Q3	4.900, 7.800	-4.000, -0.700
	SD	2.660	3.011
	Min, Max	2.40, 17.50	-10.40, 4.10
Week 44	n	52	52
	Mean	6.240	-2.411
	Median	5.800	-1.850
	Q1, Q3	4.600, 7.400	-3.775, -0.550
	SD	2.301	2.856
	Min, Max	3.09, 14.80	-11.18, 1.50
Week 48	n	53	53
	Mean	6.193	-2.690
	Median	5.700	-2.200
	Q1, Q3	4.450, 7.700	-3.700, -0.600
	SD	2.209	2.823
	Min, Max	3.00, 12.60	-12.07, 3.20
Week 52	n	55	55
	Mean	6.387	-2.359
	Median	5.940	-1.900
	Q1, Q3	4.300, 7.830	-3.500, -0.400
	SD	2.547	2.653
	Min, Max	2.14, 13.20	-10.50, 2.20
Week 56	n	48	48
	Mean	6.576	-2.459
	Median	6.150	-2.205
	Q1, Q3	4.700, 7.700	-3.500, -0.650
	SD	2.629	2.546
	Min, Max	3.10, 14.80	-10.00, 1.70
Week 60	n	54	54
	Mean	6.229	-2.540
	Median	5.600	-2.000
	Q1, Q3	4.600, 7.500	-3.900, -0.710
	SD	2.327	2.825
	Min, Max	2.72, 14.20	-12.03, 1.40
Week 64	n	53	53
	Mean	6.436	-2.498
	Median	6.200	-2.000
	Q1, Q3	4.800, 7.500	-3.300, -0.700
	SD	2.379	2.773
	Min, Max	2.70, 14.50	-11.00, 2.20
Week 68	n	49	49
	Mean	6.912	-1.993
	Median	6.300	-1.700
	Q1, Q3	5.600, 8.500	-3.400, 0.000
	SD	2.665	2.804
	Min, Max	2.30, 14.70	-9.71, 4.00
Week 72	n	49	49
	Mean	6.173	-2.377
	Median	5.700	-1.500
	Q1, Q3	4.900, 7.000	-3.500, -0.400
	SD	2.003	2.848
	Min, Max	3.20, 12.90	-12.18, 1.30
Week 76	n	45	45
	Mean	6.331	-2.272
	Median	6.000	-1.500
	Q1, Q3	4.700, 7.100	-3.600, -0.700
	SD	2.328	2.410

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Min, Max	3.70, 14.70	-8.11, 3.40
Week 80	n	37	37
	Mean	6.182	-2.556
	Median	5.500	-2.000
	Q1, Q3	4.500, 6.800	-3.300, -0.900
	SD	2.470	2.540
	Min, Max	2.59, 14.70	-12.30, 0.80
Week 84	n	44	44
	Mean	6.710	-2.285
	Median	6.350	-1.600
	Q1, Q3	4.850, 7.800	-3.100, -0.400
	SD	2.709	2.736
	Min, Max	2.47, 16.90	-11.10, 1.70
Week 88	n	36	36
	Mean	6.475	-2.236
	Median	6.000	-1.850
	Q1, Q3	5.050, 7.625	-3.800, -0.550
	SD	2.303	2.971
	Min, Max	2.68, 15.80	-12.40, 3.90
Week 92	n	32	32
	Mean	6.340	-2.332
	Median	5.900	-1.380
	Q1, Q3	4.750, 6.950	-3.350, -0.500
	SD	2.722	3.009
	Min, Max	3.10, 17.30	-11.40, 1.70
Week 96	n	35	35
	Mean	6.062	-2.602
	Median	5.600	-1.600
	Q1, Q3	4.700, 7.200	-4.500, -0.800
	SD	2.236	2.572
	Min, Max	2.50, 14.10	-8.09, 2.00
Week 100	n	28	28
	Mean	6.631	-1.720
	Median	5.850	-1.750
	Q1, Q3	4.700, 7.740	-2.850, -0.200
	SD	3.420	2.654
	Min, Max	1.66, 17.20	-7.29, 4.80
Week 104	n	23	23
	Mean	6.580	-1.797
	Median	6.200	-1.100
	Q1, Q3	4.200, 7.500	-3.230, 0.400
	SD	3.248	2.850
	Min, Max	2.15, 17.50	-8.50, 2.30
Week 108	n	22	22
	Mean	5.818	-2.505
	Median	5.100	-1.400
	Q1, Q3	4.300, 6.800	-4.000, -0.700
	SD	2.625	2.525
	Min, Max	3.20, 15.80	-8.73, 0.50
Week 112	n	25	25
	Mean	5.722	-3.087
	Median	5.600	-2.600
	Q1, Q3	3.800, 7.340	-6.200, -0.100
	SD	2.177	3.214
	Min, Max	2.43, 9.90	-9.00, 1.20
Week 116	n	19	19
	Mean	5.627	-2.050
	Median	5.100	-1.600
	Q1, Q3	4.200, 6.500	-2.300, -0.600
	SD	1.817	1.977
	Min, Max	1.76, 9.04	-7.06, 0.30
Week 120	n	38	38

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Mean	6.377	-2.784
	Median	6.200	-2.100
	Q1, Q3	4.200, 7.500	-4.500, -0.900
	SD	3.211	2.937
	Min, Max	1.56, 20.60	-10.80, 4.10
Week 128	n	40	40
	Mean	6.323	-2.351
	Median	5.900	-1.750
	Q1, Q3	5.000, 6.810	-3.715, -0.550
	SD	2.300	2.917
	Min, Max	3.70, 17.60	-12.00, 4.10
Week 136	n	42	42
	Mean	6.099	-2.342
	Median	5.900	-1.900
	Q1, Q3	4.900, 6.800	-3.900, 0.300
	SD	2.267	3.156
	Min, Max	3.00, 15.90	-12.30, 3.00
Week 144	n	39	39
	Mean	5.921	-2.497
	Median	5.200	-1.900
	Q1, Q3	4.200, 7.000	-4.600, -0.400
	SD	2.718	3.322
	Min, Max	3.00, 17.40	-14.00, 4.90
Week 152	n	42	42
	Mean	6.262	-2.276
	Median	6.050	-1.700
	Q1, Q3	4.700, 7.730	-4.300, 0.000
	SD	2.201	3.298
	Min, Max	2.90, 14.70	-12.00, 3.70
Week 160	n	39	39
	Mean	5.893	-2.587
	Median	5.300	-1.600
	Q1, Q3	4.500, 7.000	-3.300, -0.700
	SD	2.227	3.217
	Min, Max	2.80, 13.60	-13.50, 2.00
Week 168	n	37	37
	Mean	6.305	-2.018
	Median	6.100	-1.200
	Q1, Q3	4.600, 8.100	-3.300, -0.300
	SD	2.412	2.880
	Min, Max	3.00, 14.50	-11.70, 3.40
Week 176	n	29	29
	Mean	6.131	-1.997
	Median	5.100	-1.300
	Q1, Q3	4.700, 6.700	-3.100, -0.600
	SD	3.911	2.595
	Min, Max	2.70, 24.30	-8.70, 4.50
Week 184	n	31	31
	Mean	5.865	-2.224
	Median	5.500	-1.600
	Q1, Q3	4.300, 6.600	-2.500, -0.300
	SD	2.157	2.827
	Min, Max	2.52, 12.10	-12.80, 0.70
Week 192	n	28	28
	Mean	6.266	-1.547
	Median	6.050	-1.300
	Q1, Q3	4.150, 7.325	-2.550, 0.500
	SD	2.621	2.388
	Min, Max	2.51, 13.60	-8.70, 1.20
Week 200	n	28	28
	Mean	6.714	-1.534
	Median	5.750	-1.200

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Q1, Q3	4.850, 7.390	-2.150, -0.200
	SD	3.122	2.684
	Min, Max	3.40, 17.60	-9.70, 5.60
Week 208	n	19	19
	Mean	6.697	-1.584
	Median	6.700	-1.000
	Q1, Q3	4.600, 7.600	-2.500, -0.370
	SD	3.002	2.365
	Min, Max	3.80, 17.00	-7.42, 3.20
Week 216	n	18	18
	Mean	5.542	-1.630
	Median	5.150	-1.300
	Q1, Q3	4.800, 6.400	-2.000, -0.600
	SD	1.278	2.360
	Min, Max	3.60, 8.00	-8.10, 1.20
Week 224	n	17	17
	Mean	6.106	-2.173
	Median	5.400	-2.100
	Q1, Q3	4.400, 7.400	-2.620, -0.500
	SD	2.783	2.315
	Min, Max	3.30, 14.60	-7.10, 0.30

Lab Test: Lymphocytes (10^9/L)

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
Baseline	n	144	
	Mean	1.940	
	Median	1.700	
	Q1, Q3	1.290, 2.445	
	SD	0.962	
	Min, Max	0.29, 4.93	
Week 4	n	98	96
	Mean	1.924	0.071
	Median	1.685	0.140
	Q1, Q3	1.250, 2.500	-0.250, 0.485
	SD	0.889	0.648
	Min, Max	0.20, 4.76	-2.81, 1.64
Week 8	n	135	133
	Mean	1.909	0.030
	Median	1.670	0.030
	Q1, Q3	1.200, 2.590	-0.300, 0.400
	SD	1.021	0.712
	Min, Max	0.20, 4.89	-2.78, 2.59
Week 12	n	126	124
	Mean	1.987	0.067
	Median	1.700	0.075
	Q1, Q3	1.300, 2.600	-0.330, 0.425
	SD	1.052	0.743
	Min, Max	0.25, 5.10	-1.85, 3.20
Week 16	n	75	75
	Mean	1.858	-0.056
	Median	1.580	-0.030
	Q1, Q3	1.280, 2.330	-0.410, 0.300
	SD	0.973	0.762
	Min, Max	0.30, 5.18	-2.34, 3.28
Week 20	n	93	93
	Mean	2.084	0.171
	Median	1.730	0.090
	Q1, Q3	1.430, 2.730	-0.350, 0.520
	SD	0.983	0.765
	Min, Max	0.33, 5.11	-1.10, 3.23

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
Week 24	n	89	89
	Mean	2.067	0.109
	Median	1.720	0.070
	Q1, Q3	1.300, 2.710	-0.380, 0.660
	SD	1.003	0.863
	Min, Max	0.43, 4.94	-3.08, 2.32
Week 28	n	70	70
	Mean	19.029	17.130
	Median	1.765	0.145
	Q1, Q3	1.300, 2.570	-0.190, 0.420
	SD	141.990	142.039
	Min, Max	0.58, 1190.00	-2.75, 1188.51
Week 32	n	62	62
	Mean	2.064	0.079
	Median	1.815	0.020
	Q1, Q3	1.430, 2.700	-0.340, 0.460
	SD	0.968	0.799
	Min, Max	0.20, 5.27	-2.04, 2.48
Week 36	n	56	56
	Mean	1.854	-0.067
	Median	1.605	-0.100
	Q1, Q3	1.190, 2.205	-0.555, 0.450
	SD	1.045	0.943
	Min, Max	0.40, 5.03	-2.10, 2.35
Week 40	n	54	54
	Mean	1.979	0.125
	Median	1.740	-0.140
	Q1, Q3	1.140, 2.640	-0.470, 0.570
	SD	1.094	0.863
	Min, Max	0.15, 4.84	-1.16, 2.05
Week 44	n	52	52
	Mean	1.943	-0.017
	Median	1.685	-0.045
	Q1, Q3	1.205, 2.570	-0.505, 0.505
	SD	1.037	0.663
	Min, Max	0.51, 4.69	-1.33, 1.38
Week 48	n	53	53
	Mean	1.974	-0.012
	Median	1.770	-0.040
	Q1, Q3	1.180, 2.600	-0.520, 0.430
	SD	1.094	0.764
	Min, Max	0.40, 5.59	-1.67, 2.34
Week 52	n	55	55
	Mean	1.932	-0.024
	Median	1.650	-0.020
	Q1, Q3	1.290, 2.310	-0.530, 0.430
	SD	1.143	0.856
	Min, Max	0.10, 5.77	-2.24, 2.85
Week 56	n	48	48
	Mean	1.819	-0.058
	Median	1.595	-0.065
	Q1, Q3	1.070, 2.600	-0.535, 0.315
	SD	1.050	0.755
	Min, Max	0.30, 5.46	-1.40, 2.61
Week 60	n	52	52
	Mean	1.933	-0.030
	Median	1.790	-0.015
	Q1, Q3	1.245, 2.555	-0.425, 0.410
	SD	0.939	0.750
	Min, Max	0.42, 4.25	-1.71, 2.35
Week 64	n	53	53
	Mean	1.922	-0.058

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	Median	1.890	0.100
	Q1, Q3	1.300, 2.530	-0.600, 0.540
	SD	0.899	0.849
	Min, Max	0.30, 5.22	-2.45, 2.37
Week 68	n	48	48
	Mean	1.909	-0.041
	Median	1.745	0.005
	Q1, Q3	1.240, 2.335	-0.300, 0.370
	SD	1.010	0.777
	Min, Max	0.25, 4.09	-1.93, 2.19
Week 72	n	48	48
	Mean	1.894	-0.006
	Median	1.785	0.040
	Q1, Q3	1.350, 2.235	-0.560, 0.535
	SD	0.775	0.773
	Min, Max	0.59, 3.87	-1.56, 1.97
Week 76	n	44	44
	Mean	1.838	-0.082
	Median	1.690	-0.045
	Q1, Q3	1.175, 2.130	-0.525, 0.240
	SD	0.902	0.702
	Min, Max	0.59, 4.80	-1.41, 1.67
Week 80	n	35	35
	Mean	1.863	-0.111
	Median	1.680	-0.040
	Q1, Q3	1.390, 2.140	-0.490, 0.340
	SD	0.801	0.727
	Min, Max	0.60, 4.01	-1.64, 2.11
Week 84	n	44	44
	Mean	1.897	-0.099
	Median	1.760	0.090
	Q1, Q3	1.340, 2.385	-0.580, 0.410
	SD	0.819	0.796
	Min, Max	0.43, 4.23	-1.63, 1.48
Week 88	n	36	36
	Mean	2.006	-0.014
	Median	1.870	0.010
	Q1, Q3	1.360, 2.505	-0.370, 0.370
	SD	0.867	0.772
	Min, Max	0.59, 4.25	-1.61, 2.05
Week 92	n	30	30
	Mean	1.893	-0.038
	Median	1.610	-0.100
	Q1, Q3	1.260, 2.280	-0.500, 0.340
	SD	0.949	0.615
	Min, Max	0.46, 4.62	-0.98, 1.77
Week 96	n	36	36
	Mean	1.844	-0.124
	Median	1.705	-0.075
	Q1, Q3	1.370, 2.420	-0.545, 0.380
	SD	0.774	0.808
	Min, Max	0.57, 3.40	-1.63, 1.67
Week 100	n	28	28
	Mean	1.869	-0.014
	Median	1.690	-0.005
	Q1, Q3	1.300, 2.525	-0.465, 0.420
	SD	0.780	0.668
	Min, Max	0.48, 3.60	-1.10, 1.70
Week 104	n	23	23
	Mean	1.749	-0.063
	Median	1.880	-0.030
	Q1, Q3	0.980, 2.290	-0.460, 0.280

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
	SD	0.765	0.700
	Min, Max	0.43, 3.23	-1.67, 1.47
Week 108	n	22	22
	Mean	1.738	-0.106
	Median	1.610	-0.085
	Q1, Q3	1.400, 1.940	-0.490, 0.240
	SD	0.754	0.658
	Min, Max	0.50, 3.52	-1.30, 1.62
Week 112	n	25	25
	Mean	1.827	-0.011
	Median	1.790	0.020
	Q1, Q3	1.130, 2.300	-0.600, 0.250
	SD	0.841	0.679
	Min, Max	0.52, 3.32	-1.30, 1.35
Week 116	n	19	19
	Mean	1.811	0.062
	Median	1.690	0.080
	Q1, Q3	1.340, 2.100	-0.500, 0.450
	SD	0.989	0.745
	Min, Max	0.41, 4.53	-1.60, 1.96
Week 120	n	38	38
	Mean	1.811	-0.151
	Median	1.815	-0.155
	Q1, Q3	1.120, 2.170	-0.590, 0.170
	SD	0.810	0.683
	Min, Max	0.44, 3.73	-1.50, 1.43
Week 128	n	40	40
	Mean	1.677	-0.237
	Median	1.655	-0.250
	Q1, Q3	1.060, 2.065	-0.620, 0.400
	SD	0.729	0.818
	Min, Max	0.43, 3.54	-2.50, 1.02
Week 136	n	42	42
	Mean	1.585	-0.290
	Median	1.580	-0.175
	Q1, Q3	1.120, 1.980	-0.750, 0.180
	SD	0.743	0.627
	Min, Max	0.40, 3.49	-1.83, 0.98
Week 144	n	39	39
	Mean	1.638	-0.210
	Median	1.610	-0.130
	Q1, Q3	1.100, 2.070	-0.620, 0.280
	SD	0.704	0.683
	Min, Max	0.62, 3.30	-1.90, 1.02
Week 152	n	42	42
	Mean	1.644	-0.235
	Median	1.615	-0.050
	Q1, Q3	1.220, 1.940	-0.700, 0.190
	SD	0.685	0.739
	Min, Max	0.55, 3.35	-2.00, 1.05
Week 160	n	39	39
	Mean	1.762	-0.112
	Median	1.530	-0.060
	Q1, Q3	1.230, 2.160	-0.500, 0.250
	SD	0.833	0.753
	Min, Max	0.40, 4.90	-1.58, 2.04
Week 168	n	37	37
	Mean	1.628	-0.252
	Median	1.620	-0.250
	Q1, Q3	1.130, 2.120	-0.670, 0.210
	SD	0.642	0.819
	Min, Max	0.47, 2.90	-2.48, 1.71

Time Point	Statistic	Fostamatinib (N=146)	
		Value	Change from Baseline
Week 176	n	29	29
	Mean	1.597	-0.211
	Median	1.550	-0.200
	Q1, Q3	1.230, 1.850	-0.390, 0.100
	SD	0.670	0.550
	Min, Max	0.44, 3.32	-1.44, 0.76
Week 184	n	30	30
	Mean	1.507	-0.153
	Median	1.360	-0.185
	Q1, Q3	1.000, 1.860	-0.590, 0.340
	SD	0.793	0.824
	Min, Max	0.55, 4.39	-1.77, 2.49
Week 192	n	28	28
	Mean	1.474	-0.143
	Median	1.345	-0.180
	Q1, Q3	0.830, 2.020	-0.625, 0.175
	SD	0.835	0.582
	Min, Max	0.30, 3.73	-1.20, 0.99
Week 200	n	28	28
	Mean	1.558	-0.237
	Median	1.665	-0.165
	Q1, Q3	1.145, 1.845	-0.695, 0.320
	SD	0.658	0.791
	Min, Max	0.30, 3.23	-2.68, 1.33
Week 208	n	19	19
	Mean	1.722	-0.019
	Median	1.650	-0.130
	Q1, Q3	1.220, 2.250	-0.700, 0.410
	SD	0.866	0.870
	Min, Max	0.44, 4.01	-1.66, 2.11
Week 216	n	19	19
	Mean	1.573	-0.104
	Median	1.570	-0.040
	Q1, Q3	0.890, 2.190	-0.500, 0.250
	SD	0.706	0.621
	Min, Max	0.50, 3.00	-1.46, 1.12
Week 224	n	17	17
	Mean	1.636	-0.153
	Median	1.740	-0.250
	Q1, Q3	1.230, 1.930	-0.530, 0.250
	SD	0.672	0.703
	Min, Max	0.38, 3.37	-1.25, 1.47

Note: The baseline value is the last measurement for the given lab test prior to the first dose of fostamatinib. If both central and local lab data are available for a subject at a given time point, the central lab data were given priority and were used in the analyses.
(Source: 5.3.5.3.2, Table 5.1.1.2)

表 2.7.4.9-150 Immunoglobulin Tests – C788-047, C788-048 and C788-049 study

Fostamatinib Exposure Period
Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Baseline	145	11.96	6.10	2.7	8.6	10.6	13.1	49.1
	Week 4	4	25.73	20.50	9.8	12.5	18.8	39.0	55.5
	Week 8	2	5.05	0.37	4.8	4.8	5.1	5.3	5.3
	Week 12	56	11.65	4.71	6.1	8.7	10.3	13.5	27.7
	Week 16	5	7.97	1.43	6.6	6.7	8.0	8.5	10.1
	Week 20	9	10.20	6.63	5.0	6.8	8.4	10.5	26.7
	Week 24	44	9.87	3.86	3.0	7.6	9.2	11.0	27.5
	Week 28	3	8.83	1.10	7.6	7.6	9.4	9.6	9.6
	Week 36	6	9.00	1.59	6.1	8.6	9.4	10.0	10.6
	Week 40	8	9.56	2.71	6.2	8.1	9.2	10.2	15.4
	Week 44	5	8.68	2.88	4.7	7.1	8.7	11.1	11.7
	Week 48	18	10.93	4.86	2.7	8.6	9.9	11.6	25.8
	Week 52	15	10.27	4.05	5.1	7.2	9.8	12.7	19.7
	Week 64	8	9.08	2.79	5.7	7.0	8.7	10.6	14.3
	Week 68	1	15.36	---	15.4	15.4	15.4	15.4	15.4
	Week 72	3	12.43	9.94	5.4	5.4	8.0	23.8	23.8
	Week 76	20	9.60	2.64	5.3	7.8	10.1	11.1	15.8
	Week 88	2	9.95	1.68	8.8	8.8	9.9	11.1	11.1
	Week 92	1	9.83	---	9.8	9.8	9.8	9.8	9.8
	Week 96	2	7.15	2.84	5.1	5.1	7.2	9.2	9.2
	Week 100	8	10.44	2.63	7.3	8.5	9.9	12.4	14.7
	Week 104	3	9.57	3.37	5.8	5.8	10.7	12.2	12.2
	Week 128	3	11.24	2.30	9.4	9.4	10.6	13.8	13.8
	Week 136	1	7.34	---	7.3	7.3	7.3	7.3	7.3
	Week 144	3	8.62	2.70	5.9	5.9	8.6	11.3	11.3
	Week 152	2	7.25	0.28	7.1	7.1	7.3	7.5	7.5
	Week 176	1	9.12	---	9.1	9.1	9.1	9.1	9.1
	Week 184	3	11.19	3.02	8.7	8.7	10.4	14.5	14.5
	Week 192	4	13.75	10.43	7.7	8.1	9.0	19.5	29.4
	Week 200	4	12.66	6.22	4.1	8.5	13.9	16.8	18.8
	Week 208	4	10.83	2.80	6.8	9.0	11.8	12.7	13.0
	Week 216	2	8.64	2.50	6.9	6.9	8.6	10.4	10.4
	Week 224	13	10.75	2.26	7.4	9.6	10.5	12.1	15.6

（Source: 1.13.3-10, 付録 C-02-①-8）

表 2.7.4.9-151 Change from Baseline in Immunoglobulin Tests – C788-047, C788-048 and C788-049 study

Fostamatinib Exposure Period
Parameter: Immunoglobulin G (g/L)

