2.7.6　　個々の試験のまとめの目次

CTD 項番号	項題名
2.7.6.1	【国外試験】急性症候性深部静脈血栓症患者を対象とした第Ⅲ相臨床試験：試験番号 11702（試験 11702-DVT）[報告書番号 MRR-00292]
2.7.6.2	【国外試験】急性症候性肺塞栓症患者を対象とした第Ⅲ相臨床試験： 試験番号 11702 EINSTEIN-PE（試験 11702-PE） [報告書番号 A53042]
2.7.6.3	【国外試験】症候性静脈血栓塞栓症患者を対象とした第Ⅲ相臨床試験(長期投与)：試験番号 11899 [報告書番号 MRR-00273]
2.7.6.4	【国内試験】症候性肺塞栓症を伴わない急性症候性深部静脈血栓症患者を対象とした第Ⅲ相臨床試験：試験番号 14568（J-EINSTEIN-DVT 試験） [報告書番号 PH-37602]
2.7.6.5	【国内試験】急性症候性肺塞栓症患者を対象とした第Ⅲ相臨床試験：試験番号 15960（J-EINSTEIN-PE 試験） [報告書番号 PH-37586]
2.7.6.6	【国外試験】強力な CYP3A4 誘導薬を使用中の急性症候性深部静脈血栓症（DVT）又は急性症候性肺塞栓症（PE）患者を対象としたリバーロキサバンのコホート試験：試験番号 13238 [報告書番号 A50672]
2.7.6.7	【国内試験】健康成人男性被験者を対象とした第Ⅰ相臨床試験：リバーロキサバン 15mg 錠を用いた食事の影響試験：試験番号 15921 [報告書番号 A57650]
2.7.6.8	【国外試験】健康白人男性被験者を対象とした第Ⅰ相臨床試験：リバーロキサバン 2.5、5 及び 10mg 錠を空腹時投与したときの用量比例性を検討した試験：試験番号 12361 [報告書番号 PH-36607]
2.7.6.9	【国外試験】健康成人男女被験者を対象とした第Ⅰ相臨床試験：リバーロキサバン錠を粉砕投与したときの相対バイオアベイラビリティ及び薬物動態を検討した試験：試験番号 16151 [報告書番号 R-8736]
2.7.6.10	【国外試験】腎障害被験者及び正常腎機能被験者を対象としたリバーロキサバン単回投与時のリバーロキサバンの薬物動態、薬力学及び安全性に対するエリスロマイシン反復投与の影響の検討：試験番号 15692 [報告書番号 R-8735]
2.7.6.11	【国外試験】健康成人男女被験者を対象としたリバーロキサバンからワルファリンへ切り替えたときの薬力学的特性に関する相互作用試験：試験番号 15923 [報告書番号 R-8743]
2.7.6.12	【国外試験】急性症候性近位深部静脈血栓症患者を対象とした第Ⅱ相臨床試験：試験番号 11223（ODIXa-DVT 試験） [報告書番号 MRR-00150]
2.7.6.13	【国外試験】急性症候性近位深部静脈血栓症患者を対象とした第Ⅱ相臨床試験：試験番号 11528（EINSTEIN-DVT 試験） [報告書番号 MRR-00223]

2.7.6.1 【国外試験】急性症候性深部静脈血栓症患者を対象とした第Ⅲ相臨床試験：試験番号 11702（試験 11702-DVT）[報告書番号 MRR-00292]

参照項目：5.3.5.1.1 MRR-00292

2.7.6.1.1 試験計画

治験の標題：急性症候性深部静脈血栓症（DVT）患者を対象とした経口直接作用型第Ｘa 因子阻害薬リバーロキサバンの多施設共同、無作為化、非盲検、実薬対照、盲検下評価、並行群間比較、イベント主導型、非劣性検証、第Ⅲ相試験

治験調整医師：
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実施医療機関：32 ヵ国 253 施設（括弧内は施設数）
オーストラリア（19）、オーストリア（5）、ベルギー（11）、ブラジル（8）、カナダ（5）、中国（14）、チェコ共和国（7）、デンマーク（3）、フランス（28）、ドイツ（22）、香港（1）、ハンガリー（8）、インド（4）、インドネシア（5）、イスラエル（12）、イタリア（13）、韓国（2）、マレーシア（1）、オランダ（7）、ニュージーランド（6）、ノルウェイ（4）、フィリピン（2）、ポーランド（11）、シンガポール（2）、南アフリカ（11）、スペイン（4）、スウェーデン（4）、スイス（5）、台湾（3）、タイ（2）、イギリス（4）、米国（20）

公表論文：The EINSTEIN Investigators, N Engl J Med 2010;363:2499-2510

治験期間：	**開発のフェーズ**：第Ⅲ相
最初の患者の組み入れ日：2007 年 3 月 22 日 最後の患者の最終来院日：2010 年 4 月 12 日	

目的：

有効性：

症候性肺塞栓症（PE）を伴わない急性症候性深部静脈血栓症（DVT)患者における静脈血栓塞栓症（VTE）の再発抑制効果について、リバーロキサバンの有効性をエノキサパリン／ビタミン K 拮抗薬（VKA：ワルファリン又は acenocoumarol）と比較検討する。

安全性：

「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」を検討する。

試験方法：

本試験は、PE を伴わない、確定診断された急性症候性 DVT 患者を対象とした、多施設共同、無作為化、非盲検、実薬対照、盲検下評価、並行群間比較、イベント主導型、非劣性検証の第Ⅲ相試験であった。治験薬の予定投与期間は 3、6 及び 12 ヵ月のいずれかとした。

図 2.7.6.1- 1に本試験の全般的デザイン、表 2.7.6.1- 1に本試験のスケジュールを示す。

被験者はリバーロキサバン群又はエノキサパリン／VKA 群に無作為に割り付けられた。無作為割り付けは音声応答システム（IVRS）により行い、参加国及び予定投与期間を割り付け調整因子として用いた。

無作為割り付け前に最大 48 時間（治験実施計画書改訂 4 までは最大 36 時間）の抗凝固薬による治療は可とし、VKA 治療は単回投与のみ可とした。無作為割り付け後、リバーロキサバン群に割り付けられた被験者には、リバーロキサバン 15mg を 1 日 2 回 3 週間経口投与し、続いてリバーロキサバン 20mg の 1 日 1 回投与を 3、6 又は 12 ヵ月まで継続した。

エノキサパリン／VKA 群に割り付けられた被験者には、少なくとも 5 日間エノキサパリン 1mg/kg

の 1 日 2 回皮下投与と VKA の経口投与を併用（4～5 日間）し、24 時間以上の間隔をおいて測定したプロトロンビン時間国際標準比（PT-INR）が 2 回連続で 2 以上となった後は、VKA のみの投与を 3、6 又は 12 ヵ月まで継続した。VKA の投与は PT-INR が目標とする 2.5（2.0～3.0 の範囲）になるように用量調節した。VKA としてはワルファリン又は acenocoumarol を使用可とした。

すべての VTE、出血事象及び心血管事象が疑われる事象並びに死亡は、盲検下で独立中央判定委員会（CIAC）により判定され、判定結果に基づいて解析を行った。安全性データモニタリング委員会（DSMB）は試験期間中の被験者の安全性をモニターし、試験執行委員会に勧告を行った。

治験責任（分担）医師は、すべての被験者とのコンタクト時に、コンタクトレポートを使用して、下記の評価を行った。有効性又は安全性に関するイベント発現の疑いがある被験者については確認検査を行った。

- DVT 又は PE の発現、悪化あるいは再発
- 出血事象を含む有害事象（重篤な有害事象）
- 併用薬
- リバーロキサバン投与又はエノキサパリン／VKA 投与の遵守状況及び PT-INR モニタリング

更に、試験スケジュールに示す時点で中央臨床検査用の血液採取を行った。また、医療資源利用（HCRU）のためのデータを収集し、一部の被験者では抗凝固薬治療に関する評価尺度（ACTS）による被験者満足度アンケートを実施した。

無作為割り付けされたが治験薬の投与を受けなかった、又は治験薬投与を中止した被験者には、同意の撤回、追跡不能あるいは死亡がない限り、被験者の予定投与期間の終了時に来院を設定した。

予定投与期間にかかわらず、治験薬投与後に 30 日間のフォローアップ期間を設けた。治験薬投与を中止した被験者にも同様のフォローアップ期間を設定した。本試験での治験薬投与終了後、引き続き継続投与試験である試験 11899 に移行する被験者は、30 日間のフォローアップ期間を設けず、中断なく試験 11899 に移行した。

フォローアップ期間終了時に、すべての被験者にコンタクトを取ることとした。すべての疑わしい事象について治験薬投与期間と同じ方法で判定した。フォローアップ期間中に発現したすべての事象は記録のみとし、正式な解析は実施しなかった。すべての疑わしい事象について治験薬投与期間と同じ方法で判定した。フォローアップ期間中に発現したすべての事象は記録のみとし、正式な解析は実施しなかった。

予定投与期間は、下記のリスク評価及び出血の可能性に基づき、治験責任（分担）医師が、無作為割り付け時に 3、6 及び 12 ヵ月のいずれかに決定した。

下記のような一過性の危険因子を有する被験者では、多くの場合投与期間を 3 ヵ月とした。

- 最近の手術又は外傷
- 活動性の制限
- エストロゲン含有医薬品の使用
- 産褥期

特発性 VTE 又は下記のような永続的危険因子を有する被験者では、多くの場合投与期間を 6 ヵ月又は 12 ヵ月とした。

- 活動性の悪性腫瘍
- DVT/PE の既往

- 既知の血栓性素因〔アンチトロンビンⅢ、プロテインS又はプロテインCの欠乏、血液凝固第Ⅴ因子（FaV）又はプロトロンビン遺伝子突然変異、あるいは抗リン脂質抗体〕

診断と選択基準：

選択基準

(1)　症候性PEを伴わない急性症候性近位DVTと確定診断されたもの
(2)　試験開始前に文書及び口頭による詳細な説明を受け、文書による同意が得られたもの

除外基準

(3)　法的未成年者（治験参加国により異なる）
(4)　現在のDVT治療のために血栓除去術、下大静脈フィルター留置、又は血栓溶解剤による治療を受けているもの
(5)　DVT以外のVKAの適応があるもの
(6)　無作為割り付け前に、ヘパリン〔低分子量ヘパリン（LMWH）を含む〕／フォンダパリヌクスの治療用量での投与を48時間を超えて受けた、又はVKAを2回以上投与されたもの
(7)　試験開始前30日以内にほかの薬物療法試験に参加したもの
(8)　クレアチニンクリアランス（CL_{CR}）が30mL/min未満のもの
(9)　臨床的に問題となる肝障害（例：急性肝炎、慢性の活動性肝炎、肝硬変）、又はアラニン・アミノトランスフェラーゼ（ALT）が基準値上限の3倍を超えるもの
(10)　細菌性心内膜炎を有するもの
(11)　生命予後が3ヵ月未満と考えられるもの
(12)　エノキサパリン又はVKAによる治療が禁忌となる活動性出血又は高い出血リスクを有するもの。
(13)　コントロール不良の高血圧（収縮期血圧が180mmHgを超える又は拡張期血圧が110mmHgを超える）を合併しているもの
(14)　妊娠中、授乳中、又は妊娠可能な女性で適切な避妊を行わないもの
(15)　ワルファリン、acenocoumarol又はエノキサパリンの添付文書に記載されているそのほかの禁忌があるもの
(16)　強力なチトクロームP450酵素3A4（CYP3A4）阻害薬（例：HIVプロテアーゼ阻害薬、ケトコナゾール経口剤）、又は強力なCYP3A4誘導剤（例：リファンピシン）の投与が治験薬投与期間中に予定されているもの（治験実施計画書改訂2）

有効性の評価項目：

主要評価項目：症候性VTE〔「症候性DVT」又は「症候性PE（非致死的及び致死的）」の複合エンドポイント（ただしPEの可能性が否定できない原因不明の死亡を含む）〕

副次的評価項目：

- 症候性VTE〔「症候性DVT」又は「症候性PE（非致死的）」〕又は全死亡の複合エンドポイント
- 総合有用性評価指標－1：有効性主要評価項目の各構成要素又は「重大な出血事象」の複合エンドポイント
- 総合有用性評価指標－2：有効性主要評価項目の各構成要素、「重大な出血事象」、心血管死、心筋梗塞、虚血性脳卒中又は非中枢神経系塞栓症の複合エンドポイント

安全性の評価項目：

主要評価項目：「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイント

副次的評価項目：全死亡、心血管事象及び臨床検査値

薬力学的作用の評価項目：別途報告書を作成した。

リバーロキサバンの血漿中濃度のトラフ時及びピーク時におけるプロトロンビン時間及びプロトロンビナーゼ誘発凝固時間の測定（一部の被験者のみ）

症例数：

計画時：

本試験はイベント主導型の試験であり、VTE のイベント数が目標とする 88 イベントに達する見込みを得た時点を終了とするため、症例数は症候性 VTE の発現頻度に基づく。割り付け例数は 2,930 例（各群 1,465 例）と想定された。

症例数の設定根拠

リバーロキサバンが対照薬と同じ有効性を示すと仮定して、リバーロキサバンが少なくとも対照薬に対して非劣性であることを示すためには、ハザード比の 95%信頼区間の上限が非劣性マージンの 2.0 未満となる必要があることを考慮すると、検出力 90%（両側有意水準 0.05）で検出するためには合計 88 のイベント数が必要と考えられた。大部分の再発イベントが最初のイベント発現後 1 ヵ月以内に起こるとの知見に基づき、VTE の再発率は 3 ヵ月で 2.5%、6 ヵ月で 3%、12 ヵ月で 3.5%と想定される。従って、有効性主要評価項目の平均発現頻度は両群とも 3%と推定され、これにより、少なくとも 1 群 1,465 例が必要とされることから設定した。

解析時：

3,459 例（組み入れ被験者）

intention-to-treat（ITT）解析対象集団：3,449 例（リバーロキサバン：1,731 例、エノキサパリン／VKA：1,718 例）

安全性解析対象集団：3,429 例（リバーロキサバン：1,718 例、エノキサパリン／VKA：1,711 例）

治験実施計画書に適合した（PP）解析対象集団：3,096 例（リバーロキサバン：1,525 例、エノキサパリン／VKA：1,571 例）

解析方法：

解析対象集団

ITT 解析対象集団は、無作為割り付けされたすべての被験者とした。被験者番号と割り付けられた投与は IVRS によりデータベースに登録され、それに従って解析を行った。

安全性解析対象集団は、無作為割り付けされ、治験薬が少なくとも 1 回投与されたすべての被験者と規定した。被験者の解析は、実際に受けた治験薬投与に従って行われた。

ITT on treatment 解析対象集団〔（統計解析計画書（SAP）補遺に規定〕は、安全性解析対象集団の部分集団であった。無作為割り付け後に、治験薬を無作為割り付けに従って少なくとも 1 回投与されたすべての被験者とした。割り付けと異なる治験薬を投与された被験者は本解析から除外された。

PP 解析対象集団は、無作為割り付けされたすべての被験者のうち、治験実施計画書からの重大な逸脱がない被験者とした。以下の被験者は PP 解析対象集団から除外された。

- ベースライン時の DVT〔index イベント（治験対象として診断されたイベント）〕が CIAC で DVT と判定されなかった被験者
- IVRS で割り付けられた治験薬投与を受けなかった、又は治験薬の投与を一回も受けなかった被験者
- SAP version 1.0 に規定された、治験薬の投与が適切に行われなかった被験者

有効性

すべての有効性の解析はITT解析対象集団で実施した。更に、主要評価項目の補助的解析をPP解析対象集団及びITT on treatment解析対象集団で実施した。有効性評価における解析対象集団ごとの対象イベントと打ち切りまでの期間の定義を表2.7.6.1- 2に示す。

有効性の主要解析に関して、すべての主要評価項目は、実際の投与期間にかかわらず、予定投与期間の終了まで検討された。予定投与期間の後に発現したイベントは記録するのみとし、解析には含めなかった。また、予定投与期間終了時まで、及び実際の治験薬投与終了後30日目までに発現したイベントについて記述した。

すべての被験者の予定投与期間別における累積イベント発現率について、Kaplan-Meier推定値により表示した。

主要解析として、有効性主要評価項目の初回イベント発現までの時間について、予定投与期間（3、6又は12ヵ月）で層別化し、ベースライン時の活動性悪性腫瘍の有無で調整したCox比例ハザードモデルを用いて解析を行った。対照薬のエノキサパリン／VKAに対するリバーロキサバンのハザード比及び両側95%信頼区間を算出した。このモデルに基づき、95%信頼区間の上限が2.0未満の場合に、リバーロキサバンはエノキサパリン／VKAに対して非劣性を示すと考えられた。

逐次的検定：

逐次的検定ついて次の階層を適用した。有効性主要評価項目に関する非劣性が示された場合、有効性主要評価項目に関する優越性について、ハザード比（リバーロキサバン／対照薬）の両側95%信頼区間により検定を行うこととした。更に、有効性主要評価項目で非劣性が示された場合、以下のとおり閉検定手順を実施することとした。

a）安全性解析対象集団を対象とした、治験薬投与下での安全性主要評価項目に関する優越性

b）安全性解析対象集団を対象とした、治験薬投与下での「重大な出血事象」に関する優越性

共変量の影響に関する部分集団解析：

ベースラインの共変量（活動性悪性腫瘍の有無、特発性DVT/PE、DVT/PEの既往、既知の血栓性素因、性別、年齢、体重、腎機能、肺疾患、心疾患及び無作為割り付け時の可動性）及び有効性主要評価項目におけるほかの部分集団の影響を、治療効果の調整済みハザード比とその95%信頼区間を算出することにより分析した。

安全性

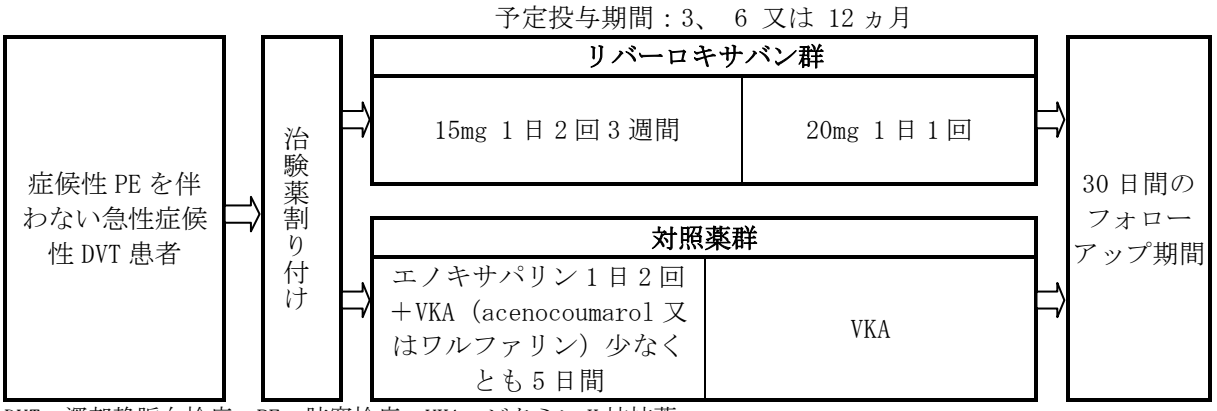
安全性解析対象集団において、すべての安全性の解析を実施した。出血事象の解析は、治験薬投与下（無作為割り付け後から治験薬投与終了後2日目まで）に発現したイベントを対象とした。その後にみられた出血事象は別途記述した。また、出血事象と死亡の解析はITT解析対象集団でも行った。

有効性及び安全性の主要解析に関して、第1種の過誤を両側0.05に維持するため、閉手順を適用し、安全性の主要解析について逐次的検定手法を用いた。有効性の主要解析において、リバーロキサバンがエノキサパリン／VKAに非劣性を示した場合、安全性主要評価項目であるイベントの発現までの時間（患者年）について、層別Cox比例ハザードモデルを用いて、有効性主要解析と同様の層及び共変量で投与群間の比較を行った。群間差が統計学的に有意（両側有意水準0.05）にリバーロキサバン群で優れていた場合、「重大な出血事象」の発現までの時間のみについて同じ有意水準で検定を行うこととした。対数（部分）尤度比検定を優越性の検定に適用した。

中間解析

該当せず。

試験の全般的デザインを図 2.7.6.1- 1に、試験スケジュールを表 2.7.6.1- 1に示す。



DVT：深部静脈血栓症、PE：肺塞栓症、VKA：ビタミン K 拮抗薬
引用元：5.3.5.1.1 MRR-00292/Text Table 7-1

図 2.7.6.1- 1 試験の全般的デザイン

表 2.7.6.1- 1 試験スケジュール

3ヵ月のコホート	スクリーニング	治験薬投与期間						フォローアップ期間
月							3	
日		1	8±1	15±1	30±7	60±7	91～98	121～128
コンタクト方法		来院	電話	来院	来院	来院	来院	来院
DVT の診断 診断のための検査	○ ○							
- 選択／除外基準の確認 [a] - VTE 危険因子 - 病歴 - 抗凝固、抗血小板療法の確認 [b] - 人口統計学的特性	○							
血小板数、Hb、aPTT、PT-INR	○[i]	出血が疑われた場合：血小板数、Hb、 aPTT、PT-INR[i] DVT / PE が疑われた場合： 血小板数、aPTT、PT-INR[i]						
ALT、クレアチニン	○[j]							
中央測定（採血） - 肝機能検査 [c,d] （全被験者） - 薬力学的検査 [e]	○ ○			○ ○	○	○ ○	○ ○	○
IVRS		○		○			○	
コンタクトレポート			○	○	○	○	○	○
HCRU			○	○	○	○	○	
ACTS [f]				○	○	○	○	
TSQM [f]					○		○	
併用薬・療法の確認 [g]	○		○	○	○	○	○	○
診断のための観察検査	○	DVT / PE、出血事象、死亡、心血管事象が疑われた場合						
対照薬群								
	[k]	エノキサパリンを少なくとも 5 日間投与						
VKA 投与（PT-INR で調整）		PT-INR は最初少なくとも 2～3 日ごと、その後少なくとも毎月測定						
リバーロキサバン群								
リバーロキサバン投与	[k]	15 mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回投与						
安全性								
(重篤な)有害事象、 出血事象、血管事象	同意取得後に収集された事象							

表 2.7.6.1- 1　試験スケジュール（続き）

6ヵ月のコホート	スクリーニング	治験薬投与期間									フォローアップ期間
月							3	4	5	6	
日		1	8 ±1	15 ±1	30 ±7	60 ±7	91～98	120 ±7	150 ±7	178～185	208～215
コンタクト方法		来院	電話	来院	来院	来院	来院	LVP [h]	LVP [h]	来院	来院
DVT の診断 診断のための検査	○ ○										
- 選択／除外基準の確認 [a] - VTE 危険因子 - 病歴 - 抗凝固、抗血小板療法の確認 [b] - 人口統計学的特性	○										
血小板数、Hb、aPTT、PT-INR	○[i]	出血が疑われた場合：血小板数、Hb、 aPTT、PT-INR[i] DVT / PE が疑われた場合： 血小板数、aPTT、PT-INR[i]									
ALT、クレアチニン	○[j]										
中央測定（採血） - 肝機能検査 [c,d] （全被験者） - 薬力学的検査 [e]	○ ○			○ ○	○	○ ○	○ ○	○	○	○ ○	○
IVRS		○					○			○	
コンタクトレポート			○	○	○	○	○	○	○	○	○
HCRU			○	○	○	○	○	○	○	○	
ACTS [f]				○	○	○	○			○	
TSQM [f]					○		○			○	
併用薬・療法の確認 [g]	○		○	○	○	○	○	○	○	○	○
診断のための観察検査	○	DVT / PE、出血事象、死亡、心血管事象が疑われた場合									
対照薬群											
	[k]	エノキサパリンを少なくとも 5 日間投与									
VKA 投与 （PT-INR で調整）		PT-INR は最初少なくとも 2～3 日ごと、その後少なくとも毎月測定									
リバーロキサバン群											
リバーロキサバン投与	[k]	15 mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回投与									
安全性											
(重篤な)有害事象、出血事象、血管事象	同意取得後に収集された事象										

表 2.7.6.1- 1　試験スケジュール（続き）

12 ヵ月のコホート	スクリーニング	治験薬投与期間															フォローアップ期間
月							3	4	5	6	7	8	9	10	11	12	13
日		1	8 ±1	15 ±1	30 ±7	60 ±7	91 ～ 98	120 ±7	150 ±7	178 ～ 185	210 ±7	240 ±7	265 ～ 272	300 ±7	330 ±7	352 ～ 359	382 ～ 389
コンタクト方法		来院	電話	来院	来院	来院	来院	LVP[h]	LVP[h]	来院	LVP[h]	LVP[h]	来院	LVP[h]	LVP[h]	来院	来院
DVT の診断 診断のための検査	○ ○																
- 選択／除外基準の確認[a] - VTE 危険因子 - 病歴 - 抗凝固、抗血小板療法の確認[b] - 人口統計学的特性	○																
血小板数、Hb、aPTT、PT-INR	○[i]	出血が疑われた場合：血小板数、Hb、 aPTT、PT-INR[i] DVT / PE が疑われた場合： 血小板数、aPTT、PT-INR[i]															
ALT、クレアチニン	○[j]																
中央測定（採血） - 肝機能検査[c,d]（全被験者） - 薬力学的検査[e]	○ ○			○ ○	○	○ ○	○ ○	○	○	○ ○	○	○	○	○	○	○ ○	○
IVRS		○		○			○			○			○			○	
コンタクトレポート			○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
HCRU			○	○	○	○	○	○	○	○	○	○	○	○	○	○	
ACTS[f]				○	○	○	○			○						○	
TSQM[f]					○		○			○						○	
併用薬・療法の確認[g]	○		○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
診断のための観察検査		DVT / PE、出血事象、死亡、心血管事象が疑われた場合															
対照薬群																	
	[k]	エノキサパリンを少なくとも 5 日間投与															
VKA 投与（PT-INR で調整）		PT-INR は最初少なくとも 2～3 日ごと、その後少なくとも毎月測定															
リバーロキサバン群																	
リバーロキサバン投与	[k]	15 mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回投与															
安全性																	
(重篤な)有害事象、出血事象、血管事象	同意取得後に収集された事象																

HCRU：医療資源の利用、ACTS：抗凝固薬治療に関する評価尺度、TSQM：薬物治療の満足度に関する質問票

a：妊娠の可能性がある女性に対し妊娠検査を実施

b：無作為割り付け前 7 日以内の抗凝固、抗血小板療法

表 2.7.6.1- 1　試験スケジュール（続き）

c：肝機能検査（LFT）はビリルビン（総ビリルビン、抱合型）、ALT、AST、AP を含む。治験薬投与期間又はフォローアップ期間に臨床的に重要な肝機能異常が発現した際に広範囲に肝機能検査を行うためベースライン時の血液検体を保管した。
d：アミラーゼ測定用採血。3 ヵ月のコホート：ベースラインと第 3 ヵ月。6 ヵ月のコホート：ベースラインと第 6 ヵ月。12 ヵ月のコホート：ベースラインと第 6 及び 12 ヵ月。
e：すべての被験者を対象に治験薬投与前のスクリーニング時に薬力学的検査を実施。リバーロキサバン群のみ第 15 日に 2 回〔治験薬投与直前（トラフ状態）で 1 回、投与 2～4 時間後（ピーク状態）で 1 回〕、第 60 日及び第 6 ヵ月の治験薬投与直前のトラフ状態、及び第 3 ヵ月、12 ヵ月の治験薬投与後のピーク状態で採血する。
f：ACTS と TSQM は米国、イギリス、カナダ、ドイツ、フランス、イタリア、オランダの被験者のみ実施。
g：新たな又は継続中の治療法あるいは投与量の変更を記録する（フォローアップ期間中は抗凝固療法のみだが、イベントが発現した場合はすべての治療法）
h：LVP（Laboratory visit phone）：必ずしも来院を必要としない。中央測定（肝機能検査）のための採血を実施、コンタクトレポート及び HCRU は電話でも可。
i：血液検体は地域の検査機関で測定された。
j：ALT、クレアチニンの血液検体は被験者の適格性を確認するため地域の検査機関で測定された。
k：無作為割り付け前の抗凝固療法は最大 48 時間許容されたが、VKA は単回投与のみ許容された。
引用元：5.3.5.1.1 MRR-00292/Text Figure 7-2

表 2.7.6.1- 2　有効性評価における解析対象集団ごとの対象イベントと打ち切りまでの期間

解析対象集団	ITT	ITT on treatment[a]	PP
有効性主要解析対象イベント	○ 予定投与期間（3、6 又は 12 ヵ月）の最終日までに発現したイベント。期間は、3 ヵ月では 98 日、6 ヵ月では 185 日、12 ヵ月では 359 日を最長とする	× ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間に発現したイベント	× ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間に発現したイベント
試験を完了した被験者における打ち切り日	無作為割り付けから治験薬の最終投与時来院までの日数と、予定投与期間の日数のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間
試験を中止した被験者における打ち切り日	無作為割り付けから最後の適切なコンタクトまでの日数と、予定投与期間の日数のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間

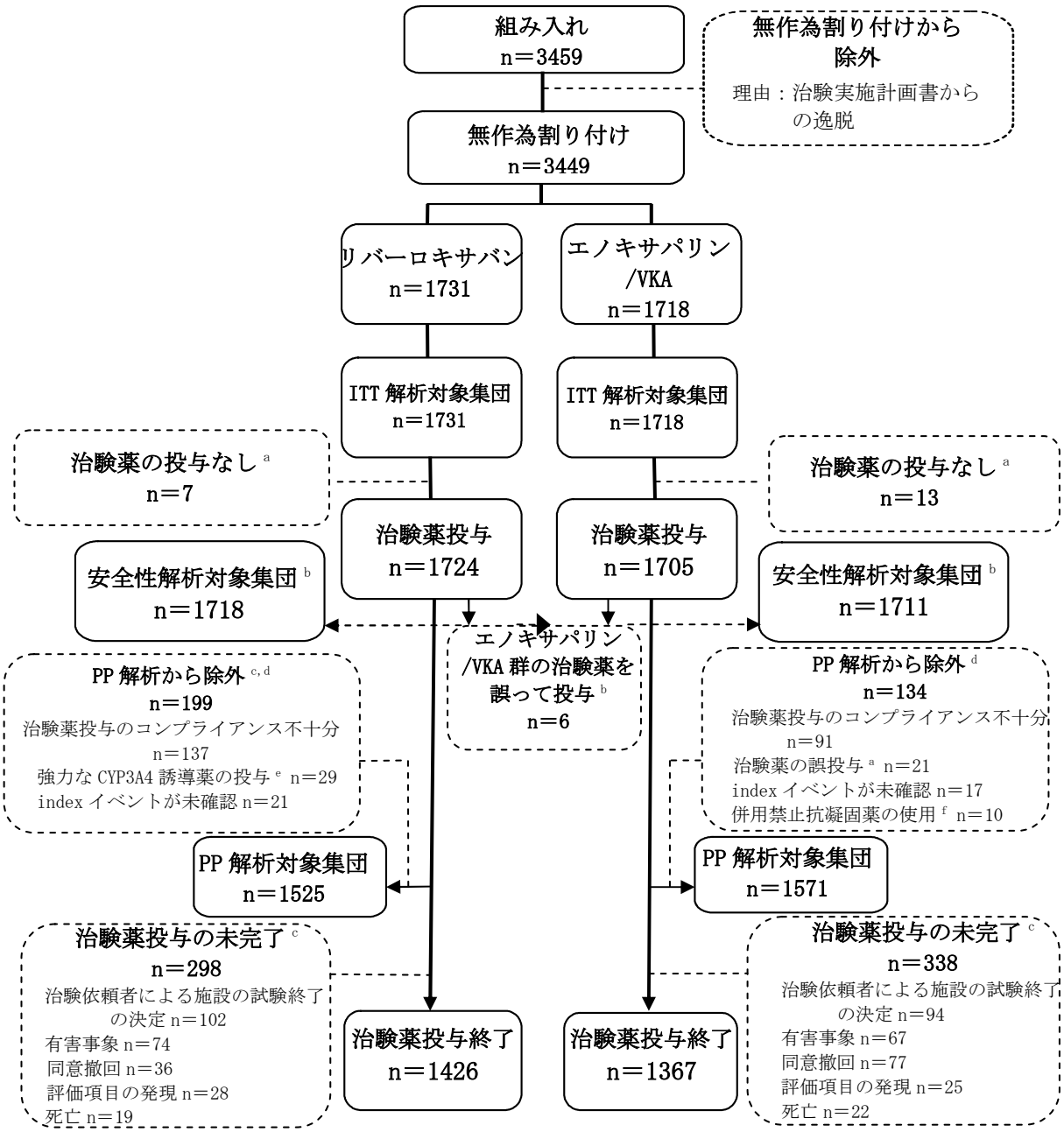
ITT：intention-to-treat、 PP：治験実施計画書に適合した
a 無作為割り付けされた治験薬投与を受けた期間のみを ITT on treatment 解析の対象とした。
引用元：5.3.5.1.1 MRR-00292/Text Table 7-2

2.7.6.1.2　成績

2.7.6.1.2.1　被験者の背景

2.7.6.1.2.1.1　被験者の内訳

被験者の内訳を図 2.7.6.1- 2に示す。32 ヵ国の 253 施設で 3,459 例が組み入れられ、3,449 例（リバーロキサバン群 1,731 例、エノキサパリンナトリウム（以下、エノキサパリン）／VKA 群 1,718 例）が無作為に割り付けられた。3,459 例の組み入れられた被験者のうち、10 例が治験実施計画書からの逸脱により割り付けられなかった。



VKA：ビタミン K 拮抗薬（acenocoumarol 又はワルファリン）、ITT：intention-to-treat 解析対象集、PP：治験実施計画書に適合した、CYP3A4：チトクローム P450 酵素 3A4

a：詳細情報なし

b： 6 例はリバーロキサバン群に割り付けられたが、実際はエノキサパリン／VKA が投与されたため、安全性解析対象集団ではエノキサパリン／VKA 群に含めた。

c：多く認められた理由

d：被験者によって 2 つ以上の理由があるため、合計数は合わない。

e：治験薬投与期間に強力な CYP3A4 誘導薬を 2 日間以上投与された場合、リバーロキサバン群から除外した。

f：割り付け前の 48 時間を超える非経口の抗凝固薬の使用、又は 2 回以上の VKA 投与

引用元：5.3.5.1.1 MRR-00292/Table 14.1/7、Table 14.1/8、Table 14.1/17、Table 14.1/18、Table 14.1/23

図 2.7.6.1- 2　被験者の内訳

予定投与期間として 3、6 又は 12 ヵ月の投与期間を無作為割り付け前に治験責任（分担）医師が決定した。予定投与期間別の被験者数を表 2.7.6.1- 3に示す。各予定投与期間の被験者の割合は、3 ヵ月が 11.9%、6 ヵ月が 62.8%、12 ヵ月が 25.3%であった。

表 2.7.6.1- 3　予定投与期間別の被験者の内訳（無作為割り付けされた被験者）

	リバーロキサバン N＝1731 (100%)	エノキサパリン／VKA N＝1718 (100%)	合計 N=3449 (100%)
予定投与期間　3 ヵ月	208 (12.0%)	203 (11.8%)	411 (11.9%)
予定投与期間　6 ヵ月	1083 (62.6%)	1083 (63.0%)	2166 (62.8%)
予定投与期間　12 ヵ月	440 (25.4%)	432 (25.1%)	872 (25.3%)

VKA：ビタミン K 拮抗薬
引用元：5.3.5.1.1 MRR-00292/Table 14.2/1

2.7.6.1.2.1.1.1　治験薬投与の完了及び未完了

すべての無作為割り付けされた被験者について、治験薬投与の完了及び未完了の内訳を表 2.7.6.1- 4に示す。リバーロキサバン群の 298 例（17.2%）及びエノキサパリン／VKA 群の 338 例（19.7%）が治験薬投与未完了であった。約 81%の被験者が治験薬投与を予定どおり終了した。本試験はイベント主導型試験であり、有効性の主要評価項目の評価に必要な目標イベント発現数の 88 件に達する見込みを得た時点で組み入れを終了した。これによる試験終了（治験依頼者による試験終了の決定）は、リバーロキサバン群 5.9%、エノキサパリン／VKA 群 5.5%であった。治験薬投与の中止理由で多かったものは、有害事象（リバーロキサバン群 4.3%、エノキサパリン／VKA 群 3.9%）、同意撤回（リバーロキサバン 2.1%、エノキサパリン／VKA 群 4.5%）、評価項目の発現（リバーロキサバン群 1.6%、エノキサパリン／VKA 群 1.5%）であった。

表 2.7.6.1- 4　治験薬投与の完了及び未完了の内訳（無作為割り付けされた被験者）

	リバーロキサバン N=1731（100%）	エノキサパリン／VKA N=1718（100%）
治験薬投与完了	1426（82.4%）	1367（79.6%）
治験薬未投与	7（ 0.4%）	13（ 0.8%）
治験薬投与未完了	298（17.2%）	338（19.7%）
有害事象	74（ 4.3%）	67（ 3.9%）
治験薬投与のコンプライアンス不十分	8（ 0.5%）	15（ 0.9%）
同意撤回	36（ 2.1%）	77（ 4.5%）
治療効果不十分	0	1（<0.1%）
追跡不能	12（ 0.7%）	18（ 1.0%）
死亡	19（ 1.1%）	22（ 1.3%）
治験実施計画書からの逸脱	8（ 0.5%）	4（ 0.2%）
治験依頼者による試験終了の決定[a]	102（ 5.9%）	94（ 5.5%）
治験責任（分担）医師による施設の試験中止[b]	0	2（ 0.1%）
治験実施計画書の規定によるもの	2（ 0.1%）	2（ 0.1%）
治験責任（分担）医師の判断（治験実施計画書の規定によるものではない）	3（ 0.2%）	6（ 0.3%）
市販薬への切り替え	0	2（ 0.1%）
評価項目の発現[c]	28（ 1.6%）	25（ 1.5%）
技術的問題	1（<0.1%）	1（<0.1%）
被験者都合	5（ 0.3%）	2（ 0.1%）

VKA：ビタミン K 拮抗薬
治験責任（分担）医師の判断による主な中止理由を示しているため、有害事象による中止の例数は、有害事象を発現し、その措置として「治験薬の中止」と記録された例数と一致しないことがある。
a：予定した目標イベント発現数に達したことによる治験依頼者による試験終了の決定
b：実施管理上の理由
c：評価項目の発現後、治験薬投与を中止するか否かを治験責任（分担）医師が判断することとした。中止と判断された被験者のみを示す。
引用元：5.3.5.1.1 MRR-00292/Table 14.1/8

2.7.6.1.2.1.1.2　　予定した治験薬投与期間の完了及び未完了

予定した治験薬投与期間の完了に関して、被験者が予定投与期間の来院日の許容範囲のうち最短の日又はそれ以降のコンタクトレポートを有していた、来院の許容範囲の最長の日（3、6 及び 12 ヵ月について、それぞれ第 98 日、第 185 日及び第 359 日）までに有効性の評価項目又は死亡が判定された、又は治験依頼者が試験を終了した場合に、予定した治験薬投与期間を完了したこととした。

リバーロキサバン群の 94.7% 、エノキサパリン／VKA 群の 91.9%の被験者は、上記定義のいずれかであった（ITT 解析対象集団）。予定投与期間を完了しなかった被験者における主な未完了の理由は、同意撤回（リバーロキサバン群 2.0%、エノキサパリン／VKA 群 3.9%）、有害事象（リバーロキサバン群 1.2%、エノキサパリン／VKA 群 0.9%）、追跡不能（リバーロキサバン群 0.9%、エノキサパリン／VKA 群 1.0%）、治験実施計画書からの逸脱（リバーロキサバン群 0.5%、エノキサパリン／VKA 群 0.4%）、予定投与期間の完了前に治験責任（分担）医師の判断により予定投与期間を完了し試験 11899 に参加（リバーロキサバン群 0.2%、エノキサパリ

ン／VKA 群 0.5%）、及び治験薬投与のコンプライアンス不十分（リバーロキサバン群 0.2%、エノキサパリン／VKA 群 0.5%）であった（表 2.7.6.1- 5）。

表 2.7.6.1- 5　予定した治験薬投与期間の完了及び未完了の内訳（無作為割り付けされた被験者）

	リバーロキサバン N=1731（100%）	エノキサパリン／VKA N=1718（100%）
予定投与期間完了／有効性主要評価項目の発現／予定投与期間終了前に死亡／治験依頼者による試験終了の決定[a]	1639（94.7%）	1579（91.9%）
同意撤回	34（ 2.0%）	67（ 3.9%）
治験責任（分担）医師の判断による施設の試験中止[b]	0	1（＜0.1%）
治験責任（分担）医師の判断により予定投与期間終了前に治験薬投与期間を終了し、フォローアップ期間なしで試験 11899 へ参加	3（ 0.2%）	8（ 0.5%）
そのほかの理由による予定投与期間未完了[c]	55（ 3.2%）	63（ 3.7%）
有害事象	20（ 1.2%）	16（ 0.9%）
治験薬投与のコンプライアンス不十分	3（ 0.2%）	8（ 0.5%）
追跡不能	15（ 0.9%）	18（ 1.0%）
治験実施計画書からの逸脱	8（ 0.5%）	7（ 0.4%）
治験実施計画書の規定によるもの	0	1（＜0.1%）
治験責任（分担）医師の判断（治験実施計画書の規定によるものではない）	0	8（ 0.5%）
市販薬への切り替え	0	1（＜0.1%）
評価項目の発現	2（ 0.1%）	1（＜0.1%）
技術的問題	1（＜0.1%）	0（ 0.0%）
被験者都合	4（ 0.2%）	3（ 0.2%）
治験責任（分担）医師の判断により予定投与期間終了前に治験薬投与期間を終了	2（ 0.1%）	0

VKA：ビタミン K 拮抗薬
治験実施計画書に定めた最終の予定投与来院は、3 ヵ月のコホートでは第 91～98 日、6 ヵ月のコホートでは第 178～185 日、12 か月のコホートでは第 352～359 日であった。各コホートの被験者がそれぞれ第 91、178、352 日もしくはそれ以降にコンタクトレポートが作成された場合、又は各コホートの被験者がそれぞれ第 98、185、359 日以前に有効性評価項目を発現もしくは死亡した場合、又は治験依頼者が試験を終了した場合、被験者は予定投与期間を完了したと取り扱った。
a：予定した目標イベント発現数に達したことによる治験依頼者による試験終了の決定
b：実施管理上の理由
c：特に eCRF に記載されなかったため、直近のエンドポイント時の理由を採用した〔治験責任（分担）医師の判断による〕。
引用元： 5.3.5.1.1 MRR-00292/Table 14.1/14

予定投与期間にかかわらず、治験薬投与終了後に 30 日間のフォローアップ期間を設定した。両投与群の被験者の 82.1%がフォローアップ期間に参加し、それぞれの群の被験者の 81.9%が完了した（5.3.5.1.1 MRR-00292/Table 14.1/11）。予定したフォローアップ期間に参加しなかった大部分の被験者は、試験 11899（リバーロキサバン：12.0%、エノキサパリン／VKA：10.8%）に参加した。

2.7.6.1.2.1.2 症例の取扱い及び解析対象集団

ITT 解析、安全性解析及び PP 解析対象集団の被験者数、並びに除外理由を表 2.7.6.1- 6に示す。

3,449 例が無作為割り付けされ、ITT 解析対象集団はリバーロキサバン群 1,731 例、エノキサパリン／VKA 群 1,718 例であった。

ITT 解析対象集団の約 90%（3,096/3,449 例）が PP 解析対象集団であり、リバーロキサバン群：1,525 例、エノキサパリン／VKA 群：1,571 例であった。PP 解析対象集団からの除外例に多くみられた理由は、治験薬の不十分な服薬コンプライアンス、治験対象として診断されたイベント（index イベント）が CIAC によって判定されなかった、及び投与期間中に 2 日間を超えて強力な CYP3A4 誘導薬を服用（PT-INR により VKA の治療効果のモニターを行ったため、エノキサパリン／VKA 投与群で当該薬剤を服用した被験者は PP 解析対象集団の対象に含めた）であった。

安全性解析対象集団は、リバーロキサバン群 1,718 例、エノキサパリン／VKA 群 1,711 例であった。

ITT on treatment 解析対象集団は、リバーロキサバン群：1,718 例、エノキサパリン／VKA 群：1,705 例であった。リバーロキサバン群に無作為に割り付けられた被験者のうち 6 例は、実際は試験中にエノキサパリン／VKA の投与を受けた。よって、これらの被験者を安全性解析対象集団の解析時に限りエノキサパリン／VKA 群に含め、ITT 解析対象集団の解析時にはリバーロキサバン群のままとした。また、これらの被験者は ITT on treatment 解析対象集団及び PP 解析対象集団には含めなかった。

20 例（リバーロキサバン群 7 例、エノキサパリン／VKA 群 13 例）が治験薬の投与を一回も受けなかった。これらの被験者は有効性の主要解析（ITT 解析対象集団）に含めたが、安全性解析対象集団、ITT on treatment 解析対象集団、PP 解析対象集団には含めなかった。治験薬投与を行わなかった理由は、ベースライン時に DVT と判定されなかった、治験実施計画書違反、同意撤回、試験前に有効性主要評価項目の発現などであった。

表 2.7.6.1- 6 各解析対象集団の内訳及び主な除外理由（無作為割り付けされた被験者）

	リバーロキサバン	エノキサパリン／VKA
無作為割り付け	1731/1731 (100.0%)	1718/1718 (100.0%)
ITT 解析対象集団	1731/1731 (100.0%)	1718/1718 (100.0%)
安全性解析対象集団	1718/1725 (99.6%)	1711/1724 (99.2%)
PP 解析対象集団	1525/1731 (88.1%)	1571/1718 (91.4%)
安全性解析対象集団からの除外[a]	7/1725[a] (0.4%)	13/1724[a] (0.8%)
治験薬の投与なし	7/1725 (0.4%)	13/1724 (0.8%)
PP 解析対象集団からの除外[b]	199/1731 (11.5%)	134/1718 (7.8%)
治験薬投与へのコンプライアンス不十分	137/1731 (7.9%)	91/1718 (5.3%)
治験薬の誤投与[c]	0/1731	21/1718 (1.2%)
治験薬投与時における誤り[d]	1/1731 (<0.1%)	0/1718
割り付け以外の治験薬投与	6/1731 (0.3%)	0/1718
CIAC により index イベントが DVT と判定されなかった	21/1731 (1.2%)	17/1718 (1.0%)
投与期間中における強力な CYP3A4 阻害薬／P-gp 阻害薬の投与	1/1731 (<0.1%)	0/1718
投与期間中における強力な CYP3A4 誘導薬の 3 日間以上の投与	29/1731 (1.7%)	N/A
投与期間中における 1 週間を超えるその他の抗凝固薬の使用（抗凝固薬の医療上の必要性がある場合を除く）	11/1731 (0.6%)	N/A
無作為割り付け前の 48 時間を超える治療用量での非経口抗凝固薬の投与又は 2 回以上の VKA の投与	10/1731 (0.6%)	10/1718 (0.6%)

N/A：該当なし（症例検討会の検討結果にしたがって、リバーロキサバン群へ割り付けられた被験者にのみ適用）、VKA：ビタミン K 拮抗薬、CYP3A4：チトクローム P450 3A4 分子種、P-gp：P 糖たん白、ITT：intention-to-treat、PP: 治験実施計画書に適合した
無作為割り付け、ITT 及び PP 解析対象集団は割り付けられた投与群に基づく。安全性解析対象集団は、投与された治験薬に基づく。
被験者は解析対象集団から複数の理由により除外される場合がある。
a：6 例はリバーロキサバン群に割り付けられたが、実際はエノキサパリン／VKA が投与されたため、安全性解析対象集団ではエノキサパリン／VKA 群に含めた。
b：安全性解析対象集団から除外された被験者は、PP 解析対象集団からも除外された。
c：初期のエノキサパリン投与下での治験薬の誤投与
d：治験薬投与時における誤り（割付時間、治験薬開始時間及び有害事象に関連する治験薬の開始時間に対して矛盾がある）。
引用元：5.3.5.1.1 MRR-00292/Table 14.1/17 及び Table 14.1/18

2.7.6.1.2.1.3 人口統計学的特性

ITT 解析対象集団の人口統計学的特性を表 2.7.6.1- 7に示す。人口統計学的特性は、ITT 解析対象集団と PP 解析対象集団及び安全性解析対象集団で同様であった。

全体として、ITT 解析対象集団の被験者背景は投与群間で類似していた。男性は、リバーロキサバン群では 57.4%、エノキサパリン／VKA 群では 56.3%で、人種では白人が 76.7%及び

76.8%、アジア人が 13.2%及び 12.7%であった。約 7%の被験者については、当該地域の法令により人種情報の収集が許可されなかったため、不明とされた。

年齢範囲はリバーロキサバン群では 18～95 歳、エノキサパリン／VKA 群では 18～97 歳であり、平均年齢は 55.8 歳及び 56.4 歳であった。年齢（区分 1）の分類では、18～＜40 歳が 18.1%及び 16.2%、40～＜60 歳が 37.1%及び 38.5%、60～＜75 歳が 30.6%及び 30.2%、≧75 歳が 14.2%及び 15.0%であった。年齢（区分 2）の分類では、65 歳未満が約 2/3（リバーロキサバン群：66%、エノキサパリン／VKA 群：65%）で、65 歳以上が 1/3 を占めた。

平均体重〔平均値±標準偏差（SD）〕はリバーロキサバン群で 82.1±18.4kg、エノキサパリン／VKA 群で 81.6±18.9kg、体重範囲はそれぞれ 33.0～192.8kg 及び 34.1～163.5kg、平均 BMI（平均値±SD）は 27.82±5.35kg/m^2、27.78±5.52kg/m^2 であった。

リバーロキサバン群の 6 例（0.3%）及びエノキサパリン／VKA 群の 9 例（0.5%）は、CL_{CR} が 30mL/min 未満（除外基準に抵触）であった。

表 2.7.6.1- 7　人口統計学的特性（ITT 解析対象集団）

	リバーロキサバン N＝1731（100%）	エノキサパリン／VKA N＝1718（100%）
性別		
男性	993（57.4%）	967（56.3%）
女性	738（42.6%）	751（43.7%）
人種		
白人	1327（76.7%）	1319（76.8%）
黒人	38（ 2.2%）	44（ 2.6%）
アジア人	229（13.2%）	219（12.7%）
アメリカンインディアン又はアラスカ先住民	1（<0.1%）	2（ 0.1%）
ヒスパニック系	9（ 0.5%）	9（ 0.5%）
分類不能	5（ 0.3%）	2（ 0.1%）
不明	122（ 7.0%）	123（ 7.2%）
年齢		
N	1731	1718
平均値±SD	55.8 ± 16.4	56.4 ± 16.3
範囲	18-95	18-97
年齢（区分 1）		
18～＜40 歳	314（18.1%）	279（16.2%）
40～＜60 歳	642（37.1%）	662（38.5%）
60～＜75 歳	530（30.6%）	519（30.2%）
≧75 歳	245（14.2%）	258（15.0%）
年齢（区分 2）		
＜65 歳	1145（66.1%）	1111（64.7%）
65～75 歳	371（21.4%）	382（22.2%）
＞75 歳	215（12.4%）	225（13.1%）
体重（kg）		
欠測	6	1
N	1725	1717
平均値±SD	82.1 ± 18.4	81.6 ± 18.9
範囲	33.0-192.8	34.1-163.5
体重		
欠測	6（ 0.3%）	1（<0.1%）
≦50kg	37（ 2.1%）	49（ 2.9%）
50＜～60kg	165（ 9.5%）	176（10.2%）
60＜～70kg	292（16.9%）	299（17.4%）
70＜～80kg	383（22.1%）	392（22.8%）
80＜～90kg	357（20.6%）	315（18.3%）
90＜～100kg	246（14.2%）	240（14.0%）
100＜～110kg	126（ 7.3%）	132（ 7.7%）
＞110kg	119（ 6.9%）	114（ 6.6%）

表 2.7.6.1- 7　人口統計学的特性（ITT 解析対象集団）（続き）

	リバーロキサバン N＝1731（100%）	エノキサパリン／VKA N＝1718（100%）
BMI（kg/m²）		
N	1717	1706
平均値±SD	27.82 ± 5.35	27.78 ± 5.52
範囲	14.9-56.8	13.3-64.9
BMI		
欠測	14（ 0.8%）	12（ 0.7%）
＜18.5kg/m²	21（ 1.2%）	24（ 1.4%）
18.5～＜25kg/m²	525（30.3%）	536（31.2%）
25～＜30kg/m²	660（38.1%）	662（38.5%）
30～＜35kg/m²	356（20.6%）	312（18.2%）
35～＜40kg/m²	103（ 6.0%）	122（ 7.1%）
≧40kg/m²	52（ 3.0%）	50（ 2.9%）
クレアチニンクリアランス		
欠測	24（ 1.4%）	20（ 1.2%）
＜30mL/min	6（ 0.3%）[a]	9（ 0.5%）[a]
30～＜50mL/min	115（ 6.6%）	120（ 7.0%）
50～＜80mL/min	393（22.7%）	399（23.2%）
≧80mL/min	1193（68.9%）	1170（68.1%）

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、BMI：body mass index（体格指数）
a：測定値の範囲は 22.3 mL/min～29.9 mL/min であった
頻度（%）は欠測値を含めて算出した。
人種の不明は、法律上の理由による未回答である。
クレアチニンクリアランスは、割り付け日までの直近の測定値を基に、Cockroft Gault 式を用いて計算した。
引用元：5.3.5.1.1 MRR-00292/Table 14.1/24

2.7.6.1.2.1.4　　血栓塞栓症の危険因子

血栓塞栓症の危険因子のうち保有率の高かったものは、最近の手術又は外傷、活動性の制限及びエストロゲン含有薬剤の使用からなる「一過性」危険因子と、特発性 DVT／PE、活動性悪性腫瘍及び DVT／PE の既往からなる「永続的」危険因子に分類される（表 2.7.6.1- 8）。最も多く報告された VTE の危険因子は特発性 DVT（被験者の約 48%）であり、続いて最近の手術又は外傷（約 20%）、DVT／PE の既往（約 19%）、活動性の制限（約 15%）であった。

表 2.7.6.1- 8　血栓塞栓症の危険因子（ITT 解析対象集団）

	リバーロキサバン N＝1731（100%）	エノキサパリン／VKA N＝1718（100%）
特発性 DVT／PE	807（46.6%）	862（50.2%）
最近の手術又は外傷	338（19.5%）	335（19.5%）
DVT／PE の既往	336（19.4%）	330（19.2%）
活動性の制限	265（15.3%）	260（15.1%）
エストロゲン含有医薬品の使用	140（ 8.1%）	115（ 6.7%）
既知の血栓性素因 [a]	107（ 6.2%）	116（ 6.8%）
第Ｖ因子 Leiden 変異	52（48.6%）	77（66.4%）
高ホモシステイン血症	22（20.6%）	17（14.7%）
抗リン脂質抗体	12（11.2%）	14（12.1%）
プロテインＳ欠損症	10（ 9.3%）	10（ 8.6%）
プロテインＣ欠損症	10（ 9.3%）	7（ 6.0%）
プロトロンビン遺伝子変異	8（ 7.5%）	9（ 7.8%）
第Ⅷ因子高値	7（ 6.5%）	2（ 1.7%）
アンチトロンビンに関するもの	5（ 4.7%）	2（ 1.7%）
活動性悪性腫瘍	118（ 6.8%）	89（ 5.2%）
VTE の家族歴	35（ 2.0%）	18（ 1.0%）
肥満	15（ 0.9%）	19（ 1.1%）
ニコチン乱用	10（ 0.6%）	15（ 0.9%）
産褥	6（ 0.3%）	11（ 0.6%）
静脈瘤	8（ 0.5%）	6（ 0.3%）
炎症／感染症	5（ 0.3%）	4（ 0.2%）
静脈炎／表在性静脈血栓症	5（ 0.3%）	2（ 0.1%）
副腎皮質ステロイドの使用	4（ 0.2%）	3（ 0.2%）
静脈不全	1（<0.1%）	5（ 0.3%）
悪性腫瘍の既往	2（ 0.1%）	3（ 0.2%）
年齢	1（<0.1%）	1（<0.1%）
丹毒	0	1（<0.1%）
心不全	0	1（<0.1%）
そのほかの危険因子	9（ 0.5%）	11（ 0.6%）

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症、VTE：静脈血栓塞栓症
被験者は 2 つ以上の危険因子や血栓性素因を有する場合もあるため、合計は一致しない。
特発性 DVT は治験責任（分担）医師の評価により分類された。
a：比較的多く報告された血栓性素因を示す。
引用元：5.3.5.1.1 MRR-00292/Table 14.1/34 及び Table 14.1/43

予定投与期間別の危険因子を表 2.7.6.1- 9に示す。予定投与期間が 3 ヵ月のコホートでは、永続的危険因子である特発性 DVT、DVT／PE の既往、先天性凝固異常症の保有割合が最も低かった。一方、このコホートでは一過性危険因子である最近の手術又は外傷、活動性の制限を伴った割合が高かった。

予定投与期間が 6 ヵ月のコホートでは、3 ヵ月のコホートに比べて永続的危険因子の保有割合が高く、一過性の危険因子の保有割合が低かった。

予定投与期間が 12 ヵ月のコホートでも 3 ヵ月のコホートと比べて永続的危険因子の保有割合が高く、一過性危険因子の保有割合が低かった。予定投与期間が 6 ヵ月のコホートと比べた場合は、永続的危険因子である DVT／PE の既往、先天性凝固異常症、VTE の家族歴が高かった。

表 2.7.6.1- 9 予定投与期間別の血栓塞栓症の危険因子（いずれかの投与群で 4%以上：ITT 解析対象集団）

	リバーロキサバン	エノキサパリン／VKA
3 ヵ月のコホート	(N=208)	(N=203)
最近の手術又は外傷	102 (49.0%)	104 (51.2%)
活動性の制限	71 (34.1%)	54 (26.6%)
特発性 DVT／PE	49 (23.6%)	54 (26.6%)
エストロゲン含有医薬品の使用	24 (11.5%)	22 (10.8%)
DVT／PE の既往	6 (2.9%)	14 (6.9%)
活動性悪性腫瘍	9 (4.3%)	6 (3.0%)
6 ヵ月のコホート	(N=1083)	(N=1083)
特発性 DVT／PE	571 (52.7%)	597 (55.1%)
最近の手術又は外傷	187 (17.3%)	196 (18.1%)
活動性の制限	164 (15.1%)	166 (15.3%)
DVT／PE の既往	142 (13.1%)	135 (12.5%)
エストロゲン含有医薬品の使用	102 (9.4%)	77 (7.1%)
活動性悪性腫瘍	83 (7.7%)	63 (5.8%)
既知の血栓性素因 [a]	49 (4.5%)	62 (5.7%)
12 か月のコホート	(N=440)	(N=432)
特発性 DVT／PE	187 (42.5%)	211 (48.8%)
DVT／PE の既往	188 (42.7%)	181 (41.9%)
既知の血栓性素因 [a]	56 (12.7%)	52 (12.0%)
最近の手術又は外傷	49 (11.1%)	35 (8.1%)
活動性の制限	30 (6.8%)	40 (9.3%)
活動性悪性腫瘍	26 (5.9%)	20 (4.6%)
VTE の家族歴	21 (4.8%)	12 (2.8%)
エストロゲン含有医薬品の使用	14 (3.2%)	16 (3.7%)

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症
被験者は 2 つ以上の危険因子や血栓性素因を有する場合もあるため、合計は一致しない。
特発性 DVT／PE は治験責任（分担）医師の評価により分類された。
a：血栓性素因 の種類はコホート毎に分類されなかった。
引用元：5.3.5.1.1 MRR-00292/Table 14.1/35

2.7.6.1.2.1.5 index イベント（DVT）

ITT 解析対象集団において、ベースライン時に本試験対象として組み入れた DVT（index イベント）の CIAC による判定結果を表 2.7.6.1- 10に示す。ITT 解析対象集団の 98.7%の被験者が

CIAC によって症候性近位 DVT と判定された。症候性 DVT ではないと判定された被験者が両投与群共に 0.9%で、評価不可能が共に 0.3%であった

表 2.7.6.1- 10　CIAC による index イベント（DVT）の判定（ITT 解析対象集団）

	リバーロキサバン群 N=1731(100%)	エノキサパリン／VKA 群 N=1718(100%)
欠測	1 (＜0.1%)	1 (＜0.1%)
評価不可能	6 (　0.3%)	5 (　0.3%)
症候性 DVT ではないと判定	16 (　0.9%)	15 (　0.9%)
遠位 DVT のみと判定	0	1 (＜0.1%)
近位 DVT と判定	1708 (98.7%)	1696 (98.7%)

ITT： intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症
引用元: 5.3.5.1.1 MRR-00292/Table 14.1/53

DVT（index イベント）は、治験責任（分担）医師により報告された血栓塞栓症の危険因子により、原発性又は二次性 DVT に分類された。最近の手術又は外傷、活動性の制限、エストロゲンを含んだ薬剤の使用、活動性悪性腫瘍、及び産褥のうち少なくとも一つの危険因子が治験責任（分担）医師により特定されれば、DVT は二次性 DVT に分類し、これら以外の場合は原発性 DVT と考えた。DVT（index イベント）が原発性 DVT とされた被験者の割合は、リバーロキサバン群では 60.9%、エノキサパリン／VKA 群では 63.0%であり、二次性 DVT とされた被験者の割合はそれぞれ 39.1%、37.0%であった（表 2.7.6.1- 11）。

表 2.7.6.1- 11　index イベント（DVT）の分類（ITT 解析対象集団）

	リバーロキサバン N＝1731 (100%)	エノキサパリン／VKA N＝1718 (100%)
原発性 DVT／PE	1055 (60.9%)	1083 (63.0%)
二次性 DVT／PE	676 (39.1%)	635 (37.0%)
最近の手術又は外傷	338 (19.5%)	335 (19.5%)
活動性の制限	265 (15.3%)	260 (15.1%)
エストロゲンを含んだ薬剤の使用	140 (8.1%)	115 (6.7%)
産褥	6 (0.3%)	11 (0.6%)
活動性悪性腫瘍	118 (6.8%)	89 (5.2%)

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症
被験者は 2 つ以上の二次性 DVT／PE の危険因子を有する可能性がある。原発性 DVT／PE と二次性 DVT／PE の区分は、本評価の対象である DVT（PE を伴わない）を有する被験者のみに使用した。
引用元：5.3.5.1.1 MRR-00292/Table 14.1/44

index イベント（DVT）発現から無作為割り付けまでの期間：

ITT 解析対象集団における、index イベント（DVT）兆候発現から無作為割り付けまでの期間の中央値（四分位範囲）はリバーロキサバン群で 5 日（3～10 日）、エノキサパリン／VKA 群で 5 日（3～10 日）であった（5.3.5.1.1 MRR-00292/Table 14.1/62）。PP 解析対象集団においても同様であった（5.3.5.1.1 MRR-00292/Table 14.1/68）。

また、3 ヵ月コホート（441 例）やベースライン時の活動性悪性腫瘍を有する被験者（207 例）の被験者数が少ないことを考慮しても、予定投与期間別、又はベースライン時の活動性悪性腫瘍の有無別においても両投与群間で大きな差はなかった（5.3.5.1.1 MRR-00292/Table 14.1/63、Table 14.1/64）。

2.7.6.1.2.1.6 病歴

病歴は、両投与群の約 90%の被験者から報告された。器官別大分類の病歴で報告の多かったものは、血管障害（リバーロキサバン群とエノキサパリン／VKA 群で 45%）、外科および内科処置（リバーロキサバン群：34%、エノキサパリン／VKA 群：33%）、代謝および栄養障害（リバーロキサバン群 27%、エノキサパリン／VKA 群：31%）であった（5.3.5.1.1 MRR-00292/Table14.1/144）。

2.7.6.1.2.1.7 前治療薬及び併用薬

無作為割り付け日以前に投与された薬剤は前治療薬とみなした。ITT 解析対象集団では、リバーロキサバン群に無作為割り付けされた被験者の 73.0%及びエノキサパリン／VKA 群に無作為割り付けされた被験者の 70.6%が、無作為割り付け前に DVT 治療として LMWH、ヘパリン（未分画）又はフォンダパリヌクスの投与を受けていた（5.3.5.1.1 MRR-00292/Table 14.1/71 及び 14.1/110）。ATC 医薬品分類で報告の多かった併用薬は、鎮痛薬、制酸薬、レニン・アンジオテンシン系に作用する薬剤、抗菌薬及び眼科用薬であった。

抗血栓薬を含む併用薬については投与開始又は中止時刻が記録されていない。抗血栓薬の投与が治験薬投与開始日に中止された場合、あるいは治験薬投与中止日に開始された場合、併用とみなした。

ITT 解析対象集団での無作為割り付けから治験薬投与終了日までの抗血栓薬（治験薬を除く）使用の割合は、リバーロキサバン群で 20.9%、及びエノキサパリン／VKA 群で 27.8%であった。使用頻度の高い薬剤は、エノキサパリン（リバーロキサバン群：4.6%、エノキサパリン／VKA 群：11.5%）、アセチルサリチル酸（9.7%及び 9.8%）及びワルファリン（2.9%及び 2.8%）であった。抗凝固薬の併用は、有害事象への対処又は予定手術・処置とのつなぎのためと推察される。エノキサパリン又は VKA を併用薬と治験薬のいずれに分類するかは治験責任（分担）医師が行った分類に従った（5.3.5.1.1 MRR-00292/Table 14.1/108）。

抗血栓薬使用の割合は、予定投与期間の長さにしたがって上昇する傾向が認められ、またベースライン時に活動性悪性腫瘍を有する被験者で高い傾向が認められた（5.3.5.1.1 MRR-00292/Table 14.1/109 及び 14.1/110）。

2.7.6.1.2.1.8 服薬状況

2.7.6.1.2.1.8.1 服薬期間

試験デザインがイベント主導型であったため、既に試験に組み入れた被験者で、主要評価項目の目標イベント発現数の 88 件に達する見込みを得た時点で被験者の組み入れを終了した。その後、予定投与期間が 3 ヵ月のコホートに割り付けられた場合は 3 ヵ月に達するまで、6 又は 12 ヵ月のコホートに割り付けられた場合は 6 ヵ月に達するまで治験薬を投与することとした。

その結果、予定投与期間 12 ヵ月のコホートが、治験依頼者によるこの試験終了の影響を受け、投与を完了した被験者は 3 ヵ月のコホート（89.1%）、6 ヵ月のコホート（86.6%）と比べ、12 ヵ月のコホート（63.2%）で低かった（5.3.5.1.1　MRR-00292/Table 14.1/9）。