Group	Week	N	Mean	SD	Min	Q1	Median	Q3	Max
R788	Baseline	0	---	---	---	---	---	---	---
	Week 4	4	0.49	4.82	-5.4	-2.7	0.5	3.7	6.4
	Week 8	2	-1.48	1.93	-2.8	-2.8	-1.5	-0.1	-0.1
	Week 12	55	-0.66	2.49	-9.4	-1.7	-0.6	0.6	4.6
	Week 16	5	0.01	0.91	-0.8	-0.7	-0.3	0.3	1.4
	Week 20	9	-1.30	2.40	-4.4	-3.0	-1.0	0.0	3.0
	Week 24	44	-2.01	4.11	-13.5	-2.3	-0.9	-0.1	6.4
	Week 28	3	-2.26	1.52	-3.2	-3.2	-3.0	-0.5	-0.5
	Week 36	6	-1.15	1.36	-2.6	-2.3	-1.4	-0.2	1.1
	Week 40	8	-1.17	1.97	-4.0	-2.3	-1.2	-0.4	2.6
	Week 44	5	-0.45	2.22	-3.3	-1.6	-0.9	1.4	2.2
	Week 48	18	-1.00	5.71	-17.8	-1.3	-0.1	0.9	8.0
	Week 52	15	-2.79	6.18	-14.7	-1.7	-0.7	0.0	4.5
	Week 64	8	-1.16	2.20	-3.9	-2.9	-1.4	0.3	2.5
	Week 68	1	-11.94	---	-11.9	-11.9	-11.9	-11.9	-11.9
	Week 72	3	-5.47	7.38	-13.9	-13.9	-2.6	0.0	0.0
	Week 76	20	-1.25	4.60	-14.8	-1.3	0.0	0.6	6.6
	Week 88	2	0.18	4.05	-2.7	-2.7	0.2	3.0	3.0
	Week 92	1	-0.91	---	-0.9	-0.9	-0.9	-0.9	-0.9
	Week 96	2	-0.87	2.84	-2.9	-2.9	-0.9	1.1	1.1
	Week 100	8	-0.89	5.76	-13.2	-1.7	0.1	1.2	7.1
	Week 104	3	-1.44	1.91	-3.0	-3.0	-2.1	0.7	0.7
	Week 128	3	-6.28	6.79	-14.1	-14.1	-2.6	-2.2	-2.2
	Week 136	1	-0.67	---	-0.7	-0.7	-0.7	-0.7	-0.7
	Week 144	3	-0.03	1.24	-1.5	-1.5	0.6	0.8	0.8
	Week 152	2	-2.07	1.55	-3.2	-3.2	-2.1	-1.0	-1.0
	Week 176	1	-1.54	---	-1.5	-1.5	-1.5	-1.5	-1.5
	Week 184	3	1.52	1.79	-0.1	-0.1	1.2	3.4	3.4
	Week 192	4	3.46	10.09	-2.6	-2.3	-1.0	9.2	18.5
	Week 200	4	-2.21	8.64	-15.0	-7.3	1.5	2.9	3.3
	Week 208	4	-0.25	1.91	-1.7	-1.4	-0.9	0.9	2.6
	Week 216	2	0.41	1.61	-0.7	-0.7	0.4	1.6	1.6
	Week 224	13	-1.75	5.75	-15.6	-1.5	-0.3	1.3	4.7

（Source: 1.13.3-10, 付録 C-02-①-8）

表 2.7.4.9-152　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（C788-047、C788-048 及び C788-049 試験）

被験者番号	該当した異常低値	プラセボ対照期投与群	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	治験薬に対する処置	転帰	発現日	転帰日
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Liver Function Test Abnormal	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 81*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Leukopenia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 15*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pain In Extremity	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 30*	Day 31*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemorrhoids	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 31*	Day 47*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 70*	Day 100*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Upper Respiratory Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 142*	Day 146*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 210*	Day 212*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Vomiting	MILD	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 231*	Day 232*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Melaena	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 263*	Day 270*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Gastrointestinal Haemorrhage	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 263*	Day 270*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemoglobin Decreased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 267*	Day 270*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Gastric Antral Vascular Ectasia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 267*	Day 270*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Aortic Stenosis	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE	Day 268*	Day 319*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemoglobin Decreased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 295*	Day 304*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Head Injury	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 303*	Day 303*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Fall	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 303*	Day 303*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dyspnoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 303*	Day 303*

被験者番号	該当した異常低値	プラセボ対照期投与群	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	治験薬に対する処置	転帰	発現日	転帰日
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemoglobin Decreased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 304*	Day 305*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemoglobin Decreased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 323*	Day 326*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pain In Extremity	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 410*	Day 438*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Liver Function Test Abnormal	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 410*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Gastrointestinal Haemorrhage	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 490*	Day 495*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Basosquamous Carcinoma Of Skin	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 502*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 524*	Day 564*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Oedema Peripheral	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 564*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Anaemia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 564*	Day 1492*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypertension	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 625*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 698*	Day 726*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Neutropenia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 698*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Renal Failure	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 774*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Nasopharyngitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 774*	Day 803*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Aortic Stenosis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 774*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypertension	SEVERE	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 831*	Day 847*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blister	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 831*	Day 831*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Melaena	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 839*	Day 846*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Eye Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 877*	Day 887*

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 887*	Day 895*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Transaminases Increased	SEVERE	Y	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 890*	Day 901*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypertension	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 891*	Day 891*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urosepsis	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 895*	Day 901*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Fungal Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 967*	Day 1130*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Creatinine Increased	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1009*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Chronic Kidney Disease	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1009*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Urea Increased	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1009*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dizziness	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1060*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urinary Tract Infection Bacterial	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1060*	Day 1067*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Gait Disturbance	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1060*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Sepsis	SEVERE	Y	POSSIBLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 1061*	Day 1067*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypokalaemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1061*	Day 1064*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypophosphataemia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1063*	Day 1064*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Precancerous Skin Lesion		N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1072*	Day 1072*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Creatinine Increased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1072*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Creatinine Increased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1072*	Day 1191*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Lactate Dehydrogenase Increased	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1130*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Contusion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1130*	Day 1130*

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Trigger Finger	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1130*	Day 1212*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Arthritis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1152*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Contusion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1158*	Day 1212*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hyperuricaemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1191*	Day 1460*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypotension	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1198*	Day 1198*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Tendon Sheath Disorder	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1212*	Day 1230*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dacryostenosis Congenital	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1212*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypertension	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1226*	Day 1247*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Contusion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1230*	Day 1310*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Escherichia Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1244*	Day 1249*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haematoma	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1247*	Day 1310*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Skin Lesion	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1247*	Day 1331*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Basal Cell Carcinoma	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1310*	Day 1331*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Skin Ulcer	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1310*	Day 1310*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dyspnoea Exertional	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1310*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urinary Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1310*	Day 1318*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Micrographic Skin Surgery		N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1331*	Day 1331*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Eye Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1331*	Day 1425*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pollakiuria	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1362*	

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1363*	Day 1373*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Paraesthesia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1366*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Blister	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1366*	Day 1425*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Onychomycosis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1366*	Day 1446*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypoaesthesia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1366*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Blister	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1366*	Day 1425*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Neck Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1398*	Day 1425*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Peripheral Swelling	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1398*	Day 1425*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pain In Extremity	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1402*	Day 1425*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Papule	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1425*	Day 1446*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Papule	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1425*	Day 1446*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Thrombocytopenia	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1438*	Day 1446*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Joint Injury	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1448*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Aplastic Anaemia	SEVERE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1485*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Squamous Cell Carcinoma Of Skin	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1488*	Day 1488*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Fall	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1489*	Day 1489*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Cellulitis	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1489*	Day 1495*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Escherichia Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1489*	Day 1492*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Acute Kidney Injury	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1489*	

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Troponin Increased	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1490*	Day 1490*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Urosepsis	SEVERE	Y	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 1490*	Day 1497*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Ecchymosis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1491*	Day 1492*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Graft Complication	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1491*	Day 1491*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypokalaemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1491*	Day 1491*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Cough	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1492*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Nasal Congestion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1492*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Mental Status Changes	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1492*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Atrial Fibrillation	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1492*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Anaemia	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1493*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Oropharyngeal Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1495*	Day 1495*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Subacute Endocarditis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1495*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dysarthria	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1497*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Decreased Appetite	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1498*	Day 1506*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dysphagia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1498*	Day 1506*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Cerebral Haemorrhage	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1498*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dry Mouth	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1499*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypernatraemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1499*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Arthralgia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1501*	Day 1501*

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Blood Bicarbonate Increased	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1506*	Day 1513*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Mobility Decreased	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1506*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pyrexia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1510*	Day 1510*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Chills	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1510*	Day 1510*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemorrhagic Stroke	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1513*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Muscular Weakness	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1513*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypotension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1513*	Day 1514*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Somnolence	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1513*	Day 1514*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pyrexia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1514*	Day 1514*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Endocarditis Bacterial	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	FATAL	Day 1516*	Day 1516*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Rectal Haemorrhage	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 125*	Day 125*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Nausea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 3*	Day 3*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Fatigue	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 12*	Day 12*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Cushingoid	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 12*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Gastrooesophageal Reflux Disease	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 13*	Day 13*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Myalgia	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 15*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Pneumonia	SEVERE	Y	PROBABLY RELATED	DRUG WITHDRAWN	RECOVERED/RESOLVED	Day 23*	Day 36*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dyspnoea	SEVERE	N	PROBABLY RELATED	DRUG INTERRUPTED	RECOVERING/RESOLVING	Day 23*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Asthenia	MILD	N	UNLIKELY RELATED	UNKNOWN	NOT RECOVERED/NOT RESOLVED	Day 23*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Fatigue	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 23*	

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Pyrexia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 23*	Day 36*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Ecchymosis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 23*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Tachycardia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 23*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Chills	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 23*	Day 34*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Leukocytosis	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 24*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Hypoxia	SEVERE	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 24*	Day 36*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Urinary Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 24*	Day 36*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Chest Pain	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 24*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Cough	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 24*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Hepatic Cyst	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	UNKNOWN	Day 24*	Day 24*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	4[redacted]	F	WHITE	Blood Pressure Diastolic Increased	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 48*	Day 48*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Decreased Appetite	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 3*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Dizziness	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 3*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 4*	Day 14*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Nausea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 4*	Day 14*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Abdominal Pain	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 4*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Nausea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 17*	Day 30*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Headache	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 23*	Day 26*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Neuropathy Peripheral	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 37*	Day 37*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Flatulence	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 49*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 50*	Day 50*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Diarrhoea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 51*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	F	WHITE	Influenza Like Illness		N		DRUG INTERRUPTED	NOT RECOVERED/NOT RESOLVED	Day 57*	

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[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Febrile Neutropenia	MODERATE	N	PROBABLY RELATED	DOSE REDUCED	RECOVERED/RESOLVED	Day 100*	Day 105*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Febrile Neutropenia	SEVERE	Y	POSSIBLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 103*	Day 108*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 103*	Day 137*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Upper Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 133*	Day 139*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Upper Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 182*	Day 290*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Upper Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 211*	Day 229*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Gastrointestinal Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 299*	Day 321*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 475*	Day 484*
[redacted]	Leukocytes (10^9/L)	Fostamatinib	3[redacted]	M	WHITE	Platelet Count Decreased	MODERATE	N	POSSIBLY RELATED	DRUG WITHDRAWN	RECOVERING/RESOLVING	Day 967*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Sleep Apnoea Syndrome	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 17*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Dizziness	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 20*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Hypertension	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 30*	Day 94*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Diarrhoea	MODERATE	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE	Day 61*	Day 87*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Abdominal Distension	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 75*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Urinary Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 88*	Day 101*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Haematuria	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 88*	Day 90*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Diarrhoea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 88*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Oral Candidiasis	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 128*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Erectile Dysfunction	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 128*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Myalgia	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 143*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Hypertension	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 143*	Day 156*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Myalgia	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 143*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Mouth Haemorrhage	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 375*	Day 382*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Increased Tendency To Bruise	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 375*	Day 382*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	M	WHITE	Petechiae	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 375*	Day 382*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Influenza Like Illness	MILD	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 9*	Day 13*

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Platelet Count Decreased	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 15*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Contusion	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 43*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Blood Blister	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 30*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Epistaxis	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 30*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Platelet Count Decreased	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 15*	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Hypertension	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 30*	Day 187*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Aspartate Aminotransferase Increased	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 71*	Day 99*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Alanine Aminotransferase Increased	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 71*	Day 99*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Dysgeusia	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 92*	Day 198*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Lymphocyte Count Decreased	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 99*	Day 127*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Blood Blister	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 173*	Day 180*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Epistaxis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 179*	Day 180*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Mouth Haemorrhage	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 180*	Day 181*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 196*	Day 257*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 215*	Day 221*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Diarrhoea	MODERATE	N	PROBABLY RELATED	DRUG WITHDRAWN	RECOVERED/RESOLVED	Day 257*	Day 291*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Viral Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 272*	Day 276*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Headache	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1*	Day 17*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Lethargy	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 48*	Day 82*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Dyspnoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 56*	Day 82*

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[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Dizziness	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 57*	Day 82*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Migraine	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 59*	Day 63*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Nausea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 59*	Day 63*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Dizziness	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 33*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Fatigue	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 33*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 167*	Day 172*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 172*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Nausea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 248*	Day 304*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Vomiting	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 248*	Day 304*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Urinary Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 385*	Day 388*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Muscle Spasms	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 510*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Fatigue	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1030*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Arthritis Viral	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1235*	Day 1277*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	4[redacted]	F	WHITE	Arthritis Viral	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1292*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 2*	Day 7*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Hypertension	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 127*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 25*	Day 26*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 28*	Day 124*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Epistaxis	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 41*	Day 41*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Dizziness	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 50*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Nausea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 70*	Day 126*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Epistaxis	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 116*	Day 116*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Dizziness	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 117*	Day 121*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Hypertension	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 128*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Immune Thrombocytopenic Purpura	MILD	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 134*	Day 139*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Chondrocalcinosis Pyrophosphate	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 134*	Day 139*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Thrombocytosis	MILD	N	POSSIBLY RELATED	DOSE REDUCED	RECOVERED/RESOLVED	Day 139*	Day 148*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	8[redacted]	F	WHITE	Joint Swelling	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 148*	Day 166*

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[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Bone Lesion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 166*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Abscess	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 166*	Day 197*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Musculoskeletal Pain	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 233*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Haemarthrosis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 237*	Day 267*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Rotator Cuff Syndrome	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 237*	Day 267*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dehydration	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 244*	Day 267*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Nausea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 244*	Day 246*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Vomiting	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 244*	Day 246*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Gastroenteritis	MODERATE	Y	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 246*	Day 258*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Epistaxis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 314*	Day 314*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 316*	Day 316*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 336*	Day 515*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Epistaxis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 357*	Day 357*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Ecchymosis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 371*	Day 400*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 396*	Day 396*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Asthenia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 512*	Day 523*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Presyncope	MILD	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 512*	Day 523*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MODERATE	Y	PROBABLY RELATED	DRUG WITHDRAWN	RECOVERED/RESOLVED	Day 516*	Day 523*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Hypokalaemia	MILD	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 519*	Day 523*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Dyspnoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 82*	Day 96*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Hypertension	MILD	N	PROBABLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 124*	Day 131*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Hypertension	MODERATE	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 145*	Day 187*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Hypoaesthesia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 175*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Nail Discolouration	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 190*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Eye Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 229*	Day 234*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 255*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Rhinitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 292*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Influenza	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 617*	Day 626*

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[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Palatal Disorder	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 802*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Pneumonia	MODERATE	N	PROBABLY RELATED	DOSE REDUCED	RECOVERING/RESOLVING	Day 851*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1000*	Day 1015*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Rhinorrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1039*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Cough	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1039*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Post Procedural Infection	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1196*	Day 1204*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Headache	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1223*	Day 1224*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1240*	Day 1260*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1316*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	F	WHITE	Oral Mucosal Blistering	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1461*	Day 1464*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Abdominal Discomfort	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 85*	Day 414*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Skin Lesion	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 127*	Day 295*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Hypertension	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 176*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Back Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 250*	Day 323*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Nasopharyngitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 259*	Day 295*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Procedural Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 392*	Day 398*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Cough	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 405*	Day 407*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Eczema	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 463*	Day 652*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Viral Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 621*	Day 680*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Nasopharyngitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 625*	Day 639*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Viral Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 717*	Day 718*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Nasopharyngitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 793*	Day 827*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Nephrolithiasis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 858*	Day 888*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Nasopharyngitis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 981*	Day 1010*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Viral Infection	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1042*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Viral Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 38*	Day 45*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Epistaxis	MODERATE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 42*	Day 42*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Retinal Tear	MODERATE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 47*	Day 52*

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[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Epistaxis	MODERATE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 48*	Day 52*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Nasal Congestion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 43*	Day 60*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Peripheral Swelling	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE	Day 57*	Day 140*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Rash Macular	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 109*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Rash Macular	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 109*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Fatigue	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 127*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 135*	Day 135*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 137*	Day 137*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Peripheral Swelling	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 140*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Rash	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 140*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Oedema Peripheral	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 140*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 154*	Day 155*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Muscle Injury	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 199*	Day 295*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Skin Lesion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 204*	Day 260*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Blood Pressure Measurement	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 232*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Fungal Skin Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 295*	Day 469*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Blood Pressure Measurement	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 295*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Tinea Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 303*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Joint Injury	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 325*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Fall	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 325*	Day 469*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 330*	Day 330*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Joint Injury	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 337*	Day 469*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Blood Pressure Measurement	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 358*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Muscle Spasms	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 386*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Blood Pressure Measurement	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 386*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Peroneal Nerve Palsy	MODERATE	N	POSSIBLY RELATED	DRUG WITHDRAWN	RECOVERING/RESOLVING	Day 441*	Day 469*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Blood Pressure Measurement	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 441*	

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[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Pneumonia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	FATAL	Day 469*	Day 469*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Muscle Spasms	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 117*	Day 328*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Abdominal Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 117*	Day 183*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Back Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 117*	Day 152*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Petechiae	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 152*	Day 169*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 161*	Day 201*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Neutropenia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 201*	Day 201*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 257*	Day 262*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 262*	Day 262*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Pyrexia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 298*	Day 298*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 314*	Day 328*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Muscle Spasms	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 314*	Day 328*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Back Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 356*	Day 391*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 454*	Day 518*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Back Pain	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 510*	Day 518*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Nasopharyngitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 512*	Day 514*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Chest Discomfort	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 522*	Day 526*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Dizziness	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 538*	Day 568*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Fatigue	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 538*	Day 568*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Chronic Obstructive Pulmonary Disease	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 561*	Day 564*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Cough	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 699*	Day 718*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Feeling Cold	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 699*	Day 718*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 699*	Day 718*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Vomiting	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 699*	Day 702*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 700*	Day 702*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Chronic Obstructive Pulmonary Disease	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 704*	Day 718*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Vomiting	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 714*	Day 714*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 964*	Day 971*

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[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Lower Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 1559*	Day 1574*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1624*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1699*	Day 1818*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Liver Function Test Abnormal	MILD	N	UNLIKELY RELATED	DOSE REDUCED	NOT RECOVERED/NOT RESOLVED	Day 1763*	
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dysgeusia	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 49*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Alanine Aminotransferase Increased	MODERATE	N	PROBABLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 43*	Day 71*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Aspartate Aminotransferase Increased	MODERATE	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 43*	Day 61*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Dysgeusia	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 72*	Day 94*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 73*	Day 81*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Nausea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 73*	Day 81*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 83*	Day 94*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Alanine Aminotransferase Increased	MILD	N	PROBABLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 85*	Day 99*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Aspartate Aminotransferase Increased	MILD	N	PROBABLY RELATED	DOSE REDUCED	RECOVERED/RESOLVED	Day 85*	Day 99*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Nausea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 90*	Day 91*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	[redacted]	F	WHITE	Abdominal Pain	MODERATE	N	PROBABLY RELATED	DRUG WITHDRAWN	RECOVERED/RESOLVED	Day 90*	Day 94*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Atrial Fibrillation	MODERATE	Y	POSSIBLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 236*	Day 237*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Angina Pectoris	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 236*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Chest Discomfort	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 236*	Day 236*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Oedema Peripheral	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 236*	Day 236*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Hypomagnesaemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 236*	Day 236*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Atrial Fibrillation	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 323*	Day 323*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Liver Function Test Abnormal	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 358*	Day 365*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Skin Wound	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 620*	Day 642*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Squamous Cell Carcinoma Of Skin	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 682*	Day 728*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Platelet Count Decreased	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 806*	Day 809*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 806*	Day 820*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	[redacted]	M	WHITE	Nausea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 10*	Day 10*

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	2[redacted]	M	WHITE	Nausea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 21*	Day 28*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	2[redacted]	M	WHITE	Pyrexia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 42*	Day 42*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	2[redacted]	M	WHITE	Bronchitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 66*	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	2[redacted]	M	WHITE	Vomiting	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 66*	Day 73*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	2[redacted]	M	WHITE	Pyrexia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 105*	Day 107*
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	Fostamatinib	2[redacted]	M	WHITE	Oral Herpes	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 112*	Day 114*
[redacted]	Lymphocytes (10^9/L)	Placebo	2[redacted]	F	WHITE	Pyrexia	MODERATE	Y	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 153*	Day 155*
[redacted]	Lymphocytes (10^9/L)	Placebo	2[redacted]	F	WHITE	Cough	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 153*	
[redacted]	Lymphocytes (10^9/L)	Placebo	2[redacted]	F	WHITE	Thrombocytopenia	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 153*	Day 155*
[redacted]	Lymphocytes (10^9/L)	Placebo	2[redacted]	F	WHITE	Upper Respiratory Tract Infection	MODERATE	Y	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 153*	Day 155*
[redacted]	Lymphocytes (10^9/L)	Placebo	2[redacted]	F	WHITE	Chills	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 153*	Day 155*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	6[redacted]	M	WHITE	Hydrocele	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 41*	Day 83*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	6[redacted]	M	WHITE	Hepatic Enzyme Increased	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 69*	Day 83*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	Fostamatinib	6[redacted]	M	WHITE	Petechiae	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 251*	Day 314*
[redacted]	Lymphocytes (10^9/L)	Fostamatinib	5[redacted]	M	WHITE	Leukopenia	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 15*	Day 85*
[redacted]	Lymphocytes (10^9/L)												
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	6[redacted]	F	WHITE	Neuralgia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 12*	Day 72*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	6[redacted]	F	WHITE	Diarrhoea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 30*	Day 32*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	6[redacted]	F	WHITE	Bronchitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 57*	Day 72*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	6[redacted]	F	WHITE	Diarrhoea	MODERATE	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 71*	Day 72*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	5[redacted]	F	WHITE	Hypertension	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 27*	Day 63*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	5[redacted]	F	WHITE	Epistaxis	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 43*	Day 44*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	5[redacted]	F	WHITE	Alanine Aminotransferase Increased	MILD	N	PROBABLY RELATED	DOSE REDUCED	RECOVERED/RESOLVED	Day 43*	Day 56*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	5[redacted]	F	WHITE	Upper Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 57*	Day 63*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	5[redacted]	F	WHITE	Petechiae	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 57*	Day 64*

＊新薬承認情報提供時に置き換え

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[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Nausea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 154*	Day 154*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Transaminases Increased	SEVERE	Y	PROBABLY RELATED	DRUG WITHDRAWN	RECOVERED/RESOLVED	Day 156*	Day 168*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Diarrhoea	MODERATE	N	PROBABLY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 233*	Day 475*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Polycythaemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 293*	Day 321*
[redacted]	Immunoglobulin G (g/L)												
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Cardio-Respiratory Arrest	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	FATAL	Day 1507*	Day 1507*
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)												
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Cellulitis Staphylococcal	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 716*	Day 723*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Cellulitis Staphylococcal	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 724*	Day 867*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Cardiac Failure Congestive	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1340*	Day 1345*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Aortic Valve Incompetence	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1340*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Tricuspid Valve Incompetence	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1340*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Mitral Valve Incompetence	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1340*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Pleural Effusion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE	Day 1340*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Ascites	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1340*	Day 1357*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Cardiac Failure Chronic	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1346*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Ascites	MODERATE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1358*	Day 1363*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Hepatic Cirrhosis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1358*	
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Portal Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 1358*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 43*	Day 48*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 216*	Day 282*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Petechiae	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 279*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Haemorrhage Subcutaneous	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 128*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Rash Papular	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 365*	Day 386*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Rhinorrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 365*	Day 374*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Dry Throat	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 365*	Day 374*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Dermatitis Allergic	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 402*	Day 408*

被験者番号	該当した異常低値	プラセボ対照期投与群	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	治験薬に対する処置	転帰	発現日	転帰日
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Loss Of Consciousness	MILD	Y	UNLIKELY RELATED	DRUG INTERRUPTED	RECOVERED/RESOLVED	Day 404*	Day 409*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Contusion	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 616*	Day 687*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Pneumonia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 671*	Day 683*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Pyrexia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 805*	Day 805*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Gastrointestinal Haemorrhage	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 911*	Day 987*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Anaemia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 925*	Day 987*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 945*	Day 949*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Anaemia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 988*	Day 1043*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Gastrointestinal Haemorrhage	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 988*	Day 1034*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Polyp	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1039*	Day 1039*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Diverticulitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 1039*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Abdominal Pain Upper	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1097*	Day 1107*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Oropharyngeal Pain	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1097*	Day 1112*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Upper Respiratory Tract Infection	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1097*	Day 1112*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Asthenia	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1107*	Day 1107*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Vomiting	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1107*	Day 1107*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Epistaxis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1109*	Day 1109*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Thrombocytopenia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1478*	Day 1484*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 81*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Diarrhoea	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 81*	Day 184*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Oedema Peripheral	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 240*	Day 257*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Limb Injury	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 281*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Respiratory Tract Infection	MILD	N	PROBABLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 362*	Day 366*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	M	WHITE	Pain In Extremity	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 523*	Day 529*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Flatulence	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 12*	Day 27*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Hypertension	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 41*	Day 41*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Osteoporosis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 55*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Mouth Haemorrhage	MODERATE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*

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[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Arthralgia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Petechiae	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Ecchymosis	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Mouth Haemorrhage	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Asthenia	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Dizziness	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 128*	Day 130*
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Haematoma	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERING/RESOLVING	Day 174*	
[redacted]	Immunoglobulin G (g/L)	Fostamatinib	[redacted]	F	WHITE	Platelet Count Decreased	SEVERE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 174*	Day 181*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Thrombocytopenia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 85*	Day 86*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 419*	Day 805*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 806*	Day 986*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	M	WHITE	Hypertension	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 987*	Day 1044*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 123*	Day 197*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Thrombocytopenia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 160*	Day 161*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Thrombocytopenia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 181*	Day 187*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Viral Pharyngitis	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 230*	Day 259*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MODERATE	N	POSSIBLY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 243*	Day 245*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Purpura	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 245*	Day 250*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Hypertension	MODERATE	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 315*	Day 354*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Diarrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1443*	Day 1445*
[redacted]	Immunoglobulin G (g/L)	Placebo	[redacted]	F	WHITE	Thrombocytopenia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 1444*	Day 1446*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Headache	MILD	N	POSSIBLY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 85*	
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Rhinorrhoea	MILD	N	UNLIKELY RELATED	DOSE NOT CHANGED	RECOVERED/RESOLVED	Day 85*	Day 132*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Blood Pressure Inadequately Controlled	MILD	N	PROBABLY RELATED	DOSE REDUCED	RECOVERED/RESOLVED	Day 98*	Day 114*
[redacted]	Lymphocytes (10^9/L)	Placebo	[redacted]	M	WHITE	Thrombocytopenia	SEVERE	Y	UNLIKELY RELATED	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED	Day 113*	

（Source: 1.13.3-10, 付録 C-02-①-9）

表 2.7.4.9-153　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（C788-047、C788-048 及び C788-049 試験）

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間（Y: R788 投与中）
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CALCIUM CITRATE	CONCOMITANT MEDICATION	TO SUPPORT BONE HEALTH	2	TABLET	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CALCIUM CITRATE	CONCOMITANT MEDICATION	PROPHYLACTIC FOR BONE HEALTH	2	TABLET	QD	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMBIEN	CONCOMITANT MEDICATION	SLEEP DEPRIVATION	0.5	TABLET	PRN	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ASCORBIC ACID	CONCOMITANT MEDICATION	TO INCREASE VITAMIN C	500	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	VITAMIN C 500 MG OR TABS	CONCOMITANT MEDICATION	VITAMIN	1	TABLET	BID	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	400	mg	BID	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]		
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FERROUS SULFATE	CONCOMITANT MEDICATION	INCREASE IRON	325	mg	QOD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FERROUS SULFATE	CONCOMITANT MEDICATION	PROPHYLACTIC IRON SUPPLEMENT	325	mg	BID	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CALCIUM-PHOSPHORUS-VITAMIN D (CITRACAL +D3 OR)	CONCOMITANT MEDICATION	VITAMIN	400	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DARBOPOIETIN ALFA	CONCOMITANT MEDICATION	TO INCREASE RED BLOOD CELLS	200	ug	PRN	SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	TRANEXAMIC ACID	CONCOMITANT MEDICATION	BLEEDING	650	mg	TID	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG - GAMMA GLOBULIN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	PRN	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	SITZ BATH - INGREDIENTS UNKNOWN	CONCOMITANT MEDICATION	WORSENING HEMORRHOIDS		UNKNOWN	PRN	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	200	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間(Y: R788投与中)
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BENZONATATE	CONCOMITANT MEDICATION	COUGH SUPPRESSANT FOR URI	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FLUTICASONE	CONCOMITANT MEDICATION	NASAL SPRAY FOR URI	1	PUFF	PRN	NASAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	GUAIFENESIN SYRUP	CONCOMITANT MEDICATION	EXPECTORANT FOR URI	1	tsp	Q6H	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LEVOFLOXACIN	CONCOMITANT MEDICATION	ANTIBIOTIC TO TREAT URI	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOLE	CONCOMITANT MEDICATION	ACID REFLUX	20	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOLE	CONCOMITANT MEDICATION	ACID REFLUX	20	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ESOMEPRAZOLE	CONCOMITANT MEDICATION	GASTRIC ANTRAL VASCULAR ECTASIA	40	mg	Q12H	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ESOMEPRAZOLE	CONCOMITANT MEDICATION	GASTRIC ANTRAL VASCULAR ECTASIA	40	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FERROUS SULFATE	CONCOMITANT MEDICATION	ANEMIA DURING GAVE	325	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PACKED RED BLOOD CELLS	CONCOMITANT MEDICATION	ANEMIA DURING GAVE	350	mL	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FOLIC ACID	CONCOMITANT MEDICATION	ANEMIA	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ZOLPIDEM	CONCOMITANT MEDICATION	INSOMNIA	5	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PACKED RED BLOOD CELLS	CONCOMITANT MEDICATION	ANEMIA DURING GAVE	350	mL	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CYANOCOBALAMIN	CONCOMITANT MEDICATION	NUTRITIONAL SUPPLEMENT	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DOCUSATE	CONCOMITANT MEDICATION	CONSTIPATION	100	mg	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	TRAZODONE	CONCOMITANT MEDICATION	INSOMNIA	100	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FOLIC ACID	CONCOMITANT MEDICATION	ANEMIA	0.8	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	BID	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	LIMIT SALT ABSORPTION POST SURGERY	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	MAGNESIUM	CONCOMITANT MEDICATION	POST TAVR SURGERY - AORTIC STENOSIS	400	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL	CONCOMITANT MEDICATION	HYPERTENSION	75	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	POTASSIUM	CONCOMITANT MEDICATION	POST TAVR SURGERY - AORTIC STENOSIS	20	mEq	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ASPIRIN	CONCOMITANT MEDICATION	AORTIC STENOSIS	81	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL	CONCOMITANT MEDICATION	HYPERTENSION	25	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	25	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FOLIC ACID	CONCOMITANT MEDICATION	INPATIENT MED FOR GASTROINTESTINAL HEMORRHAGE SAE	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	25	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA (DISCHARGE MEDICATION)	10	mg	QOD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMBIEN	CONCOMITANT MEDICATION	INSOMNIA	2.5	mg	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	TID 5 DAYS PER WEEK BID 2 DAYS PER WEEK	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	TID 3 DAYS PER WEEK BID 4 DAYS PER WEEK	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL SUCCINATE	CONCOMITANT MEDICATION	HYPERTENSION	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ASCORBIC ACID	CONCOMITANT MEDICATION	NUTRITIONAL SUPPLEMENT	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PACKED RBCS	CONCOMITANT MEDICATION	INCREASE HEMOGLOBIN - MELENA SAE INPATIENT	1	U	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	CONCOMITANT MEDICATION	EDEMA	200	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FLUTICASONE PROPIONATE (FLONASE NA)	CONCOMITANT MEDICATION	CONGESTION	1	SPRAY	PRN	NASAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LOSARTAN POTASSIUM	CONCOMITANT MEDICATION	HYPERTENSION	25	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LOSARTAN POTASSIUM	CONCOMITANT MEDICATION	HYPERTENSION	50	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LIDOCAINE 5 % OINTMENT	CONCOMITANT MEDICATION	SHOULDER PAIN	1	APPLICATION	PRN	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	7.5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CLOTRIMAZOLE	CONCOMITANT MEDICATION	BILATERAL LEG FUNGUS, ERYTHEMATOUS WITH CENTRAL CLEARING - CUTANEOUS	1	APPLICATION	BID PRN	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LOSARTAN POTASSIUM	CONCOMITANT MEDICATION	HYPERTENSION	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LOSARTAN POTASSIUM-HCTZ 100-12.5 MG TABLET	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL SUCCINATE (TOPROL XL) 100 MG TABLET EXTENDED RELEASE 24 HOUR	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOLE SODIUM 40 MG TABLET DELAYED RELEASE	CONCOMITANT MEDICATION	ACID REFLUX	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOLE SODIUM 20	CONCOMITANT MEDICATION	ACID REFLUX	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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		MG TAB EC										
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOLE SODIUM 40 MG TABLET DELAYED RELEASE	CONCOMITANT MEDICATION	ACID REFLUX	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HYDROCHLOROTHIAZIDE 12.5 MG TABLET	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	FEVER - SEPSIS	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CEFTRIAXONE	CONCOMITANT MEDICATION	KLEBSIELLA UTI	1	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DANAZOL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	200	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE	CONCOMITANT MEDICATION	HYPERTENSION	25	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE	CONCOMITANT MEDICATION	HYPERTENSION	100	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	NYSTATIN	CONCOMITANT MEDICATION	SEPSIS	5	mL	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	POTASSIUM CHLORIDE	CONCOMITANT MEDICATION	HYPOKALEMIA	60	mEq	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMPICILLIN	CONCOMITANT MEDICATION	SEPSIS	2	g	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMPICILLIN	CONCOMITANT MEDICATION	SEPSIS	3	g	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ALBUTEROL	CONCOMITANT MEDICATION	FOR WHEEZING AS NEEDED	3	mL	PRN	RESPIRATORY (INHALATION)	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HYDROCHLOROTHIAZIDE 12.5 MG TABLET	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HYDROCHLOROTHIAZIDE 12.5 MG TABLET	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	SODIUM POTASSIUM PHOSPHATE TAB (PHOSPHA 250)	CONCOMITANT MEDICATION	HYPOPHOSPHATEMIA	2	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FLUTICASONE 0.05% NASAL SPRAY	CONCOMITANT MEDICATION	CONGESTION	1	SPRAY	BID	NASAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	GUAIFENESIN	CONCOMITANT MEDICATION	COUGH	5	mL	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	POTASSIUM CHLORIDE	CONCOMITANT MEDICATION	HYPOKALEMIA	60	mEq	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMPICILLIN	CONCOMITANT MEDICATION	SEPSIS	2	g	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	SODIUM CHLORIDE 0.9% FLUSH INJ	CONCOMITANT MEDICATION	LUMEN FLUSH	10	mL	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOLE	CONCOMITANT MEDICATION	ACID REFLUX	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN COD #3 ORAL	CONCOMITANT MEDICATION	FOR COUGH AS NEEDED	1	TABLET	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	4	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PENICILLIN G POTASSIUM IN D5W (PENICILLIN G POT IN DEXTROSE) 20000 UNIT/ML SOLUTION	CONCOMITANT MEDICATION	SEPSIS	1	INFUSION	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AMOXICILLIN	CONCOMITANT MEDICATION	PPX ANTIBIOTICS FOR DENTAL CLEANING	1	UNKNOWN	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DOXAZOSIN	CONCOMITANT MEDICATION	HYPERURICEMIA/HTN	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FOLIC ACID	CONCOMITANT MEDICATION	ANEMIA	0.8	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DOXAZOSIN	CONCOMITANT MEDICATION	HYPERURICEMIA/HTN	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CEPHALEXIN 500 MG CAPSULE	CONCOMITANT MEDICATION	E. COLI UTI	1	CAPSULE	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CEPHALEXIN	CONCOMITANT MEDICATION	UTI	250	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ESTRADIOL	CONCOMITANT MEDICATION	FREQUENT UTIS	10	ug	2 TIMES PER WEEK	VAGINAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DICLOFENAC SODIUM (VOLTAREN) 1 % GEL	CONCOMITANT MEDICATION	PAIN IN UPPER LEFT ARM	1	APPLICATION	PRN	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	1	TABLET	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HEPARIN 5000 UNIT	CONCOMITANT MEDICATION	VTE PPX	1	SYRINGE	BID	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PIPERACILLIN TAZOBACTAM 4500 MG INFUSE OVER 30 MIN	CONCOMITANT MEDICATION	SEPSIS	1	INFUSION	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CALCIUM CITRATE TAB 1500 MG + VIT D 250 (315 MG OF ELEMENTAL CA)	CONCOMITANT MEDICATION	VITAMIN	315	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	POTASSIUM CHLORIDE ORAL LIQ	CONCOMITANT MEDICATION	HYPOKALEMIA	40	mEq	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	SEPSIS	650	mg	ONCE	RECTAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	1	TABLET	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	1	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	MEROPENEM 500 MG IN NS 50 ML INFUSE OVER 30 MIN	CONCOMITANT MEDICATION	UROSEPSIS - MORGANELLA BACTEREMIA	1	INFUSION	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE INJ	CONCOMITANT MEDICATION	AFIB WITH RVR	5	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	VANCOMYCIN INJ 750 MG IN NS 250 ML INFUSE OVER 60 MIN	CONCOMITANT MEDICATION	SEPSIS	1	INFUSION	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	SEPSIS	650	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE ORAL SUSP 12.5 MG	CONCOMITANT MEDICATION	AFIB WITH RVR	1	UNKNOWN	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	SEPSIS	650	mg	ONCE	RECTAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	SEPSIS	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DIGOXIN	CONCOMITANT MEDICATION	AFIB WITH RVR	125	ug	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE INJ	CONCOMITANT MEDICATION	AFIB WITH RVR	2.5	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CEFTRIAXONE IV INJ 2000 MG IN D5W 50 ML INFUSE OVER 30 MIN	CONCOMITANT MEDICATION	SEPSIS	1	INFUSION	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DIGOXIN 62.5 MICROGRAM	CONCOMITANT MEDICATION	AFIB WITH RVR	1	UNKNOWN	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ERTAPENEM INJ 1000 MG IN NORMAL SALINE 50 ML INFUSE OVER 30 MIN	CONCOMITANT MEDICATION	SEPSIS	1	INFUSION	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BENZOCAINE-MENTHOL	CONCOMITANT MEDICATION	COUGH	1	LOZENGE	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BENZONATATE	CONCOMITANT MEDICATION	COUGH	100	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	GUAIFENESIN + DEXTROMETHORPHAN ORAL LIQ	CONCOMITANT MEDICATION	COUGH	10	mL	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LIDOCAINE INJ 1%	CONCOMITANT MEDICATION	FOR PICC INSERTION	0.5	mL	ONCE	INTRADERMAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	50	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	SODIUM CHLORIDE 0.9% FLUSH INJ	CONCOMITANT MEDICATION	IV FLUSH	10	mL	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DIGOXIN INJ	CONCOMITANT MEDICATION	AFIB WITH RVR	125	ug	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE INJ	CONCOMITANT MEDICATION	AFIB WITH RVR	2.5	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE ORAL SUSP 12.5 MG	CONCOMITANT MEDICATION	AFIB WITH RVR	1	UNKNOWN	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DIGOXIN INJ	CONCOMITANT MEDICATION	AFIB WITH RVR	125	ug	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	SEPSIS	650	mg	ONCE	RECTAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE INJ	CONCOMITANT MEDICATION	AFIB WITH RVR	2.5	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE ORAL SUSP	CONCOMITANT MEDICATION	AFIB WITH RVR	25	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BENEPROTEIN (PROTEIN MODULE - 6 G PROTEIN/7 G PACKET)	CONCOMITANT MEDICATION	POOR APPETITE/NUTRITIONAL SUPPLEMENT	1	PACKET	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HYDRALAZINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	2	TABLET	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HYDRALAZINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	2	TABLET	BID	ORAL	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	2	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	SEPSIS	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DOXAZOSIN	CONCOMITANT MEDICATION	HYPERTENSION	1	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	DOXAZOSIN	CONCOMITANT MEDICATION	HYPERTENSION	1	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	MULTIVITAMIN ORAL LIQ	CONCOMITANT MEDICATION	VITAMINS	15	mL	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAZOLAMIDE	CONCOMITANT MEDICATION	ELEVATED HCO3	125	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CARVEDIOL 3.125 MG TABLET	CONCOMITANT MEDICATION	AFIB WITH RVR	1	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	POLYETHYLENE GLYCOL	CONCOMITANT MEDICATION	GI PPX	1	PACKET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	SENNA 17.2 MG	CONCOMITANT MEDICATION	GI PPX	1	UNKNOWN	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	FEVER - SEPSIS	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACETAZOLAMIDE	CONCOMITANT MEDICATION	ELEVATED HCO3	125	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUROSEMIDE	CONCOMITANT MEDICATION	EDEMA	40	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ERTAPENEM INJ 1000 MG IN NORMAL SALINE 50 ML INFUSE OVER 30 MIN	CONCOMITANT MEDICATION	SEPSIS	1	INFUSION	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LORAZEPAM	CONCOMITANT MEDICATION	SEDATIVE - MRI SPINE	0.5	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL TARTRATE ORAL SUSP 6.25 MG	CONCOMITANT MEDICATION	AFIB WITH RVR	1	UNKNOWN	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	METOPROLOL XL SUSTAINED RELEASE ORAL	CONCOMITANT MEDICATION	AFIB WITH RVR	25	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ASPIRIN	CONCOMITANT MEDICATION	AFIB WITH RVR	81	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	OTHER: NEEDED BECAUSE FOSTAMATINIB WITHHELD DUE TO LFTS.								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	OTHER: DOSE OF FOSTAMATINIB WITHHELD DUE TO LFTS AND NEEDED RESCUE								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	OTHER: FOSTAMINIB WITHHELD DUE TO LFTS NEEDED RESCUE THERAPY								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	OTHER: TAPERING OFF PREDNISONE								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	OTHER: TAPERING OFF PREDNISONE								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	OTHER: TAPERING OFF								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	CENTRUM	CONCOMITANT MEDICATION	MULTI-VITAMIN	1	CAPSULE	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	CENTRUM	CONCOMITANT MEDICATION	MULTI-VITAMIN	1	CAPSULE	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	THYROXINE	CONCOMITANT MEDICATION	HYPOTHYROIDISM	125	CAPSULE	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	THYROXINE	CONCOMITANT MEDICATION	HYPOTHYROIDISM	125	CAPSULE	QD	ORAL		19[redacted]		Y

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[redacted]	Lymphocytes (10^9/L)	VITAMIN D	CONCOMITANT MEDICATION	INCREASE VITAMIN D INTAKE	3	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	VITAMIN D	CONCOMITANT MEDICATION	INCREASE VITAMIN D INTAKE	3	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	METOPROLOL	CONCOMITANT MEDICATION	TAKEN AFTER POTENTIAL AORTIC ANEURYSM	50	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	METOPROLOL	CONCOMITANT MEDICATION	PROPHYLAXIS FOR BLOOD PRESSURE	50	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CELLCEPT	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CELLCEPT	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DANAZOL	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DANAZOL	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRIN	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRIN	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	

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[redacted]	Lymphocytes (10^9/L)	DAPSONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DAPSONE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	COLACE	CONCOMITANT MEDICATION	CONSTIPATION	100	mg	PRN	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	COLACE	CONCOMITANT MEDICATION	CONSTIPATION	100	mg	PRN	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IRON	CONCOMITANT MEDICATION	PREVENTATIVE	2	TABLET	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IRON	CONCOMITANT MEDICATION	INCREASE IRON INTAKE, PREVENTATIVE	2	TABLET	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PREVENT ALLERGIC REACTION TO IVIG	25	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	25	mg	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	INTRAVENOUS IMMUNOGLOBULIN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	PRN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PREVENT INFLAMMATION FROM IVIG INFUSION	650	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	650	mg	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DECADRON (DEXAMETHASONE)	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	40	mg	EVER Y WEEK	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	TRANEXAMIC ACID	CONCOMITANT MEDICATION	BLEEDING	650	mg	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	50	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	50	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	50	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE AS RESCUE THERAPY	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	NPLATE RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	530	ug	PRN	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	NPLATE RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	530	ug	ONCE	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	INPATIENT MEDICATION FOR SAE	2.5	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	25	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	60	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MED FOR IVIG	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	60	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	25	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	60	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MED FOR IVIG	650	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	FOR REASONS RELATED TO IVIG	650	mg	PRN	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BENADRYL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	50	mg	ONCE	ORAL	FOLLOW-UP	20[redacted]	20[redacted] Y	
[redacted]	Lymphocytes (10^9/L)	IVIG RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	FOLLOW-UP	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	NPLATE RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	530	ug	ONCE	SUBCUTANEOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TYLENOL	CONCOMITANT MEDICATION	PRE-MEDICATION FOR IVIG	650	mg	ONCE	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	OTHER: PLATELET COUNT 4,000								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	OTHER: PLATELET COUNT 4,000								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT								

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				BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT								

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				BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	RITUXAN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE 2.5MG	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	OSCAL ULTRA	CONCOMITANT MEDICATION	SUPPLEMENT	90	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PROMACTA	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PROMACTA	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	FERRALET	CONCOMITANT MEDICATION	ANEMIA	90	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	10	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE 10 MG	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	MILLIPRED 5MG	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ACETAMINOPHEN	CONCOMITANT MEDICATION	FEBRILE	650	mg	PRN	RECTAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AZITHROMYCIN	CONCOMITANT MEDICATION	PNEUMONIA	500	mg	Q12H	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	LACTOBACILLUS ACIDOPHILUS	CONCOMITANT MEDICATION	GENERAL HEALTH/SUPPLEMENT	1	g	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	MEROPENEM	CONCOMITANT MEDICATION	PNEUMONIA	1	g	Q12H	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PANTROPRAZOLE	CONCOMITANT MEDICATION	REFLUX/NAUSEA	40	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE	CONCOMITANT MEDICATION	PNEUMONIA	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	SODIUM CHLORIDE	CONCOMITANT MEDICATION	PNEUMONIA	250	mL	QH	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	VANCOMYCIN	CONCOMITANT MEDICATION	PNEUMONIA	1	g	Q12H	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	LEVOTHYROXINE	CONCOMITANT MEDICATION	HYPOTHYROIDISM	75	ug	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	BUPROPION HYDROCHLORIDE (WELLBUTRIN XL)	CONCOMITANT MEDICATION	DEPRESSION	300	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	TOPIRAMATE (TOPOMAX)	CONCOMITANT MEDICATION	MIGRAINES	200	mg	BID	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXAN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	POTASSIUM CHLORIDE	CONCOMITANT MEDICATION	LOW POTASSIUM	10	mEq	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	FUROSEMIDE (LASIX)	CONCOMITANT MEDICATION	HYPERTENSION	20	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHEA	4	mg	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	SIMETHACONE	CONCOMITANT MEDICATION	FLATULENCE	125	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	30	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/UL AND AT 2 IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Leukocytes (10^9/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]		Y