実際の投与期間は、3 ヵ月以上がリバーロキサバン群 92.2%及びエノキサパリン／VKA 群 89.4%、6 ヵ月以上がリバーロキサバン群 68.4%及びエノキサパリン／VKA 群 63.0%、12 ヵ月以上がリバーロキサバン群 2.8%及びエノキサパリン／VKA 群 2.4%であった（表 2.7.6.1- 12）。この実際の服薬期間に関する解析において、1 ヵ月は 30 日間で計算したため 12 ヵ月以上は 360 日間以上であった。一方、治験薬投与の完了・未完了の判断基準はこれとは異なり、12 ヵ月の場合は 352 日間以上投与を受けた被験者を完了と判断した。

安全性解析対象集団における服薬期間の中央値と四分位範囲（IQR）は、リバーロキサバン群で 182 日（178～190 日）、エノキサパリン／VKA 群で 181.0 日（176.0～189.0 日）であった（表 2.7.6.1- 12）。約半数の被験者（リバーロキサバン群：50.0%、エノキサパリン／VKA 群：45.0%）が 6～9 ヵ月の投与を受けた。また、リバーロキサバン群とエノキサパリン／VKA 群の実際の投与期間の長さは同程度であった。実投与期間の平均値はリバーロキサバン群 194.4 日間、エノキサパリン／VKA 群 188.7 日間であった（表 2.7.6.1- 12）。

表 2.7.6.1- 12　実際の服薬期間（安全性解析対象集団）

		リバーロキサバン N＝1718 (100%)	エノキサパリン／VKA N＝1711 (100%)
服薬期間	＜1 週間	22 (1.3%)	22 (1.3%)
期間（区分）	1 週間～＜1 ヵ月	49 (2.9%)	83 (4.9%)
	1 ヵ月～＜3 ヵ月	51 (3.0%)	68 (4.0%)
	3 ヵ月～＜6 ヵ月	412 (24.0%)	454 (26.5%)
	6 ヵ月～＜9 ヵ月	859 (50.0%)	770 (45.0%)
	9 ヵ月～＜12 ヵ月	276 (16.1%)	272 (15.9%)
	≧12 ヵ月	49 (2.9%)	41 (2.4%)
服薬期間（日）	中央値（IQR）	182.0 (178～190)	181.0 (175～189)
	平均値±SD	194.4±89.7	188.2±92.8
	範囲	1～401	1～390

ITT：intention-to-treat、IQR：四分位範囲、VKA：ビタミン K 拮抗薬
30 日間を 1 ヵ月とした。
服薬期間（日）の計算は、日付が判明している場合、治験薬投与終了日－初回投与日＋1 とした。投与終了日が欠測の場合は、SAP 補遺に定義した補完を行った。
%は欠測値を含む。
引用元：5.3.5.1.1 MRR-00292/Table 14.2/34

2.7.6.1.2.1.8.2　服薬コンプライアンス

リバーロキサバン群の服薬率は、服薬した錠剤数を実際の投与期間に必要とされた錠剤数で除した計算値に基づいて算出した。服薬率は、最初の 3 週間の 1 日 2 回投与期と、それ以降の 1 日 1 回投与期に分けて評価した。ITT 解析対象集団において、リバーロキサバン群では 91.3%の被験者が服薬率 80%以上であった（表 2.7.6.1- 13）。

表 2.7.6.1- 13　服薬率（リバーロキサバン群）

		ITT 解析対象集団 N＝1731 （100%）	PP 解析対象集団 N＝1525 （100%）
全服薬率	治験薬の投与なし	13（ 0.8%）	0
	欠測	17（ 1.0%）	0
	＜50%	51（ 2.9%）	2[a]（ 0.1%）
	50～＜80%	69（ 4.0%）	1[a]（<0.1%）
	≧80%	1581（91.3%）	1522（99.8%）
服薬率：15mg 1 日 2 回投与期間（最初の 3 週間）	治験薬の投与なし	13（ 0.8%）	0
	該当期間に治験薬投与なし	0	0
	欠測	13（ 0.8%）	6（ 0.4%）
	＜50%	56（ 3.2%）	16（ 1.0%）
	50～＜80%	45（ 2.6%）	36（ 2.4%）
	≧80%	1604（92.7%）	1467（96.2%）
服薬率：20mg 1 日 1 回投与期間（投与開始 3、6 及び 12 ヵ月後まで）	治験薬の投与なし	13（ 0.8%）	0
	該当期間に治験薬投与なし	60（ 3.5%）	40（ 2.6%）
	欠測	25（ 1.4%）	9（ 0.6%）
	＜50%	58（ 3.4%）	2（ 0.1%）
	50～＜80%	48（ 2.8%）	11（ 0.7%）
	≧80%	1527（88.2%）	1463（95.9%）

VKA：ビタミン K 拮抗薬、ITT：intention-to-treat、PP：治験実施計画書に適合した
平均服薬率は、実際に使用された錠数を治験薬の初回処方から投与終了日（中止した場合も含む）までの投与期間における予定服薬錠数で除して算出した。
服薬率は、実際に使用された錠数をそれぞれの投与期間で治験薬の初回処方から投与終了日までの予定服薬錠数で除して算出した。
a：3 例ともリバーロキサバン投与を 1 日 2 回投与期間中に中止した。症例検討会の検討結果にしたがって調整した服薬率は、いずれも 80%を超えていたため、PP 解析対象集団から除外しなかった。
引用元：5.3.5.1.1 MRR-00292/Table 14.2/61、Table 14.2/63、Table 14.2/64、Table 14.2/66、Table 14.2/67 及び Table 14.2/69

エノキサパリン／VKA 群の服薬率は、予定投与スケジュールにおける初期のエノキサパリン投与の期間と、VKA 投与期間中の PT-INR の測定頻度に基づいて算出した。治験実施計画書では、初期のエノキサパリン投与の期間を「24 時間以上間隔をおいた 2 回連続の測定で PT-INR が 2.0 以上となるまで最低 5 日間エノキサパリン投与」とし、VKA 投与期間中の PT-INR の測定頻度を「月 1 回の PT-INR の測定」と規定した。全服薬率が 80%以上の被験者の割合は ITT 解析対象集団では 93.8%、PP 解析対象集団では 99.8%であった（表 2.7.6.1- 14）。

表 2.7.6.1- 14　服薬率（エノキサパリン／VKA 群）

		ITT 解析対象集団 N＝1718 (100%)	PP 解析対象集団 N＝1571 (100%)
全服薬率	治験薬の投与なし	13 (0.8%)	0
	欠測	0	0
	＜50%	29 (1.7%)	1[a] (<0.1%)
	50～＜80%	64 (3.7%)	2[a] (0.1%)
	≧80%	1612 (93.8%)	1568 (99.8%)
服薬率：エノキサパリン投与（治験実施計画書に従い、少なくとも 5 日間）	治験薬の投与なし	13 (0.8%)	0
	該当期間に治験薬投与なし	9 (0.5%)	7 (0.4%)
	欠測	4 (0.2%)	4 (0.3%)
	＜50%	17 (1.0%)	1 (<0.1%)
	50～＜80%	17 (1.0%)	1 (<0.1%)
	≧80%	1658 (96.5%)	1558 (99.2%)
服薬率：VKA 投与（投与開始 3、6 及び 12 ヵ月間の PT-INR の測定頻度 ）	治験薬の投与なし	13 (0.8%)	0
	該当期間に治験薬投与なし	1 (<0.1%)	1 (<0.1%)
	欠測	14 (0.8%)	6 (0.4%)
	＜50%	13 (0.8%)	0
	50～＜80%	52 (3.0%)	1 (<0.1%)
	≧80%	1625 (94.6%)	1563 (99.5%)

ITT：intention-to-treat、PP：治験実施計画書に適合した、VKA ：ビタミン K 拮抗薬、PT-INR：プロトロンビン時間国際標準比
服薬率：最初のエノキサパリン投与期間と VKA 投与期間の PT-INR 測定回数を基に算出した。全体の服薬遵守については、最初のエノキサパリン投与期間及び VKA 投与期間の両方において少なくとも 80%の服薬率が必要である。
a：3 例中 2 例がエノキサパリン投与期間中に中止し、症例検討会の検討結果にしたがって、この期間で服薬を遵守していると考えられた。その他の 1 例はエノキサパリン投与期間終了時に PT-INR が目標範囲内であったため、服薬を遵守しているとみなし、いずれも PP 解析対象集団から除外しなかった。
引用元：5.3.5.1.1 MRR-00292/Table 14.2/61、Table 14.2/63、Table 14.2/64、Table 14.2/66、Table 14.2/67、Table 14.2/69

2.7.6.1.2.1.8.3　PT-INR が目標範囲内に達するまでの期間

エノキサパリン／VKA 群において、VKA 投与期間（VKA 投与開始後の初期治療のエノキサパリン投与後から VKA の投与終了までの期間）に PT-INR の目標範囲 2.0～3.0 の達成度を評価した。

PT-INR が目標範囲の下限（PT-INR が 2.0）以上に達するまでの期間及び初期の LMWH 投与中止時の PT-INR を表 2.7.6.1- 15に示す。PT-INR が目標範囲内に達するまでの期間は、エノキサパリン／ワルファリン群では 8.7 日、エノキサパリン／acenocoumarol 群では 6.2 日、両投与群全体では 8.1 日であった。

初期の LMWH 投与中止の時点において、PT-INR が目標範囲内（2.0～3.0）にあった被験者の割合は 62.4%（安全性解析対象集団）、2.0 を下回っていたのは 17.5%、3.0 を上回っていたのは 19.1%であった。予定投与期間 3、6 及び 12 ヵ月のコホートの各データは、全体のデータと一貫していた（5.3.5.1.1 MRR-00292/Table 14.2/282）。

表 2.7.6.1- 15　PT-INR が目標範囲の下限以上に達するまでの期間及び初期の LMWH 投与中止時の PT-INR（安全性解析対象集団）

	エノキサパリン/ワルファリン (N＝1278)	エノキサパリン/acenocoumarol (N＝426)	合計 (N＝1704)
PT-INR が目標範囲下限（PT-INR≧2）以上に達するまでの期間（無作為割り付けからの日数）			
N	1248	419	1667
欠測	30	7	37
平均値	8.7	6.2	8.1
SD	9.4	7.3	9.0
最小値	1	1	1
Q1	5.0	3.0	4.0
中央値	7.0	5.0	6.0
Q3	9.0	7.0	9.0
最大値	152	97	152
初期の LWMH 投与中止時の PT-INR			
N	1278（100.0%）	426（100.0%）	1704（100.0%）
初期の LMWH 未投与	1（ <0.1%）	1（ 0.2%）	2（ 0.1%）
初期の LMWH 投与時に PT-INR 未測定	12（ 0.9%）	3（ 0.7%）	15（ 0.9%）
＜2.0（欠測値なし）	254（ 19.9%）	44（ 10.3%）	298（ 17.5%）
2.0≦～≦3.0	812（ 63.5%）	252（ 59.2%）	1064（ 62.4%）
＞3.0	199（ 15.6%）	126（ 29.6%）	325（ 19.1%）

LMWH：低分子量ヘパリン、PT-INR：プロトロンビン時間国際標準比
値は実測及び推定（すなわち、線形補間）された PT-INR を基にしている。
引用元：5.3.5.1.1 MRR-00292/ Table 14.2/281

2.7.6.1.2.1.8.4　PT-INR が目標範囲内であった期間割合（TTR）

VKA 投与期間中に被験者の PT-INR が目標範囲内（2.0～3.0）であった期間割合（TTR）の平均値を未調整で表 2.7.6.1- 16に示す。未調整 PT-INR の解析には、以下の期間を問わず VKA 投与期間のすべての PT-INR 測定値を含めた。

- 治験責任（分担）医師による意図的な VKA 投与中断期間（CIAC 判定による）、及び VKA 投与再開後の 8 日間
- 別の抗凝固薬を追加使用した期間（ヘパリン、フォンダパリヌクス、その他の VKA）

有効性の主要評価項目又は「重大な出血事象」報告後の期間

VKA 単独投与期間中、1 ヵ月目の TTR は 54.1%（週平均値の範囲：51.6%～57.3%）、それ以降の 11 ヵ月のうち 9 ヵ月は 60%超であった。全試験期間の未調整 TTR は 57.7%であった。

表 2.7.6.1- 16　PT-INR が目標範囲内であった期間割合（未調整 TTR、安全性解析対象集団、エノキサパリン／VKA 群、N=1704）

VKA 投与期間	エノキサパリン／VKA 群（平均）	VKA 投与期間	エノキサパリン／VKA 群（平均）
1 週目	57.3%	1 ヵ月目	54.1%
2 週目	51.6%	2 ヵ月目	58.0%
3 週目	55.2%	3 ヵ月目	61.0%
4 週目	55.4%	4 ヵ月目	61.2%
		5 ヵ月目	62.0%
		6 ヵ月目	60.5%
		7 ヵ月目	61.2%
		8 ヵ月目	64.9%
		9 ヵ月目	65.2%
		10 ヵ月目	66.4%
		11 ヵ月目	63.8%
		12 ヵ月目	57.2%
		全 VKA 投与期間	57.7%

PT-INR：プロトロンビン時間国際標準比、VKA ：ビタミン K 拮抗薬
VKA 投与期間において目標範囲内（2.0～3.0）であった実測 PT-INR の割合を示した。VKA 投与期間は、予定投与期間中の VKA の投与開始後及び最初のエノキサパリンの投与中止後から VKA の投与終了までの期間とした。
引用元：5.3.5.1.1 MRR-00292/Table Table 14.2/298

TTR を上記の期間を除いて調整した結果を表 2.7.6.1- 17に示す（治験総括報告書作成後の事後解析）。

表 2.7.6.1- 17 PT-INR 目標範囲内であった期間割合（調整 TTR、ITT on treatment 解析対象集団、エノキサパリン／VKA 群、N=1704）

VKA 投与期間	エノキサパリン／VKA 群（平均）	VKA 投与期間	エノキサパリン／VKA 群（平均）
1 週目	58.8%	1 ヵ月目	55.8%
2 週目	52.4%	2 ヵ月目	59.1%
3 週目	56.5%	3 ヵ月目	62.3%
4 週目	56.3%	4 ヵ月目	62.1%
		5 ヵ月目	63.1%
		6 ヵ月目	63.8%
		7 ヵ月目	64.3%
		8 ヵ月目	67.4%
		9 ヵ月目	66.3%
		10 ヵ月目	68.0%
		11 ヵ月目	65.3%
		12 ヵ月目	59.1%
		全 VKA 投与期間	60.3%

DVT：深部静脈血栓症、PE：肺塞栓症、VKA：ビタミン K 拮抗薬
VKA 投与期間は、VKA 投与開始及び初期の LMWH 投与中止から VKA 最終投与までの期間と規定した。
下記に該当するものを除き、VKA 投与期間中に実測及び推定（線形補間、最終観察の繰り越し）された PT-INR を基に目標範囲内であった期間を示した。

- 治験責任（分担）医師による意図的な VKA 投与中断期間（CIAC 判定による）及び VKA 投与再開後の 8 日間
- ヘパリン、フォンダパリヌクス及びその他の VKA を含む抗凝固薬を追加投与した期間
- 有効性主要評価項目又は「重大な出血事象」の報告後の期間

引用元：5.3.5.3.7 PH-36746/ Table 14.2/409

2.7.6.1.2.2 有効性の結果

2.7.6.1.2.2.1 有効性主要評価項目

2.7.6.1.2.2.1.1 有効性の主要解析

有効性主要評価項目は、症候性 VTE〔「症候性 DVT」又は「症候性 PE（非致死的及び致死的）」の複合エンドポイント〕であった。ITT 解析対象集団における、予定投与期間終了時までの有効性主要評価項目のイベント発現頻度は、リバーロキサバン群では 2.1%（36/1,731 例）、エノキサパリン／VKA 群では 3.0%（51/1,718 例）であった（表 2.7.6.1- 18）。

有効性主要評価項目の各構成要素について、ITT 解析対象集団における予定投与期間終了時までの発現頻度を以下に示す。

- PE による死亡：リバーロキサバン群で 0.1%未満（1/1,731 例）、エノキサパリン／VKA 群で 0%
- 死亡理由として PE の可能性を否定できない死亡：リバーロキサバン群で 0.2%（3/1,731 例）、エノキサパリン／VKA 群で 0.3%（6/1,718 例）
- 症候性 PE 及び DVT：リバーロキサバン群で 0.1%未満（1/1,731 例）、エノキサパリン／VKA 群で 0%

- 症候性 PE のみ：リバーロキサバン群で 1.2%（20/1,731 例）、エノキサパリン／VKA 群で 1.0%（18/1,718 例）
- 症候性 DVT のみ：リバーロキサバン群で 0.8%（14/1,731 例）、エノキサパリン／VKA 群で 1.6%（28/1,718 例）

表 2.7.6.1- 18　予定投与期間終了までに発現した有効性評価項目の発現頻度（ITT 解析対象集団）

評価項目/構成要素	リバーロキサバン N＝1731（100%）	エノキサパリン／VKA N＝1718（100%）
有効性主要評価項目（事前に規定）	36（ 2.1%）	51（ 3.0%）
死亡（PE）	1（<0.1%）	0
死亡（PE の可能性を否定できない）	3（ 0.2%）	6（ 0.3%）
症候性 PE 及び DVT	1（<0.1%）	0
症候性 PE	20（ 1.2%）	18（ 1.0%）
症候性 DVT	14（ 0.8%）	28（ 1.6%）
有効性副次的評価項目（事前に規定）	69（ 4.0%）	87（ 5.1%）
死亡（PE）	1（<0.1%）	0
死亡（PE の可能性を否定できない）	3（ 0.2%）	6（ 0.3%）
死亡（出血事象）	1（<0.1%）	5（ 0.3%）
死亡（心血管死）	2（ 0.1%）	4（ 0.2%）
死亡（その他）	31（ 1.8%）	34（ 2.0%）
症候性 PE 及び DVT	1（<0.1%）	0
症候性 PE	20（ 1.2%）	18（ 1.0%）
症候性 DVT	14（ 0.8%）	28（ 1.6%）
症候性 DVT	14（ 0.8%）	28（ 1.6%）
DVT（近位）	13（ 0.8%）	27（ 1.6%）
DVT（遠位）	1（<0.1%）	1（<0.1%）
総合有用性評価指標-1（事前に規定）	51（ 2.9%）	73（ 4.2%）
死亡（PE）	1（<0.1%）	0
死亡（PE の可能性を否定できない）	3（ 0.2%）	6（ 0.3%）
症候性 PE 及び DVT	1（<0.1%）	0
症候性 PE	20（ 1.2%）	18（ 1.0%）
症候性 DVT	14（ 0.8%）	28（ 1.6%）
重大な出血事象	15（ 0.9%）	23（ 1.3%）
総合有用性評価指標-2（事後に規定）	62（ 3.6%）	81（ 4.7%）
死亡（PE）	1（<0.1%）	0
死亡（PE の可能性を否定できない）	3（ 0.2%）	6（ 0.3%）
死亡（心血管死）	2（ 0.1%）	4（ 0.2%）
症候性 PE 及び DVT	1（<0.1%）	0
症候性 PE	20（ 1.2%）	18（ 1.0%）
症候性 DVT	14（ 0.8%）	28（ 1.6%）
重大な出血事象	15（ 0.9%）	23（ 1.3%）
ST 上昇型心筋梗塞（STEMI）	1（<0.1%）	0
非 ST 上昇型心筋梗塞（NSTEMI）	5（ 0.3%）	1（<0.1%）
虚血性脳卒中	3（ 0.2%）	5（ 0.3%）
非中枢神経系塞栓症	2（ 0.1%）	2（ 0.1%）

ITT：intention-to-treat、DVT：深部静脈血栓症、PE：肺塞栓症

発現頻度：割り付けから治験薬投与終了までにイベントが報告された例数/各群の例数、同一症例に複数のイベントが発現した場合、該当症例はいくつかの構成要素で数えられ、構成要素の合計と複合エンドポイントが合わない。

引用元：5.3.5.1.1 MRR-00292/Table14.2-113

有効性の主要解析として、予定投与期間で層別化し、ベースライン時の活動性悪性腫瘍の有無で調整し、予定投与期間終了までの有効性主要評価項目に適合させた Cox 比例ハザードモデルを用いた（表 2.7.6.1- 19）。リバーロキサバン群とエノキサパリン／VKA 群の比較では、ハザード比 0.680（95%信頼区間：0.443～1.042）であった。信頼区間の上限は事前に規定した非劣性マージンである 2.0 を下回り、非劣性の片側 p 値は＜0.0001 であったことから、リバーロキサバンの有効性はエノキサパリン／VKA に対して非劣性であることが検証された。リバーロキサバンの優越性検定では、統計学的有意差はみられなかった（p＝0.0764）。

有効性の主要解析に加え、ITT on treatment 解析対象集団の解析も実施した。有効性主要評価項目の発現頻度はリバーロキサバン群で 2.0%（34/1,718 例）、エノキサパリン／VKA 群で 2.9%（49/1,705 例）であった。層別 Cox 比例ハザードモデルによる有効性主要評価項目のハザード比は 0.671、95%信頼区間は 0.433～1.039（p＜0.0001）であった。

PP 解析対象集団では、有効性主要評価項目の発現頻度はリバーロキサバン群で 2.1%（32/1,525 例）、エノキサパリン／VKA 群で 2.9%（46/1,571 例）であった。層別 Cox 比例ハザードモデルによる有効性主要評価項目のハザード比は 0.698、95%信頼区間は 0.444～1.097（p＜0.0001）であった。

表 2.7.6.1- 19 有効性主要評価項目の概要

解析対象集団	ITT	ITT on treatment	PP
有効性主要評価項目の発現頻度			
リバーロキサバン	36/1731 (2.1%)	34/1718 (2.0%)	32/1525 (2.1%)
エノキサパリン／VKA	51/1718 (3.0%)	49/1705 (2.9%)	46/1571 (2.9%)
Cox 比例ハザードモデルを用いた解析：リバーロキサバン vs エノキサパリン／VKA			
ハザード比	0.680	0.671	0.698
95%信頼区間	0.443～1.042	0.433～1.039	0.444～1.097
非劣性に関する p 値	＜0.0001	＜0.0001	＜0.0001
優越性に関する p 値	0.0764	0.0737	0.1191

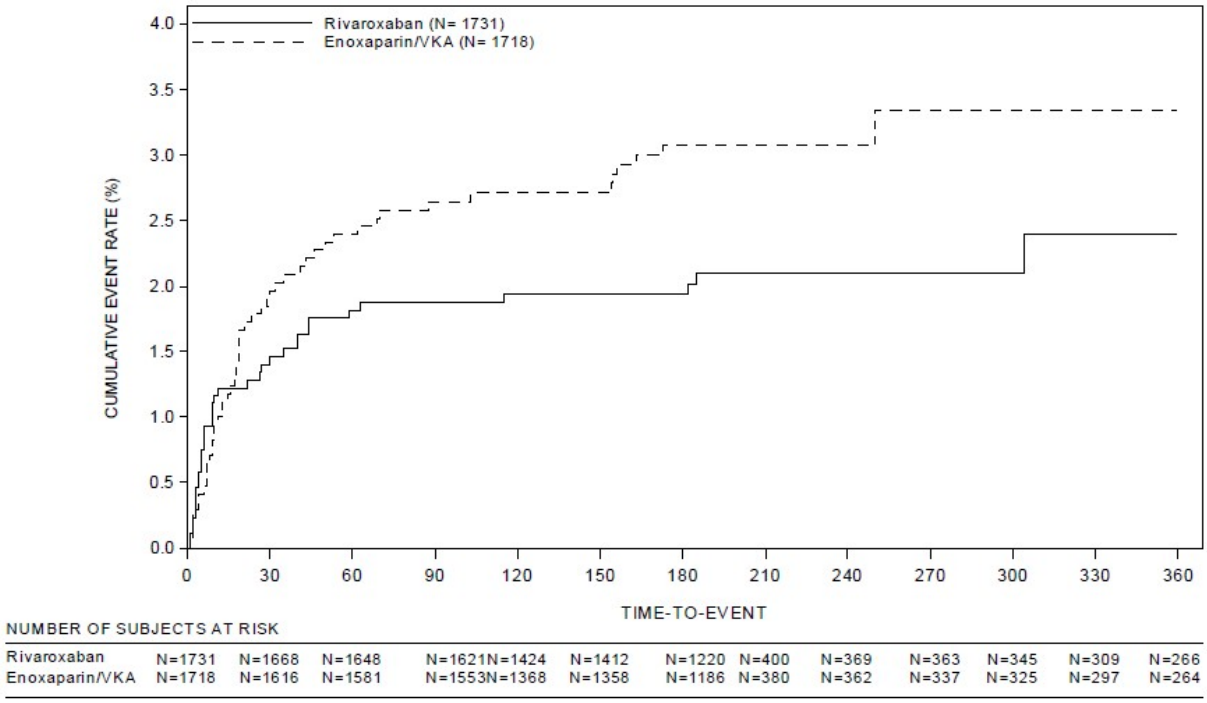
ITT：intention-to-treat、PP：治験実施計画書に適合した、VKA：ビタミン K 拮抗薬。
p 値とハザード比の推定値は層別 Cox 比例ハザードモデルを用いて算出した。層調整には無作為割り付けから予定投与期間終了までのイベント（ITT 解析対象集団）又は治験薬初回投与後から治験薬投与終了後 2 日目までのイベント（ITT on treatment 解析対象集団及び PP 解析対象集団）を用いて算出した。エノキサパリン／VKA 群に対するリバーロキサバン群の対数ハザード比の推定値、標準誤差及び非劣性マージン、2.0 の対数値に基づき、非劣性に関する漸近的片側 p 値を算出した。
引用元：5.3.5.1.1 MRR-00292/Table 14.2/113、Table 14.2/125、Table 14.2/128、Table 14.2/243、Table 14.2/254、Table 14.2/258

ITT 解析対象集団における、有効性主要評価項目の累積発現率の Kaplan-Meier 曲線を図 2.7.6.1- 3に示す。

Kaplan Meier 法による 3、6 又は 12 ヵ月（それぞれ第 99～120 日、第 186～210 日、第 331～359 日）の有効性主要評価項目の累積イベント発現率の差（リバーロキサバンからエノキサパリ

ン／VKA を減じる）は、それぞれ－0.77％、－0.97％及び－0.95％であった（5.3.5.1.1 MRR-00292/Table 14.2/146）。

両投与群の曲線がほぼ重なっている第 14 日までの期間を除く予定投与期間終了までの各時点において、Kaplan-Meier 法による累積イベント発現率（ITT 解析対象集団）は、リバーロキサバン群の方がエノキサパリン／VKA 群より数値的に低かった（図 2.7.6.1- 3）。PP 解析対象集団における Kaplan-Meier 法による累積イベント発現率は、ITT 解析対象集団と類似していた。リバーロキサバン群とエノキサパリン／VKA 群共に、大部分のイベント発現は投与開始後 1 ヵ月間にみられた。リバーロキサバン群では 2 週目終了までにイベントの 50％が発現し、エノキサパリン／VKA では 3 週目までにイベントの 50％が発現した。6 ヵ月目以降は有効性主要評価項目の発現はほとんど認められなかった（5.3.5.1.1 MRR-00292/Table 14.2/146）。



Timepoint: Event or censoring up to the intended treatment duration
引用元：5.3.5.3.1 MR-00292/Figure 14.2/1

図 2.7.6.1- 3　Kaplan-Meier 法による有効性主要評価項目の累積イベント発現率（ITT 解析対象集団）

有効性評価項目及び各構成要素の最初の発現頻度に関して以下の時期別に解析した。

- 0～3 ヵ月　　（無作為割り付けから第 98 日までにイベント発現）
- 3～6 ヵ月　　（第 99 日から 185 日目までにイベント発現）
- 6～12 ヵ月　　（第 186 日から 359 日目までにイベント発現）

イベントの大半は 0～3 ヵ月の期間に発現した。有効性評価項目のイベントの発現頻度は、リバーロキサバン群のほうがエノキサパリン／VKA 群よりおおむね低かった。3～6 ヵ月の期間の発現頻度は 0～3 ヵ月の期間よりおおむね低く、6～12 ヵ月の期間の発現頻度はおおむね 3～6 ヵ月の期間より更に低かった。6～12 ヵ月の期間に有効性主要評価項目のイベントを発現した被験者は各投与群で 1 症例のみであった。

0～3 ヵ月の期間に関して、予定投与期間が 3 ヵ月であったコホートにおいて検討すると、リバーロキサバン群のほうがエノキサパリン／VKA 群より有効性主要評価項目のイベントを発現した被験者の数が数値的に多かった〔リバーロキサバン群：2.4%（5/208 例）、エノキサパリン／VKA 群：1.5%（3/203 例）〕。一方、予定投与期間が 6 ヵ月のコホートでは、エノキサパリン／VKA 群のほうがイベントを発現した被験者数が多く〔リバーロキサバン群：2.1%（23/1,083 例）、エノキサパリン／VKA 群：2.4%（26/1,083 例）〕、予定投与期間が 12 ヵ月のコホートにおいても同様であった〔リバーロキサバン群：0.9%（4/440 例）、エノキサパリン／VKA 群：3.5%（15/432 例）〕（5.3.5.1.1 MRR-00292/Table 14.2/98）。

2.7.6.1.2.2.1.2　フォローアップ期間

治験薬投与終了後 2 日目から 30 日目までの期間の有効性主要評価項目の発現頻度は、リバーロキサバン群で 0.8%（12/1,425 例）、エノキサパリン／VKA 群で 0.5%（7/1,408 例）であった。発現したイベントの内訳は、死亡（PE の可能性が除外できない）が両投与群共に 1 例、症候性 PE のみがリバーロキサバン群 4 例及びエノキサパリン／VKA 群 2 例、症候性 DVT のみがリバーロキサバン群 8 例及びエノキサパリン／VKA 群 4 例であった（5.3.5.1.1 MRR-00292/Table 14.2/131）。

治験薬投与終了後 3 日目から 30 日目までのフォローアップ期間についての事後解析を行った。有効性主要評価項目の発現頻度はリバーロキサバン群で 0.8%（11/1,425 例）、エノキサパリン／VKA 群で 0.5%（7/1,408 例）であった（表 2.7.6.1- 20）。

治験薬投与終了後 2 日目から 30 日目までの解析では、3 日目から 30 日目までの解析と比較して、リバーロキサバン群に症候性 PE が 1 件多く発現しているが、結果の解釈に意味のある影響は認められなかった。

表 2.7.6.1- 20　投与終了後 3 日目から 30 日目までの期間における有効性評価項目及び各構成要素の発現頻度（ITT 解析対象集団、事後解析）

評価項目 構成要素	リバーロキサバン	エノキサパリン／VKA
有効性の主要評価項目	11/1425　(0.8%)	7/1408　(0.5%)
死亡（PE）	0/1425	0/1408
死亡（PE の可能性が否定できない）	1/1425　(<0.1%)	1/1408　(<0.1%)
症候性 PE 及び DVT	0/1425	0/1408
症候性 PE のみ	3/1425　(0.2%)	2/1408　(0.1%)
症候性 DVT のみ	8/1425　(0.6%)	4/1408　(0.3%)

発現頻度＝イベント発現数／該当集団の被験者数
イベント発現数＝治験薬投与終了後 3 日目から 30 日目までにイベントが発現した被験者数
フォローアップ期間に移行した被験者は、当該被験者のフォローアップ期間への移行、あるいは投与終了後 3 日目から投与終了後 30 日目までに複合評価項目の 1 つとしてイベントの発現の判定について、治験責任(分担)医師により eCRF に記載された被験者に該当する。
引用元：5.3.5.1.14 PH-36761/Table 1/6

2.7.6.1.2.2.2　有効性副次的評価項目

ITT 解析対象集団における有効性の副次的評価項目の予定投与期間終了までの発現頻度を表 2.7.6.1- 18に示す。有効性の副次的評価項目は、症候性 VTE〔「症候性 DVT」、「症候性 PE(非致死的)」〕又は全死亡の複合エンドポイントであった。予定投与期間終了までの有効性の副次的評価項目の発現頻度は、リバーロキサバン群で 4.0%（69/1,731 例）、エノキサパリン／VKA 群で 5.1%（87/1,718 例）であった。予定投与期間で層別し、ベースライン時の活動性悪性腫瘍の有無で調整した Cox 比例ハザードモデルにより、予定投与期間終了までのリバーロキサバン投与とエノキサパリン／VKA 投与を比較したときのハザード比は 0.722（95%信頼区間：0.526～0.991、p 値＝0.0436）であった（5.3.5.1.1 MRR-00292/ Table 14.2/245, Table 14.2/246, Table 14.2/247）。

総合有用性評価指標 - 1 の評価項目は、有効性主要評価項目の各構成要素又は「重大な出血事象」の複合エンドポイントであった。予定投与期間終了までの総合有用性評価指標 - 1 の発現頻度は、リバーロキサバン群で 2.9%（51/1,731 例）、エノキサパリン／VKA 群で 4.2%（73/1,718 例）であった。Cox 比例ハザードモデルによるリバーロキサバン投与とエノキサパリン／VKA 投与を比較したハザード比は 0.667（95%信頼区間：0.466～0.954、p 値＝0.027）であった（5.3.5.1.1 MRR-00292/ Table 14.2/245, Table 14.2/246, Table 14.2/247）。

総合有用性評価指標 - 2 の評価項目（事後解析）は、有効性主要評価項目の各構成要素又は「重大な出血事象」、心血管死、心筋梗塞、虚血性脳卒中又は非中枢神経系全身性塞栓症の複合エンドポイントであった。予定投与期間終了までの総合有用性評価指標 - 2 の発現頻度は、リバーロキサバン群で 3.6%（62/1,731 例）、エノキサパリン／VKA 群で 4.7%（81/1,718）であった。Cox 比例ハザードモデルによるリバーロキサバン投与とエノキサパリン／VKA 投与を比較したハザード比は 0.727（95%信頼区間：0.522～1.013、p＝0.059）であった（5.3.5.1.1 MRR-00292/ Table 14.2/245, Table 14.2/246, Table 14.2/247）。

PP 解析対象集団及び ITT on treatment 解析対象集団における有効性の副次的評価項目の発現頻度は ITT 解析対象集団の結果と同様であった（5.3.5.1.1 MRR-00292/ Table 14.2/259, Table 14.2/260, Table 14.2/261）。

2.7.6.1.2.2.3 有効性主要評価項目の部分集団解析

有効性主要評価項目に関するイベント発現頻度をベースライン及び人口統計学的因子に基づいて部分集団解析を行った（図 2.7.6.1- 4）。主な部分集団の結果を以下に示した。数値上、イベント発現頻度は、ほとんどの部分集団でエノキサパリン／VKA 群よりもリバーロキサバン群のほうが低かった。有効性主要評価項目で、ハザード比の点推定値が 1 を上回っていたのは、予定投与期間が 3 ヵ月の部分集団のみであった。

DVT/PE の既往：

DVT/PE の既往を有する被験者におけるリバーロキサバン群とエノキサパリン／VKA 群のイベント発現頻度は、リバーロキサバン群 1.2%（4/336 例）、エノキサパリン／VKA 群 4.8%（16/330 例）であり、DVT/PE の既往のない被験者における発現頻度は、リバーロキサバン群 2.3%（32/1,395 例）、エノキサパリン／VKA 群 2.5%（35/1,388 例）であった。両部分集団ともにハザード比は 1 を下回っていた（DVT/PE の既往あり： 0.232、DVT/PE の既往なし： 0.884）（5.3.5.1.1 MRR-00292/ Table 14.2/271）。

活動性悪性腫瘍の有無：

ベースライン時に活動性悪性腫瘍を有していた被験者は、ベースライン時に悪性腫瘍のなかった被験者と比べて VTE の発現頻度が高く、ハザード比は 1.971、95%信頼区間は 0.987～3.937 であった（5.3.5.1.1 MRR-00292/ Table 14.2/243）。

ベースライン時に悪性腫瘍を有していたリバーロキサバン群の被験者 118 例のうち、4 例（3.4%）に VTE が発現したのに対し、エノキサパリン／VKA 群の被験者は 89 例中 5 例（5.6%）に発現し、ハザード比は 0.607（95%信頼区間：0.163～2.264）であった。また、ベースライン時に悪性腫瘍のなかったリバーロキサバン群の被験者 1,613 例のうち、32 例（2.0%）に VTE が発現したのに対し、エノキサパリン／VKA 群の被験者は 1,629 例中 46 例（2.8%）に発現し、ハザード比は 0.692（95%信頼区間：0.441～1.087）であった（5.3.5.1.1 MRR-00292/Table 14.2/271、Figure 14.2/195、Figure 14.2/196）。

予定投与期間：

予定投与期間が 3 ヵ月のコホートにおける有効性主要評価項目の発現頻度は、リバーロキサバン群で 2.4%（5/208 例）、エノキサパリン／VKA 群で 1.5%（3/203 例）であった。予定投与期間が 6 ヵ月のコホートでは、リバーロキサバン群が 2.3%（25/1,083 例）、エノキサパリン／VKA 群が 2.7%（29/1,083 例）であった。予定投与期間が 12 ヵ月のコホートでは、リバーロキサバン群が 1.4%（6/440 例）、エノキサパリン／VKA 群が 4.4%（19/432 例）であった（5.3.5.1.1 MRR-00292/ Table 14.2/89）。3 ヵ月の期間ではハザード比が 1 を上回ったのに対し、6 及び 12 ヵ月の期間ではハザード比は 1 を下回った。交互作用の p 値は 0.087 であったが、質的交互作用の p 値は 0.48 であった（5.3.5.1.1 MRR-00292/Table 14.2/271、Table 16.1.9.1/11）。

地域：

地域別にみた有効性主要評価項目の発現頻度を以下に示す（5.3.5.1.1 MRR-00292/ Table 14.2/271）。西欧：リバーロキサバン群 2.0%（15/758 例）、エノキサパリン／VKA 群 2.3%（17/740 例）、東欧： 0.4%（1/255 例）及び 1.5%（4/260 例）、アジア： 1.4%（3/211 例）及び 3.8%（8/211 例）、オーストラリア及びニュージーランド： 3.4%（6/179 例）及び

5.0%（9/179 例）、北米： 3.1%（5/163 例）及び 4.9%（8/163 例）であった。イベント発現頻度及びハザード比に関して地域間で数値的な差がみられるが、ばらつきによるものと考えられた（交互作用の p 値：0.78）。

特別な被験者集団：

追加的な事後解析として、75 歳超、体重≦50kg、CL_{CR}（計算値）＜50mL/min の基準のうち、少なくとも 1 つに該当する被験者の部分集団における有効性主要評価項目の発現頻度を検討した。クレアチニンクリアランスは Cockcroft-Gault の式を用いて算出した（5.3.5.1.1 MRR-00292//Table 16.1.9.1/19）。当該部分集団における有効性主要評価項目の発現頻度は、リバーロキサバン群で 2.5%（7/281 例）、エノキサパリン／VKA 群で 4.3%（13/305 例）であったのに対し、当該部分集団以外の被験者における発現頻度は、リバーロキサバン群で 2.0%（29/1,450 例）、エノキサパリン／VKA 群で 2.7%（38/1,413 例）であった。リバーロキサバン群とエノキサパリン／VKA 群において、各レベルの説明変数を別々に適合させた Cox 比例ハザードモデルによるハザード比は、当該部分集団の被験者で 0.572（95%信頼区間：0.228～1.437）、当該部分集団以外の被験者で 0.721（95%信頼区間：0.444～1.170）であった。

無作為割り付け前の治療：

無作為割り付け前の（LMW）ヘパリン（LMWH を含むヘパリン）／フォンダパリヌクスの使用は最大 48 時間まで許容された。無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスを使用しなかった被験者は 972 例（28.2%）であったのに対し、2,477 例（71.8%）は無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスを使用していた（5.3.5.1.1 MRR-00292/Figure 14.2/195）。後者では、無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスを使用した被験者のうち 90%以上が 1 日以内の使用であった。

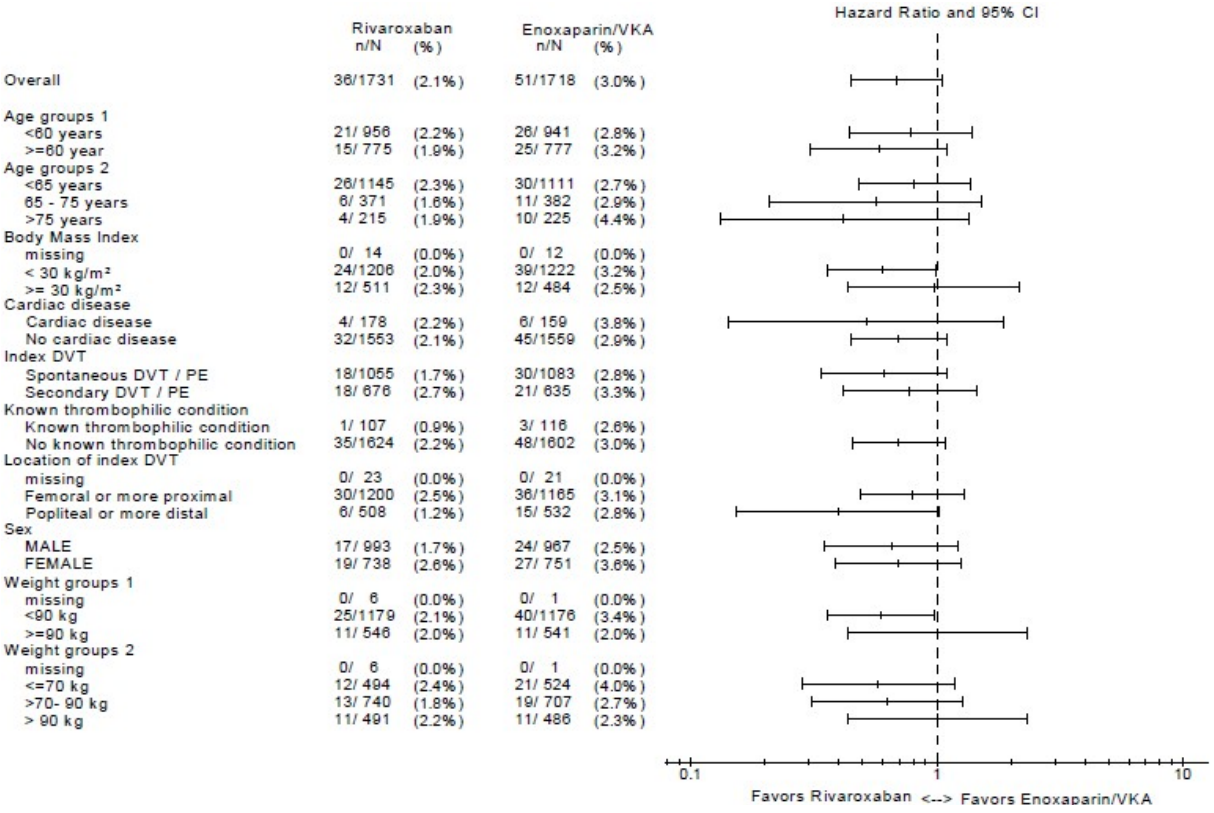
無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスの投与を受けなかった被験者のうち、リバーロキサバン群 467 例中 9 例（1.9%）、エノキサパリン／VKA 群 505 例中 10 例（2.0%）に有効性主要評価項目の発現が認められ、ハザード比は 0.98 であった（95%信頼区間：0.40～2.41）。無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスの投与を受けた被験者のうち、リバーロキサバン群 1,264 例中 27 例（2.1%）、エノキサパリン／VKA 群 1,213 例中 41 例（3.4%）に有効性主要評価項目の発現が認められ、ハザード比は 0.61 であった（95%信頼区間：0.38～0.99）。リバーロキサバン群の被験者では無作為割り付け前の（LMW）ヘパリン／フォンダパリヌクス投与の有無による差は認められなかった。

対照薬の種類による解析：ワルファリンと acenocoumarol：

試験 11702-DVT では、acenocoumarol とワルファリンのいずれかを使用した被験者において部分集団ごとに解析を行った（5.3.5.1.1 MRR-00292/Table 14.2/137, Table 14.2/139, Table 14.2/262, Table 14.2/266）。ワルファリンの部分集団にはワルファリンのみを投与した施設を含め、acenocoumarol の部分集団には acenocoumarol のみを投与した施設を含めた。ワルファリンの部分集団では、有効性主要評価項目の発現頻度はリバーロキサバン群で 2.2%（28/1,249 例）、エノキサパリン／ワルファリン群で 3.3%（41/1,256 例）であり、ハザード比は 0.669（95%信頼区間：0.414～1.082）であった。acenocoumarol の部分集団では、有効性主要評価項目の発現頻度はリバーロキサバン群で 1.9%（7/377 例）、エノキサパリン／acenocoumarol 群で 2.4%（9/380 例）であり、ハザード比は 0.768（95%信頼区間：0.285～2.065）であった。

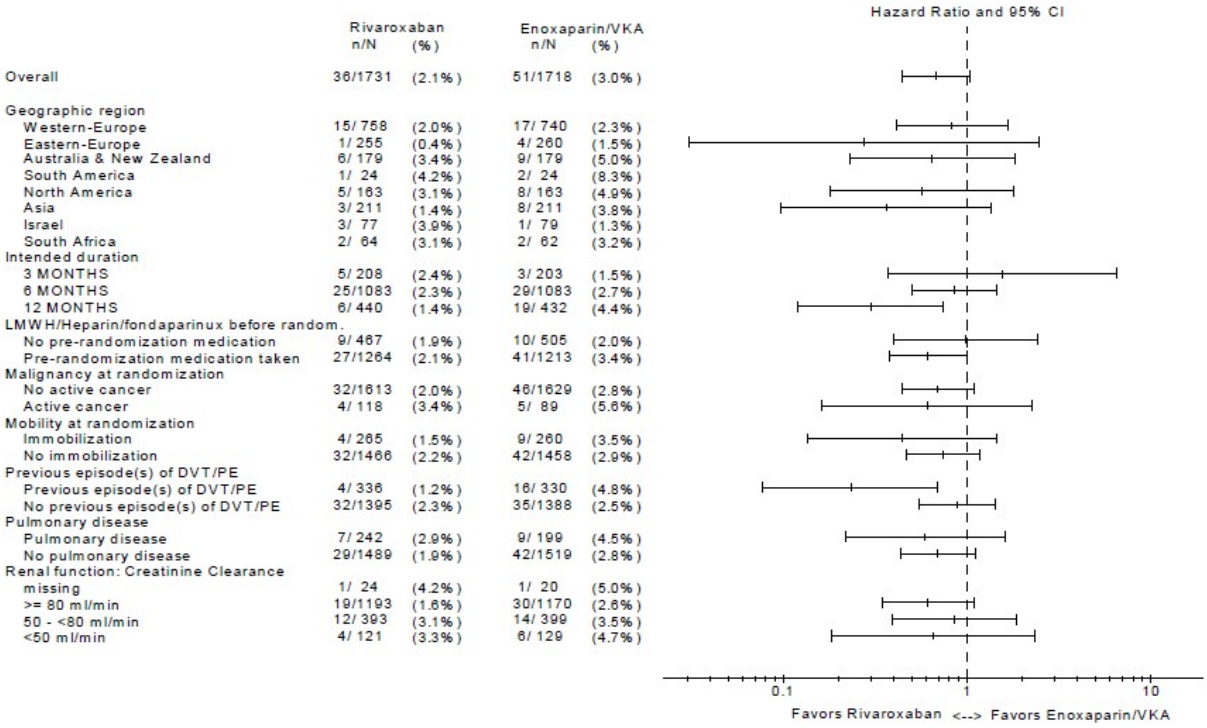
PT-INR：凝固状況による解析：

ITT 解析対象集団におけるエノキサパリン／VKA 群の検討では、主要有効性評価項目のイベント発現時に PT-INR が 3 を上回っていた場合（実測値又は補完値）、イベント発現頻度がわずかに高かった（3 人月の発現頻度：イベント発現時の PT-INR が 3 を超える場合 1.9%、全 PT-INR 範囲 1.3%）。この結果については、ワルファリンと acenocoumarol の部分集団間でやや違いが認められた。イベント発現時に PT-INR が 2.0 を下回っていた被験者では、3 人月の発現頻度はワルファリンの部分集団（1.1%）のほうが acenocoumarol の部分集団（1.6%）よりわずかに低かった。イベント発現時に PT-INR が目標範囲内（2.0～3.0）であった被験者では、3 人月の発現頻度はワルファリンの部分集団（1.3%）のほうが acenocoumarol の部分集団（0.8%）より高かった。また、イベント発現時に PT-INR が 3.0 を上回っていた症例でも、3 人月の発現頻度はワルファリンの部分集団（2.2%）のほうが acenocoumarol の部分集団（1.5%）より高かった（5.3.5.1.1 MRR-00292/Table 14.2/330）。



引用元：5.3.5.1.1 MRR-00292/Figure14.2/195、Figure14.2/196

図 2.7.6.1- 4　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）



引用元：5.3.5.1.1 MR-00292/Figure 14.2/195、Figure 14.2/196

図 2.7.6.1- 4　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

2.7.6.1.2.2.4　　有効性の結論

有効性主要評価項目は、症候性 VTE〔「症候性 DVT」又は「症候性 PE（非致死的及び致死的）」〕の複合エンドポイント（ただし PE の可能性が否定できない原因不明の死亡を含む）であった。致死的 PE は、客観的な診断検査又は剖検に基づく PE、あるいは原因が特定されない死亡及び DVT/PE の可能性が否定できない死亡（原因不明の死亡）のいずれかと定義した。

本試験において、有効性主要評価項目に関して、リバーロキサバン群（リバーロキサバン 15mg、1 日 2 回、3 週間投与に続いて、20mg 1 日 1 回投与）のエノキサパリン／VKA 群に対するハザード比は 0.680（95%信頼区間：0.443～1.042、ITT 解析対象集団）であり、その信頼区間の上限は事前に規定した非劣性マージンである 2.0 を下回っており、非劣性の片側 p 値は 0.0001 未満であったことから、リバーロキサバンのエノキサパリン／VKA に対する非劣性が検証された。

有効性主要評価項目の発現頻度（ITT 解析対象集団）はエノキサパリン／VKA 群（現在の標準治療）で 3.0%であり、治験実施計画書における例数設定の根拠とした推定発現頻度に合致していた。

本試験の結果は、有効性主要評価項目の個々の構成要素を通して一貫しており、また、事前に規定された、地域、予定投与期間、人口統計学とベースライン特性及び凝固状態を通じて一貫していた。

リバーロキサバン群のエノキサパリン／VKA 群に対する比較結果は、すべての副次的評価項目を通して維持されており、イベント発現頻度は一貫してリバーロキサバン群で低く、有効性主要評価項目に「重大な出血事象」を含めた場合（総合有用性評価指標-1）でも同様であった。

2.7.6.1.2.3　安全性の結果

2.7.6.1.2.3.1　有害事象の要約

表 2.7.6.1- 21に安全性解析対象集団における有害事象の要約を投与群ごとに示す。本試験では、治験薬投与下で発現した有害事象（TEAE）とは、無作為割り付け後、治験薬の投与終了後 2 日目までに発現した有害事象とした。

有害事象の発現頻度は、リバーロキサバン群 64.2%、エノキサパリン／VKA 群 64.7%であった。治験薬投与終了後 3 日目以降に発現した有害事象の発現頻度は、リバーロキサバン群 8.8%、エノキサパリン／VKA 群 9.3%であった。

TEAE は、リバーロキサバン群 62.7%、エノキサパリン／VKA 群 63.1%であった。治験薬投与下で発現した出血関連有害事象〔治験責任（分担）医師の報告による〕を除く有害事象の発現頻度は、リバーロキサバン群 57.6%、エノキサパリン／VKA 群 58.3%であった。治験責任（分担）医師の報告による、治験薬投与下で発現した出血関連有害事象の発現頻度は、エノキサパリン／VKA 群（23.3%）に比べてリバーロキサバン群（25.2%）でやや高かった。

治験薬との因果関係が否定できない TEAE の発現頻度は、エノキサパリン／VKA 群（23.0%）とリバーロキサバン群（23.3%）で同程度であった。

出血関連有害事象〔治験責任（分担）医師の報告による〕を除く、治験薬との因果関係が否定できない TEAE の発現頻度は、リバーロキサバン群 9.6%、エノキサパリン／VKA 群 9.8%であり、両群で同程度であった。

安全性解析対象集団で 93 例の死亡が報告された〔リバーロキサバン群：41 例（2.4%）、 エノキサパリン／VKA 群：52 例（3.0%）〕。治験薬投与下で発現した死亡は、36 例であった〔リバーロキサバン群：17 例（1.0%）、エノキサパリン／VKA 群：19 例（1.1%）〕。

重篤な TEAE の発現頻度は、リバーロキサバン群で 12.0%、エノキサパリン／VKA 群で 13.6%）であった。

治験薬の投与中止に至った有害事象の発現頻度は、リバーロキサバン群で 4.9%、エノキサパリン／VKA 群で 4.7%であった。

表 2.7.6.1- 21 有害事象の要約（安全性解析対象集団）

有害事象	リバーロキサバン N=1718 (100%)	エノキサパリン／VKA N=1711 (100%)
AE	1103 (64.2%)	1107 (64.7%)
SAE	222 (12.9%)	254 (14.8%)
死亡（無作為割り付け後のすべての死亡）	41 (2.4%)	52 (3.0%)
治験薬投与下の死亡 [a]	17 (1.0%)	19 (1.1%)
TEAE [a]	1078 (62.7%)	1080 (63.1%)
TEAE（出血関連有害事象を除く） [a, b]	989 (57.6%)	998 (58.3%)
治験薬投与下の出血関連有害事象 [a, b]	433 (25.2%)	399 (23.3%)
治験薬投与終了後 3 日目以降の AE	152 (8.8%)	159 (9.3%)
治験薬との因果関係が否定できない TEAE [a]	401 (23.3%)	394 (23.0%)
治験薬との因果関係が否定できない TEAE（出血関連有害事象を除く） [a, b]	165 (9.6%)	167 (9.8%)
治験薬投与下の治験薬との因果関係が否定できない出血性有害事象 [a, b]	303 (17.6%)	279 (16.3%)
治験薬投与終了後 3 日目以降の治験薬との因果関係が否定できない AE	11 (0.6%)	16 (0.9%)
重篤な TEAE[a]	207 (12.0%)	233 (13.6%)
重篤な TEAE（出血関連有害事象を除く） [a, b]	176 (10.2%)	207 (12.1%)
治験薬との因果関係が否定できない 重篤な TEAE [a]	42 (2.4%)	51 (3.0%)
治験薬投与終了後 3 日目以降の SAE	31 (1.8%)	45 (2.6%)
治験薬投与終了後 3 日目以降の治験薬との因果関係が否定できない SAE	1 (<0.1%)	3 (0.2%)
治験薬の投与中止に至った AE	85 (4.9%)	81 (4.7%)
入院（入院期間の延長）に至った AE	193 (11.2%)	211 (12.3%)

VKA：ビタミン K 拮抗薬、AE：有害事象、SAE：重篤な有害事象
VTE 及び非致死的 PE は AE 又は SAE とみなさないため、本表には含まれない。
a：治験薬投与下、すなわち治験薬投与終了 2 日目までに発現した有害事象。
b：出血関連有害事象は治験責任（分担）医師による報告に基づく。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/1, Table 14.3.1/42

2.7.6.1.2.3.2 比較的よくみられる有害事象

2.7.6.1.2.3.2.1 治験薬投与下で発現した有害事象（TEAE）

いずれかの投与群における発現頻度が 2%以上の TEAE を表 2.7.6.1- 22に示す。全体として、TEAE の発現頻度は両群間で同様であった（リバーロキサバン群 62.7%、エノキサパリン／VKA 群 63.1%）。発現頻度の高かった TEAE は、鼻咽頭炎（リバーロキサバン群：5.4%、エノキサパリン／VKA 群：4.9%）、四肢痛（4.4%、3.9%）、頭痛（5.3%、4.0%）、咳嗽（4.2%、3.0%）及び鼻出血（5.2%、4.3%）であった。

リバーロキサバン群でエノキサパリン／VKA 群より 1%以上発現頻度が高かった TEAE は、背部痛（リバーロキサバン群：2.9%、エノキサパリン／VKA 群：1.8%）、頭痛（5.3%、4.0%）、月経過多（2.9%、1.1%）、咳嗽（4.2%、3.0%）であった。リバーロキサバン群に比べてエノ

キサパリン／VKA 群で 1%以上発現頻度が高かった TEAE は、INR 増加（リバーロキサバン群：＜0.1%、エノキサパリン／VKA 群：2.2%）及びアラニン・アミノトランスフェラーゼ増加（リバーロキサバン群：1.2%、エノキサパリン／VKA 群：3.0%）であった。

TEAE の重症度はほとんどは軽度又は中等度とされ、高度とされた TEAE の発現頻度はリバーロキサバン群 7.9%及びエノキサパリン／VKA 群 7.8%であった（5.3.5.1.1 MRR-00292/Table 14.3.1/147）。

MedDRA 器官別大分類で、発現頻度が高かったのは、「感染症および寄生虫症」（リバーロキサバン群：20.4%、エノキサパリン／VKA 群：20.9%）、「胃腸障害」（19.6%、17.2%）、「筋骨格系および結合組織障害」（14.7%、13.3%）、「呼吸器、胸郭および縦隔障害」（13.6%、12.0%）、「一般・全身障害および投与部位の状態」（11.5%、10.4%）、及び「神経系障害」（11.5%、7.8%）であった。「心臓障害」は 3.1%、2.7%であった（5.3.5.1.1 MRR-00292/Table 14.3.1/18）。

表 2.7.6.1- 22　TEAE の発現頻度（いずれかの投与群で 2%以上、安全性解析対象集団）

MedDRA 器官別大分類／基本語	リバーロキサバン N＝1718（100%）	エノキサパリン／VKA N＝1711（100%）
全事象	1078（62.7%）	1080（63.1%）
胃腸障害		
便秘	48（ 2.8%）	43（ 2.5%）
下痢	54（ 3.1%）	40（ 2.3%）
歯肉出血	36（ 2.1%）	28（ 1.6%）
悪心	47（ 2.7%）	38（ 2.2%）
直腸出血	36（ 2.1%）	19（ 1.1%）
全身障害および投与局所様態		
胸痛	36（ 2.1%）	31（ 1.8%）
末梢性浮腫	41（ 2.4%）	41（ 2.4%）
発熱	43（ 2.5%）	38（ 2.2%）
感染症および寄生虫症		
インフルエンザ	38（ 2.2%）	38（ 2.2%）
鼻咽頭炎	93（ 5.4%）	84（ 4.9%）
尿路感染	37（ 2.2%）	32（ 1.9%）
傷害、中毒および処置合併症		
挫傷	53（ 3.1%）	68（ 4.0%）
臨床検査		
アラニン・アミノトランスフェラーゼ増加	20（ 1.2%）	52（ 3.0%）
INR 増加	1（<0.1%）	38（ 2.2%）
筋骨格系および結合組織障害		
関節痛	43（ 2.5%）	38（ 2.2%）
背部痛	50（ 2.9%）	31（ 1.8%）
四肢痛	76（ 4.4%）	66（ 3.9%）
神経系障害		
浮動性めまい	38（ 2.2%）	22（ 1.3%）
頭痛	91（ 5.3%）	68（ 4.0%）
腎および尿路障害		
血尿	39（ 2.3%）	41（ 2.4%）
生殖系および乳房障害		
月経過多	49（ 2.9%）	19（ 1.1%）
呼吸器、胸郭および縦隔障害		
咳嗽	72（ 4.2%）	51（ 3.0%）
呼吸困難	33（ 1.9%）	37（ 2.2%）
鼻出血	89（ 5.2%）	74（ 4.3%）
血管障害		
血腫	37（ 2.2%）	59（ 3.4%）
高血圧	38（ 2.2%）	40（ 2.3%）

MedDRA：ICH 国際医薬用語集、VKA：ビタミン K 拮抗薬、INR：（プロトロンビン時間）国際標準比
MedDRA version 13.0
治験薬最終投与後 2 日目までに発現した有害事象のみが含まれている。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/18

2.7.6.1.2.3.2.2 治験薬との因果関係が否定できないTEAE

いずれかの投与群の発現頻度が 2%以上の治験薬との因果関係が否定できない TEAE を表 2.7.6.1- 23に示した。

治験薬との因果関係が否定できない TEAE（いずれかの投与群で発現頻度 2%以上）の発現頻度は、リバーロキサバン群（23.3%）とエノキサパリン／VKA 群（23.0%）で同程度であった。個々の事象で発現頻度 2%以上の治験薬との因果関係が否定できない TEAE は 4 事象であり、鼻出血、月経過多では、リバーロキサバン群（それぞれ 3.9%及び 2.3%）の発現頻度がエノキサパリン／VKA 群（それぞれ 3.3%及び 0.9%）よりも高く、一方、挫傷、血腫では、エノキサパリン／VKA 群（それぞれ 2.3%及び 2.2%）の発現頻度がリバーロキサバン群（それぞれ 1.6%及び 1.5%）よりも高かった。

表 2.7.6.1- 23 治験薬との因果関係が否定できないTEAEの発現頻度（いずれかの投与群で2%以上、安全性解析対象集団）

MedDRA器官別大分類／基本語	リバーロキサバン N＝1718（100%）	エノキサパリン／VKA N＝1711（100%）
全事象	401（23.3%）	394（ 3.0%）
傷害、中毒および処置合併症		
挫傷	28（ 1.6%）	40（ 2.3%）
生殖系および乳房障害		
月経過多	40（ 2.3%）	16（ 0.9%）
呼吸器、胸郭および縦隔障害		
鼻出血	67（ 3.9%）	56（ 3.3%）
血管障害		
血腫	25（ 1.5%）	38（ 2.2%）

MedDRA：ICH国際医薬用語集、VKA：ビタミンK拮抗薬
MedDRA version 13.0
治験薬投与終了後2日目までに発現した有害事象のみが含まれている。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/23

2.7.6.1.2.3.2.3 治験薬投与終了後3日目以降に発現した有害事象

治験薬投与終了後 3 日目以降に発現した有害事象の発現頻度は、リバーロキサバン群 8.8%、エノキサパリン／VKA 群 9.3%であった。治験薬投与終了後 3 日目以降に発現した有害事象のうち両群間で差が大きかったのは、器官別大分類による「臨床検査」（リバーロキサバン群 0.6%、エノキサパリン／VKA 群 1.2%）、「筋骨格系および結合組織障害」（1.5%、0.8%）であった。個々の事象の四肢痛（0.4%、0.1%未満）以外に臨床的に意味のある差は認められなかった（5.3.5.1.1 MRR-00292/Table 14.3.1/9）。

2.7.6.1.2.3.3 有害事象の部分集団解析

TEAE 又は出血関連有害事象〔治験責任（分担）医師の報告〕を除く TEAE に関し、リバーロキサバン群とエノキサパリン／VKA 群間において、予定投与期間、性別、地域、年齢（60 歳未満と 60 歳以上）について、顕著な差は認められなかった。

ベースライン時に活動性悪性腫瘍を有する被験者において、出血関連有害事象を含む TEAE の発現頻度は、リバーロキサバン群で 81.4%、エノキサパリン／VKA 群で 76.1%であり、出血関連有害事象を除く TEAE の発現頻度は、リバーロキサバンで 71.2%、エノキサパリン／VKA 群で 69.3%であった。ベースライン時に活動性悪性腫瘍が認められなかった被験者においては、出血関連有害事象を含む TEAE の発現頻度（リバーロキサバン群：61.4%、エノキサパリン／VKA 群：62.4%）と、出血性有害事象を除く TEAE の発現頻度（56.6%、57.7%）はベースライン時に活動性悪性腫瘍の有無にかかわらず同程度であった（5.3.5.1.1 MRR-00292/Table 14.3.1/2 から Table 14.3.1/6）。

2.7.6.1.2.3.4 死亡

すべての死亡について、CIAC が判定した。安全性解析対象集団において 93 例の死亡が報告された（表 2.7.6.1- 24）。死亡の発現頻度は、数値上エノキサパリン／VKA 群〔3.0%（52/1,711 例）〕よりもリバーロキサバン群〔2.4%（41/1,718 例）〕の方が低かった。CIAC 判定による死亡理由で両群に多かったものは、悪性腫瘍〔リバーロキサバン群: 1.6%（27/1,718 例）、エノキサパリン／VKA 群：1.2%（20/1,711 例）〕、PE の可能性を否定できない原因不明の死亡〔0.2%（3/1,718 例）、0.4%（6/1,711 例）〕、感染症〔0.2%（3/1,718 例）、0.5%（9/1,711 例）〕及び出血〔0.1%（2/1,718 例）、0.3%（5/1,711 例）〕であった。

表 2.7.6.1- 24 無作為割り付け後の死因別の死亡（安全性解析対象集団）

死因（CIAC 判定）	リバーロキサバン N＝1718（100%）	エノキサパリン／VKA N＝1711（100%）
全事象	41（ 2.4%）	52（ 3.0%）
判定なし	0	1（<0.1%）
肺塞栓症	1（<0.1%）	0
出血	2（ 0.1%）	5（ 0.3%）
悪性腫瘍	27（ 1.6%）	20（ 1.2%）
敗血症	0	2（ 0.1%）
PE の可能性が否定できない原因不明の死亡 [a]	3（ 0.2%）	6（ 0.4%）
虚血性脳卒中	1（<0.1%）	4（ 0.2%）
そのほかの心血管事象	1（<0.1%）	1（<0.1%）
感染症	3（ 0.2%）	9（ 0.5%）
その他の呼吸不全	0	1（<0.1%）
悪液質	1（<0.1%）	0
肺炎	0	1（<0.1%）
腎不全	1（<0.1%）	0
糖尿病性昏睡	1（<0.1%）	0
自殺	0	1（<0.1%）
肝疾患	0	1（<0.1%）

CIAC：中央独立判定委員会、VKA：ビタミン K 拮抗薬
すべての死亡例について、CIAC は事前に定義された選択リストに基づいて死因を分類した。安全性解析対象集団における投与群は、実際に投与された治験薬の群を示す（無作為割り付けされた群ではない）。
a：データベースでの原文は“unexplained PE and PE cannot be ruled out”。
引用元：5.3.5.1.1 MRR-00292/Table 16.1.9.1/41

治験薬投与下で発現した死亡例は 36 例であり、発現頻度はリバーロキサバン群〔1.0%（17/1718）〕とエノキサパリン／VKA 群〔1.1%（19/1711）〕で同程度であった。両投与群に

おいて死因のうち頻度が高かったものは、悪性腫瘍〔リバーロキサバン群：0.5%（8/1718）、エノキサパリン／VKA 群：0.2%（4/1711）〕、PE の可能性が否定できない原因不明の死亡〔0.1%（2/1718）、0.3%（5/1711）〕、感染症〔0.2%（3/1718）、0.2%（4/1711）〕であった（5.3.5.1.1 MRR-00292/Table 14.3.1/42）。