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[redacted]	Leukocytes (10^9/L)	PREDNISONE	PREVIOUSITP MEDICATIONS							20[redacted]		
[redacted]	Leukocytes (10^9/L)	POTASSIUM	CONCOMITANT MEDICATION	HYPOKALEMIC PREVENTION	1	g	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	POTASSIUM	CONCOMITANT MEDICATION	HYPOKALEMIC PREVENTION	1	g	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	CONTROLOC	CONCOMITANT MEDICATION	GASTRIC ULCER PREVENTION	40	mg	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	CONTROLOC	CONCOMITANT MEDICATION	GASTRIC ULCER PREVENTION	40	mg	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	COVERCARD	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	COVERCARD	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	REVOLADE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	REVOLADE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Leukocytes (10^9/L)	MEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	12	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	MEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	12	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	MEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	125	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	MEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	64	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	FLUIMUCIL	CONCOMITANT MEDICATION	FEVER NEUTROPENIC	200	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	NIVESTIM	CONCOMITANT MEDICATION	NEUTROPENIC FEVER	48	IU	QD	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	RINGER	CONCOMITANT MEDICATION	NEUTROPENIC FEVER	100	mL	QD	INTRAVENOUS	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Leukocytes (10^9/L)	TAZOCIN	CONCOMITANT MEDICATION	NEUTROPENIC FEVER	4.5	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	KLION	CONCOMITANT MEDICATION	DIARRHEA	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	PROBIOTICS	CONCOMITANT MEDICATION	GASTROINTESTINAL INFECTION	250	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted] Y	

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[redacted]	Leukocytes (10^9/L)	PROBIOTICS	CONCOMITANT MEDICATION	DIARRHEA		VIAL	UNKNOWN	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	NORMIX	CONCOMITANT MEDICATION	DIARRHEA	400	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	MEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	32	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Leukocytes (10^9/L)	MEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	12	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AMITRIPTYLINE	CONCOMITANT MEDICATION	INTERMITTENT HEADACHE	75	mg	PRN	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AMITRIPTYLENE	CONCOMITANT MEDICATION	INTERMITTENT HEADACHES	75	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	10	mg	3 TIMES PER WEEK	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	IMODIUM	CONCOMITANT MEDICATION	DIARRHEA	2	mg	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IMODIUM	CONCOMITANT MEDICATION	DIARRHEA	2	mg	PRN	ORAL	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	HYDROCHLORTHIAZIDE	CONCOMITANT MEDICATION	HYPERTENSION	25	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CIPROFLOXACIN	CONCOMITANT MEDICATION	POSSIBLE URINARY TRACT INFECTION	500	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MIRACLE MOUTHWASH	CONCOMITANT MEDICATION	ORAL THRUSH	10	mL	QID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	MIRACLE MOUTHWASH (TETRACYCLINE, NYSTATIN, DEXAMETHASONE, DIPHENHYDRAMINE)	CONCOMITANT MEDICATION	ORAL THRUSH	10	mL	QID	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DIFLUCAN	CONCOMITANT MEDICATION	ORAL THRUSH	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LISINOPRIL	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	LISINOPRIL	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IBUPROFEN	CONCOMITANT MEDICATION	MYALGIA	400	mg	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IBUPROFEN	CONCOMITANT MEDICATION	MYALGIA	400	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	7.5	mg	3 TIMES PER WEEK	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	3 TIMES PER WEEK	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIFLUCAN	CONCOMITANT MEDICATION	ORAL THRUSH	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	2 TIMES PER WEEK	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	10	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ADCAL-D3	CONCOMITANT MEDICATION	BONE PROTECTION	1	TABLET	UNKNOWN	UNKNOWN		20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ADCAL D3.	CONCOMITANT MEDICATION	PREVENTION OF OSTEOPOROSIS	11	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	OMEPRAZOLE	CONCOMITANT MEDICATION	STOMACH PROTECTION	20	mg	QD	ORAL	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	30	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	10	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ALENDRONIC ACID	CONCOMITANT MEDICATION	PROPHYLACTIC - BONE PROTECTION	20	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ALENDRONIC ACID	CONCOMITANT MEDICATION	BONE PROTECTION	70	mg	EVER Y WEEK	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	RESCUE PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	TRANEXAMIC ACID	CONCOMITANT MEDICATION	EPISTAXIS	1	g	TID	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HIGH BLOOD PRESSURE	2.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QOD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QOD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHOEA	2	mg	UNKNOWN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	LISINOPRIL	CONCOMITANT MEDICATION	HIGH BLOOD PRESSURE	2.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	RESCUE PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	30	mg	QD	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	20	mg	QD	ORAL	FOLLOW-UP	[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	STEROIDS	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	MMF	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	GEDAREL	CONCOMITANT MEDICATION	CONTRACEPTIVE PILL	20	ug	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GEDAREL	CONCOMITANT MEDICATION	CONTRACEPTIVE PILL	20	20/150 ug TABLET	QD	ORAL		20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	RESCUE MEDICATION-IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	55	g	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	TRAMADOL	CONCOMITANT MEDICATION	MIGRAINE		UNKNOWN	UNKNOWN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FERROUS SUPLHATE	CONCOMITANT MEDICATION	IRON DEFICIENCY	200	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	FERROUS SULPHATE	CONCOMITANT MEDICATION	LOW IRON STORES	200	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CHLORPHENAMINE	CONCOMITANT MEDICATION	PRE-MED FOR IVIG TREATMENT	10	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	HYDROCORTISONE	CONCOMITANT MEDICATION	PRE-MEDS FOR IVIG TREATMENT	100	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	PRE-MEDS FOR IVIG TREATMENT	1	g	ONCE	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	RESCUE IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	56	g	ONCE	SUBCUTANEOUS	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIORALYTE	CONCOMITANT MEDICATION	DIARRHOEA	1	SACHET	3 TIMES PER WEEK	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	NITROFURANTOIN	CONCOMITANT MEDICATION	URNINARY TRACT INFECTION	1	TABLET	BID	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIORALYTE	CONCOMITANT MEDICATION	DIARRHOEA	1	SACHET	QD	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHOEA	20	mg	QID	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	CONCOMITANT MEDICATION	VIRAL ARTHRITIS	15	mg	QD	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	HYDROXYCHLOROQUINE	CONCOMITANT MEDICATION	VIRAL ARTHRITIS	200	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS							19[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DAPSONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DAPSONE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	REVOLADE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	REVOLADE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CELLCEPT	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CELLCEPT	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	7.5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CORTISONE	CONCOMITANT MEDICATION	ARTHRITIS BILATERAL HANDS		UNKNOWN	ONCE	INTRA-ARTICULAR	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	CONCOMITANT MEDICATION	CALCIUM PYROPHOSPHATE DEPOSITION DISEASE (CPPD)	15	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	VENOFER	CONCOMITANT MEDICATION	LOW IRON	600	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	FUCIDIN CREAM	CONCOMITANT MEDICATION	SACIO-COCCYGEAL NODULE? EARLY ABCESS		FINGER TIP UNIT	ONCE	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	FUCIDIN CREAM	CONCOMITANT MEDICATION	SACIO-COCCYGEAL NODULE, EARLY ABCESS		FINGER TIP UNIT	ONCE	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CALCIUM CARBONATE	CONCOMITANT MEDICATION	GASTROENTERITIS	125	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	100	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ONDANSETRON	CONCOMITANT MEDICATION	GASTROENTERITIS	4	mg	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	VITAMIN D3	CONCOMITANT MEDICATION	OSTEOPOROSIS	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	VITAMIN B12	CONCOMITANT MEDICATION	IRON DEFICIENCY	1	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	AMLODOPINE	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CALCIUM CARBONATE	CONCOMITANT MEDICATION	GASTROENTERITIS	1	TABLET	QD	ORAL	FOLLOW-UP	20[redacted]		Y

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[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PLATELET TRANSFUSION	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	1	U	ONCE	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	POTASSIUM EXTENDED-RELEASE	CONCOMITANT MEDICATION	HYPOGLYCEMIA	40	mmol	ONCE	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	VITAMIN D3 (CHOLECALCIFEROL)	CONCOMITANT MEDICATION	OSTEOPOROSIS	1	TABLET	QD	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	POTASSIUM CHLORIDE LIQUID	CONCOMITANT MEDICATION	HYPOKALEMIA	40	mmol	ONCE	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	RISEDRONATE	CONCOMITANT MEDICATION	OSTEOPOROSIS	35	mg	EVERY WEEK	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	g	ONCE	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	OTHER: SUBJECT RECEIVED IVIG AT AN UNSCHEDULED VISIT ON JULY 9, 2015								

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[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					INTRAVENOUS		19[redacted]	19[redacted]	

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[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	ANTI-D	PREVIOUSITP MEDICATIONS					INTRAVENOUS		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS					INTRAVENOUS		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	MYCOPHENOLATE MOFETIL (MMF)	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	ANTI-D	PREVIOUSITP MEDICATIONS							19[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUSITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS							19[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	MYCOPHENOLATE MOFETIL (MMF)	PREVIOUSITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUSITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUSITP MEDICATIONS							20[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLONE	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLONE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ROMIPLOSTIM	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS		20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ROMIPLOSTIM	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	MYCOPHENOLATE MOFETIL	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	

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		(MMF)										
[redacted]	Lymphocytes (10^9/L)	MYCOPHENOLATE MOFETIL (MMF)	PREVIOUS ITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	MYCOPHENOLATE MOFETIL (MMF)	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	MYCOPHENOLATE MOFETIL (MMF)	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CO-TRIMOXAZOLE FORTE	CONCOMITANT MEDICATION	PROPHYLAXIS	960	mg	3 TIMES PER WEEK	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	FLUCONAZOLE	CONCOMITANT MEDICATION	PROPHYLAXIS	50	mg	BID	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	g	QD	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	g	QD	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	g	OVER TWO DAYS	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	g	OVER 2 DAYS	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	

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[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	g	OVER 2 DAYS	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	60	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	500	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	30	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	METHLYPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	500	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	30	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	500	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CHLORAMPHENICOL	CONCOMITANT MEDICATION	EYE INFECTION	1	%	QID	INTRAOCULAR	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	500	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	30	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMOXICILLIN	CONCOMITANT MEDICATION	CHEST INFECTION	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	SALBUTAMOL	CONCOMITANT MEDICATION	CHEST INFECTION	100	ug	PRN	RESPIRATORY (INHALATION)	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	MUPIROCIN	CONCOMITANT MEDICATION	NOSE INFECTION	2	%	TID	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	CHEST INFECTION	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	CHEST INFECTION	100	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	35	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	30	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	25	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	15	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	COUGH MEDICINE (PATIENT COULDN'T REMEMBER THE NAME)	CONCOMITANT MEDICATION	CHEST INFECTION			QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	PNEUMONIA	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PNEUMOCOCCAL VACCINE (PPV RECOMBINANT	CONCOMITANT MEDICATION	PNEUMONIA	0.5	mL	ONCE	INTRAMU SCULAR	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	AZITHROMYCIN	CONCOMITANT MEDICATION	PNEUMONIA	250	mg	ONE CAPSULE ON MON, WED AND FRI EVERY WEEK	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AUGMENTIN	CONCOMITANT MEDICATION	PNEUMONIA	375	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CLARITHROMYCIN	CONCOMITANT MEDICATION	RHINORRHOEA & COUGH	500	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	RHINORRHOEA & COUGH	625	mg	TID	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	FLUCLOXACILLIN	CONCOMITANT MEDICATION	INFECTION POST WART REMOVAL	500	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	HEADACHE	1	g	ONCE	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CLARITHROMYCIN	CONCOMITANT MEDICATION	CHEST INFECTION	500	mg	BID	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	LOSARTAN	CONCOMITANT MEDICATION	HYPERTENSION	500	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	CO-AMOXICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL		[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	MOXIFLOXACIN	CONCOMITANT MEDICATION	CHEST INFECTION	400	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	SEPTRIN	CONCOMITANT MEDICATION	CHEST INFECTION	950	mg	3 TIMES PER WEEK	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS							19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	PREVIOUSITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS							20[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	MYCOPHENOLATE	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	MYCOPHENOLATE	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	HEADACHES	2	TABLET	PRN	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELOCON	CONCOMITANT MEDICATION	SKIN RASH	1	FINGER	QD	TOPICAL	TREATMENT	20[redacted]	[redacted]	

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						TIP UNIT						
[redacted]	Immunoglobulin G (g/L)	EMULSIFYING OINTMENT	CONCOMITANT MEDICATION	SKIN RASH	1	FINGER TIP UNIT	QD	TOPICAL	TREATMENT	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	LAMISIL CREAM	CONCOMITANT MEDICATION	SKIN RASH	1	FINGER TIP UNIT	QD	TOPICAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	RANITIDINE	CONCOMITANT MEDICATION	EPIGASTRIC PAIN	150	mg	BID	ORAL	FOLLOW-UP	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	RANITIDINE	CONCOMITANT MEDICATION	UPPER GASTRIC DISCOMFORT ON EATING	150	mg	BID	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTESNION	5	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	BISOPROLOL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	COUGH	2	TABLET	QD	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	VIRAL INFECTION	2	TABLET	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	COLD	2	TABLET	TID	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	VIRAL INFECTION	1	g	BID	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	COLD	1	g	BID	ORAL	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	COLD	1	g	BID	ORAL	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LEMSIP	CONCOMITANT MEDICATION	VIRAL INFECTION	1	SACHET	QD	ORAL	FOLLOW-UP	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	VIRAL INFECTION	1	g	TID	ORAL	FOLLOW-UP	[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	STEROIDS	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	FOLIC ACID	CONCOMITANT MEDICATION	CHRON'S DISASE	5	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	CITALOPRAM	CONCOMITANT MEDICATION	DEPRESSION	20	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	LANSOPRAZOLE	CONCOMITANT MEDICATION	CHRON'S DISEASE	30	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	AZATHIOPINE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	CYCLOSPORIN	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	

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[redacted]	Lymphocytes (10^9/L)	ELTROMBOPAG	PREVIOUS ITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	LOPERAMIDE	CONCOMITANT MEDICATION	CHRON'S DISEASE	2	mg	PRN	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	MERCAPTOPURINE	CONCOMITANT MEDICATION	CHRON'S DISEASE	50	mg	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PENTASA	CONCOMITANT MEDICATION	CHRON'S DISEASE	4	TABLET	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	MESALAZINE	CONCOMITANT MEDICATION	CHRON'S DISEASE	1	g	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IVIG	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS		[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	ELTROMBOPAG	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	VIRAL INFECTION	2	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	0.4	/kg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TRANEXAMIC ACID	CONCOMITANT MEDICATION	BLEEDING	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PLATELETS	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	2	POOLS	ONCE	INTRAVENOUS	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	RED BLOOD CELLS	CONCOMITANT MEDICATION	BLEEDING	2	BAG	PRN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	NASEPTIN CREAM	CONCOMITANT MEDICATION	EPISTAXIS		FINGER TIP UNIT	BID	TOPICAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PLATELETS	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	1	POOL	ONCE	INTRAVENOUS	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TRANEXAMIC ACID	CONCOMITANT MEDICATION	BLEEDING	0.5	g	BID	ORAL	TREATMENT	[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	OTHER: VIRAL INFECTION - SAE COMPLETED								
[redacted]	Lymphocytes (10^9/L)	ALLOPURINOL	CONCOMITANT MEDICATION	GOUT	200	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	ATENOLOL	CONCOMITANT MEDICATION	HYPERTENSION	100	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	BENDROFLUMETHIAZIDE	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL		19[redacted]		Y

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[redacted]	Lymphocytes (10^9/L)	COCODAMOL	CONCOMITANT MEDICATION	PAIN	16	16 mg / 1000 mg	QID OR PRN	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	LERCANIDIPINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL		19[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PERINDOPRIL	CONCOMITANT MEDICATION	HYPERTENSION	8	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PERINDOPRIL	CONCOMITANT MEDICATION	HYPERTENSION	8	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RE COMBINANT ANTI D	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	RE COMBINANT ANTI D	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	SUDAFED	CONCOMITANT MEDICATION	NASAL CONGESTION		0.10%	QD	NASAL		20[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ACEMETACIN	CONCOMITANT MEDICATION	GOUT	120	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DOXAZOCIN	CONCOMITANT MEDICATION	HYPERTENSION	1	mg	QD	ORAL	TREATMENT	20[redacted]	19[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TRANEXAMIC ACID	CONCOMITANT MEDICATION	EPISTAXIS	1.5	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BETNOVATE CREAM	CONCOMITANT MEDICATION	MACULAR RASH, BOTH FEET		0.12%	QD	TOPICAL	SCREENING	20[redacted]	20[redacted] Y	
[redacted]	Lymphocytes (10^9/L)	BETNOVATE CREAM	CONCOMITANT MEDICATION	MACULAR RASH - BOTH FEET		0.122% W/W	BID	TOPICAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	HYDRAMOL EMOLIENT	CONCOMITANT MEDICATION	RASH - GREAT TOE, DORSUM FOOT & MEDIAL ASPECT OF BOTH FEET - MACULAR RASH		FINGER TIP UNIT	BID	TOPICAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	HYDROMOL EMOLIENT	CONCOMITANT MEDICATION	MACULAR RASH, BOTH FEET		FINGER TIP UNIT	BID	TOPICAL	SCREENING	20[redacted]		Y

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[redacted]	Lymphocytes (10^9/L)	NASEPTIN NASAL OINTMENT: CHLORHEXIDINE 0.1% / NEOMYCIN 0.5%	CONCOMITANT MEDICATION	EPISTAXIS		UNKNOWN	PRN	TOPICAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DERMOVATE	CONCOMITANT MEDICATION	MACULAR RASH, BOTH FEET		FINGER TIP UNIT	BID	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	LERCANIDIPINE	CONCOMITANT MEDICATION	HYPERTENSION	20	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	CHLORPHENARIMINE	CONCOMITANT MEDICATION	MACULAR RASH, BOTH FEET	4	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	MEPILEX DRESSING	CONCOMITANT MEDICATION	TO PROTECT BIOPSY SITE			PRN	DRESSING	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	SHOLDER INJURY	1	g	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DERMOL 500	CONCOMITANT MEDICATION	MACULAR RASH		USE AS A BODY WASH IN PLACE OF SOAP	PRN	TOPICAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	FUCIDIN	CONCOMITANT MEDICATION	POST SKIN BIOPSY	20	20 mg/g	TID	TOPICAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DERMOVATE CREAM	CONCOMITANT MEDICATION	MACULAR RASH, BOTH FEET		FINGER TIP UNIT	PRN	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	TURBINAFINE	CONCOMITANT MEDICATION	TINEA INCOGNITO	1	%	PRN	TOPICAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IBUPROFEN	CONCOMITANT MEDICATION	R SHOULDER PAIN FOLLOWING FALL (AE9)	400	mg	TID	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	IBUPROFEN	CONCOMITANT MEDICATION	INTERMITTENT SPASM RIGHT THIGH	400	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	ALLUPURINOL	CONCOMITANT MEDICATION	GOUT	200	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	ATTENOLOL	CONCOMITANT MEDICATION	HYPERTENSION	100	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	BENDROFLUMETHIAZIDE	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	COCODAMOL	CONCOMITANT MEDICATION	PAIN	16	16/1000 mg	PRN	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	COMPRESSION STOCKINGS	CONCOMITANT MEDICATION	VTE PREVENTION			PRN	STOCKINGS				Y

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[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ANTI D	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ANTI D	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IV IMMUNOGLOBULIN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IV IMMUNOGLOBULIN	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	CO-CODAMOL	CONCOMITANT MEDICATION	PAIN IN KNEES	500	mg	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	CO CODAMOL	CONCOMITANT MEDICATION	PAIN IN KNEES	500	mg	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	COLECALCIFEROL	CONCOMITANT MEDICATION	PAIN IN KNEES SUSPECTED BONE DEGENERATION DUE TO STEROID USE - CALCIUM AND VITAMIN D		IU	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	COLECALCIFEROL	CONCOMITANT MEDICATION	PAIN IN KNEES-SUSPECTED BONE DEGENERATION DUE TO STEROID USE - CONTAINS CALCIUM AND VITAMIN D		IU	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SALBUTAMOL NEB	CONCOMITANT MEDICATION	EXACERBATION OF COPD	5	mg	PRN	RESPIRATORY (INHALATION)	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SERITIDE	CONCOMITANT MEDICATION	EXACERBATION OF COPD	250	PUFF	BID	RESPIRATORY (INHALATION)	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	SIMPLE LINCTUS	CONCOMITANT MEDICATION	NON PRODUCTIVE COUGH	5	mL	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SPIRIVA	CONCOMITANT MEDICATION	EXACERBATION OF COPD	18	PUFF	QD	RESPIRATORY (INHALATION)	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	TRANSEXAMIC ACID	CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	1	g	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	SERETIDE	CONCOMITANT MEDICATION	LOWER RESPIRATORY TRACT INFECTION	250	PUFF	BID	RESPIRATORY (INHALATION)	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SPIRIVA	CONCOMITANT MEDICATION	LOWER RESPIRATORY TRACT INFECTION	18	PUFF	QD	RESPIRATORY (INHALATION)	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	COPD EXACERBATION	100	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	CONCOMITANT MEDICATION	COPD	40	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	SIMPLE LINCTUS	CONCOMITANT MEDICATION	COUGH	5	mL	QID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	290	mL	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	SALBUTAMOL	CONCOMITANT MEDICATION	LOWER RESPIRATORY TRACT INFECTION	100	PUFF	PRN	RESPIRATORY (INHALATION)	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	30	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	CHEST INFECTION	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CO-AMOICLAV	CONCOMITANT MEDICATION	CHEST INFECTION	625	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	QUININE SULPHATE	CONCOMITANT MEDICATION	CRAMPS IN BOTH HANDS	300	mg	QD	ORAL	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST TIGHTNESS	40	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	CONCOMITANT MEDICATION	COPD	30	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	COUGH	200	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	COUGH	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	AMOXICILLIN	CONCOMITANT MEDICATION	EXAC COPD	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	AMOXICILLIN	CONCOMITANT MEDICATION	CHEST INFECTION	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	AMOXICILLIN	CONCOMITANT MEDICATION	CHEST INFECTION	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CLARITHROMYCIN	CONCOMITANT MEDICATION	CHEST INFECTION	500	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	CONCOMITANT MEDICATION	CHEST INFECTION	30	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHOEA	2	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	OTHER: EPISTAXIS WHILST AN INPATIENT WITH COPD EXACERBATION								
[redacted]	Lymphocytes (10^9/L)	AZATHIOPRINE	PREVIOUS ITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	RITUXIMAB	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUS ITP MEDICATIONS					ORAL		19[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	BLACKMORES HAIR SKIN AND NAILS	CONCOMITANT MEDICATION	NUTRITIONAL SUPPLEMENT		TABLET	UNKNOWN	ORAL		20[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	FOULDING PROBIOTIC	CONCOMITANT MEDICATION	SUPPLEMENT	1	TABLET	QD	ORAL		20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	13	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PREDNISOLONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	MAGNESIUM	CONCOMITANT MEDICATION	NUTRITIONAL SUPPLEMENT	2	TABLET	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DOXYCYCLINE	CONCOMITANT MEDICATION	UPPER RESPIRATORY TRACT INFECTION		mg	UNKNOWN	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	AUGMENTIN DUO FORTE	CONCOMITANT MEDICATION	UPPER RESPIRATORY TRACT INFECTION		mg	UNKNOWN	ORAL	SCREENING	20[redacted]	20[redacted]	