死亡例に関する詳細情報は付表 2.7.6.1-2 に示す。

2.7.6.1.2.3.5　重篤な有害事象

2.7.6.1.2.3.5.1　重篤な TEAE

いずれかの投与群で MedDRA 器官別大分類で 1%以上の発現頻度で認められた重篤な TEAE を表 2.7.6.1- 25に示す。

重篤な TEAE の発現頻度は、リバーロキサバン群 12.0%、エノキサパリン／VKA 群 13.6%で同程度であった。重篤な TEAE のうち発現頻度が高かったのは、リバーロキサバン群では、貧血（0.6%）、月経過多（0.3%）及び尿路感染（0.3%）であった。エノキサパリン／VKA 群では、肺炎（0.6%）、貧血（0.4%）、アラニン・アミノトランスフェラーゼ増加（0.4%）、血尿（0.4%）及び肝酵素上昇（0.3%）であった。投与群間に臨床的に重要な差は認められなかった。詳細は 5.3.5.1.1 MRR-00292/Table 14.3.1/28 に示す。

表 2.7.6.1- 25　重篤な TEAE の発現頻度（いずれかの投与群で 1%以上、安全性解析対象集団）

MedDRA 器官別大分類	リバーロキサバン N＝1718（100%）	エノキサパリン／VKA N＝1711（100%）
全事象	207（12.0%）	233（13.6%）
胃腸障害	27（ 1.6%）	31（ 1.8%）
感染症および寄生虫症	28（ 1.6%）	48（ 2.8%）
臨床検査	8（ 0.5%）	20（ 1.2%）
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	47（ 2.7%）	42（ 2.5%）
神経系障害	18（ 1.0%）	17（ 1.0%）
血管障害	10（ 0.6%）	19（ 1.1%）

MedDRA：ICH 国際医薬用語集
MedDRA version 13.0
治験薬投与下（無作為割り付け後から治験薬投与終了後 2 日目まで）に発現した有害事象のみが含まれている。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/28

治験薬との因果関係が否定できない重篤な TEAE の発現頻度は、エノキサパリン／VKA 群〔3.0%（51/1,711 例）〕よりもリバーロキサバン群〔2.4%（42/1,718 例）〕のほうがやや低かった（5.3.5.1.1 MRR-00292/ Section 10.4.3.2、Table14.3.1/33）。この差は、器官別大分類での「臨床検査」（リバーロキサバン群：0.3%、エノキサパリン／VKA 群：0.8%）及び「筋骨格系および結合組織障害」（リバーロキサバン群：0%、エノキサパリン／VKA 群：0.3%）の発現頻度の差によるものと思われる。これら 2 つの器官別大分類での個々の事象では、アラニン・アミノトランスフェラーゼ増加（0.1%、0.2%）、肝酵素上昇（0%、0.2%）、INR 増加（0%、0.2%）及び筋肉内出血（0%、0.2%）が多く認められた。

器官別大分類の「血液およびリンパ系障害」（個々の事象では貧血、小球性貧血、特発性血腫、血小板減少症）において、治験薬との因果関係が否定できない重篤な TEAE の発現頻度はリバー

ロキサバン群でやや高かった（0.6%、0.2%）。また、「生殖系および乳房障害」（個々の事象では月経過多、膣出血）でもリバーロキサバン群の発現頻度がやや高かった（リバーロキサバン群：0.3%、エノキサパリン／VKA 群：0.1%）。

2.7.6.1.2.3.5.2 治験薬投与終了後 3 日目以降に発現した重篤な有害事象

治験薬投与終了後 3 日目以降に発現した重篤な有害事象の発現頻度は、リバーロキサバン群に比べてエノキサパリン／VKA 群でわずかに高かった（リバーロキサバン群：1.8%、エノキサパリン／VKA 群：2.6%。エノキサパリン／VKA 群に比べてリバーロキサバン群で発現頻度が 0.2%以上低かったのは、器官別大分類で「胃腸障害」（リバーロキサバン群：0.2%、エノキサパリン／VKA 群：0.6%）、「感染症および寄生虫症」（リバーロキサバン群：0.1%、エノキサパリン／VKA 群：0.5%）、及び「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）」（リバーロキサバン群：0.4%、エノキサパリン／VKA 群：0.6%）であった（5.3.5.1.1 MRR-00292/Table 14.3.1/13）。

治験薬投与終了後 3 日目以降に発現した治験薬との因果関係が否定できない重篤な TEAE は 4 例〔リバーロキサバン群 1 例（0.1%未満）、エノキサパリン／VKA 群 3 例（0.2%）〕にみられた。内訳はリバーロキサバン群の 1 例（被験者 300074142）が貧血、エノキサパリン／VKA 群の 3 例（被験者 140374037、540014003、540024030）がそれぞれ下部消化管出血、上部消化管出血、及び多臓器不全であった（5.3.5.1.1 MRR-00292/Table 14.3.1/15）。

2.7.6.1.2.3.6 治験薬の投与中止に至った有害事象

治験薬の投与中止に至った有害事象の発現頻度は、リバーロキサバン群が 4.9%、エノキサパリン／VKA 群が 4.7%であった。治験薬の投与中止に至った有害事象のうち器官別大分類で発現頻度の高かったものは「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）」（リバーロキサバン群：1.0%、エノキサパリン／VKA 群：1.1%）、「胃腸障害」（0.6%、0.6%）、「神経系障害」（0.6%、0.3%）、「呼吸器、胸郭および縦隔障害」（0.5%、0.4%）、及び「感染症および寄生虫症」（0.3%、0.5%）であった（表 2.7.6.1- 26）。

個々の事象で、リバーロキサバン群で発現頻度が高かった事象（5 例以上に発現）は、貧血（0.3%）のみであった。エノキサパリン／VKA 群では 5 例以上に発現した事象はなかった（5.3.5.1.1 MRR-00292/Table 14.3.1/35）。個々の事象では発現頻度が低く、臨床的に意味のある投与群間の差について評価できなかった。

表 2.7.6.1- 26 治験薬の投与中止に至った有害事象（いずれかの投与群で 5 例以上、安全性解析対象集団）

MedDRA 器官別大分類/基本語	リバーロキサバン (N＝1718)	エノキサパリン／VKA (N＝1711)
全事象	85 (4.9%)	81 (4.7%)
血液およびリンパ系障害	7 (0.4%)	4 (0.2%)
貧血	5 (0.3%)	2 (0.1%)
胃腸障害	11 (0.6%)	11 (0.6%)
感染症および寄生虫症	5 (0.3%)	8 (0.5%)
臨床検査	6 (0.3%)	4 (0.2%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	18 (1.0%)	19 (1.1%)
神経系障害	10 (0.6%)	5 (0.3%)
腎および尿路障害	5 (0.3%)	3 (0.2%)
生殖系および乳房障害	5 (0.3%)	1 (<0.1%)
呼吸器、胸郭および縦隔障害	8 (0.5%)	7 (0.4%)
皮膚および皮下組織障害	4 (0.2%)	5 (0.3%)
血管障害	6 (0.3%)	5 (0.3%)

MedDRA version 13.0
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/35

2.7.6.1.2.3.7 出血事象

2.7.6.1.2.3.7.1 安全性主要評価項目

安全性主要評価項目は、安全性解析対象集団における「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイントであった。出血事象に関して治験薬投与下とする期間の定義は、無作為割り付けから治験薬投与終了 2 日後までとした。出血事象（疑い）は有害事象又は重篤な有害事象として報告され、CIAC により「重大な出血事象」、「重大ではないが臨床的に問題となる出血事象」、「軽微な出血事象」、又は「出血事象ではない」に分類された。

安全性解析対象集団における、予定投与期間終了までに治験薬投与下の初回発現の出血事象の要約を表 2.7.6.1- 27に示す。安全性主要評価項目の発現頻度は、両群とも 8.1%（リバーロキサバン群：139/1,718 例、エノキサパリン／VKA 群：138/1,711 例）であった。

表 2.7.6.1- 27　治験薬投与下で初回に発現した安全性主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）の発現頻度の部位別内訳（安全性解析対象集団）

安全性評価項目	リバーロキサバン (N＝1718)	エノキサパリン／VKA (N＝1711)
「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」のいずれか	139 (8.1%)	138 (8.1%)
重大な出血事象	13 (0.8%)	19 (1.1%)
致死的出血	1 (<0.1%)	5 (0.3%)
頭蓋内	0	2 (0.1%)
消化管	1 (<0.1%)	2 (0.1%)
胸部	0	1 (<0.1%)
重要な臓器の非致死的出血事象	3 (0.2%)	3 (0.2%)
頭蓋内	2 (0.1%)	0
後腹膜	0	1 (<0.1%)
関節内	0	1 (<0.1%)
眼内	1 (<0.1%)	0
硝子体	0	1 (<0.1%)
重要な臓器以外の非致死的出血事象（2g/dL 以上のヘモグロビン減少、又は 2 単位以上の輸血）	9 (0.5%)	11 (0.6%)
皮膚（注射部位以外）	0	2 (0.1%)
泌尿生殖器	1 (<0.1%)	3 (0.2%)
子宮	4 (0.2%)	0
消化管	2 (0.1%)	4 (0.2%)
直腸	1 (<0.1%)	2 (0.1%)
筋肉内	1 (<0.1%)	0
重大ではないが臨床的に問題となる出血事象	126 (7.3%)	119 (7.0%)
手術部位	1 (<0.1%)	2 (0.1%)
皮膚（注射部位以外）	10 (0.6%)	26 (1.5%)
泌尿生殖器	33 (1.9%)	29 (1.7%)
子宮	27 (1.6%)	15 (0.9%)
歯肉	0	2 (0.1%)
消化管	9 (0.5%)	13 (0.8%)
直腸	21 (1.2%)	10 (0.6%)
肛門	1 (<0.1%)	0
鼻	14 (0.8%)	13 (0.8%)
気管	4 (0.2%)	0
咽頭	0	1 (<0.1%)
関節内	0	1 (<0.1%)
結膜	1 (<0.1%)	3 (0.2%)
眼内	1 (<0.1%)	0
耳	1 (<0.1%)	2 (0.1%)
筋肉内	2 (0.1%)	3 (0.2%)
脚	0	1 (<0.1%)
不確定	1 (<0.1%)	0

被験者の初回に発現した出血事象の出血部位が2つ以上の場合、出血したすべての部位にカウントした。
治験薬投与下：無作為割り付けから治験薬投与終了後2日目までに発現した事象。
致死的出血に関して、事象はこの期間内に発現したが、その後に死に至る場合もある〔被験者160194013（エノキサパリン／VKA群）及び被験者540024030（エノキサパリン／VKA群）：CIACによって致死的出血と判定された〕。
引用元：5.3.5.1.1 MR-00292/Table 14.3.1/48

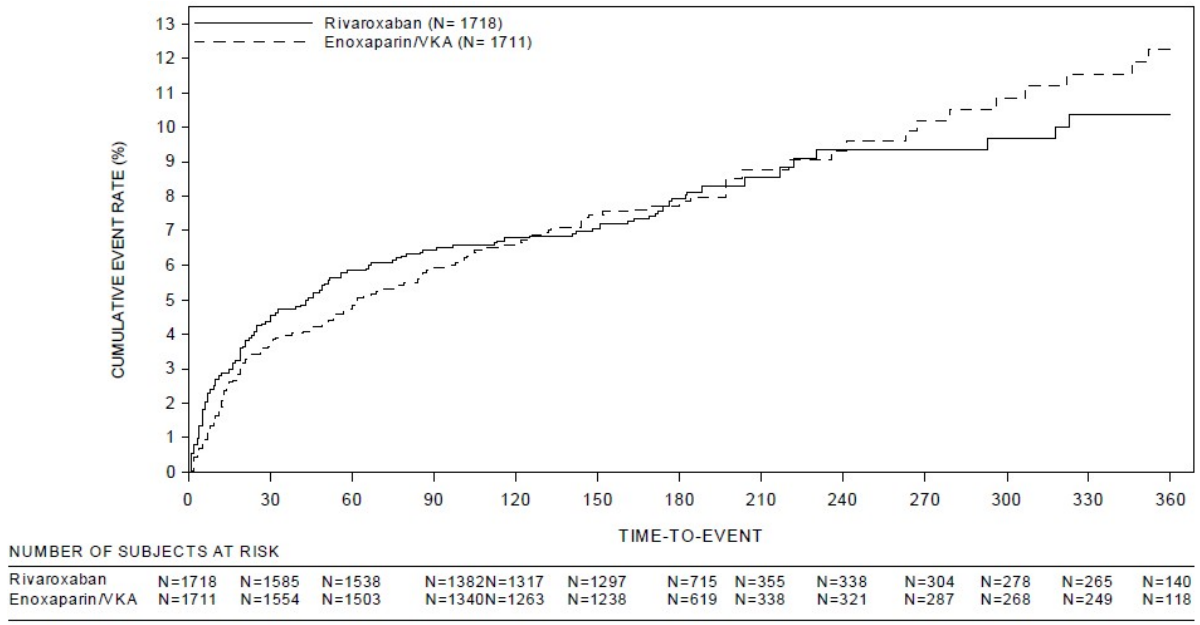
両群における発現頻度は同程度であり、安全性主要評価項目のハザード比（リバーロキサバン群対エノキサパリン／VKA 群）は 1 に近かった（表 2.7.6.1- 28）。

表 2.7.6.1- 28　治験薬投与下で発現したすべての出血事象の発現頻度及び Cox 比例ハザードモデルでの解析結果（安全性解析対象集団）

評価項目	リバーロキサバン (N＝1718)	エノキサパリン／VKA (N＝1711)	ハザード比	95%信頼区間	p 値[a]
安全性の主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）	139 (　8.1%)	138 (　8.1%)	0.966	0.763-1.222	0.7709
重大な出血事象	14 (　0.8%)	20 (　1.2%)	0.646	0.326-1.282	0.2117
全出血事象	412 (24.0%)	379 (22.2 %)			

VKA：ビタミン K 拮抗薬
p 値及びハザード比の推定値は層別化 Cox 比例ハザードモデルに基づき、予定投与期間を層別因子としベースライン時の悪性腫瘍の有無で調整した。
＊：リバーロキサバン投与スケジュールは 15mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回
a：名目 p 値、多重性の調整は行わなかった。
無作為割付けから治験薬の投与終了後 2 日目までに発現した事象。
引用元：5.3.5.1.1 MR-00292/Table 14.3.1/48、Table14.3.1/84、Table 14.3.1/117、Table 14.3.1/120

Kaplan-Meier 法による、安全性主要評価項目の出血事象の累積イベント発現率を投与群ごとに図 2.7.6.1- 5に示す。



引用元：5.3.5.1.1 MR-00292/Figure 14.3.1/13

図 2.7.6.1- 5　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）の Kaplan-Meier 法による累積イベント発現率（安全性解析対象集団）

2.7.6.1.2.3.7.2　　重大な出血事象

治験薬投与下に発現した「重大な出血事象」は、エノキサパリン／VKA 群〔1.2%（20/1,711 例）〕に比べ、リバーロキサバン群〔0.8%（14/1,718 例）〕で数値上低く、ハザード比は 0.646（95%信頼区間：0.326～1.282）及び p 値は 0.2117 であった（表 2.7.6.1- 28及び表 2.7.6.1- 29）。

両投与群の「重大な出血事象」のほとんどは「重要な臓器以外の非致死的出血事象」（ヘモグロビン減少 2g/dL 以上又は輸血 2 単位以上）に分類され、リバーロキサバン群 0.6%（10/1,718 例）、エノキサパリン／VKA 群 0.7%（12/1,711 例）であった。両投与群における「重要な臓器の非致死的出血事象」の発現頻度は 0.2%であった（表 2.7.6.1- 29）。

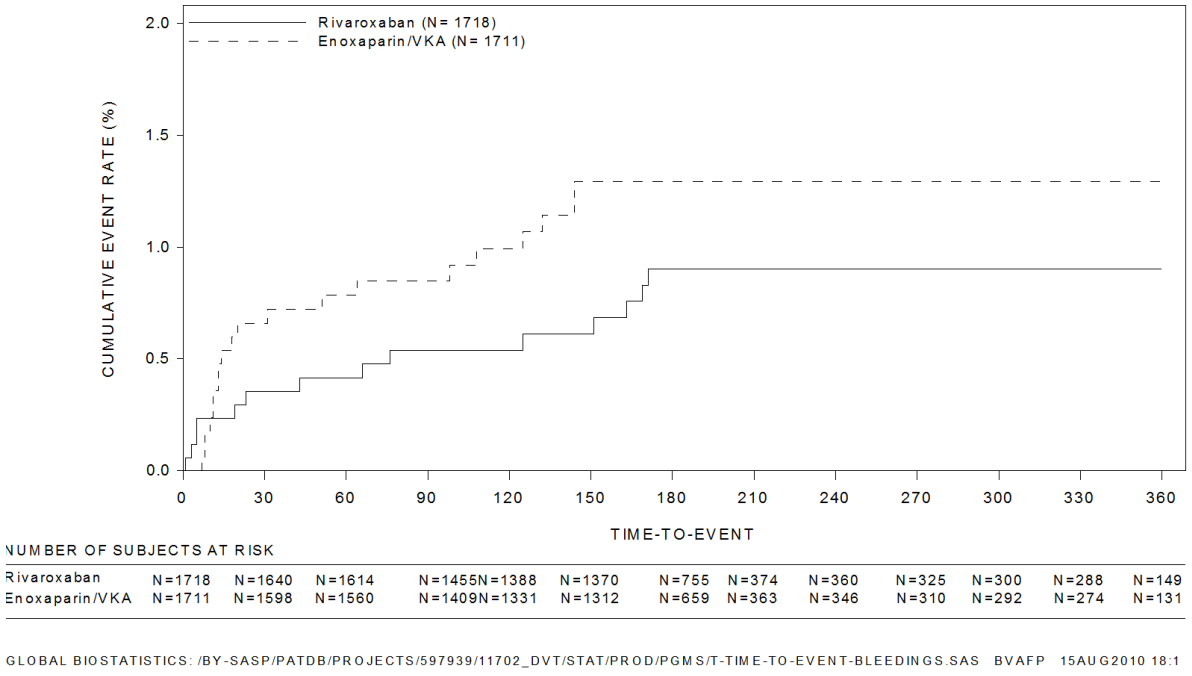
治験薬投与下に発現した致死的出血事象が 6 例に認められ、リバーロキサバン群が 1 例（1/1,718 例：＜0.1%）、エノキサパリン／VKA 群 5 例（5/1,711 例：0.3%）であり、リバーロキサバン群の 1 例は消化管出血による死亡であった。エノキサパリン／VKA 群の 5 例のうち 2 例は消化管出血、1 例は胸部出血、2 例は頭蓋内出血による死亡であった（表 2.7.6.1- 29）。

治験薬投与下に発現した「重大な出血事象」の累積イベント発現率の推移を図 2.7.6.1- 6に示す。両投与群間の数値上の差は投与 2 週間後にみられ、投与期間終了まで持続がみられた。

表 2.7.6.1- 29　治験薬投与下で発現した「重大な出血事象」（安全性解析対象集団）

出血事象	リバーロキサバン (N＝1718)	エノキサパリン／VKA (N＝1711)
重大な出血事象	14 (0.8%)	20 (1.2%)
致死的出血事象	1 (<0.1%)	5 (0.3%)
頭蓋内	0	2 (0.1%)
消化管	1 (<0.1%)	2 (0.1%)
胸部	0	1 (<0.1%)
重要な臓器の非致死的出血事象	3 (0.2%)	3 (0.2%)
頭蓋内	2 (0.1%)	0
後腹膜	0	1 (<0.1%)
関節内	0	1 (<0.1%)
眼内	1 (<0.1%)	0
硝子体	0	1 (<0.1%)
重要な臓器以外の非致死的出血事象（Hb 減少 2g/dL 以上及び／又は輸血 2 単位以上）	10 (0.6%)	12 (0.7%)
皮膚（注射部位以外）	0	2 (0.1%)
泌尿生殖器	1 (<0.1%)	3 (0.2%)
子宮	5 (0.3%)	0
消化管	3 (0.2%)	4 (0.2%)
直腸	1 (<0.1%)	3 (0.2%)
筋肉内	1 (<0.1%)	0

Hb：ヘモグロビン、VKA：ビタミン K 拮抗薬
無作為割り付けから治験薬の投与終了後 2 日目までに発現した有害事象とした。
引用元： 5.3.5.1.1 MR-00292/Table 14.3.1/84



引用元： 5.3.5.1.1 MR-00292/Figure14.3.1/1

図 2.7.6.1- 6　治験薬投与下で発現した「重大な出血事象」の Kaplan-Meier 法による累積イベント発現率（安全性解析対象集団）

2.7.6.1.2.3.7.3　　重大ではないが臨床的に問題となる出血事象

「重大ではないが臨床的に問題となる出血事象」の発現頻度は、リバーロキサバン群 7.5%、エノキサパリン／VKA 群 7.1％であり、両投与群で同程度であった（5.3.5.1.1 MRR-00292/Table 14.3.1/84）。部位別では、「重大ではないが臨床的に問題となる出血事象」のうち、リバーロキサバン群で発現頻度が高かった事象は、泌尿生殖器〔リバーロキサバン群：2.0％（35/1,718 例）、エノキサパリン／VKA 群：1.7％（29/1,711 例）〕、直腸〔1.3％（22/1,718 例）、0.6％（10/1,711 例）〕、子宮〔1.7％（29/1,718 例）、0.9％（16/1,711 例）〕、気管〔0.3％（6/1,718 例）、0％〕であった（5.3.5.1.1 MRR-00292/Table 14.3.1/84）。エノキサパリン／VKA 群で発現頻度が高かった事象は、皮膚（注射部位以外）〔0.6％（11/1,718 例）、1.6％（28/1,711 例）〕、消化管〔0.6％（11/1,718 例）、0.8％（14/1,711 例）〕であった。なお、エノキサパリン／VKA 群には臨床所見に基づき CIAC が「重大ではないが臨床的に問題となる出血事象」と判定した関節内（重要な臓器）出血事象が 1 件あった。

2.7.6.1.2.3.7.4　　軽微な出血事象

「重大な出血事象」及び「重大ではないが臨床的に問題となる出血事象」のいずれの基準にも合致しない、臨床的に明らかな出血は CIAC により「軽微な出血」に分類された。「軽微な出血

事象」の発現頻度は、エノキサパリン／VKA 群で 17.2%（295/1,711 例）で、リバーロキサバン群で〔18.5%（318/1,718 例）〕であった。報告が多かった「軽微な出血事象」は、皮膚出血（リバーロキサバン：6.9%、エノキサパリン／VKA：10.1%）、鼻出血（リバーロキサバン：4.8%、エノキサパリン／VKA：3.7%）、子宮出血（3.3%、1.4%）であった（5.3.5.1.1 MRR-00292/Table 14.3.1/84）。

2.7.6.1.2.3.7.5 致死的出血事象

治験薬投与下で発現した致死的出血事象は 6 例でみられた。リバーロキサバン群の 1 例（消化管出血）及び、エノキサパリン／VKA 群の 5 例（消化管出血による 2 例、胸部出血による 1 例及び頭蓋内出血による 2 例）であった（表 2.7.6.1- 29）。

治験薬投与終了後の事象として、リバーロキサバン群において致死的出血が 1 例認められた。本症例は被験者 550034027 で、治験薬の最終投与から 8 日後に致死的消化管出血事象が発現した（5.3.5.1.1 MRR-00292/Table 14.3.2/5、Section 15 参照）。

2.7.6.1.2.3.7.6 頭蓋内出血

治験薬投与下に発現した重大な出血事象には頭蓋内出血 4 件が含まれた（リバーロキサバン群：2 件、エノキサパリン／VKA 群：2 件）。そのうち 2 件は致死的で、エノキサパリン／VKA 群で発現し、内訳は脳内出血事象が 1 件、硬膜下血腫が 1 件であった。両被験者のイベント発現時の PT-INR 測定値は、目標範囲を超えていた。

頭蓋内の重大な出血が発現した被験者に関する詳細は 5.3.5.1.1 MR-00292 /Table 14.3.2/5 及び Section 15 に示す。

2.7.6.1.2.3.7.7 消化管出血

治験薬投与下に発現した重大な消化管出血の発現頻度（「重要な臓器以外の非致死的出血事象」）は、リバーロキサバン群（2 例）とエノキサパリン群（4 例）で同程度であった（表 2.7.6.1- 28）。また、リバーロキサバン群では致死的な消化管出血事象が 1 例、エノキサパリン／VKA 群では 2 例に認められた。「重大ではないが臨床的に問題となる出血事象」と判定された消化管出血も投与群間で同程度であった〔リバーロキサバン群 9 例（0.5%）、エノキサパリン群 13 例（0.8%）〕。

2.7.6.1.2.3.7.8 子宮出血

重大又は重大ではないが臨床的に問題となる子宮からの出血事象の発現頻度は、リバーロキサバン群の方が高かった。年齢グループ（55 歳未満と 55 歳超）別の出血事象の解析において、年齢グループ 55 歳未満の方で多く認められた（5.3.5.3.2 PH-36346/Table 1.1/3、Table 1.1/4）。「重大な出血事象」が 5 例で認められた（リバーロキサバン群の 55 歳未満 5 例、エノキサパリン／VKA 群なし）。5 例には重要な医学的所見が認められ〔性器部位の基質病変（4 例）又は血小板減少症（1 例）〕、いずれも転帰は回復であった。「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の発現頻度は、年齢グループ 55 歳未満でリバーロキサバン群が 32/363 例、エノキサパリン／VKA 群が 14/352 例であった（5.3.5.3.2 PH-36346/Table 1.1/3）。最初の投与 30 日間で高い発現頻度が既に観察されたが、この期間にはリバーロキサバ

ン 15mg 1 日 2 回の投与期が含まれる。第 30 日以降、投与群間差は大きくならなかった（5.3.5.3.2 PH-36346/Figure1.1/5）。

治験責任（分担）医師の報告による治験薬の投与中止に至った出血事象の解析から、子宮出血が認められたほとんどの女性が投与を継続したことが示された（5.3.5.1.1 MRR-00292/Table 14.3.1/36）。

2.7.6.1.2.3.7.9 安全性主要評価項目の部分集団解析

安全性の主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）及び「重大な出血事象」について、有効性主要評価項目の部分集団解析と同様に、事前に規定したベースライン特性及び人口統計学による部分集団解析の結果を表 2.7.6.1- 30、図 2.7.6.1- 7及び図 2.7.6.1- 8に示す。

試験 11702 DVT の SAP 補遺に詳述したとおり（5.3.5.1.1 MR-00292/SAP 補遺）、性別、年齢、体重、ベースライン時の活動性悪性腫瘍の有無、予定投与期間、腎機能、無作為割り付け前の治療、無作為割り付け前の治療及び人種に関する部分集団別に、安全性主要評価項目と「重大な出血事象」の発現頻度について部分集団解析を行った。

出血事象が発現した被験者数が少ないことを考慮し、安全性の主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）の部分集団解析結果の解釈、特に「重大な出血事象」（更に発現数が少ないため）については慎重に行う必要がある。いくつかの部分集団は被験者数が少なく、また事象の発現頻度が低かった。事象の総数が 5 件以上で統計学的解析を行った。

ハザード比とその 95%信頼区間からは、両投与群の安全性主要評価項目の発現頻度が同程度で、事前に規定したすべての部分集団を通じ一貫性があることが示された。結果は以下のとおりであった（表 2.7.6.1- 30）。

- 活動性悪性腫瘍：両投与群共に活動性悪性腫瘍と診断された被験者では出血リスクが高かった。両投与群間では差は認められなかった。
- 性別:安全性主要評価項目での出血リスクは女性より男性で数値的に低かった。「重大な出血事象」も同様の結果であり、両投与群間で差は認められなかった。
- 年齢：60 歳未満の部分集団での安全性主要評価項目の発現頻度は、エノキサパリン／VKA 群に比べリバーロキサバン群で数値的に高かった。60 歳以上の部分集団ではリバーロキサバン群で数値上低かった。この不均質性は有意ではなかった（交互作用の p 値：0.11、Gail と Simon の方法による質的交互作用の p 値：0.19）（5.3.5.1.1 MRR-00292/Table 14.3.1/126、Table 16.1.9.1/12）。また、60 歳未満の部分集団での「重大な出血事象」の発現頻度はエノキサパリン／VKA 群に比べリバーロキサバン群で数値上高かった。60 歳以上の部分集団ではリバーロキサバン群で数値上低かった。この不均質性は示されなかった（交互作用の p 値：0.063、Gail と Simon の方法による質的交互作用の p 値：0.24）（5.3.5.1.1 MRR-00292/Table 14.3.1/125、Table 16.1.9.1/13）。
- 体重：50 ㎏未満の部分集団での安全性主要評価項目の発現頻度は、エノキサパリン／VKA 群に比べリバーロキサバン群で数値上高く、50 歳以上の部分集団での発現頻度は両投与群で同様であった。この不均質性は有意ではなかった（交互作用の p 値：0.14、Gail と Simon の方法による質的交互作用の p 値：0.32）（5.3.5.1.1 MRR-00292/Table 14.3.1/126、Table 16.1.9.1/12）。

- 予定投与期間：安全性主要評価項目の発現頻度は、3 ヵ月コホートではリバーロキサバン群 7.7%、エノキサパリン／VKA 群 8.0%、6 ヵ月コホートでは 8.4%、7.2%、12 ヵ月コホートでは 7.6%、10.2%であった。
- クレアチニンクリアランス：CL_{CR} が 80mL/分以上（リバーロキサバン群：7.5%、エノキサパリン／VKA 群：7.4%）又は 50～80mL/分未満（リバーロキサバン群：9.2%、エノキサパリン／VKA 群：10.3%）の部分集団における発現頻度は、投与群間で同程度であった。CL_{CR} が 50mL/分未満の被験者ではエノキサパリン／VKA 群に比べ、リバーロキサバン群のほうが発現頻度が数値上高かった〔リバーロキサバン群：10.8%（13/120 例）、エノキサパリン／VKA 群：7.8%（10/128 例）〕（5.3.5.1.1 MRR-00292/Table 14.3.1/37）。
- 特殊な被験者集団：この被験者集団には、75 歳超、体重 50kg 以下又はクレアチニンクリアランス 50mL/分未満の基準を満たす被験者が含まれた。この部分集団における「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の発現頻度（事後解析で算出）は、エノキサパリン／VKA 群に比べ、リバーロキサバン群のほうが高かった（リバーロキサバン群：11.8%、エノキサパリン／VKA 群：9.6%）。この特殊集団以外の被験者集団における発現頻度は、投与群間で同程度であった（リバーロキサバン群：7.4%、エノキサパリン／VKA 群：7.7%）（5.3.5.1.1 MRR-00292/Table 16.1.9.1/21）。

統計学的に有意な質的な交互作用は示されなかった。部分集団解析では、エノキサパリン／VKA 群に比べリバーロキサバン群の部分集団で高い出血リスクは示唆されなかった。ベースライン特性及び人口統計学的因子別の「重大な出血事象」の発現は、幾つかの例外はあるものの、概ね安全性の主要評価項目での結果を裏付けるものであった。例外の事例としては、CL_{CR} において、50mL/分未満の集団で「重大な出血」が認められたのが、リバーロキサバン群 120 例中 1 例に対しエノキサパリン／VKA 群では 128 例中 7 例であったことなどであった（5.3.5.1.1 MRR-00292/Table 14.3.1/125）。

表 2.7.6.1- 30　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（安全性解析対象集団）

因子	区分	発現頻度		ハザード比	ハザード比の95%信頼区間の下限値	ハザード比の95%信頼区間の上限値	交互作用のｐ値[a]
		リバーロキサバン	エノキサパリン／VKA				
年齢（区分1）	＜60歳	74/947	60/939	1.168	0.830	1.643	0.114
	≧60歳	65/771	78/772	0.806	0.579	1.120	
年齢（区分2）	＜65歳	86/1134	79/1107	1.014	0.746	1.377	0.883
	65～75歳	34/369	39/381	0.894	0.564	1.416	
	＞75歳	19/215	20/223	0.971	0.517	1.826	
予定投与期間	3ヵ月	16/207	16/201	0.948	0.474	1.898	0.272
	6ヵ月	90/1074	78/1079	1.109	0.818	1.502	
	12ヵ月	33/437	44/431	0.715	0.455	1.123	
（LMW）ヘパリン／フォンダパリヌクスによる前治療	なし	47/465	47/500	1.022	0.680	1.535	0.664
	あり	92/1253	91/1211	0.940	0.703	1.256	
活動性悪性腫瘍	なし	122/1600	124/1623	0.979	0.762	1.257	0.755
	あり	17/118	14/88	0.840	0.413	1.710	
人種	N.A.	13/122	10/123	1.281	0.561	2.922	0.695
	白人	101/1316	97/1315	1.012	0.766	1.338	
	黒人	4/38	5/43	0.888	0.231	3.419	
	アジア人	19/227	25/217	0.676	0.371	1.231	
	アメリカンインディアン	0/1	1/2	.	.	.	
	ヒスパニック	0/9	0/9	.	.	.	
	分類不能	2/5	0/2	.	.	.	

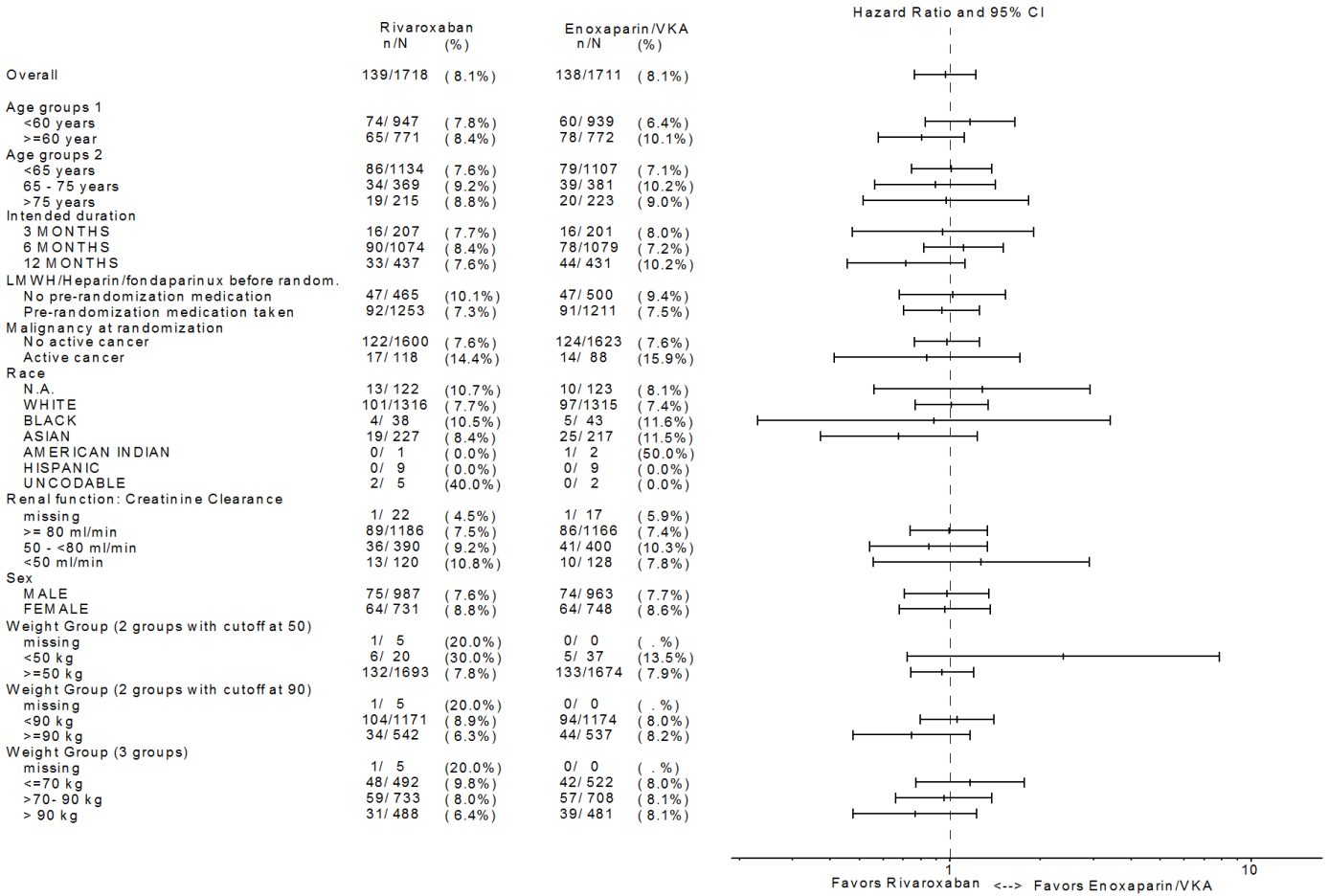
表 2.7.6.1- 30　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（安全性解析対象集団）（続き）

因子	区分	発現頻度		ハザード比	ハザード比の95%信頼区間の下限値	ハザード比の95%信頼区間の上限値	交互作用のｐ値[a]
		リバーロキサバン	エノキサパリン／VKA				
腎機能：クレアチニン・クリアランス（区分）	欠測	1/22	1/17	.	.	.	.
	≧80mL/min	89/1186	86/1166	0.993	0.738	1.336	.
	50～＜80mL/min	36/390	41/400	0.851	0.543	1.333	0.415
	＜50mL/min	13/120	10/128	1.271	0.556	2.905	
性別	男性	75/987	74/963	0.976	0.708	1.347	
	女性	64/731	64/748	0.961	0.679	1.360	0.233
体重（50kg で区分）	欠測	1/5	0/0	.	.	.	
	＜50kg	6/20	5/37	2.384	0.722	7.870	0.824
	≧50kg	132/1693	133/1674	0.943	0.741	1.200	
体重（90kg で区分）	欠測	1/5	0/0	.	.	.	0.381
	＜90kg	104/1171	94/1174	1.057	0.799	1.399	
	≧90kg	34/542	44/537	0.748	0.478	1.170	0.031
体重（3 区分）	欠測	1/5	0/0	.	.	.	
	≦70kg	48/492	42/522	1.169	0.772	1.771	0.400
	＞70～90kg	59/733	57/708	0.955	0.662	1.377	
	＞90kg	31/488	39/481	0.766	0.478	1.227	

表 2.7.6.1- 30 安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（安全性解析対象集団）（続き）

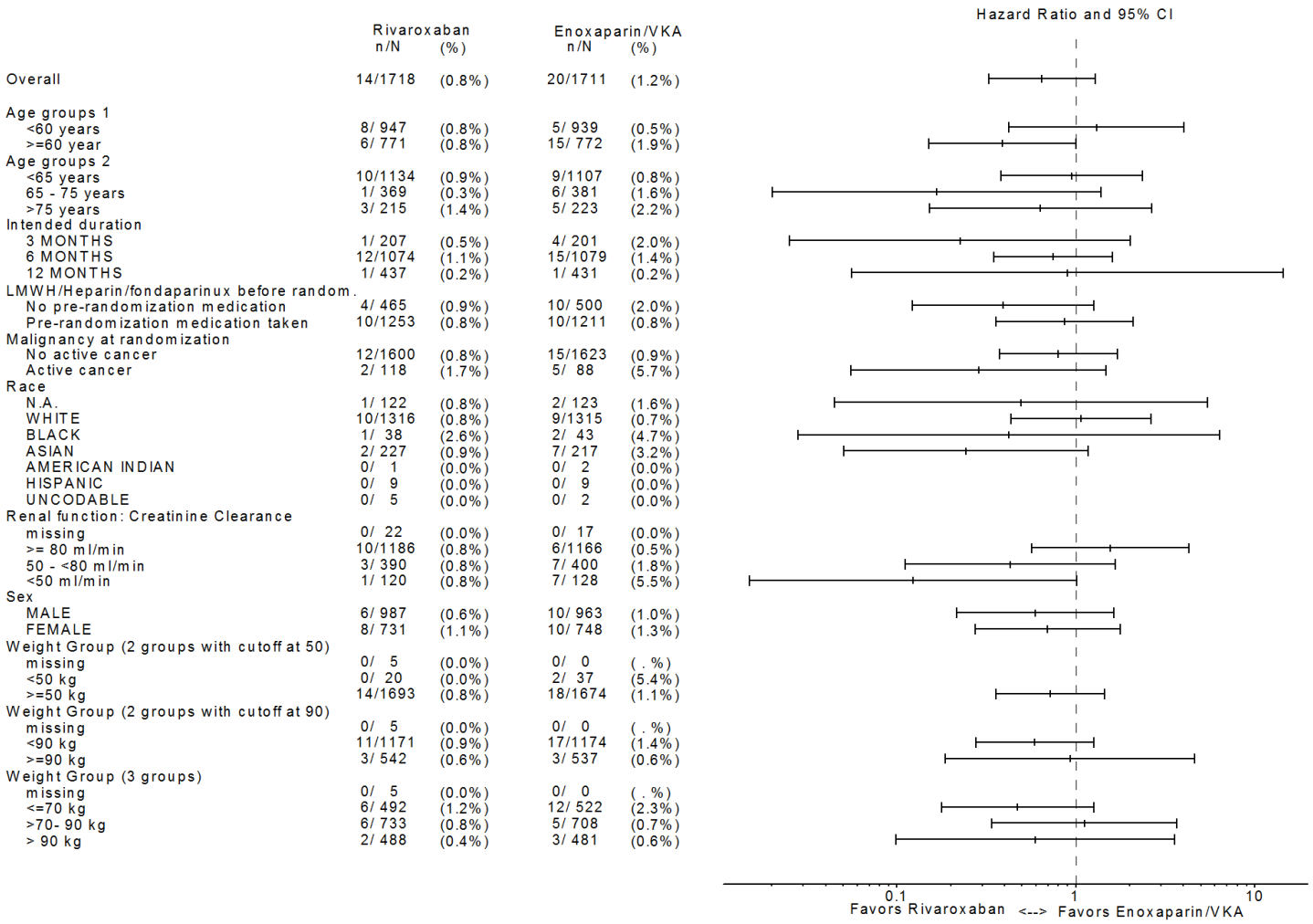
因子	区分	発現頻度		ハザード比	ハザード比の95%信頼区間の下限値	ハザード比の95%信頼区間の上限値	交互作用のｐ値[a、c]
		リバーロキサバン	エノキサパリン／VKA				
（LMW）ヘパリン／フォンダパリヌクスの前治療	なし	47/465	47/ 500	1.022	0.680	1.535	0.713
	あり	92/1253	91/1211	0.940	0.703	1.256	
（LMW）ヘパリン／フォンダパリヌクスの前治療期間（区分）	なし	47/465	47/500	1.022	0.680	1.535	0.953
	1日間	87/1184	85/1135	0.945	0.701	1.275	
	2日間	4/66	4/68	0.978	0.244	3.928	
	＞2日間	1/3	2/8	2.121	0.127	35.359	
特殊な被験者集団[b]	いいえ	106/1438	109/1408	0.918	0.702	1.199	0.356
	はい	33/280	29/303	1.225	0.743	2.021	

VKA：ビタミンK拮抗薬、（LMW）ヘパリン：LMWHを含むヘパリン
層別化されたCox比例ハザードモデルを用いた解析はカテゴリに少なくても5事象あるときだけ実施した。層として予定投与期間、ベースライン時の活動性悪性腫瘍の有無を共変量として各モデルに含められた。ベースライン時の悪性腫瘍の有無別の解析において、この共変量はモデルに含まれなかった。予定投与期間ごとの解析において、その変数は層としてモデルに含まれなかった。
a：交互作用に対するｐ値は投与群、投与群と部分集団の交互作用、ベースライン時の活動性悪性腫瘍の有無を含めたモデルで計算された。交互作用に対する値は、ベースライン及び被験者背景に関する記録が欠測のものを除いて計算された。
b：被験者の年齢が75歳超、もしくは体重が50kg以下、もしくはクレアチニン・クリアランスが50mL/min未満のいずれかに該当する被験者を特殊な被験者集団とした。
c：SAP補遺に基づく。
引用元：5.3.5.1.1 MRR-00292/ Table 14.3.1/126及びTable 16.1.9.1/21



引用元：5.3.5.1.1 MRR-00292/Figure 14.3.1/37

図 2.7.6.1- 7 安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（安全性解析対象集団）



引用元：5.3.5.1.1 MRR-00292/Figure 14.3.1/38

図 2.7.6.1- 8 治験薬投与下で発現した「重大な出血事象」のベースライン及び人口統計学的因子別解析（安全性解析対象集団）

2.7.6.1.2.3.7.10 出血事象に関する事後解析

2.7.6.1.2.3.7.10.1 出血事象と注目する併用薬

出血事象と注目する併用薬の解析の詳細は 5.3.5.3.1/PH-36306 に示す。部分集団によっては、被験者数が少なく、また事象発現頻度が低いため、結果は慎重に解釈する必要がある。

注目する併用薬についてベースライン時の併用薬使用別に提示した安全性主要評価項目（CIAC の判定）の forest プロットは 5.3.5.1.14 PH-36761/Figure 1/2 に示す。ベースライン時の注目する併用薬別の「重大な出血事象」の forest プロット及び注目する併用薬（時間依存性共変量とする）別の安全性主要評価項目及び「重大な出血事象」について 5.3.5.1.14 PH-36761 に示す。

一般に、アセチルサリチル酸（ASA）、CYP3A4 阻害薬、クロピドグレル又はチクロピジン、非ステロイド性抗炎症薬（NSAID）、NSAID 及び／又は抗血小板薬、P-糖たん白質（P-gp）阻害薬、PAI 又は ASA、及びスタチンの投与を受けている被験者では、これらの投与を受けていない被験者に比べ出血の発現頻度が高かった。しかし、エノキサパリン／VKA 群の被験者に比べた時リバーロキサバン群の被験者でこれらの併用薬の影響が異なることを示す傾向は認められなかった。事前に規定した併用薬の投与グループと非投与グループの 2 つを比較した場合、「重大な出血事象」及び「重大ではないが臨床的に問題となる出血事象」の複合エンドポイントに関するハザード比の信頼区間に重なりが認められた。

2.7.6.1.2.3.7.10.2 治験薬投与開始後初期の出血

本試験において、リバーロキサバン群では、その試験デザインにより、最初の 21 日間は 30mg/日と、その後の期間における 20mg/日よりも高い 1 日用量が用いられた。そのため両投与群において無作為割付け後最初の 21 日間に発現した出血事象の解析を行った。

第 21 日までの主要な安全性評価項目の発現頻度は、リバーロキサバン群で 3.8%（65/1718）、エノキサパリン／VKA 群で 3.2%（55/1711）であった（5.3.5.1.14/PH-36761/Table1/1）。第 22 日以後投与期間終了までの発現頻度は、リバーロキサバン群で 4.6%（74/1605）、エノキサパリン／VKA 群で 5.3%（83/1580）であった（5.3.5.1.14 PH-36761/Table 1/2）。

第 21 日までの「重大な出血事象」の発現頻度は、エノキサパリン／VKA 群〔0.6%（11/1711）〕に比べリバーロキサバン群〔0.3%（5/1718）〕で数値上低かった（5.3.5.1.14 PH-36761/Table 1/1 参照）。リバーロキサバン群の「重大な出血事象」（5 件）はすべて「重要な臓器以外の非致死的出血事象」であった。エノキサパリン／VKA 群の「重大な出血事象」11 件は、「致死的」（3 件）、「重要な臓器の非致死的」（1 件）、「重要な臓器以外の非致死的」（7 件）であった。一方、第 21 日以後投与期間終了までの「重大な出血事象」の発現頻度は両群ともに 0.5%（8/1,605 例、8/1,580 例）であった（5.3.5.1.14 PH-36761/Table 1/2）。

第 21 日までの「重大ではないが臨床的に問題となる出血事象」の発現頻度は、エノキサパリン／VKA 群〔2.6%（44/1711）〕に比べリバーロキサバン群〔3.5%（60/1718）〕で高かった（5.3.5.1.14 PH-36761/Table 1/1）。器官別大分類で報告が多かった「重大ではないが臨床的に問題となる出血事象」のうち、リバーロキサバン群の発現頻度の方が高かったものは、泌尿生殖器の出血事象（リバーロキサバン：1.1%、エノキサパリン／VKA：0.6%）、直腸の出血事象（0.6%、0.1%）、子宮出血事象（0.9%、0.3%）であった。皮膚（注射部位以外）の出血事象はリバーロキサバン群（0.2%）に比べエノキサパリン／VKA 群（1.0%）で頻度が高かった。第

21 日以後投与期間終了までの発現頻度は、リバーロキサバン群で 4.1%、エノキサパリン／VKA 群で 4.7%（5.3.5.1.14 PH-36761/Table 1/2）であった。

2.7.6.1.2.3.7.10.3 治験薬投与終了後 3 日目から 30 日目までの出血事象

治験実施計画書では、無作為化後投与を受けなかった被験者又は治験薬投与を中止した被験者は少なくとも予定投与期間の終了時（3、6 又は 12 ヵ月目）に受診するよう規定した。また各投与期間の後には治験薬投与期間にかかわらず、フォローアップ期間 30 日間を設定した。投与終了時又は中止時、治験責任（分担）医師の判断により他の抗凝固療法を行うことが認められた。

治験薬投与終了後 3 日目から 30 日目までにに発現した出血事象の要約を以下に示す（5.3.5.1.14 PH-36761/Table 1/7）。

- 全出血事象の発現頻度は、リバーロキサバン群で 1.8%、エノキサパリン／VKA 群で 1.9%であった。
- 「重大な出血事象」の発現頻度はリバーロキサバン群で 0.2%、エノキサパリン／VKA 群で 0.4%であった。
- 先にリバーロキサバンの投与を受けた被験者（550034027）1 例で致死的消化管出血事象が認められた。
- 両投与群における「重大ではないが臨床的に問題となる出血事象」の発現頻度は共に 0.4%であった。
- 「軽微な出血事象」の発現頻度はリバーロキサバン群で 1.4%、エノキサパリン／VKA 群で 1.1%であった。

これらの結果から、治験薬投与終了後 3 日目から 30 日目までの両投与群間の出血事象の発現頻度が同程度であることが示された。

2.7.6.1.2.3.7.10.4 複数回発現した出血事象

複数回発現した出血事象のすべての解析は治験薬投与下に限定して行った。これらは探索的解析であった。複数回発現した出血事象は異なる手法、すなわち記述的要約、人年ごとの事象発現頻度、事象再発までの期間の解析法及び平均累積関数を用いて解析した。

出血事象の発現した 70%を超える被験者における事象の発現は 1 回であった。「重大な出血事象」で複数回発現したものはなかった。安全性解析対象集団において、「臨床的に問題となる出血事象」が発現したのは、リバーロキサバン群で 139/1,718 例、エノキサパリン／VKA 群で 138/1,711 例であった（5.3.5.1.5 PH-36338/Table 14.3.1/2）。90%を超える被験者では出血事象の発現は 1 回で、また臨床的に問題となる出血事象の発現回数が最も多かったのは 1 被験者で 3 件であった。投与群間に差は認められなかった。

結果からはまた、Anderson-Gill モデルから導かれる再発性出血事象に対する治療効果（すなわちハザード比）が、出血事象初回発現までの期間に関して Cox モデルから得られる投与効果と実質的に差がないことが示された（5.3.5.1.5 PH-36338/Table 14.3.1/18）。

2.7.6.1.2.3.7.10.5 PT-INR と出血事象

本試験では、エノキサパリン／VKA 群の被験者で PT-INR の測定を行った。

「重大な出血事象」の発現頻度を事象発現時の PT-INR 別に表 2.7.6.1- 31に示す。「重大な出血事象」が少ないことを考慮する必要はあるが、「重大な出血事象」の発現頻度が最も低いのは PT-INR が目標範囲内の 2～3 を呈した被験者であった（0.1%／3 人月）。それに対して、PT-INR が目標範囲を下回る 2.0 未満での発現頻度は 0.8%／3 人月、目標範囲を超える 3.0 超での発現頻度は更に高く、2.1%／3 人月であった。

表 2.7.6.1- 31　発現時の PT-INR 別、治験薬投与下に発現した「重大な出血事象」の発現頻度（エノキサパリン/VKA 群、安全性解析対象集団）

		発現率	
PT-INR	／3 人月	発現例数／人年	1000 人年当たりの発現例数
＜2.0	0.8%	6 /　2379	2.5
2.0～≦3.0	0.1%	2 /　6218	0.3
＞3.0	2.1%	11 /　1580	7.0

PT-INR：プロトロンビン時間国際標準比、VKA：ビタミン K 拮抗薬
低分子量ヘパリン（LMWH）の最初の投与の中止日又はそれ以前に事象が発現した被験者は解析から除外した。人年は VKA 投与期の期間に基づく。事象発現例の期間は、VKA 投与期開始（VKA 開始かつ最初の LMWH 中止の後）から治験薬投与下で発現した「重大な出血事象」の初回発現（発現日含む、予定投与期間内）までとした。該当事象非発現例の期間は、VKA 投与期開始から出血事象発現の最終連絡又は VKA 最終投与までの期間の短い方（予定投与期間内）。PT-INR は事象発現日の測定値とした。測定値がない場合、直前の PT-INR（16 日以内の測定値）を使用した。
引用元： 5.3.5.1.1 MRR-00292/Table 14.3.1/127

施設 TTR は、各治験実施施設におけるエノキサパリン／VKA 群の TTR の平均値と規定した。

調整 TTR から計算した施設 TTR 値に基づき施設を 3 つの部分集団（エノキサパリン／VKA 群の被験者がほぼ均等になるよう）に分類した。この 3 つの部分集団の施設 TTR は、55.9%未満、55.9%～65.3%、65.3%超であった。3 つの部分集団別の安全性の主要評価項目を表 2.7.6.1-32に示す。

エノキサパリン／VKA 群では施設 TTR と安全性の主要評価項目の発現頻度との間に関連は認められなかった（施設 TTR 55.9%未満、55.9%～65.3%、65.3%超の頻度はそれぞれ、8.57%、6.62%、9.09%）。3 区分におけるハザード比（リバーロキサバン：エノキサパリン／VKA）は全体でのハザード比 0.966 と同程度であった（表 2.7.6.1- 32）。

表 2.7.6.1- 32　施設 TTR 別の安全性主要評価項目の発現頻度（PT-INR の目標範囲内は 2～3、安全性解析対象集団）

共変量	区分	発現頻度		ハザード比	ハザード比の95%信頼区間下限値	ハザード比の95%信頼区間上限値	交互作用の P 値[a]
		リバーロキサバン	エノキサパリン／VKA				
施設 TTR	施設 TTR のない被験者	6/ 42 (14.29%)	0/ 5 (0.00%)	.	.	.	0.746
	< 55.9%	41/541 (7.58%)	48/560 (8.57%)	0.813	0.535	1.236	
	55.9% - 65.3%	40/578 (6.92%)	38/574 (6.62%)	1.015	0.651	1.584	
	> 65.3%	52/557 (9.34%)	52/572 (9.09%)	1.012	0.689	1.487	

PT-INR：プロトロンビン時間国際標準比、TTR：PT-INR が目標範囲内の 2～3 に入っている期間の平均値、VKA：ビタミン K 拮抗薬
施設 TTR は施設の個別被験者全員の調整 TTR を平均して算出。対照群の PT-INR がない施設は除外した。
施設を施設 TTR で層別化して例数が均等になるよう 3 つの部分集団に分類した。
1 区分の事象数が 5 件以上の場合に限り層別 Cox 比例ハザードモデルを用いて解析した（予定投与期間に基づき層別し、各モデルではベースライン時の活動性悪性腫瘍を共変量とする）。
a：交互作用の p 値は、投与群、部分集団、投与群*部分集団及びベースライン時の活動性悪性腫瘍を共変量とするモデルにより計算した。交互作用の p 値の計算は施設 TTR のない被験者を除外して行なった。
引用元： 5.3.5.1.12 PH-36754/Table 1/18

2.7.6.1.2.3.7.10.6 出血事象とプロトロンビン時間延長との関係

リバーロキサバン群の安全性解析対象集団において、Neoplastin®を用いてベースライン及びベースライン後のトラフ時かつピーク時のプロトロンビン時間を測定した（5.3.5.1.4 PH-36329）。

出血事象発現例と出血事象非発現例で、ピーク時のプロトロンビン時間が異なるという結果はみられなかった。部分集団解析も行ったが、出血事象の有無によらず同様であった。

2.7.6.1.2.3.7.11 出血関連有害事象

治験責任（分担）医師の報告による治験薬投与下に発現した出血関連有害事象は、リバーロキサバン群で 433/1,718 例（25.2%）、エノキサパリン／VKA 群で 399/1,711 例（23.3%）で、そのうち各投与群で 303/1,718 例（17.6%）及び 279/1,711 例（16.3%）が治験責任（分担）医師により治験薬との関連ありと判断された（5.3.5.1.1 MRR-00292/ Table14.3.1/22 及び Table14.3.1/27）。重篤な出血関連有害事象の発現頻度は、リバーロキサバン群で 2.7%（47/1,718 例）、エノキサパリン／VKA 群で 2.7%（47/1,711 例）であった（5.3.5.1.1 MRR-00292/Table14.3.1/32）。

治験責任（分担）医師が報告した出血関連有害事象で治験薬の投与中止に至った事象の発現頻度は、リバーロキサバン群で 2.0%（34/1,718 例）、エノキサパリン／VKA 群で 1.3%（22/1,711 例）であった（5.3.5.1.1 MRR-00292/Table 14.3.1/36）。治験薬の投与中止に至った出血関連有害事象で最も頻度の高い事象は貧血であり、リバーロキサバン群で 0.3%（5/1,718 例）、エノキサパリン／VKA 群で 0.1%（2/1,711 例）であった。

2.7.6.1.2.3.8 心血管事象

CIAC が心血管事象（急性冠症候群、虚血性脳卒中、一過性脳虚血発作、非中枢神経系塞栓症及び心血管死）を盲検下で判定した。この項においては、特に明記しない限り心血管事象は、CIAC により判定された事象を指す。

「投与中」及び「投与終了後」に発現した心血管事象の頻度について概要を表 2.7.6.1- 33に示す。「投与中」に発現した事象とは治験薬の投与終了後 1 日目までに発現した事象とした。一方、「投与終了後」に発現した事象とは治験薬の投与終了後 2 日目から 30 日目までに発現した事象とした。

発現頻度の検討から「投与中」及び「投与終了後」における心血管事象の発現頻度が低いことが示された。「投与中」の心血管事象の発現は、リバーロキサバン群で 12/1,718 例（0.7%）、エノキサパリン／VKA 群で 14/1,711 例（0.8%）であった。「投与終了後」の発現は、リバーロキサバン群で 2/1,423 例（0.1%）、エノキサパリン／VKA 群で 6/1,410 例（0.4%）であった。なお、3 例（リバーロキサバン群 1 例、エノキサパリン／VKA 群 2 例）で「投与中」に虚血性脳卒中が発現し、それにより投与終了後に死亡したことには留意が必要である。これらの死亡例は「投与終了後」に発現した事象〔死亡（虚血性脳卒中）〕として集計した。試験結果からは、急性冠症候群（ST 上昇心筋梗塞、非 ST 上昇心筋梗塞、不安定狭心症）、脳血管事象（虚血性脳卒中又は一過性脳虚血発作）、心血管死、又は非中枢神経系塞栓症について、リバーロキサバン群で「投与中」又は「投与終了後」の発現頻度は高くはなかった。

表 2.7.6.1- 33 「投与中」及び「投与終了後」の期間における心血管事象の発現頻度（安全性解析対象集団）

評価項目／構成要素	リバーロキサバン (N＝1718)	エノキサパリン／VKA (N＝1711)
「投与中」に発現した事象		
全心血管事象	12 (0.7%)	14 (0.8%)
全虚血性脳卒中（死因又は心血管事象として判定）	3 (0.2%)	5 (0.3%)
死亡（心血管死）	1 (<0.1%)	0
死亡（そのほかの心血管事象）	1 (<0.1%)	0
STEMI	1 (<0.1%)	0
NSTEMI	4 (0.2%)	1 (<0.1%)
UA	1 (<0.1%)	1 (<0.1%)
TIA	1 (<0.1%)	5 (0.3%)
虚血性脳卒中[a]	3 (0.2%)	5 (0.3%)
非中枢神経系全身性塞栓症	2 (0.1%)	2 (0.1%)
「投与終了後」に発現した事象 （安全性対象集団のうちフォローアップ期間に参加した被験者）		
	(N＝1423)	(N＝1410)
全心血管事象	2 (0.1%)	6 (0.4%)
全虚血性脳卒中（死因又は心血管事象として判定）	1 (<0.1%)	4 (0.3%)
死亡（心血管死）	1 (<0.1%)	5 (0.4%)
死亡（虚血性脳卒中）[a]	1 (<0.1%)	4 (0.3%)
死亡（そのほかの心血管事象）	0	1 (<0.1%)
NSTEMI	1 (<0.1%)	0
虚血性脳卒中	0	1 (<0.1%)
非中枢神経系全身性塞栓症	0	1 (<0.1%)

(N) STEMI：（非）ST 部分上昇型心筋梗塞、TIA：一過性脳虚血発作、UA：不安定狭心症、VKA：ビタミン K 拮抗薬

心血管事象の定義：急性冠症候群、虚血性脳卒中、一過性脳虚血発作、非中枢神経系塞栓症及び心血管系死亡

a：「投与中」に発現した事象として虚血性脳卒中が 3 例（リバーロキサバン群 1 例、エノキサパリン／VKA 群 2 例）あり、これらはその虚血性脳卒中による「投与終了後」に発現した事象としての死亡例であることに留意。これらは「投与終了後」に発現した事象「死亡（虚血性脳卒中）」にも集計。

「投与中」に発現した事象とは治験薬最終服用 1 日後までに発現した事象とした。「投与終了後」に発現した事象とは治験薬の投与終了後 2 日目から 30 日目までに発現した事象とした。「全虚血性脳卒中」の区分は「虚血性脳卒中及び死亡（虚血性脳卒中）」区分の略であることに留意。

引用元： 5.3.5.1.1 MRR-00292/Table 14.3.1/139、Table 14.3.1/140、Table 14.3.1/142、Table 14.3.1/143

心血管死:

「投与中」に起きた心血管死は、リバーロキサバン群で 1 例、エノキサパリン／VKA 群はなかった。一方「投与終了後」の死亡は、リバーロキサバン群で 1 例、エノキサパリン／VKA 群で 5 例であった。虚血性脳卒中による死亡は 5 例（リバーロキサバン群：1 例、エノキサパリン／VKA 群：4 例）あり、これらは治験薬投与終了後 2 日以降の死亡であった（5.3.5.1.1 MRR-00292/Table 14.3.1/143）。

エノキサパリン／VKA 群で治験薬投与終了後 31 日以降の死亡例が 1 例（160264014）あった（被験者の死亡日 2009 年 6 月 16 日、治験薬の最終投与日 2009 年 5 月 13 日）。CIAC は死因を虚血性脳卒中によるものと判定した（5.3.5.1.1 MRR-00292/Table 14.3.1/143）。

虚血性脳卒中:

「投与中」に発現した虚血性脳卒中は、リバーロキサバン群で 3 例、エノキサパリン／VKA 群で 5 例であった。うちリバーロキサバン群の 1 例及びエノキサパリン／VKA 群の 2 例が治験薬中止 2 日以降に虚血性脳卒中のため死亡した。「投与終了後」に、エノキサパリン／VKA 群で致死的虚血性脳卒中の新たな事象の報告が 1 例あったが、リバーロキサバン群では報告はなかった（5.3.5.1.1 MRR-00292/ Table 14.3.1/142、Table 14.3.1/143）。

一過性脳虚血発作:

「投与中」に発現した一過性脳虚血発作は、リバーロキサバン群で 1 例、エノキサパリン／VKA 群で 5 例であった。「投与終了後」には一過性脳虚血発作の発現はなかった。

急性冠症候群:

「投与中」に発現した心筋梗塞は、リバーロキサバン群で 5 例、エノキサパリン／VKA 群で 1 例であった。リバーロキサバン群の 5 例のうち 4 例は非 ST 上昇心筋梗塞であった。両群共に不安定狭心症の報告が 1 例ずつあった。「投与終了後」にリバーロキサバン群で心筋梗塞（NSTEMI）の報告が 1 例あったが、エノキサパリン／VKA 群での報告はなかった。

非中枢神経系塞栓症:

「投与中」に発現した非中枢神経系塞栓症は、両群ともに 2 例ずつであった。「投与終了後」にエノキサパリン群で非中枢神経系塞栓症が更に 1 例発現した。

2.7.6.1.2.3.9　肝臓安全性

2.7.6.1.2.3.9.1　肝臓関連臨床検査値異常

表 2.7.6.1- 34に、ベースライン後のアスパラギン酸アミノトランスフェラーゼ（AST）、ALT、アルカリフォスファターゼ（ALP）、総ビリルビン、直接ビリルビンの各臨床検査値の閾値逸脱頻度及びこれらの複数の検査値が同時に基準値上限を超える発現（ALT とビリルビン、AST とビリルビン及び総ビリルビン＋直接ビリルビンの組み合わせ）の発現頻度を示す。ベースライン後の期間は、無作為割り付けから各被験者での最終観察日までとした。

基準値上限の 3 倍を超えるベースライン後の ALT 増加は、リバーロキサバン群で 1.5%（25/1680 例）、エノキサパリン／VKA 群で 3.8%（62/1649 例）であった。また、これらの事象の大部分は治験薬投与下に発現したものであった（リバーロキサバン群：19/25 例、エノキサパリン／VKA 群：54/62 例）（表 2.7.6.1- 34）。ベースライン後に認められた基準値上限の 5、8 及び 10 倍を超える ALT 増加は、エノキサパリン／VKA 群に比べ、リバーロキサバン群で数字上低い、もしくは同程度であった。基準値上限の 20 倍を超えた被験者は認められなかった。

ALP、AST 及び総ビリルビンの臨床検査パラメータに関し、ベースライン後かつ治験薬投与下に発現した基準値上限（各閾値は異なる）を超える増加の頻度は、概ねエノキサパリン／VKA 群とリバーロキサバン群でほぼ同程度であった（5.3.5.1.1 MRR-00292/Table 14.3.2/14）。詳細は 5.3.5.1.1 MRR-00292/Section 10.4.3.4.3 を参照。

表 2.7.6.1- 34　ベースライン後の臨床検査値異常の発現頻度（中央測定、安全性解析対象集団）

基準	リバーロキサバン Num/Den	%	エノキサパリン／VKA Num/Den	%	差：リバーロキサバンエノキサパリン／VKA (%)	95%信頼区間
ALT＞3×ULN 及び総ビリルビン＞2×ULN（同時発現）	1/1680	＜0.1	1/1648	＜0.1	-0.0	-0.3 ～ 0.3
AST＞3×ULN 及び総ビリルビン＞2×ULN（同時発現）	0/1680	0.0	2/1648	0.1	-0.1	-0.4 ～ 0.1
ALT＞3×ULN、総ビリルビン＞2×ULN 及び直接/総ビリルビン≧50%（同時発現）	0/1676	0.0	1/1639	＜0.1	-0.1	-0.3 ～ 0.2
AST＞3×ULN、総ビリルビン＞2×ULN 及び直接/総ビリルビン≧50%（同時発現）	0/1676	0.0	1/1639	＜0.1	-0.1	-0.3 ～ 0.2
総ビリルビン＞2×ULN 及び直接/総ビリルビン≧50%（同時発現）	1/1676	＜0.1	4/1639	0.2	-0.2	-0.6 ～ 0.1
総ビリルビン＞2×ULN 及び直接ビリルビン＞2×ULN（同時発現）	9/1676	0.5	7/1639	0.4	0.1	-0.4 ～ 0.6
SGOT/AST						
＞ 3×ULN	21/1680	1.3	27/1649	1.6	-0.4	-1.2 ～ 0.4
＞ 5×ULN	9/1680	0.5	8/1649	0.5	0.1	-0.5 ～ 0.6
＞ 8×ULN	2/1680	0.1	4/1649	0.2	-0.1	-0.5 ～ 0.2
＞10×ULN	2/1680	0.1	4/1649	0.2	-0.1	-0.5 ～ 0.2
＞20×ULN	0/1680	0.0	0/1649	0.0	0.0	-0.2 ～ 0.2
SGPT/ALT						
＞ 3×ULN	25/1680	1.5	62/1649	3.8	-2.3	-3.4 ～-1.2
＞ 5×ULN	6/1680	0.4	18/1649	1.1	-0.7	-1.4 ～-0.2
＞ 8×ULN	4/1680	0.2	7/1649	0.4	-0.2	-0.7 ～ 0.2
＞10×ULN	3/1680	0.2	3/1649	0.2	-0.0	-0.4 ～ 0.4
＞20×ULN	0/1680	0.0	0/1649	0.0	0.0	-0.2 ～ 0.2

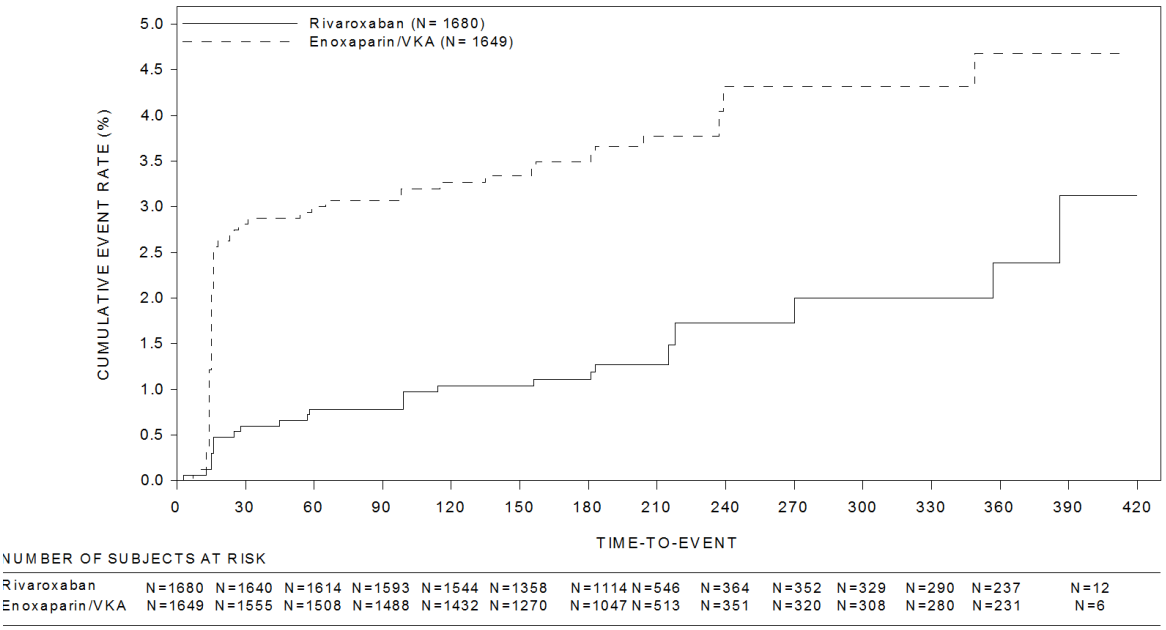
表 2.7.6.1- 34 ベースライン後の臨床検査値異常の発現頻度（中央測定、安全性解析対象集団）（続き）

基準	リバーロキサバン Num/Den	%	エノキサパリン／VKA Num/Den	%	差：リバーロキサバンエノキサパリン／VKA（%）	95%信頼区間
アルカリフォスファターゼ						
＞ 3×ULN	7/1683	0.4	10/1649	0.6	-0.2	-0.7 ～ 0.3
＞ 5×ULN	2/1683	0.1	4/1649	0.2	-0.1	-0.5 ～ 0.2
＞ 8×ULN	0/1683	0.0	1/1649	＜0.1	-0.1	-0.3 ～ 0.2
＞10×ULN	0/1683	0.0	0/1649	0.0	0.0	-0.2 ～ 0.2
＞20×ULN	0/1683	0.0	0/1649	0.0	0.0	-0.2 ～ 0.2
総ビリルビン						
＞1.5×ULN	35/1683	2.1	27/1649	1.6	0.4	-0.5 ～ 1.4
＞ 2×ULN	14/1683	0.8	14/1649	0.8	-0.0	-0.7 ～ 0.6
＞ 3×ULN	1/1683	＜0.1	5/1649	0.3	-0.2	-0.7 ～ 0.1
＞ 5×ULN	0/1683	0.0	0/1649	0.0	0.0	-0.2 ～ 0.2
＞ 8×ULN	0/1683	0.0	0/1649	0.0	0.0	-0.2 ～ 0.2
直接ビリルビン						
＞1.5×ULN	49/1676	2.9	42/1639	2.6	0.4	-0.8 ～ 1.5
＞ 2×ULN	19/1676	1.1	19/1639	1.2	-0.0	-0.8 ～ 0.7
＞ 3×ULN	7/1676	0.4	7/1639	0.4	-0.0	-0.5 ～ 0.5
＞ 5×ULN	1/1676	＜0.1	4/1639	0.2	-0.2	-0.6 ～ 0.1
＞ 8×ULN	0/1676	0.0	4/1639	0.2	-0.2	-0.6 ～-0.0

ULN：基準値上限、VKA：ビタミン K 拮抗薬、ベースライン後：無作為割り付け日後の臨床検査値、Numerator（Num）：該当する検査値異常が認められた被験者数、Denominator（Den）：ベースライン後に該当する検査値が存在する被験者数、SGPT/ALT: アラニン・アミノトランスフェラーゼ、SGOT/AST：アスパラギン酸アミノトランスフェラーゼ
信頼区間は正確な方法を用いて計算された。
直接／総ビリルビン≧50%：直接ビリルビンの値が、総ビリルビンの少なくとも 50%であること。
信頼区間は漸近的な方法（標準化されたスコア統計量）を用いて計算された。そのため低い頻度の時は解釈に注意を要する。ベースライン後は割付から各被験者の最後の観察までの期間とする。
ベースライン後の期間は、無作為割り付けから各被験者での最終観察日までである。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.2/14 及び Table 14.3.2/21

基準値上限の 3 倍を超える ALT 増加の初回発現（ベースライン後）に関する累積発現率の Kaplan-Meier 推定値は、無作為割り付けから 30 日目までが、リバーロキサバン群とエノキサパリン／VKA 群でそれぞれ 0.6%及び 2.8%、180 日目までがそれぞれ 1.1%及び 3.5%であった（初回承認時 CTD 5.3.5.3.2/Appendix 3.1.1/Table ISLS1.10.1）。

基準値上限の 3 倍を超える ALT の初回発現までの Kaplan-Meier 曲線を図 2.7.6.1- 9に示す。2 曲線間の乖離の大部分は最初の 2 週間にみられた。この期間において、エノキサパリン／VKA 群の被験者は PT-INR が目標範囲に到達するまで VKA に加えてエノキサパリンの投与を受けていた（5.3.5.1.1 MRR-00292/Section 10.4.3.4.3 参照）。



引用元：5.3.5.1.1 MRR-00292/Figure 14.3.2/1

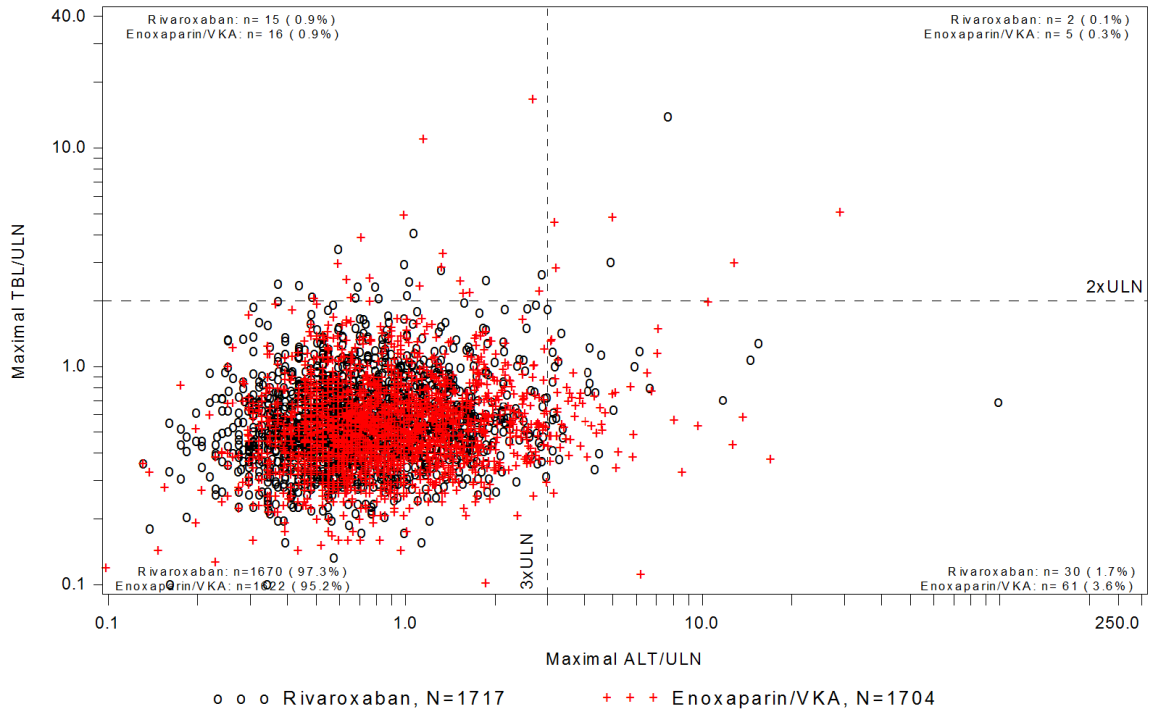
図 2.7.6.1- 9 Kaplan-Meier 法による、基準値上限の 3 倍を超える ALT 増加の累積発現率（中央測定、安全性解析対象集団）

2.7.6.1.2.3.9.2 ALT が基準値上限の 3 倍かつ総ビリルビンが基準値上限の 2 倍を超える被験者

eDISH プロット（図 2.7.6.1- 10）の右上象限にある 7 例（リバーロキサバン群：2 例、エノキサパリン／VKA 群：5 例）は、中央測定及び各施設で測定した ALT が基準値上限の 3 倍を超えるかつ総ビリルビンが基準値上限の 2 倍を超える増加を呈した被験者を表す。この 7 例中、エノキサパリン／VKA 群の 1 例で ALT 増加後 31 日以上経過して総ビリルビン増加が認められ、この症例は肝臓関連事象評価委員会（HEAC）のレビューに送られなかった。

中央測定又は施設測定において、基準値上限の 3 倍を超える ALT と基準値上限の 2 倍を超える総ビリルビンがベースライン後に同時発現した被験者は 6 例（リバーロキサバン群：2 例、エノキサパリン／VKA 群：4 例）であった。（5.3.5.1.1 MRR-00292/Section10.4.3.4.3.1、Table 14.3.2/20）。

ベースライン後に基準値上限の 3 倍を超える AST と基準値上限の 2 倍を超える総ビリルビンが同時に発現した被験者は 6 例（リバーロキサバン群：1 例、エノキサパリン／VKA 群：5 例）であった。またそのうち 4 例では ALT が基準値上限の 3 倍を超える増加をも伴った。総じて AST と総ビリルビン共に増加した症例はごくわずかであった（初回承認時 CTD 5.3.5.3.2 R-8569/Appendix 3.1.1/Table ISLS1.05）。



Note: At any time: Including screening period, baseline and postbaseline periods.
Note: Values lower than 0.1 are plotted with value 0.1

引用元：初回承認時 CTD 5.3.5.3.2 R-8569/Appendix 3.1.1/Figure ISLS1.13

図 2.7.6.1- 10　ALT 最高値と総ビリルビン最高値別の散布図（中央測定及び施設測定に基づく随時測定値、安全性解析対象集団）

2.7.6.1.2.3.9.3　　肝臓関連有害事象

肝臓関連有害事象の特定には肝障害に関する標準 MedDRA 検索式（SMQ）を用いた。

肝臓関連有害事象の発現頻度を表 2.7.6.1- 35に示す。大部分の肝臓関連有害事象は臨床検査値異常であり、リバーロキサバン群で 3.1%（54/1,718 例）、エノキサパリン／VKA 群で 8.2%（141/1,711 例）であった。これらの臨床検査値の有害事象として、肝機能検査値異常と報告されたものに加えてアラニン・アミノトランスフェラーゼ、アスパラギン酸アミノトランスフェラーゼ及び INR の増加が多く報告された。肝障害 SMQ による肝臓関連有害事象の発現頻度は、リバーロキサバン群で 4.8%（83/1,718 例）、エノキサパリン／VKA 群で 9.4%（161/1,711 例）であった。サブ SMQ では「肝臓関連臨床検査、徴候及び症状」の発現頻度が高く（リバーロキサバン群 3.67%、エノキサパリン／VKA 群 6.31%）、次いで「肝臓に関連する凝固および出血障害」（0.17%、2.57%）であった（5.3.5.3.10 PH-36312 Table 14.3.1/21）。

肝障害 SMQ からサブ SMQ「肝臓に関連する凝固および出血障害」を除外した後の肝臓患関連有害事象について、ベースライン後の発現頻度はエノキサパリン／VKA 群（7.19%）に比べ、リバーロキサバン群（4.48%）で低かった（絶対差：－2.71%、95%信頼区間：－4.27～－1.14、初回承認時 CTD 5.3.5.3.2 R-8569/Appendix 3.1.2/Table ISLS2.01.2）。このパターンは TEAE でも同様であった。これはエノキサパリン／VKA 群に比べ、リバーロキサバン群で肝トランスア

ミナーゼ増加の報告が少ないことによる（初回承認時 CTD 5.3.5.3.2 R-8569/Setion 3.1.3.3 参照）。これ以外の区分では両群の発現頻度は同様でありハザード比の 95%信頼区間が 1 をまたいだ。

サブ SMQ「肝臓に関連する凝固および出血障害」及び「肝臓関連臨床検査、徴候および症状」を除外した後のすべての有害事象の区分における発現率は投与群間で同様で、最大の絶対差はわずか－0.06％であった（初回承認時 CTD 5.3.5.3.2 R-8569/Appendix 3.1.2/Table ISLS2.01.4）。

表 2.7.6.1- 35　肝臓関連有害事象の発現頻度（いずれかの投与群で 0.5%以上、安全性解析対象集団）

MedDRA 器官別大分類/基本語	リバーロキサバン (N＝1718) n（%）	エノキサパリン／VKA (N＝1711) n（%）
全事象	83（ 4.8%）	161（ 9.4%）
肝胆道系障害	21（ 1.2%）	21（ 1.2%）
脂肪肝	10（ 0.6%）	9（ 0.5%）
臨床検査	54（ 3.1%）	141（ 8.2%）
アラニン・アミノトランスフェラーゼ増加	25（ 1.5%）	55（ 3.2%）
アスパラギン酸アミノトランスフェラーゼ増加	14（ 0.8%）	21（ 1.2%）
血中アルカリホスファターゼ増加	7（ 0.4%）	10（ 0.6%）
肝酵素上昇	1（＜0.1%）	15（ 0.9%）
INR 増加	2（ 0.1%）	41（ 2.4%）
肝機能検査異常	9（ 0.5%）	21（ 1.2%）

VKA：ビタミン K 拮抗薬、INR：（プロトロンビン時間）国際標準比
MedDRA version 13.0
肝臓関連の有害事象は SMQ を基に抽出した。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/38

肝臓関連の重篤な有害事象の発現頻度を表 2.7.6.1- 36に示す。全体として、肝臓関連の重篤な有害事象の発現頻度はリバーロキサバン群で 0.8%（13/1,718 例）、エノキサパリン／VKA 群で 1.4%（24/1,711 例）であった。これらの事象の大部分は臨床検査値異常であり、リバーロキサバン群で 0.4%（7/1,718 例）、エノキサパリン／VKA 群で 1.2%（20/1,711 例）であった。これらの臨床検査値の有害事象として、肝機能検査異常及び肝酵素上昇と報告されたものに加えて、アラニン・アミノトランスフェラーゼ増加及び INR 増加が多く報告された。サブ SMQ では「肝臓関連臨床検査、徴候及び症状」の発現頻度が高く（リバーロキサバン群：0.52%、エノキサパリン／VKA 群：0.88%）で、次いで「肝臓に関連する凝固および出血障害」（0%、0.29%）であった（5.3.5.3.10 PH-36312 Table 14.3.1/25）。

サブ SMQ「肝臓に関連する凝固および出血障害」及び「肝臓関連臨床検査、徴候および症状」を除外した後のベースライン後の肝臓関連の重篤な有害事象の発現頻度は両投与群ともに 0.3%に低下した（初回承認時 CTD 5.3.5.3.2 R-8569/Appendix 3.1.2/Table ISLS2.05.4）。

表 2.7.6.1- 36　肝臓関連の重篤な有害事象の発現頻度（安全性解析対象集団）

MedDRA 器官別大分類/基本語	リバーロキサバン (N＝1718) n（%）	エノキサパリン／VKA (N＝1711) n（%）
全事象	13（ 0.8%）	24（ 1.4%）
胃腸障害	1（＜0.1%）	0
腹水	1（＜0.1%）	0
肝胆道系障害	2（ 0.1%）	3（ 0.2%）
急性肝不全	0	1（＜0.1%）
肝不全	0	1（＜0.1%）
肝腫瘤	1（＜0.1%）	0
脂肪肝	0	1（＜0.1%）
急性肝炎	1（＜0.1%）	0
胆汁うっ滞性黄疸	0	1（＜0.1%）
臨床検査	7（ 0.4%）	20（ 1.2%）
アラニン・アミノトランスフェラーゼ増加	2（ 0.1%）	6（ 0.4%）
血中ビリルビン増加	1（＜0.1%）	0
肝酵素上昇	1（＜0.1%）	5（ 0.3%）
INR 増加	0	5（ 0.3%）
肝機能検査異常	2（ 0.1%）	4（ 0.2%）
トランスアミナーゼ上昇	2（ 0.1%）	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3（ 0.2%）	2（ 0.1%）
転移性肝癌	1（＜0.1%）	0
肝の悪性新生物	2（ 0.1%）	2（ 0.1%）

MedDRA：ICH 国際医薬用語集、VKA：ビタミン K 拮抗薬、INR：（プロトロンビン時間）国際標準比
MedDRA version 13.0
肝臓関連の有害事象は SMQ を基に抽出した。
引用元：5.3.5.1.1 MRR-00292/Table 14.3.1/39

治験薬の投与中止に至ったベースライン後の肝臓関連有害事象の発現頻度は、両投与群ともに 0.4%であった（リバーロキサバン群：7/1,718 例、エノキサパリン／VKA 群：6/1,711 例）。個々の事象の発現頻度は、投与群間でほぼ同程度であった（5.3.5.1.1 MRR-00292/Table 14.3.1/40）。

死亡に至った肝臓関連有害事象を発現した被験者は計 5 例であった。内訳はリバーロキサバン群が 2 例、エノキサパリン／VKA 群が 3 例であった。すべての死因は基礎疾患によるとされた。リバーロキサバン群の 2 例には基礎疾患として悪性腫瘍があり、死因は悪性腫瘍と判定された。エノキサパリン／VKA 群の 2 例は悪性腫瘍、1 例は総胆管結石を伴う胆管炎で外科手術を受けた後、肝不全が発現し死亡した。初めの 2 例の死因は悪性腫瘍、3 例目については胆石による肝臓と判定された。

HEAC による評価：

HEAC は、事前に規定した肝臓に関連する以下の基準に該当する被験者について評価した。

- 死亡前 30 日以内に基準値上限の 3 倍を超える ALT の増加を伴う全死亡
- ALT が基準値上限の 3 倍を超え、かつ総ビリルビンが基準値上限の 2 倍を超える場合
  - 同時発現（同一検体の臨床検査評価で検査値増加が認められた場合）
  - 非同時発現（ALT 増加後 30 日以内に総ビリルビンが増加した場合）
- ALT が基準値上限の 8 倍を超える場合（症候性、無症候性を問わない）
- その他〔MedDRA 標準検索式（SMQ）「肝臓関連」を用いて検索した基本語に基づく〕

HEAC のレビューのために送付されたのは 20 例（リバーロキサバン群：8 例、エノキサパリン／VKA 群：12 例）であった。死亡の 30 日以内に基準値上限の 3 倍を超える ALT が発現した死亡例（それぞれの投与群で 3 例ずつ認められた）を除き、HEAC の基準に合致した症例の数は、エノキサパリン／VKA 群に比べ、リバーロキサバン群で数値上低かった。エノキサパリン／VKA 群ではエノキサパリン投与中に基準値上限の 8 倍を超える ALT 増加が認められた例は 5 例であった。

5 例の死亡例のうち、HEAC の基準に合致したのは 1 例のみ（被験者 540024033）で、評価のため同委員会に送られた。3 人の委員全員が、死亡原因は肝事象であり治験薬との因果関係はないと判断した（初回承認時 CTD 5.3.5.3.2./Table ISLS2.08.4 参照）。肝移植又は HEAC 判定により治験薬と関連する肝臓事象関連死とされたものはなかった（初回承認時 CTD 5.3.5.3.2 R-8569 参照）。

肝臓の安全性の要約：

全体的に、本試験における肝機能検査異常はリバーロキサバン群に比べエノキサパリン／VKA 群で発現頻度が高かった。この大部分は投与開始初期（対照群の被験者には VKA 投与に加えてエノキサパリン投与が行なわれた）に認められた。それ以降は両投与群間に差は認められなかった。したがって、これにはエノキサパリン投与が影響している可能性が考えられる。死亡の 30 日以内に基準値上限の 3 倍を超える ALT が発現したすべての死亡例並びに 2 つの異常の合併（基準値上限の 3 倍を超える ALT 及び基準値上限の 2 倍を超える総ビリルビン）が発現した死亡例には合理的に説明できる死因があり治験薬との関連性はなかった。本試験ではこれ以外に肝臓の安全性上問題となる事象の兆候は認められなかった。

2.7.6.1.2.3.10 そのほかの臨床検査値評価

本試験において中央測定を行ったほかの臨床検査（肝機能検査以外）は、ベースライン時及び投与終了時のアミラーゼのみであった。予定投与期間が 12 ヵ月間の被験者ではベースライン時、6 ヵ月後及び投与終了時アミラーゼの測定を行った。ベースライン後の上昇としてアミラーゼが基準値上限の 3 倍を超えた症例は認められなかった（5.3.5.1.1 MRR-00292/Table 14.3.2/14）。

2.7.6.1.2.3.11 身体的所見及び安全性に関連するほかの観察項目

バイタルサイン及び心電図は通常検査としては行わなかった。

2.7.6.1.2.3.12　　安全性の結論

無作為割り付けされた 3,449 例のうち、3,429 例（リバーロキサバン群：1,718 例、エノキサパリン／VKA 群：1,711 例）が安全性解析対象集団に含まれた。安全性解析の結果、リバーロキサバンの安全性プロファイルはエノキサパリン／VKA と同様であった。この結論は以下の結果に基づく。

- TEAE の発現頻度は両群間で同様であった（両群とも 63%）。治験薬との因果関係が否定できない TEAE の発現頻度は両群とも 23%であった。治験実施計画書では再発性 DVT 及び非致死的 PE は有害事象又は重篤な有害事象とはみなさないと規定していることに留意すべきである。
- 重篤な TEAE の発現頻度はリバーロキサバン群で 12%、エノキサパリン／VKA 群で 14%であった。
- TEAE による治験薬の投与中止に至った被験者の割合は、リバーロキサバン群で 4.9%、エノキサパリン／VKA 群で 4.7%であった。
- 安全性解析対象集団で合計 93 例の死亡〔リバーロキサバン群：41 例（2.4%）、エノキサパリン／VKA 群：52 例（3.0%）〕がみられた。CIAC 判定による、両群の死亡の最も多かった 4 つの理由は悪性腫瘍〔リバーロキサバン群：1.6%（27/1,718 例）、エノキサパリン／VKA 群：1.2%　（20/1,711 例）〕、PE を否定できない原因不明の死亡〔リバーロキサバン群：0.2%（3/1,718 例）、エノキサパリン／VKA 群：0.4%（6/1,711 例）〕、感染性疾患〔リバーロキサバン群：0.2%（3/1,718 例）、エノキサパリン／VKA 群：0.5%（9/1,711 例）〕及び出血〔リバーロキサバン群：0.1%（2/1,718 例）、エノキサパリン／VKA 群：0.3%（5/1,711 例）〕であった。
- 安全性主要評価項目（治験薬投与下の最初の「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」に基づく）の発現頻度は、両群で同程度であった（両群とも 8.1%）。ハザード比（リバーロキサバン群対エノキサパリン／VKA 群）は 1 に近かった（ハザード比 0.966、95%信頼区間：0.763～1.222、優越性の p 値：0.77）。
- 「重大な出血事象」の初回発現頻度は、リバーロキサバン群〔0.8%（13/1,718 例）〕とエノキサパリン／VKA 群〔1.1%（19/1,711 例）〕で同様であった。「重大な出血事象」の構成要素及びその発現頻度は、致死的出血〔リバーロキサバン群：＜0.1%（1/1,718 例）、エノキサパリン／VKA 群：0.3%　（5/1,711 例）〕、重要な臓器の非致死的出血〔リバーロキサバン群：0.2%（3/1,718 例）、エノキサパリン／VKA 群：0.2%（3/1,711 例）〕及び重要な臓器以外の非致死的出血〔リバーロキサバン群：0.5%（9/1,718 例）、エノキサパリン／VKA 群：0.6%（11/1,711 例）〕であった。
- 「重大ではないが臨床的に問題となる出血事象」の発現頻度は、両群で同様であった：リバーロキサバン群 7.3%（126/1,718 例）、エノキサパリン／VKA 群 7.0%（119/1,711 例）。両群で発現頻度の差が大きかった事象は、直腸出血（リバーロキサバン群：1.2%、エノキサパリン／VKA 群：0.6%）、子宮出血（リバーロキサバン群：1.6%、エノキサパリン／VKA 群：0.9%）及び皮膚出血（リバーロキサバン群：0.6%、エノキサパリン／VKA 群：1.5%）であった。
- 致死的な出血事象が 6 例にみられた：リバーロキサバン群 1 例（消化管出血）、エノキサパリン／VKA 群で 5 例（消化管出血 2 例、胸部出血 1 例及び頭蓋内出血 2 例）。
- 頭蓋内出血に関連した「重大な出血事象」が 4 例（リバーロキサバン群：2 例、エノキサパリン／VKA 群：2 例）にみられ、このうち 2 例は致死的（いずれもエノキサパリン／VKA

群）であった。エノキサパリン／VKA 群の 2 例はいずれも、イベント発現日の PT-INR は目標範囲を超えていた。

- 安全性主要評価項目の部分集団解析では、事前に規定したすべての部分集団を通して一貫して両群の発現頻度は同程度であった。
- 治験薬投与下で発現した心血管事象（急性冠症候群、虚血性脳卒中、一過性脳虚血発作、非中枢性全身性塞栓症及び心血管死）はリバーロキサバン群で 12/1,718 例（0.7%）、エノキサパリン／VKA 群で 14/1,711 例（0.8%）にみられた。治験薬投与終了後における心血管事象の発現頻度はリバーロキサバン群で 2/1,423 例（0.1%）、エノキサパリン／VKA 群で 6/1,410 例（0.4%）であった。投与中にリバーロキサバン群で 1 例の死亡がみられた。治験薬投与終了後には 6 例の死亡（リバーロキサバン群：1 例、エノキサパリン／VKA 群：5 例）が報告された。本試験では投与中又は投与終了後で発現した心血管事象の発現頻度には、報告数が少ないことを考慮すると投与群間で差はみられなかった。
- 肝移植又は HEAC 判定により治験薬と関連する肝臓事象関連死とされたものはなかった基準値上限の 3 倍を超える（＞3×ULN）ALT の発現頻度は、リバーロキサバン群で 1.5%（25/1,680 例）、エノキサパリン／VKA 群で 3.8%（62/1,649 例）であった。大部分の被験者では、検査値は治験期間中に基準値範囲内又は開始時のレベルまで戻った。エノキサパリン／VKA 群の約 50%の被験者では、異常値は投与開始の最初の 2 週間に発現した。その後は両群間で違いはみられなかった。ALT＞3×ULN 及び総ビリルビン＞2×ULN（中央又は各医療機関での測定値）の複数検査値の同時上昇はリバーロキサバン群で 0.1%（2/1,682）、エノキサパリン／VKA 群で 0.2%（4/1,648）に発現した。本試験のデータは、エノキサパリン／VKA 群で投与開始時に ALT 増加の頻度が高かった以外、肝臓関連検査値異常に関して両群間に違いがないことを示している。肝臓関連有害事象（MedDRA 肝障害 SMQ に基づく）の両群での報告頻度の差は小さく、差の多くは臨床検査値異常に関連するものであった。

2.7.6.1.3 結論

症候性 PE を伴わない急性症候性 DVT の被験者において、有効性主要評価項目とした症候性 VTE の発現頻度について、リバーロキサバン群の標準治療（エノキサパリン／VKA）群に対するハザード比は 0.680（95%信頼区間：0.443～1.042）で、リバーロキサバンの標準治療に対する非劣性が検証され、有効性に関する本試験の主目的が達成された。更に、CL_{CR}、性別、BMI、年齢及び種々の危険因子にかかわらず、有効性の結果は一貫していた。

同様に、安全性主要評価項目、すなわち、「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイントについて、リバーロキサバンはエノキサパリン／VKA と同様の安全性プロファイルを示した（ハザード比：0.966、95％信頼区間：0.763～1.222）。安全性主要評価項目の結果も事前に規定した部分集団を通して一貫していた。「重大な出血事象」の発現頻度はエノキサパリン／VKA 群よりもリバーロキサバン群で数値上低かった。結果として、総合有用性評価指標－1（症候性 VTE と「重大な出血事象」との複合エンドポイント）のイベント発現の頻度は、数値上リバーロキサバン群の方が低かった。

本試験により、リバーロキサバン 15mg 1 日 2 回経口投与に続く 20mg 1 日 1 回経口投与は、体重補正したエノキサパリン 1 日 2 回皮下投与と PT-INR で用量調節した経口 VKA 投与の 2 剤を用いる標準的抗凝固療法と同様の有効性と安全性が示された。

2.7.6.1　付表

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団） 2

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例） 33

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Number of subjects (%) with at least one adverse event		1103 (64.2%)	1107 (64.7%)	403 (23.5%)	404 (23.6%)
Blood and lymphatic system disorders	血液およびリンパ系障害	59 (3.4%)	57 (3.3%)	20 (1.2%)	11 (0.6%)
Anaemia	貧血	32 (1.9%)	30 (1.8%)	13 (0.8%)	6 (0.4%)
Anaemia haemolytic autoimmune	自己免疫性溶血性貧血	1 (<0.1%)	0		
Anaemia macrocytic	大球性貧血	1 (<0.1%)	0		
Anaemia megaloblastic	巨赤芽球性貧血	0	1 (<0.1%)		
Autoimmune thrombocytopenia	自己免疫性血小板減少症	0	1 (<0.1%)		
Bone marrow failure	骨髄機能不全	1 (<0.1%)	0		
Deficiency anaemia	欠乏性貧血	1 (<0.1%)	0		
Febrile neutropenia	発熱性好中球減少症	1 (<0.1%)	1 (<0.1%)		
Haemorrhagic anaemia	出血性貧血	1 (<0.1%)	3 (0.2%)	0	1 (<0.1%)
Haemorrhagic diathesis	出血性素因	1 (<0.1%)	2 (0.1%)	1 (<0.1%)	2 (0.1%)
Hypercoagulation	凝固亢進	2 (0.1%)	2 (0.1%)		
Iron deficiency anaemia	鉄欠乏性貧血	3 (0.2%)	3 (0.2%)	2 (0.1%)	1 (<0.1%)
Leukocytosis	白血球増加症	0	3 (0.2%)		
Leukopenia	白血球減少症	2 (0.1%)	4 (0.2%)		
Lymphadenitis	リンパ節炎	1 (<0.1%)	1 (<0.1%)		
Lymphadenopathy	リンパ節症	3 (0.2%)	2 (0.1%)		
Lymphadenopathy mediastinal	縦隔リンパ節腫脹	2 (0.1%)	1 (<0.1%)		
Microcytic anaemia	小球性貧血	1 (<0.1%)	0	1 (<0.1%)	0
Nephrogenic anaemia	腎性貧血	1 (<0.1%)	1 (<0.1%)		
Neutropenia	好中球減少症	1 (<0.1%)	1 (<0.1%)		
Normochromic normocytic anaemia	正色素性正球性貧血	1 (<0.1%)	0		
Pernicious anaemia	悪性貧血	1 (<0.1%)	0		
Polycythaemia	赤血球増加症	1 (<0.1%)	0	1 (<0.1%)	0
Splenic haemorrhage	脾臓出血	0	1 (<0.1%)		
Splenomegaly	脾腫	1 (<0.1%)	0		
Spontaneous haematoma	特発性血腫	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
Thrombocytopenia	血小板減少症	3 (0.2%)	6 (0.4%)	2 (0.1%)	1 (<0.1%)
Thrombocytosis	血小板増加症	0	1 (<0.1%)		
Cardiac disorders	心臓障害	59 (3.4%)	51 (3.0%)	7 (0.4%)	1 (<0.1%)
Acute coronary syndrome	急性冠動脈症候群	1 (<0.1%)	0		
Acute myocardial infarction	急性心筋梗塞	5 (0.3%)	1 (<0.1%)		
Angina pectoris	狭心症	3 (0.2%)	3 (0.2%)		
Angina unstable	不安定狭心症	1 (<0.1%)	4 (0.2%)		
Aortic valve disease	大動脈弁疾患	0	1 (<0.1%)		
Aortic valve incompetence	大動脈弁閉鎖不全症	2 (0.1%)	0		
Arrhythmia	不整脈	1 (<0.1%)	0		
Atrial fibrillation	心房細動	4 (0.2%)	10 (0.6%)		
Atrial flutter	心房粗動	1 (<0.1%)	0		
Atrioventricular block	房室ブロック	0	2 (0.1%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Atrioventricular block second degree	第二度房室ブロック	1 (<0.1%)	0		
Bradycardia	徐脈	3 (0.2%)	1 (<0.1%)		
Bundle branch block left	左脚ブロック	0	1 (<0.1%)		
Cardiac arrest	心停止	0	3 (0.2%)		
Cardiac disorder	心障害	1 (<0.1%)	0		
Cardiac failure	心不全	3 (0.2%)	4 (0.2%)		
Cardiac failure chronic	慢性心不全	1 (<0.1%)	1 (<0.1%)		
Cardiac failure congestive	うっ血性心不全	0	2 (0.1%)		
Cardio-respiratory arrest	心肺停止	1 (<0.1%)	0		
Coronary artery disease	冠動脈疾患	0	1 (<0.1%)		
Cyanosis	チアノーゼ	1 (<0.1%)	3 (0.2%)	1 (<0.1%)	0
Diastolic dysfunction	拡張機能障害	1 (<0.1%)	0	1 (<0.1%)	0
Hypertensive heart disease	高血圧性心疾患	0	1 (<0.1%)		
Left ventricular hypertrophy	左室肥大	1 (<0.1%)	2 (0.1%)		
Mitral valve incompetence	僧帽弁閉鎖不全症	1 (<0.1%)	3 (0.2%)		
Mitral valve prolapse	僧帽弁逸脱	0	1 (<0.1%)		
Myocardial infarction	心筋梗塞	0	1 (<0.1%)		
Myocardial ischaemia	心筋虚血	0	2 (0.1%)		
Palpitations	動悸	15 (0.9%)	5 (0.3%)	2 (0.1%)	1 (<0.1%)
Pericardial cyst	心膜嚢胞	1 (<0.1%)	0		
Pericarditis	心膜炎	1 (<0.1%)	0		
Right ventricular failure	右室不全	1 (<0.1%)	0		
Sick sinus syndrome	洞不全症候群	0	1 (<0.1%)		
Sinoatrial block	洞房ブロック	0	1 (<0.1%)		
Sinus arrhythmia	洞性不整脈	0	2 (0.1%)		
Sinus tachycardia	洞性頻脈	1 (<0.1%)	0		
Supraventricular tachycardia	上室性頻脈	0	1 (<0.1%)		
Tachyarrhythmia	頻脈性不整脈	1 (<0.1%)	0		
Tachycardia	頻脈	11 (0.6%)	6 (0.4%)	3 (0.2%)	0
Tricuspid valve incompetence	三尖弁閉鎖不全症	0	1 (<0.1%)		
Ventricular extrasystoles	心室性期外収縮	1 (<0.1%)	0		
Ventricular tachycardia	心室性頻脈	0	1 (<0.1%)		
Congenital, familial and genetic disorders	先天性、家族性および遺伝性障害	22 (1.3%)	16 (0.9%)		
Adenomatous polyposis coli	大腸腺腫性ポリポーシス	0	1 (<0.1%)		
Antithrombin III deficiency	アンチトロンビンＩＩＩ欠乏症	2 (0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Congenital cystic kidney disease	先天性嚢胞性腎疾患	1 (<0.1%)	1 (<0.1%)		
Congenital urethral anomaly	先天性尿道異常	1 (<0.1%)	0		
Dolichocolon	過長結腸	1 (<0.1%)	0		
Dysplastic naevus syndrome	異形成母斑症候群	1 (<0.1%)	0		
Factor II mutation	第ＩＩ因子突然変異	4 (0.2%)	2 (0.1%)		
Factor V Leiden mutation	第Ｖ因子ライデン変異	8 (0.5%)	8 (0.5%)		
Gene mutation	遺伝子突然変異	2 (0.1%)	4 (0.2%)		
Hip dysplasia	股関節形成不全	0	1 (<0.1%)		
Mixed hyperlipidaemia	混合型高脂血症	2 (0.1%)	0		
Phimosis	包茎	0	1 (<0.1%)		
Pyloric stenosis	幽門狭窄	1 (<0.1%)	0		
Ear and labyrinth disorders	耳および迷路障害	26 (1.5%)	24 (1.4%)	6 (0.3%)	2 (0.1%)
Deafness	難聴	1 (<0.1%)	0		
Deafness neurosensory	感音性難聴	1 (<0.1%)	0	1 (<0.1%)	0
Deafness unilateral	片耳難聴	0	1 (<0.1%)		
Ear discomfort	耳不快感	2 (0.1%)	1 (<0.1%)		
Ear haemorrhage	耳出血	2 (0.1%)	4 (0.2%)	1 (<0.1%)	2 (0.1%)
Ear pain	耳痛	2 (0.1%)	2 (0.1%)	1 (<0.1%)	0
External ear inflammation	外耳の炎症	0	1 (<0.1%)		
Hearing impaired	聴覚障害	1 (<0.1%)	0	1 (<0.1%)	0
Hypoacusis	聴力低下	1 (<0.1%)	1 (<0.1%)		
Sudden hearing loss	突発難聴	0	1 (<0.1%)		
Tinnitus	耳鳴	4 (0.2%)	2 (0.1%)		
Vertigo	回転性めまい	15 (0.9%)	11 (0.6%)	3 (0.2%)	0
Vertigo labyrinthine	迷路性回転性めまい	0	1 (<0.1%)		
Endocrine disorders	内分泌障害	4 (0.2%)	10 (0.6%)		
Basedow's disease	バセドウ病	1 (<0.1%)	0		
Cushingoid	クッシング様	0	1 (<0.1%)		
Goitre	甲状腺腫	2 (0.1%)	3 (0.2%)		
Hyperthyroidism	甲状腺機能亢進症	0	2 (0.1%)		
Hypothyroidism	甲状腺機能低下症	1 (<0.1%)	4 (0.2%)		
Eye disorders	眼障害	42 (2.4%)	46 (2.7%)	14 (0.8%)	21 (1.2%)
Asthenopia	眼精疲労	1 (<0.1%)	0		
Blepharochalasis	眼瞼皮膚弛緩症	0	1 (<0.1%)		
Cataract	白内障	4 (0.2%)	4 (0.2%)		
Cataract cortical	皮質白内障	1 (<0.1%)	0		
Chorioretinitis	脈絡網膜炎	0	1 (<0.1%)		
Conjunctival haemorrhage	結膜出血	12 (0.7%)	23 (1.3%)	9 (0.5%)	15 (0.9%)
Conjunctivitis	結膜炎	4 (0.2%)	3 (0.2%)		
Diabetic retinopathy	糖尿病性網膜症	2 (0.1%)	1 (<0.1%)		
Diplopia	複視	1 (<0.1%)	0		
Dry eye	眼乾燥	1 (<0.1%)	1 (<0.1%)		
Entropion	眼瞼内反	0	1 (<0.1%)		
Eye haemorrhage	眼出血	2 (0.1%)	4 (0.2%)	2 (0.1%)	4 (0.2%)
Eye inflammation	眼の炎症	1 (<0.1%)	0		
Eye movement disorder	眼運動障害	1 (<0.1%)	0		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Eye pain	眼痛	1 (<0.1%)	0		
Eye pruritus	眼そう痒症	2 (0.1%)	0		
Hypermetropia	遠視	1 (<0.1%)	0		
Hyphaema	前房出血	1 (<0.1%)	0	1 (<0.1%)	0
Keratoconjunctivitis sicca	乾性角結膜炎	0	1 (<0.1%)		
Lacrimal haemorrhage	涙器出血	0	1 (<0.1%)		
Macular hole	黄斑円孔	1 (<0.1%)	0		
Maculopathy	黄斑症	1 (<0.1%)	0		
Ocular hyperaemia	眼充血	0	3 (0.2%)	0	2 (0.1%)
Retinal detachment	網膜剥離	1 (<0.1%)	0		
Retinal exudates	網膜滲出物	1 (<0.1%)	0	1 (<0.1%)	0
Retinopathy	網膜症	1 (<0.1%)	0		
Vision blurred	霧視	3 (0.2%)	2 (0.1%)	1 (<0.1%)	0
Visual impairment	視力障害	1 (<0.1%)	1 (<0.1%)		
Vitreous detachment	硝子体剥離	1 (<0.1%)	0	1 (<0.1%)	0
Vitreous haemorrhage	硝子体出血	0	1 (<0.1%)		
Gastrointestinal disorders	胃腸障害	352 (20.5%)	309 (18.1%)	119 (6.9%)	90 (5.3%)
Abdominal discomfort	腹部不快感	14 (0.8%)	9 (0.5%)	4 (0.2%)	1 (<0.1%)
Abdominal distension	腹部膨満	5 (0.3%)	5 (0.3%)	2 (0.1%)	0
Abdominal pain	腹痛	28 (1.6%)	16 (0.9%)	2 (0.1%)	0
Abdominal pain lower	下腹部痛	7 (0.4%)	1 (<0.1%)	2 (0.1%)	0
Abdominal pain upper	上腹部痛	18 (1.0%)	9 (0.5%)	3 (0.2%)	1 (<0.1%)
Abdominal wall cyst	腹壁嚢胞	1 (<0.1%)	0		
Abdominal wall haematoma	腹壁血腫	1 (<0.1%)	1 (<0.1%)		
Aerophagia	空気嚥下	0	1 (<0.1%)		
Anal fissure	裂肛	1 (<0.1%)	0		
Anal haemorrhage	肛門出血	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Anal skin tags	肛門皮膚垂	0	1 (<0.1%)		
Aphthous stomatitis	アフタ性口内炎	0	1 (<0.1%)		
Ascites	腹水	4 (0.2%)	2 (0.1%)		
Barrett's oesophagus	バレット食道	1 (<0.1%)	0		
Chapped lips	口唇のひび割れ	1 (<0.1%)	0		
Coeliac artery stenosis	腹腔動脈狭窄	0	1 (<0.1%)		
Coeliac disease	セリアック病	1 (<0.1%)	0		
Colitis	大腸炎	0	1 (<0.1%)		
Colitis ulcerative	潰瘍性大腸炎	1 (<0.1%)	1 (<0.1%)		
Colonic polyp	結腸ポリープ	3 (0.2%)	6 (0.4%)		
Constipation	便秘	50 (2.9%)	45 (2.6%)	1 (<0.1%)	3 (0.2%)
Crohn's disease	クローン病	0	4 (0.2%)		
Dental caries	齲歯	5 (0.3%)	4 (0.2%)		
Diabetic gastropathy	糖尿病性胃障害	0	1 (<0.1%)		
Diarrhoea	下痢	58 (3.4%)	43 (2.5%)	8 (0.5%)	3 (0.2%)
Diverticulum	憩室	2 (0.1%)	0		
Diverticulum intestinal	腸憩室	3 (0.2%)	5 (0.3%)		
Dry mouth	口内乾燥	4 (0.2%)	4 (0.2%)	2 (0.1%)	0
Duodenal polyp	十二指腸ポリープ	0	1 (<0.1%)		
Duodenal ulcer	十二指腸潰瘍	2 (0.1%)	3 (0.2%)	1 (<0.1%)	0
Duodenitis	十二指腸炎	3 (0.2%)	3 (0.2%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Dyspepsia	消化不良	19 (1.1%)	14 (0.8%)	4 (0.2%)	2 (0.1%)
Dysphagia	嚥下障害	1 (<0.1%)	0		
Enterocutaneous fistula	腸管皮膚瘻	2 (0.1%)	0		
Eructation	おくび	0	1 (<0.1%)		
Faecaloma	糞塊	1 (<0.1%)	0		
Faeces discoloured	変色便	1 (<0.1%)	1 (<0.1%)		
Faeces hard	硬便	1 (<0.1%)	0		
Flatulence	鼓腸	4 (0.2%)	4 (0.2%)	2 (0.1%)	0
Food poisoning	食中毒	2 (0.1%)	2 (0.1%)		
Frequent bowel movements	排便回数増加	1 (<0.1%)	0		
Gastric haemorrhage	胃出血	0	1 (<0.1%)	0	1 (<0.1%)
Gastric ulcer	胃潰瘍	3 (0.2%)	3 (0.2%)		
Gastric ulcer haemorrhage	出血性胃潰瘍	1 (<0.1%)	1 (<0.1%)		
Gastric ulcer perforation	穿孔性胃潰瘍	0	1 (<0.1%)		
Gastritis	胃炎	8 (0.5%)	6 (0.4%)	1 (<0.1%)	0
Gastritis atrophic	萎縮性胃炎	1 (<0.1%)	0		
Gastritis erosive	びらん性胃炎	2 (0.1%)	0		
Gastrointestinal disorder	胃腸障害	1 (<0.1%)	0		
Gastrointestinal haemorrhage	胃腸出血	4 (0.2%)	0	3 (0.2%)	0
Gastrointestinal necrosis	消化管壊死	0	1 (<0.1%)		
Gastrointestinal tract mucosal discolouration	消化管粘膜変色	0	1 (<0.1%)		
Gastrooesophageal reflux disease	胃食道逆流性疾患	14 (0.8%)	3 (0.2%)	3 (0.2%)	0
Gastrooesophageal sphincter insufficiency	胃食道括約筋機能不全	1 (<0.1%)	0		
Gingival bleeding	歯肉出血	37 (2.2%)	29 (1.7%)	32 (1.9%)	24 (1.4%)
Gingival pain	歯肉痛	0	1 (<0.1%)		
Gingival recession	歯肉退縮	0	1 (<0.1%)	0	1 (<0.1%)
Gingival swelling	歯肉腫脹	0	1 (<0.1%)	0	1 (<0.1%)
Gingivitis	歯肉炎	2 (0.1%)	3 (0.2%)		
Haematemesis	吐血	2 (0.1%)	7 (0.4%)	2 (0.1%)	6 (0.4%)
Haematochezia	血便排泄	7 (0.4%)	8 (0.5%)	4 (0.2%)	6 (0.4%)
Haemorrhoidal haemorrhage	痔出血	14 (0.8%)	8 (0.5%)	8 (0.5%)	4 (0.2%)
Haemorrhoids	痔核	8 (0.5%)	9 (0.5%)	1 (<0.1%)	0
Hernial eventration	内臓ヘルニア	0	1 (<0.1%)		
Hiatus hernia	裂孔ヘルニア	5 (0.3%)	5 (0.3%)		
Hyperchlorhydria	胃酸過多	0	1 (<0.1%)		
Hypoaesthesia oral	口の感覚鈍麻	1 (<0.1%)	0		
Inguinal hernia	鼠径ヘルニア	1 (<0.1%)	1 (<0.1%)		
Inguinal hernia, obstructive	閉塞性鼠径ヘルニア	0	1 (<0.1%)		
Intestinal cyst	腸管嚢胞	1 (<0.1%)	0		
Intestinal dilatation	腸管拡張症	1 (<0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Intestinal haemorrhage	腸出血	0	3 (0.2%)	0	2 (0.1%)
Intestinal infarction	腸梗塞	0	1 (<0.1%)		
Intestinal ischaemia	腸管虚血	0	1 (<0.1%)		
Intestinal mass	腸管腫瘤	0	1 (<0.1%)		
Intestinal obstruction	腸閉塞	2 (0.1%)	1 (<0.1%)		
Intestinal perforation	腸管穿孔	1 (<0.1%)	0		
Intestinal polyp	腸管ポリープ	3 (0.2%)	0		
Intra-abdominal haematoma	腹腔内血腫	1 (<0.1%)	13 (0.8%)	0	11 (0.6%)
Intra-abdominal haemorrhage	腹腔内出血	0	1 (<0.1%)	0	1 (<0.1%)
Large intestine perforation	大腸穿孔	1 (<0.1%)	1 (<0.1%)		
Lip dry	口唇乾燥	1 (<0.1%)	0		
Lip haemorrhage	口唇出血	2 (0.1%)	0		
Lip ulceration	口唇潰瘍	0	1 (<0.1%)		
Lower gastrointestinal haemorrhage	下部消化管出血	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
Mallory-Weiss syndrome	マロリー・ワイス症候群	1 (<0.1%)	0		
Melaena	メレナ	8 (0.5%)	4 (0.2%)	8 (0.5%)	3 (0.2%)
Melanosis coli	結腸メラノーシス	0	1 (<0.1%)		
Mouth haemorrhage	口腔内出血	6 (0.3%)	2 (0.1%)	5 (0.3%)	2 (0.1%)
Mouth ulceration	口腔内潰瘍形成	2 (0.1%)	1 (<0.1%)		
Nausea	悪心	51 (3.0%)	41 (2.4%)	10 (0.6%)	11 (0.6%)
Oesophageal pain	食道痛	1 (<0.1%)	0		
Oesophageal ulcer	食道潰瘍	0	1 (<0.1%)		
Oesophageal ulcer haemorrhage	食道潰瘍出血	0	1 (<0.1%)		
Oesophagitis	食道炎	4 (0.2%)	2 (0.1%)		
Oral pain	口腔内痛	1 (<0.1%)	1 (<0.1%)		
Pancreas lipomatosis	膵脂肪腫症	2 (0.1%)	0		
Pancreatic cyst	膵嚢胞	0	2 (0.1%)		
Pancreatitis	膵炎	1 (<0.1%)	2 (0.1%)		
Pancreatitis acute	急性膵炎	0	3 (0.2%)		
Paraesthesia oral	口の錯感覚	1 (<0.1%)	0	1 (<0.1%)	0
Peptic ulcer	消化性潰瘍	0	1 (<0.1%)		
Pericoronitis	歯冠周囲炎	0	1 (<0.1%)		
Periodontal disease	歯周病	1 (<0.1%)	0		
Periodontitis	歯周炎	2 (0.1%)	3 (0.2%)		
Peritonitis	腹膜炎	1 (<0.1%)	0		
Proctalgia	肛門周囲痛	1 (<0.1%)	0		
Rectal haemorrhage	直腸出血	38 (2.2%)	20 (1.2%)	28 (1.6%)	12 (0.7%)
Rectal polyp	直腸ポリープ	2 (0.1%)	0		
Reflux oesophagitis	逆流性食道炎	3 (0.2%)	5 (0.3%)		
Retroperitoneal fibrosis	後腹膜線維症	0	1 (<0.1%)		
Small intestinal obstruction	小腸閉塞	0	1 (<0.1%)		
Stomatitis haemorrhagic	出血性口内炎	1 (<0.1%)	0		
Stress ulcer	ストレス潰瘍	0	1 (<0.1%)		
Subileus	亜イレウス	1 (<0.1%)	1 (<0.1%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Tongue haemorrhage	舌出血	2 (0.1%)	1 (<0.1%)		
Tooth disorder	歯の障害	1 (<0.1%)	2 (0.1%)		
Toothache	歯痛	7 (0.4%)	7 (0.4%)		
Umbilical hernia	臍ヘルニア	1 (<0.1%)	2 (0.1%)		
Upper gastrointestinal haemorrhage	上部消化管出血	0	3 (0.2%)	0	2 (0.1%)
Vomiting	嘔吐	19 (1.1%)	25 (1.5%)	4 (0.2%)	3 (0.2%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	214 (12.5%)	190 (11.1%)	22 (1.3%)	27 (1.6%)
Asthenia	無力症	11 (0.6%)	7 (0.4%)		
Axillary pain	腋窩痛	1 (<0.1%)	0		
Catheter site haemorrhage	カテーテル留置部位出血	0	1 (<0.1%)		
Chest discomfort	胸部不快感	1 (<0.1%)	5 (0.3%)		
Chest pain	胸痛	38 (2.2%)	32 (1.9%)	0	1 (<0.1%)
Chills	悪寒	3 (0.2%)	0	1 (<0.1%)	0
Cyst	嚢胞	1 (<0.1%)	1 (<0.1%)		
Death	死亡	2 (0.1%)	1 (<0.1%)		
Device breakage	医療機器破損	0	1 (<0.1%)		
Device leakage	医療機器リーク	1 (<0.1%)	0		
Device occlusion	医療機器閉塞	1 (<0.1%)	0		
Drug resistance	薬剤耐性	0	1 (<0.1%)	0	1 (<0.1%)
Exercise tolerance decreased	運動耐性低下	2 (0.1%)	0		
Facial pain	顔面痛	1 (<0.1%)	1 (<0.1%)		
Fatigue	疲労	26 (1.5%)	16 (0.9%)	6 (0.3%)	2 (0.1%)
Feeling abnormal	異常感	3 (0.2%)	2 (0.1%)		
Feeling cold	冷感	2 (0.1%)	0		
Feeling hot	熱感	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Feeling of body temperature change	体温変動感	1 (<0.1%)	0	1 (<0.1%)	0
Gait disturbance	歩行障害	0	2 (0.1%)		
General physical health deterioration	全身健康状態低下	1 (<0.1%)	2 (0.1%)		
Generalised oedema	全身性浮腫	1 (<0.1%)	0		
Haemorrhagic cyst	出血性嚢胞	1 (<0.1%)	0		
Hernia	ヘルニア	1 (<0.1%)	1 (<0.1%)		
Impaired healing	治癒不良	0	1 (<0.1%)		
Inflammation	炎症	2 (0.1%)	3 (0.2%)		
Influenza like illness	インフルエンザ様疾患	5 (0.3%)	2 (0.1%)		
Infusion site phlebitis	注入部位静脈炎	0	1 (<0.1%)		
Injection site extravasation	注射部位血管外漏出	0	2 (0.1%)	0	2 (0.1%)
Injection site haematoma	注射部位血腫	2 (0.1%)	12 (0.7%)	2 (0.1%)	12 (0.7%)
Injection site haemorrhage	注射部位出血	0	1 (<0.1%)	0	1 (<0.1%)
Injection site pain	注射部位疼痛	0	1 (<0.1%)	0	1 (<0.1%)
Injection site reaction	注射部位反応	0	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Injection site swelling	注射部位腫脹	0	1 (<0.1%)	0	1 (<0.1%)
Irritability	易刺激性	1 (<0.1%)	0		
Local swelling	局所腫脹	1 (<0.1%)	0		
Malaise	倦怠感	5 (0.3%)	5 (0.3%)	3 (0.2%)	0
Medical device complication	医療機器合併症	0	1 (<0.1%)		
Multi-organ failure	多臓器不全	3 (0.2%)	2 (0.1%)	0	1 (<0.1%)
Non-cardiac chest pain	非心臓性胸痛	2 (0.1%)	1 (<0.1%)		
Oedema	浮腫	16 (0.9%)	10 (0.6%)	1 (<0.1%)	0
Oedema peripheral	末梢性浮腫	44 (2.6%)	47 (2.7%)	5 (0.3%)	1 (<0.1%)
Pain	疼痛	8 (0.5%)	6 (0.4%)	0	1 (<0.1%)
Pelvic mass	骨盤腔内腫瘤	0	1 (<0.1%)		
Polyp	ポリープ	2 (0.1%)	0		
Puncture site haemorrhage	穿刺部位出血	1 (<0.1%)	2 (0.1%)	0	2 (0.1%)
Pyrexia	発熱	47 (2.7%)	40 (2.3%)	1 (<0.1%)	1 (<0.1%)
Sudden cardiac death	心突然死	1 (<0.1%)	0		
Sudden death	突然死	0	1 (<0.1%)		
Systemic inflammatory response syndrome	全身性炎症反応症候群	1 (<0.1%)	0		
Thirst	口渇	1 (<0.1%)	0		
Vessel puncture site haematoma	血管穿刺部位血腫	3 (0.2%)	1 (<0.1%)	1 (<0.1%)	0
Vessel puncture site haemorrhage	血管穿刺部位出血	2 (0.1%)	1 (<0.1%)	2 (0.1%)	1 (<0.1%)
Vessel puncture site reaction	血管穿刺部位反応	1 (<0.1%)	0		
Hepatobiliary disorders	肝胆道系障害	29 (1.7%)	28 (1.6%)	2 (0.1%)	2 (0.1%)
Acute hepatic failure	急性肝不全	0	1 (<0.1%)		
Bile duct stenosis	胆管狭窄	1 (<0.1%)	0		
Biliary colic	胆道仙痛	1 (<0.1%)	1 (<0.1%)		
Cholangitis	胆管炎	1 (<0.1%)	1 (<0.1%)		
Cholecystitis	胆嚢炎	0	1 (<0.1%)		
Cholecystitis acute	急性胆嚢炎	0	2 (0.1%)		
Cholecystitis chronic	慢性胆嚢炎	1 (<0.1%)	0		
Cholelithiasis	胆石症	7 (0.4%)	7 (0.4%)		
Gallbladder polyp	胆嚢ポリープ	1 (<0.1%)	1 (<0.1%)		
Hepatic cirrhosis	肝硬変	1 (<0.1%)	0		
Hepatic cyst	肝嚢胞	6 (0.3%)	4 (0.2%)		
Hepatic failure	肝不全	0	1 (<0.1%)		
Hepatic function abnormal	肝機能異常	3 (0.2%)	1 (<0.1%)	1 (<0.1%)	0
Hepatic mass	肝腫瘤	1 (<0.1%)	1 (<0.1%)		
Hepatic steatosis	脂肪肝	10 (0.6%)	9 (0.5%)		
Hepatitis acute	急性肝炎	1 (<0.1%)	0	1 (<0.1%)	0
Hepatocellular injury	肝細胞損傷	0	1 (<0.1%)		
Hepatomegaly	肝腫大	1 (<0.1%)	0		
Hydrocholecystis	水腫性胆嚢炎	0	1 (<0.1%)		
Hyperbilirubinaemia	高ビリルビン血症	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Hypertransaminasaemia	高トランスアミナーゼ血症	0	1 (<0.1%)	0	1 (<0.1%)
Jaundice cholestatic	胆汁うっ滞性黄疸	0	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Liver disorder	肝障害	0	1 (<0.1%)		
Immune system disorders	免疫系障害	19 (1.1%)	14 (0.8%)	1 (<0.1%)	1 (<0.1%)
Antiphospholipid syndrome	抗リン脂質抗体症候群	3 (0.2%)	2 (0.1%)		
Behcet's syndrome	ベーチェット症候群	1 (<0.1%)	1 (<0.1%)		
Contrast media allergy	造影剤アレルギー	0	1 (<0.1%)		
Drug hypersensitivity	薬物過敏症	4 (0.2%)	2 (0.1%)	0	1 (<0.1%)
House dust allergy	家塵アレルギー	1 (<0.1%)	0		
Humoral immune defect	体液性免疫不全	1 (<0.1%)	0		
Hypersensitivity	過敏症	7 (0.4%)	5 (0.3%)	1 (<0.1%)	0
Liver transplant rejection	肝移植拒絶反応	0	1 (<0.1%)		
Perfume sensitivity	香水過敏症	0	1 (<0.1%)		
Seasonal allergy	季節性アレルギー	2 (0.1%)	2 (0.1%)		
Infections and infestations	感染症および寄生虫症	373 (21.7%)	379 (22.2%)	8 (0.5%)	2 (0.1%)
Abdominal abscess	腹部膿瘍	0	2 (0.1%)		
Abdominal sepsis	腹部敗血症	1 (<0.1%)	0		
Abscess	膿瘍	1 (<0.1%)	0		
Abscess limb	四肢膿瘍	2 (0.1%)	2 (0.1%)		
Acute tonsillitis	急性扁桃炎	1 (<0.1%)	1 (<0.1%)		
Anal abscess	肛門膿瘍	0	1 (<0.1%)		
Appendicitis	虫垂炎	0	1 (<0.1%)		
Arthritis infective	感染性関節炎	0	2 (0.1%)		
Asymptomatic bacteriuria	無症候性細菌尿	1 (<0.1%)	0		
Bacteraemia	菌血症	1 (<0.1%)	1 (<0.1%)		
Bacterial infection	細菌感染	2 (0.1%)	0		
Bacterial sepsis	細菌性敗血症	0	1 (<0.1%)		
Balanitis candida	カンジダ性亀頭炎	1 (<0.1%)	0		
Blister infected	感染性水疱	0	1 (<0.1%)		
Body tinea	体部白癬	0	1 (<0.1%)		
Bone tuberculosis	骨結核	1 (<0.1%)	0		
Bronchiectasis	気管支拡張症	1 (<0.1%)	0		
Bronchitis	気管支炎	29 (1.7%)	34 (2.0%)	0	1 (<0.1%)
Bronchopneumonia	気管支肺炎	4 (0.2%)	1 (<0.1%)		
Candidiasis	カンジダ症	0	1 (<0.1%)		
Cardiac valve vegetation	心臓弁疣贅	0	1 (<0.1%)		
Catheter site infection	カテーテル留置部位感染	0	1 (<0.1%)		
Cellulitis	蜂巣炎	17 (1.0%)	23 (1.3%)		
Cerebral toxoplasmosis	脳トキソプラズマ症	0	1 (<0.1%)		
Chlamydial infection	クラミジア感染	1 (<0.1%)	0		
Clostridial infection	クロストリジウム感染	1 (<0.1%)	0		
Conjunctivitis infective	感染性結膜炎	0	1 (<0.1%)		
Cystitis	膀胱炎	10 (0.6%)	14 (0.8%)		
Dengue fever	デング熱	0	1 (<0.1%)		
Dermatophytosis	皮膚糸状菌症	1 (<0.1%)	0		
Dermo-hypodermitis	皮膚皮下組織炎	0	2 (0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Device related infection	医療機器関連感染	0	1 (<0.1%)		
Disseminated tuberculosis	播種性結核	0	1 (<0.1%)		
Diverticulitis	憩室炎	2 (0.1%)	1 (<0.1%)		
Dysentery	赤痢	1 (<0.1%)	0		
Ear infection	耳感染	1 (<0.1%)	5 (0.3%)		
Endocarditis staphylococcal	ブドウ球菌性心内膜炎	0	1 (<0.1%)		
Enterocolitis bacterial	細菌性腸炎	1 (<0.1%)	0		
Epiglottitis	喉頭蓋炎	1 (<0.1%)	1 (<0.1%)		
Epstein-Barr virus infection	エプスタイン・バーウイルス感染	1 (<0.1%)	0		
Erysipelas	丹毒	5 (0.3%)	6 (0.4%)		
Escherichia sepsis	大腸菌性敗血症	0	1 (<0.1%)		
Escherichia urinary tract infection	大腸菌性尿路感染	1 (<0.1%)	0		
Eye infection	眼感染	2 (0.1%)	1 (<0.1%)		
Folliculitis	毛包炎	2 (0.1%)	1 (<0.1%)		
Fungal infection	真菌感染	1 (<0.1%)	0		
Fungal skin infection	皮膚真菌感染	3 (0.2%)	2 (0.1%)		
Furuncle	せつ	4 (0.2%)	1 (<0.1%)		
Gastroenteritis	胃腸炎	13 (0.8%)	18 (1.1%)		
Gastroenteritis viral	ウイルス性胃腸炎	6 (0.3%)	0		
Genital candidiasis	性器カンジダ症	1 (<0.1%)	0		
Genital infection fungal	真菌性性器感染	0	1 (<0.1%)		
Gingival infection	歯肉感染	2 (0.1%)	0		
Helicobacter gastritis	ヘリコバクター性胃炎	2 (0.1%)	0		
Helicobacter infection	ヘリコバクター感染	0	1 (<0.1%)		
Hepatitis A	A型肝炎	0	1 (<0.1%)		
Herpes simplex	単純ヘルペス	1 (<0.1%)	0		
Herpes zoster	帯状疱疹	8 (0.5%)	3 (0.2%)		
Hordeolum	麦粒腫	1 (<0.1%)	1 (<0.1%)		
Incision site abscess	切開部位膿瘍	1 (<0.1%)	1 (<0.1%)		
Incision site infection	切開部位感染	0	2 (0.1%)		
Infected cyst	感染性嚢腫	0	1 (<0.1%)		
Infected skin ulcer	感染性皮膚潰瘍	0	1 (<0.1%)		
Infection	感染	1 (<0.1%)	3 (0.2%)		
Infective aneurysm	感染性動脈瘤	1 (<0.1%)	0		
Infective exacerbation of chronic obstructive airways disease	感染による慢性閉塞性気道疾患の増悪	2 (0.1%)	2 (0.1%)		
Influenza	インフルエンザ	39 (2.3%)	38 (2.2%)		
Injection site infection	注射部位感染	0	1 (<0.1%)		
Kidney infection	腎感染	0	1 (<0.1%)		
Laryngitis	喉頭炎	1 (<0.1%)	0		
Lobar pneumonia	大葉性肺炎	1 (<0.1%)	4 (0.2%)		
Localised infection	限局性感染	8 (0.5%)	6 (0.4%)	1 (<0.1%)	0