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[redacted]	Lymphocytes (10^9/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHEA	2	mg	ONCE	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	OXYCODONE	CONCOMITANT MEDICATION	ABDOMINAL PAIN	5	mg	PRN	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	ABDOMINAL PAIN	1	g	PRN	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PLAQUENIL	CONCOMITANT MEDICATION	SYSTEMIC LUPUS ERYTHEMATOSUS	200	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PLAQUENIL (HYDROXYCHLOROQUINE SULFATE)	CONCOMITANT MEDICATION	SYSTEMIC LUPUS ERYTHEMATOSUS	200	mg	QD	ORAL		19[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	PREVIOUSITP MEDICATIONS							19[redacted]		
[redacted]	Immunoglobulin G (g/L)	ATENOLOL	CONCOMITANT MEDICATION	HYPERTENSION	50	mg	BID	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ATENOLOL	CONCOMITANT MEDICATION	HYPERTENSION	50	mg	BID	ORAL		19[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	INDAPAMIDE	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	INDAPAMIDE	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DANAZOL	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOL	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ATORVASTATIN	CONCOMITANT MEDICATION	HYPERCHOLESTEROLAEMIA	10	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ATORVASTATIN	CONCOMITANT MEDICATION	HYPERCHOLESTEROLAEMIA	10	mg	QD	ORAL		20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ESOMEPRAZOLE	CONCOMITANT MEDICATION	GASTRO-OESOPHAGEAL REFLUX DISEASE	20	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PANADOL OSTEO	CONCOMITANT MEDICATION	OSTEOARTHRITIS	1.3	g	TID	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ESOMEPRAZOLE	CONCOMITANT MEDICATION	GASTRO-OESOPHAGEAL REFLUX DISEASE	20	mg	QD	ORAL		19[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	PANADOL OSTEO	CONCOMITANT MEDICATION	OSTEOARTHRITIS	1.3	g	PRN	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SYSTANE LUBRICATING EYE DROPS	CONCOMITANT MEDICATION	DRY EYES	1	gtt	TID	INTRAOCULAR	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SYSTANE LUBRICATING EYE DROPS	CONCOMITANT MEDICATION	DRY EYES	1	gtt	TID	INTRAOCULAR	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	4	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	OSTEVIT-D	CONCOMITANT MEDICATION	VITAMIN D DEFICIENCY	25	ug	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	OSTEVIT-D	CONCOMITANT MEDICATION	VITAMIN D DEFICIENCY	25	ug	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	INTRAVENOUS IMMUNOGLOGULIN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	INTRAVENOUS IMMUNOGLOGULIN	PREVIOUS ITP MEDICATIONS							20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	GLYCERYL TRINITRATE PATCH	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	TRANSDERMAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GLYCERYL TRINITRATE TRANSDERMAL PATCH	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	TRANSDERMAL		20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	7.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	7.5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	4	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	4	mg	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	4	mg	QD	ORAL	SCREENING	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	4	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	4	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CALCIUM CITRATE	CONCOMITANT MEDICATION	OSTEOPOROSIS	250	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DIGOXIN	CONCOMITANT MEDICATION	ATRIAL FIBRILLATION	250	ug	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FERROUS SULPHATE	CONCOMITANT MEDICATION	PROPHYLAXIS OF IRON DEFICIENCY	325	mg	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GLYCERYL TRINITRATE SPRAY	CONCOMITANT MEDICATION	ANGINA	400	ug	PRN	SUBLINGUAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	MAGNESIUM	CONCOMITANT MEDICATION	HYPOMAGNESEMIA	20	mmol	ONCE	INTRAVENOUS	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIGOXIN	CONCOMITANT MEDICATION	ATRIAL FIBRILLATION	63	ug	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	ATORVASTATIN	CONCOMITANT MEDICATION	HYPERCHOLESTEROLAEMIA	40	mg	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	BISOPROLOL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	FLECAINIDE/TAMBOCOR	CONCOMITANT MEDICATION	ATRIAL FIBRILLATION	100	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	FLUCLOXACILLIN	CONCOMITANT MEDICATION	PREVENTION WOUND INFECTION	250	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted] Y	
[redacted]	Immunoglobulin G (g/L)	CEPHALEXIN	CONCOMITANT MEDICATION	INFECTION PREVENTION	500	mg	TID	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FLUOROURACIL	CONCOMITANT MEDICATION	BOWENOID KERATOSIS	5	%	BID	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	25	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	OTHER: PLATELETS 16000, NO BLEEDING BUT SIGNIFICANT RISK FOR BLEEDING. USUAL PLATELET COUNT GREATER THAN 20 000.								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	APREDNISOLON	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	REVOLADE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	APREDNISOLON	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PANTOPRAZOL	CONCOMITANT MEDICATION	GASTRIC PROTECTION	40	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	NPLATE	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	OLEOVIT D3	CONCOMITANT MEDICATION	VITAMIN D DEFICIENCY	30	gtt	EVERY WEEK	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	APREDNISOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	100	mg	TAPERED	ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CYKLOKAPRON	CONCOMITANT MEDICATION	BLEEDING	2	TABLET	TID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PRIVIGEN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PRIVIGEN	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CIPROXIN	CONCOMITANT MEDICATION	INFECTION PROPHYLAXIS	500	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ERYCYTOL	CONCOMITANT MEDICATION	VITAMIN B12 DEFICIENCY PROPHYLAXIS	1	AMPULE	ONCE	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	VALACICLOVIR	CONCOMITANT MEDICATION	INFECTION PROPHYLAXIS	500	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IMMUNOPRIN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	100	mg	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PRIVIGEN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	30	g	QD	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ZOFRAN ZYDIS	CONCOMITANT MEDICATION	NAUSEA	8	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PRIVIGEN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	30	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ZOFRAN ZYDIS	CONCOMITANT MEDICATION	NAUSEA	8	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PRIVIGEN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	30	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PRIVIGEN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	30	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	TAVANIC	CONCOMITANT MEDICATION	BRONCHITIS	500	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	AVELOX	CONCOMITANT MEDICATION	FEVER	400	mg	QD	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/μL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	BELARA	CONCOMITANT MEDICATION	CONTRACEPTION	1	TABLET	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	BELARA	CONCOMITANT MEDICATION	CONTRACEPTION	1	TABLET	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	APREDNISOLON	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	APREDNISOLON	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CYCLOCAPRON	CONCOMITANT MEDICATION	MENSTRUAL BLEEDING	1	g	TID, DURING MENSTRUAL BLEEDING	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	CYCLOKAPRON	CONCOMITANT MEDICATION	MENSTRUAL BLEEDING	1	g	TID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DESLORATADIN	CONCOMITANT MEDICATION	RASH	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DIPROGENTA	CONCOMITANT MEDICATION	RASH	1	APPLICATION	QD	TOPICAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	FERRLECIT	CONCOMITANT MEDICATION	IRON DEFICIENCY	1	AMPULE	EVERY WEEK	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DIBONDRIN	CONCOMITANT MEDICATION	PREMEDICATION BEFORE RESCUE THERAPY	30	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	FAMOTIDIN	CONCOMITANT MEDICATION	PREMEDICATION BEFORE RESCUE THERAPY	20	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PANTOPRAZOL	CONCOMITANT MEDICATION	PREMEDICATION BEFORE RESCUE THERAPY	40	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	

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[redacted]	Lymphocytes (10^9/L)	PRIVIGEN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	20	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DIBONDRIN	CONCOMITANT MEDICATION	CHILLS	30	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	MOXIFLOXACIN	CONCOMITANT MEDICATION	CHILLS	400	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	CHILLS	1	g	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ULCUSAN	CONCOMITANT MEDICATION	CHILLS	20	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	URBASON	CONCOMITANT MEDICATION	CHILLS	96	mg	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	MOXIFLOXACIN	CONCOMITANT MEDICATION	ELEVATED CRP	400	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	HEADACHE	500	mg	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	TRADOLAN	CONCOMITANT MEDICATION	HEADACHE	24	gtt	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	METROGASTRON	CONCOMITANT MEDICATION	VOMITING	4	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PARACETAMOL	CONCOMITANT MEDICATION	HEADACHE	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	METAMIZOL-NATRIUM	CONCOMITANT MEDICATION	HEADACHE	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	AVELOX	CONCOMITANT MEDICATION	INFECTION	400	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	HALCION	CONCOMITANT MEDICATION	SLEEP AID	0.2	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	URBASON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	96	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	URBASON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	60	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	URBASON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

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[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMLATOR	CONCOMITANT MEDICATION	ARTERIAL HYPETENSION	10	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMLATOR	CONCOMITANT MEDICATION	ARTERIAL HYPERTEN SION	10	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	CICLOSPORIN - SANDIMUN	PREVIOUS ITP MEDICATIONS					ORAL		19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	KIOVIG	PREVIOUS ITP MEDICATIONS					INTRAVE NOUS		19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	KIOVIG	PREVIOUS ITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	CICLOSPORIN - SANDIMUN	PREVIOUS ITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	HELICID	CONCOMITANT MEDICATION	PROFYLAXIS OF GI ULCERS	20	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	HELICID	CONCOMITANT MEDICATION	PROFYLAXIS OF GI ULCERS	20	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	15	mg	QD	ORAL	SCREENING	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	15	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	ONCE	INTRAVE NOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	AMLODIGAMMA	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	AMLODIGAMMA	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	LORISTA H	CONCOMITANT MEDICATION	HYPERTENSION	50	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	LORISTA H	CONCOMITANT MEDICATION	HYPERTENSION	50	mg	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	80	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	ROMIPLOSTIN	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ROMIPLOSTIN	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	15	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	15	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	RANITIDINE	CONCOMITANT MEDICATION	STOMACH IRRITATION CAUSED BY STEROIDS	150	mg	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	RANITIDINE	CONCOMITANT MEDICATION	STOMACH IRRITATION CAUSED BY STEROIDS	150	mg	BID	ORAL	SCREENING	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	HEMOFER	CONCOMITANT MEDICATION	PRAPHYLAXIS OF LOW FERRITIN LEVEL	1	TABLET	QD	ORAL	SCREENING	20[redacted]		Y

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[redacted]	Lymphocytes (10^9/L)	HEMOFER	CONCOMITANT MEDICATION	PROPHYLAXIS OF LOW FERRITIN LEVEL	1	TABLET	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS							20[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOLUM	PREVIOUSITP MEDICATIONS					ORAL		[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOLUM	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS					ORAL		[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS					ORAL		[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	AMLODIPINUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	10	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AMLODIPINUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	10	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	OMEPRAZOLUM	CONCOMITANT MEDICATION	PROPHYLAXIS OF GASTRITIS	20	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	OMEPRAZOLUM	CONCOMITANT MEDICATION	PROPHYLAXIS OF GASTRITIS	20	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS					ORAL		[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	PREVIOUSITP MEDICATIONS					INTRAVENOUS		[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHRIOPRINE	PREVIOUSITP MEDICATIONS					ORAL		[redacted]	[redacted]	

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[redacted]	Immunoglobulin G (g/L)	AZATHRIOPRINE	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	CARVEDILOLUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	125	ugX100	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	CARVEDILOLUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	125	ugX100	QD	ORAL		[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FENOFIBRATUM	CONCOMITANT MEDICATION	HYPERTRIGLICERYDEMIA	160	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	FENOFIBRATUM	CONCOMITANT MEDICATION	HIPERTRIGLICERYDEMIA	160	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GLIMEPIRIDUM	CONCOMITANT MEDICATION	DIABETES MELLITUS	2	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GLIMEPIRIDUM	CONCOMITANT MEDICATION	DIABETES MELLITUS	2	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METFORMINI HYDROCHLORIDUM	CONCOMITANT MEDICATION	DIABETES MELLITUS	1	g	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METFORMINI HYDROCHLORIDUM	CONCOMITANT MEDICATION	DIABETES MELLITUS	1	g	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNIZONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SPIRONOLACTONUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	25	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNIZONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	5	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SPIRONOLACTONUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	25	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	NEURALGIA	500	mg	QD	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	TRAMADOLI HYDROCHLORIDUM	CONCOMITANT MEDICATION	NEURALGIA	100	mg	QD	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	AMOXICILLINUM	CONCOMITANT MEDICATION	BRONCHITIS	500	mg	BID	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHEA	2	mg	PRN	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	BISOPROLOLI FUMARAS	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	REVOLADE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	REVOLADE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	MEDROL	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	MEDROL	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	

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[redacted]	Immunoglobulin G (g/L)	MEDROL TAB 4 MG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	8	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	MEDROL TAB 4 MG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	8	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PRESTARIUM CO	CONCOMITANT MEDICATION	HYPERTENSION		mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MEDROL TAB 4 MG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	NASIC NASAL SPRAY	CONCOMITANT MEDICATION	UPPER RESPIRATORY TRACT INFECTION.	1	ONE SPRAY AT A TIME IN EACH NOSTRIL.	TID	NASAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	SOLVOLAN	CONCOMITANT MEDICATION	UPPER RESPIRATORY TRACT INFECTION.	30	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	GLUCOSE 5%	CONCOMITANT MEDICATION	ALT AND AST >10 ULN; SAE LINE 2	500	mL	QD	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MEDROL TAB 4MG-RESCUE MED	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	48	mg	QD	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLONE AS RESCUE MEDICATION DUE TO SAE 1	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	80	mg	QD	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PANTOPRAZOLE	CONCOMITANT MEDICATION	ALT AND AST >10 ULN; SAE LINE 2	40	mg	QD	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	VITAMIN C	CONCOMITANT MEDICATION	ALT AND AST >10 ULN; SAE LINE 2	400	mg	QD	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	ULCOPROL	CONCOMITANT MEDICATION	ACID REFLUX AFTER SAE, LINE 2	20	mg	BID	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET								

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				PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND REQUIRES URGENT OR EMERGENT SURGERY								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUS ITP MEDICATIONS					INTRAVENOUS		19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUS ITP MEDICATIONS							19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	CYCLONAMINE	CONCOMITANT MEDICATION	BLEEDING PROPHYLAXIS	750	mg	TID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	CYCLONAMINUM	CONCOMITANT MEDICATION	BLEEDING PROPHYLAXIS	750	mg	TID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNIZOLONUM	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNIZOLONUM	PREVIOUS ITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHIOPRINUM	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHIOPRINUM	PREVIOUS ITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOLUM	PREVIOUS ITP MEDICATIONS					ORAL		[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOLUM	PREVIOUS ITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUS ITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUS ITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PRAZOL	CONCOMITANT MEDICATION	GASTRITIS PROPHYLAXIS	20	mg	QD	ORAL	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PRAZOL	CONCOMITANT MEDICATION	GASTRITIS PROPHYLAXIS	20	mg	QD	ORAL	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNIZOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	4	mg	QD	ORAL		[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNIZOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	4	mg	QD	ORAL		[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE-RM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	100	mg	QD	ORAL	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDI HYDROCHLORIDUM	CONCOMITANT MEDICATION	DIARRHEA	2	mg	QD PRN	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	VENESECTION	CONCOMITANT MEDICATION	POLYCYTHEMIA	400	mL	ONCE	INTRAVENOUS	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNIZOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	4	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	OMEPRAZOLE	CONCOMITANT MEDICATION	PROPHYLAXIS OF GASTRITIS DURING STERYTHERAPY	20	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	VALZEK	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	80	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	CYCLONAMINA	CONCOMITANT MEDICATION	BLEEDING PROPHYLAXIS	500	mg	TID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GLUCOPHAGE	CONCOMITANT MEDICATION	DIABETES	750	mg	BID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	KALIPOZ PROLONGATUM	CONCOMITANT MEDICATION	HIPOKALIEMIA PROPHYLAXIS	391	mg	QD	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	VIGANTOLETTEN	CONCOMITANT MEDICATION	PROPHYLAXIS OF OSTEOPOROSIS	1	1000 IU	BID	ORAL		[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	15	mg	QD	ORAL	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	100	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	100	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	NEBIVOLOL	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL		19[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	AMLODIPINE	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	NEBIVOLOL	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL		20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	KALII CHLORIDUM	CONCOMITANT MEDICATION	PROPHYLAXIS	391	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	KALII CHLORIDUM	CONCOMITANT MEDICATION	PROPHYLAXIS	391	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	LOSARTANUM KALCIUM (LORISTA H 50/12.5)	CONCOMITANT MEDICATION	HYPERTENSION	62	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	LOSARTANUM KALUM (LORISTA H 50/12.5)	CONCOMITANT MEDICATION	HYPERTENSION	62	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	SPIRONOLACTON	CONCOMITANT MEDICATION	HYPERTENSION	25	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	SPIRONOLACTON	CONCOMITANT MEDICATION	HYPERTENSION	25	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	BISOPROLOLI FUMARANS	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	BISOPROLOLI FUMARANS	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISON	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	PREDNISON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	BETALOC ZOK	CONCOMITANT MEDICATION	CHRONIC ATRIAL FIBRILLATION ; HYPERTENSION	50	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	BETALOC ZOK	CONCOMITANT MEDICATION	CHRONIC ATRIAL FIBRILLATION ; HYPERTENSION	50	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUS ITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLPTEDNISOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	8	mg	BID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	16	mg	QD	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	NORVASC	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	NORVASC	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	METAMIZOL	CONCOMITANT MEDICATION	PAIN DUE TO STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	1	g	BID	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	TRAMADOL	CONCOMITANT MEDICATION	PAIN DUE TO STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	50	mg	TID	ORAL	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	KETOPROFEN	CONCOMITANT MEDICATION	INFLAMMATION DUE TO STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	100	mg	BID	INTRAMUSCULAR	TREATMENT	20[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	OMEPRAZOL	CONCOMITANT MEDICATION	GASTROPROTECTOR	20	mg	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PENTOXIFYLLINE	CONCOMITANT MEDICATION	INFLAMMATION DUE TO STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	100	mg	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIAZEPAM	CONCOMITANT MEDICATION	HOSPITALIZATION DUE TO STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FRAXIPARINE	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	0.6	mg	QD	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MEDOCEF	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM DATA VALUE CHANGED	2	g	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISOLON	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	60	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	METRONIDAZOLE	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	500	mg	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MERONEM	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM DATA VALUE CHANGED	1	g	TID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	VANCOMYCINE	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	1	g	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MILGAMMA	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM	50	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Immunoglobulin G (g/L)	UNASYN	CONCOMITANT MEDICATION	STAPHILOCOCCUS EPIDERMIDIS PHLEGMONE OF THE LEFT HAND AND FOREARM DATA VALUE CHANGED	1.5	g	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	ARIXTRA	CONCOMITANT MEDICATION	HRONIC ATRIAL FIBRILLATION	2.5	mg	QD	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CONCOR	CONCOMITANT MEDICATION	HRONIC ATRIAL FIBRILLATION	2.5	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FURANTHRIL	CONCOMITANT MEDICATION	CHRONIC CONGESTIVE HEART FAILURE	80	mg	BID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	KALINOR- 2,17 G/2,0 G/2,057 G EFFERVESCENT TABLET POTASSIUM CITRATE/POTASSIUM HYDROGENCARBONATE/CITR IC ACID ANHYDROUS	CONCOMITANT MEDICATION	HYPOKALIEMIA	1	TABLET	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	SPIRONOLACTON	CONCOMITANT MEDICATION	ASCITES	25	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	FURANTHRIL	CONCOMITANT MEDICATION	CHRONIC CONGESTIVE HEART FAILURE	40	mg	TID	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CONCOR	CONCOMITANT MEDICATION	HRONIC ATRIAL FIBRILLATION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	SPIRONOLACTONE	CONCOMITANT MEDICATION	ASCITES	25	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	TRIFAS	CONCOMITANT MEDICATION	HRONIC HEART FAILURE	10	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ACIDI FOLICI	CONCOMITANT MEDICATION	CIRRHOSIS HEPATIS	0.4	mg	TID	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CARSIL (SYLIMARIN)	CONCOMITANT MEDICATION	HEPATIS CIROSIS	90	mg	TID	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	HEPA-MERZ	CONCOMITANT MEDICATION	HEPATIS CIRRHOSIS	5	g	BID	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	MAGNERICH	CONCOMITANT MEDICATION	ASCITES	500	mg	TID	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	OMEPRAZID (OMEPRAZOLE)	CONCOMITANT MEDICATION	REFLUX OESOPHAGITIS	20	mg	BID	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	SPIRONOLACTONE	CONCOMITANT MEDICATION	CHRONIC HEART FAILURE	25	mg	TID	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	TRANSMETIL	CONCOMITANT MEDICATION	HEPATIS CIRRHOSIS	500	mg	BID	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	HUMAN ALBUMIN	CONCOMITANT MEDICATION	CIRRHOSIS HEPATIS/HYPOALBUMINEMIA	100	g	QD	INTRAVENOUS	FOLLOW-UP	[redacted]	20[redacted]	Y

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[redacted]	Immunoglobulin G (g/L)	LEGALON	CONCOMITANT MEDICATION	CIRRHOSIS HEPATIS	140	mg	TID	ORAL	FOLLOW-UP	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASON	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASON	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATIOPRYNA	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	50	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AZATIOPRYNA	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	CYCLONAMINE	CONCOMITANT MEDICATION	HYPERTENSION	750	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	5	g	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	50	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AXTIL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	RAMIPRYL	CONCOMITANT MEDICATION	HYPERTENSION	5	g	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMID	CONCOMITANT MEDICATION	DIARRHEA	2	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMID	CONCOMITANT MEDICATION	DIARHHEA	2	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	CONTINUES HEADACHES	500	mg	PRN	ORAL				Y
[redacted]	Immunoglobulin G (g/L)	PAREACETAMOL	CONCOMITANT MEDICATION	CONTINUES HEADACHES	500	mg	PRN	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ENCORTON	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	DANAZOL	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	DANAZOL	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CYCLOSPORIN	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	CYCLOSPORIN	PREVIOUSITP MEDICATIONS							20[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL		19[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	MICARDIS	CONCOMITANT MEDICATION	HYPERTENSION	80	mg	QD	ORAL		19[redacted]		Y

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[redacted]	Lymphocytes (10^9/L)	MICARDIS	CONCOMITANT MEDICATION	HYPERTENSION	80	mg	QD	ORAL		19[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	10	mg	QOD	ORAL		20[redacted]	[redacted]	
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	20	mg	QOD	ORAL		20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	7.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	7.5	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CLEMASTIN	CONCOMITANT MEDICATION	PROPHYLAXIS OF ATOPIC SKIN ALLERGY	2	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	15	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IV IG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	90	g	ONCE	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	CLEXANE	CONCOMITANT MEDICATION	PROPHYLAXIS OF VEIN THROMBOSIS	0.4	mL	QD	SUBCUTANEOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CLEXANE	CONCOMITANT MEDICATION	VEIN THROMBOSIS PROPHYLAXIS	0.4	mL	QD	SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	KEFZOL - CEFAZOLIN	CONCOMITANT MEDICATION	INFECTION PREVENTION			QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	KEFZOL/CEFAZOLIN	CONCOMITANT MEDICATION	INFECTION PREVENTION			QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	30	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTOM	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	CHLORQUINALDOLUM	CONCOMITANT MEDICATION	DRYNESS IN THROAT	2	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CHLORQUINALDOLUM	CONCOMITANT MEDICATION	RUNNY NOSE	2	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	RUNNY NOSE	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	DRYNESS IN THROAT	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CHLORQUINALDOLUM	CONCOMITANT MEDICATION	DRYNESS IN THROAT	2	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CHLORQUINALDOLUM	CONCOMITANT MEDICATION	RUNNY NOSE	2	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	RUNNY NOSE	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	DRYNESS IN THROAT	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	FUCIBET	CONCOMITANT MEDICATION	SKIN ALLERGY	21	mg	QD	TOPICAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMLOZEK	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	CONTROLOC	CONCOMITANT MEDICATION	LOSS OF CONCIOUSSNESS	40	mg	UNKNOWN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	METOCLOPRAMID	CONCOMITANT MEDICATION	LOSS OF CONCIOUSSNESS	10	mg	UNKNOWN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PLASMALYTE	CONCOMITANT MEDICATION	LOSS OF CONCIOUSSNESS	500	mL	UNKNOWN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	SALINE	CONCOMITANT MEDICATION	LOSS OF CONCIOUSSNESS	500	mL	UNKNOWN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMLOZEK	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	ENCORTON	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	BISOCARD	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	PNEUMONIA	1	TABLET	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AUGMENTIN	CONCOMITANT MEDICATION	PNEUMONIA	1	g	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PARACETAMOLUM	CONCOMITANT MEDICATION	FEVERISH CONDITION	500	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	AMOKSIKLAV	CONCOMITANT MEDICATION	RESPIRATORY TRACT INFECTION	1	TABLET	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y