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Lower respiratory tract infection	下気道感染	9 (0.5%)	5 (0.3%)		
Lung infection	肺感染	2 (0.1%)	2 (0.1%)		
Lymphangitis	リンパ管炎	0	1 (<0.1%)		
Mastitis	乳腺炎	0	1 (<0.1%)		
Mumps	ムンプス	0	1 (<0.1%)		
Myringitis	鼓膜炎	1 (<0.1%)	0		
Nail bed infection	爪床感染	0	1 (<0.1%)		
Nail infection	爪感染	1 (<0.1%)	0		
Nasopharyngitis	鼻咽頭炎	100 (5.8%)	91 (5.3%)	1 (<0.1%)	1 (<0.1%)
Oesophageal candidiasis	食道カンジダ症	1 (<0.1%)	1 (<0.1%)		
Onychomycosis	爪真菌症	0	1 (<0.1%)		
Opisthorchiasis	タイ肝吸虫症	0	1 (<0.1%)		
Oral candidiasis	口腔カンジダ症	5 (0.3%)	2 (0.1%)		
Oral fungal infection	口腔真菌感染	2 (0.1%)	1 (<0.1%)	1 (<0.1%)	0
Oral herpes	口腔ヘルペス	4 (0.2%)	2 (0.1%)		
Oropharyngitis fungal	真菌性口腔咽頭炎	0	1 (<0.1%)		
Otitis externa	外耳炎	1 (<0.1%)	1 (<0.1%)		
Otitis media	中耳炎	3 (0.2%)	2 (0.1%)		
Paronychia	爪囲炎	2 (0.1%)	1 (<0.1%)		
Pharyngitis	咽頭炎	10 (0.6%)	2 (0.1%)		
Pharyngitis streptococcal	レンサ球菌性咽頭炎	1 (<0.1%)	0		
Pneumonia	肺炎	20 (1.2%)	21 (1.2%)		
Pneumonia bacterial	細菌性肺炎	0	2 (0.1%)		
Post procedural infection	処置後感染	1 (<0.1%)	0		
Post procedural pneumonia	処置後肺炎	1 (<0.1%)	0		
Post procedural sepsis	処置後敗血症	1 (<0.1%)	1 (<0.1%)		
Postoperative wound infection	術後創感染	1 (<0.1%)	3 (0.2%)		
Pseudomembranous colitis	偽膜性大腸炎	0	1 (<0.1%)		
Pulmonary sepsis	肺敗血症	0	1 (<0.1%)		
Pulmonary tuberculosis	肺結核	1 (<0.1%)	3 (0.2%)		
Pyelonephritis	腎盂腎炎	2 (0.1%)	3 (0.2%)		
Pyelonephritis acute	急性腎盂腎炎	0	1 (<0.1%)		
Rash pustular	膿疱性皮疹	1 (<0.1%)	0	1 (<0.1%)	0
Renal abscess	腎膿瘍	1 (<0.1%)	0		
Respiratory tract infection	気道感染	11 (0.6%)	5 (0.3%)		
Rhinitis	鼻炎	10 (0.6%)	7 (0.4%)		
Sepsis	敗血症	4 (0.2%)	9 (0.5%)		
Septic shock	敗血症性ショック	1 (<0.1%)	6 (0.4%)		
Sinusitis	副鼻腔炎	13 (0.8%)	11 (0.6%)	1 (<0.1%)	0
Skin infection	皮膚感染	2 (0.1%)	4 (0.2%)	1 (<0.1%)	0
Sputum purulent	膿性痰	0	1 (<0.1%)		
Staphylococcal skin infection	ブドウ球菌皮膚感染	1 (<0.1%)	0		
Strongyloidiasis	糞線虫症	0	1 (<0.1%)		
Subacute endocarditis	亜急性心内膜炎	1 (<0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Tinea cruris	股部白癬	0	2 (0.1%)		
Tinea pedis	足部白癬	0	2 (0.1%)		
Tonsillitis	扁桃炎	0	1 (<0.1%)		
Tooth abscess	歯膿瘍	2 (0.1%)	4 (0.2%)		
Tooth infection	歯感染	3 (0.2%)	3 (0.2%)	1 (<0.1%)	0
Tracheitis	気管炎	0	1 (<0.1%)		
Tracheobronchitis	気管気管支炎	1 (<0.1%)	1 (<0.1%)		
Upper respiratory tract infection	上気道感染	15 (0.9%)	25 (1.5%)		
Urinary tract infection	尿路感染	38 (2.2%)	36 (2.1%)	1 (<0.1%)	0
Vaginal infection	膣感染	1 (<0.1%)	1 (<0.1%)		
Vaginitis bacterial	細菌性膣炎	1 (<0.1%)	0		
Viral infection	ウイルス感染	6 (0.3%)	6 (0.4%)		
Viral upper respiratory tract infection	ウイルス性上気道感染	7 (0.4%)	5 (0.3%)		
Vulvovaginal candidiasis	外陰部膣カンジダ症	3 (0.2%)	0		
Vulvovaginal mycotic infection	外陰膣真菌感染	1 (<0.1%)	2 (0.1%)		
Wound abscess	創部膿瘍	1 (<0.1%)	0		
Wound infection	創傷感染	5 (0.3%)	2 (0.1%)		
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	166 (9.7%)	190 (11.1%)	50 (2.9%)	72 (4.2%)
Accident	事故	1 (<0.1%)	1 (<0.1%)		
Accidental overdose	偶発的過量投与	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Alcohol poisoning	アルコール中毒	0	1 (<0.1%)		
Anaemia postoperative	術後貧血	0	1 (<0.1%)		
Animal bite	動物咬傷	4 (0.2%)	1 (<0.1%)		
Animal scratch	動物による引っかき傷	1 (<0.1%)	0		
Ankle fracture	足関節部骨折	0	1 (<0.1%)		
Arthropod bite	節足動物咬傷	2 (0.1%)	1 (<0.1%)		
Arthropod sting	節足動物刺傷	1 (<0.1%)	2 (0.1%)		
Bursa injury	滑液包損傷	0	1 (<0.1%)		
Cartilage injury	軟骨損傷	0	1 (<0.1%)		
Clavicle fracture	鎖骨骨折	1 (<0.1%)	0		
Concussion	脳振盪	0	1 (<0.1%)		
Contusion	挫傷	57 (3.3%)	69 (4.0%)	28 (1.6%)	40 (2.3%)
Crushing injury of trunk	体幹の圧挫損傷	1 (<0.1%)	0		
Drug exposure during pregnancy	妊娠時の薬物曝露	0	1 (<0.1%)		
Drug toxicity	薬物毒性	1 (<0.1%)	0	1 (<0.1%)	0
Epicondylitis	上顆炎	0	1 (<0.1%)		
Eschar	焼痂	1 (<0.1%)	0		
Excoriation	擦過傷	5 (0.3%)	5 (0.3%)	1 (<0.1%)	0
Eye injury	眼外傷	1 (<0.1%)	0		
Face injury	顔面損傷	0	1 (<0.1%)		
Facial bones fracture	顔面骨骨折	1 (<0.1%)	0		
Fall	転倒	11 (0.6%)	10 (0.6%)		
Femoral neck fracture	大腿骨頚部骨折	0	2 (0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Femur fracture	大腿骨骨折	0	1 (<0.1%)		
Fibula fracture	腓骨骨折	1 (<0.1%)	0		
Foot fracture	足骨折	2 (0.1%)	1 (<0.1%)		
Forearm fracture	前腕骨折	0	1 (<0.1%)		
Gastroenteritis radiation	放射線胃腸炎	1 (<0.1%)	0		
Gastrointestinal disorder postoperative	術後胃腸障害	1 (<0.1%)	0		
Graft haemorrhage	移植部位出血	0	1 (<0.1%)		
Hand fracture	手骨折	2 (0.1%)	0		
Heat stroke	熱射病	1 (<0.1%)	0		
Humerus fracture	上腕骨骨折	2 (0.1%)	1 (<0.1%)		
Induced abortion haemorrhage	人工流産による出血	1 (<0.1%)	0		
Inflammation of wound	創部炎症	1 (<0.1%)	0		
Injury	損傷	1 (<0.1%)	0		
Joint dislocation	関節脱臼	2 (0.1%)	2 (0.1%)		
Joint injury	関節損傷	2 (0.1%)	3 (0.2%)		
Joint sprain	関節捻挫	11 (0.6%)	8 (0.5%)		
Ligament injury	靱帯損傷	0	1 (<0.1%)		
Ligament rupture	靱帯断裂	1 (<0.1%)	1 (<0.1%)		
Limb injury	四肢損傷	4 (0.2%)	2 (0.1%)		
Mouth injury	口腔内損傷	0	1 (<0.1%)	0	1 (<0.1%)
Muscle rupture	筋断裂	1 (<0.1%)	1 (<0.1%)		
Muscle strain	筋挫傷	5 (0.3%)	3 (0.2%)		
Open wound	開放創	0	1 (<0.1%)		
Operative haemorrhage	術中出血	1 (<0.1%)	2 (0.1%)		
Overdose	過量投与	2 (0.1%)	2 (0.1%)	1 (<0.1%)	2 (0.1%)
Pelvic fracture	骨盤骨折	0	1 (<0.1%)		
Periorbital haematoma	眼窩周囲血腫	2 (0.1%)	1 (<0.1%)		
Pneumothorax traumatic	外傷性気胸	0	1 (<0.1%)		
Post procedural haematoma	処置後血腫	1 (<0.1%)	0	1 (<0.1%)	0
Post procedural haematuria	処置後血尿	2 (0.1%)	0	2 (0.1%)	0
Post procedural haemorrhage	処置後出血	8 (0.5%)	10 (0.6%)	4 (0.2%)	5 (0.3%)
Post procedural swelling	処置後腫脹	0	2 (0.1%)		
Post-traumatic pain	外傷後疼痛	2 (0.1%)	0		
Postoperative hernia	術後ヘルニア	0	1 (<0.1%)		
Procedural hypertension	処置による高血圧	0	1 (<0.1%)		
Procedural hypotension	処置による低血圧	1 (<0.1%)	0		
Procedural pain	処置による疼痛	2 (0.1%)	3 (0.2%)		
Radiation pneumonitis	放射線性肺臓炎	0	1 (<0.1%)		
Radius fracture	橈骨骨折	0	2 (0.1%)		
Rib fracture	肋骨骨折	3 (0.2%)	2 (0.1%)		
Road traffic accident	交通事故	2 (0.1%)	1 (<0.1%)		
Scratch	引っかき傷	2 (0.1%)	0		
Skeletal injury	骨格損傷	5 (0.3%)	2 (0.1%)	1 (<0.1%)	1 (<0.1%)
Skin injury	皮膚損傷	0	1 (<0.1%)		
Skin laceration	皮膚裂傷	10 (0.6%)	5 (0.3%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Soft tissue injury	軟部組織損傷	0	2 (0.1%)		
Spinal column injury	脊柱損傷	1 (<0.1%)	0		
Spinal compression fracture	脊椎圧迫骨折	1 (<0.1%)	1 (<0.1%)		
Stress fracture	ストレス骨折	1 (<0.1%)	1 (<0.1%)		
Subcutaneous haematoma	皮下血腫	9 (0.5%)	17 (1.0%)	8 (0.5%)	12 (0.7%)
Subdural haematoma	硬膜下血腫	0	1 (<0.1%)		
Synovial rupture	滑膜断裂	1 (<0.1%)	1 (<0.1%)		
Tendon injury	腱損傷	0	1 (<0.1%)		
Tendon rupture	腱断裂	1 (<0.1%)	1 (<0.1%)		
Therapeutic agent toxicity	治療薬毒性	0	2 (0.1%)	0	2 (0.1%)
Thermal burn	熱傷	0	2 (0.1%)		
Thoracic vertebral fracture	胸椎骨折	0	2 (0.1%)		
Tooth fracture	歯牙破折	2 (0.1%)	5 (0.3%)		
Tooth injury	歯牙損傷	1 (<0.1%)	0		
Traumatic fracture	外傷性骨折	0	1 (<0.1%)		
Traumatic haematoma	外傷性血腫	3 (0.2%)	5 (0.3%)	2 (0.1%)	3 (0.2%)
Traumatic haemorrhage	外傷性出血	4 (0.2%)	1 (<0.1%)	1 (<0.1%)	0
Ulna fracture	尺骨骨折	0	2 (0.1%)		
Upper limb fracture	上肢骨折	0	1 (<0.1%)		
Vascular pseudoaneurysm	血管偽動脈瘤	1 (<0.1%)	0		
Wound	創傷	5 (0.3%)	6 (0.4%)		
Wound dehiscence	創し開	1 (<0.1%)	0		
Wound haemorrhage	創傷出血	20 (1.2%)	22 (1.3%)	5 (0.3%)	9 (0.5%)
Wrist fracture	手首関節骨折	0	1 (<0.1%)		
Investigations	臨床検査	96 (5.6%)	191 (11.2%)	28 (1.6%)	76 (4.4%)
Activated partial thromboplastin time prolonged	活性化部分トロンボプラスチン時間延長	1 (<0.1%)	0	1 (<0.1%)	0
Activated partial thromboplastin time shortened	活性化部分トロンボプラスチン時間短縮	0	1 (<0.1%)	0	1 (<0.1%)
Alanine aminotransferase increased	アラニン・アミノトランスフェラーゼ増加	25 (1.5%)	55 (3.2%)	11 (0.6%)	21 (1.2%)
Angiogram	血管造影	0	1 (<0.1%)		
Antiphospholipid antibodies positive	抗リン脂質抗体陽性	1 (<0.1%)	0		
Arthroscopy	関節鏡検査	0	1 (<0.1%)		
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	14 (0.8%)	21 (1.2%)	7 (0.4%)	3 (0.2%)
Bilirubin conjugated increased	抱合ビリルビン増加	2 (0.1%)	2 (0.1%)	1 (<0.1%)	0
Biopsy breast	乳房生検	0	2 (0.1%)		
Biopsy kidney	腎生検	2 (0.1%)	0		
Biopsy lung	肺生検	1 (<0.1%)	0		
Biopsy lymph gland	リンパ節生検	0	1 (<0.1%)		
Biopsy prostate	前立腺生検	1 (<0.1%)	2 (0.1%)		
Biopsy stomach	胃生検	1 (<0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Blood albumin increased	血中アルブミン増加	1 (<0.1%)	0	1 (<0.1%)	0
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	7 (0.4%)	10 (0.6%)	2 (0.1%)	1 (<0.1%)
Blood amylase increased	血中アミラーゼ増加	1 (<0.1%)	4 (0.2%)	0	1 (<0.1%)
Blood bicarbonate decreased	血中重炭酸塩減少	0	1 (<0.1%)		
Blood bilirubin increased	血中ビリルビン増加	6 (0.3%)	5 (0.3%)	3 (0.2%)	0
Blood cholesterol increased	血中コレステロール増加	1 (<0.1%)	2 (0.1%)		
Blood creatinine increased	血中クレアチニン増加	1 (<0.1%)	0		
Blood folate decreased	血中葉酸減少	1 (<0.1%)	0		
Blood glucose decreased	血中ブドウ糖減少	1 (<0.1%)	0		
Blood glucose fluctuation	血中ブドウ糖変動	1 (<0.1%)	0		
Blood glucose increased	血中ブドウ糖増加	0	1 (<0.1%)		
Blood homocysteine increased	血中ホモシステイン増加	2 (0.1%)	2 (0.1%)		
Blood potassium decreased	血中カリウム減少	2 (0.1%)	1 (<0.1%)		
Blood potassium increased	血中カリウム増加	1 (<0.1%)	0		
Blood pressure increased	血圧上昇	2 (0.1%)	2 (0.1%)		
Blood thromboplastin decreased	血中トロンボプラスチン減少	1 (<0.1%)	0	1 (<0.1%)	0
Blood thyroid stimulating hormone increased	血中甲状腺刺激ホルモン増加	1 (<0.1%)	0		
Blood urine present	尿中血陽性	1 (<0.1%)	0	1 (<0.1%)	0
Body temperature increased	体温上昇	1 (<0.1%)	0		
C-reactive protein increased	Ｃ－反応性蛋白増加	1 (<0.1%)	0		
Carbohydrate antigen 125 increased	糖鎖抗原１２５増加	0	1 (<0.1%)		
Carcinoembryonic antigen increased	癌胎児性抗原増加	1 (<0.1%)	0		
Chest X-ray	胸部Ｘ線	0	1 (<0.1%)		
Chest X-ray abnormal	胸部Ｘ線異常	0	1 (<0.1%)		
Coagulation factor VII level decreased	凝固第ＶＩＩ因子量減少	1 (<0.1%)	0	1 (<0.1%)	0
Coagulation factor VIII level increased	凝固第ＶＩＩＩ因子量増加	0	1 (<0.1%)		
Coagulation factor X level decreased	凝固第Ｘ因子量減少	1 (<0.1%)	0	1 (<0.1%)	0
Colonoscopy	結腸内視鏡検査	3 (0.2%)	2 (0.1%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Computerised tomogram	コンピュータ断層撮影	0	1 (<0.1%)		
Computerised tomogram abdomen	腹部コンピュータ断層撮影	0	1 (<0.1%)		
Culture throat positive	咽頭培養陽性	0	1 (<0.1%)		
Free prostate-specific antigen decreased	遊離前立腺特異性抗原減少	1 (<0.1%)	0		
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	3 (0.2%)	2 (0.1%)	3 (0.2%)	0
Glomerular filtration rate decreased	糸球体濾過率減少	0	1 (<0.1%)		
Haematocrit decreased	ヘマトクリット減少	0	1 (<0.1%)		
Haemoglobin decreased	ヘモグロビン減少	5 (0.3%)	3 (0.2%)	2 (0.1%)	1 (<0.1%)
Heart rate decreased	心拍数減少	0	1 (<0.1%)	0	1 (<0.1%)
Heart rate irregular	心拍数不整	2 (0.1%)	0		
Hepatic enzyme increased	肝酵素上昇	1 (<0.1%)	15 (0.9%)	1 (<0.1%)	7 (0.4%)
Influenza A virus test positive	A型インフルエンザウイルス検査陽性	0	1 (<0.1%)		
International normalised ratio abnormal	ＩＮＲ異常	0	2 (0.1%)	0	2 (0.1%)
International normalised ratio decreased	ＩＮＲ減少	0	5 (0.3%)	0	2 (0.1%)
International normalised ratio fluctuation	ＩＮＲ変動	0	2 (0.1%)	0	2 (0.1%)
International normalised ratio increased	ＩＮＲ増加	2 (0.1%)	41 (2.4%)	0	29 (1.7%)
Intraocular pressure increased	眼圧上昇	0	1 (<0.1%)		
Lipids increased	脂質増加	2 (0.1%)	0		
Lipoprotein (a) increased	リポ蛋白（ａ）増加	1 (<0.1%)	0		
Liver function test abnormal	肝機能検査異常	9 (0.5%)	21 (1.2%)	4 (0.2%)	4 (0.2%)
Low density lipoprotein increased	低比重リポ蛋白増加	0	1 (<0.1%)		
Lymph node palpable	リンパ節触知	1 (<0.1%)	0		
Lymphocyte count increased	リンパ球数増加	0	1 (<0.1%)		
Neutrophil count decreased	好中球数減少	0	1 (<0.1%)		
Occult blood	便潜血	0	1 (<0.1%)	0	1 (<0.1%)
Oesophagogastroduodenoscopy	食道胃十二指腸内視鏡検査	1 (<0.1%)	1 (<0.1%)		
Platelet count decreased	血小板数減少	0	3 (0.2%)	0	2 (0.1%)

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Platelet count increased	血小板数増加	1 (<0.1%)	0		
Prostatic specific antigen decreased	前立腺特異性抗原減少	1 (<0.1%)	0		
Prostatic specific antigen increased	前立腺特異性抗原増加	1 (<0.1%)	2 (0.1%)		
Protein total increased	総蛋白増加	1 (<0.1%)	0	1 (<0.1%)	0
Prothrombin time prolonged	プロトロンビン時間延長	0	1 (<0.1%)	0	1 (<0.1%)
Red blood cell count decreased	赤血球数減少	0	1 (<0.1%)		
Red blood cells urine positive	尿中赤血球陽性	0	1 (<0.1%)		
Staphylococcus test positive	ブドウ球菌検査陽性	0	1 (<0.1%)		
Transaminases increased	トランスアミナーゼ上昇	4 (0.2%)	2 (0.1%)	2 (0.1%)	1 (<0.1%)
Troponin I increased	トロポニンＩ増加	1 (<0.1%)	0		
Troponin increased	トロポニン増加	0	1 (<0.1%)		
Tumour marker increased	腫瘍マーカー上昇	1 (<0.1%)	0		
Ultrasound Doppler	ドップラー超音波	0	1 (<0.1%)		
Ultrasound liver abnormal	肝超音波検査異常	1 (<0.1%)	0		
Ultrasound scan	超音波スキャン	1 (<0.1%)	0		
Urine ketone body present	尿中ケトン体陽性	0	1 (<0.1%)		
Urogram	尿路造影	1 (<0.1%)	0		
Vitamin B12 decreased	ビタミンＢ１２減少	0	1 (<0.1%)		
Weight decreased	体重減少	4 (0.2%)	1 (<0.1%)	2 (0.1%)	0
Weight increased	体重増加	0	4 (0.2%)		
White blood cell count decreased	白血球数減少	1 (<0.1%)	2 (0.1%)	0	1 (<0.1%)
White blood cell count increased	白血球数増加	0	1 (<0.1%)		
White blood cells urine positive	尿中白血球陽性	0	1 (<0.1%)		
Metabolism and nutrition disorders	代謝および栄養障害	87 (5.1%)	87 (5.1%)	9 (0.5%)	2 (0.1%)
Acidosis	アシドーシス	0	1 (<0.1%)		
Decreased appetite	食欲減退	7 (0.4%)	2 (0.1%)	5 (0.3%)	0
Dehydration	脱水	1 (<0.1%)	3 (0.2%)		
Diabetes mellitus	糖尿病	4 (0.2%)	8 (0.5%)	0	1 (<0.1%)
Diabetes mellitus inadequate control	コントロール不良の糖尿病	1 (<0.1%)	0		
Diabetic foot	糖尿病性足病変	0	1 (<0.1%)		
Diabetic ketoacidosis	糖尿病性ケトアシドーシス	1 (<0.1%)	0		
Dyslipidaemia	脂質異常症	0	1 (<0.1%)		
Electrolyte imbalance	電解質失調	0	1 (<0.1%)		
Failure to thrive	成長障害	1 (<0.1%)	0		
Folate deficiency	葉酸欠乏	1 (<0.1%)	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Gout	痛風	14 (0.8%)	12 (0.7%)	0	1 (<0.1%)
Haemochromatosis	ヘモクロマトーシス	1 (<0.1%)	0		
Hypercalcaemia	高カルシウム血症	1 (<0.1%)	0		
Hypercholesterolaemia	高コレステロール血症	8 (0.5%)	9 (0.5%)		
Hyperglycaemia	高血糖	2 (0.1%)	1 (<0.1%)		
Hyperhomocysteinaemia	高ホモシステイン血症	2 (0.1%)	5 (0.3%)		
Hyperinsulinaemia	高インスリン血症	0	1 (<0.1%)		
Hyperkalaemia	高カリウム血症	1 (<0.1%)	2 (0.1%)		
Hyperlipidaemia	高脂血症	2 (0.1%)	7 (0.4%)		
Hypernatraemia	高ナトリウム血症	1 (<0.1%)	0		
Hyperproteinaemia	高蛋白血症	1 (<0.1%)	0		
Hypertriglyceridaemia	高トリグリセリド血症	0	1 (<0.1%)		
Hyperuricaemia	高尿酸血症	2 (0.1%)	1 (<0.1%)	1 (<0.1%)	0
Hypoalbuminaemia	低アルブミン血症	4 (0.2%)	1 (<0.1%)		
Hypocalcaemia	低カルシウム血症	1 (<0.1%)	3 (0.2%)		
Hypochloraemia	低クロール血症	1 (<0.1%)	0		
Hypoglycaemia	低血糖症	4 (0.2%)	2 (0.1%)		
Hypokalaemia	低カリウム血症	12 (0.7%)	16 (0.9%)		
Hypolipidaemia	低脂血症	0	1 (<0.1%)		
Hypomagnesaemia	低マグネシウム血症	1 (<0.1%)	0		
Hyponatraemia	低ナトリウム血症	0	3 (0.2%)		
Hypophosphataemia	低リン酸血症	0	1 (<0.1%)		
Hypoproteinaemia	低蛋白血症	1 (<0.1%)	0		
Hypovitaminosis	ビタミン欠乏症	0	1 (<0.1%)		
Hypovolaemia	血液量減少症	0	1 (<0.1%)		
Iron deficiency	鉄欠乏	5 (0.3%)	1 (<0.1%)	1 (<0.1%)	0
Lactose intolerance	ラクトース不耐性	1 (<0.1%)	0		
Lipid metabolism disorder	脂質代謝障害	1 (<0.1%)	0		
Malnutrition	栄養障害	0	2 (0.1%)		
Metabolic acidosis	代謝性アシドーシス	1 (<0.1%)	1 (<0.1%)		
Metabolic disorder	代謝障害	0	1 (<0.1%)		
Methylenetetrahydrofolate reductase polymorphism	メチレンテトラヒドロ葉酸還元酵素多型	6 (0.3%)	9 (0.5%)		
Obesity	肥満	0	1 (<0.1%)		
Tetany	テタニー	1 (<0.1%)	0	1 (<0.1%)	0
Type 2 diabetes mellitus	２型糖尿病	2 (0.1%)	1 (<0.1%)		
Vitamin B12 deficiency	ビタミンＢ１２欠乏	3 (0.2%)	1 (<0.1%)	1 (<0.1%)	0
Vitamin D deficiency	ビタミンＤ欠乏	3 (0.2%)	2 (0.1%)		
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	267 (15.5%)	238 (13.9%)	5 (0.3%)	17 (1.0%)
Arthralgia	関節痛	45 (2.6%)	40 (2.3%)		
Arthritis	関節炎	6 (0.3%)	13 (0.8%)		
Back pain	背部痛	54 (3.1%)	34 (2.0%)		
Bone pain	骨痛	5 (0.3%)	1 (<0.1%)		
Bursitis	滑液包炎	6 (0.3%)	3 (0.2%)		
Chondrocalcinosis	軟骨石灰化症	0	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Coccydynia	尾骨痛	1 (<0.1%)	0		
Costochondritis	肋軟骨炎	1 (<0.1%)	0		
Exostosis	外骨腫	2 (0.1%)	1 (<0.1%)		
Fistula discharge	瘻孔分泌物	1 (<0.1%)	0		
Flank pain	側腹部痛	0	4 (0.2%)		
Foot deformity	足変形	0	2 (0.1%)		
Gouty arthritis	痛風性関節炎	1 (<0.1%)	3 (0.2%)		
Groin pain	鼠径部痛	8 (0.5%)	6 (0.4%)		
Haemarthrosis	出血性関節症	0	5 (0.3%)	0	4 (0.2%)
Intervertebral disc disorder	椎間板障害	1 (<0.1%)	0		
Intervertebral disc protrusion	椎間板突出	3 (0.2%)	2 (0.1%)		
Jaw cyst	顎骨嚢胞	0	1 (<0.1%)		
Joint effusion	関節滲出液	1 (<0.1%)	2 (0.1%)		
Joint range of motion decreased	関節可動域減少	1 (<0.1%)	0		
Joint stiffness	関節硬直	1 (<0.1%)	1 (<0.1%)		
Joint swelling	関節腫脹	10 (0.6%)	5 (0.3%)		
Juvenile arthritis	若年性関節炎	0	1 (<0.1%)		
Kyphosis	脊柱後弯症	1 (<0.1%)	0		
Ligament pain	靭帯痛	0	2 (0.1%)		
Limb discomfort	四肢不快感	3 (0.2%)	7 (0.4%)	0	1 (<0.1%)
Lower extremity mass	下肢腫瘤	1 (<0.1%)	1 (<0.1%)		
Medial tibial stress syndrome	脛骨内側過労性症候群	1 (<0.1%)	0		
Monarthritis	単関節炎	0	1 (<0.1%)		
Muscle atrophy	筋萎縮	0	1 (<0.1%)		
Muscle contracture	筋拘縮	1 (<0.1%)	0		
Muscle fatigue	筋肉疲労	2 (0.1%)	0		
Muscle haemorrhage	筋肉内出血	0	5 (0.3%)	0	4 (0.2%)
Muscle rigidity	筋固縮	1 (<0.1%)	0		
Muscle spasms	筋痙縮	23 (1.3%)	15 (0.9%)	2 (0.1%)	1 (<0.1%)
Muscle tightness	筋緊張	0	1 (<0.1%)		
Muscle twitching	筋攣縮	1 (<0.1%)	0		
Muscular weakness	筋力低下	1 (<0.1%)	1 (<0.1%)		
Musculoskeletal chest pain	筋骨格系胸痛	5 (0.3%)	3 (0.2%)		
Musculoskeletal discomfort	筋骨格不快感	2 (0.1%)	2 (0.1%)		
Musculoskeletal pain	筋骨格痛	8 (0.5%)	16 (0.9%)	0	1 (<0.1%)
Musculoskeletal stiffness	筋骨格硬直	2 (0.1%)	2 (0.1%)		
Myalgia	筋肉痛	11 (0.6%)	8 (0.5%)		
Myosclerosis	筋硬化症	1 (<0.1%)	0		
Myositis	筋炎	2 (0.1%)	0		
Neck mass	頚部腫瘤	1 (<0.1%)	1 (<0.1%)		
Neck pain	頚部痛	3 (0.2%)	1 (<0.1%)	0	1 (<0.1%)
Osteitis	骨炎	1 (<0.1%)	2 (0.1%)		
Osteoarthritis	変形性関節症	6 (0.3%)	7 (0.4%)		
Osteoarthropathy	骨関節障害	1 (<0.1%)	0		
Osteopenia	骨減少症	1 (<0.1%)	1 (<0.1%)		
Osteoporosis	骨粗鬆症	4 (0.2%)	2 (0.1%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Pain in extremity	四肢痛	82 (4.8%)	68 (4.0%)	3 (0.2%)	6 (0.4%)
Pain in jaw	顎痛	1 (<0.1%)	3 (0.2%)		
Pathological fracture	病的骨折	1 (<0.1%)	0		
Periarthritis	関節周囲炎	1 (<0.1%)	0		
Plantar fasciitis	足底筋膜炎	1 (<0.1%)	3 (0.2%)		
Polymyalgia rheumatica	リウマチ性多発筋痛	1 (<0.1%)	0		
Rotator cuff syndrome	肩回旋筋腱板症候群	2 (0.1%)	4 (0.2%)		
Sacroiliitis	仙腸骨炎	1 (<0.1%)	1 (<0.1%)		
Scoliosis	側弯症	1 (<0.1%)	0		
Spinal osteoarthritis	変形性脊椎症	6 (0.3%)	3 (0.2%)		
Spondylitis	脊椎炎	0	1 (<0.1%)		
Synovial cyst	滑液嚢腫	3 (0.2%)	4 (0.2%)		
Synovitis	滑膜炎	0	2 (0.1%)		
Systemic lupus erythematosus	全身性エリテマトーデス	1 (<0.1%)	0		
Tendon pain	腱痛	0	2 (0.1%)		
Tendonitis	腱炎	7 (0.4%)	6 (0.4%)		
Tenosynovitis	腱鞘炎	0	1 (<0.1%)		
Torticollis	斜頚	1 (<0.1%)	0		
Upper extremity mass	上肢腫瘤	1 (<0.1%)	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	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）	77 (4.5%)	81 (4.7%)		
Acute leukaemia	急性白血病	0	1 (<0.1%)		
Acute lymphocytic leukaemia	急性リンパ性白血病	1 (<0.1%)	0		
Adenocarcinoma	腺癌	1 (<0.1%)	0		
Adenoma benign	良性腺腫	1 (<0.1%)	0		
Adrenal adenoma	副腎腺腫	1 (<0.1%)	3 (0.2%)		
Angiomyolipoma	血管筋脂肪腫	1 (<0.1%)	0		
Angiosarcoma	血管肉腫	1 (<0.1%)	0		
B-cell lymphoma	Ｂ細胞性リンパ腫	1 (<0.1%)	0		
Basal cell carcinoma	基底細胞癌	2 (0.1%)	1 (<0.1%)		
Benign lung neoplasm	肺の良性新生物	0	1 (<0.1%)		
Benign mediastinal neoplasm	縦隔の良性新生物	0	1 (<0.1%)		
Bile duct cancer	胆管癌	1 (<0.1%)	0		
Bladder cancer	膀胱癌	2 (0.1%)	0		
Bladder transitional cell carcinoma stage I	膀胱移行上皮癌第１期	0	1 (<0.1%)		
Brain neoplasm	脳新生物	0	1 (<0.1%)		
Breast cancer	乳癌	3 (0.2%)	1 (<0.1%)		
Breast cancer metastatic	転移性乳癌	1 (<0.1%)	0		
Cervix cancer metastatic	転移性子宮頚部癌	1 (<0.1%)	0		
Cervix carcinoma	子宮頚部癌	2 (0.1%)	7 (0.4%)		
Cervix carcinoma stage III	子宮頚部癌第３期	1 (<0.1%)	0		
Colon adenoma	大腸腺腫	0	1 (<0.1%)		
Colon cancer	結腸癌	3 (0.2%)	4 (0.2%)		
Colorectal cancer	結腸直腸癌	2 (0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Ear neoplasm malignant	耳の悪性新生物	0	1 (<0.1%)		
Endometrial cancer	子宮内膜癌	1 (<0.1%)	1 (<0.1%)		
Erythroplasia	紅色肥厚症	0	1 (<0.1%)		
Fibroadenoma of breast	乳腺線維腺腫	0	1 (<0.1%)		
Fibroma	線維腫	0	1 (<0.1%)		
Gastric cancer	胃癌	1 (<0.1%)	1 (<0.1%)		
Gastric cancer recurrent	再発胃癌	1 (<0.1%)	0		
Glioblastoma	神経膠芽細胞腫	1 (<0.1%)	0		
Haemangioma of liver	肝臓血管腫	2 (0.1%)	2 (0.1%)		
Hepatic cancer metastatic	転移性肝癌	1 (<0.1%)	0		
Hepatic neoplasm malignant	肝の悪性新生物	2 (0.1%)	2 (0.1%)		
Hodgkin's disease	ホジキン病	0	1 (<0.1%)		
Large cell carcinoma of the respiratory tract stage unspecified	呼吸器大細胞癌、病期不明	0	1 (<0.1%)		
Large intestine carcinoma	大腸癌	1 (<0.1%)	0		
Lipoma	脂肪腫	3 (0.2%)	2 (0.1%)		
Lung adenocarcinoma	肺腺癌	0	3 (0.2%)		
Lung cancer metastatic	転移性肺癌	1 (<0.1%)	0		
Lung carcinoma cell type unspecified recurrent	再発肺癌、細胞タイプ不明	1 (<0.1%)	0		
Lung neoplasm	肺新生物	3 (0.2%)	6 (0.4%)		
Lung neoplasm malignant	肺の悪性新生物	2 (0.1%)	3 (0.2%)		
Lymphoma	リンパ腫	3 (0.2%)	1 (<0.1%)		
Lymphoma cutis	皮膚型リンパ腫	1 (<0.1%)	0		
Malignant melanoma	悪性黒色腫	1 (<0.1%)	1 (<0.1%)		
Malignant melanoma in situ	表皮内悪性黒色腫	1 (<0.1%)	0		
Meningioma	髄膜腫	0	1 (<0.1%)		
Metastases to abdominal cavity	腹腔内転移	0	1 (<0.1%)		
Metastases to central nervous system	中枢神経系転移	1 (<0.1%)	1 (<0.1%)		
Metastases to liver	肝転移	2 (0.1%)	5 (0.3%)		
Metastases to lung	肺転移	1 (<0.1%)	2 (0.1%)		
Metastases to lymph nodes	リンパ節転移	2 (0.1%)	2 (0.1%)		
Metastases to peritoneum	腹膜転移	1 (<0.1%)	0		
Metastases to spine	脊椎転移	0	1 (<0.1%)		
Metastatic neoplasm	転移性新生物	2 (0.1%)	1 (<0.1%)		
Metastatic squamous cell carcinoma	転移性扁平上皮癌	0	1 (<0.1%)		
Non-Hodgkin's lymphoma	非ホジキンリンパ腫	2 (0.1%)	0		
Non-small cell lung cancer	非小細胞肺癌	0	1 (<0.1%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

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		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Oesophageal adenocarcinoma	食道腺癌	1 (<0.1%)	0		
Oesophageal carcinoma	食道癌	0	1 (<0.1%)		
Ovarian cancer	卵巣癌	2 (0.1%)	2 (0.1%)		
Ovarian cancer metastatic	転移性卵巣癌	0	1 (<0.1%)		
Ovarian cancer recurrent	再発卵巣癌	0	1 (<0.1%)		
Ovarian epithelial cancer	卵巣上皮癌	0	1 (<0.1%)		
Pancreatic carcinoma	膵癌	3 (0.2%)	0		
Pancreatic carcinoma metastatic	転移性膵癌	0	2 (0.1%)		
Pelvic neoplasm	骨盤新生物	1 (<0.1%)	0		
Penile wart	陰茎疣贅	0	1 (<0.1%)		
Penis carcinoma	陰茎癌	0	1 (<0.1%)		
Pleural neoplasm	胸膜新生物	1 (<0.1%)	0		
Polycythaemia vera	真性多血症	0	1 (<0.1%)		
Prostate cancer	前立腺癌	1 (<0.1%)	2 (0.1%)		
Prostate cancer metastatic	転移性前立腺癌	0	1 (<0.1%)		
Pyogenic granuloma	化膿性肉芽腫	0	1 (<0.1%)		
Rectal adenoma	直腸腺腫	0	1 (<0.1%)		
Rectal cancer	直腸癌	2 (0.1%)	2 (0.1%)		
Rectal cancer recurrent	再発直腸癌	1 (<0.1%)	0		
Renal cancer metastatic	転移性腎癌	1 (<0.1%)	0		
Renal cell carcinoma	腎細胞癌	1 (<0.1%)	0		
Renal cell carcinoma recurrent	再発腎細胞癌	0	1 (<0.1%)		
Renal neoplasm	腎新生物	1 (<0.1%)	1 (<0.1%)		
Retroperitoneal neoplasm	後腹膜新生物	0	1 (<0.1%)		
Rhabdomyosarcoma	横紋筋肉腫	1 (<0.1%)	0		
Seborrhoeic keratosis	脂漏性角化症	1 (<0.1%)	0		
Skin cancer	皮膚癌	1 (<0.1%)	1 (<0.1%)		
Small cell lung cancer metastatic	転移性小細胞肺癌	1 (<0.1%)	0		
Squamous cell carcinoma of skin	皮膚有棘細胞癌	0	2 (0.1%)		
Superficial spreading melanoma stage unspecified	表在拡大型黒色腫、病期不明	1 (<0.1%)	0		
Uterine cancer	子宮癌	0	1 (<0.1%)		
Uterine leiomyoma	子宮平滑筋腫	4 (0.2%)	3 (0.2%)		
Uterine neoplasm	子宮新生物	1 (<0.1%)	0		
Waldenstrom's macroglobulinaemia	ワルデンストローム・マクログロブリン血症	1 (<0.1%)	0		
Nervous system disorders	神経系障害	202 (11.8%)	141 (8.2%)	36 (2.1%)	16 (0.9%)
Amnesia	健忘	0	2 (0.1%)		
Aphonia	失声症	1 (<0.1%)	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

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		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Ataxia	運動失調	1 (<0.1%)	0		
Balance disorder	平衡障害	0	1 (<0.1%)		
Brain injury	脳損傷	0	1 (<0.1%)		
Burning sensation	灼熱感	2 (0.1%)	1 (<0.1%)		
Carpal tunnel syndrome	手根管症候群	0	1 (<0.1%)		
Cerebral arteriosclerosis	脳動脈硬化症	1 (<0.1%)	0		
Cerebral atrophy	大脳萎縮	0	1 (<0.1%)		
Cerebral haemorrhage	脳出血	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
Cervical root pain	頚髄神経根痛	1 (<0.1%)	0		
Cervicobrachial syndrome	頚腕症候群	1 (<0.1%)	1 (<0.1%)		
Cognitive disorder	認知障害	1 (<0.1%)	0		
Complex regional pain syndrome	複合性局所疼痛症候群	0	2 (0.1%)		
Convulsion	痙攣	0	1 (<0.1%)		
Dementia	認知症	1 (<0.1%)	1 (<0.1%)		
Diabetic neuropathy	糖尿病性ニューロパチー	0	1 (<0.1%)		
Dizziness	浮動性めまい	39 (2.3%)	25 (1.5%)	5 (0.3%)	3 (0.2%)
Dizziness postural	体位性めまい	0	1 (<0.1%)		
Dysaesthesia	異常感覚	1 (<0.1%)	0	1 (<0.1%)	0
Dysgeusia	味覚異常	3 (0.2%)	0		
Epilepsy	てんかん	2 (0.1%)	1 (<0.1%)		
Facial neuralgia	顔面部神経痛	0	1 (<0.1%)		
Facial palsy	顔面神経麻痺	1 (<0.1%)	0		
Grand mal convulsion	大発作痙攣	1 (<0.1%)	0		
Haemorrhage intracranial	頭蓋内出血	1 (<0.1%)	2 (0.1%)	1 (<0.1%)	1 (<0.1%)
Head discomfort	頭部不快感	1 (<0.1%)	0		
Headache	頭痛	92 (5.4%)	72 (4.2%)	21 (1.2%)	9 (0.5%)
Hyperaesthesia	知覚過敏	1 (<0.1%)	0	1 (<0.1%)	0
Hypoaesthesia	感覚鈍麻	3 (0.2%)	7 (0.4%)	0	1 (<0.1%)
Hypoglycaemic coma	低血糖昏睡	1 (<0.1%)	0		
IIIrd nerve paresis	第３脳神経不全麻痺	0	1 (<0.1%)		
Ischaemic stroke	虚血性脳卒中	4 (0.2%)	7 (0.4%)	0	1 (<0.1%)
Lethargy	嗜眠	5 (0.3%)	2 (0.1%)	1 (<0.1%)	1 (<0.1%)
Meralgia paraesthetica	感覚異常性大腿神経痛	1 (<0.1%)	0		
Metabolic encephalopathy	代謝性脳症	1 (<0.1%)	0		
Migraine	片頭痛	2 (0.1%)	1 (<0.1%)	1 (<0.1%)	0
Mononeuritis	単神経炎	1 (<0.1%)	0		
Motor dysfunction	運動機能障害	0	1 (<0.1%)		
Movement disorder	運動障害	0	1 (<0.1%)		
Multiple sclerosis	多発性硬化症	1 (<0.1%)	0		
Muscle contractions involuntary	不随意性筋収縮	0	1 (<0.1%)		
Myelitis	脊髄炎	0	1 (<0.1%)		
Nerve compression	神経圧迫	0	1 (<0.1%)		
Neuralgia	神経痛	1 (<0.1%)	2 (0.1%)	0	1 (<0.1%)
Neuritis cranial	脳神経炎	0	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Neuropathy peripheral	末梢性ニューロパチー	2 (0.1%)	3 (0.2%)		
Paraesthesia	錯感覚	18 (1.0%)	8 (0.5%)	4 (0.2%)	1 (<0.1%)
Parkinson's disease	パーキンソン病	1 (<0.1%)	0		
Parkinsonism	パーキンソニズム	0	1 (<0.1%)		
Peripheral nerve palsy	末梢神経麻痺	1 (<0.1%)	0		
Peripheral sensorimotor neuropathy	末梢性感覚運動ニューロパチー	1 (<0.1%)	0		
Polyneuropathy	多発ニューロパチー	1 (<0.1%)	0		
Post herpetic neuralgia	ヘルペス後神経痛	1 (<0.1%)	0		
Presyncope	失神寸前の状態	3 (0.2%)	2 (0.1%)		
Pseudoradicular syndrome	偽性根症候群	1 (<0.1%)	0		
Restless legs syndrome	下肢静止不能症候群	2 (0.1%)	0		
Sciatica	坐骨神経痛	8 (0.5%)	4 (0.2%)	1 (<0.1%)	0
Senile dementia	老年認知症	0	1 (<0.1%)		
Sensory disturbance	感覚障害	2 (0.1%)	0	1 (<0.1%)	0
Somnolence	傾眠	4 (0.2%)	0	1 (<0.1%)	0
Spinal cord compression	脊髄圧迫	1 (<0.1%)	0		
Syncope	失神	11 (0.6%)	6 (0.4%)	1 (<0.1%)	0
Tension headache	緊張性頭痛	2 (0.1%)	1 (<0.1%)		
Transient ischaemic attack	一過性脳虚血発作	1 (<0.1%)	4 (0.2%)		
Tremor	振戦	2 (0.1%)	2 (0.1%)		
Vascular encephalopathy	血管性脳症	0	1 (<0.1%)		
Vertebrobasilar insufficiency	椎骨脳底動脈不全	0	1 (<0.1%)		
Pregnancy, puerperium and perinatal conditions	妊娠、産褥および周産期の状態	2 (0.1%)	2 (0.1%)		
Abortion	流産	0	1 (<0.1%)		
Post abortion haemorrhage	流産後の出血	1 (<0.1%)	1 (<0.1%)		
Pregnancy	妊娠	1 (<0.1%)	2 (0.1%)		
Psychiatric disorders	精神障害	80 (4.7%)	62 (3.6%)	1 (<0.1%)	2 (0.1%)
Acute psychosis	急性精神病	0	1 (<0.1%)		
Affective disorder	感情障害	1 (<0.1%)	0		
Agitation	激越	1 (<0.1%)	0		
Alcohol abuse	アルコール乱用	0	1 (<0.1%)		
Alcohol withdrawal syndrome	アルコール離脱症候群	0	1 (<0.1%)		
Anxiety	不安	27 (1.6%)	14 (0.8%)		
Attention deficit/hyperactivity disorder	注意欠陥多動性障害	0	1 (<0.1%)		
Completed suicide	自殺既遂	0	1 (<0.1%)		
Confusional state	錯乱状態	3 (0.2%)	2 (0.1%)		
Delirium	譫妄	0	1 (<0.1%)		
Depressed mood	抑うつ気分	2 (0.1%)	1 (<0.1%)		
Depression	うつ病	20 (1.2%)	11 (0.6%)		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Insomnia	不眠症	30 (1.7%)	19 (1.1%)	1 (<0.1%)	1 (<0.1%)
Libido decreased	リビドー減退	2 (0.1%)	0		
Major depression	大うつ病	1 (<0.1%)	0		
Mental status changes	精神状態変化	0	1 (<0.1%)		
Mood swings	気分動揺	1 (<0.1%)	0		
Panic attack	パニック発作	2 (0.1%)	2 (0.1%)		
Psychotic disorder	精神病性障害	1 (<0.1%)	0		
Restlessness	落ち着きのなさ	0	1 (<0.1%)		
Senile psychosis	老人性精神病	0	1 (<0.1%)		
Sleep disorder	睡眠障害	2 (0.1%)	6 (0.4%)	0	1 (<0.1%)
Stress	ストレス	1 (<0.1%)	1 (<0.1%)		
Suicide attempt	自殺企図	1 (<0.1%)	0		
Renal and urinary disorders	腎および尿路障害	76 (4.4%)	83 (4.9%)	28 (1.6%)	34 (2.0%)
Acute prerenal failure	急性腎前性腎不全	1 (<0.1%)	0		
Anuria	無尿	1 (<0.1%)	1 (<0.1%)		
Bladder diverticulum	膀胱憩室	0	1 (<0.1%)		
Calculus ureteric	尿管結石	2 (0.1%)	1 (<0.1%)		
Calculus urinary	尿路結石	1 (<0.1%)	1 (<0.1%)		
Chromaturia	着色尿	0	2 (0.1%)	0	2 (0.1%)
Cystitis haemorrhagic	出血性膀胱炎	1 (<0.1%)	0		
Cystitis noninfective	非感染性膀胱炎	0	1 (<0.1%)		
Dysuria	排尿困難	2 (0.1%)	3 (0.2%)		
Glomerulonephritis chronic	慢性糸球体腎炎	1 (<0.1%)	0		
Haematuria	血尿	42 (2.4%)	44 (2.6%)	27 (1.6%)	32 (1.9%)
Haemorrhage urinary tract	尿路出血	0	1 (<0.1%)		
Hydronephrosis	水腎症	1 (<0.1%)	3 (0.2%)		
Lupus nephritis	ループス腎炎	1 (<0.1%)	0		
Nephrolithiasis	腎結石症	5 (0.3%)	8 (0.5%)		
Nephropathy	腎症	1 (<0.1%)	2 (0.1%)		
Nephrotic syndrome	ネフローゼ症候群	1 (<0.1%)	0		
Nocturia	夜間頻尿	0	2 (0.1%)		
Oliguria	乏尿	0	1 (<0.1%)		
Pollakiuria	頻尿	3 (0.2%)	0	1 (<0.1%)	0
Pyelocaliectasis	腎盂腎杯拡張症	1 (<0.1%)	0		
Renal colic	腎仙痛	0	2 (0.1%)		
Renal cyst	腎嚢胞	9 (0.5%)	12 (0.7%)		
Renal failure	腎不全	3 (0.2%)	1 (<0.1%)		
Renal failure acute	急性腎不全	2 (0.1%)	7 (0.4%)		
Renal failure chronic	慢性腎不全	0	2 (0.1%)		
Residual urine	残尿	1 (<0.1%)	0		
Urethral haemorrhage	尿道出血	0	1 (<0.1%)	0	1 (<0.1%)
Urinary incontinence	尿失禁	1 (<0.1%)	1 (<0.1%)		
Urinary retention	尿閉	3 (0.2%)	2 (0.1%)		
Urinary tract obstruction	尿路閉塞	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Urine odour abnormal	尿臭異常	0	1 (<0.1%)	0	1 (<0.1%)
Reproductive system and breast disorders	生殖系および乳房障害	115 (6.7%)	70 (4.1%)	76 (4.4%)	33 (1.9%)
Adenomyosis	腺筋症	1 (<0.1%)	0		
Adnexa uteri cyst	子宮付属器嚢胞	1 (<0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Benign prostatic hyperplasia	良性前立腺肥大症	6 (0.3%)	10 (0.6%)		
Breast engorgement	乳房うっ滞	0	1 (<0.1%)		
Breast hyperplasia	乳房過形成	1 (<0.1%)	0		
Breast mass	乳房腫瘤	2 (0.1%)	1 (<0.1%)		
Breast pain	乳房痛	1 (<0.1%)	0		
Cervical polyp	子宮頚管ポリープ	2 (0.1%)	0		
Dysfunctional uterine bleeding	機能障害性子宮出血	1 (<0.1%)	0	1 (<0.1%)	0
Dysmenorrhoea	月経困難症	3 (0.2%)	6 (0.4%)	1 (<0.1%)	2 (0.1%)
Endometrial hyperplasia	子宮内膜増殖症	1 (<0.1%)	0		
Epididymitis	精巣上体炎	0	1 (<0.1%)		
Erectile dysfunction	勃起不全	3 (0.2%)	3 (0.2%)	1 (<0.1%)	1 (<0.1%)
Fibrocystic breast disease	線維嚢胞性乳腺疾患	1 (<0.1%)	0		
Genital cyst	生殖器嚢胞	1 (<0.1%)	0		
Genital discharge	性器分泌物	0	1 (<0.1%)		
Genital haemorrhage	性器出血	0	1 (<0.1%)	0	1 (<0.1%)
Genital pain	生殖器痛	0	1 (<0.1%)		
Gynaecomastia	女性化乳房	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	0
Haemorrhagic ovarian cyst	出血性卵巣嚢胞	1 (<0.1%)	0		
Menometrorrhagia	機能性子宮出血	2 (0.1%)	0	1 (<0.1%)	0
Menorrhagia	月経過多	50 (2.9%)	19 (1.1%)	40 (2.3%)	16 (0.9%)
Menstrual disorder	月経障害	2 (0.1%)	0	2 (0.1%)	0
Menstruation irregular	不規則月経	1 (<0.1%)	0	1 (<0.1%)	0
Metrorrhagia	不正子宮出血	10 (0.6%)	3 (0.2%)	8 (0.5%)	3 (0.2%)
Oedema genital	性器浮腫	1 (<0.1%)	0		
Oligomenorrhoea	希発月経	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)
Ovarian cyst	卵巣嚢胞	3 (0.2%)	2 (0.1%)		
Ovarian mass	卵巣腫瘤	1 (<0.1%)	1 (<0.1%)		
Pelvic pain	骨盤痛	0	1 (<0.1%)		
Penile haemorrhage	陰茎出血	0	1 (<0.1%)	0	1 (<0.1%)
Penile swelling	陰茎腫脹	0	1 (<0.1%)		
Postmenopausal haemorrhage	閉経後出血	1 (<0.1%)	1 (<0.1%)		
Premenstrual syndrome	月経前症候群	0	1 (<0.1%)		
Prostatitis	前立腺炎	1 (<0.1%)	2 (0.1%)		
Prostatomegaly	前立腺腫大	1 (<0.1%)	0		
Pruritus genital	陰部そう痒症	0	1 (<0.1%)		
Scrotal swelling	陰嚢腫脹	0	2 (0.1%)		
Uterine enlargement	子宮肥大	1 (<0.1%)	0		
Uterine haemorrhage	子宮出血	0	1 (<0.1%)	0	1 (<0.1%)
Uterine polyp	子宮ポリープ	1 (<0.1%)	0		
Vaginal discharge	膣分泌物	2 (0.1%)	1 (<0.1%)		
Vaginal haemorrhage	膣出血	28 (1.6%)	12 (0.7%)	25 (1.5%)	8 (0.5%)
Vulvovaginal pain	外陰膣痛	0	1 (<0.1%)	0	1 (<0.1%)
Vulvovaginal pruritus	外陰膣そう痒症	0	1 (<0.1%)		
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	242 (14.1%)	214 (12.5%)	85 (4.9%)	68 (4.0%)
Acute respiratory failure	急性呼吸不全	0	1 (<0.1%)		

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

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		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Allergic pharyngitis	アレルギー性咽頭炎	0	1 (<0.1%)		
Asthma	喘息	4 (0.2%)	4 (0.2%)		
Atelectasis	無気肺	2 (0.1%)	1 (<0.1%)		
Bronchitis chronic	慢性気管支炎	2 (0.1%)	0		
Bronchospasm	気管支痙攣	1 (<0.1%)	3 (0.2%)		
Chronic obstructive pulmonary disease	慢性閉塞性肺疾患	7 (0.4%)	4 (0.2%)		
Cough	咳嗽	73 (4.2%)	54 (3.2%)	3 (0.2%)	1 (<0.1%)
Dysphonia	発声障害	3 (0.2%)	2 (0.1%)		
Dyspnoea	呼吸困難	33 (1.9%)	38 (2.2%)	2 (0.1%)	1 (<0.1%)
Dyspnoea at rest	安静時呼吸困難	1 (<0.1%)	0		
Dyspnoea exertional	労作性呼吸困難	7 (0.4%)	6 (0.4%)	3 (0.2%)	0
Emphysema	肺気腫	1 (<0.1%)	0		
Epistaxis	鼻出血	91 (5.3%)	75 (4.4%)	67 (3.9%)	57 (3.3%)
Haemoptysis	喀血	20 (1.2%)	17 (1.0%)	13 (0.8%)	10 (0.6%)
Haemothorax	血胸	0	1 (<0.1%)	0	1 (<0.1%)
Hiccups	しゃっくり	1 (<0.1%)	0		
Hyperventilation	過換気	0	1 (<0.1%)		
Hypoxia	低酸素症	0	1 (<0.1%)		
Increased upper airway secretion	上気道分泌増加	1 (<0.1%)	0		
Interstitial lung disease	間質性肺疾患	0	1 (<0.1%)		
Lung consolidation	肺硬化	0	1 (<0.1%)		
Lung disorder	肺障害	2 (0.1%)	1 (<0.1%)		
Nasal congestion	鼻閉	4 (0.2%)	2 (0.1%)		
Oropharyngeal blistering	口腔咽頭水疱形成	0	1 (<0.1%)		
Oropharyngeal pain	口腔咽頭痛	16 (0.9%)	6 (0.4%)		
Orthopnoea	起坐呼吸	1 (<0.1%)	0		
Painful respiration	呼吸時疼痛	1 (<0.1%)	0		
Paranasal cyst	副鼻腔嚢胞	1 (<0.1%)	0		
Pharyngeal inflammation	咽頭の炎症	1 (<0.1%)	0		
Pleural effusion	胸水	4 (0.2%)	6 (0.4%)		
Pleural fibrosis	胸膜線維症	0	1 (<0.1%)		
Pleurisy	胸膜炎	0	1 (<0.1%)		
Pleuritic pain	胸膜痛	0	1 (<0.1%)		
Postnasal drip	後鼻漏	0	1 (<0.1%)		
Productive cough	湿性咳嗽	3 (0.2%)	3 (0.2%)	1 (<0.1%)	1 (<0.1%)
Pulmonary embolism	肺塞栓症	1 (<0.1%)	2 (0.1%)		
Pulmonary fibrosis	肺線維症	1 (<0.1%)	0		
Pulmonary hypertension	肺高血圧症	0	3 (0.2%)		
Pulmonary infarction	肺梗塞	0	1 (<0.1%)		
Pulmonary mass	肺腫瘤	1 (<0.1%)	0		
Pulmonary oedema	肺水腫	0	1 (<0.1%)		
Rales	ラ音	0	1 (<0.1%)		
Respiratory distress	呼吸窮迫	0	1 (<0.1%)		
Respiratory failure	呼吸不全	3 (0.2%)	1 (<0.1%)		
Respiratory tract congestion	気道うっ血	1 (<0.1%)	1 (<0.1%)		
Respiratory tract inflammation	気道の炎症	0	1 (<0.1%)		

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Rhinitis allergic	アレルギー性鼻炎	0	3 (0.2%)		
Rhinitis atrophic	萎縮性鼻炎	1 (<0.1%)	0		
Rhinorrhoea	鼻漏	2 (0.1%)	8 (0.5%)		
Sinus congestion	副鼻腔うっ血	1 (<0.1%)	2 (0.1%)		
Sleep apnoea syndrome	睡眠時無呼吸症候群	0	1 (<0.1%)		
Sputum retention	痰貯留	1 (<0.1%)	0		
Tachypnoea	頻呼吸	2 (0.1%)	2 (0.1%)		
Throat irritation	咽喉刺激感	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	0
Upper airway obstruction	上気道閉塞	2 (0.1%)	0		
Wegener's granulomatosis	ウェゲナー肉芽腫症	1 (<0.1%)	0		
Wheezing	喘鳴	2 (0.1%)	1 (<0.1%)		
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	152 (8.8%)	170 (9.9%)	50 (2.9%)	52 (3.0%)
Acne	ざ瘡	1 (<0.1%)	0	1 (<0.1%)	0
Actinic keratosis	日光性角化症	0	1 (<0.1%)		
Alopecia	脱毛症	10 (0.6%)	14 (0.8%)	5 (0.3%)	9 (0.5%)
Blister	水疱	1 (<0.1%)	2 (0.1%)		
Blood blister	血性水疱	0	1 (<0.1%)		
Decubitus ulcer	褥瘡性潰瘍	4 (0.2%)	2 (0.1%)		
Dermal cyst	皮膚嚢腫	1 (<0.1%)	1 (<0.1%)		
Dermatitis	皮膚炎	4 (0.2%)	6 (0.4%)	0	1 (<0.1%)
Dermatitis allergic	アレルギー性皮膚炎	1 (<0.1%)	4 (0.2%)	1 (<0.1%)	0
Dermatitis contact	接触性皮膚炎	2 (0.1%)	2 (0.1%)		
Dermatitis exfoliative	剥脱性皮膚炎	0	2 (0.1%)	0	1 (<0.1%)
Dermatitis herpetiformis	疱疹状皮膚炎	1 (<0.1%)	0		
Dermatosis	皮膚症	0	1 (<0.1%)		
Drug eruption	薬疹	1 (<0.1%)	3 (0.2%)	1 (<0.1%)	0
Dry skin	皮膚乾燥	6 (0.3%)	10 (0.6%)	3 (0.2%)	1 (<0.1%)
Ecchymosis	斑状出血	4 (0.2%)	7 (0.4%)	2 (0.1%)	7 (0.4%)
Eczema	湿疹	6 (0.3%)	8 (0.5%)	1 (<0.1%)	0
Ephelides	雀卵斑	1 (<0.1%)	0		
Erythema	紅斑	4 (0.2%)	10 (0.6%)	2 (0.1%)	0
Erythema multiforme	多形紅斑	0	1 (<0.1%)		
Excessive granulation tissue	過剰肉芽組織	0	1 (<0.1%)		
Exfoliative rash	剥脱性発疹	1 (<0.1%)	0		
Generalised erythema	全身紅斑	1 (<0.1%)	0		
Haemorrhage subcutaneous	皮下出血	1 (<0.1%)	0	1 (<0.1%)	0
Haemorrhagic urticaria	出血性蕁麻疹	0	1 (<0.1%)		
Henoch-Schonlein purpura	ヘノッホ・シェーンライン紫斑病	0	1 (<0.1%)		
Hyperhidrosis	多汗症	6 (0.3%)	2 (0.1%)	1 (<0.1%)	0
Hypoaesthesia facial	顔面感覚鈍麻	1 (<0.1%)	0		
Increased tendency to bruise	挫傷発生の増加傾向	1 (<0.1%)	2 (0.1%)	1 (<0.1%)	2 (0.1%)
Leukocytoclastic vasculitis	白血球破砕性血管炎	0	1 (<0.1%)	0	1 (<0.1%)
Livedo reticularis	網状皮斑	0	1 (<0.1%)		
Nail bed bleeding	爪床出血	1 (<0.1%)	0	1 (<0.1%)	0

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Nail bed inflammation	爪床の炎症	0	1 (<0.1%)		
Night sweats	寝汗	7 (0.4%)	5 (0.3%)	5 (0.3%)	5 (0.3%)
Onychoclasis	爪破損	1 (<0.1%)	0		
Panniculitis	脂肪織炎	1 (<0.1%)	0		
Petechiae	点状出血	2 (0.1%)	6 (0.4%)	2 (0.1%)	3 (0.2%)
Photosensitivity allergic reaction	アレルギー性光線過敏性反応	1 (<0.1%)	0		
Pigmentation disorder	色素沈着障害	1 (<0.1%)	1 (<0.1%)		
Pruritus	そう痒症	29 (1.7%)	33 (1.9%)	9 (0.5%)	8 (0.5%)
Pruritus allergic	アレルギー性そう痒症	0	1 (<0.1%)		
Pruritus generalised	全身性そう痒症	1 (<0.1%)	1 (<0.1%)		
Psoriasis	乾癬	2 (0.1%)	1 (<0.1%)		
Purpura	紫斑	0	3 (0.2%)		
Rash	発疹	27 (1.6%)	28 (1.6%)	10 (0.6%)	3 (0.2%)
Rash erythematous	紅斑性皮疹	0	2 (0.1%)	0	1 (<0.1%)
Rash generalised	全身性皮疹	0	1 (<0.1%)	0	1 (<0.1%)
Rash macular	斑状皮疹	0	1 (<0.1%)		
Rash papular	丘疹	1 (<0.1%)	1 (<0.1%)		
Rash pruritic	そう痒性皮疹	0	2 (0.1%)	0	1 (<0.1%)
Scab	痂皮	1 (<0.1%)	0		
Scar	瘢痕	0	1 (<0.1%)		
Seborrhoeic dermatitis	脂漏性皮膚炎	1 (<0.1%)	0		
Skin discolouration	皮膚変色	4 (0.2%)	2 (0.1%)		
Skin disorder	皮膚障害	1 (<0.1%)	1 (<0.1%)		
Skin exfoliation	皮膚剥脱	1 (<0.1%)	0	1 (<0.1%)	0
Skin fragility	皮膚脆弱性	1 (<0.1%)	0		
Skin haemorrhage	皮膚出血	9 (0.5%)	8 (0.5%)	6 (0.3%)	6 (0.4%)
Skin hyperpigmentation	皮膚色素過剰	1 (<0.1%)	0		
Skin induration	皮膚硬結	1 (<0.1%)	0		
Skin irritation	皮膚刺激	0	2 (0.1%)		
Skin lesion	皮膚病変	5 (0.3%)	3 (0.2%)	0	1 (<0.1%)
Skin mass	皮膚腫瘤	0	1 (<0.1%)		
Skin oedema	皮膚浮腫	0	1 (<0.1%)		
Skin striae	皮膚線条	0	1 (<0.1%)		
Skin swelling	皮膚腫脹	0	1 (<0.1%)		
Skin ulcer	皮膚潰瘍	7 (0.4%)	9 (0.5%)	0	2 (0.1%)
Skin ulcer haemorrhage	出血性皮膚潰瘍	0	1 (<0.1%)	0	1 (<0.1%)
Spider naevus	くも状母斑	1 (<0.1%)	0	1 (<0.1%)	0
Stasis dermatitis	うっ滞性皮膚炎	0	1 (<0.1%)	0	1 (<0.1%)
Telangiectasia	毛細血管拡張症	0	1 (<0.1%)		
Urticaria	蕁麻疹	5 (0.3%)	4 (0.2%)	0	1 (<0.1%)
Surgical and medical procedures	外科および内科処置	14 (0.8%)	13 (0.8%)		
Abortion induced	人工流産	0	1 (<0.1%)		
Bariatric gastric balloon insertion	肥満症に対する胃内バルーン挿入	0	1 (<0.1%)		
Bladder catheter removal	膀胱カテーテル除去	1 (<0.1%)	0		
Cataract operation	白内障手術	1 (<0.1%)	0		
Central venous catheterisation	中心静脈カテーテル留置	0	1 (<0.1%)		
Cerumen removal	耳垢除去	1 (<0.1%)	0		