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[redacted]	Lymphocytes (10^9/L)	APAP (PARACETAMOLUM)	CONCOMITANT MEDICATION	UPPER RESPIRATORY TRACT INFECTION	1	TABLET	TID	ORAL	TREATMENT	[redacted]	[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	MIOCARDIS	CONCOMITANT MEDICATION	HYPERTENSION	80	mg	QD	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	MICARDIS PLUS	CONCOMITANT MEDICATION	HYPERTENSION	1	TABLET	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DEXAMETHAZONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QID	ORAL	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PRENOME(OMEPRAZOLE)	CONCOMITANT MEDICATION	PROPHYLAXIS OF GASTRITIS	20	mg	QD	ORAL	FOLLOW-UP	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	REVOLADE	CONCOMITANT MEDICATION	QUALIFICATION FOR TRANSPLANTATION	50	mg	QD	ORAL	FOLLOW-UP	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	ENCORTON	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ENCORTON	PREVIOUSITP MEDICATIONS							20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHAZON	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHAZON	PREVIOUSITP MEDICATIONS							[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOL	PREVIOUSITP MEDICATIONS					ORAL		[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DANAZOL	PREVIOUSITP MEDICATIONS							[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	CYCLOSPORINE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	CYCLOSPORINE	PREVIOUSITP MEDICATIONS						SCREENING	[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARHHEA	2	mg	BID	ORAL	TREATMENT	[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	XALATA	CONCOMITANT MEDICATION	PROPHYLAXIS GLAUCOMA	1	gtt	QD	TOPICAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	CORTICOIDS	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	PARIET	CONCOMITANT MEDICATION	GASTRIC PROTECTION	20	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PARIET	CONCOMITANT MEDICATION	GASTRIC PROTECTION	20	mg	QD	ORAL		19[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	PREVIOUSITP MEDICATIONS					ORAL		19[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	RITUXIMAB	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	

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[redacted]	Immunoglobulin G (g/L)	DANAZOL	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	GAMMAGLOBULIN	PREVIOUSITP MEDICATIONS					INTRAVENOUS		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	MYCOPHENOLATE	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	PREVIOUSITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	PREVIOUSITP MEDICATIONS					INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ROMIPLOSTIM	PREVIOUSITP MEDICATIONS					SUBCUTANEOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	SIROLIMUS	PREVIOUSITP MEDICATIONS					ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	MANIDON	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION			BID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	MANIDON	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION			BID	ORAL		20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	CYCLOPHOSPHAMIDE	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	ELTROMBOPAG	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLPREDNISONE	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATIOPRIN 75MG/12H	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	CYCLOPHOSPHAMIDE	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	GAMMAGLOBULINE 40 G	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	GAMMAGLOBULINE 40 G	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	GAMMAGLOBULINE 40 G	PREVIOUSITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	AMARYL	CONCOMITANT MEDICATION	DIABETES MELLITUS	1	g	PRN	ORAL	SCREENING	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	AMARYL	CONCOMITANT MEDICATION	DIABETES MELLITUS	1	g	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	PAIN MUSCLE	1	g	PRN	ORAL	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	PAIN MUSCLE	1	g	PRN	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	GAMMAGLOBULINE 40 G	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	GAMMAGLOBULINE 40 G	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	15	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	15	mg	QD	ORAL	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AERO-RED	CONCOMITANT MEDICATION	FLATULENCE	120	mg	QD	ORAL	TREATMENT	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PROLIA	CONCOMITANT MEDICATION	OSTEOPOROSIS	60	mg	Q6M	SUBCUTANEOUS	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL	SCREENING	[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PROLIA	CONCOMITANT MEDICATION	OSTEOPOROSIS	60	mg	Q6M	SUBCUTANEOUS	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	1	g/kg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	IMMUNOGLOBULIN	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	1	g/kg	ONCE	INTRAVENOUS	FOLLOW-UP	[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND REQUIRES URGENT OR EMERGENT SURGERY								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	XALATA	CONCOMITANT MEDICATION	PROPHYLAXIS GLAUCOMA	1	gtt	QD	TOPICAL				Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASON	PREVIOUS ITP MEDICATIONS					INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	

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[redacted]	Immunoglobulin G (g/L)	DEXAMETHASON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISON	PREVIOUS ITP MEDICATIONS					ORAL	SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISON	PREVIOUS ITP MEDICATIONS						SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	20	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	RAMIPRYL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	DIURESIN SR	CONCOMITANT MEDICATION	HYPERTENSION		mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	NEBIVOLOL	CONCOMITANT MEDICATION	HYPERTENSION	2.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	POLPRAZOLE	CONCOMITANT MEDICATION	PROPHILAXIS OF GASTRIC ULCER	20	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	POLPRAZOLE	CONCOMITANT MEDICATION	PROPHILAXIS OF GASTRITIS	20	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	LEVOTHYROXINE	CONCOMITANT MEDICATION	HYPOTHYREOSIS	143	ug	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LEVOTHYROXINE	CONCOMITANT MEDICATION	HYPOTHYREOSIS	143	ug	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	FOLIC ACID	CONCOMITANT MEDICATION	PROPHILAXIS OF ANEMIA	15	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	FOLIC ACID	CONCOMITANT MEDICATION	PROPHILAXIS OF ANEMIA	15	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	INSULINE	CONCOMITANT MEDICATION	DIABETES MELLITUS	6	IU	TID	SUBCUTANEOUS	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	INSULINE	CONCOMITANT MEDICATION	DIABETES MELLITUS	6	IU	TID	SUBCUTANEOUS	SCREENING	20[redacted]	20[redacted]	

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[redacted]	Immunoglobulin G (g/L)	PREDNISONUM	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PREDNISONUM	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	AZATHIOPRINE	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	CALCII CARBONAS	CONCOMITANT MEDICATION	PROPHILAXIS OF OSTEOPOROSIS	1	g	QD	ORAL		19[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CHOLOCACIFEROLUM	CONCOMITANT MEDICATION	PROPHILAXIS OF OSTEOPOROSIS	25	ug	QD	ORAL		19[redacted]	[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNISOLONUM	PREVIOUSITP MEDICATIONS					ORAL	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNISOLONUM	PREVIOUSITP MEDICATIONS						SCREENING	20[redacted]	[redacted]	
[redacted]	Immunoglobulin G (g/L)	HYDROCORTISONE	CONCOMITANT MEDICATION	PROPHILAXIS OF ADRENAL FAILURE	10	mg	QD	ORAL	SCREENING	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	HYDROCORTISONE	CONCOMITANT MEDICATION	PROPHILAXIS OF ADRENAL FAILURE	10	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	70	g	QD	INTRAVENOUS	SCREENING	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	1.5	g	TOTAL DOSE	INTRAVENOUS		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PLT CONCENTRATE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	1	U	ONCE	IN	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	50	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHEA	2	mg	UNKNOWN	ORAL		20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	70	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	70	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	1 g		QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	

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[redacted]	Immunoglobulin G (g/L)	METHYLOPREDNISOLONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	500	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	60	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	PARACETAMOL	CONCOMITANT MEDICATION	HEADACHE	1	g	PRN	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	AMLODIPINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	
[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHEA	2	mg	PRN	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	IVIG	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	70	g	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	INDAPAMIDE	CONCOMITANT MEDICATION	HYPERTENSION	1.5	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	LEVOTHYROXINE	CONCOMITANT MEDICATION	HYPOTHYREOSIS	137	ug	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CYCLONAMINA	CONCOMITANT MEDICATION	TROMBOCYTOPENIA	500	mg	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	PLT CONCENTRATE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	5	U	ONCE	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	CARBO MEDICINALIS	CONCOMITANT MEDICATION	DIARRHEA	2	g	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIOSMECTITE	CONCOMITANT MEDICATION	DIARRHEA	2	PUFF	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DIOSMECTITE	CONCOMITANT MEDICATION	DIARRHEA	1	PUFF	TID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	METRONIDAZOL	CONCOMITANT MEDICATION	DIARRHEA	250	mg	QID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LEVOTHYROXINE	CONCOMITANT MEDICATION	HYPOTHYREOSIS	125	ug	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	AMLODYPINE	CONCOMITANT MEDICATION	HYPERTENSION	5	mg	QD	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	LERCANIDIPINE	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	TREATMENT	20[redacted]		Y

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[redacted]	Immunoglobulin G (g/L)	RAMIPRIL	CONCOMITANT MEDICATION	HYPERTENSION	10	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Immunoglobulin G (g/L)	LOPERAMIDE	CONCOMITANT MEDICATION	DIARRHEA	2	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	40	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	20	mg	BID	ORAL	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間(Y: R788投与中)
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間(Y: R788投与中)
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Immunoglobulin G (g/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/µL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISON	PREVIOUS ITP MEDICATIONS					ORAL		19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISON	PREVIOUS ITP MEDICATIONS							19[redacted]	19[redacted]	
[redacted]	Lymphocytes (10^9/L)	REVOLADE	PREVIOUS ITP MEDICATIONS					ORAL		19[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	REVOLADE	PREVIOUS ITP MEDICATIONS							19[redacted]	20[redacted]	
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA	15	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	15	mg	QD	ORAL	SCREENING	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DILATREND	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	25	mg	QD	ORAL	TREATMENT	20[redacted]		Y
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	16	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	14	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	DEXAMETHASONE	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	12	mg	QD	INTRAVENOUS	TREATMENT	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	SOLUMEDROL	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	1 g		QD	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	IMMUNOGOBULINE IV	ITP CONCOMITANT MEDICATION	IMMUNE THROMBOCYTOPENIC PURPURA (ITP)	25	g	QD	INTRAVENOUS	FOLLOW-UP	20[redacted]	20[redacted]	Y
[redacted]	Lymphocytes (10^9/L)	ATACAND	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	32	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	ATACAND	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	32	mg	QD	ORAL				Y

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	投与量	単位	用法	投与経路	投与開始時期	投与開始日	投与終了日	投与期間(Y: R788投与中)
[redacted]	Lymphocytes (10^9/L)	DILATREND	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	25	mg	QD	ORAL			20[redacted]	
[redacted]	Lymphocytes (10^9/L)	NEFRIX	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	25	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	NORVASC	CONCOMITANT MEDICATION	ARTERIAL HYERTENSION	5	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	IVIG	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	NEFRIX	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	25	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	TENAXUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	1	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	NORVASC	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	5	mg	QD	ORAL				Y
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	PREDNISONE	RESCUE MEDICATION	PLATELET COUNT <50,000/uL AND AT IMMEDIATE RISK OF BLEEDING OR WITH CLINICALLY SIGNIFICANT BLEEDING OR WET PURPURA								
[redacted]	Lymphocytes (10^9/L)	TENAXUM	CONCOMITANT MEDICATION	ARTERIAL HYPERTENSION	1	mg	QD	ORAL				Y

(Source: 1.13.3-10, 付録 C-02-①-10)

表 2.7.4.9-154　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（C788-047、C788-048 及び C788-049 試験）

被験者番号	該当した異常低値	病歴名	開始日	区分（合併/既往）
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	FUNCTIONAL HEART MURMUR	[redacted]	合併
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BREAST CANCER	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	CATARACT EXTRACTION OF BOTH EYES	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ACOUSTIC NEUROMA/RESECTION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	COLONOSCOPY - INTERNAL HEMORRHOIDS	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ENDOMETRIAL CANCER/HYSTERECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BLEEDING	[redacted]	合併
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	SLEEP DEPRIVATION/PROBLEMS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BREAST BIOPSY FOR BENIGN PARENCHYMAL HEMATOMA/DRAINAGE	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ENDOSCOPY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	ARTERIOVENOUS MALFORMATION/ARGON PLASMA COAGULATION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	GASTRITIS W/ HELICOBACTER PYLORI	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BASAL CELL RESECTION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	RIGHT PATELLAR FRACTURE	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BASAL CELL CARCINOMA/RESECTION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	BILATERAL PATELLAR FRACTURE	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	LOWER EXTREMITY EDEMA	[redacted]	既往
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	PERSISTENT TOE PAIN	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HYPOTHYROIDISM	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	GALL BLADDER REMOVED	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	APPENDECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	PLASTIC SURGERY POST PLANE CRASH	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	FRONTAL ARTERITIS -POST PLANE CRASH	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	HYSTERECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	R BREAST TUMOR EXCISION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	BREAST IMPLANTATION AND REMOVAL	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	HYPERCHOLESTEREMIAS	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	BREAST CANCER	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	LUMPECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	AORTIC ANEURYSM OF UNSPECIFIED SITE WITHOUT MENTION OF RUPTURE	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	TRIGGER FINGER" RELEASE SURGERY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	BLEEDING	[redacted]	合併
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ANEMIA	[redacted]	合併
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	WEIGHT GAIN	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HYPOTHYROIDISM	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HYPERTENSION	[redacted]	合併

被験者番号	該当した異常低値	病歴名	開始日	区分 （合併/既往）
[redacted]	Lymphocytes (10^9/L)	CHOLECYSTECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	BREAST REDUCTION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	HYSTERECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	SPINAL FUSION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	DEPRESSION	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	MIGRAINES	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	PANCYTOPENIA	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	PETECHIAE	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	NAUSEA	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	LOW POTASSIUM	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	INCREASED URINARY FREQUENCEY	[redacted]	合併
[redacted]	Leukocytes (10^9/L)	HYPERTHYREOSIS	[redacted]	既往
[redacted]	Leukocytes (10^9/L)	LIPOMA SURGERY	[redacted]	既往
[redacted]	Leukocytes (10^9/L)	CARDIOVASCULAR	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	OCCASIONAL SMALL BRUISES AND PETECHIAE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	INTERMITTENT HEADACHE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	INTERMITTENT FATIGUE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	TRAUMATIC BRAIN INJURY	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	INTERMITTENT HEARTBURN	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	INTERMITTENT ACNE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	AUTOIMMUNE HEMOLYTIC ANEMIA	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	RASH	[redacted]	合併
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	APPENDECTOMY	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	OVARIAN CYST NOS	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	SKIN BLEEDING	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	FATIGUE	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	OSTEOPOROSIS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	MYELOFIBROSIS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	TOTAL ABDOMINAL HYSTERECTOMY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	WHITE COAT HYPERTENSION	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	COLONIC RESECTION FOR COLORECTAL CANCER STAGE 2	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	COLON CANCER	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	SUBDURAL HEMATOMA (IN CONTEXT OF SEVERE THROMBOCYTOPENIA	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	MONOCLONAL GAMMOPATHY OF UNKNOWN SIGNIFICANCE	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	IRON DEFICIENCY	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HEMORRHOIDAL BLEEDING	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	VARICOSE VEINS	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	DISCOID LUPUS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	GALL BLADDER REMOVED	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	SKIN RASH	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	EPIGASTRIC PAIN	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	BILATERAL HIP REPLACEMENT	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	BILATERAL HIP REPLACEMENT	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	CROHNS DISEASE	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HERNIA REPAIR	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	GOUT	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HYPERTENSION	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	PREVIOUS ALCOHOL EXCESS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	CHRONIC KIDNEY DISEASE:STAGE THREE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	DEPRESSION	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	KNEE PAIN	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	ACID REFLUX	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	TENNIS ELBOW	[redacted]	既往

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[redacted]	Immunoglobulin G (g/L)	JOINT PAIN DUE TO ITP	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	BACK PAIN	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	CHRONIC IRON DEFICIENCY	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	ENDOMETRIAL ABLATION	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	COELIAC DISEASE	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	OSTEOPOROSIS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	ARTHRITIS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	UPPER RESPIRATORY TRACT INFECTION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	SYSTEMIC LUPUS ERYTHEMATOSIS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	HYPERCHOLESTEROLAEMIA	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	DIVERTICULAR DISEASE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	GASTRO-OESOPHAGEAL REFLUX DISEASE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	OSTEOARTHRITIS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	DRY EYES	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	VITAMIN D DEFICIENCY	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	MODERATE, CHRONIC BILATERAL VENOUS ECZEMA	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	EXTRACTION OF LENS, ASPIRATION OF CATARACT AND INSERTION OF ARTIFICIAL LENS (LEFT)	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	LAPAROSCOPIC CHOLECYSTECTOMY	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	EXTRACTION OF LENS, ASPIRATION OF CATARACT AND INSERTION OF ARTIFICIAL LENS (RIGHT)	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	SOLAR KERATOSES	[redacted]	合併
[redacted]	Lymphocytes (10^9/L), Leukocytes (10^9/L)	HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	AMPUTATION - TRAUMA	[redacted]	既往
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ARTERIAL HYPERTENSION	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	HYPERTENSION	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	CATARACTA SENILIS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	ADRENAL ADENOMA	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	ARTERIAL HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	DIABETES MELLITUS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	HYPERTRIGLICERYDEMIA	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	MYOMA.	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	CARIES	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	FRACTURE OF RIGHT CLAVICULAR BONE	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	OBESITAS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	WARTS OF TRUNK AND UPPER LIMBS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	ARTERIAL HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	LEFT LOWER LIMB THROMBOSIS	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	DIABETES	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	FATTY LIVER	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	LIPID DISORDERS	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	ARTERIAL HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	DEPRESSION	[redacted]	既往
[redacted]	Immunoglobulin G (g/L), Lymphocytes (10^9/L)	ABDOMINAL OBESITY	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	POLYPOSIS COLON	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	HYDROCELE RIGHT TESTICLE	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	CHRONIC ATRIAL FIBHRILATION;	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	HYPERTENSION	[redacted]	合併

被験者番号	該当した異常低値	病歴名	開始日	区分 （合併/既往）
[redacted]	Immunoglobulin G (g/L)	INTRACEREBRAL BLEEDING IN THE LEFT BRAIN HEMISPHERE	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	INFECTION OF MIDDLE EAR	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	ACUTE PANCREATITIS	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	APPENDIX REMOVAL	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	CONTINUES HEADACHES		合併
[redacted]	Lymphocytes (10^9/L)	HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	DIABETES MELLITUS	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	OPEN-ANGLE GLAUCOMA	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	ARTERIAL HYPERTENSION GRADE 1	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	PAIN MUSCLE	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	TONSILECTOMY	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	HEMANGIOMAS OF LIVER	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	HYPOTHYROIDISM	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	HYPERTENSION	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	DIABETES	[redacted]	合併
[redacted]	Immunoglobulin G (g/L)	CHOLECYSTECTOMY	[redacted]	既往
[redacted]	Immunoglobulin G (g/L)	THROMBOCYTOPENIA	[redacted]	既往
[redacted]	Lymphocytes (10^9/L)	ARTERIAL HYPERTENSION	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	OBESITY	[redacted]	合併
[redacted]	Lymphocytes (10^9/L)	TROMBOCYTOPENIA (ON 14 JAN PLATELET =14)	[redacted]	合併

（Source: 1.13.3-10, 付録 C-02-①-11）

表 2.7.4.9-155 Summary of Clinical Laboratory Results by Time (Hematology) – Safety Population – D4300-022 study

Parameter: LEUKOCYTES (10^9/L)

Time Point	N	Mean	(Std Dev)	Median	Range	Number of Subjects		
						Low	WNL	High
SCREENING	18	9.489	(3.7780)	8.300	3.90 - 20.90	0	15	3
BASELINE	18	8.234	(1.8647)	8.355	4.68 - 11.42	0	17	1
WEEK 1	18	7.932	(2.5145)	7.285	3.86 - 14.30	0	16	2
WEEK 2	17	7.308	(2.1141)	6.610	4.90 - 12.93	0	16	1
WEEK 3	15	6.314	(1.8559)	6.330	3.10 - 10.42	1	14	0
WEEK 4	16	6.736	(2.9249)	6.045	3.46 - 14.45	0	14	2
WEEK 5	12	6.006	(1.8095)	6.545	2.74 - 8.97	1	11	0
WEEK 6	15	5.859	(1.6025)	5.870	2.80 - 8.34	1	14	0
WEEK 7	13	5.872	(2.1672)	5.200	3.11 - 8.77	1	12	0
WEEK 8	13	6.255	(2.6388)	6.890	2.05 - 11.74	2	10	1
WEEK 9	13	6.552	(2.2763)	5.830	3.97 - 11.51	0	12	1
WEEK 10	12	6.249	(2.2536)	6.115	3.19 - 9.65	1	11	0
WEEK 11	10	6.054	(1.7213)	6.425	3.80 - 9.00	0	10	0
WEEK 12	10	6.174	(1.4984)	5.795	3.53 - 8.70	0	10	0
WEEK 14	11	6.870	(1.9300)	6.290	3.83 - 9.73	0	11	0
WEEK 16	9	6.678	(2.4394)	5.560	4.51 - 12.18	0	8	1
WEEK 18	11	6.438	(1.2466)	6.530	3.63 - 7.99	0	11	0
WEEK 20	10	6.525	(1.4066)	6.715	3.40 - 8.63	0	10	0
WEEK 22	9	6.692	(1.3942)	6.910	4.15 - 8.94	0	9	0
WEEK 24	7	7.446	(1.5297)	7.990	4.07 - 8.45	0	7	0
MONTH 7	11	6.552	(1.8190)	5.600	3.69 - 9.57	0	11	0
MONTH 8	11	6.627	(2.0634)	6.080	3.56 - 10.09	0	11	0
MONTH 9	11	6.532	(1.5527)	6.310	4.00 - 9.23	0	11	0
MONTH 10	10	6.950	(1.9023)	6.485	4.45 - 9.79	0	10	0
MONTH 11	10	6.659	(1.9243)	7.130	3.13 - 9.85	1	9	0
MONTH 12	10	6.276	(1.5049)	6.115	3.79 - 9.10	0	10	0
MONTH 13	8	7.190	(2.6995)	6.600	3.61 - 12.30	0	7	1
MONTH 14	10	6.492	(2.0258)	6.330	3.45 - 9.80	0	10	0
MONTH 15	8	6.415	(2.3212)	6.200	3.81 - 10.16	0	8	0
MONTH 16	7	6.626	(2.0940)	6.270	3.89 - 10.30	0	7	0
MONTH 17	8	7.175	(2.1040)	7.380	4.14 - 10.52	0	8	0
MONTH 18	7	6.984	(1.7189)	7.010	3.84 - 9.21	0	7	0
MONTH 19	8	8.023	(2.6827)	7.750	3.59 - 12.49	0	7	1
MONTH 20	7	6.256	(1.4841)	6.430	3.53 - 7.91	0	7	0
MONTH 21	8	7.649	(2.6468)	7.585	3.52 - 10.90	0	8	0
MONTH 22	8	8.093	(3.0380)	7.915	3.86 - 12.85	0	7	1
MONTH 23	8	7.318	(1.9373)	7.930	4.27 - 9.88	0	8	0
MONTH 24	7	7.110	(1.5283)	6.560	5.44 - 8.92	0	7	0
MONTH 25	8	6.780	(2.0698)	7.980	4.06 - 8.63	0	8	0
MONTH 26	7	8.483	(2.6915)	8.590	3.97 - 12.14	0	6	1
MONTH 27	7	6.174	(2.2684)	7.350	3.10 - 8.80	2	5	0
MONTH 28	6	8.037	(6.2381)	5.980	2.68 - 19.56	1	4	1
MONTH 29	6	6.170	(2.6361)	5.375	3.48 - 10.36	0	6	0
MONTH 30	6	6.473	(2.6765)	6.675	3.26 - 9.83	1	5	0
MONTH 31	5	8.348	(4.7905)	6.000	4.14 - 15.34	0	3	2
MONTH 32	5	5.624	(2.0235)	5.740	2.98 - 8.26	1	4	0
MONTH 33	5	5.860	(1.6981)	6.200	3.65 - 7.58	0	5	0
MONTH 34	5	7.276	(2.1040)	7.270	4.40 - 10.03	0	5	0
MONTH 35	5	6.164	(2.5186)	6.760	3.41 - 9.50	0	5	0
MONTH 36	5	6.232	(2.9116)	6.690	3.23 - 9.60	2	3	0
MONTH 37	4	6.825	(2.7566)	7.305	3.09 - 9.60	1	3	0
MONTH 38	2	7.940	(0.7920)	7.940	7.38 - 8.50	0	2	0
MONTH 39	2	5.030	(3.7760)	5.030	2.36 - 7.70	1	1	0
MONTH 40	1	9.010		9.010	9.01 - 9.01	0	1	0
FOLLOW-UP	6	7.630	(3.7051)	6.820	3.46 - 12.13	0	4	2

Note: Low = Number of patients with a value below lower limit of normal. WNL = Number of patients with a value within the limits of normal range. High = Number of patients with a value above upper limit of normal.