付表 2.7.6.1- 1　すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Colon polypectomy	結腸ポリープ切除	0	1 (<0.1%)		
Dental cleaning	歯牙清掃	1 (<0.1%)	0		
Dental implantation	歯科インプラント埋込み	2 (0.1%)	0		
Ear tube insertion	耳チューブ挿入	1 (<0.1%)	0		
High frequency ablation	高周波アブレーション	1 (<0.1%)	0		
Hip arthroplasty	股関節形成	1 (<0.1%)	0		
Ileostomy closure	回腸瘻閉鎖	1 (<0.1%)	0		
Incisional hernia repair	瘢痕ヘルニア修復	1 (<0.1%)	0		
Inguinal hernia repair	鼠径部ヘルニア修復	1 (<0.1%)	0		
Intervertebral disc operation	椎間板手術	0	1 (<0.1%)		
Intestinal polypectomy	腸ポリープ切除	0	1 (<0.1%)		
Intra-uterine contraceptive device insertion	子宮内避妊具挿入	1 (<0.1%)	0		
Knee operation	膝手術	1 (<0.1%)	0		
Meniscus operation	半月板手術	1 (<0.1%)	0		
Removal of internal fixation	内固定除去	0	1 (<0.1%)		
Sinus operation	副鼻腔手術	1 (<0.1%)	0		
Skin neoplasm excision	皮膚新生物切除	0	1 (<0.1%)		
Tooth extraction	抜歯	0	2 (0.1%)		
Transurethral prostatectomy	経尿道的前立腺摘除	0	1 (<0.1%)		
Uterine polypectomy	子宮ポリープ切除	0	1 (<0.1%)		
Vasectomy	精管切除	1 (<0.1%)	0		
Vena cava filter insertion	大静脈フィルター挿入	0	1 (<0.1%)		
Vascular disorders	血管障害	150 (8.7%)	184 (10.8%)	35 (2.0%)	46 (2.7%)
Angiosclerosis	血管硬化	1 (<0.1%)	0		
Aortic aneurysm	大動脈瘤	1 (<0.1%)	3 (0.2%)		
Aortic arteriosclerosis	大動脈硬化症	4 (0.2%)	1 (<0.1%)		
Aortic stenosis	大動脈狭窄	1 (<0.1%)	0		
Arterial haemorrhage	動脈出血	0	1 (<0.1%)		
Arterial thrombosis limb	四肢動脈血栓症	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Arteriosclerosis	動脈硬化症	2 (0.1%)	4 (0.2%)		
Arteriosclerosis obliterans	閉塞性動脈硬化症	0	1 (<0.1%)		
Bleeding varicose vein	出血性静脈瘤	2 (0.1%)	0		
Blue toe syndrome	青趾症候群	0	1 (<0.1%)	0	1 (<0.1%)
Circulatory collapse	循環虚脱	1 (<0.1%)	0	1 (<0.1%)	0
Collateral circulation	側副血行	4 (0.2%)	6 (0.4%)		
Essential hypertension	本態性高血圧症	2 (0.1%)	1 (<0.1%)		
Extremity necrosis	四肢壊死	0	1 (<0.1%)		
Femoral artery occlusion	大腿動脈閉塞	1 (<0.1%)	0		
Haematoma	血腫	42 (2.4%)	61 (3.6%)	25 (1.5%)	39 (2.3%)
Hot flush	ほてり	2 (0.1%)	3 (0.2%)	1 (<0.1%)	1 (<0.1%)

付表 2.7.6.1- 1 すべての有害事象及び治験薬との因果関係が否定できないすべての有害事象の発現頻度（試験 11702-DVT、安全性解析対象集団）（続き）

Primary System Organ Class / Preferred Term MedDRA version{13.0}		All		All study drug-related	
		Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)	Rivaroxaban N=1718 (100%)	Enoxaparin/VKA N=1711 (100%)
Hypertension	高血圧	39 (2.3%)	45 (2.6%)	0	1 (<0.1%)
Hypertensive crisis	高血圧クリーゼ	0	1 (<0.1%)		
Hypotension	低血圧	4 (0.2%)	8 (0.5%)	1 (<0.1%)	0
Iliac artery stenosis	腸骨動脈狭窄	0	1 (<0.1%)		
Intermittent claudication	間欠性跛行	1 (<0.1%)	0		
Jugular vein thrombosis	頚静脈血栓症	0	1 (<0.1%)		
Lymphoedema	リンパ浮腫	1 (<0.1%)	0		
Lymphorrhoea	リンパ漏	0	1 (<0.1%)		
May-Thurner syndrome	マイ・トゥルナー症候群	0	1 (<0.1%)		
Neovascularisation	血管新生	2 (0.1%)	0		
Orthostatic hypotension	起立性低血圧	3 (0.2%)	1 (<0.1%)		
Peripheral arterial occlusive disease	末梢動脈閉塞性疾患	3 (0.2%)	2 (0.1%)		
Peripheral artery aneurysm	末梢動脈瘤	1 (<0.1%)	0		
Peripheral coldness	末梢冷感	3 (0.2%)	0	3 (0.2%)	0
Peripheral embolism	末梢血管塞栓症	0	1 (<0.1%)		
Peripheral ischaemia	末梢性虚血	1 (<0.1%)	2 (0.1%)		
Peripheral vascular disorder	末梢血管障害	1 (<0.1%)	1 (<0.1%)		
Phlebitis	静脈炎	1 (<0.1%)	2 (0.1%)	0	1 (<0.1%)
Phlebitis superficial	表在性静脈炎	3 (0.2%)	1 (<0.1%)		
Post thrombotic syndrome	血栓後症候群	11 (0.6%)	11 (0.6%)	1 (<0.1%)	0
Raynaud's phenomenon	レイノー現象	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)
Shock	ショック	0	1 (<0.1%)		
Shock haemorrhagic	出血性ショック	0	1 (<0.1%)	0	1 (<0.1%)
Superficial vein prominence	表在静脈隆起	1 (<0.1%)	0		
Thrombophlebitis	血栓性静脈炎	1 (<0.1%)	4 (0.2%)		
Thrombophlebitis migrans	遊走性血栓静脈炎	0	1 (<0.1%)		
Thrombophlebitis superficial	表在性血栓性静脈炎	3 (0.2%)	1 (<0.1%)		
Thrombosis	血栓症	2 (0.1%)	2 (0.1%)		
Varicose ulceration	静脈瘤性潰瘍	0	1 (<0.1%)		
Varicose vein	静脈瘤	6 (0.3%)	9 (0.5%)	1 (<0.1%)	0
Vasodilatation	血管拡張	3 (0.2%)	1 (<0.1%)	1 (<0.1%)	0
Vasospasm	血管痙攣	0	1 (<0.1%)		
Vein pain	静脈痛	1 (<0.1%)	3 (0.2%)		
Venous insufficiency	静脈不全	6 (0.3%)	8 (0.5%)		
Venous thrombosis limb	四肢静脈血栓症	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	0

Adverse events are sorted in alphabetical order by primary SOC and preferred term.
A subject is counted only once within each preferred term of any primary SOC.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-1-2.sas erjli 21MAR2013 9:58
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）

Subject ID: 100034004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/47/WHITE/GERMANY/YES
Medical history	Hyperlipidaemia, Malignant melanoma, Stasis dermatitis, Knee operation, Knee operation, Skin ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARIXTRA, HEPARIN, NEXIUM, SIMVAHEXAL, WARFARIN
Adverse Events (AE) Preferred term	1. Leukocytoclastic vasculitis 2. Leukocytoclastic vasculitis 3. Leukocytoclastic vasculitis 4. Skin ulcer 5. Skin ulcer
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MODERATE/YES/YES/YES 3. MODERATE/YES/NO/YES 4. MODERATE/YES/YES/YES 5. MILD/YES/NO/NO
Start/stop date of event with relative date	1. 27DEC2007 (22) - 29DEC2007 (24) 2. 29DEC2007 (24) - 30DEC2007 (25) 3. 30DEC2007 (25) - --------- (.) 4. 15JAN2008 (41) - 04JUN2008 (182) 5. 05JUN2008 (183) - --------- (.)
Duration of AE	1. 3 2. 2 3. . 4. 142 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 5. NONE
Outcome of event	1. WORSENED 2. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034004

Parameter	Value
	3. UNCHANGED
	4. IMPROVED
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100034004[1)]	ULCERA CRURUM VENOSA LEFT LOWER LEG（PT：皮膚潰瘍） 治験担当医はワルファリンと報告事象との関連性があると判断した。弊社は、合併症（静脈怒張及びアレルギー性血管炎）によるものであり、ワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/78/WHITE/GERMANY/YES
Medical history	Cystitis, Hypertension, Hysterectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARDIODORON, CIPROFLOXACIN, CIPROHEXAL, ENOXAPARIN, INFECTOTRIMET, ISOPTIN, LASIX, NITROLINGUAL SPRAY, OMEPRAZOL, RAMIPRIL, URO-VAXOM [ESCHERICHIA COLI], WARFARIN
Adverse Events (AE) Preferred term	1. Cystitis 2. Cystitis 3. Cystitis 4. Atrial fibrillation 5. Bundle branch block left 6. Hypertensive crisis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 02FEB2008 (19) - 28FEB2008 (45) 2. 14OCT2008 (274) - 19OCT2008 (279) 3. 12DEC2008 (333) - 16DEC2008 (337) 4. 05JAN2009 (357) - 14JAN2009 (366) 5. 05JAN2009 (357) - 14JAN2009 (366) 6. 05JAN2009 (357) - 14JAN2009 (366)
Duration of AE	1. 27 2. 6 3. 5 4. 10 5. 10 6. 10
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034008

Parameter	Value
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034009/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/33/WHITE/GERMANY/YES
Medical history	Acetabulum fracture, Laparotomy, Small intestinal resection, Osteosynthesis, Retinal degeneration
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	NEXIUM
Adverse Events (AE) Preferred term	1. Maculopathy 2. Maculopathy
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. --APR2008 (.) - 04AUG2008 (196) 2. 04AUG2008 (196) - 09AUG2008 (201)
Duration of AE	1. . 2. 6
Dose on AE onset	1. 2. 20 mg
Dose status on AE onset	1. 2. F
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. WORSENED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034014/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/75/WHITE/GERMANY/YES
Medical history	Varices oesophageal, Hip arthroplasty, Hypertension, Hypothyroidism, Knee arthroplasty, Mitral valve incompetence, Mitral valve prolapse, Renal failure, Osteoarthritis, Cholelithiasis, Aortic valve incompetence, Sjogren's syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CONCOR 5 [BISOPROLOL ALONE = BISOPROLOLHEMIFUMARAT], FERRO SANOL, L-THYROXIN 100, NOVALGIN, OMEPRAZOL, TRAMAL LONG
Adverse Events (AE) Preferred term	1. Facial pain 2. Osteoarthritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 14MAR2008 (4) - 15MAR2008 (5) 2. 28SEP2008 (202) - 31OCT2008 (235)
Duration of AE	1. 2 2. 34
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034020/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/GERMANY/YES
Medical history	Depression, Gastritis, Hypertension, Hypothyroidism, Constipation, Pulmonary fibrosis, Thrombosis, Thrombosis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACC, ACETYLCYSTEINE, ATMADISC, AZATHIOPRIN, CORTISONE, DELIX, ENDOXAN, L- THYROXIN, MCP, MOVICOL, NAVOBAN, NEXIUM, PREDNISOLON, ROXITHROMYCIN, SERTRALIN, SPIZEF, UROMITEXAN
Adverse Events (AE) Preferred term	1. Pulmonary fibrosis 2. Bronchopneumonia 3. Pulmonary fibrosis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 07AUG2008 (69) - 12AUG2008 (74) 2. 12FEB2009 (258) - 24FEB2009 (270) 3. 12MAR2009 (286) - 26MAR2009 (300)
Duration of AE	1. 6 2. 13 3. 15
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. I 3. I
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034021/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/52/WHITE/GERMANY/YES
Medical history	Hip arthroplasty, Hip arthroplasty
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Atrial fibrillation 3. Atrial fibrillation 4. Hypertension
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/NO 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 18AUG2008 (43) - 09SEP2008 (65) 2. 07JAN2009 (185) - 28JAN2009 (206) 3. 29JAN2009 (207) - 30JAN2009 (208) 4. 29JAN2009 (207) - --------- (.)
Duration of AE	1. 23 2. 22 3. 2 4. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. F 4. F
Action taken	1. OTHER 2. NONE 3. REMEDIAL DRUG THERAPY,OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. WORSENED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034021

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034024

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034024/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/GERMANY/YES
Medical history	Anxiety, Hypertension, Drug hypersensitivity, Hyperlipidaemia, Hyperthyroidism
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALCIUM D 3, DELIX, DYSTO LOGES, ENOXAPARIN, MONO EMBOLEX, RANITIDIN, SIMVAHEXAL, UNACID, WARFARIN
Adverse Events (AE) Preferred term	1. Abdominal abscess 2. Hypocalcaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 08MAY2009 (284) - 16MAY2009 (292) 2. 10MAY2009 (286) - 14MAY2009 (290)
Duration of AE	1. 9 2. 5
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100034031

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100034031/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/75/WHITE/GERMANY/YES
Medical history	Hyperlipidaemia, Hypertension, Obesity, Back pain
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARCOXIA, BISOPROLOL 5, DELIX, ENOXAPARIN, NEXIUM, SIMVAHEXAL, WARFARIN
Adverse Events (AE) Preferred term	1. Back pain
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 01DEC2008 (18) - 05DEC2008 (22)
Duration of AE	1. 5
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100054001/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/67/WHITE/GERMANY/YES
Medical history	Diverticulum intestinal, Cough, Hypertension, Sciatica, Spinal column stenosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACCUZIDE, ACERCOMP, ARCOXIA, BIFITERAL, CITALOPRAM, DUROGESIC, GABAPENTIN, GABAPENTIN HEXAL, GARYDOL, ISOMOL, KATADOLON, LACTULOSE, MCP HECAL, MEAVERIN 1% [MEPIVACAIN-HYDROCHLORIDE], MORPHINE SANDOZ, MUCOSOLVAN, NOVALGIN, NOVAMINSULFON, PERFALGAN, SEVREDOL, TARGIN, TRAMAL, VALORON N, VALORON N RETARD
Adverse Events (AE) Preferred term	1. Decreased appetite 2. Weight decreased 3. Constipation 4. Sciatica 5. Sciatica 6. Wound haemorrhage 7. Sciatica 8. Hyperhidrosis 9. Hyperhidrosis 10. Chills 11. Sciatica 12. Chills 13. Oropharyngeal pain 14. Paraesthesia 15. Intervertebral disc protrusion 16. Sciatica 17. Paraesthesia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/YES/NO/YES 5. MODERATE/YES/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/YES/NO/YES 8. MILD/YES/NO/YES 9. MILD/YES/NO/YES 10. MILD/YES/NO/YES 11. MILD/NO/NO/YES 12. MILD/YES/NO/YES 13. MILD/NO/NO/YES 14. MODERATE/NO/NO/NO 15. SEVERE/NO/YES/NO 16. MILD/NO/NO/NO 17. MILD/NO/NO/NO

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054001

Parameter	Value
Start/stop date of event with relative date	1. 31AUG2007 (1) - 15JAN2008 (138) 2. 31AUG2007 (1) - 15JAN2008 (138) 3. 03SEP2007 (4) - 14JAN2008 (137) 4. 01OCT2007 (32) - 09OCT2007 (40) 5. 12OCT2007 (43) - 13NOV2007 (75) 6. 16OCT2007 (47) - 16OCT2007 (47) 7. 30NOV2007 (92) - 13DEC2007 (105) 8. 01DEC2007 (93) - 12DEC2007 (104) 9. 14JAN2008 (137) - 20JAN2008 (143) 10. 14JAN2008 (137) - 20JAN2008 (143) 11. 20JAN2008 (143) - 17MAR2008 (200) 12. 22JAN2008 (145) - 30JAN2008 (153) 13. 13FEB2008 (167) - 17FEB2008 (171) 14. 11MAR2008 (194) - 18MAR2008 (201) 15. 17MAR2008 (200) - 18MAR2008 (201) 16. 23MAR2008 (206) - --------- (.) 17. 23MAR2008 (206) - --------- (.)
Duration of AE	1. 138 2. 138 3. 134 4. 9 5. 33 6. 1 7. 14 8. 12 9. 7 10. 7 11. 58 12. 9 13. 5 14. 8 15. 2 16. . 17. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054001

Parameter	Value
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
	16. 20 mg
	17. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .
	13. .
	14. F
	15. F
	16. F
	17. F
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. OTHER
	5. OTHER
	6. REMEDIAL DRUG THERAPY,OTHER
	7. OTHER
	8. OTHER
	9. NONE
	10. NONE
	11. OTHER
	12. NONE
	13. REMEDIAL DRUG THERAPY
	14. OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054001

Parameter	Value
	15. OTHER
	16. NONE
	17. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. RESOLVED
	15. RESOLVED
	16. UNCHANGED
	17. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100054010/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/GERMANY/YES
Medical history	Cystitis noninfective, Colon polypectomy, Varices oesophageal, Haemorrhoids, Hypertension, Mitral valve incompetence, Benign prostatic hyperplasia, Hepatic steatosis, Post thrombotic syndrome, Carotid arteriosclerosis, Oedema, Haemorrhoid operation, Anal prolapse
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACC BRAUSE, AMOXICILLIN AL, DOLANTIN, DOLOMO NT, DORMICUM, MAGNESIUM, ORALAV, PANTOZOL, PREPACOL, PROPOFOL, RAMIPRIL, TRANSPULMIN [CINEOL, LEVOMENTHOL, D-CAMPHER]
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Pain in extremity 3. Cough 4. Toothache 5. Tooth infection 6. Post procedural haemorrhage 7. Rectal haemorrhage 8. Cough 9. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/YES/NO/YES 7. MODERATE/YES/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 08NOV2008 (4) - 11NOV2008 (7) 2. 25NOV2008 (21) - 07JAN2009 (64) 3. 07FEB2009 (95) - 20MAR2009 (136) 4. 12JUN2009 (220) - 21JUN2009 (229) 5. 16JUN2009 (224) - 22JUN2009 (230) 6. 18JUN2009 (226) - 18JUN2009 (226) 7. 20JUL2009 (258) - 30JUL2009 (268) 8. 06AUG2009 (275) - 27SEP2009 (327) 9. 19AUG2009 (288) - 19AUG2009 (288)
Duration of AE	1. 4 2. 44 3. 42 4. 10 5. 7 6. 1 7. 11

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054010

Parameter	Value
	8. 53
	9. 1
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. I
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	2. OTHER
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY,OTHER
	6. OTHER
	7. OTHER
	8. REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100054010

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100064005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100064005/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/57/WHITE/GERMANY/YES
Medical history	Wegener's granulomatosis, Prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CALCIUM, CIPROFLOXACIN, DIFLUCAN, FOLSAN, METHOTREXAT, NOVAMINSULFON, PANTOPRAZOLE, PREDNISOLON, PREDNISOLONE, RITUXIMAB, TAMSULOSIN, VITAMIN D3
Adverse Events (AE) Preferred term	1. Muscle spasms 2. Bronchitis 3. Conjunctival haemorrhage 4. Conjunctival haemorrhage 5. Conjunctival haemorrhage 6. Headache 7. Conjunctival haemorrhage 8. Tooth fracture 9. Pyrexia 10. Wegener's granulomatosis 11. Cystitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MODERATE/YES/NO/YES 5. MILD/YES/NO/YES 6. MODERATE/NO/NO/YES 7. MILD/YES/NO/YES 8. MODERATE/NO/NO/YES 9. SEVERE/NO/NO/YES 10. MODERATE/NO/YES/YES 11. MILD/NO/NO/YES
Start/stop date of event with relative date	1. -----2009 (.) - --JUN2009 (.) 2. --FEB2009 (.) - --FEB2009 (.) 3. 27OCT2008 (5) - -----2008 (.) 4. 10NOV2008 (19) - 17NOV2008 (26) 5. 09DEC2008 (48) - 15DEC2008 (54) 6. 22DEC2008 (61) - 13MAY2009 (203) 7. 14JAN2009 (84) - 16JAN2009 (86) 8. 26JAN2009 (96) - 02FEB2009 (103) 9. 12APR2009 (172) - --MAY2009 (.) 10. 14MAY2009 (204) - 27MAY2009 (217) 11. 10OCT2009 (353) - 15OCT2009 (358)
Duration of AE	1. . 2. . 3. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100064005

Parameter	Value
	4. 8
	5. 7
	6. 143
	7. 3
	8. 8
	9. .
	10. 14
	11. 6
Dose on AE onset	1.
	2.
	3. 15 mg
	4. 15 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
Dose status on AE onset	1.
	2.
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
Action taken	1. NONE
	2. NONE
	3. NONE
	4. STUDY DRUG DISCONTINUED AND RESTARTED
	5. NONE
	6. NONE
	7. NONE
	8. STUDY DRUG DISCONTINUED AND RESTARTED
	9. NONE
	10. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100064005

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100074001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100074001/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/68/WHITE/GERMANY/YES
Medical history	Cerebrovascular accident, Cerebrovascular accident, Back pain, Breast cancer, Gastritis erosive, Hypercholesterolaemia, Hypertension, Restlessness, Postmenopause, Dyssomnia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMITRIPTYLIN, ATROPIN, BELOC ZOK, CIPRALEX, CIPROBAY [CIPROFLOXACIN-HCL], CIPROHEXAL, COTRIM FORTE, DEXAMETHASON, DISOPRIVAN 1%, EUTHYROX, GABAPENTIN, GRANOCYTE, IBUPROFEN, ISCOVER, LISINOPRIL, MORPHINE, NEXIUM, NOVALGIN, PROPOFOL, SIMVASTATIN, SOLUTIONS FOR PARENTERAL NUTRITION, TILIDIN, TRANXILIUM, ULTIVA, VALORON N RETARD, ZANTIC
Adverse Events (AE) Preferred term	1. Goitre 2. Cataract 3. Epistaxis 4. Circulatory collapse 5. Fall 6. Haematuria 7. Urinary tract infection 8. Urinary tract infection 9. Circulatory collapse 10. Epistaxis 11. Back pain 12. Urinary tract infection 13. Epistaxis 14. Epistaxis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/YES/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/YES/NO/YES 7. MODERATE/YES/NO/YES 8. MODERATE/YES/YES/YES 9. MILD/YES/YES/YES 10. MILD/YES/NO/YES 11. SEVERE/NO/YES/YES 12. MODERATE/NO/NO/YES 13. MODERATE/YES/NO/YES 14. MILD/YES/NO/YES
Start/stop date of event with relative date	1. -----2008 (.) - --------- (.) 2. --APR2008 (.) - 22SEP2008 (322) 3. 18NOV2007 (13) - 20NOV2007 (15) 4. 24NOV2007 (19) - 24NOV2007 (19)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100074001

Parameter	Value
	5. 24NOV2007 (19) - 15JAN2008 (71)
	6. 20JAN2008 (76) - 03FEB2008 (90)
	7. 20JAN2008 (76) - 03FEB2008 (90)
	8. 05MAR2008 (121) - 15MAR2008 (131)
	9. 08MAR2008 (124) - 10MAR2008 (126)
	10. 26MAY2008 (203) - 03JUN2008 (211)
	11. 13JUN2008 (221) - 15JUN2008 (223)
	12. 16JUN2008 (224) - 21JUN2008 (229)
	13. 19JUN2008 (227) - 20JUN2008 (228)
	14. 26AUG2008 (295) - 26AUG2008 (295)
Duration of AE	1. .
	2. .
	3. 3
	4. 1
	5. 53
	6. 15
	7. 15
	8. 11
	9. 3
	10. 9
	11. 3
	12. 6
	13. 2
	14. 1
Dose on AE onset	1.
	2.
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
Dose status on AE onset	1.
	2.
	3. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100074001

Parameter	Value
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .
	13. .
	14. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	3. NONE
	4. OTHER
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. OTHER
	14. NONE
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100074001

Parameter	Value
	14. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100074001[1),1)]	CIRCULATORY COLLAPSE（PT：循環虚脱） 治験担当医はリバーロキサバンと報告事象との関連性があると判断した。弊社は、合併症（尿路感染）からの脱水によるものであり、リバーロキサバンとの因果関係は否定できると考える。 URINARY TRACT INFECTION（PT：尿路感染） 治験担当医はリバーロキサバンと報告事象との関連性があると判断した。弊社は、細菌感染による偶発的発現によるものであり、リバーロキサバンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100074006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100074006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/59/WHITE/GERMANY/YES
Medical history	Goitre, Pneumonia, Hypercholesterolaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BUSCOPAN, DORMICUM, ENOXAPARIN, EUTHYROX, KLYSMA [NATRIUMDIHYDROGENPHOSPHAT FOR PURGATION OF INTESTINE, COLOSCOPY], PRAVASIN, PROPOFOL, SIMVASTATIN, SUPRARENIN AND NACL MIX, THYRONAJOD, WARFARIN
Adverse Events (AE) Preferred term	1. Rectal adenoma 2. Influenza 3. Epistaxis 4. Rectal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. -----2009 (.) - 19JUN2009 (235) 2. 07DEC2008 (41) - 15DEC2008 (49) 3. 08DEC2008 (42) - 14DEC2008 (48) 4. 20JUN2009 (236) - 23JUN2009 (239)
Duration of AE	1. . 2. 9 3. 7 4. 4
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. NONE 3. NONE 4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100074006

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100094033

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100094033/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/69/WHITE/GERMANY/YES
Medical history	Breast cancer, Breast cancer, Chronic lymphocytic leukaemia, Hyperthyroidism, Hypothyroidism, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLCYSTEIN, ADUMBRAN, CEC, CEFUROXIM, EUTHYROX, NOVAMINSULFON, RINGER-LACTAT
Adverse Events (AE) Preferred term	1. Bronchitis 2. Humoral immune defect
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07JUL2009 (41) - 17JUL2009 (51) 2. 13JUL2009 (47) - --------- (.)
Duration of AE	1. 11 2. .
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100094038

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100094038/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/71/WHITE/GERMANY/YES
Medical history	Breast cancer, Cholecystectomy, Constipation, Depression, Diverticulum intestinal, Folate deficiency, Gastritis, Hysterectomy, Lung neoplasm malignant, Pneumonia, Sleep disorder, Gamma-glutamyltransferase increased
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADUMBRAN, ALLOPURINOL, AMBROXOL, ATOSIL, BALDRIAN, BISACODYL, CEFTRIAXON, CEFUROXIM, CHEMOTHERAPY, CLEXANE, ENOXAPARIN, FLUNINOC, FLUNUNOC, FOLIC ACID, HALDOL, IBUPROFEN, JONOSTERIL, KCL, KLACID, MCP (METOCLOPRAMID), MELNEURIN, MIDAZOLAM, MORPHINE, NACL, NACL 10%, NEUROCIL, NEXIUM, NIFEDIPIN, NOVAMINSULFON, PARACETAMOL, RANITIDIN, RINGER-LACTAT, TAVOR [LORAZEPAM], TETRAZEPAM, TRAMAL, ULCOGANT [SUCRALFATE], VOMEX A, WARFARIN, ZOPICLON
Adverse Events (AE) Preferred term	1. Reflux oesophagitis 2. Tension headache 3. Hypokalaemia 4. Periodontitis 5. Oesophageal ulcer haemorrhage 6. Acute psychosis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 15SEP2009 (54) - 03OCT2009 (72) 2. 16SEP2009 (55) - 25SEP2009 (64) 3. 16SEP2009 (55) - --------- (.) 4. 17SEP2009 (56) - 25SEP2009 (64) 5. 21SEP2009 (60) - 22SEP2009 (61) 6. 21SEP2009 (60) - 25SEP2009 (64)
Duration of AE	1. 19 2. 10 3. . 4. 9 5. 2 6. 5
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100094038

Parameter	Value
	2.
	3.
	4.
	5.
	6.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY,OTHER
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. INSUFFICIENT FOLLOW-UP
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100094038[2)]	BLEEDING ESOPHAGEAL ULCER（PT：食道潰瘍出血） 治験担当医は、合併症（逆流性食道炎及び再発性胃炎）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100124002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100124002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/73/WHITE/GERMANY/YES
Medical history	Aortic aneurysm, Cholecystectomy, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BISOPROLOL, ENOXAPARIN, IBUPROFEN, PARACETAMOL, WARFARIN
Adverse Events (AE) Preferred term	1. Muscle haemorrhage 2. Procedural pain 3. Sleep disorder 4. Procedural hypertension 5. Sleep disorder
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES 2. SEVERE/NO/NO/YES 3. MODERATE/NO/NO/NO 4. MODERATE/NO/NO/NO 5. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 01DEC2008 (7) - 23DEC2008 (29) 2. 08DEC2008 (14) - 23DEC2008 (29) 3. 13DEC2008 (19) - 15DEC2008 (21) 4. 18DEC2008 (24) - 18DEC2008 (24) 5. 18DEC2008 (24) - 18DEC2008 (24)
Duration of AE	1. 23 2. 16 3. 3 4. 1 5. 1
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100124002

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100124002[3)]	COMPARTMENT SYNDROME（PT：コンパートメント症候群） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100134008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/45/WHITE/GERMANY/YES
Medical history	Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	FOLICOMBIN
Adverse Events (AE) Preferred term	1. Menorrhagia 2. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/NO/YES
Start/stop date of event with relative date	1. 26FEB2008 (27) - 29FEB2008 (30) 2. 26FEB2008 (27) - --------- (.)
Duration of AE	1. 4 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100134008[2)]	HYPERMENORRHOE（PT：月経過多） 治験担当医は、合併症によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性および抗凝固作用から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100134015/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/78/WHITE/GERMANY/YES
Medical history	Angina pectoris, Chronic obstructive pulmonary disease, Diabetes mellitus, Gout, Hyperlipidaemia, Hypertension, Oesophagitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALLOPURINOL, ATROVENT, GLIMEPIRID, LORZAAR, OXIS-SPRAY, PANTOZOL, PENTALONG, PULMICORT-SPRAY, SIMVASTATIN, SULTANOL
Adverse Events (AE) Preferred term	1. Oesophageal adenocarcinoma
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 02SEP2008 (106) - 31DEC2008 (226)
Duration of AE	1. 121
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100134016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/69/WHITE/GERMANY/YES
Medical history	Breast cancer, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, ENOXAPARIN, TAMOXIFEN, WARFARIN
Adverse Events (AE) Preferred term	1. Meningioma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 16DEC2008 (204) - 05FEB2009 (255)
Duration of AE	1. 52
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134024

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100134024/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/84/WHITE/GERMANY/YES
Medical history	Hypertension, Prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	KONAKION, LISINOPRIL, PPSB
Adverse Events (AE) Preferred term	1. Thrombocytopenia 2. Epistaxis 3. Haematoma 4. Thrombocytopenia 5. Drug hypersensitivity
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES 2. SEVERE/YES/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/YES/NO/NO 5. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 26NOV2008 (65) - 09DEC2008 (78) 2. 26NOV2008 (65) - 09DEC2008 (78) 3. 27NOV2008 (66) - --------- (.) 4. 09DEC2008 (78) - 17FEB2009 (148) 5. 07JAN2009 (107) - --------- (.)
Duration of AE	1. 14 2. 14 3. . 4. 71 5. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. F 5. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY 3. NONE 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134024

Parameter	Value
	2. RESOLVED
	3. INSUFFICIENT FOLLOW-UP
	4. RESOLVED
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134036

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100134036/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/50/WHITE/GERMANY/YES
Medical history	Ankylosing spondylitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, ENBREL (ETANERCEPT), ENOXAPARIN, SYMPAL(DEXKETOPROFEN), WARFARIN
Adverse Events (AE) Preferred term	1. Thoracic vertebral fracture 2. Skin laceration
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 17JUL2009 (94) - 24JUL2009 (101) 2. 17JUL2009 (94) - 17JUL2009 (94)
Duration of AE	1. 8 2. 1
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134038

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100134038/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/54/WHITE/GERMANY/YES
Medical history	Gout, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CELLIDRIN (ALLOPURINOL), CONCOR, FURESIS, GENTAMICIN, HEPARIN, MERONEM, METOHEXAL RETARD(METOPROLOLTARTRAT), PANTOZOL, SPIRONOLACTONE, VANCOMYCIN
Adverse Events (AE) Preferred term	1. Multi-organ failure 2. Subacute endocarditis 3. Renal failure 4. Oesophagitis 5. Hepatic cirrhosis 6. Bile duct cancer
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/NO 6. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 28JUL2009 (84) - 21AUG2009 (108) 2. 28JUL2009 (84) - --------- (.) 3. 28JUL2009 (84) - --------- (.) 4. 28JUL2009 (84) - --------- (.) 5. 31JUL2009 (87) - --------- (.) 6. 31JUL2009 (87) - --------- (.)
Duration of AE	1. 25 2. . 3. . 4. . 5. . 6. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. F 6. F

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100134038

Parameter	Value
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
Outcome of event	1. DEATH
	2. UNCHANGED
	3. UNCHANGED
	4. UNCHANGED
	5. UNCHANGED
	6. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100224001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100224001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/48/WHITE/GERMANY/YES
Medical history	Gastritis, Menorrhagia, Uterine leiomyoma, Anaemia, Hyperthyroidism
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FERRLECIT, MINISISTON, PANTOZOL, WARFARIN
Adverse Events (AE) Preferred term	1. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 01DEC2008 (21) - 06DEC2008 (26)
Duration of AE	1. 6
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100224001[3)]	HYPERMENORRHEA（PT：月経過多） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、クマジン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100224022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100224022/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/63/WHITE/GERMANY/YES
Medical history	Diabetes mellitus, Hypercholesterolaemia, Hypertension, Rhinitis allergic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMLODIPIN, BLOPRESS, CRESTOR, ENOXAPARIN, EZETROL, JANUVIA, METFORMIN, WARFARIN
Adverse Events (AE) Preferred term	1. Angina pectoris
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 29MAY2009 (74) - 30MAY2009 (75)
Duration of AE	1. 2
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100224049

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100224049/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/GERMANY/YES
Medical history	Colitis, Hypercholesterolaemia, Hypertension, Migraine, Varicose vein, Colon adenoma, Postmenopause, Coronary artery disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BELOC ZOC MITE, DIOVAN, FENTANYL, SIMVASTATIN
Adverse Events (AE) Preferred term	1. Abdominal pain 2. Weight decreased 3. Weight decreased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 05AUG2009 (3) - 07AUG2009 (5) 2. 21SEP2009 (50) - 26SEP2009 (55) 3. 27SEP2009 (56) - 05NOV2009 (95)
Duration of AE	1. 3 2. 6 3. 40
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED 3. NONE
Outcome of event	1. RESOLVED 2. IMPROVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100224053

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100224053/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/56/WHITE/GERMANY/YES
Medical history	Appendicectomy, Haemangioma of liver, Hypertension, Hypothyroidism, Ectopic pregnancy, Tachyarrhythmia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CORDAREX, HYLO VISION, L-THYROXIN, LIPOSIC, METOHEXAL SUCC., RAMIPRIL, RAMIPRIL 7.5, RAMIPRIL COMP12.5
Adverse Events (AE) Preferred term	1. Conjunctivitis 2. Tachyarrhythmia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 11SEP2009 (16) - 20SEP2009 (25) 2. 09OCT2009 (44) - 13OCT2009 (48)
Duration of AE	1. 10 2. 5
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100224054

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100224054/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/GERMANY/YES
Medical history	Angina unstable, Diabetes mellitus, Hypertension, Carotid artery occlusion, Vertebral artery occlusion, Obesity, Hyperlipidaemia, Lip neoplasm, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARVEDILOL, ENOXAPARIN, ISCOVER, RAMIPRIL, RAMIPRIL 5 PLUS, SIMVASTATIN, WARFARIN
Adverse Events (AE) Preferred term	1. Arterial thrombosis limb
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 03DEC2009 (98) - 18JAN2010 (144)
Duration of AE	1. 47
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-100224054[4)]	ARTERIAL THROMBOSIS OF SUPERFICIAL FEMORALIS ART.（PT：末梢動脈血栓症） 治験担当医は、エノキサパリンについて、因果関係評価を行っていない。弊社は、エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer Pharma 社及び治験依頼者の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer Pharma 社及び治験依頼者が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer Pharma 社及び治験依頼者が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer Pharma 社及び治験依頼者が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer Pharma 社及び治験依頼者が「関連なし」の場合
5）治験担当医師及び治験依頼者が「関連あり」、Bayer Pharma 社が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100264003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100264003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/57/WHITE/GERMANY/YES
Medical history	Diabetes mellitus, Disability, Hypertension, Obesity, Paraesthesia, Subarachnoid haemorrhage, Subarachnoid haemorrhage, Dyspnoea exertional, Tobacco abuse
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BIFITERAL, FORMOTEROL, HEPARIN, JANUVIA, METFORMIN, METOPROLOL, PANTOZOL, RAMIPRIL
Adverse Events (AE) Preferred term	1. Hypercholesterolaemia 2. Acute myocardial infarction 3. Troponin I increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. --OCT2009 (.) - --------- (.) 2. 03OCT2009 (327) - 13OCT2009 (337) 3. 03OCT2009 (327) - --OCT2009 (.)
Duration of AE	1. . 2. 11 3. .
Dose on AE onset	1. 2. 20 mg 3. 20 mg
Dose status on AE onset	1. 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 3. OTHER
Outcome of event	1. UNCHANGED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100394026

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/100394026/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/30/WHITE/GERMANY/YES
Medical history	Rhinitis allergic, Appendicectomy, Endometriosis, Ovarian cyst
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BROMHEXIN, BRONCHIKUM [PLANTAGO LANCEOL, PRIMULA SPP: FL EXT,THYM: VULG:FL EXT.], ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Cough 2. External ear inflammation 3. Eczema 4. Ovarian cyst
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 06JUN2009 (24) - 15JUN2009 (33) 2. 22AUG2009 (101) - 26AUG2009 (105) 3. 29NOV2009 (200) - 02DEC2009 (203) 4. 01FEB2010 (264) - 02FEB2010 (265)
Duration of AE	1. 10 2. 5 3. 4 4. 2
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. NONE 4. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 100394026

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/120034001/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/40/WHITE/UNITED KINGDOM/YES
Medical history	Arteriovenous fistula operation, Asthma, Colonic polyp, Depression, Tongue disorder, Polyuria, Endometrial cancer, Fatigue, Lethargy, Diarrhoea, Meningioma, Vaginal haemorrhage, Postmenopause, Cowden's disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	FLUOXETINE, LOPERAMIDE, LORAZEPAM, PARACETAMOL, SALBUTAMOL, SOLIFENACIN, ZOPICLONE
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Anxiety 3. Insomnia 4. Rectal haemorrhage 5. Vaginal haemorrhage 6. Vaginal haemorrhage 7. Vaginal haemorrhage 8. Endometrial cancer 9. Diarrhoea 10. Contusion 11. Dizziness 12. Oedema peripheral 13. Cough 14. Oedema peripheral 15. Anaemia 16. Pain in extremity 17. Pyrexia 18. Dizziness 19. Anxiety
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/NO 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/YES/NO/YES 5. MILD/YES/NO/YES 6. MILD/YES/NO/YES 7. MILD/YES/NO/YES 8. SEVERE/NO/YES/YES 9. MODERATE/YES/NO/YES 10. MILD/YES/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/NO/NO/YES 14. MODERATE/NO/NO/YES 15. SEVERE/YES/YES/YES 16. MILD/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034001

Parameter	Value
	17. MILD/NO/NO/YES
	18. MODERATE/NO/NO/YES
	19. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 10APR2008 (0) - 11APR2008 (1)
	2. 12APR2008 (2) - 16JUL2008 (97)
	3. 12APR2008 (2) - --------- (.)
	4. 15APR2008 (5) - --------- (.)
	5. 18APR2008 (8) - 19APR2008 (9)
	6. 20APR2008 (10) - 20APR2008 (10)
	7. 23APR2008 (13) - --------- (.)
	8. 12MAY2008 (32) - 07SEP2008 (150)
	9. 15MAY2008 (35) - 15MAY2008 (35)
	10. 26MAY2008 (46) - --------- (.)
	11. 30MAY2008 (50) - 17JUL2008 (98)
	12. 31MAY2008 (51) - 02JUN2008 (53)
	13. 31MAY2008 (51) - 31MAY2008 (51)
	14. 02JUN2008 (53) - --------- (.)
	15. 02JUN2008 (53) - --------- (.)
	16. 02JUN2008 (53) - --------- (.)
	17. 17JUL2008 (98) - 17JUL2008 (98)
	18. 17JUL2008 (98) - 18JUL2008 (99)
	19. 17JUL2008 (98) - --------- (.)
Duration of AE	1. 2
	2. 96
	3. .
	4. .
	5. 2
	6. 1
	7. .
	8. 119
	9. 1
	10. .
	11. 49
	12. 3
	13. 1
	14. .
	15. .
	16. .
	17. 1
	18. 2
	19. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034001

Parameter	Value
Dose on AE onset	1.
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
	16. 20 mg
	17. 20 mg
	18. 20 mg
	19. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .
	13. .
	14. .
	15. .
	16. .
	17. .
	18. .
	19. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034001

Parameter	Value
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. STUDY DRUG DISCONTINUED PERMANENTLY
	9. NONE
	10. NONE
	11. NONE
	12. OTHER
	13. NONE
	14. OTHER
	15. OTHER
	16. NONE
	17. NONE
	18. NONE
	19. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. IMPROVED
	3. UNCHANGED
	4. UNCHANGED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. DEATH
	9. RESOLVED
	10. UNCHANGED
	11. WORSENED
	12. WORSENED
	13. RESOLVED
	14. UNCHANGED
	15. IMPROVED
	16. UNCHANGED
	17. RESOLVED
	18. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034001

Parameter	Value
	19. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/120034010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/39/WHITE/UNITED KINGDOM/YES
Medical history	Depression, Diabetes mellitus, Eczema, Hyperlipidaemia, Hypothyroidism, Pain in extremity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	50:50 PARAFIN EMOLLIENT, ATROVENT, BETAMETHASONE WITH SALICYLIC ACID, DIHYDROCODENE, ENOXAPARIN, FLUCCLOXACILLAN, FLUCLOXACILLAN, GLIPIZIDE, LEVEMIR, LEVOTHYROXINE, METFORMIN, MICROGYNON 30, NOVORAPID, PARACETAMOL, SALBUTAMOL, SERTRALINE, SIMVASTIN, WARFARIN
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Pain in extremity 3. Pain in extremity 4. Cellulitis 5. Cellulitis 6. Asthma 7. Asthma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --JUN2009 (.) - --------- (.) 2. 23MAY2009 (2) - 31MAY2009 (10) 3. 31MAY2009 (10) - --JUN2009 (.) 4. 01JUN2009 (11) - 08JUN2009 (18) 5. 08JUN2009 (18) - --------- (.) 6. 09JUN2009 (19) - 10JUN2009 (20) 7. 10JUN2009 (20) - 14JUN2009 (24)
Duration of AE	1. . 2. 9 3. . 4. 8 5. . 6. 2 7. 5
Dose on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 120034010

Parameter	Value
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP
	2. WORSENED
	3. IMPROVED
	4. IMPROVED
	5. INSUFFICIENT FOLLOW-UP
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140034002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140034002/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/51/BLACK/UNITED STATES/YES
Medical history	Anxiety, Asthenia, Asthma, Bronchitis, Cholecystectomy, Diabetes mellitus, Hypertension, Hysterectomy, Obesity, Restless legs syndrome, Status asthmaticus, Sleep apnoea syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUTEROL, ALDACTONE [SPIRONOLACTONE], AMITRIPTYLINE, ATROVENT, CLARITIN, COLACE, COZAAR, DARVOCET, FLUTICASONE, GLIPIZIDE, HUMALOG INSULIN, HYDROCHLOROTHIAZIDE, KLONOPIN, LASIX, LORTAB [HYDROCODONE + PARACETAMOL], MORPHINE, NEURONTIN, NEXIUM, PEPCID [FAMOTIDINE], PHENERGAN [PROMETHAZINE], PREDNISONE, PROTONIX, REGLAN, REQUIP, SALMETEROL, SINGULAIR, SOLUMEDROL, TRAZODONE, WARFARIN, ZITHROMAX, ZOLOFT
Adverse Events (AE) Preferred term	1. Skin laceration 2. Asthma 3. Gastrooesophageal reflux disease 4. Dermatitis contact 5. Oedema peripheral 6. Hypoglycaemia 7. Headache
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07JUL2007 (3) - --------- (.) 2. 16JUL2007 (12) - 22JUL2007 (18) 3. 16JUL2007 (12) - --------- (.) 4. 16JUL2007 (12) - --------- (.) 5. 16JUL2007 (12) - 22JUL2007 (18) 6. 19JUL2007 (15) - 19JUL2007 (15) 7. 19JUL2007 (15) - 19JUL2007 (15)
Duration of AE	1. . 2. 7 3. . 4. . 5. 7 6. 1 7. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140034002

Parameter	Value
	5. 15 mg
	6. 15 mg
	7. 15 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. OTHER
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. NONE
Outcome of event	1. INSUFFICIENT FOLLOW-UP
	2. RESOLVED
	3. INSUFFICIENT FOLLOW-UP
	4. INSUFFICIENT FOLLOW-UP
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140154013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140154013/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/UNITED STATES/YES
Medical history	Acute sinusitis, Osteoarthritis, Benign prostatic hyperplasia, Chronic sinusitis, Drug hypersensitivity, Headache, Constipation, Insomnia, Intervertebral disc degeneration, Nasal polyps, Peripheral vascular disorder, Pneumonia, Seasonal allergy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, ACTIVASE, ANCEF, BENADRYL CREAM, ENOXAPARIN, FENTANYL, FLONASE, HEPARIN, HYDROCODONE, KEFZOL, MAGNESIUM HYDROXIDE, NASOCORT, OXYCODONE, SENNA S, UNFRACTIONATED HEPARIN, VERSED, WARFARIN
Adverse Events (AE) Preferred term	1. Hot flush 2. Hyperhidrosis 3. Cough 4. Hepatic enzyme increased 5. Post thrombotic syndrome 6. Pain in extremity 7. Thrombosis 8. Rash 9. May-Thurner syndrome 10. Constipation 11. Contusion
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. SEVERE/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MILD/NO/NO/YES 9. SEVERE/NO/YES/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07MAY2009 (1) - 15JUN2009 (40) 2. 07MAY2009 (1) - 15JUN2009 (40) 3. 13MAY2009 (7) - 04JUN2009 (29) 4. 20MAY2009 (14) - 12AUG2009 (98) 5. 22MAY2009 (16) - 02JUN2009 (27) 6. 22MAY2009 (16) - 02JUN2009 (27) 7. 22MAY2009 (16) - --------- (.) 8. 28MAY2009 (22) - 04JUN2009 (29) 9. 29MAY2009 (23) - 02JUN2009 (27) 10. 29MAY2009 (23) - 04JUN2009 (29) 11. 08AUG2009 (94) - 16AUG2009 (102)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140154013

Parameter	Value
Duration of AE	1. 40
	2. 40
	3. 23
	4. 85
	5. 12
	6. 12
	7. .
	8. 8
	9. 5
	10. 7
	11. 9
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY,OTHER
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	8. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140154013

Parameter	Value
	9. REMEDIAL DRUG THERAPY,OTHER
	10. REMEDIAL DRUG THERAPY
	11. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. IMPROVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140164005/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/52/WHITE/UNITED STATES/YES
Medical history	Decreased appetite, Blood cholesterol increased, Hypertension, Knee arthroplasty, Epistaxis, Pain in extremity, Small cell lung cancer stage unspecified, Tonsillectomy, Tobacco user, Alcohol use, Decreased appetite, Lower limb fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALOXI, ARANESP, BENADRYL, BENADRYL [DIPHENHYDRAMINE], CARBOPLATIN, DECADRON, DEXAMETHASONE, ETOPOSIDE, EZETIMIBE/SIMVASTATIN, HYDROCODONE/APAP 10/325, K-DUR, KYTRIL, LASIX, MEGACE ES, NEULASTA, TOPOTECAN, TOPROL, VITAMIN K
Adverse Events (AE) Preferred term	1. Anaemia 2. Pain in extremity 3. Thrombocytopenia 4. Thrombocytopenia 5. Fatigue 6. Pruritus 7. Oedema 8. Nausea 9. Bone pain 10. Contusion 11. Contusion 12. Rectal haemorrhage 13. Constipation 14. Diarrhoea 15. Epistaxis 16. Hypokalaemia 17. Orthopnoea 18. Oedema peripheral 19. Small cell lung cancer metastatic
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/YES/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/NO/NO/YES 14. MILD/NO/NO/YES 15. MILD/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164005

Parameter	Value
	16. MILD/NO/NO/YES
	17. MILD/NO/NO/YES
	18. MILD/NO/NO/YES
	19. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 14MAY2007 (1) - --------- (.)
	2. 15MAY2007 (2) - 19MAY2007 (6)
	3. 24MAY2007 (11) - 29MAY2007 (16)
	4. 29MAY2007 (16) - --------- (.)
	5. 29MAY2007 (16) - --------- (.)
	6. 03JUN2007 (21) - --------- (.)
	7. 11JUN2007 (29) - --------- (.)
	8. 11JUN2007 (29) - --------- (.)
	9. 02JUL2007 (50) - --------- (.)
	10. 09JUL2007 (57) - --------- (.)
	11. 27JUL2007 (75) - 04AUG2007 (83)
	12. 01AUG2007 (80) - --------- (.)
	13. 01AUG2007 (80) - --------- (.)
	14. 01AUG2007 (80) - --------- (.)
	15. 03SEP2007 (113) - --------- (.)
	16. 04SEP2007 (114) - 27NOV2007 (198)
	17. 22OCT2007 (162) - --------- (.)
	18. 05NOV2007 (176) - --------- (.)
	19. 12NOV2007 (183) - 22DEC2007 (223)
Duration of AE	1. .
	2. 5
	3. 6
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. 9
	12. .
	13. .
	14. .
	15. .
	16. 85
	17. .
	18. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164005

Parameter	Value
	19. 41
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164005

Parameter	Value
	3. OTHER
	4. OTHER
	5. OTHER
	6. REMEDIAL DRUG THERAPY,OTHER
	7. NONE
	8. NONE
	9. NONE
	10. NONE
	11. NONE
	12. NONE
	13. NONE
	14. NONE
	15. NONE
	16. REMEDIAL DRUG THERAPY
	17. NONE
	18. NONE
	19. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. WORSENED
	4. UNCHANGED
	5. UNCHANGED
	6. UNCHANGED
	7. UNCHANGED
	8. UNCHANGED
	9. UNCHANGED
	10. UNCHANGED
	11. RESOLVED
	12. UNCHANGED
	13. UNCHANGED
	14. UNCHANGED
	15. UNCHANGED
	16. RESOLVED
	17. UNCHANGED
	18. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164005

Parameter	Value
	19. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140164006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/53/WHITE/UNITED STATES/YES
Medical history	Abdominal pain, Anaemia, Asthma, Cholecystitis, Hearing impaired, Haemorrhoids, Hiatus hernia, Dyspepsia, Neck pain, Hypoaesthesia, Arthralgia, Thrombocytopenia, Urinary incontinence, Intervertebral disc protrusion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADRIAMYCIN, ALLOPURINOL, ALOXI, AMBIEN, ARANESP, ATIVAN, AUGMENTIN, B-12, CEPHALEXIN, CYTOXAN, DECADRON, DEMEROL, KYTRIL, LEVAQUIN, LORTAB, NEULASTA, PREDNISONE, RITUXAN, ROCEPHIN, TAGAMET, TYLENOL [ACETAMINOPHEN], VALIUM [DIAZEPAM], VESICARE, VINCRISTINE
Adverse Events (AE) Preferred term	1. Non-Hodgkin's lymphoma 2. Insomnia 3. Pyrexia 4. Asthenia 5. Constipation 6. Back pain 7. Renal cell carcinoma 8. Neutropenia 9. Anaemia 10. Localised infection 11. Neutropenia 12. Skin disorder
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MODERATE/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/NO/NO/YES 11. MODERATE/NO/NO/YES 12. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 23MAY2007 (3) - 08FEB2008 (264) 2. 05JUN2007 (16) - --------- (.) 3. 13JUN2007 (24) - 05JUL2007 (46) 4. 13JUN2007 (24) - 15FEB2008 (271) 5. 19JUN2007 (30) - 21JUN2007 (32) 6. 26JUN2007 (37) - 05JUL2007 (46) 7. 10JUL2007 (51) - 24AUG2007 (96) 8. 26JUL2007 (67) - 02AUG2007 (74) 9. 02AUG2007 (74) - 03OCT2007 (136) 10. 19AUG2007 (91) - 18SEP2007 (121)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164006

Parameter	Value
	11. 19OCT2007 (152) - 24OCT2007 (157)
	12. 14MAR2008 (299) - --------- (.)
Duration of AE	1. 262
	2. .
	3. 23
	4. 248
	5. 3
	6. 10
	7. 46
	8. 8
	9. 63
	10. 31
	11. 6
	12. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. I
	8. .
	9. .
	10. .
	11. .
	12. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY,OTHER
	3. REMEDIAL DRUG THERAPY,OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164006

Parameter	Value
	4. NONE
	5. NONE
	6. NONE
	7. STUDY DRUG DISCONTINUED AND RESTARTED
	8. REMEDIAL DRUG THERAPY
	9. NONE
	10. REMEDIAL DRUG THERAPY,OTHER
	11. REMEDIAL DRUG THERAPY,OTHER
	12. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140164012/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/UNITED STATES/YES
Medical history	Abdominal discomfort, Benign prostatic hyperplasia, Diarrhoea, Diverticulitis, Oesophageal candidiasis, Haemorrhoids, Hyperlipidaemia, Hypertension, Knee arthroplasty, Splenectomy, Transurethral prostatectomy, Hypersensitivity, Hypoacusis, Limb discomfort
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CYMBALTA, DIOVAN [VALSARTAN], FLORA Q2, FUROSEMIDE, LEVOQUIN, MACROBID, MIRALAX, SPIRONOLACTONE, ZOCOR
Adverse Events (AE) Preferred term	1. Haematuria 2. Urinary tract infection 3. Haematuria 4. Diarrhoea 5. Constipation 6. Depression 7. Abdominal pain upper
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 15AUG2007 (1) - 26AUG2007 (12) 2. 15AUG2007 (1) - 09SEP2007 (26) 3. 25AUG2007 (11) - 25AUG2007 (11) 4. 26AUG2007 (12) - 07SEP2007 (24) 5. 07SEP2007 (24) - 14SEP2007 (31) 6. 07SEP2007 (24) - --------- (.) 7. 27NOV2007 (105) - 29NOV2007 (107)
Duration of AE	1. 12 2. 26 3. 1 4. 13 5. 8 6. . 7. 3
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 20 mg 6. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164012

Parameter	Value
	7. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164024

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140164024/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/87/WHITE/UNITED STATES/YES
Medical history	Hypertension, Diverticulum, Gastritis erosive, Glaucoma, Blood cholesterol increased, Haemorrhoids, Iron deficiency anaemia, Amnesia, Seasonal allergy, Subdural haematoma, Vertigo, Mycotic allergy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAZOLAMIDE, ARANESP, ASPIRIN, BENADRYL, CALCIUM +D, CLARITIN, COSOPT, HYDROCORTISON, KDUR, KLONOPIN WAFER, LASIX, LIPITOR, LORATADINE, MEDRODOSE PAK, MULTI-VITAMIN, NAMENDA, QUINAPRIL, SLOW FE (IRON), VITAMIN E, XALATAN
Adverse Events (AE) Preferred term	1. Faeces discoloured 2. Rash 3. Anaemia 4. Gastrointestinal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/YES/NO/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 22JUL2008 (23) - 05AUG2008 (37) 2. 09SEP2008 (72) - 15SEP2008 (78) 3. 29SEP2008 (92) - 29OCT2008 (122) 4. 29SEP2008 (92) - 20OCT2008 (113)
Duration of AE	1. 15 2. 7 3. 31 4. 22
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164024

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-140164024[2)]	GASTROINTESTINAL BLEED（PT：胃腸出血） 治験担当医は、リバーロキサバン投与中止後も事象が継続していることから、因果関係は否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164029

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140164029/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/39/HISPANIC/UNITED STATES/YES
Medical history	Asthma, Bartholin's cyst, Hypertension, Diabetes mellitus, Myocardial infarction, Hypocalcaemia, Iron deficiency anaemia, Thrombophlebitis superficial, Uterine leiomyoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTOPLUS, ALBUTEROL, ATIVAN, BENADRYL, IRON DEXTRAN, LIPITOR, LISINOPRIL, METFORMIN, METOPROLOL, NIFEREX, NITROFURANTOIN MONO/MAC, PLAVIX, SOLU MEDROL, SYNTHROID, TAGAMET, TYLENOL [PSUEDOEPHEDRINE + PARACETAMOL], ZANTAC
Adverse Events (AE) Preferred term	1. Menstruation irregular 2. Dyspnoea 3. Fatigue 4. Iron deficiency 5. Anaemia 6. Escherichia urinary tract infection 7. Drug hypersensitivity 8. Hypothyroidism 9. Anaemia 10. Uterine leiomyoma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/NO/YES 9. SEVERE/YES/YES/YES 10. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 25JUL2008 (2) - 01AUG2008 (9) 2. 25JUL2008 (2) - 01AUG2008 (9) 3. 25JUL2008 (2) - 01AUG2008 (9) 4. 31JUL2008 (8) - --------- (.) 5. 31JUL2008 (8) - --------- (.) 6. 06AUG2008 (14) - 20AUG2008 (28) 7. 07AUG2008 (15) - 07AUG2008 (15) 8. 29OCT2008 (98) - --------- (.) 9. 30NOV2008 (130) - 02DEC2008 (132) 10. 04DEC2008 (134) - 04DEC2008 (134)
Duration of AE	1. 8 2. 8 3. 8 4. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164029

Parameter	Value
	5. .
	6. 15
	7. 1
	8. .
	9. 3
	10. 1
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. F
	10. F
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	10. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164029

Parameter	Value
	6. RESOLVED
	7. RESOLVED
	8. UNCHANGED
	9. RESOLVED
	10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164040

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140164040/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/48/HISPANIC/UNITED STATES/YES
Medical history	Anaemia, Anxiety, Cervix carcinoma, Depression, Increased appetite, Proctalgia, Insomnia, Pain, Pelvic exenteration, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMBIEN, BENADRYL, DURAGESIC, FENTANYL PATCH, HEPARIN, HYDROCODONE, MEGACE, MEPHYTON, MORPHINE SULFATE, NORCO 10/325, NOVOLIN R, PROTONIX, REGLAN, ROXANOL UD, TYLENOL [CHLORPHENAMINE + DEXTROMETHORPHAN + PARACETAMOL + PSEUDOEPHEDRINE], XANAX, ZOFRAN, ZOLOFT
Adverse Events (AE) Preferred term	1. Nausea 2. Vomiting 3. Cervix carcinoma 4. Pain 5. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 13JAN2009 (28) - --------- (.) 2. 13JAN2009 (28) - --------- (.) 3. 13JAN2009 (28) - 11FEB2009 (57) 4. 16JAN2009 (31) - 11FEB2009 (57) 5. 17JAN2009 (32) - 26JAN2009 (41)
Duration of AE	1. . 2. . 3. 30 4. 27 5. 10
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140164040

Parameter	Value
Outcome of event	4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 5. OTHER 1. UNCHANGED 2. UNCHANGED 3. DEATH 4. WORSENED 5. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140174004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140174004/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/48/WHITE/UNITED STATES/YES
Medical history	Pain in extremity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, CIPROFLOXACIN, IBUPROFEN, INDOCIN, MOTRIN IB
Adverse Events (AE) Preferred term	1. Back pain 2. Nasopharyngitis 3. Haemoptysis 4. Joint sprain 5. Skeletal injury 6. Clavicle fracture
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/NO 6. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 24DEC2007 (5) - 28DEC2007 (9) 2. 07JAN2008 (19) - 10JAN2008 (22) 3. 08JAN2008 (20) - 10JAN2008 (22) 4. 17JAN2008 (29) - 02FEB2008 (45) 5. 12APR2008 (115) - --------- (.) 6. 24APR2008 (127) - 25APR2008 (128)
Duration of AE	1. 5 2. 4 3. 3 4. 17 5. . 6. 2
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. F 6. F

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140174004

Parameter	Value
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140174012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140174012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/UNITED STATES/YES
Medical history	Cholecystectomy, Gastrooesophageal reflux disease, Mycosis fungoides
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AZITHROMYCIN, BENADRYL ALLERGY 25, CEFTAZIDIME, CEPHALEXIN, COLACE, COMPAZINE, DOCUSATE, DOXIL [DOXORUBICIN HYDROCHLORIDE], ENOXAPARIN, GEMCITABINE, ONTAK, PREDNISONE, PRILOSEC OTC, PROPXYPHEN, TRIAMCINOLONE, TYLENOL [ACETAMINOPHEN ALONE], VANCOMYCIN, WARFARIN, ZOFRAN
Adverse Events (AE) Preferred term	1. Device related infection 2. Pneumonia 3. Tooth abscess 4. Liver function test abnormal
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 23APR2009 (30) - 25APR2009 (32) 2. 25APR2009 (32) - 30APR2009 (37) 3. 18MAY2009 (55) - --JUN2009 (.) 4. 17JUL2009 (115) - 17AUG2009 (146)
Duration of AE	1. 3 2. 6 3. . 4. 32
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140174012

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140194003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/57/WHITE/UNITED STATES/YES
Medical history	Rhinitis allergic, Constipation, Ear infection, Epistaxis, Rash papular, Faeces discoloured, Dyspepsia, Hyponatraemia, Insomnia, Nausea, Oedema peripheral, Sinusitis, Vertigo, Vomiting, Anaemia, Head and neck cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	5 FU, ANTIVERT [MECLOZINE HCL (ANTIVERT)], ARANESP, AUGMENTIN, AVELOX, CALCIUM CARBONATE (TUMS), CARBOPLATIN, CISPLATIN, DECADRON, DOCETAXEL, DOXYCYCLINE, ERBITUX, HYDROCODONE, KYTRIL, LEVAQUIN, LODINE, MARINOL, MIRALAX, MUCINEX, NASONEX, NEULASTA, PRILOSEC, PROMETHAZINE, PROMETHAZINE HCL (PHENERGAN), REGLAN, UNASYN, VANCOMYCIN, VECTIBIX, VISTARIL, XELODA, ZOFRAN
Adverse Events (AE) Preferred term	1. Haemoglobin decreased 2. Increased upper airway secretion 3. Pyrexia 4. Dysphagia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07AUG2007 (7) - 13AUG2007 (13) 2. 06DEC2007 (128) - --------- (.) 3. 10JUL2008 (345) - 11JUL2008 (346) 4. 26JUL2008 (361) - 26JUL2008 (361)
Duration of AE	1. 7 2. . 3. 2 4. 1
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. F
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194003

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140194005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/46/BLACK/UNITED STATES/YES
Medical history	Abdominal pain, Anaemia, Asthma, Back pain, Hydronephrosis, Transfusion, Vision blurred, Cervix carcinoma, Dysuria, Rash papular, Headache, Haematuria, Hypertension, Insomnia, Nausea, Oedema peripheral, Arthralgia, Renal failure, Dyspnoea, Female sterilisation, Umbilical hernia, Vomiting, Hypoacusis, Ureteral stent insertion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUTEROL, AMBIEN, ARANESP, ATIVAN, BENADRYL CREAM 2%, CETUXIMAB, CISPLATIN, CLINDAMYCIN PHOSPHATE 1%, CLONIDINE HCL, COMPAZINE, LORTAB
Adverse Events (AE) Preferred term	1. Vaginal haemorrhage 2. Anaemia 3. Vaginal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MODERATE/YES/YES/YES 3. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 02SEP2007 (19) - 03SEP2007 (20) 2. 06SEP2007 (23) - 08SEP2007 (25) 3. 20SEP2007 (37) - 22SEP2007 (39)
Duration of AE	1. 2 2. 3 3. 3
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. NONE 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140194007/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/46/WHITE/UNITED STATES/YES
Medical history	Gastrooesophageal reflux disease, Anaemia, Vision blurred, Constipation, Depression, Diarrhoea, Dysuria, Vitreous floaters, Genital herpes, Hypertension, Hypothyroidism, Insomnia, Pain in extremity, Nausea, Palpitations, Radiotherapy, Proctalgia, Urinary tract infection, Rhinitis seasonal, Anal cancer, Tinnitus, Vulvovaginal discomfort, Bladder spasm, Radical hysterectomy, Haemorrhoidal haemorrhage
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMBIEN, CIPRO, COLACE, COMPAZINE, FLAGYL, GENTIAN VIOLET 1%, HYDROCHLOROTHIAZIDE, HYOSCYAMINE, IMODIUM [LOPERAMIDE HCL], KLOR-CON (POTASSIUM CHLORIDE), LASIX, LEVOTHYROXIN, LIDOCAINE HCL 2%, LISINOPRIL, LOMOTIL [ATROPINE SULFATE + DIPHENOXYLATE HCL], LOTREL, METOPROLOL, MORPHINE SULFATE, NEXIUM, PHENERGAN, POTASSIUM CHLORIDE (KCL), PRENATAL VITAMINS, PROCTOFOAM HC 1%, PROCTOSOL HC 2.5%, SENOKOT, TANDEM F, VALTREX, XENADERM, ZOFRAN, ZYRTEC [CETIRIZINE HCL]
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Clostridial infection
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 15DEC2007 (53) - 19DEC2007 (57) 2. 15DEC2007 (53) - 29DEC2007 (67)
Duration of AE	1. 5 2. 15
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140194012/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/51/WHITE/UNITED STATES/YES
Medical history	Blood alkaline phosphatase increased, Alanine aminotransferase increased, Anaemia, Aspartate aminotransferase increased, Back pain, Bronchitis, Dermatitis contact, Ear infection, Pyrexia, Blood glucose increased, Osteoarthritis, Headache, Hepatitis A, Hypokalaemia, Hyponatraemia, Pain in extremity, Menometrorrhagia, Palpitations, Sinusitis, Oedema peripheral, Tooth loss, Uterine leiomyoma, Seasonal allergy, Myopia, Poor personal hygiene
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXICILLIN, DARVOCET N-100, DIPHENHYDRAMINE, FLEXERIL, HYDROCHLOROTHIAZIDE, POTASSIUM CHLORIDE ER, PROVERA, SLOW FE, VITAMIN D, ZOFRAN, ZOSYN
Adverse Events (AE) Preferred term	1. Vaginal haemorrhage 2. Vitamin D deficiency 3. Bacteraemia 4. Hypokalaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12DEC2008 (116) - 01FEB2009 (167) 2. 22DEC2008 (126) - --------- (.) 3. 02JAN2009 (137) - 09FEB2009 (175) 4. 20JAN2009 (155) - --------- (.)
Duration of AE	1. 52 2. . 3. 39 4. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194012