Parameter: NEUTROPHILS (10^9/L)

Time Point	N	Mean	(Std Dev)	Median	Range	Number of Subjects		
						Low	WNL	High
SCREENING	18	6.719	(3.7140)	5.100	1.90 - 16.90	0	11	7
BASELINE	18	5.134	(1.9024)	4.740	2.40 - 9.26	0	15	3
WEEK 1	18	4.703	(2.4232)	4.385	1.41 - 9.90	3	14	1
WEEK 2	16	4.224	(2.2795)	3.925	1.04 - 9.26	1	13	2
WEEK 3	15	3.398	(1.6071)	3.060	0.90 - 5.90	2	13	0
WEEK 4	16	4.251	(2.9502)	3.975	0.80 - 11.04	3	11	2
WEEK 5	11	3.095	(1.6709)	3.100	0.87 - 5.39	4	7	0
WEEK 6	14	3.126	(1.6323)	3.065	0.70 - 5.80	3	11	0
WEEK 7	13	3.165	(1.9473)	2.370	1.06 - 7.00	3	10	0
WEEK 8	13	3.445	(2.1210)	3.040	1.33 - 8.85	3	9	1
WEEK 9	13	3.486	(1.9398)	2.560	1.40 - 7.93	2	10	1
WEEK 10	12	3.280	(1.8318)	3.235	0.83 - 6.14	4	8	0
WEEK 11	10	3.273	(1.5336)	3.575	1.54 - 6.07	3	7	0
WEEK 12	10	3.126	(1.2442)	3.405	1.07 - 4.79	2	8	0
WEEK 14	11	3.566	(1.4677)	3.490	1.21 - 5.68	2	9	0
WEEK 16	9	3.462	(1.7216)	3.040	1.15 - 6.44	2	7	0
WEEK 18	11	3.500	(1.6131)	3.230	1.69 - 6.60	2	9	0
WEEK 20	10	3.608	(1.0769)	3.810	1.60 - 5.10	1	9	0
WEEK 22	9	3.707	(1.4648)	3.250	1.90 - 6.20	0	9	0
WEEK 24	7	4.684	(1.1903)	4.760	2.86 - 6.26	0	7	0
MONTH 7	10	3.634	(1.6661)	3.145	1.71 - 6.80	1	9	0
MONTH 8	10	4.054	(1.9162)	4.035	1.40 - 7.95	1	8	1
MONTH 9	10	3.625	(1.6109)	3.930	1.35 - 5.91	2	8	0
MONTH 10	10	3.971	(1.9335)	4.220	1.28 - 7.17	1	9	0
MONTH 11	10	3.742	(1.6798)	3.490	1.50 - 6.97	2	8	0
MONTH 12	9	3.414	(1.4309)	3.800	1.19 - 5.32	2	7	0
MONTH 13	8	4.121	(2.9068)	4.020	1.07 - 10.50	1	6	1
MONTH 14	10	3.801	(1.8365)	3.435	1.06 - 6.80	2	8	0
MONTH 15	8	3.761	(2.0116)	3.025	1.28 - 6.70	1	7	0
MONTH 16	7	4.089	(2.2284)	3.610	1.46 - 8.10	1	5	1
MONTH 17	8	3.740	(1.7467)	3.550	1.60 - 6.79	1	7	0
MONTH 18	6	3.933	(1.6111)	3.975	1.99 - 6.25	0	6	0
MONTH 19	8	4.961	(2.5482)	4.620	2.10 - 10.02	0	7	1
MONTH 20	6	3.615	(1.3419)	3.975	1.81 - 5.24	0	6	0
MONTH 21	8	4.603	(2.0862)	4.815	1.30 - 7.70	1	7	0
MONTH 22	8	4.953	(2.2188)	5.405	1.70 - 7.35	1	7	0
MONTH 23	8	4.143	(1.6217)	4.400	2.10 - 6.10	0	8	0
MONTH 24	7	4.121	(1.4651)	3.730	2.30 - 6.13	0	7	0
MONTH 25	8	3.880	(2.0534)	4.900	0.79 - 5.87	2	6	0
MONTH 26	7	5.536	(2.4867)	5.360	1.23 - 8.98	1	5	1
MONTH 27	7	3.366	(1.8883)	4.200	1.20 - 5.40	3	4	0
MONTH 28	6	5.393	(6.2124)	2.880	1.31 - 17.42	3	2	1
MONTH 29	6	3.433	(2.4951)	3.000	1.13 - 7.65	2	4	0
MONTH 30	6	3.222	(2.3461)	3.150	0.95 - 5.53	3	3	0
MONTH 31	5	5.564	(5.0324)	3.100	1.19 - 13.30	1	2	2
MONTH 32	5	2.856	(1.7495)	1.820	1.60 - 5.59	2	3	0
MONTH 33	5	2.972	(1.1925)	2.970	1.35 - 4.69	1	4	0
MONTH 34	5	3.828	(1.6262)	3.610	2.34 - 6.53	0	5	0
MONTH 35	5	3.542	(2.2656)	3.140	1.18 - 7.30	1	4	0
MONTH 36	5	3.196	(2.1442)	3.070	1.16 - 6.70	1	4	0
MONTH 37	4	3.818	(2.4029)	3.065	1.84 - 7.30	0	4	0
MONTH 38	2	4.545	(1.3506)	4.545	3.59 - 5.50	0	2	0
MONTH 39	2	3.370	(3.0123)	3.370	1.24 - 5.50	1	1	0
MONTH 40	1	5.720		5.720	5.72 - 5.72	0	1	0
FOLLOW-UP	6	4.988	(2.5313)	4.535	2.03 - 8.33	0	5	1

Note: Low = Number of patients with a value below lower limit of normal. WNL = Number of patients with a value within the limits of normal range. High = Number of patients with a value above upper limit of normal.

Parameter: LYMPHOCYTES (10^9/L)

Time Point	N	Mean	(Std Dev)	Median	Range	Number of Subjects		
						Low	WNL	High
SCREENING	18	2.032	(1.0602)	1.750	0.50 - 4.30	2	15	1
BASELINE	18	2.187	(0.9557)	2.060	0.90 - 4.08	2	14	2
WEEK 1	18	2.643	(1.2071)	2.245	0.90 - 5.26	1	15	2
WEEK 2	16	2.453	(1.3244)	2.130	0.44 - 5.52	1	13	2
WEEK 3	15	2.319	(1.1291)	1.890	1.00 - 5.09	0	14	1
WEEK 4	16	1.956	(1.0061)	1.690	0.76 - 4.75	1	14	1
WEEK 5	11	2.549	(1.0719)	2.500	0.99 - 4.63	1	9	1
WEEK 6	14	2.269	(0.9240)	2.000	1.17 - 4.40	0	13	1
WEEK 7	13	2.191	(1.0545)	1.660	1.24 - 4.68	0	12	1
WEEK 8	13	2.210	(1.1197)	2.110	0.40 - 4.25	2	10	1
WEEK 9	13	2.402	(1.0358)	1.960	1.02 - 4.50	0	11	2
WEEK 10	12	2.348	(0.9011)	2.240	1.05 - 3.91	0	12	0
WEEK 11	10	2.154	(0.8017)	1.830	1.48 - 4.01	0	9	1
WEEK 12	10	2.389	(0.9304)	2.170	1.30 - 4.10	0	9	1
WEEK 14	11	2.637	(1.0754)	2.540	1.12 - 4.43	0	9	2
WEEK 16	9	2.627	(1.2602)	2.570	1.15 - 5.05	0	8	1
WEEK 18	11	2.320	(0.9930)	2.330	0.80 - 4.33	1	9	1
WEEK 20	10	2.358	(0.9642)	2.315	1.00 - 4.14	0	9	1
WEEK 22	9	2.423	(1.0753)	1.950	1.17 - 4.28	0	8	1
WEEK 24	7	2.096	(0.9386)	1.850	0.88 - 3.80	1	6	0
MONTH 7	10	2.186	(0.9333)	1.845	1.17 - 3.96	0	10	0
MONTH 8	10	2.174	(0.9141)	2.030	0.92 - 4.02	1	8	1
MONTH 9	10	2.300	(0.8847)	2.235	0.97 - 4.08	1	8	1
MONTH 10	10	2.399	(1.0680)	2.205	1.21 - 4.07	0	9	1
MONTH 11	10	2.299	(0.9562)	2.055	1.29 - 4.00	0	10	0
MONTH 12	9	2.258	(1.1622)	1.830	0.97 - 4.55	1	7	1
MONTH 13	8	2.373	(1.4372)	1.730	1.00 - 4.98	0	7	1
MONTH 14	10	2.108	(0.8544)	1.755	1.33 - 4.15	0	9	1
MONTH 15	8	2.053	(0.6180)	2.015	1.37 - 2.93	0	8	0
MONTH 16	7	1.931	(0.5887)	1.800	1.32 - 3.19	0	7	0
MONTH 17	8	2.696	(1.1699)	2.110	1.68 - 4.79	0	7	1
MONTH 18	6	2.403	(0.9973)	2.115	1.16 - 3.70	0	6	0
MONTH 19	8	2.418	(0.9836)	2.120	1.10 - 4.08	0	7	1
MONTH 20	6	2.005	(0.9171)	1.740	0.96 - 3.29	1	5	0
MONTH 21	8	2.319	(1.0974)	2.015	1.00 - 4.45	0	7	1
MONTH 22	8	2.345	(1.0629)	2.075	1.10 - 4.38	0	7	1
MONTH 23	8	2.424	(1.1668)	1.880	1.17 - 4.20	0	6	2
MONTH 24	7	2.351	(0.6807)	2.110	1.51 - 3.32	0	7	0
MONTH 25	8	2.210	(0.7742)	1.975	1.34 - 3.33	0	8	0
MONTH 26	7	2.220	(1.2290)	1.920	0.69 - 4.41	1	5	1
MONTH 27	7	2.167	(0.9260)	1.990	1.00 - 3.54	0	7	0
MONTH 28	6	2.025	(0.8992)	1.920	0.98 - 3.09	1	5	0
MONTH 29	6	2.108	(0.7920)	2.225	1.05 - 2.90	0	6	0
MONTH 30	6	2.218	(1.3710)	2.170	0.18 - 3.99	1	5	0
MONTH 31	5	2.130	(0.7929)	2.300	1.20 - 3.00	0	5	0
MONTH 32	5	2.246	(0.9701)	2.580	0.88 - 3.41	1	4	0
MONTH 33	5	2.278	(0.8983)	2.050	1.24 - 3.53	0	5	0
MONTH 34	5	2.814	(1.2306)	2.340	1.68 - 4.88	0	4	1
MONTH 35	5	2.066	(1.0485)	2.010	0.85 - 3.44	1	4	0
MONTH 36	5	2.510	(1.2611)	2.100	1.19 - 4.48	0	4	1
MONTH 37	4	2.365	(1.3541)	2.365	0.95 - 3.78	1	3	0
MONTH 38	2	2.985	(0.9687)	2.985	2.30 - 3.67	0	2	0
MONTH 39	2	1.140	(0.3677)	1.140	0.88 - 1.40	1	1	0
MONTH 40	1	2.290		2.290	2.29 - 2.29	0	1	0
FOLLOW-UP	6	1.783	(1.1259)	1.480	0.73 - 3.65	2	4	0

Note: Low = Number of patients with a value below lower limit of normal. WNL = Number of patients with a value within the limits of normal range. High = Number of patients with a value above upper limit of normal.
（Source: 1.13.3-10, 付録 C-02-①-1）

表 2.7.4.9-156　　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（D4300-022 試験）

被験者番号	該当した異常低値	投与量	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	発現日	転帰日
[redacted]	LYMPHOCYTES	R788 75 MG BID	[redacted]	M	WHITE	EPISTAXIS	MILD	N	POSSIBLY RELATED	Day 15*	Day 25*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EPISTAXIS	MILD	N	UNLIKELY RELATED	Day 15*	Day 25*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	STOMATITIS	MILD	N	POSSIBLY RELATED	Day 15*	Day 25*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD ALKALINE PHOSPHATASE INCREASED	MILD	N	POSSIBLY RELATED	Day 25*	Day 39*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 25*	Day 39*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 25*	Day 86*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 25*	Day 52*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	MUSCULOSKELETAL PAIN	SEVERE	N	POSSIBLY RELATED	Day 37*	Day 39*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BACK PAIN	MILD	N	POSSIBLY RELATED	Day 39*	Day 46*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	PAIN	MILD	N	NOT RELATED	Day 39*	Day 52*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	STOMATITIS	MILD	N	POSSIBLY RELATED	Day 39*	Day 46*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	NECK PAIN	MILD	N	POSSIBLY RELATED	Day 39*	Day 46*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EPISTAXIS	MILD	N	POSSIBLY RELATED	Day 39*	Day 46*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD ALKALINE PHOSPHATASE INCREASED	MILD	N	POSSIBLY RELATED	Day 46*	Day 52*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 46*	Day 52*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	MUSCULOSKELETAL PAIN	MILD	N	POSSIBLY RELATED	Day 46*	Day 52*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD ALKALINE PHOSPHATASE INCREASED	MILD	N	POSSIBLY RELATED	Day 57*	Day 57*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 66*	Day 66*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 66*	Day 71*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD ALKALINE PHOSPHATASE INCREASED	MILD	N	POSSIBLY RELATED	Day 71*	Day 78*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 71*	Day 78*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	STOMATITIS	MILD	N	UNLIKELY RELATED	Day 71*	Day 78*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	STOMATITIS	MILD	N	POSSIBLY RELATED	Day 71*	Day 71*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	PETECHIAE	MILD	N	POSSIBLY RELATED	Day 78*	Day 78*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD ALKALINE PHOSPHATASE INCREASED	MILD	N	POSSIBLY RELATED	Day 84*	Day 86*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 92*	Day 92*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 92*	Day 99*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 92*	Day 106*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 92*	Day 99*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	GINGIVAL BLEEDING	MILD	N	POSSIBLY RELATED	Day 92*	Day 106*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD BLISTER	MILD	N	POSSIBLY RELATED	Day 106*	Day 113*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 106*	Day 106*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 106*	Day 123*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	SKIN DISCOLOURATION	MILD	N	POSSIBLY RELATED	Day 106*	Day 113*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD BLISTER	MILD	N	POSSIBLY RELATED	Day 106*	Day 113*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	CONSTIPATION	MILD	N	POSSIBLY RELATED	Day 134*	Day 165*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 134*	Day 165*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 134*	Day 165*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	RASH PAPULAR	MODERATE	N	POSSIBLY RELATED	Day 162*	Day 192*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD ALKALINE PHOSPHATASE INCREASED	MILD	N	POSSIBLY RELATED	Day 165*	Day 178*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	RASH PAPULAR	MILD	N	POSSIBLY RELATED	Day 168*	Day 178*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 178*	Day 426*

＊新薬承認情報提供時に置き換え

被験者番号	該当した異常低値	投与量	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	発現日	転帰日
[redacted]	LYMPHOCYTES	R788 75 MG BID	[redacted]	M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 178*	Day 332*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	CONSTIPATION	MILD	N	POSSIBLY RELATED	Day 192*	Day 218*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD PRESSURE INCREASED	MILD	N	UNLIKELY RELATED	Day 192*	Day 218*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	MOUTH HAEMORRHAGE	MILD	N	UNLIKELY RELATED	Day 192*	Day 218*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ECCHYMOSIS	MODERATE	N	POSSIBLY RELATED	Day 218*	Day 247*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EPISTAXIS	MODERATE	N	POSSIBLY RELATED	Day 275*	Day 277*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	GINGIVAL BLEEDING	SEVERE	N	POSSIBLY RELATED	Day 276*	Day 277*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	GINGIVAL BLEEDING	SEVERE	N	POSSIBLY RELATED	Day 276*	Day 277*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EPISTAXIS	MILD	N	POSSIBLY RELATED	Day 277*	Day 277*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD PRESSURE INCREASED	MILD	N	POSSIBLY RELATED	Day 287*	Day 303*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	DYSURIA	MILD	N	POSSIBLY RELATED	Day 297*	Day 303*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	URINE ABNORMALITY	MILD	N	POSSIBLY RELATED	Day 297*	Day 303*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	OSTEOMYELITIS	MODERATE	N	NOT RELATED	Day 313*	Day 332*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ECCHYMOSIS	MILD	N	POSSIBLY RELATED	Day 332*	Day 360*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EYE HAEMORRHAGE	MILD	N	POSSIBLY RELATED	Day 332*	Day 360*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	CONSTIPATION	MILD	N	UNLIKELY RELATED	Day 360*	Day 360*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EYE HAEMORRHAGE	MILD	N	POSSIBLY RELATED	Day 465*	Day 465*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	OCULAR HYPERAEMIA	MILD	N	POSSIBLY RELATED	Day 608*	Day 639*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	HERPES ZOSTER	MODERATE	N	UNLIKELY RELATED	Day 613*	Day 639*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	CONSTIPATION	MILD	N	UNLIKELY RELATED	Day 703*	Day 1086*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	INFLUENZA	MODERATE	N	POSSIBLY RELATED	Day 703*	Day 748*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	HYPERTENSION	MODERATE	N	POSSIBLY RELATED	Day 708*	Day 722*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ECCHYMOSIS	MODERATE	N	UNLIKELY RELATED	Day 721*	Day 1127*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD BLISTER	MILD	N	UNLIKELY RELATED	Day 735*	Day 1127*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ARTHRALGIA	MILD	N	UNLIKELY RELATED	Day 735*	Day 737*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD UREA INCREASED	MILD	N	POSSIBLY RELATED	Day 750*	Day 799*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	PROTEIN TOTAL DECREASED	MILD	N	POSSIBLY RELATED	Day 771*	Day 799*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	FATIGUE	MILD	N	POSSIBLY RELATED	Day 771*	Day 773*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 771*	Day 866*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	MOUTH HAEMORRHAGE	MILD	N	NOT RELATED	Day 799*	Day 799*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ECCHYMOSIS	MILD	N	NOT RELATED	Day 799*	Day 799*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	STOMATITIS	MILD	N	POSSIBLY RELATED	Day 800*	Day 806*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	NECK PAIN	MODERATE	N	POSSIBLY RELATED	Day 846*	Day 890*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	RASH PRURITIC	MODERATE	N	POSSIBLY RELATED	Day 862*	Day 890*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	GOUT	MODERATE	N	POSSIBLY RELATED	Day 883*	Day 883*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	CONSTIPATION	MODERATE	N	POSSIBLY RELATED	Day 886*	Day 886*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	STOMATITIS	MILD	N	UNLIKELY RELATED	Day 887*	Day 892*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	CONTUSION	MILD	N	UNLIKELY RELATED	Day 890*	Day 937*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	PETECHIAE	MILD	N	UNLIKELY RELATED	Day 918*	Day 939*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	MUSCULOSKELETAL STIFFNESS	MILD	N	UNLIKELY RELATED	Day 939*	Day 941*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	ARTHRALGIA	MODERATE	N	UNLIKELY RELATED	Day 946*	Day 974*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	MUSCULOSKELETAL PAIN	SEVERE	N	UNLIKELY RELATED	Day 989*	Day 1002*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	PROSTATITIS	MODERATE	N	UNLIKELY RELATED	Day 1007*	Day 1031*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	BLOOD BLISTER	MILD	N	UNLIKELY RELATED	Day 1017*	Day 1080*
	LYMPHOCYTES	R788 75 MG BID		M	WHITE	EPISTAXIS	MILD	N	UNLIKELY RELATED	Day 1063*	Day 1063*

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被験者番号	該当した異常低値	投与量	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	発現日	転帰日
[redacted]	LYMPHOCYTES	R788 75 MG BID	7	M	WHITE	RASH	MODERATE	N	UNLIKELY RELATED	Day 1119*	Day 1127*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 1*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	HEART RATE INCREASED	MILD	N	POSSIBLY RELATED	Day 1*	Day 9*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	BLOOD BILIRUBIN INCREASED	MODERATE	N	POSSIBLY RELATED	Day 9*	Day 57*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	PAIN IN EXTREMITY	MODERATE	N	UNLIKELY RELATED	Day 22*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	EYE HAEMORRHAGE	MILD	N	POSSIBLY RELATED	Day 22*	Day 60*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	HEADACHE	MODERATE	N	POSSIBLY RELATED	Day 22*	Day 29*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	PETECHIAE	MILD	N	POSSIBLY RELATED	Day 22*	Day 52*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	TONGUE BLISTERING	MILD	N	POSSIBLY RELATED	Day 22*	Day 29*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	FATIGUE	MODERATE	N	POSSIBLY RELATED	Day 36*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	NAUSEA	MODERATE	N	POSSIBLY RELATED	Day 36*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	MUSCLE SPASMS	MODERATE	N	POSSIBLY RELATED	Day 45*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 57*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	BLOOD PRESSURE INCREASED	MODERATE	N	POSSIBLY RELATED	Day 57*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	EPISTAXIS	MILD	N	POSSIBLY RELATED	Day 57*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	VOMITING	MODERATE	N	POSSIBLY RELATED	Day 57*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	EYE HAEMORRHAGE	MODERATE	N	POSSIBLY RELATED	Day 60*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	SKIN HAEMORRHAGE	MODERATE	N	POSSIBLY RELATED	Day 60*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	7	M	WHITE	MUCOSAL HAEMORRHAGE	MODERATE	N	POSSIBLY RELATED	Day 60*	Day 65*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	OEDEMA PERIPHERAL	MODERATE	N	POSSIBLY RELATED	Day 1*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	PETECHIAE	MILD	N	POSSIBLY RELATED	Day 1*	Day 15*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	PURPURA	MILD	N	POSSIBLY RELATED	Day 1*	Day 15*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	HYPERTENSION	MILD	N	POSSIBLY RELATED	Day 15*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	VISION BLURRED	MILD	N	POSSIBLY RELATED	Day 70*	Day 93*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	POLLAKIURIA	MODERATE	N	POSSIBLY RELATED	Day 94*	Day 111*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	OEDEMA PERIPHERAL	MODERATE	N	POSSIBLY RELATED	Day 94*	Day 111*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	TONGUE DISORDER	MILD	N	POSSIBLY RELATED	Day 94*	Day 111*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	MUSCULOSKELETAL STIFFNESS	MILD	N	POSSIBLY RELATED	Day 94*	Day 111*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	PNEUMONIA	MODERATE	Y	NOT RELATED	Day 111*	Day 117*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	THROMBOSIS	MODERATE	N	UNLIKELY RELATED	Day 129*	Day 146*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	CHEST PAIN	MODERATE	N	POSSIBLY RELATED	Day 204*	Day 204*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	OEDEMA PERIPHERAL	MILD	N	POSSIBLY RELATED	Day 210*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	ERYTHEMA	MILD	N	POSSIBLY RELATED	Day 239*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	OEDEMA PERIPHERAL	MILD	N	POSSIBLY RELATED	Day 239*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	CATARACT	MODERATE	N	POSSIBLY RELATED	Day 260*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	ECCHYMOSIS	MILD	N	POSSIBLY RELATED	Day 267*	Day 323*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	HYPOACUSIS	MILD	N	UNLIKELY RELATED	Day 275*	Day 295*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	GOUT	MILD	N	POSSIBLY RELATED	Day 275*	Day 386*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	POLLAKIURIA	MILD	N	POSSIBLY RELATED	Day 275*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	POLLAKIURIA	MILD	N	POSSIBLY RELATED	Day 275*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	EYE PAIN	MILD	N	POSSIBLY RELATED	Day 289*	Day 295*
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	FAECAL INCONTINENCE	MILD	N	POSSIBLY RELATED	Day 323*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	BLOOD GLUCOSE INCREASED	MILD	N	POSSIBLY RELATED	Day 374*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	BLOOD UREA INCREASED	MILD	N	POSSIBLY RELATED	Day 394*	
	LYMPHOCYTES	R788 150 MG BID	8	M	WHITE	BLOOD CREATININE INCREASED	MILD	N	POSSIBLY RELATED	Day 394*	Day 409*