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140194014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/40/WHITE/UNITED STATES/YES
Medical history	Gastrooesophageal reflux disease, Anaemia, Anxiety, Constipation, Headache, Hyperlipidaemia, Insomnia, Pain in extremity, Metrorrhagia, Squamous cell carcinoma of the cervix, Oedema peripheral, Denture wearer, Nicotine dependence, Myopia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, ALOXI, ATIVAN, CARBOPLATIN, COMPAZINE, CRESTOR, DEXAMETHASONE, DIPHENHYDRAMINE, DOCUSATE SODIUM, ENOXAPARIN, LUNESTA, OXYCODONE HCL/ACETAMINOPHEN, RANITIDINE, TAXOL, VITAMIN C, WARFARIN
Adverse Events (AE) Preferred term	1. Nausea 2. Vomiting 3. Vaginal haemorrhage 4. Mental status changes 5. Haematuria 6. Renal failure acute 7. International normalised ratio increased 8. Hydronephrosis 9. Fatigue 10. Cervix carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/NO 4. MODERATE/NO/NO/NO 5. MODERATE/NO/YES/NO 6. SEVERE/NO/YES/NO 7. MODERATE/NO/YES/NO 8. MODERATE/NO/YES/NO 9. MODERATE/NO/NO/NO 10. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 16OCT2008 (38) - 04DEC2008 (87) 2. 16OCT2008 (38) - 04DEC2008 (87) 3. 05JAN2009 (119) - 12JAN2009 (126) 4. 05JAN2009 (119) - --------- (.) 5. 06JAN2009 (120) - --------- (.) 6. 06JAN2009 (120) - 21FEB2009 (166) 7. 06JAN2009 (120) - 10JAN2009 (124) 8. 06JAN2009 (120) - 07JAN2009 (121) 9. 06JAN2009 (120) - --------- (.) 10. 05MAR2009 (178) - 12MAR2009 (185)
Duration of AE	1. 50 2. 50 3. 8

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194014

Parameter	Value
	4. .
	5. .
	6. 47
	7. 5
	8. 2
	9. .
	10. 8
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. NONE
	10. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140194014

Parameter	Value
	5. IMPROVED 6. RESOLVED 7. RESOLVED 8. RESOLVED 9. UNCHANGED 10. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-140194014[2),2),2)]	ELEVATED LAB VALUE: INR（PT：国際標準比増加） 治験担当医は、合併症（末期子宮頸部癌）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。 HEMATURIA（PT：血尿） 治験担当医は、合併症（末期子宮頸部癌）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。 VAGINAL BLEEDING, INCREASED（PT：腟出血） 治験担当医は、合併症（末期子宮頸部癌）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140204002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140204002/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/UNITED STATES/YES
Medical history	Gastrooesophageal reflux disease, Anxiety, Asthma, Cellulitis, Chronic obstructive pulmonary disease, Colon cancer, Electrolyte imbalance, Blood cholesterol increased, Hysterectomy, Neuropathy peripheral, Epistaxis, Vitamin B12 deficiency, Hypersensitivity, Colectomy, Hernia repair, Gastrooesophageal reflux disease, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADJUVANT-5FU, ADVAIR, ALBUTEROL NEBULIZER, CALCIUM CARBONATE WITH VIT. D, DECADRON, DIPHENHYDRAMINE, FLONASE, HEPARIN, HUMALOG, K-DUR, LANTUS, LASIX, LEUCOVORIN, LOPERAMIDE HCL, LORCET, MAGNESIUM GLUCONATE, MERREM, METFORMIN, MULTI-VITAMIN, NOVOLOG, PEPTO-BISMOL, PERCOCET, PROTONIX, SINGULAIR, TRICOR, VANCOMYCIN, VITAMIN B-12, XANAX, ZITHROMAX, ZOFRAN
Adverse Events (AE) Preferred term	1. Pain 2. Paraesthesia 3. Somnolence 4. Arthralgia 5. Pyrexia 6. Diarrhoea 7. Cellulitis 8. Hypersensitivity 9. Asthma 10. Nasopharyngitis 11. Abdominal pain 12. Nausea
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. SEVERE/NO/YES/YES 8. MODERATE/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MODERATE/NO/NO/YES 11. SEVERE/NO/NO/NO 12. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 02AUG2007 (11) - 08AUG2007 (17) 2. 02AUG2007 (11) - 08AUG2007 (17) 3. 02AUG2007 (11) - 08AUG2007 (17) 4. 05AUG2007 (14) - 05AUG2007 (14) 5. 07AUG2007 (16) - 09AUG2007 (18) 6. 07AUG2007 (16) - 08AUG2007 (17) 7. 08AUG2007 (17) - 23AUG2007 (32)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140204002

Parameter	Value
	8. 08AUG2007 (17) - 09AUG2007 (18)
	9. 12OCT2007 (82) - 31OCT2007 (101)
	10. 24OCT2007 (94) - 31OCT2007 (101)
	11. 10FEB2008 (203) - --------- (.)
	12. 10FEB2008 (203) - 11FEB2008 (204)
Duration of AE	1. 7
	2. 7
	3. 7
	4. 1
	5. 3
	6. 2
	7. 16
	8. 2
	9. 20
	10. 8
	11. .
	12. 2
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 15 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. I
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. F
	12. F

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140204002

Parameter	Value
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
	2. STUDY DRUG DISCONTINUED AND RESTARTED
	3. STUDY DRUG DISCONTINUED AND RESTARTED
	4. NONE
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. NONE
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. UNCHANGED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140204035

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140204035/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/UNITED STATES/YES
Medical history	Arthralgia, Gastrooesophageal reflux disease, Hyperlipidaemia, Hysterectomy, Knee arthroplasty, Nausea, Osteoarthritis, Caesarean section
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, COLACE, DARVOCET, DILAUDID, FAMOTIDINE, FERROUS SULFATE, IMODIUM, MORPHINE SULFATE, MULTI-VITAMIN, NEURONTIN, VITAMIN B COMPLEX, VITAMIN D
Adverse Events (AE) Preferred term	1. Joint range of motion decreased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 17MAR2009 (61) - 18MAR2009 (62)
Duration of AE	1. 2
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140314005/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/55/WHITE/UNITED STATES/YES
Medical history	Anxiety, Arthroscopy, Asthma, Cholecystectomy, Depression, Diabetes mellitus, Hepatic steatosis, Hypercholesterolaemia, Hypertension, Hypothyroidism, Hysterectomy, Insomnia, Leukocytosis, Obesity, Osteoarthritis, Pneumonia, Restless legs syndrome, Varicose vein, Thyroidectomy, Thyroid cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATIVAN, ATROVENT, BACTRIM DS, BENADRYL [DIPHENHYDRAMINE HYDROCHLORIDE], CELEBREX, DECADRON, ENOXAPARIN, LORTAB [HYDROCODONE BITARTRATE], MORPHINE, PERCOCET, PREDNISONE, PREVACID, RACEMIC EPINEPHRINE, ROCEPHIN, SINGULAIR, SOLUMEDROL, SYNTHROID, UNASYN, VALIUM [DIAZEPAM ALONE], VERAMYST, WARFARIN
Adverse Events (AE) Preferred term	1. Oropharyngeal pain 2. Epiglottitis 3. Ocular hyperaemia 4. Rhinorrhoea 5. Gastroenteritis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 20OCT2007 (65) - 24OCT2007 (69) 2. 24OCT2007 (69) - 26OCT2007 (71) 3. 15NOV2007 (91) - 11DEC2007 (117) 4. 15NOV2007 (91) - 18FEB2008 (186) 5. 03DEC2007 (109) - 06DEC2007 (112)
Duration of AE	1. 5 2. 3 3. 27 4. 96 5. 4
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314005

Parameter	Value
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
Outcome of event	1. WORSENED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140314012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/67/WHITE/UNITED STATES/YES
Medical history	Anaemia, Asthma, Epistaxis, Fatigue, Goitre, Hiatus hernia, Hypercalcaemia, Hypertension, Peripheral vascular disorder, Renal failure, Splenectomy, Thyroidectomy, Aneurysm repair, Oesophageal dilatation, Cough
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, METOPROLOL, NORVASC, SYNTHROID, WARFARIN
Adverse Events (AE) Preferred term	1. Sepsis 2. Intestinal ischaemia 3. Gastric ulcer perforation 4. Post procedural haemorrhage 5. Thrombocytopenia 6. Liver function test abnormal 7. Gastrointestinal necrosis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/YES/NO 5. MODERATE/NO/NO/NO 6. MODERATE/NO/NO/NO 7. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 04MAR2008 (6) - 21MAR2008 (23) 2. 08MAR2008 (10) - 15MAR2008 (17) 3. 08MAR2008 (10) - 08MAR2008 (10) 4. 12MAR2008 (14) - 13MAR2008 (15) 5. 12MAR2008 (14) - --------- (.) 6. 13MAR2008 (15) - --------- (.) 7. 15MAR2008 (17) - --------- (.)
Duration of AE	1. 18 2. 8 3. 1 4. 2 5. . 6. . 7. .
Dose on AE onset	1. 2. 3. 4. 5. 6. 7.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314012

Parameter	Value
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	2. OTHER
	3. NONE
	4. OTHER
	5. OTHER
	6. NONE
	7. NONE
Outcome of event	1. DEATH
	2. WORSENED
	3. RESOLVED
	4. RESOLVED
	5. IMPROVED
	6. UNCHANGED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140314013/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/51/WHITE/UNITED STATES/YES
Medical history	Appendicectomy, Intestinal obstruction, Cerebrovascular accident, Cholecystectomy, Depression, Diarrhoea, Headache, Hysterectomy, Tobacco abuse, Tuberculin test positive, Uterine cancer, Contrast media allergy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, IBUPROFEN, LEXAPRO, LOVENOX, MORPHINE, VALIUM, WARFARIN
Adverse Events (AE) Preferred term	1. Small intestinal obstruction 2. Wrist fracture 3. Pelvic fracture 4. Pelvic pain 5. Hypertension
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/YES/NO 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 28MAR2009 (313) - 31MAR2009 (316) 2. 13MAY2009 (359) - 14MAY2009 (360) 3. 13MAY2009 (359) - 01JUL2009 (408) 4. 21MAY2009 (367) - 22MAY2009 (368) 5. 21MAY2009 (367) - --------- (.)
Duration of AE	1. 4 2. 2 3. 50 4. 2 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY 5. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314013

Parameter	Value
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED 4. RESOLVED 5. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-140314013[4)]	SMALL BOWEL OBSTRUCTION（PT：小腸閉塞） 治験担当医はエノキサパリンとの因果関係評価を行っていない。弊社は小腸閉塞の既往歴があるため、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314032

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140314032/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/53/WHITE/UNITED STATES/YES
Medical history	Arthralgia, Asthma, Carpal tunnel syndrome, Drug hypersensitivity, Eczema, Hepatitis C, Hypertension, Insomnia, Oedema peripheral, Muscular weakness, Nephrolithiasis, Neutropenia, Peptic ulcer, Serum ferritin increased, Dyspnoea, Thrombocytopenia, Hypoaesthesia, Meniscus lesion, Bowel movement irregularity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMBIEN, CARAFATE, DURAGESIC PATCH, ENOXAPARIN, FLAGYL, HYDROCORTISONE CREAM, HYDROMORPHONE, LEVAQUIN, LISINOPRIL, MORPHINE, MULTIVITAMIN, PEGASYS, RIBAVIRIN, TYLENOL [ACETAMINOPHEN ONLY], WARFARIN, ZOFRAN, ZOSYN
Adverse Events (AE) Preferred term	1. Back pain 2. Abdominal pain 3. Nausea
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 18AUG2009 (21) - 02SEP2009 (36) 2. 18AUG2009 (21) - 20AUG2009 (23) 3. 18AUG2009 (21) - 19AUG2009 (22)
Duration of AE	1. 16 2. 3 3. 2
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140314033

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140314033/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/35/WHITE/UNITED STATES/YES
Medical history	Abdominal pain, Anaemia, Depression, Diabetes mellitus, Duodenal ulcer, Oesophageal ulcer, Hiatus hernia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARAFATE, DILAUDID, HUMALOG, LEVEMIR, LEXAPRO, PHENERGAN, REGLAN, REGULAR INSULIN, ZOFRAN
Adverse Events (AE) Preferred term	1. Diabetic ketoacidosis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 19SEP2009 (24) - 21SEP2009 (26)
Duration of AE	1. 3
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140324005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140324005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/83/WHITE/UNITED STATES/YES
Medical history	Rhinitis allergic, Anxiety, Asthma, Bronchitis, Chronic obstructive pulmonary disease, Depression, Foot fracture, Glaucoma, Hyperlipidaemia, Hypertension, Insomnia, Muscle spasms, Nephrolithiasis, Osteoporosis, Pneumonia, Restless legs syndrome, Transient ischaemic attack, Urinary incontinence, Gastrooesophageal reflux disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADVAIR, AMBIEN, AVELOX, BONIVA, COZAAR, DETROL LA, HYDROCHLOROTHIAZIDE, IPRATROPIUM NEBULIZER, MOTRIN, MUCINEX, MULTIVITAMIN, NORVASC, PEPCID [FAMOTIDINE], PREMARIN [ESTROGENS CONJUGATED], QUININE SULFATE, REQUIP, SOLUMEDROL, XALATAN, XANAX, XOPENEX, ZOCOR, ZOLOFT
Adverse Events (AE) Preferred term	1. Chronic obstructive pulmonary disease
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 29FEB2008 (126) - 05MAR2008 (131)
Duration of AE	1. 6
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140324031

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140324031/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/87/WHITE/UNITED STATES/YES
Medical history	Anaemia, Drug hypersensitivity, Hip arthroplasty, Hypertension, Irritable bowel syndrome, Menopause, Knee arthroplasty, Knee arthroplasty, Osteoarthritis, Hypoacusis, Anxiety disorder, Major depression, Gastrooesophageal reflux disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	5%DEXTROSE/.45% SALINE, ALBUTEROL, AMLODIPINE, ATIVAN, ATROVENT, BENTYL, CALCIUM, CALCIUM GLUCONATE, CEFEPIME, CIPRO, CLONAZEPAM, DARVOCET, DIFLUCAN, DOPAMINE, EFFEXOR XR, ENOXAPARIN, FENTANYL, FERROUS SULFATE, FIBERCON, HALDOL, HYDRALAZINE, HYDROCHLORTHIAZIDE, K-DUR, LASIX, LEVOPHED, LISINOPRIL, LOPRESSOR, MAGNESIUM SULFATE, METHYLPREDNISOLONE, MULTIVITAMIN, NORMAL SALINE, PROTONIX, REMERON, SODIUM BICARBONATE, SOLUCORTEF, VANCOMYCIN, VITAMIN K, WARFARIN, ZOFRAN
Adverse Events (AE) Preferred term	1. Gastroenteritis 2. Pneumonia 3. Renal failure 4. Sepsis 5. Dehydration 6. Acute respiratory failure 7. Confusional state 8. Electrolyte imbalance 9. Septic shock 10. Hypotension 11. Anuria 12. Back pain 13. Acidosis 14. Gait disturbance 15. Hypokalaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/NO/YES 4. SEVERE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MODERATE/NO/NO/YES 8. SEVERE/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MODERATE/NO/NO/YES 11. MILD/NO/NO/YES 12. MODERATE/NO/NO/YES 13. MODERATE/NO/NO/YES 14. MODERATE/NO/NO/YES 15. MODERATE/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140324031

Parameter	Value
Start/stop date of event with relative date	1. 06DEC2008 (68) - 19DEC2008 (81) 2. 08DEC2008 (70) - 19DEC2008 (81) 3. 08DEC2008 (70) - 19DEC2008 (81) 4. 08DEC2008 (70) - 19DEC2008 (81) 5. 08DEC2008 (70) - 09DEC2008 (71) 6. 08DEC2008 (70) - 19DEC2008 (81) 7. 09DEC2008 (71) - 19DEC2008 (81) 8. 09DEC2008 (71) - 19DEC2008 (81) 9. 09DEC2008 (71) - 19DEC2008 (81) 10. 09DEC2008 (71) - 19DEC2008 (81) 11. 09DEC2008 (71) - 12DEC2008 (74) 12. 09DEC2008 (71) - 19DEC2008 (81) 13. 09DEC2008 (71) - 12DEC2008 (74) 14. 10DEC2008 (72) - 27DEC2008 (89) 15. 12DEC2008 (74) - 18DEC2008 (80)
Duration of AE	1. 14 2. 12 3. 12 4. 12 5. 2 6. 12 7. 11 8. 11 9. 11 10. 11 11. 4 12. 11 13. 4 14. 18 15. 7
Dose on AE onset	1. 2. 3. 4. 5. 6. 7. 8. 9. 10. 11.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140324031

Parameter	Value
	12.
	13.
	14.
	15.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED AND RESTARTED
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	8. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	10. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	11. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	12. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	13. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	14. NONE
	15. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140324031

Parameter	Value
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. RESOLVED
	15. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140374008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140374008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/85/HISPANIC/UNITED STATES/YES
Medical history	Bronchitis, Anxiety, Cardiac failure congestive, Gastrooesophageal reflux disease, Gout, Procedural headache, Hyperlipidaemia, Hypertension, Hypokalaemia, Hypothyroidism, Hysterectomy, Menopause, Pituitary tumour removal, Rash, Glucose tolerance impaired
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, ALBUTEROL, ASPIRIN, ATENOLOL, DOCUSATE SODIUM, ENOXAPARIN, FAMOTIDINE, HYDROCODONE, HYDROCORTISONE, LASIX, LEVOFLOXACIN, LEVOTHYROXINE, LORAZEPAM, MICONAZOLE 2%, MILK OF MAGNESIA, NITROGLYCERIN, POTASSIUM CHLORIDE, PROMETHAZINE, REGULAR INSULIN, SIMVASTATIN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Haematoma 2. International normalised ratio increased
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 13MAR2008 (19) - 07APR2008 (44) 2. 13MAR2008 (19) - 15MAR2008 (21)
Duration of AE	1. 26 2. 3
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140374037

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140374037/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/51/ASIAN/UNITED STATES/YES
Medical history	Anaemia, Back pain, Cholecystectomy, Cholelithiasis, Hepatic enzyme increased, Renal fusion anomaly, Colitis ulcerative, Abdominal pain, Gastrooesophageal reflux disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, LIALDA, WARFARIN
Adverse Events (AE) Preferred term	1. Blood alkaline phosphatase increased 2. Lower gastrointestinal haemorrhage 3. Nausea 4. Pyrexia 5. Hypokalaemia 6. Haemorrhagic anaemia 7. Sepsis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/YES/NO 3. MILD/NO/NO/NO 4. MILD/NO/NO/NO 5. MILD/NO/NO/NO 6. MODERATE/YES/NO/NO 7. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 30APR2009 (20) - --------- (.) 2. 29JUN2009 (80) - 01JUL2009 (82) 3. 29JUN2009 (80) - 01JUL2009 (82) 4. 29JUN2009 (80) - 01JUL2009 (82) 5. 29JUN2009 (80) - 01JUL2009 (82) 6. 29JUN2009 (80) - 01JUL2009 (82) 7. 29JUN2009 (80) - 01JUL2009 (82)
Duration of AE	1. . 2. 3 3. 3 4. 3 5. 3 6. 3 7. 3
Dose on AE onset	1. 2. 3. 4. 5. 6. 7.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140374037

Parameter	Value
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140414003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140414003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/68/WHITE/UNITED STATES/YES
Medical history	Catheterisation cardiac, Cholecystectomy, Coagulation factor VII level decreased, Dehydration, Diabetes mellitus, Hypertension, Knee arthroplasty, Oedema peripheral, Spinal column stenosis, Splenic abscess, Caesarean section, Vena cava filter insertion, Radical hysterectomy, Uterine dilation and curettage, Uterine dilation and curettage, Hernia repair, Urinary retention postoperative, Sticky platelet syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACCUPRIL, AMOXICILIN, ASPIRIN, ENOXAPARIN, FOLTX VITAMIN, GLUCOPHAGE, HEPARIN, NEURONTIN, NOVOLIN R INSULIN, OXYCODONE + ACETAMINOPHEN, SENOKOT-S, TENORETIC, UNFRACTIONATED HEPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Renal failure acute 2. Contusion 3. Constipation 4. Rash 5. Cough
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 22NOV2008 (2) - 24NOV2008 (4) 2. 22NOV2008 (2) - 31DEC2008 (41) 3. 24NOV2008 (4) - 24NOV2008 (4) 4. 06DEC2008 (16) - 04FEB2009 (76) 5. 30DEC2008 (40) - 13JAN2009 (54)
Duration of AE	1. 3 2. 40 3. 1 4. 61 5. 15
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY 2. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140414003

Parameter	Value
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140424011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/140424011/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/84/WHITE/UNITED STATES/YES
Medical history	Breast cancer, Chronic obstructive pulmonary disease, Gastrooesophageal reflux disease, Essential tremor, Osteoarthritis, Osteoporosis, Peripheral vascular disorder, Spinal column stenosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADVAIR, ASPIRIN, FOSAMAX, INDERAL, LETROZOLE, POTASSIUM, PREDNISONE, SPIRIVA
Adverse Events (AE) Preferred term	1. Humerus fracture 2. Ecchymosis 3. Facial bones fracture 4. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/YES/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 05NOV2008 (7) - 08DEC2008 (40) 2. 05NOV2008 (7) - 08DEC2008 (40) 3. 05NOV2008 (7) - 08DEC2008 (40) 4. 05NOV2008 (7) - 12NOV2008 (14)
Duration of AE	1. 34 2. 34 3. 34 4. 8
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 2. STUDY DRUG DISCONTINUED PERMANENTLY 3. STUDY DRUG DISCONTINUED PERMANENTLY 4. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 140424011

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160014003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160014003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/78/N.A./FRANCE/YES
Medical history	Appendicectomy, Benign prostatic hyperplasia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	EFFERALGAN, INIPOMP, OFLOXACINE, OMIX LP, OXYBUTYNINE
Adverse Events (AE) Preferred term	1. Urinary retention 2. Bladder catheter removal 3. Urinary tract infection 4. Haematuria 5. Haematuria 6. Abdominal pain upper 7. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/YES/NO/YES 5. MILD/YES/NO/YES 6. MILD/NO/NO/YES 7. MILD/YES/NO/NO
Start/stop date of event with relative date	1. 05SEP2007 (28) - 05SEP2007 (28) 2. 07SEP2007 (30) - 08SEP2007 (31) 3. 20SEP2007 (43) - 04MAR2008 (209) 4. 05NOV2007 (89) - 05NOV2007 (89) 5. 12NOV2007 (96) - 12NOV2007 (96) 6. 25NOV2007 (109) - 26NOV2007 (110) 7. 04APR2008 (240) - 20APR2008 (256)
Duration of AE	1. 1 2. 2 3. 167 4. 1 5. 1 6. 2 7. 17
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160014003

Parameter	Value
	2. .
	3. .
	4. .
	5. .
	6. .
	7. F
Action taken	1. OTHER
	2. OTHER
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160014038

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160014038/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/70/N.A./FRANCE/YES
Medical history	Anxiety, Hypertension, Mitral valve incompetence, Glucose tolerance impaired, Bundle branch block right, Intestinal polyp, Osteoarthritis, Dyslipidaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APROVEL, ARIXTRA, CLAMOXYL, COLOPEG, DAFALGAN, DOLIPRANE, EZETROL, GENTALLINE, HEPARINE, IMMUCYST, IXPRIM, LIPANTHYL, LOVENOX, NORMACOL, XANAX
Adverse Events (AE) Preferred term	1. Back pain 2. Sciatica 3. Bladder cancer 4. Hypersensitivity 5. Rectal polyp 6. Pain in extremity 7. Post procedural haematuria 8. Post procedural haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/YES/YES 6. MILD/NO/NO/YES 7. MILD/YES/NO/YES 8. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 27SEP2008 (3) - 03OCT2008 (9) 2. 27SEP2008 (3) - 29SEP2008 (5) 3. 03OCT2008 (9) - 05MAR2009 (162) 4. 09OCT2008 (15) - 24OCT2008 (30) 5. 23OCT2008 (29) - 23OCT2008 (29) 6. 30OCT2008 (36) - 31OCT2008 (37) 7. 24DEC2008 (91) - 30DEC2008 (97) 8. 11JAN2009 (109) - 12JAN2009 (110)
Duration of AE	1. 7 2. 3 3. 154 4. 16 5. 1 6. 2 7. 7 8. 2
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160014038

Parameter	Value
	4. 15 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. I
	6. .
	7. I
	8. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. OTHER
	5. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	6. NONE
	7. NONE
	8. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160014055

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160014055/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/41/N.A./FRANCE/YES
Medical history	Depression, Hypercholesterolaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, ELUDRIL [ELUDRIL CONTAIN CHLORHEXIDINE AND CHLOROBUTANOL.], ENOXAPARIN, FENOFIBRATE, INIPOMP, IXPRIM, SEROPRAM, TERCIAN, TRANXENE, WARFARIN
Adverse Events (AE) Preferred term	1. Injection site haematoma 2. Tooth infection 3. Depression
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 30JAN2009 (3) - 10FEB2009 (14) 2. 10JUN2009 (134) - 30JUN2009 (154) 3. 26JUN2009 (150) - 11AUG2009 (196)
Duration of AE	1. 12 2. 21 3. 47
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160014061

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160014061/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/79/N.A./FRANCE/YES
Medical history	Diabetes mellitus, Hypertension, Osteoporosis, Venous insufficiency, Dyslipidaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARIMIDEX, ATACAND [ATACAND ACTIF INGREDIENT IS CANDESARTAN ALONE], DAFFALGAN, ELISOR, NOVONORM
Adverse Events (AE) Preferred term	1. Breast cancer 2. Procedural pain
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 04MAY2009 (42) - --------- (.) 2. 07MAY2009 (45) - 10MAY2009 (48)
Duration of AE	1. . 2. 4
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. I 2. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160054002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160054002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/N.A./FRANCE/YES
Medical history	Benign prostatic hyperplasia, Intracranial aneurysm, Cerebrovascular accident, Vascular operation, Intervertebral disc protrusion, Peripheral ischaemia, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BIPROFENID, ENOXAPARIN, ILOMEDINE, INEXIUM, KARDEGIC [ACETYLSALYCILATE LYSINE], LASILIX, MICROLAX [SORBITOL, CITRATE OF SODIUM & LAURYLSULFOAC?TATE OF SODIUM], NORMACOL [GOMME DE STERCULIA], PARACETAMOL, PERFALGAN, PERMIXON, PLAVIX, PRIMPERAN, WARFARIN, XATRAL
Adverse Events (AE) Preferred term	1. Constipation 2. International normalised ratio fluctuation 3. Peripheral ischaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/YES/YES 3. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 16FEB2008 (22) - 18FEB2008 (24) 2. 20MAR2008 (55) - 21MAR2008 (56) 3. 16DEC2008 (326) - --------- (.)
Duration of AE	1. 3 2. 2 3. .
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-160054002[4)]	INR NOT STABILIZED（PT：国際標準比変動） 治験担当医はエノキサパリンと報告事象の因果関係評価を行なっていない。弊社は、ワルファリンの用量を増量することで回復したことから、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160074003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160074003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/40/N.A./FRANCE/YES
Medical history	Depression, Hypothyroidism, Female sterilisation, Headache
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DOLIPRANE, ENOXAPARIN, INNOHEP, LEVOTHYROX, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. International normalised ratio increased 2. International normalised ratio increased 3. Haematoma 4. Joint sprain 5. International normalised ratio decreased
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MILD/YES/YES/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 20DEC2007 (15) - 02JAN2008 (28) 2. 02JAN2008 (28) - 07JAN2008 (33) 3. 02JAN2008 (28) - 29JAN2008 (55) 4. 11MAR2008 (97) - 15APR2008 (132) 5. 06MAY2008 (153) - 10MAY2008 (157)
Duration of AE	1. 14 2. 6 3. 28 4. 36 5. 5
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. DOSE OF STUDY DRUG REDUCED 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. WORSENED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160074003

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160104010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/46/N.A./FRANCE/YES
Medical history	Renal cell carcinoma, Anaemia, Depression, Nephrectomy, Vena cava thrombosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACUPAN, DEPAKOTE, ENOXAPARIN, LASILIX 20, PERFALGAN, SEROPLEX, TARDYFERON, WARFARIN
Adverse Events (AE) Preferred term	1. Epistaxis 2. Renal cell carcinoma recurrent 3. Splenic haemorrhage 4. Incision site abscess
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/NO/YES/YES 3. SEVERE/NO/YES/NO 4. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 19JUN2008 (95) - 19JUN2008 (95) 2. 19SEP2008 (187) - --------- (.) 3. 11NOV2008 (240) - 12NOV2008 (241) 4. 29JAN2009 (319) - 18FEB2009 (339)
Duration of AE	1. 1 2. . 3. 2 4. 21
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. DOSE OF STUDY DRUG REDUCED 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 3. OTHER 4. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. WORSENED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104010

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160104015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/56/N.A./FRANCE/YES
Medical history	Anxiety, Cholecystectomy, Hypertension, Lung neoplasm malignant, Myocardial infarction, Cerebrovascular accident, Restrictive pulmonary disease, Dyslipidaemia, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADANCOR, ATROVENT, AUGMENTIN, BRICANYL, CIFLOX, CORVASAL, DERMOVAL [CLOBETASOL PROPIONATE], DIPROSONE, DOLIPRANE 1000, ENOXAPARIN, FORLAX, INEXIUM, ISOPTINE LP 120, IXPRIM 37,5 MG/325 MG, KETODERM, LEXOMIL, LYSANXIA, MICROLAX [SODIUM CITRATE + SODIUM LAURYL SULFOACETATE + SORBITOL], NAABACK [ACIDE N-ACETYL ASPARTYL GLUTAMIQUE,SEL DE SODIUM], NICOPATCH, NOCTAMIDE, NOCTRAN, PRAVASTATINE, SECTRAL, SINGULAIR, SPIRIVA, TORENTALL LP 400, VASTAREL, VASTEN, WARFARIN, XYZAL
Adverse Events (AE) Preferred term	1. Chest X-ray abnormal 2. Eczema 3. Insomnia 4. Haemoptysis 5. Brain injury 6. Weight decreased 7. Constipation 8. Pneumonia bacterial 9. Liver function test abnormal
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. SEVERE/NO/YES/YES 9. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 03FEB2009 (22) - --------- (.) 2. 02APR2009 (80) - --------- (.) 3. 25MAY2009 (133) - 23OCT2009 (284) 4. 09OCT2009 (270) - 15OCT2009 (276) 5. 13OCT2009 (274) - --OCT2009 (.) 6. 13NOV2009 (305) - --------- (.) 7. 13NOV2009 (305) - 06DEC2009 (328) 8. 21NOV2009 (313) - 22DEC2009 (344) 9. 21NOV2009 (313) - 25NOV2009 (317)
Duration of AE	1. . 2. . 3. 152 4. 7

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104015

Parameter	Value
	5. .
	6. .
	7. 24
	8. 32
	9. 5
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. OTHER
	7. REMEDIAL DRUG THERAPY
	8. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	9. NONE
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED
	8. DEATH

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104015

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-160104015[2)]	ELEVATED LIVER FUNCTION TEST（PT：肝機能検査異常） 治験担当医は、肺炎治療中の偶発症であり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160104020/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/58/N.A./FRANCE/YES
Medical history	Breast neoplasm, Cholecystectomy, Mastectomy, Menopause, Nephrectomy, Obesity, Oophorectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTISKENAN, ACUPAN, ATARAX, BROMAZEPAM, CYMBALTA, CYTEAL, DOLIPRANE, DUROGESIC 75 MCG/H, ENDOTHELON, FUCIDINE CREAM, LYRICA, MOPRAL, NORMACOL, ORBENINE, OXYGEN, PERFALGAN, PULMICORT, RELISTOR, SOLUMEDROL, SPASFON, TAVANIC, TELFAST, TETRAZEPAM, TRIMEBUTINE, ZOLPIDEM
Adverse Events (AE) Preferred term	1. Bronchitis 2. Rectal haemorrhage 3. Staphylococcal skin infection 4. Chest pain 5. Abdominal pain 6. Pleural effusion 7. Metastases to liver
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/YES/YES 5. SEVERE/NO/NO/YES 6. MILD/NO/YES/YES 7. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 11MAR2009 (3) - 18MAR2009 (10) 2. 04APR2009 (27) - 04APR2009 (27) 3. 05AUG2009 (150) - --------- (.) 4. 21AUG2009 (166) - 31AUG2009 (176) 5. 12OCT2009 (218) - --------- (.) 6. 13OCT2009 (219) - --------- (.) 7. 09NOV2009 (246) - 08DEC2009 (275)
Duration of AE	1. 8 2. 1 3. . 4. 11 5. . 6. . 7. 30
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160104020

Parameter	Value
	7. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	7. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. INSUFFICIENT FOLLOW-UP
	4. RESOLVED
	5. UNCHANGED
	6. UNCHANGED
	7. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160124008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160124008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/81/N.A./FRANCE/YES
Medical history	Arrhythmia, Diabetes mellitus, Prostatic adenoma, Cerebrovascular accident, Colorectal cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CYMBALTA, FLECAINE, HEPARINE, INEXIUM, LEVEMIR PENFILL, MOVICOL, NAFTIDROFURYL, NOVORAPID, OMIX, PLAVIX
Adverse Events (AE) Preferred term	1. Syncope 2. Subileus 3. Urinary tract infection
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/NO 3. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 29MAY2008 (4) - 29MAY2008 (4) 2. 04JUN2008 (10) - 05JUN2008 (11) 3. 05JUN2008 (11) - 24JUN2008 (30)
Duration of AE	1. 1 2. 2 3. 20
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg
Dose status on AE onset	1. . 2. F 3. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160124014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160124014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/58/N.A./FRANCE/YES
Medical history	Hypertension, Skin necrosis, Diabetes mellitus, Erysipelas, Hypercholesterolaemia, Obesity, Hypokalaemia, Sleep apnoea syndrome, Myocardial ischaemia, Skin ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMOXICILLINE, ASPEGIC, CONTRAMAL, CORDIPATCH, DIFFU-K, ENOXAPARIN, FORZAR, JANUVIA, LYRICA, METFORMINE, NOVONORM, TAHOR
Adverse Events (AE) Preferred term	1. Rotator cuff syndrome 2. Arterial haemorrhage 3. Oedema 4. Joint sprain 5. Arthralgia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 18DEC2008 (3) - 29JUN2009 (196) 2. 03JAN2009 (19) - 03JAN2009 (19) 3. 19JAN2009 (35) - --FEB2009 (.) 4. 06APR2009 (112) - 18APR2009 (124) 5. 15JUN2009 (182) - --------- (.)
Duration of AE	1. 194 2. 1 3. . 4. 13 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. OTHER 2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 3. NONE 4. NONE 5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160124014

Parameter	Value
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED 4. RESOLVED 5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-160124014[2)]	BLEEDING ARTERIOLE（PT：潰瘍性出血） 治験担当医は、合併症（脚潰瘍）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160124020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160124020/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/76/N.A./FRANCE/YES
Medical history	Alcoholism, Blindness unilateral, Depression, Diabetes mellitus, Erysipelas, Fibula fracture, Glaucoma, Menopause, Obesity, Osteoporosis, Polyneuropathy, Colitis ulcerative, Macular degeneration
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APRIDA, BETNESOL, CACIT VITAMINE D3, CARTRABACK [CARTEOLOL], DAFALGAN, EVISTA, HUMIRA, IMUREL, INEXIUM, LANTUS, LAROXYL, LASILIX, LYRICA, NOVONORM, OFLOCET, PENTASA, SKENAN, SMECTA [DIOSMECTITE], SOLUPRED, VITAMINE B1 B6
Adverse Events (AE) Preferred term	1. Oedema 2. Oedema peripheral 3. Hypoalbuminaemia 4. Anaemia 5. Urinary tract infection 6. Colitis ulcerative 7. Anaemia 8. Melaena
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. SEVERE/NO/YES/YES 7. SEVERE/YES/YES/YES 8. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 08SEP2009 (14) - 13SEP2009 (19) 2. 14SEP2009 (20) - 25SEP2009 (31) 3. 14SEP2009 (20) - 25SEP2009 (31) 4. 15SEP2009 (21) - 11FEB2010 (170) 5. 24SEP2009 (30) - 01OCT2009 (37) 6. 16OCT2009 (52) - 26OCT2009 (62) 7. 12FEB2010 (171) - 22FEB2010 (181) 8. 12FEB2010 (171) - 22FEB2010 (181)
Duration of AE	1. 6 2. 12 3. 12 4. 150 5. 8 6. 11 7. 11 8. 11
Dose on AE onset	1. 15 mg 2. 15 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160124020

Parameter	Value
	3. 15 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	8. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. WORSENED
	2. RESOLVED
	3. RESOLVED
	4. WORSENED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160134003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160134003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/70/N.A./FRANCE/YES
Medical history	Hypertension, Depression, Insomnia, Prostate cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMLODIPINE, ANAFRANIL, IMOVANE, LASILIX, LEXOMIL, NORSET, PERINDOPRIL
Adverse Events (AE) Preferred term	1. Depression 2. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 11JUN2008 (34) - 09SEP2008 (124) 2. 05JUL2008 (58) - 05JUL2008 (58)
Duration of AE	1. 91 2. 1
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160134004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160134004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/49/N.A./FRANCE/YES
Medical history	Hysterectomy, Sciatica
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DIANTALVIC, ENOXAPARIN, GLUCOSE 5%, LANSOYL, NORMACOL, PARACETAMOL, SPASFON, WARFARIN
Adverse Events (AE) Preferred term	1. Renal colic
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 30MAY2008 (16) - 02JUN2008 (19)
Duration of AE	1. 4
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160174031

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160174031/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/70/N.A./FRANCE/YES
Medical history	Anaemia, Asthma, Drug hypersensitivity, Drug hypersensitivity, Goitre, Haematoma, Hypertension, Hypothyroidism, Pain, Umbilical hernia repair, Umbilical hernia repair, Osteoarthritis, Depression
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATHYMIL, CALCIPARINE, COLCHICINE, COLCHIMAX [COLCHICINE, PAPAVER SOMNIFERUM POWDER, TIEMONIUM METHYLSULPHATE], CONTRAMAL, EFFEXOR, HEXAQUINE, HYTACAND, IMOVANE, INEXIUM, LEVOTHYROX, NORCET, PARACETAMOL, SERETIDE
Adverse Events (AE) Preferred term	1. Goitre 2. Gout 3. Back pain
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 25MAR2009 (108) - 27MAR2009 (110) 2. 09SEP2009 (276) - --------- (.) 3. 01OCT2009 (298) - --------- (.)
Duration of AE	1. 3 2. . 3. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. I 2. . 3. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. IMPROVED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160174041

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160174041/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/79/N.A./FRANCE/YES
Medical history	Angioplasty, Cataract, Renal failure chronic, Coronary artery insufficiency, Diabetes mellitus, Hypercholesterolaemia, Hypertension, Inguinal hernia, Memory impairment, Arthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID, ADANCOR, BIPRETERAX, CHONDROSULF, CRESTOR, DEXERYL [GLYCEROL, VASELINE, PARAFFIN LIQUID], DIANTALVIC, DOLIPRANE, INSULIN, KETUM, LASILIX, NOVOMIX INSULIN, PLAVIX, TANAKAN, TRANSIPEG [MACROCOL 3350], TRINITRINE
Adverse Events (AE) Preferred term	1. Pruritus 2. Epistaxis 3. Diabetes mellitus inadequate control
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 30APR2009 (4) - 19MAY2009 (23) 2. 23AUG2009 (119) - 23AUG2009 (119) 3. 31OCT2009 (188) - 18NOV2009 (206)
Duration of AE	1. 20 2. 1 3. 19
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. F
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160184002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160184002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/57/N.A./FRANCE/YES
Medical history	Dermatitis exfoliative, Lung neoplasm malignant, Gastrointestinal ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACIDE FOLIQUE, ACTISKENAN, ALIMTA, ARANESP, B 26 [B 26 IS COMPOSED WITH PERFUSION OF GLUCOSE AT 5% AND NACL 3G/L AND KCL 1G/, DERMOVAL [CLOBETASOL PROPIONATE], DEXERYL [GLYCEROL, PARAFFIN LIQUID, VASELINE], DI ANTALVIC, DIPROSONE, DUPHALAC [DUPHALAC LACTULOSE], ENOXAPARIN, FLAMMAZINE, KETODERM, MACOFLEX, PREDNISONE, PRIMPERAN, STARCH, TARDYFERON [FERROUS SULFATE], TAXOTERE, TINZAPARINE, VITAMIN B 12, WARFARIN, ZOPHREN
Adverse Events (AE) Preferred term	1. Dermatitis exfoliative 2. International normalised ratio increased 3. Anaemia 4. Fatigue 5. Asthenia 6. Septic shock
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/YES 4. SEVERE/NO/NO/YES 5. SEVERE/NO/NO/YES 6. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 21JAN2008 (95) - 28JAN2008 (102) 2. 03MAR2008 (137) - 07MAR2008 (141) 3. 24MAR2008 (158) - 25MAR2008 (159) 4. 26MAR2008 (160) - --------- (.) 5. 26MAR2008 (160) - --------- (.) 6. 01APR2008 (166) - 02APR2008 (167)
Duration of AE	1. 8 2. 5 3. 2 4. . 5. . 6. 2
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160184002

Parameter	Value
	3.
	4.
	5.
	6.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER
	2. STUDY DRUG DISCONTINUED AND RESTARTED
	3. OTHER
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. WORSENED
	5. UNCHANGED
	6. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160194005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160194005/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/72/N.A./FRANCE/YES
Medical history	Inguinal hernia, Myocardial infarction, Myocardial infarction, Dyslipidaemia, Prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMYLASE, CRESTOR, KARDEGIC [ACETYLSALICYLATE LYSINE], MAGNESIUM B6, SPIRAMYCINE METRONIDAZOLE, WARFARIN
Adverse Events (AE) Preferred term	1. Haematuria 2. Myalgia 3. Gingivitis 4. Oropharyngeal pain
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 06MAR2008 (50) - 07MAR2008 (51) 2. 06APR2008 (81) - --------- (.) 3. 14APR2008 (89) - 25APR2008 (100) 4. 06MAY2008 (111) - 09MAY2008 (114)
Duration of AE	1. 2 2. . 3. 12 4. 4
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160194005

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160194013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160194013/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/81/N.A./FRANCE/YES
Medical history	Anal fistula, Depression, Appendicectomy, Arrhythmia, Chronic obstructive pulmonary disease, Hypertension, Pulmonary tuberculosis, Prostatomegaly, Sleep apnoea syndrome, Prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMIODARONE, CORDARONE, DIPROSONE, ENOXAPARIN, FORTZAAR, INNOHEP, SERETIDE 500, SPIRIVA, WARFARIN
Adverse Events (AE) Preferred term	1. Eczema 2. Haemorrhage intracranial
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 29MAR2008 (2) - 09APR2008 (13) 2. 03JUL2008 (98) - 05JUL2008 (100)
Duration of AE	1. 12 2. 3
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号：11702-160194013

死亡に至るまでの経過

被験者は81歳、男性。2008年3月26日に深部静脈血栓症と診断され、2008年3月28日にエノキサパリン（18,000IU）／用量調節ワルファリンの投与を開始した。

2008年7月3日、被験者は頭蓋内出血（報告用語：頭蓋内出血、以下同様）を発現した。本事象は重大な医学的事象であり、また被験者は入院し死亡に至ったため、重篤な有害事象とされた。本事象により被験者の治験は中止された。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「あり」と判断した。被験者は、高血圧及び無呼吸症候群の病歴を有していた。2008年7月2日夜、被験者は倒れ、翌日入院した。午前中に嘔吐しその後昏睡状態に陥った。頭部CTスキャンにより硬膜下血腫が認められた。PT-INRが上昇（5.1）したため2008年7月1日に治験薬の投与は中断されていたが、本事象の発現によりそのまま中止された。2008年7月3日のPT-INRは2.9であった。2008年7月3日、本事象に対してビタミンKが投与された。2008年7月5日、EEGは脳活動を示さず、同日、本事象により被験者は死亡に至った。剖検は実施されなかった。

独立中央判定委員会（CIAC）は、頭蓋内出血（頭蓋内出血）を「重大な出血事象」と考え、死亡原因を出血と判定した。

Laboratory Parameter	Normal Range	Date	Result
Hemoglobin	13.0-17.0 g/dL	26 Mar 2008	14.9 g/dL
Platelets	150-400 giga/L	26 Mar 2008	163 giga/L
Creatinine	0.70-1.20 mg/dL	26 Mar 2008	**1.33 mg/dL (H)**
PICT Seconds		28 Mar 2008	**53.10 S (H)**

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160194017

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160194017/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/66/N.A./FRANCE/YES
Medical history	Hypertension, Hysterectomy, Uterine cancer, Dermo-hypodermitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, EXACYL, WARFARIN
Adverse Events (AE) Preferred term	1. Lung neoplasm 2. Haemoptysis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 02MAY2008 (3) - --------- (.) 2. 11MAY2008 (12) - 13MAY2008 (14)
Duration of AE	1. . 2. 3
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160194023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160194023/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/N.A./FRANCE/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CALCIPARINE, CELTRIAXONE, ENOXAPARIN, FUROSEMIDE, LEVOFLOXACINE, PERFALGAN, SOLMUCOL, TINZAPARINE, WARFARIN
Adverse Events (AE) Preferred term	1. Urinary tract infection 2. Pneumonia 3. Cardiac failure 4. Haematuria 5. Urinary tract infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/YES/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07OCT2008 (1) - 08OCT2008 (2) 2. 20JAN2009 (106) - 26JAN2009 (112) 3. 20JAN2009 (106) - 26JAN2009 (112) 4. 21JAN2009 (107) - 26JAN2009 (112) 5. 21JAN2009 (107) - 31JAN2009 (117)
Duration of AE	1. 2 2. 7 3. 7 4. 6 5. 11
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160194023

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160214005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160214005/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/39/N.A./FRANCE/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CONTRAMAL LP, DOLIPRANE, LOVENOX, SPASFON LYOC
Adverse Events (AE) Preferred term	1. Cholelithiasis 2. Biliary colic 3. Abdominal pain 4. Chest pain
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 08NOV2007 (22) - 11NOV2007 (25) 2. 08NOV2007 (22) - --------- (.) 3. 08NOV2007 (22) - 04DEC2007 (48) 4. 08NOV2007 (22) - 04DEC2007 (48)
Duration of AE	1. 4 2. . 3. 27 4. 27
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY,OTHER 3. OTHER 4. OTHER
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160214005

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160214010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160214010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/86/N.A./FRANCE/YES
Medical history	Anxiety, Appendicectomy, Cough, Essential hypertension, Hypothyroidism, Insomnia, Myocardial ischaemia, Menopause, Oedema peripheral, Peritonitis, Rales, Vertigo, Lung disorder, Iodine allergy, Intraocular lens extraction, Cardiac valve disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADANCOR, CALCIPARINE, DIFFU K, EFFEXOR, ENOXAPARIN, FUROSEMIDE, HEMIGOXINE, WARFARIN, ZINNAT, ZOLPIDEM
Adverse Events (AE) Preferred term	1. Red blood cell count decreased 2. Muscle haemorrhage 3. Renal failure acute 4. Shock haemorrhagic
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/YES/YES/YES 3. SEVERE/NO/NO/YES 4. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 27APR2008 (12) - 15MAY2008 (30) 2. 28APR2008 (13) - 16MAY2008 (31) 3. 28APR2008 (13) - --------- (.) 4. 28APR2008 (13) - 16MAY2008 (31)
Duration of AE	1. 19 2. 19 3. . 4. 19
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. OTHER 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 3. NONE 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160214010

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702- 160214010[2),1),1),1)]	ACUTE RENAL FAILURE（PT：急性腎不全） 治験担当医は、ワルファリンとの因果関係を否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。 HEMORRHAGIC SHOCK（PT：出血性ショック） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投薬終了9日後の発現であることから、因果関係は否定できると考える。 LOSS OF ERYTHROCYTES（PT：赤血球数減少） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投薬終了9日後の発現であることから、因果関係は否定できると考える。 PSOAS HAEMATOMA（PT：筋肉内出血） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投薬終了9日後の発現であることから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160234001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/58/N.A./FRANCE/YES
Medical history	Arteritis, Hypercholesterolaemia, Insomnia, Alcoholism, Tobacco poisoning
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATARAX, COLCHICINE, CRESTOR, DOLIPRANE, ENOXAPARIN, HYPNOVEL, INIPOMP, PLAVIX, STILNOX, WARFARIN
Adverse Events (AE) Preferred term	1. Joint effusion 2. Alcohol abuse
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 06JUL2007 (10) - --------- (.) 2. 12SEP2007 (78) - 14SEP2007 (80)
Duration of AE	1. . 2. 3
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160234002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/87/N.A./FRANCE/YES
Medical history	Anxiety, Glaucoma, Headache, Hypercholesterolaemia, Hypertension, Hypothyroidism, Hysterectomy, Back pain, Lung infection
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DEBRIDAT, DIANTALVIC, DOLIPRANE, ENOXAPARIN, INIPOMP, LEVOTHYROX, LEXOMIL, MOTILIUM, MOVICOL, NIFLUGEL, PENICILLINE, PYOSTACINE, TOPALGIC [TRAMADOL HYDROCHLORIDE], TRIFLUCAN, UNFRACTIONED HEPARINE, WARFARIN
Adverse Events (AE) Preferred term	1. Vitamin D deficiency 2. Arthralgia 3. Nausea 4. Constipation 5. Pain in extremity 6. Bacterial sepsis 7. Erysipelas 8. Rhinorrhoea
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/YES/YES/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/YES/YES 8. MILD/NO/NO/NO
Start/stop date of event with relative date	1. --DEC2007 (.) - --------- (.) 2. --DEC2007 (.) - --------- (.) 3. 27JUN2007 (1) - 05NOV2007 (132) 4. 02JUL2007 (6) - 18SEP2007 (84) 5. 15JUL2007 (19) - 27JUL2007 (31) 6. 20JUL2007 (24) - 27JUL2007 (31) 7. 20JUL2007 (24) - 27JUL2007 (31) 8. 19DEC2007 (176) - 21DEC2007 (178)
Duration of AE	1. . 2. . 3. 132 4. 79 5. 13 6. 8 7. 8 8. 3
Dose on AE onset	1. 2.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234002

Parameter	Value
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
Outcome of event	1. IMPROVED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-160234002[1)]	PAIN OF THE LEFT THIGH（PT：四肢痛） 治験担当医は深部静脈血栓の再発によるものであり、エノキサパリン及びワルファリンとの関連性があると判断した。弊社は、合併症（感染症）によるものであり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160234023/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/35/N.A./FRANCE/YES
Medical history	Abdominal pain, Tendon operation, Postoperative thrombosis, Duodenitis, Spinal operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AREDIA, CIPROFLOXACINE, DICLOFENAC, ENOXAPARIN, INIPOMP, OROCAL D3, PHLOROGLUCINOL, PROPOFAN [CAFFEINE+DEXTROPROPOXYPHENE+PARACETAMOL], WARFARIN
Adverse Events (AE) Preferred term	1. Arthralgia 2. Muscle atrophy 3. Inflammation 4. Complex regional pain syndrome 5. Renal colic
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. --MAR2008 (.) - --MAR2008 (.) 2. --MAR2008 (.) - --MAR2008 (.) 3. --MAR2008 (.) - --MAR2008 (.) 4. 02APR2008 (57) - 05APR2008 (60) 5. 18APR2008 (73) - 18APR2008 (73)
Duration of AE	1. . 2. . 3. . 4. 4 5. 1
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY 5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234023

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234066

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160234066/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/85/N.A./FRANCE/YES
Medical history	Anxiety, Appendicitis, Cholecystectomy, Hypertension, Osteoporosis, Tumour excision, Cataract operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, HEPARINE, STILNOX, WARFARIN, XANAX
Adverse Events (AE) Preferred term	1. Rash 2. Fall 3. Urinary tract infection 4. Subdural haematoma 5. Urinary tract infection 6. Skin infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/NO/YES 3. MILD/NO/NO/NO 4. SEVERE/NO/YES/NO 5. MILD/NO/NO/NO 6. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. --NOV2009 (.) - --DEC2009 (.) 2. 17JUN2009 (2) - 17JUN2009 (2) 3. 20JUN2009 (5) - 03JUL2009 (18) 4. 15JUL2009 (30) - 03AUG2009 (49) 5. 03AUG2009 (49) - 10AUG2009 (56) 6. 22SEP2009 (99) - 01OCT2009 (108)
Duration of AE	1. . 2. 1 3. 14 4. 20 5. 8 6. 10
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160234066

Parameter	Value
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-160234066[4),2)]	FALL（PT：転倒） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、本剤開始前の発現であり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。 SUBDURAL HEMATOMA（PT：硬膜下血腫） 治験担当医は、エノキサパリン及びワルファリンとの因果関係は否定できると判断した。弊社は、本剤開始後の発現であり、エノキサパリン及びワルファリンと報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160254002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160254002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/41/N.A./FRANCE/YES
Medical history	Thrombophlebitis superficial
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FONDAPARINUX, WARFARIN
Adverse Events (AE) Preferred term	1. Pregnancy 2. Post abortion haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/NO
Start/stop date of event with relative date	1. 30JAN2008 (13) - 17FEB2008 (31) 2. 17FEB2008 (31) - 10MAR2008 (53)
Duration of AE	1. 19 2. 23
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702- 160254002[2)]	SPONTANEOUS ABORTION（PT：自然流産） 治験担当医は、エノキサパリン及びワルファリンとの因果関係を否定できると判断した。弊社は、エノキサパリン及びワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160254003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160254003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/42/N.A./FRANCE/YES
Medical history	Appendicectomy, Embolism, Groin pain, Sepsis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Alanine aminotransferase increased 3. Epistaxis 4. Psoriasis 5. Epistaxis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/YES/YES/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 18FEB2008 (8) - 18FEB2008 (8) 2. 26FEB2008 (16) - 02APR2008 (52) 3. 03NOV2008 (267) - 03NOV2008 (267) 4. 01DEC2008 (295) - --------- (.) 5. 05JAN2009 (330) - 05JAN2009 (330)
Duration of AE	1. 1 2. 37 3. 1 4. . 5. 1
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160254003

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160254010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160254010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/65/N.A./FRANCE/YES
Medical history	Oedema peripheral, Thrombophlebitis superficial
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	COLCHIMAX [COLCHICINE + PAPAVER SOMNIFERUM POWDER + TIEMONIUM METHYLSULPHATE], ENOXAPARIN, WARFARIN, ZYLORIC
Adverse Events (AE) Preferred term	1. Arthritis 2. Renal neoplasm 3. Arthritis 4. Hypertension
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 06MAR2009 (4) - 17MAR2009 (15) 2. 04MAY2009 (63) - 06AUG2009 (157) 3. 04MAY2009 (63) - 07MAY2009 (66) 4. 04MAY2009 (63) - --------- (.)
Duration of AE	1. 12 2. 95 3. 4 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160254010

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160254011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160254011/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/50/N.A./FRANCE/YES
Medical history	Psoriasis, Rheumatoid arthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APRANAX, REMICADE
Adverse Events (AE) Preferred term	1. Atrial flutter
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 24JUL2009 (137) - 24JUL2009 (137)
Duration of AE	1. 1
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160264001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/67/N.A./FRANCE/YES
Medical history	Anxiety, Depression, Diabetes mellitus, Hemiplegia, Hypercholesterolaemia, Hypertension, Prostatic adenoma, Cerebrovascular accident, Cerebrovascular accident
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANAFRANIL, AUGMENTIN, CLAMOXYL, DIFFU K, DOXYCYCLINE, DUPHALAC [DUPHALAC CONTAIN ONLY LACTULOSE], ENOXAPARIN, GLUCOPHAGE, KARDEGIC, LASILIX, LIORESAL, LYSANXIA, RENITEC, ROCEPHINE, SERESTA, TAHOR, WARFARIN
Adverse Events (AE) Preferred term	1. Constipation 2. Urinary tract infection 3. Oral fungal infection 4. Constipation 5. Nausea 6. Haematuria 7. Urinary tract infection 8. Haematuria 9. Haematuria 10. Hypokalaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MODERATE/YES/YES/YES 7. MILD/NO/NO/YES 8. MODERATE/YES/NO/YES 9. MODERATE/YES/YES/YES 10. MILD/NO/NO/YES
Start/stop date of event with relative date	1. -----2008 (.) - 13JUN2009 (541) 2. 25MAR2008 (96) - 04APR2008 (106) 3. 26MAR2008 (97) - -----2008 (.) 4. 14SEP2008 (269) - 22SEP2008 (277) 5. 14SEP2008 (269) - 22SEP2008 (277) 6. 06NOV2008 (322) - 08NOV2008 (324) 7. 12NOV2008 (328) - --NOV2008 (.) 8. 08DEC2008 (354) - 10DEC2008 (356) 9. 10DEC2008 (356) - 13DEC2008 (359) 10. 10DEC2008 (356) - -----2009 (.)
Duration of AE	1. . 2. 11 3. . 4. 9

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264001

Parameter	Value
	5. 9
	6. 3
	7. .
	8. 3
	9. 4
	10. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. NONE
	10. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264001

Parameter	Value
	6. RESOLVED
	7. RESOLVED
	8. WORSENED
	9. RESOLVED
	10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160264008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/56/N.A./FRANCE/YES
Medical history	Arteritis, Osteoarthritis, Diabetes mellitus, Systemic sclerosis, Gastrooesophageal reflux disease, Hypercholesterolaemia, Hypokalaemia, Menopause, Pain, Peptic ulcer, Scleroderma, Systemic lupus erythematosus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BUFLOMEDIL, CALCIPARINE, CORTANCYL, CRESTOR, DIFFU K, EFFERALGAN CODEINE, ENOXAPARIN, FLAGYL, FOSAMAX, INIPOMP, MOTILLIUM, NEURONTIN, NOVOMIX 30, NOVOMIX 50, NOVONORM, OFLOCET, ORBENINE, TOPALGIC [TOPALGIC: TRAMADOL HYDROCHLORIDE], WARFARIN
Adverse Events (AE) Preferred term	1. Skin haemorrhage 2. Extremity necrosis 3. Vomiting 4. Nausea
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01JAN2009 (133) - 04FEB2009 (167) 2. 04FEB2009 (167) - 17FEB2009 (180) 3. 07FEB2009 (170) - 07FEB2009 (170) 4. 08FEB2009 (171) - 08FEB2009 (171)
Duration of AE	1. 35 2. 14 3. 1 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. NONE 4. NONE
Outcome of event	1. WORSENED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264008

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160264014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/97/N.A./FRANCE/YES
Medical history	Anaemia, Dementia, Gastritis, Hypercholesterolaemia, Cerebrovascular accident, Acute coronary syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADANCOR, CARDENSIEL, DISCOTRINE, ELECTROLYTE TRANSFUSION, ENOXAPARIN, GELUPRANE, ICOREL, IMOVANE, INEXIUM, KARDEGIC, PERFALGAN, TAHOR, TIPRIDAL, WARFARIN
Adverse Events (AE) Preferred term	1. Insomnia 2. Anaemia 3. Epilepsy 4. General physical health deterioration
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. SEVERE/NO/YES/NO 4. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 12MAY2009 (2) - 29MAY2009 (19) 2. 13MAY2009 (3) - 15MAY2009 (5) 3. 23MAY2009 (13) - 16JUN2009 (37) 4. 24MAY2009 (14) - 16JUN2009 (37)
Duration of AE	1. 18 2. 3 3. 25 4. 24
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 3. NONE 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160264014

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-160264014[2)]	ANEMIA（PT：貧血） 治験担当医は、合併症（貧血）及び併用薬によるものであり、否定できると判断した。弊社は、エノキサパリン及びワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160274004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160274004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/79/N.A./FRANCE/YES
Medical history	Hypertension, Prostatic adenoma, Osteoarthritis, Parkinson's disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENALAPRIL/HYDROCHLOROTHIAZIDE, ENOXAPARIN, ESIDREX, LEVODOPA/BENSERAZIDE, LOVENOX, PRUNIER D'AFRIQUE, TRIVASTAL, UNFRACTIONATED HEPARIN, VITAMINE K, WARFARIN
Adverse Events (AE) Preferred term	1. Rectal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 15APR2008 (54) - 16APR2008 (55)
Duration of AE	1. 2
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160294013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160294013/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/74/N.A./FRANCE/YES
Medical history	Chronic obstructive pulmonary disease, Chronic respiratory failure, Diaphragmatic hernia, Dupuytren's contracture, Hypertension, Osteoarthritis, Atrial fibrillation, Polyneuropathy, Prostatic adenoma, Rotator cuff syndrome, Small cell lung cancer stage unspecified, Squamous cell carcinoma, Tobacco poisoning, Venous insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AERIUS, CLARYTINE, CORDARONE, CORTANCYL, FLECAINE LP, HEMIGOXINE, INEXIUM, LASILIX, MEPRONIZINE, SERETIDE, SERETIDE DISKUS, SPIRIVA, TARDYFERON [JUST FERROUS SULFATE], TEMERIT, VITAMIN B6, VITAMINE B1
Adverse Events (AE) Preferred term	1. Haematoma 2. Haematuria 3. Rectal haemorrhage 4. Haematoma 5. Lung neoplasm
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 19APR2008 (2) - 21MAY2008 (34) 2. 21APR2008 (4) - 22APR2008 (5) 3. 22APR2008 (5) - 22APR2008 (5) 4. 18JUL2008 (92) - --AUG2008 (.) 5. 04NOV2008 (201) - 09NOV2008 (206)
Duration of AE	1. 33 2. 2 3. 1 4. . 5. 6
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. F
Action taken	1. NONE 2. NONE 3. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160294013

Parameter	Value
	4. NONE
	5. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160304008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160304008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/86/N.A./FRANCE/YES
Medical history	Hypertension, Muscle spasms, Hypercholesterolaemia, Inguinal hernia repair, Insomnia, Renal failure, Dysuria, Tobacco user, Penile prosthesis insertion, Subileus, Colorectal cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CHIBROPROSCAR, COUMADINE, CRESTOR, DEBRIDAT, LEXOMIL, LIPANTHYL, NISIS, RIVOTRIL, ROCGEL, TAREG, TRIMEBUTINE
Adverse Events (AE) Preferred term	1. Contusion 2. Waldenstrom's macroglobulinaemia 3. Panic attack 4. Gastroenteritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 27JUN2008 (29) - 28JUL2008 (60) 2. 02JUL2008 (34) - --------- (.) 3. 30JUL2008 (62) - 01AUG2008 (64) 4. 02DEC2008 (187) - 07DEC2008 (192)
Duration of AE	1. 32 2. . 3. 3 4. 6
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. NONE 2. OTHER 3. NONE 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160304008

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160324003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160324003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/59/N.A./FRANCE/YES
Medical history	Anxiety, Breast cancer, Depression, Goitre, Hypertension, Insomnia, Lower limb fracture, Lymphoedema, Obesity, Schizophrenia, Calculus urinary, Impaired healing, Wound infection, Postmenopause, Wound
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALDACTONE [SPIRONOLACTONE], ARIMIDEX, ATARAX, CIFLOX, DEPAMIDE, DOLIPRANE, EFFEXOR, ENOXAPARIN, LOPRESSOR, LOVENOX, MEPRONIZINE, ORBENINE, WARFARIN, ZYPREXA
Adverse Events (AE) Preferred term	1. Post procedural sepsis 2. Post procedural sepsis 3. Impaired healing 4. Pyrexia 5. Impaired healing
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 29OCT2008 (47) - 06NOV2008 (55) 2. 07NOV2008 (56) - --------- (.) 3. 13NOV2008 (62) - 18NOV2008 (67) 4. 17NOV2008 (66) - 18NOV2008 (67) 5. 19NOV2008 (68) - --------- (.)
Duration of AE	1. 9 2. . 3. 6 4. 2 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. OTHER 4. REMEDIAL DRUG THERAPY 5. OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160324003

Parameter	Value
Outcome of event	1. IMPROVED 2. UNCHANGED 3. IMPROVED 4. RESOLVED 5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160334002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160334002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/42/N.A./FRANCE/YES
Medical history	Tobacco abuse, Varicose vein, Pain in extremity, Lumbar vertebral fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, KARDEGIC, NORSTEROIDE (19-NORTES-TOSTERONE), PROPOFAN [CAFFEINE+DEXTROPROPOXYPHENE+PARACETAMOL], WARFARIN
Adverse Events (AE) Preferred term	1. Iliac artery stenosis 2. Pain in extremity 3. Arthralgia 4. Arteriosclerosis 5. Gait disturbance 6. Iliac artery stenosis 7. Iliac artery stenosis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/NO/YES/YES 7. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 06JUN2008 (10) - 14OCT2008 (140) 2. 18JUN2008 (22) - --------- (.) 3. 18JUN2008 (22) - --------- (.) 4. 02OCT2008 (128) - --------- (.) 5. 02OCT2008 (128) - --------- (.) 6. 14OCT2008 (140) - 16OCT2008 (142) 7. 16OCT2008 (142) - --------- (.)
Duration of AE	1. 131 2. . 3. . 4. . 5. . 6. 3 7. .
Dose on AE onset	1. 2. 3. 4. 5. 6. 7.
Dose status on AE onset	1.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160334002

Parameter	Value
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY,OTHER
	3. REMEDIAL DRUG THERAPY,OTHER
	4. OTHER
	5. NONE
	6. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	7. NONE
Outcome of event	1. WORSENED
	2. IMPROVED
	3. RESOLVED
	4. UNCHANGED
	5. UNCHANGED
	6. IMPROVED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160334021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/160334021/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/72/N.A./FRANCE/YES
Medical history	Osteoarthritis, Prostatic adenoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CHIBROPROSCAR (FINASTERIDE), DOLIPRANE, ENOXAPARIN, LOVENOX, WARFARIN
Adverse Events (AE) Preferred term	1. Ear neoplasm malignant 2. Arthralgia 3. Ear haemorrhage 4. Ear neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --MAR2009 (.) - 01JUL2009 (173) 2. 11MAY2009 (122) - 16MAY2009 (127) 3. 01JUL2009 (173) - 01JUL2009 (173) 4. 01JUL2009 (173) - 01JUL2009 (173)
Duration of AE	1. . 2. 6 3. 1 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. OTHER 4. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. WORSENED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 160334021