被験者番号	該当した異常低値	投与量	年齢（歳）	性別（M：男性、F：女性	人種	有害事象名（PT）	程度	重篤性（Y：重篤、N：非重篤）	因果関係	発現日	転帰日
[redacted]	LYMPHOCYTES	R788 150 MG BID	[redacted]	M	WHITE	BLOOD LACTATE DEHYDROGENASE INCREASED	MILD	N	POSSIBLY RELATED	Day 394*	
	LYMPHOCYTES	R788 150 MG BID		M	WHITE	ASPARTATE AMINOTRANSFERASE INCREASED	MILD	N	POSSIBLY RELATED	Day 409*	Day 436*
	LYMPHOCYTES	R788 150 MG BID		M	WHITE	RASH	MILD	N	NOT RELATED	Day 432*	
	LYMPHOCYTES	R788 150 MG BID		M	WHITE	PROTEIN TOTAL DECREASED	MILD	N	POSSIBLY RELATED	Day 436*	Day 445*
	LYMPHOCYTES	R788 150 MG BID		M	WHITE	SKIN EXFOLIATION	MILD	N	POSSIBLY RELATED	Day 456*	Day 479*
	LYMPHOCYTES	R788 150 MG BID		M	WHITE	LEFT VENTRICULAR DYSFUNCTION	MODERATE	N	UNLIKELY RELATED	Day 479*	
	LYMPHOCYTES	R788 150 MG BID		M	WHITE	TOOTH INFECTION	MODERATE	N	NOT RELATED		Day 136*

（Source: 1.13.3-10, 付録 C-02-①-2）

＊新薬承認情報提供時に置き換え

表 2.7.4.9-157　　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（D4300-022 試験）

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	容量・用法	投与開始日	投与終了日
[redacted]	LYMPHOCYTES	CANDESARTAN CILEXETIL	GENERAL CONMED	HIGH BLOOD PRESSURE	60 MG BID	19[redacted]	
	LYMPHOCYTES	CARVEDILOL	GENERAL CONMED	HIGH BLOOD PRESSURE	25 MG BID	19[redacted]	
	LYMPHOCYTES	HYDROCHLOROTHIAZIDE	GENERAL CONMED	HTN	25 MG QID	19[redacted]	
	LYMPHOCYTES	LOVASTATIN	GENERAL CONMED	HYPERLIPIDEMIA	20 MG BID	19[redacted]	
	LYMPHOCYTES	ZINC	GENERAL CONMED	DIETARY SUPPLEMENT	50 MG 1X	20[redacted]	
	LYMPHOCYTES	GOSERELIN	GENERAL CONMED	HORMONE THERAPY	5.6 MG	20[redacted]	
	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TREATMENT HISTORY	ITP	50 G	20[redacted]	20[redacted]
	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TRANSFUSION HISTORY			20[redacted]	
	LYMPHOCYTES	PLATELETS, HUMAN BLOOD	ITP TRANSFUSION HISTORY			20[redacted]	
	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TREATMENT HISTORY	ITP	50 G	20[redacted]	20[redacted]
	LYMPHOCYTES	PLATELETS, HUMAN BLOOD	ITP TRANSFUSION HISTORY			20[redacted]	
	LYMPHOCYTES	ANTIBIOTICS FOR TOPICAL USE /OLD CODE/	GENERAL CONMED	RED BUMPS ON CHEST	UNKNOWN	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	AMINOCAPROIC ACID	GENERAL CONMED	MOUTH BLEED	6 TABS 500 MG OR TABS PRN (4-6 HR)	20[redacted]	
	LYMPHOCYTES	IMMUNOGLOBULINS	GENERAL CONMED	ITP	100 CC	20[redacted]	20[redacted]
	LYMPHOCYTES	CLINDAMYCIN	GENERAL CONMED	INFECTION PROPHYLAXIS	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	CIPROFLOXACIN	GENERAL CONMED	DENTAL PROPHYLACTIC	500 MG BID	20[redacted]	20[redacted]
	LYMPHOCYTES	PLANTAGO OVATA HUSK	GENERAL CONMED	LAXATIVE FOR CONSTIPATION	1 TSP	20[redacted]	
	LYMPHOCYTES	PLANTAGO OVATA	GENERAL CONMED	CONSTIPATION	UNKNOWN	20[redacted]	20[redacted]
	LYMPHOCYTES	ERYTHROMYCIN	GENERAL CONMED	SHINGLES AROUND EYE	THIN LAYER	20[redacted]	20[redacted]
	LYMPHOCYTES	TOBRAMYCIN	GENERAL CONMED	CONJUNCTIVITIS	1 DROP	20[redacted]	20[redacted]
	LYMPHOCYTES	VALACICLOVIR HYDROCHLORIDE	GENERAL CONMED	SHINGLES AROUND EYE	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	ANTIBIOTICS	GENERAL CONMED	FLU	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	OTHER RESPIRATORY SYSTEM PRODUCTS	GENERAL CONMED	FLU	UNK	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	PENICILLIN NOS	GENERAL CONMED	FLU	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	AMLODIPINE	GENERAL CONMED	HYPERTENSION	5 MG	20[redacted]	
	LYMPHOCYTES	CALCIUM CITRATE	GENERAL CONMED	DIETARY SUPPLEMENT	1500 MG 1X	20[redacted]	
	LYMPHOCYTES	ERGOCALCIFEROL	GENERAL CONMED	NUTRITION	1200 UNITS 1X	20[redacted]	
	LYMPHOCYTES	IMMUNOGLOBULINS	GENERAL CONMED	ITP	UNKNOWN	20[redacted]	20[redacted]
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	NECK PAIN	5 MG	20[redacted]	20[redacted]
	LYMPHOCYTES	HYDROCODONE + PARACETAMOL	GENERAL CONMED	NECK PAIN	5 MG/325 MG	20[redacted]	20[redacted]
	LYMPHOCYTES	VITAMINS NOS	GENERAL CONMED	NUTRITION	1X	20[redacted]	
	LYMPHOCYTES	ASCORBIC ACID	GENERAL CONMED	NUTRITION	500 MG	20[redacted]	
	LYMPHOCYTES	OTHER ANTIPRURITICS /OLD CODE/	GENERAL CONMED	PRURITIC RASH	UNKNOWN	20[redacted]	20[redacted]
	LYMPHOCYTES	ANTIINFLAMMATORY/ANTIRHEUMATIC PRODUCTS	GENERAL CONMED	R. SHOULDER PAIN	SHOT	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	CIPROFLOXACIN	GENERAL CONMED	PROSTATITIS	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	AMOXICILLIN	GENERAL CONMED	DENTAL PROPHYLAXIS	250 MG QID X7 DAYS	20[redacted]	20[redacted]
	LYMPHOCYTES	BACITRACIN	GENERAL CONMED	RASH	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	RITUXIMAB	ITP TREATMENT HISTORY	ITP	UNK	20[redacted]	
	LYMPHOCYTES	PREDNISONE	ITP TREATMENT HISTORY	ITP	10 MG BID	20[redacted]	
	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TREATMENT HISTORY	ITP	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	EPOETIN ALFA	ITP TRANSFUSION HISTORY			20[redacted]	

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	容量・用法	投与開始日	投与終了日
[redacted]	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TRANSFUSION HISTORY			20[redacted]	
	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TRANSFUSION HISTORY			20[redacted]	
	LYMPHOCYTES	PALONOSETRON	GENERAL CONMED	ANTINAUSEA	.25 MG IV	20[redacted]	20[redacted]
	LYMPHOCYTES	AMINOCAPROIC ACID	GENERAL CONMED	BLEEDS/PRN	500 TID	20[redacted]	
	LYMPHOCYTES	PALONOSETRON	GENERAL CONMED	ANTINAUSEA	.25 MG IV	20[redacted]	20[redacted]
	LYMPHOCYTES	PALONOSETRON HYDROCHLORIDE	GENERAL CONMED	ANTINAUSEA	PRN	20[redacted]	
	LYMPHOCYTES	PALONOSETRON	GENERAL CONMED	ANTIEMETICS	.25 MG IV	20[redacted]	20[redacted]
	LYMPHOCYTES	DIPHENHYDRAMIN + PARACETAMOL + PHENYLPROPANOLAMIN	GENERAL CONMED	PRE MEDS FOR PRE-IVIG TREATMENT	25 MG PO	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	IMMUNOGLOBULINS	GENERAL CONMED	ITP	1,000 GRAMS	20[redacted]	20[redacted]
	LYMPHOCYTES	PALONOSETRON	GENERAL CONMED	ANTI-NAUSEA	.25 MG IV	20[redacted]	20[redacted]
	LYMPHOCYTES	METHYLPREDNISOLONE SODIUM SUCCINATE	GENERAL CONMED	PRE MEDS FOR PRE-IVIG TREATMENT	1 GRAM IV	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	PARACETAMOL	GENERAL CONMED	PRE MEDS FOR PRE-IVIG TREATMENT	PO	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	PALONOSETRON HYDROCHLORIDE	GENERAL CONMED	ANTI NAUSEA; ANTIEMETIC	30 CC	20[redacted]	20[redacted]
	LYMPHOCYTES	PALONOSETRON	GENERAL CONMED	ANTINAUSEA; ANTIEMETIC	.25 MG IV	20[redacted]	20[redacted]
	LYMPHOCYTES	DIPHENHYDRAMIN + PARACETAMOL + PHENYLPROPANOLAMIN	GENERAL CONMED	PRE MEDS FOR PRE-IVIG TREATMENT	25 MG PO	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	IMMUNOGLOBULINS	GENERAL CONMED	ITP	80 GRAMS IV	20[redacted]	20[redacted]
	LYMPHOCYTES	METHYLPREDNISOLONE SODIUM SUCCINATE	GENERAL CONMED	PRE MEDS FOR PRE-IVIG TREATMENT	1 GRAM IV	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	PARACETAMOL	GENERAL CONMED	PRE MEDS FOR PRE-IVIG TREATMENT	650 MG PO	20[redacted]	20[redacted]
[redacted]	LYMPHOCYTES	ZOLPIDEM TARTRATE	GENERAL CONMED	SLEEP DISORDER	10 MG		
	LYMPHOCYTES	DUTASTERIDE	GENERAL CONMED	IMPROVE URINARY FLOW	.5 MG		20[redacted]
	LYMPHOCYTES	CARVEDILOL	GENERAL CONMED	HEART MED	6.25 MG BID		
	LYMPHOCYTES	LOVASTATIN	GENERAL CONMED	HYPERCHOLESTEROLEMIA	20 MG/DAILY		
	LYMPHOCYTES	METFORMIN	GENERAL CONMED	DIABETES	500 MG/DAILY		
	LYMPHOCYTES	MACROGOL	GENERAL CONMED	LAXATIVE	PRN		
	LYMPHOCYTES	MORPHINE SULFATE	GENERAL CONMED	GENERALIZED PAIN	15 MG BID		
	LYMPHOCYTES	GABAPENTIN	GENERAL CONMED	NERVE PAIN	UNKNOWN		
	LYMPHOCYTES	OXYCODONE	GENERAL CONMED	GENERALIZED PAIN	PRN/5 MG		
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	10 MG/DAY		
	LYMPHOCYTES	OMEPRAZOLE	GENERAL CONMED	HEART BURN	20 MG/DAILY		20[redacted]
	LYMPHOCYTES	METOCLOPRAMIDE	GENERAL CONMED	HEARTBURN	10 MG PRN		20[redacted]
	LYMPHOCYTES	VINCRISTINE	ITP TREATMENT HISTORY	ITP	UNK		
	LYMPHOCYTES	ONDANSETRON HYDROCHLORIDE	GENERAL CONMED	PREVIOUS NAUSEA DUE TO RIGEL	2 MG BID		
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	40 MG/DAY	20[redacted]	20[redacted]
	LYMPHOCYTES	INSULIN	GENERAL CONMED	DIABETES	8 UNITS	20[redacted]	20[redacted]
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	20 MG/DAY	20[redacted]	20[redacted]
	LYMPHOCYTES	INSULIN	GENERAL CONMED	DIABETES	5 UNITS	20[redacted]	20[redacted]
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	15 MG/DAY	20[redacted]	20[redacted]
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	10 MG/DAY	20[redacted]	20[redacted]
	LYMPHOCYTES	ACETYLSALICYLIC ACID	GENERAL CONMED	CARDIAC PROPHYLAXIS	8/MG/DAY	20[redacted]	20[redacted]
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	5 MG/DAY	20[redacted]	20[redacted]
	LYMPHOCYTES	ATENOLOL	GENERAL CONMED	HYPERTENSION	25 MG/DAY	20[redacted]	20[redacted]

被験者番号	該当した異常低値	薬剤名	投与区分	投与理由	容量・用法	投与開始日	投与終了日
[redacted]	LYMPHOCYTES	FUROSEMIDE	GENERAL CONMED	HYPERTENSION	20 MG	20[redacted]	
	LYMPHOCYTES	PENICILLIN NOS	GENERAL CONMED	PROPHYLAXIS ANTIBIOTIC	UNK	20[redacted]	20[redacted]
	LYMPHOCYTES	CLOBETASOL	GENERAL CONMED	SKIN RASH	5%	20[redacted]	
	LYMPHOCYTES	METOPROLOL	GENERAL CONMED	HYPERTENSION	50 MG	20[redacted]	
	LYMPHOCYTES	ELTROMBOPAG	GENERAL CONMED	ITP	50 MG	20[redacted]	
	LYMPHOCYTES	GLIMEPIRIDE	GENERAL CONMED	DIABETES	2 MG/DAY		
	LYMPHOCYTES	INSULIN	GENERAL CONMED	DIABETES	7 UNITS		20[redacted]
	LYMPHOCYTES	IMMUNOGLOBULINS	ITP TREATMENT HISTORY	ITP	UNK		
	LYMPHOCYTES	LOSARTAN POTASSIUM	GENERAL CONMED	HYPERTENSION	125 MG/DAY		
	LYMPHOCYTES	PREDNISONE	GENERAL CONMED	ITP	60 MG/DAY		20[redacted]
	LYMPHOCYTES	RITUXIMAB	ITP TREATMENT HISTORY	ITP	UNK		
	LYMPHOCYTES	STEROID ANTIBACTERIALS /OLD CODE/	ITP TREATMENT HISTORY	ITP	UNK		
	LYMPHOCYTES	TERAZOSIN HYDROCHLORIDE	GENERAL CONMED	HYPERTENSION	2 MG/DAY		
	LYMPHOCYTES	IMMUNOGLOBULIN HUMAN ANTI-RH	ITP TREATMENT HISTORY	ITP	UNK		
	LYMPHOCYTES	SIMVASTATIN	GENERAL CONMED	HYPERLIPIDEMIA	5 MG/DAY		

（Source: 1.13.3-10，付録 C-02-①-3）

表 2.7.4.9-158　R788 の投与中に白血球数、リンパ球数及び IgG の異常低値が認められた被験者の一覧表（D4300-022 試験）

被験者番号		該当した異常低値	病歴名（PT）
[redacted]		LYMPHOCYTES	HYPERLIPIDAEMIA
		LYMPHOCYTES	CARDIAC FAILURE
		LYMPHOCYTES	HYPERTENSION
		LYMPHOCYTES	PETECHIAE
		LYMPHOCYTES	CONTUSION
		LYMPHOCYTES	PROSTATE CANCER
		LYMPHOCYTES	LYMPHOMA
		LYMPHOCYTES	LEG AMPUTATION
		LYMPHOCYTES	DIABETES MELLITUS
		LYMPHOCYTES	VASCULITIS
		LYMPHOCYTES	INCONTINENCE
		LYMPHOCYTES	DYSPEPSIA
		LYMPHOCYTES	DRUG HYPERSENSITIVITY
		LYMPHOCYTES	ANAEMIA
		LYMPHOCYTES	LYMPHOMA
		LYMPHOCYTES	NEURALGIA
		LYMPHOCYTES	SLEEP DISORDER
		LYMPHOCYTES	HYPERCHOLESTEROLAEMIA
		LYMPHOCYTES	MYOCARDIAL INFARCTION
		LYMPHOCYTES	ATRIOVENTRICULAR BLOCK FIRST DEGREE
		LYMPHOCYTES	EJECTION FRACTION DECREASED
		LYMPHOCYTES	CONTUSION
		LYMPHOCYTES	CORONARY ARTERIAL STENT INSERTION
		LYMPHOCYTES	PULMONARY EMBOLISM
		LYMPHOCYTES	ATRIAL FIBRILLATION
		LYMPHOCYTES	HYPERLIPIDAEMIA

（Source: 1.13.3-10, 付録 C-02-①-4）

表 2.7.4.9-159　国内外の第 III 相臨床試験（R788-1301、C788-047、C788-048 及び C788-049 試験の統合）における副腎皮質ステロイドを併用した被験者割合、副腎皮質ステロイドの併用の有無別における血栓症、塞栓症及び血栓塞栓症の有害事象の発現状況

	血栓症、塞栓症及び血栓塞栓症の有害事象		
	なし	あり	Total
副腎皮質ステロイド併用なし 全被験者に占める割合（/146 例） 副腎皮質ステロイド非併用例に占める割合（/61 例） 血栓系有害事象発現例/非発現例に占める割合（/145 例、/1 例）	60 例 41.10% 98.36% 41.38%	1 例 0.68% 1.64% 100.00%	61 例 41.78%
副腎皮質ステロイド併用あり 全被験者に占める割合（/146 例） 副腎皮質ステロイド併用例に占める割合（/85 例） 血栓系有害事象発現例/非発現例に占める割合（/145 例、/1 例）	85 例 58.22% 100.00% 58.62%	0 例 0.00% 0.00% 0.00%	85 例 58.22%
Total	145 例 99.32%	1 例 0.68%	146 例 100.00%

（Source: 1.13.3-10, C-04 表 7）

表 2.7.4.9-160　海外第 II 相臨床試験（D4300-0022 試験）における副腎皮質ステロイドを併用した被験者割合、副腎皮質ステロイドの併用の有無別における血栓症、塞栓症及び血栓塞栓症の有害事象の発現状況

	血栓症、塞栓症及び血栓塞栓症の有害事象		
	なし	あり	Total
副腎皮質ステロイド併用なし 全被験者に占める割合（/18 例） 副腎皮質ステロイド非併用例に占める割合（/1 例） 血栓系有害事象非発現例/発現例に占める割合（/15 例、/3 例）	1 例 5.56% 100.00% 6.67%	0 例 0.00% 0.00% 0.00%	1 例 5.56%
副腎皮質ステロイド併用あり 全被験者に占める割合（/18 例） 副腎皮質ステロイド併用例に占める割合（/17 例） 血栓系有害事象非発現例/発現例に占める割合（/15 例、/3 例）	14 例 77.78% 82.35% 93.33%	3 例 16.67% 17.65% 100.00%	17 例 94.44%
Total	15 例 83.33%	3 例 16.67%	18 例 100.00%

（Source: 1.13.3-10, C-04 表 8）

表 2.7.4.9-161　国内外の第 III 相臨床試験（R788-1301、C788-047、C788-048 及び C788-049 試験の統合）における副腎皮質ステロイドの併用の有無別における血小板数の変化量（中央値）

	投与後	4 週	8 週	12 週	16 週	20 週	24 週	52 週	104 週	152 週	200 週
ステロイド併用なし	症例数	61	55	53	49	44	44	20	7	18	14
	変化量（/μL）	3000	6000	7000	13000	14000	10000	46000	85000	72000	71000
ステロイド併用あり	症例数	68	64	62	56	49	45	34	17	23	14
	変化量（/μL）	8000	15000	15000	20000	17000	23000	53000	47000	59000	91000

（Source: 1.13.3-10, C-04 表 9）

表 2.7.4.9-162　海外第 II 相臨床試験（D4300-0022 試験）における副腎皮質ステロイドの併用の有無別における血小板数の変化量（中央値）

	投与後	1 週	4 週	8 週	12 週	16 週	20 週	24 週	12 カ月	18 カ月	24 カ月	30 カ月	36 カ月
ステロイド併用なし	症例数	1	1	0	0	0	0	0	0	0	0	0	0
	変化量（10^9/L）	-2	4	-	-	-	-	-	-	-	-	-	-
ステロイド併用あり	症例数	17	15	13	10	9	10	7	10	7	7	6	5
	変化量（10^9/L）	13	35	12	12	4	9	49	20	24	-11	59	-16

（Source: 1.13.3-10, C-04 表 10）

表 2.7.4.9-163　国内外の第 III 相臨床試験（R788-1301、C788-047、C788-048 及び C788-049 試験の統合）における副腎皮質ステロイドを併用した被験者割合、副腎皮質ステロイドの併用の有無別におけるオーバーシュートの発現状況

	血小板数のオーバーシュート		
	なし	あり	Total
副腎皮質ステロイド併用なし	60 例	1 例	61 例
全被験者に占める割合（/146 例）	41.10%	0.68%	41.78%
副腎皮質ステロイド非併用例に占める割合（/61 例）	98.36%	1.64%	
オーバーシュート非発現例/発現例に占める割合（/141 例、/5 例）	42.55%	20.00%	
副腎皮質ステロイド併用あり	81 例	4 例	85 例
全被験者に占める割合（/146 例）	55.48%	2.74%	58.22%
副腎皮質ステロイド併用例に占める割合（/85 例）	95.29%	4.71%	
オーバーシュート非発現例/発現例に占める割合（/141 例、/5 例）	57.45%	80.00%	
Total	141 例	5 例	146 例
	96.58%	3.42%	100.00%

（Source: 1.13.3-10, C-04 表 11）

表 2.7.4.9-164　海外第 II 相臨床試験（D4300-0022 試験）における副腎皮質ステロイドを併用した被験者割合、副腎皮質ステロイドの併用の有無別におけるオーバーシュートの発現状況

	血小板数のオーバーシュート		
	なし	あり	Total
副腎皮質ステロイド併用なし	1 例	0 例	1 例
全被験者に占める割合（/18 例）	5.56%	0.00%	5.56%
副腎皮質ステロイド非併用例に占める割合（/1 例）	100.00%	0.00%	
オーバーシュート非発現例/発現例に占める割合（/16 例、/2 例）	6.25%	0.00%	
副腎皮質ステロイド併用あり	15 例	2 例	17 例
全被験者に占める割合（/18 例）	83.33%	11.11%	94.44%
副腎皮質ステロイド併用例に占める割合（/17 例）	88.24%	11.76%	
オーバーシュート非発現例/発現例に占める割合（/16 例、/2 例）	93.75%	100.00%	
Total	16 例	2 例	18 例
	88.89%	11.11%	100.00%

（Source: 1.13.3-10, C-04 表 12）