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180014008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180014008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/39/WHITE/POLAND/YES
Medical history	Thrombocytopenia, Intervertebral disc disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	OLANZAPIN, VENLAFAXIN, VENLAFAXINE
Adverse Events (AE) Preferred term	1. Major depression 2. Menorrhagia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 21AUG2008 (77) - --------- (.) 2. 08OCT2008 (125) - 10OCT2008 (127)
Duration of AE	1. . 2. 3
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. F
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180044009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180044009/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/54/WHITE/POLAND/YES
Medical history	Chronic obstructive pulmonary disease, Osteoporosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALFADIOL, AULIN, BISOCARD, BONVIVA, CEPHALOSPORIN 2ND GENERATION, ENCORTON, FLIXOTIDE, FUROSEMID, OSTEODIAG, OXODIL, POLPRAZOL, SPIRIVA, SPIRONOLAKTON
Adverse Events (AE) Preferred term	1. Pericarditis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 05OCT2009 (166) - 15OCT2009 (176)
Duration of AE	1. 11
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180094002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180094002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/POLAND/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Haemorrhage intracranial
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 05OCT2008 (151) - --------- (.)
Duration of AE	1. .
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180104013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180104013/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/POLAND/YES
Medical history	Alanine aminotransferase increased, Muscle contractions involuntary, Chronic obstructive pulmonary disease, Hyperlipidaemia, Hypertension, Nephrolithiasis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALVESCO, ATACAND [CANDESARTAN CILEXETIL ALONE], ATORIS, BISOCARD, CI-DIOVAN, CIPROPHLOXACINUM, GLYCERIN SUPPOSITORY, IMODIUM, LACTULOSA, METOPROLOL, NO-SPA, OXIS, SEREVENT, SPIRIVA, THERAFLU
Adverse Events (AE) Preferred term	1. Asthenia 2. Synovial rupture 3. Nasopharyngitis 4. Nasopharyngitis 5. Diarrhoea 6. Nasopharyngitis 7. Pyelonephritis 8. Nephrolithiasis 9. Pyelonephritis 10. Constipation 11. Renal cyst 12. Calculus ureteric 13. Bronchitis 14. Dyspepsia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/YES/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MODERATE/NO/NO/YES 13. MILD/NO/NO/NO 14. MILD/NO/NO/NO
Start/stop date of event with relative date	1. --FEB2009 (.) - --JUL2009 (.) 2. --JUN2009 (.) - --------- (.) 3. 12DEC2008 (14) - 12DEC2008 (14) 4. 28DEC2008 (30) - 29DEC2008 (31) 5. 26JAN2009 (59) - 27JAN2009 (60) 6. 26JAN2009 (59) - 27JAN2009 (60)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180104013

Parameter	Value
	7. 03OCT2009 (309) - 04OCT2009 (310)
	8. 03OCT2009 (309) - 09OCT2009 (315)
	9. 05OCT2009 (311) - 09OCT2009 (315)
	10. 08OCT2009 (314) - 09OCT2009 (315)
	11. 09OCT2009 (315) - --------- (.)
	12. 09OCT2009 (315) - --------- (.)
	13. 24NOV2009 (361) - 01DEC2009 (368)
	14. 26NOV2009 (363) - 05DEC2009 (372)
Duration of AE	1. .
	2. .
	3. 1
	4. 2
	5. 2
	6. 2
	7. 2
	8. 7
	9. 5
	10. 2
	11. .
	12. .
	13. 8
	14. 10
Dose on AE onset	1.
	2.
	3. 15 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
Dose status on AE onset	1.
	2.
	3. .
	4. .
	5. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180104013

Parameter	Value
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .
	13. F
	14. F
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. NONE
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. NONE
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. WORSENED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. UNCHANGED
	12. UNCHANGED
	13. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180104013

Parameter	Value
	14. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-180104013[3)]	HEMATURIA（PT：血尿） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180114003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180114003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/POLAND/YES
Medical history	Benign prostatic hyperplasia, Duodenal ulcer, Hypertension, Abdominal hernia, Renal failure
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	FOKUSIN
Adverse Events (AE) Preferred term	1. Bladder cancer 2. Haematuria 3. Acute myocardial infarction
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. SEVERE/YES/NO/YES 3. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 27AUG2008 (183) - --------- (.) 2. 27AUG2008 (183) - 30AUG2008 (186) 3. 30AUG2008 (186) - --------- (.)
Duration of AE	1. . 2. 4 3. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. F 2. F 3. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. RESOLVED 3. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180124002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180124002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/78/WHITE/POLAND/YES
Medical history	Anaemia, Cataract, Hypertension, Myocardial ischaemia, Myocardial infarction, Benign prostatic hyperplasia, Cerebrovascular accident, Hypoacusis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACARD, CERUTIN, CLEXANE, DOXYCYCLINUM, EFFOX LONG, ENARENAL, FITOPROST, KALIPOZ, MICROSER, NILOGRIN, NOOTROPIL, OMNIC, POLPRAZOL, REASEC, TERTENSIF SR, VINPOCETINE
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 16DEC2008 (7) - 16DEC2008 (7) 2. 12MAY2009 (154) - 27MAY2009 (169)
Duration of AE	1. 1 2. 16
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180124004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180124004/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/79/WHITE/POLAND/YES
Medical history	Prostate cancer, Dermatitis exfoliative, Hypertension, Lung disorder, Cardiovascular insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APO-DOXAN, APO-FLUTAM, ATARAX, ATROVENT, AUGMENTIN, CIPRONEX, CLARITINE, CLEXANE, DEXAVEN, ESSENTIALE, ESTAZOLAM, EUPHYLINUM, FLUMYCON, FRAXIPARINE, HYDROCORTISON, INHIBACE [CILAZAPRIL], ISOPTIN, KALIPOZ, METYPRED, MUCOSOLVAN, POLPRAZOL, PULMOTEROL, SOLUMEDROL, SPIRONOL, THEOPHYLLINE, THEOVENT, TIALORID, TRILAC, VITRUM CALCIUM
Adverse Events (AE) Preferred term	1. Oedema peripheral 2. Dyspnoea at rest 3. Lung disorder
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 04APR2009 (61) - 09APR2009 (66) 2. 09APR2009 (66) - 15APR2009 (72) 3. 09JUL2009 (157) - 14JUL2009 (162)
Duration of AE	1. 6 2. 7 3. 6
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. I 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180124005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180124005/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/59/WHITE/POLAND/YES
Medical history	Hypertension, Thyroidectomy, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ASPIRIN, CLEXANE, CLOPIDOGREL, EFFOX, ENOXAPARIN, ESTAZOLAM, EUTHYROX, LOSEC, NO-SPA, PARACETAMOL, PERFALGAN, PLAVIX, POLOCARD, SIMVASTATIN, SORTIS, TANANTRIL
Adverse Events (AE) Preferred term	1. Angina unstable 2. Metastatic neoplasm
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 25FEB2009 (6) - 10MAR2009 (19) 2. 30MAR2009 (39) - --------- (.)
Duration of AE	1. 14 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180174001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180174001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/69/WHITE/POLAND/YES
Medical history	Coronary artery disease, Hypertension, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ENOXAPARIN, MONONIT
Adverse Events (AE) Preferred term	1. Motor dysfunction 2. Movement disorder 3. Ischaemic stroke 4. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 29JUN2008 (40) - --------- (.) 2. 29JUN2008 (40) - --------- (.) 3. 01JUL2008 (42) - 06AUG2008 (78) 4. 06AUG2008 (78) - --------- (.)
Duration of AE	1. . 2. . 3. 37 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. INSUFFICIENT FOLLOW-UP 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180174001

Parameter	Value
	4. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180174002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180174002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/POLAND/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPARGIN, NEDAL [NEBIVOLOLUM], PLAVIX, POLOCARD, TORVALIPIN, TRITACE
Adverse Events (AE) Preferred term	1. Acute myocardial infarction
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 30NOV2009 (328) - 07DEC2009 (335)
Duration of AE	1. 8
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 180194001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/180194001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/86/WHITE/POLAND/YES
Medical history	Hypertension, Myocardial infarction, Cardiac failure, Atrial fibrillation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ADRENALINE, DILATREND, ENOXAPARIN, FUROSEMIDUM, KALIPOZ PROLONGATUM, POLOCARD
Adverse Events (AE) Preferred term	1. Cardiac arrest
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 22DEC2008 (4) - 22DEC2008 (4)
Duration of AE	1. 1
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/84/WHITE/ITALY/YES
Medical history	Arrhythmia, Intestinal adenocarcinoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BISOPROLOL, DOBETIN, ECOVAL, EPARMEFOLIN, FERLIXIT, FERROGRAD, FOLINA, GENTALYN, GUTTALAX 0.75%, IRON, LASITONE, MOVICOL, OMEPARZOLE, PARIET, SUPRADYN, X-PREP
Adverse Events (AE) Preferred term	1. Anaemia 2. Anaemia 3. Cardiac failure 4. Haemorrhoids 5. Gastritis atrophic 6. Adenocarcinoma 7. Anaemia 8. Constipation 9. Dermatitis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/NO/YES 2. SEVERE/YES/YES/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. SEVERE/NO/NO/YES 7. SEVERE/YES/YES/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 19NOV2007 (109) - 03DEC2007 (123) 2. 04DEC2007 (124) - 14DEC2007 (134) 3. 08DEC2007 (128) - --------- (.) 4. 10DEC2007 (130) - 03JAN2008 (154) 5. 10DEC2007 (130) - --------- (.) 6. 30DEC2007 (150) - --------- (.) 7. 16JAN2008 (167) - 08FEB2008 (190) 8. 16JAN2008 (167) - 06FEB2008 (188) 9. 30JAN2008 (181) - 30JAN2008 (181)
Duration of AE	1. 15 2. 11 3. . 4. 25 5. . 6. . 7. 24 8. 22 9. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014002

Parameter	Value
Dose on AE onset	1. 20 mg
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
Dose status on AE onset	1. .
	2. .
	3. I
	4. I
	5. I
	6. .
	7. I
	8. I
	9. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
Outcome of event	1. WORSENED
	2. RESOLVED
	3. IMPROVED
	4. RESOLVED
	5. UNCHANGED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014002

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/74/WHITE/ITALY/YES
Medical history	Chronic obstructive pulmonary disease, Cardiac failure, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETILCISTEINA, AMINOFILLINA, AMINOFILLINA RETARD, BECLOMETASONE, BETAMETILDIGOSSINA, CARDURA, CEFTRIAXONE, DEPONIT, DIGOSIN, ENALAPRIL, ENAPREN, ENOXAPARIN, FLIXOTIDE, FLUIMUCIL, FUROSEMIDE, IDROCLOROTIAZIDE, IDROPLURIVIT, LANITOP, LASIX, LEVOFLOXACINA, METHYLPREDNISOLONE, NISTATINA, OMEPRAZOLE, OSSITROPIO, PANTORC, PERINDOPRIL, POTASSIUM CHLORIDE, PREDNISONE, SERETIDE, SEREVENT, SPIRIVA, VITAMINE C, WARFARIN
Adverse Events (AE) Preferred term	1. Chronic obstructive pulmonary disease 2. Infective exacerbation of chronic obstructive airways disease 3. Asthenia 4. Hypokalaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 06NOV2007 (71) - 21NOV2007 (86) 2. 06NOV2007 (71) - 21NOV2007 (86) 3. 06NOV2007 (71) - 17NOV2007 (82) 4. 13NOV2007 (78) - 21NOV2007 (86)
Duration of AE	1. 16 2. 16 3. 12 4. 9
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014004

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/51/WHITE/ITALY/YES
Medical history	Metastases to bone, Breast cancer, Metastases to lung
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	COEFFERALGAN, CONTRAMAL, CYCLOPHOSPHAMIDE, DIFLUCAN, FUROSEMIDE, KANREONATO POTASSIO, LASIX, LEVOFLOXACINA, METILPREDNISOLONA, MYOCET, NAVOBAN, OMEPRAZOLE, PARACETAMOL, PLASIL, POTASSIO CLORURO, PREDNISONE, RANIDIL, SENNA FOGLIA, SENNA FOGLIE, SOLDESAM, TRAMADOL, URBASON, XPREP
Adverse Events (AE) Preferred term	1. Respiratory failure 2. Constipation 3. Pain 4. Nausea 5. Nausea 6. Vomiting 7. Constipation 8. Fungal infection 9. Constipation 10. Breast cancer 11. Respiratory failure 12. Arrhythmia 13. Hyperglycaemia 14. Anxiety 15. Metastases to lung 16. Pain
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/NO/YES 8. MODERATE/NO/NO/YES 9. MODERATE/NO/NO/YES 10. SEVERE/NO/YES/YES 11. SEVERE/NO/YES/YES 12. SEVERE/NO/YES/YES 13. MODERATE/NO/NO/YES 14. MODERATE/NO/NO/YES 15. SEVERE/NO/YES/YES 16. SEVERE/NO/NO/YES
Start/stop date of event with relative date	1. 25NOV2007 (54) - 17DEC2007 (76) 2. 26NOV2007 (55) - 27NOV2007 (56)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014008

Parameter	Value
	3. 29NOV2007 (58) - 30NOV2007 (59)
	4. 01DEC2007 (60) - 03DEC2007 (62)
	5. 10DEC2007 (69) - 11DEC2007 (70)
	6. 10DEC2007 (69) - 11DEC2007 (70)
	7. 14DEC2007 (73) - 16DEC2007 (75)
	8. 17DEC2007 (76) - 06JAN2008 (96)
	9. 17DEC2007 (76) - 04JAN2008 (94)
	10. 05JAN2008 (95) - --------- (.)
	11. 05JAN2008 (95) - 06JAN2008 (96)
	12. 05JAN2008 (95) - --------- (.)
	13. 05JAN2008 (95) - 05JAN2008 (95)
	14. 05JAN2008 (95) - 06JAN2008 (96)
	15. 05JAN2008 (95) - --------- (.)
	16. 05JAN2008 (95) - 06JAN2008 (96)
Duration of AE	1. 23
	2. 2
	3. 2
	4. 3
	5. 2
	6. 2
	7. 3
	8. 21
	9. 19
	10. .
	11. 2
	12. .
	13. 1
	14. 2
	15. .
	16. 2
Dose on AE onset	1. 20 mg
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014008

Parameter	Value
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
	16. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. F
	11. F
	12. F
	13. F
	14. F
	15. F
	16. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. STUDY DRUG DISCONTINUED PERMANENTLY
	11. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. REMEDIAL DRUG THERAPY
	15. STUDY DRUG DISCONTINUED PERMANENTLY
	16. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014008

Parameter	Value
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. UNCHANGED
	11. DEATH
	12. UNCHANGED
	13. RESOLVED
	14. RESOLVED
	15. UNCHANGED
	16. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/ITALY/YES
Medical history	Bronchitis chronic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AVALOX, BACAMPICILLINA, CONTRAMAL, DELTACORTENE, ENOXAPARIN, ENOXAPARINA, GASTROGEL, INSULINA RAPID, LANTUS, LEVOFLOXACINA, METILPREDNISOLONA, OMEPRAZOLE, PARACETAMOL, ROCEFIN, SELEDIE, SEVELAMER, SOFARGEN, WARFARIN
Adverse Events (AE) Preferred term	1. Henoch-Schonlein purpura 2. Haematuria 3. Diabetes mellitus
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 08NOV2007 (16) - 10MAR2008 (139) 2. 26FEB2008 (126) - 10MAR2008 (139) 3. 26FEB2008 (126) - --------- (.)
Duration of AE	1. 124 2. 14 3. .
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-220014010[2)]	PURPURA SCHONLEIN-HENOCH（PT：ヘノッホ・シェーンライン紫斑病） 治験担当医は、クマリンとの因果関係は否定できると判断した。弊社は、クマリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014021/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/77/WHITE/ITALY/YES
Medical history	Depression, Glioblastoma, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID, ALBUMINA, ANTRA, CALCIO LEVOFOLINATO, CARDIOSTENOL, CIPROFLOXACINA, ENOXAPARIN, FUROSEMIDE, HUMALOG, HUMULIN R, KONAKION, MEROPENEM, METILPREDNISOLONA, MOEXIPRIL CLORIDRATO/IDROCLOROTIAZIDE, MORFINA, NISTATINA, OMPERAZOLO, REMERON, SOLDESAM, TEMODAL, TRIMETOPRIM/SULFAMETOSSAZOLO, URBASON, WARFARIN, XANAX
Adverse Events (AE) Preferred term	1. Interstitial lung disease 2. Oral candidiasis 3. Anaemia 4. Hyperglycaemia 5. Oedema 6. International normalised ratio increased 7. Pain 8. Hyperglycaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 11JUL2008 (89) - 18JUL2008 (96) 2. 11JUL2008 (89) - 13JUL2008 (91) 3. 12JUL2008 (90) - 12JUL2008 (90) 4. 13JUL2008 (91) - 15JUL2008 (93) 5. 13JUL2008 (91) - 17JUL2008 (95) 6. 14JUL2008 (92) - 16JUL2008 (94) 7. 14JUL2008 (92) - 17JUL2008 (95) 8. 17JUL2008 (95) - 17JUL2008 (95)
Duration of AE	1. 8 2. 3 3. 1 4. 3 5. 5 6. 3 7. 4 8. 1
Dose on AE onset	1.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014021

Parameter	Value
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014022/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/59/WHITE/ITALY/YES
Medical history	Asthenia, Pyrexia, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACIDO FOLICO, AMIKACINA, ANTRA, ATRA, AUGMENTIN, CEFTAZIDIME, CONTRAMAL, DESAMETASONE, ENOXAPARIN, ENOXAPARINA, IDARUBICINA, IMIPENEM, LEVOFLOXACINA, METRONIDAZOLO, MYLICON, NISTATINA, OMEPRAZOLO, PLASIL, TRIATEC, VANCOMICINA, WARFARIN, ZOFRAN
Adverse Events (AE) Preferred term	1. Pruritus 2. Leukopenia 3. Flatulence 4. Acute leukaemia 5. Thrombocytopenia 6. Anaemia 7. Abscess limb 8. Anxiety
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 15MAY2008 (16) - 27MAY2008 (28) 2. 16MAY2008 (17) - 26MAY2008 (27) 3. 20MAY2008 (21) - 22MAY2008 (23) 4. 27MAY2008 (28) - --------- (.) 5. 08JUN2008 (40) - 20JUN2008 (52) 6. 10JUN2008 (42) - 16JUL2008 (78) 7. 12JUN2008 (44) - --------- (.) 8. 10JUL2008 (72) - --------- (.)
Duration of AE	1. 13 2. 11 3. 3 4. . 5. 13 6. 37 7. . 8. .
Dose on AE onset	1. 2.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014022

Parameter	Value
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED AND RESTARTED
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. WORSENED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014029

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014029/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/ITALY/YES
Medical history	Anaemia, Gastrointestinal carcinoma, Glaucoma, Hiatus hernia, Hypertension, Intestinal operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALPHAGAN, CAPECITABINA, CEFAZOLINA, COSOPT, DESAMETASONE, DIOSMECTAL, EFFORTIL, ENOXAPARIN, FERROGRAD, GRANISETRON, LOPERAMIDE, METRONIDAZOLO, OMEPRAZOLE, OXALIPLATINO, OXATOMIDE, PALONOSETRON, PARACETAMOLO, PLASIL, RIOPAN, WARFARIN, XALATAN
Adverse Events (AE) Preferred term	1. Abdominal pain 2. Vomiting 3. Pyrexia 4. Hypotension 5. Pyrexia 6. Iron deficiency anaemia 7. Pruritus 8. Abdominal pain 9. Diarrhoea 10. Diarrhoea 11. Vomiting 12. Haematuria 13. Anaemia 14. Abdominal pain 15. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MODERATE/NO/NO/YES 11. MODERATE/NO/NO/YES 12. MODERATE/YES/NO/YES 13. MODERATE/YES/NO/YES 14. MODERATE/NO/NO/YES 15. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 16AUG2008 (3) - 16AUG2008 (3) 2. 26AUG2008 (13) - 09SEP2008 (27) 3. 26AUG2008 (13) - 28AUG2008 (15) 4. 01SEP2008 (19) - 08SEP2008 (26)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014029

Parameter	Value
	5. 16SEP2008 (34) - 17SEP2008 (35)
	6. 10OCT2008 (58) - 03NOV2008 (82)
	7. 14OCT2008 (62) - 14OCT2008 (62)
	8. 14OCT2008 (62) - 14OCT2008 (62)
	9. 12NOV2008 (91) - 12NOV2008 (91)
	10. 14NOV2008 (93) - 18NOV2008 (97)
	11. 14NOV2008 (93) - 01DEC2008 (110)
	12. 29NOV2008 (108) - 02DEC2008 (111)
	13. 01DEC2008 (110) - 03DEC2008 (112)
	14. 01DEC2008 (110) - 01DEC2008 (110)
	15. 04DEC2008 (113) - 09DEC2008 (118)
Duration of AE	1. 1
	2. 15
	3. 3
	4. 8
	5. 2
	6. 25
	7. 1
	8. 1
	9. 1
	10. 5
	11. 18
	12. 4
	13. 3
	14. 1
	15. 6
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014029

Parameter	Value
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. REMEDIAL DRUG THERAPY
	10. DOSE OF STUDY DRUG REDUCED,REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. STUDY DRUG DISCONTINUED AND RESTARTED
	13. STUDY DRUG DISCONTINUED AND RESTARTED
	14. REMEDIAL DRUG THERAPY
	15. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014029

Parameter	Value
	12. RESOLVED
	13. WORSENED
	14. RESOLVED
	15. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-220014029[4)]	ANEMIA（PT：貧血） 治験担当医はエノキサパリンとの因果関係評価を行っていない。弊社は、エノキサパリンについては、時間的関連性が認められないため、因果関係は否定できると考える。 HEMATURIA（PT：血尿） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては、時間的関連性が認められないため、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014042

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220014042/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/ITALY/YES
Medical history	Cerebrovascular disorder, Hypertension, Hyponatraemia, Myocardial ischaemia, Parkinsonism, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXICILLIN TRIHYDRATE+POTASSIUM CLAVULANATE, CANRENOL, CARDIOASPIRIN, CIPROFLOXACIN, DICODRAL, ENOXAPARIN, ENTEROGERMINA, ENTEROLACTIS [LACTOBACILLUS CASEI], EPOETIN BETA THREE WEEKLY, FUROSEMIDE, FUROSEMIDE THREE WEEKLY, FUROSEMIDE TWICE WEEKLY, ISOSORBIDE MONONITRATE, LASIX, POTASSIUM CANRENOATE, QUETIAPINA, SELEDIE, SIMVASTATINA, SUPRADYN, WARFARIN
Adverse Events (AE) Preferred term	1. Cystitis 2. Diarrhoea 3. Anaemia 4. Cardiac failure chronic 5. Cystitis 6. Hypercholesterolaemia 7. International normalised ratio decreased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 18FEB2009 (2) - 24FEB2009 (8) 2. 21FEB2009 (5) - 25FEB2009 (9) 3. 27FEB2009 (11) - 06MAR2009 (18) 4. 27FEB2009 (11) - 06MAR2009 (18) 5. 04MAR2009 (16) - 06MAR2009 (18) 6. 22APR2009 (65) - 03JUN2009 (107) 7. 06JUL2009 (140) - 12JUL2009 (146)
Duration of AE	1. 7 2. 5 3. 8 4. 8 5. 3 6. 43 7. 7
Dose on AE onset	1. 2. 3. 4. 5.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220014042

Parameter	Value
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220034002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220034002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/ITALY/YES
Medical history	Liver disorder, Skin discolouration, Rib fracture, Spinal fracture, Traumatic lung injury
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATENOLOLO, CO-EFFERALGAN, ENOXAPARIN, LIXIDOL, WARFARIN
Adverse Events (AE) Preferred term	1. Tachycardia 2. Chest pain 3. Lung adenocarcinoma 4. Haemothorax 5. Tachycardia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. SEVERE/YES/YES/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 29AUG2007 (3) - 03SEP2007 (8) 2. 30AUG2007 (4) - 04SEP2007 (9) 3. 30AUG2007 (4) - --------- (.) 4. 03SEP2007 (8) - 04SEP2007 (9) 5. 04SEP2007 (9) - --------- (.)
Duration of AE	1. 6 2. 6 3. . 4. 2 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 5. NONE
Outcome of event	1. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220034002

Parameter	Value
	2. RESOLVED
	3. UNCHANGED
	4. DEATH
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号：11702-220034002

死亡に至るまでの経過

被験者は 72 歳、白人男性。2007 年 8 月 27 日に深部静脈血栓症と診断され、同日エノキサパリン（16,000UI）／用量調節ワルファリンの投与を開始した。

2007 年 8 月 30 日、被験者は肺腺癌（肺腺癌）を発現した。本事象は重大な医学的事象であったため、重篤とされた。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「なし」と判断した。2007 年 8 月 27 日、被験者は両下肢深部静脈血栓症に起因する潜在性悪性腫瘍の有無を検査するため入院した。同日の胸部 CT スキャンで、右肺に 3cm 大の小結節が認められた。2007 年 8 月 28 日に治験薬の投与が中断され、8 月 30 日に診断目的で肺生検術を実施した。8 月 31 日に治験薬の投与は再開された。生検の結果、肺腺癌が確認された。術後の疼痛緩和のため Co-Efferalgan 及び Lixidol が投与された。本事象の最終転帰は不変と報告された。

2007 年 9 月 3 日、被験者は血胸（出血：大量血胸）を発現した。本事象により被験者は死亡に至ったため重篤とされた。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「あり」と判断した。被験者は肺損傷の病歴を有していた。2007 年 9 月 4 日に行った CT では右胸膜腔への大量血胸、右肺虚脱及び前方気胸が認められた。血圧 70/50mmHg、心拍数 120 回/分。ヘモグロビン値は 2g/dL 以上低下した（2007 年 8 月 27 日：13.3g/dL、8 月 30 日：12.6g/dL、9 月 4 日：10.3g/dL）。PT-INR 1.32（2007 年 9 月 2 日）、1.87（2007 年 9 月 3 日）。2007 年 9 月 3 日、治験薬の投与が中止された。本事象に対する治療として、血漿増量剤の Emagel、及び Adrenaline が投与され、2007 年 9 月 4 日に濃厚赤血球が輸血された（500mL×6 回）。同日、本事象により被験者は死亡に至った。剖検は実施されなかった。

CIAC は、血胸（出血：大量血胸）を「重大な出血事象」とし、死亡原因を出血と判定した。

Laboratory Parameter	Normal Range	Date	Result	Date	Result	Date	Result
Hemoglobin	13.0-17.5 g/dL	27 Aug 2007	13.3 g/dL	30 Aug 2007	**12.6 g/dL (L)**	04 Sep 2007	**10.3 g/dL (L)**
Platelets	150-450 giga/L	27 Aug 2007	**134 giga/L (L)**	30 Aug 200	152 giga/L	04 Sep 2007	180 giga/L
Pict Seconds		27 Aug 2007	**77.30 S (H)**				
Prothrombin Time (PT)		27 Aug 2007	**15.80 S (H)**				
PT, INR	0.9-1.2 NONE	27 Aug 2007	**1.3 NONE (H)**				

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220034006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220034006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/83/WHITE/ITALY/YES
Medical history	Benign prostatic hyperplasia, Cholecystectomy, Gastritis, Gastric cancer, Hypertension, Idiopathic thrombocytopenic purpura, Knee arthroplasty, Poliomyelitis, Hypoacusis, Skin neoplasm excision, Gastritis haemorrhagic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DELTACORTENE, DIURESIX, FOLINA, GAVISCON ADVANCE, NEXIUM, OMNIC, TARGOSID, TAZOCIN, TORECAN, VERAPAMIL
Adverse Events (AE) Preferred term	1. Asthenia 2. Palpitations 3. Subcutaneous haematoma 4. Contusion 5. Vertigo 6. Anaemia 7. Cellulitis 8. Bursitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/YES/NO/YES 6. MILD/NO/YES/YES 7. SEVERE/NO/YES/YES 8. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 06FEB2008 (14) - --------- (.) 2. 23FEB2008 (31) - 23FEB2008 (31) 3. 12MAR2008 (49) - 19MAR2008 (56) 4. 12MAR2008 (49) - 19MAR2008 (56) 5. 23APR2008 (91) - 03MAY2008 (101) 6. 16MAY2008 (114) - --------- (.) 7. 11JUL2008 (170) - 29AUG2008 (219) 8. 11JUL2008 (170) - 29AUG2008 (219)
Duration of AE	1. . 2. 1 3. 8 4. 8 5. 11 6. . 7. 50 8. 50
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220034006

Parameter	Value
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220084004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220084004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/38/BLACK/ITALY/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Alanine aminotransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 08SEP2007 (16) - 19SEP2007 (27)
Duration of AE	1. 12
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. NONE
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220084042

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220084042/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/76/WHITE/ITALY/YES
Medical history	Myocardial ischaemia, Diverticulum intestinal, Essential hypertension, Atrial fibrillation, Benign prostatic hyperplasia, Cardiac ablation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMILODIPINE, AMLODIPINE, CEFIXORAL, CONTROL, DELTACORTENE, LASIX, LOBIVON, MITTOVAL, NITROGLYCERINE, POTASSIUM CANRENOATE, PROPAFENONE, PROSTIDE, RAMIPRIL
Adverse Events (AE) Preferred term	1. Headache 2. Hypertension 3. Erysipelas 4. Nephrotic syndrome 5. Nephrotic syndrome 6. Insomnia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 26MAR2009 (8) - 10APR2009 (23) 2. 27MAR2009 (9) - 30MAR2009 (12) 3. 04AUG2009 (139) - 21AUG2009 (156) 4. 18AUG2009 (153) - 26AUG2009 (161) 5. 27AUG2009 (162) - --------- (.) 6. 29AUG2009 (164) - 03SEP2009 (169)
Duration of AE	1. 16 2. 4 3. 18 4. 9 5. . 6. 6
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. I

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220084042

Parameter	Value
	6. .
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. WORSENED
	5. UNCHANGED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220084048

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220084048/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/80/WHITE/ITALY/YES
Medical history	Myocardial ischaemia, Chronic obstructive pulmonary disease, Essential hypertension, Hernia, Obesity, Pneumonitis, Metabolic syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, EUPHILLINA, LASITONE, MONOKET, SEACOR, TRIATEC, WARFARIN, ZYLORIC
Adverse Events (AE) Preferred term	1. Constipation 2. Renal cyst 3. Completed suicide
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 26NOV2009 (101) - 26NOV2009 (101) 2. 26NOV2009 (101) - --------- (.) 3. 27NOV2009 (102) - 27NOV2009 (102)
Duration of AE	1. 1 2. . 3. 1
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. NONE 2. NONE 3. NONE
Outcome of event	1. RESOLVED 2. INSUFFICIENT FOLLOW-UP 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220094002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220094002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/81/WHITE/ITALY/YES
Medical history	Metastases to bone, Prostate cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENANTONE, ESTRACYT
Adverse Events (AE) Preferred term	1. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 28DEC2007 (95) - 02JAN2008 (100)
Duration of AE	1. 6
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220104006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220104006/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/ITALY/YES
Medical history	Hypertension, Multiple myeloma, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALCIUM NADROPARIN, COUMADIN, CYCLOPHOSPHAMIDE, SOLUMEDROL, TRIATEC, ZOLEDRONATE
Adverse Events (AE) Preferred term	1. Nausea 2. Excoriation 3. Hepatitis acute 4. Cough 5. Anxiety
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/YES/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 06DEC2007 (1) - 03JAN2008 (29) 2. 07DEC2007 (2) - 03JAN2008 (29) 3. 23JAN2008 (49) - 07FEB2008 (64) 4. 31JAN2008 (57) - 07FEB2008 (64) 5. 27FEB2008 (84) - 27FEB2008 (84)
Duration of AE	1. 29 2. 28 3. 16 4. 8 5. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. F 5. F
Action taken	1. NONE 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY 4. REMEDIAL DRUG THERAPY 5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220104006

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220104008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220104008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/ITALY/YES
Medical history	Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, EFFERALGAN, LANOXIN, TACHIPIRINA
Adverse Events (AE) Preferred term	1. Pyrexia 2. Pyrexia 3. Syncope 4. Rib fracture 5. Atrial fibrillation 6. Atrial fibrillation
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01JAN2008 (20) - 03JAN2008 (22) 2. 10FEB2008 (60) - 12FEB2008 (62) 3. 27MAR2008 (106) - 27MAR2008 (106) 4. 27MAR2008 (106) - 30MAY2008 (170) 5. 27MAR2008 (106) - 27MAR2008 (106) 6. 12JUN2008 (183) - 15JUN2008 (186)
Duration of AE	1. 3 2. 3 3. 1 4. 65 5. 1 6. 4
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. . 6. F

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220104008

Parameter	Value
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220114010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220114010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/83/WHITE/ITALY/YES
Medical history	Basal cell carcinoma, Herpes zoster, Hypercholesterolaemia, Hypertension, Nephrolithiasis, Myocardial ischaemia, Squamous cell carcinoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASCRIPTIN, CARDIRENE, CLEXANE, ENOXAPARIN, KONAKION, LANSOX, LASIX, METOPROLOLO, PLAUNAZIDE, RATACAND, SERTRALINA, SIMVASTATINA, TRITTICO, WARFARIN, XANAX
Adverse Events (AE) Preferred term	1. Transient ischaemic attack 2. Asthenia 3. Depression
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 04AUG2009 (92) - 07AUG2009 (95) 2. 31AUG2009 (119) - --------- (.) 3. 31AUG2009 (119) - --------- (.)
Duration of AE	1. 4 2. . 3. .
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220134002/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/61/WHITE/ITALY/YES
Medical history	Diabetes mellitus, Endometrial cancer, Hysterectomy, Anaemia of malignant disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUMIN, EFFERALGAN (PARACETAMOL), KANRENOL, KLACID, LASIX, LEVOXACIN, REVIVAN (DOPAMINE)
Adverse Events (AE) Preferred term	1. Ischaemic stroke 2. Pyrexia 3. Acute myocardial infarction 4. Anaemia 5. Renal failure acute
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/YES/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/YES/YES 5. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 14OCT2007 (32) - 21OCT2007 (39) 2. 02NOV2007 (51) - 15NOV2007 (64) 3. 08NOV2007 (57) - 20NOV2007 (69) 4. 23NOV2007 (72) - 27NOV2007 (76) 5. 14DEC2007 (93) - 31DEC2007 (110)
Duration of AE	1. 8 2. 14 3. 13 4. 5 5. 18
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. NONE 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134002

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220134004/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/71/WHITE/ITALY/YES
Medical history	Gastric cancer, Pancreatic carcinoma, Gastrectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Haematuria 2. Hepatic enzyme increased 3. Blood bilirubin increased 4. Bile duct stenosis 5. Hepatic enzyme increased 6. Blood bilirubin increased 7. Death
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/YES/YES 4. SEVERE/NO/NO/NO 5. MILD/YES/NO/NO 6. MILD/YES/NO/NO 7. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 15OCT2007 (5) - 22OCT2007 (12) 2. 06NOV2007 (27) - 27NOV2007 (48) 3. 06NOV2007 (27) - 27NOV2007 (48) 4. 20NOV2007 (41) - 20NOV2007 (41) 5. 28NOV2007 (49) - --------- (.) 6. 28NOV2007 (49) - --------- (.) 7. 07DEC2007 (58) - 07DEC2007 (58)
Duration of AE	1. 8 2. 22 3. 22 4. 1 5. . 6. . 7. 1
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134004

Parameter	Value
	2. .
	3. .
	4. F
	5. F
	6. F
	7. F
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
	2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
	3. OTHER
	4. OTHER
	5. NONE
	6. NONE
	7. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. INSUFFICIENT FOLLOW-UP
	7. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220134008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/54/WHITE/ITALY/YES
Medical history	Endometrial cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 03DEC2007 (7) - 05DEC2007 (9)
Duration of AE	1. 3
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220134015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/36/WHITE/ITALY/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, MEPRAL, WARFARIN
Adverse Events (AE) Preferred term	1. Alanine aminotransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 28APR2008 (18) - 12JUN2008 (63)
Duration of AE	1. 46
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. NONE
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220134016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/65/WHITE/ITALY/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 01JUL2008 (70) - 02JUL2008 (71)
Duration of AE	1. 2
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220134022/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/75/WHITE/ITALY/YES
Medical history	Aortic aneurysm, Hypertension, Osteoarthritis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	KETOPROFENE, LANSOPRAZOLE, METOCLOPRAMIDE, OMEPRAZOLE, PRILACE [PRILACE'S INGREDIENTS ARE PIRETANIDE+RAMIPRIL], RISEDRONATE, TRAMADOLE
Adverse Events (AE) Preferred term	1. Osteoarthritis 2. Gastritis 3. Nausea 4. Aortic stenosis 5. Aortic valve incompetence
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 02OCT2008 (1) - 21APR2009 (202) 2. 17NOV2008 (47) - 27NOV2008 (57) 3. 19NOV2008 (49) - 27NOV2008 (57) 4. 21NOV2008 (51) - --------- (.) 5. 21NOV2008 (51) - --------- (.)
Duration of AE	1. 202 2. 11 3. 9 4. . 5. .
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220134022

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220144014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220144014/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/84/WHITE/ITALY/YES
Medical history	Chronic obstructive pulmonary disease, Hypercholesterolaemia, Hypertension, Hypothyroidism
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	COTAREG, EUTIROX, FISIOTENS
Adverse Events (AE) Preferred term	1. Chronic obstructive pulmonary disease
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/NO
Start/stop date of event with relative date	1. 24JUN2008 (189) - 14JUL2008 (209)
Duration of AE	1. 21
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. F
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220144025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220144025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/84/WHITE/ITALY/YES
Medical history	Gastritis, Hypertension, Iron deficiency, Benign prostatic hyperplasia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FERROGRAD, LUCEN, OMNIC, PRINZIDE, WARFARIN
Adverse Events (AE) Preferred term	1. Anaemia 2. Gastric haemorrhage 3. Gastric cancer
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MODERATE/YES/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 13MAY2008 (85) - 09JUL2008 (142) 2. 16MAY2008 (88) - 04JUN2008 (107) 3. 16MAY2008 (88) - 04JUN2008 (107)
Duration of AE	1. 58 2. 20 3. 20
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-220144025[3)]	BLEEDING FROM GASTRIC NEOFORMATION NOS（PT：腫瘍出血） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220144033

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220144033/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/82/WHITE/ITALY/YES
Medical history	Endometrial cancer, Erysipelas, Hypertension, Hyperuricaemia, Hepatic cirrhosis, Thrombophlebitis, Upper limb fracture, Gammopathy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXICILLIN, CLAVULANATE POTASSIUM, ENOXAPARIN, SELEPARINA, WARFARIN, ZESTRIL, ZYLORIC
Adverse Events (AE) Preferred term	1. Joint dislocation 2. Platelet count decreased
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 30MAY2008 (29) - 15JUN2008 (45) 2. 31MAY2008 (30) - 04AUG2008 (95)
Duration of AE	1. 17 2. 66
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 2. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-220144033[4)]	LUXATION LEFT SHOULDER（PT：関節脱臼） 治験担当医は報告事象とワルファリンとの因果関係評価を行っていない。弊社は、外傷性の事象であることから、ワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 220154010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/220154010/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/67/WHITE/ITALY/YES
Medical history	Foot fracture, Benign prostatic hyperplasia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	TERAFLUSS, TOBRADEX
Adverse Events (AE) Preferred term	1. Retinal detachment
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 05SEP2008 (151) - 08SEP2008 (154)
Duration of AE	1. 4
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/240024012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/49/WHITE/SPAIN/YES
Medical history	Anaemia, Mastitis, Mastitis, Septic embolus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ANESTHESIA NOS, AUGMENTINE (AMOXICILLIN 500 MG/CLAVULANIC 125 MG, AUGMENTINE RETARD, CIPROFLOXACINO, ENOXAPARIN, FEROGRADUMET, FERROPROTINA, FRAGMIN, PANTOPRAZOL, PARACETAMOL, VENOFER, ZINNAT
Adverse Events (AE) Preferred term	1. Mastitis 2. Mastitis 3. Mastitis 4. Peripheral ischaemia 5. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/NO 5. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 15DEC2008 (49) - 29DEC2008 (63) 2. 13FEB2009 (109) - 27FEB2009 (123) 3. 26MAR2009 (150) - 10AUG2009 (287) 4. 09NOV2009 (378) - 23NOV2009 (392) 5. 17NOV2009 (386) - 21NOV2009 (390)
Duration of AE	1. 15 2. 15 3. 138 4. 15 5. 5
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY,OTHER 5. OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024012

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/240024014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/70/WHITE/SPAIN/YES
Medical history	Appendicectomy, Hemiparesis, Hypertension, Insomnia, Subdural haematoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMOXICILLIN/CLAVULANIC ACID, BAYCIP, BOI K, BROADLEAF PLANTAIN COOK, CALAMIN LOTION, CAPTOPRIL, CEFIXIMA, CEFOTAXIME, CEFTAZIDIMA, CODEISAN, COLESTID, DEXCLORFENIRAMINA, DEXCLORFENIRAMINA RETARD, ENALAPRIL, ENOXAPARIN, FENITOINA, INNOHEP 20000, LACTITOL, LEVOFLOXACINO, LOPERAMIDA, LORAZEPAM, MAGNESIO LACTATO, METILPREDNISOLONA, METOCLOPRAMIDA, METRONIDAZOL, OMEPRAZOL, PANTOPRAZOL, PARACETAMOL, POLARAMINE, POTASIO CLORURO, PREDNISONA, SALAZOPIRINA, SUERO FISIOLOGICO, SUERO GLUCOSADO, ULTRA-LEVURA
Adverse Events (AE) Preferred term	1. Respiratory tract infection 2. Dermatitis exfoliative 3. Vomiting 4. Constipation 5. Urinary tract infection 6. Diarrhoea 7. Dermatitis exfoliative 8. Respiratory tract infection 9. Gastroenteritis 10. Gastroenteritis 11. Colitis ulcerative 12. Colitis ulcerative 13. Pneumonia 14. Rash 15. Pneumonia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/YES/NO/YES 7. MODERATE/YES/NO/YES 8. MODERATE/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/NO/YES/YES 11. SEVERE/NO/YES/YES 12. MILD/NO/NO/YES 13. SEVERE/NO/YES/YES 14. MILD/NO/NO/YES 15. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01NOV2008 (2) - 03NOV2008 (4)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024014

Parameter	Value
	2. 02NOV2008 (3) - 23NOV2008 (24)
	3. 03NOV2008 (4) - 03NOV2008 (4)
	4. 07NOV2008 (8) - 08NOV2008 (9)
	5. 02DEC2008 (33) - 07DEC2008 (38)
	6. 09DEC2008 (40) - 09JAN2009 (71)
	7. 14DEC2008 (45) - 29DEC2008 (60)
	8. 16DEC2008 (47) - 20DEC2008 (51)
	9. 20DEC2008 (51) - 26DEC2008 (57)
	10. 26DEC2008 (57) - 31DEC2008 (62)
	11. 09JAN2009 (71) - 05FEB2009 (98)
	12. 06FEB2009 (99) - --------- (.)
	13. 25MAR2009 (146) - 01APR2009 (153)
	14. 25MAR2009 (146) - 26MAR2009 (147)
	15. 01APR2009 (153) - 06APR2009 (158)
Duration of AE	1. 3
	2. 22
	3. 1
	4. 2
	5. 6
	6. 32
	7. 16
	8. 5
	9. 7
	10. 6
	11. 28
	12. .
	13. 8
	14. 2
	15. 6
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024014

Parameter	Value
	13.
	14.
	15.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	11. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. OTHER
	15. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024014

Parameter	Value
	9. WORSENED
	10. RESOLVED
	11. IMPROVED
	12. UNCHANGED
	13. IMPROVED
	14. RESOLVED
	15. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/240024021/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/SPAIN/YES
Medical history	Depression, Obesity, Peripheral vascular disorder, Type 2 diabetes mellitus, Umbilical hernia, Myocardial ischaemia, Dyslipidaemia, Renal impairment
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AAS, ACENOCOUMAROL, ANESTHESIC NOS, ATORVASTATINA, AUMENTINE, CALCIUM GLUCONATE, CARBEDILOL, CIPROFLOXACINO, CITALOPRAM, CLEXANE, CLINDAMICINA, DEXKETOPROFENO, DUPHALAC [LACTULOSE], ENOXAPARIN, FENTANILO 12, FUROSEMIDA, FUROSEMIDE, GABAPENTINA, GLUCOSE, GLUCOSE SERUM 40%, INSULINA NPH, IRUXOL MONO, LACTITOL, METAMIZOL, METFORMINA, MORPHYNE SULPHATE, NALOXONE, NITROPLAST 10, NORMLGEL, OMEPRAZOL, PANTOPRAZOL, PARACETAMOL, PASTA LASSAR IMBA, PENTOXIFILINA, PLASIMINE 2%, PRINPERAN, RESINCALCIO, SEVREDOL, TRAMADOL
Adverse Events (AE) Preferred term	1. Nausea 2. Constipation 3. Peripheral vascular disorder 4. Transient ischaemic attack 5. Hypertension 6. Confusional state 7. Renal failure acute 8. Hypoglycaemia 9. Peripheral vascular disorder 10. Renal failure acute 11. Atrioventricular block 12. Hyperkalaemia 13. Constipation 14. Vomiting
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/YES/YES 7. MILD/NO/NO/YES 8. MILD/NO/YES/YES 9. SEVERE/NO/YES/YES 10. MILD/NO/NO/YES 11. MODERATE/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/YES/NO/YES 14. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 25MAR2009 (6) - 27MAR2009 (8) 2. 27MAR2009 (8) - 28MAR2009 (9)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024021

Parameter	Value
	3. 10MAY2009 (52) - 10AUG2009 (144)
	4. 09JUL2009 (112) - 09JUL2009 (112)
	5. 09JUL2009 (112) - 09JUL2009 (112)
	6. 01AUG2009 (135) - 03AUG2009 (137)
	7. 02AUG2009 (136) - 03AUG2009 (137)
	8. 03AUG2009 (137) - 04AUG2009 (138)
	9. 11AUG2009 (145) - 24AUG2009 (158)
	10. 11AUG2009 (145) - --------- (.)
	11. 11AUG2009 (145) - 11AUG2009 (145)
	12. 11AUG2009 (145) - 24AUG2009 (158)
	13. 16AUG2009 (150) - 22AUG2009 (156)
	14. 17AUG2009 (151) - 17AUG2009 (151)
Duration of AE	1. 3
	2. 2
	3. 93
	4. 1
	5. 1
	6. 3
	7. 2
	8. 2
	9. 14
	10. .
	11. 1
	12. 14
	13. 7
	14. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
Dose status on AE onset	1.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024021

Parameter	Value
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5.
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	10. REMEDIAL DRUG THERAPY
	11. NONE
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. WORSENED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. IMPROVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 240024021

Parameter	Value
	14. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/69/WHITE/CANADA/YES
Medical history	Breast cancer, Hypertension, Insomnia, Pain, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, APO DOXY, APO FUROSEMIDE, APO TRIAZO, ARTIFICIAL TEARS, ATIVAN, ATROVENT, CALCIUM/MAGNESIUM/ZINC, COZAAR, DILAUDID, DOPAMINE, ENOXAPARIN, FENTANYL, GRAVOL, HALIBUT LIVER OIL, HEPARIN, HYDRALAZINE, INSULIN, KAYEXALATE, KETOCONAZOLE, KETOROLAC, LASIX, LEVAQUIN, MERREM, MERSYNDOL, MIDAZOLAM, MORPHINE, MULTIVITAMIN, NITRODUR, NORTRIPTYLINE, NOVO-SPIROTON, OXYCOCET, PANTOLOC, PREGABALIN, PREVACID, RALIVIA, RANITIDINE, SODIUM BICARBONATE, SOFLAX, TRAZODONE, VENTOLIN, VERAPAMIL, WARFARIN, ZITHROMAX
Adverse Events (AE) Preferred term	1. Tendon injury 2. Contusion 3. Epistaxis 4. Pneumonia 5. Pneumonia 6. Hyperkalaemia 7. Cardiac failure congestive
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/YES/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MODERATE/NO/NO/YES 7. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --MAY2008 (.) - 15AUG2008 (256) 2. 04DEC2007 (1) - 15JAN2008 (43) 3. 06APR2008 (125) - 06APR2008 (125) 4. 19MAY2008 (168) - 01JUN2008 (181) 5. 18SEP2008 (290) - 22SEP2008 (294) 6. 18SEP2008 (290) - 20SEP2008 (292) 7. 19SEP2008 (291) - --------- (.)
Duration of AE	1. . 2. 43 3. 1 4. 14 5. 5 6. 3 7. .
Dose on AE onset	1. 2. 3.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054001

Parameter	Value
	4.
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. DEATH
	6. RESOLVED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/48/WHITE/CANADA/YES
Medical history	Drug hypersensitivity, Depression, Hypertension, Pain in extremity, Hip arthroplasty, Colitis ulcerative, Vitamin B12 deficiency, Hernia repair, Nephrolithiasis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CIPROFLOXACIN, GRAVOL, MORPHINE, NAPROXEN, OXYCONTIN, SODIUM CHLORIDE 0.9%, TORADOL, TRAMACET, TYLENOL [ACETAMINOPHEN ALONE], VITAMIN B12
Adverse Events (AE) Preferred term	1. Skin hyperpigmentation 2. Post thrombotic syndrome 3. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/YES/YES
Start/stop date of event with relative date	1. --MAY2008 (.) - --------- (.) 2. --MAY2008 (.) - --------- (.) 3. 04FEB2008 (33) - 10APR2008 (99)
Duration of AE	1. . 2. . 3. 67
Dose on AE onset	1. 2. 3. 20 mg
Dose status on AE onset	1. 2. 3. .
Action taken	1. NONE 2. NONE 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054009/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/47/WHITE/CANADA/YES
Medical history	Dysmenorrhoea, Uterine leiomyoma, Menometrorrhagia, Drug hypersensitivity, Thrombophlebitis, Female sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DIMENHYDRINATE, EVRA TRANSDERMAL PATCH, FRAGMIN, GRAVOL, LUPRON, MIRENA IUD, MORPHINE, OVRAL, POTASSIUM CHLORIDE, PROVERA, TYLENOL #3, TYLENOL [ACETAMINOPHEN + CODEINE]
Adverse Events (AE) Preferred term	1. Menorrhagia 2. Menorrhagia 3. Cough
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES 2. SEVERE/YES/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 08JAN2008 (5) - 14JAN2008 (11) 2. 29FEB2008 (57) - 15MAR2008 (72) 3. 27APR2008 (115) - --MAY2008 (.)
Duration of AE	1. 7 2. 16 3. .
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054028/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/CANADA/YES
Medical history	Arthritis, Asthma, Blood cholesterol increased, Osteoporosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTONEL, ADVAIR PUFFER, CALCIUM, CELEBREX, CRESTOR, ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Injection site haematoma 2. Haemarthrosis 3. Haematoma 4. Excoriation
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/YES/YES/YES 3. SEVERE/YES/YES/YES 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 28MAR2008 (1) - 18APR2008 (22) 2. 05AUG2008 (131) - 15SEP2008 (172) 3. 05AUG2008 (131) - 15SEP2008 (172) 4. 10SEP2008 (167) - 15OCT2008 (202)
Duration of AE	1. 22 2. 42 3. 42 4. 36
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED PERMANENTLY 3. STUDY DRUG DISCONTINUED PERMANENTLY 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054028

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-260054028[1),1)]	HEMARTHROSIS（PT：出血性関節症） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。 HEMATOMA（PT：血腫） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054034

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054034/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/44/WHITE/CANADA/YES
Medical history	Alcohol abuse, Drug abuse, Insomnia, Psychotic disorder, Suicide attempt, Scrotal infection, Depression
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BENZTROPINE, CELEXA, IMOVANE, LANSOPRAZOLE EC, LORAZEPAM, LOXAPINE, NICOTINE PATCH, PERCOCET, RISPERIDONE, SEROQUEL, TRAMACET
Adverse Events (AE) Preferred term	1. Depression 2. Psychotic disorder 3. Depression 4. Psychotic disorder
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 16DEC2008 (202) - 19DEC2008 (205) 2. 16DEC2008 (202) - 19DEC2008 (205) 3. 04APR2009 (311) - 19JUN2009 (387) 4. 04APR2009 (311) - 19JUN2009 (387)
Duration of AE	1. 4 2. 4 3. 77 4. 77
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054034

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054048

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054048/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/81/WHITE/CANADA/YES
Medical history	Dry eye, Post gastric surgery syndrome, Duodenal ulcer, Hip fracture, Urinary tract infection, Lumbar vertebral fracture, Prostatomegaly, Duodenal operation, Intervertebral disc degeneration
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEFTRIAXONE, CIPROFLOXACIN, DALTEPARIN, DEXTROSE 5% WTER/ 0.45 % NORMAL SALINE, DEXTROSE 5%WATER/0.9% NORMAL SALINE, HYPROMELLOSE, MIRTAZAPINE, TAMSULOSIN, TYLENOL [ACETAMINOPHEN ALONE], TYLENOL [THE INGREDIENTS FOR THE TYLENOL ARE ACETAMINOPHEN ALONE], VITAMIN C
Adverse Events (AE) Preferred term	1. Urinary tract infection 2. Haematuria 3. Hypernatraemia 4. Depression 5. Spinal compression fracture 6. Epistaxis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MILD/YES/NO/YES
Start/stop date of event with relative date	1. --NOV2008 (.) - 19DEC2008 (106) 2. 12DEC2008 (99) - 13DEC2008 (100) 3. 13DEC2008 (100) - 19DEC2008 (106) 4. 13DEC2008 (100) - 19DEC2008 (106) 5. 15DEC2008 (102) - --------- (.) 6. 30JAN2009 (148) - 03FEB2009 (152)
Duration of AE	1. . 2. 2 3. 7 4. 7 5. . 6. 5
Dose on AE onset	1. 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. 2. . 3. I

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054048

Parameter	Value
	4. I
	5. I
	6. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. IMPROVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054053

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054053/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/71/WHITE/CANADA/YES
Medical history	Adrenal adenoma, Renal cyst, Gastrooesophageal reflux disease, Hydronephrosis, Hyperlipidaemia, Hypertension, Injury, Explorative laparotomy, Prostate cancer, Prostatectomy, Type 1 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLCYSTEINE, APO-HYDRO, APO-RAMIPRIL, AVANDIA, CRESTOR, DALTEPARIN, DETROL, DEXTROSE 5% WATER, DIAMICRON MR, HUMULIN 70/30, HYDROCHLOROTHIAZIDE, INSULIN ASPART, INSULIN REGULAR, LUPRON DEPOT, METFORMIN, MORPHINE, OXYCODONE, PANTOPRAZOLE, RABEPRAZOLE, TYLENOL ES
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Melaena 3. Hypoglycaemia 4. Rib fracture 5. Overdose 6. Chest pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 23SEP2008 (9) - --------- (.) 2. 30SEP2008 (16) - 30SEP2008 (16) 3. 10DEC2008 (87) - 10DEC2008 (87) 4. 10DEC2008 (87) - 06JAN2009 (114) 5. 12DEC2008 (89) - 06JAN2009 (114) 6. 20AUG2009 (340) - --NOV2009 (.)
Duration of AE	1. . 2. 1 3. 1 4. 28 5. 26 6. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054053

Parameter	Value
	4. .
	5. .
	6. .
Action taken	1. NONE
	2. NONE
	3. OTHER
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. NONE
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054054

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054054/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/44/WHITE/CANADA/YES
Medical history	Cellulitis, Drug dependence, Hypertension, Panic attack, Osteosynthesis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASA, ATACAND [CANDESARTAN CILEXETIL], CELEBREX, CEPHALEX, ENOXAPARIN, FLAGYL, LEVOQUIN, OPIOIDS, PAROXETINE, WARFARIN
Adverse Events (AE) Preferred term	1. Pneumonia 2. Scrotal swelling 3. Penile swelling 4. Haematuria 5. Urethral haemorrhage 6. Urinary retention 7. International normalised ratio increased 8. Thrombosis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES 3. SEVERE/NO/YES/YES 4. MILD/YES/NO/YES 5. MILD/YES/NO/YES 6. MODERATE/NO/NO/YES 7. MODERATE/YES/NO/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 10APR2009 (206) - 10MAY2009 (236) 2. 23APR2009 (219) - 28APR2009 (224) 3. 23APR2009 (219) - 28APR2009 (224) 4. 24APR2009 (220) - 27APR2009 (223) 5. 24APR2009 (220) - 27APR2009 (223) 6. 24APR2009 (220) - 26APR2009 (222) 7. 24APR2009 (220) - 27APR2009 (223) 8. 28JUL2009 (315) - 05AUG2009 (323)
Duration of AE	1. 31 2. 6 3. 6 4. 4 5. 4 6. 3 7. 4 8. 9
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054054

Parameter	Value
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054058

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054058/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/52/WHITE/CANADA/YES
Medical history	Alcoholism, Thrombocytopenia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	COLCHICINE, TYLENOL #3
Adverse Events (AE) Preferred term	1. Epistaxis 2. Gout 3. Transaminases increased 4. Nausea 5. Blister 6. Transaminases increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 31OCT2008 (3) - 31OCT2008 (3) 2. 01NOV2008 (4) - 08NOV2008 (11) 3. 12NOV2008 (15) - 27OCT2009 (364) 4. 15NOV2008 (18) - 17NOV2008 (20) 5. 12AUG2009 (288) - --------- (.) 6. 28OCT2009 (365) - --------- (.)
Duration of AE	1. 1 2. 8 3. 350 4. 3 5. . 6. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. . 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054058

Parameter	Value
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. NONE 4. NONE 5. NONE 6. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. WORSENED 4. RESOLVED 5. UNCHANGED 6. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-260054058[2),2)]	INCREASED TRANSAMINITIS（PT：トランスアミナーゼ上昇）2 事象有 1）治験担当医は、合併症（飲酒）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。 2）治験担当医は、合併症（飲酒）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054065

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054065/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/20/WHITE/CANADA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	GABAPENTIN, SEASONALE, TORADOL, TYLENOL #3, TYLENOL ES
Adverse Events (AE) Preferred term	1. Migraine 2. Paranasal cyst
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07DEC2008 (4) - 15DEC2008 (12) 2. 14DEC2008 (11) - --------- (.)
Duration of AE	1. 9 2. .
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054069

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054069/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/76/WHITE/CANADA/YES
Medical history	Alcohol abuse, Arrhythmia, Blood cholesterol increased, Diverticulum, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALTACE, ATIVAN, FRESH FROZEN PLASMA, LANOXIN, LIPITOR, MICARDIS, PICA-SALAX, TYLENOL [PARACETAMOL ALONE]
Adverse Events (AE) Preferred term	1. Gastrointestinal haemorrhage 2. Headache 3. Agitation
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 08JUL2009 (204) - 09JUL2009 (205) 2. 09JUL2009 (205) - 09JUL2009 (205) 3. 09JUL2009 (205) - 10JUL2009 (206)
Duration of AE	1. 2 2. 1 3. 2
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. I 3. I
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054085

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260054085/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/54/BLACK/CANADA/YES
Medical history	Diabetes mellitus, Hypercholesterolaemia, Hypertension, Prolactinoma, Uveitis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALTACE, CRESTOR, ENOXAPARIN, EZETROL, INSULIN HUMULLIN, INSULIN LENTES, METFORMIN, WARFARIN
Adverse Events (AE) Preferred term	1. Liver function test abnormal 2. Pancreatic carcinoma metastatic 3. Nausea 4. Hyponatraemia 5. Tachycardia 6. Cough 7. Vomiting 8. Upper gastrointestinal haemorrhage 9. Pancreatic carcinoma metastatic 10. Oedema 11. Hypokalaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/NO 3. MILD/NO/NO/NO 4. MILD/NO/NO/NO 5. MILD/NO/NO/NO 6. MILD/NO/NO/NO 7. MILD/NO/NO/NO 8. SEVERE/NO/YES/NO 9. SEVERE/NO/YES/NO 10. MODERATE/NO/NO/NO 11. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 19JUN2009 (25) - --------- (.) 2. 21JUN2009 (27) - 04JUL2009 (40) 3. 22JUN2009 (28) - --------- (.) 4. 22JUN2009 (28) - --------- (.) 5. 22JUN2009 (28) - 26JUN2009 (32) 6. 23JUN2009 (29) - --------- (.) 7. 23JUN2009 (29) - --------- (.) 8. 05JUL2009 (41) - 07JUL2009 (43) 9. 05JUL2009 (41) - 20JUL2009 (56) 10. 05JUL2009 (41) - --------- (.) 11. 08JUL2009 (44) - 09JUL2009 (45)
Duration of AE	1. . 2. 14 3. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054085

Parameter	Value
	4. .
	5. 5
	6. .
	7. .
	8. 3
	9. 16
	10. .
	11. 2
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. OTHER
	2. OTHER
	3. REMEDIAL DRUG THERAPY,OTHER
	4. OTHER
	5. OTHER
	6. REMEDIAL DRUG THERAPY,OTHER
	7. REMEDIAL DRUG THERAPY,OTHER
	8. REMEDIAL DRUG THERAPY,OTHER
	9. REMEDIAL DRUG THERAPY,OTHER
	10. REMEDIAL DRUG THERAPY,OTHER
	11. REMEDIAL DRUG THERAPY,OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260054085

Parameter	Value
Outcome of event	1. UNCHANGED
	2. WORSENED
	3. UNCHANGED
	4. UNCHANGED
	5. RESOLVED
	6. UNCHANGED
	7. UNCHANGED
	8. RESOLVED
	9. DEATH
	10. UNCHANGED
	11. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260124016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260124016/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/82/WHITE/CANADA/YES
Medical history	Arthritis, Constipation, Hypercholesterolaemia, Hypothyroidism, Lung neoplasm malignant, Gastrooesophageal cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLSALICYLIC ACID, ARTHROTEC [THE INGREDIENTS OF ARTHROTEC ARE DICLOFENAC SODIUM PLUS MISOPROSTOL.], DECADRON, ELTROXIN, ENSURE DIETARY SUPPLEMENT, FENOFIBRATE, GLUCOSAMINE, GLYCERINE SUPPOSITORY, MAGNESIUM, MAXERAN, MORPHINE, MULTIVITAMIN, PARIET, SENOKOT, SOFLAX, TARCEVA, VITAMIN C
Adverse Events (AE) Preferred term	1. Melaena 2. Abdominal discomfort 3. Lung carcinoma cell type unspecified recurrent 4. Gastric cancer recurrent 5. Failure to thrive
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/YES/YES 5. SEVERE/NO/NO/YES
Start/stop date of event with relative date	1. 20MAR2008 (1) - --------- (.) 2. 24MAR2008 (5) - --------- (.) 3. 25AUG2008 (159) - --------- (.) 4. 25AUG2008 (159) - --------- (.) 5. 25AUG2008 (159) - 19SEP2008 (184)
Duration of AE	1. . 2. . 3. . 4. . 5. 26
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260124016

Parameter	Value
Outcome of event	5. NONE 1. UNCHANGED 2. UNCHANGED 3. UNCHANGED 4. UNCHANGED 5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 260124058

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/260124058/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/58/WHITE/CANADA/YES
Medical history	Genital herpes, Gastrooesophageal reflux disease, Hepatic cyst, Hypertension, Menopause, Congenital cystic kidney disease, Female sterilisation, Seasonal allergy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AVAMYS NASAL SPRAY, CILAZAPRIL, DOCUSATE SODIUM, FAMCICLOVIR, FRAGMIN, HYDROMORPHONE, ONDANSETRON, PANTOLOC, PLENDIL, ZOVIRAX
Adverse Events (AE) Preferred term	1. Ovarian cancer
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 29MAY2009 (43) - --------- (.)
Duration of AE	1. .
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280034001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280034001/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/76/WHITE/BELGIUM/YES
Medical history	Pneumonia, Parkinson's disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACEDICON, AMANTAN, AUGMENTIN, CIPROXINE, DAFALGAN, DUOVENT, LAXOBERON, LYSOMUCIL, MONURIL, MOTILIUM INSTANT, PROLOPA, REDOXON, STALEVO, STILNOCT, TAZOCIN
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Decubitus ulcer 3. Urinary tract infection 4. Urinary retention 5. Urinary tract infection 6. Cough 7. Sputum retention 8. Device occlusion
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/YES/YES 7. MILD/NO/YES/YES 8. MILD/NO/YES/YES
Start/stop date of event with relative date	1. --JAN2008 (.) - --------- (.) 2. 28JUN2007 (4) - 18AUG2007 (55) 3. 06JUL2007 (12) - 16JUL2007 (22) 4. 12JUL2007 (18) - 12JUL2007 (18) 5. 26JUL2007 (32) - 07AUG2007 (44) 6. 25AUG2007 (62) - 30AUG2007 (67) 7. 25AUG2007 (62) - 30AUG2007 (67) 8. 09SEP2007 (77) - 10SEP2007 (78)
Duration of AE	1. . 2. 52 3. 11 4. 1 5. 13 6. 6 7. 6 8. 2
Dose on AE onset	1. 2. 15 mg 3. 15 mg 4. 15 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280034001

Parameter	Value
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. OTHER
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY,OTHER
	7. REMEDIAL DRUG THERAPY,OTHER
	8. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280034004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280034004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/82/WHITE/BELGIUM/YES
Medical history	Hypertension, Hysterectomy, Insomnia, Osteoporosis, Pneumonia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ALDACTAZINE, DEPOMEDROL, DULCOLAX [THE INGREDIENTS OF DULCOLAX ARE BISACODYL], ENOXAPARIN, FOSAMAX, IBUPROFEN, MICARDIS, MOTILIUM INSTANT, NAPROZINE, STILNOCT
Adverse Events (AE) Preferred term	1. Constipation 2. Carpal tunnel syndrome 3. Pneumonia 4. Disseminated tuberculosis 5. Diarrhoea
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/NO/NO 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 24OCT2007 (3) - 25OCT2007 (4) 2. 30OCT2007 (9) - 18DEC2007 (58) 3. 22NOV2007 (32) - 04FEB2008 (106) 4. 28NOV2007 (38) - --------- (.) 5. 30NOV2007 (40) - 30NOV2007 (40)
Duration of AE	1. 2 2. 50 3. 75 4. . 5. 1
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY 5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280034004

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280054003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280054003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/53/WHITE/BELGIUM/YES
Medical history	Alcohol abuse, Gastritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXICILLINE, ANTABUSE, BEFACT FORTE [CYANOCOBALAMINE , PYRIDOXINEHYDROCHLORIDE : RIBOFLAVINEAND THIAMIN, ENOXAPARIN, ETUMINE, LORAMET, PARACETAMOL + CODEINE, SEROXAT, TRAZOLAN, WARFARIN
Adverse Events (AE) Preferred term	1. Toothache 2. Haematoma 3. Alcohol poisoning
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 13MAY2008 (75) - --------- (.) 2. 20JUN2008 (113) - --------- (.) 3. 20JUN2008 (113) - 23JUN2008 (116)
Duration of AE	1. . 2. . 3. 4
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280064004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280064004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/64/WHITE/BELGIUM/YES
Medical history	Arrhythmia, Diabetes mellitus, Hepatic steatosis, Hypercholesterolaemia, Hypertension, Hyperuricaemia, Insomnia, Ischaemic cardiomyopathy, Colonic polyp, Gastric bypass, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUMINE, AUGMENTIN, BICARBONATE SODIUM 1.4%, CACO3, CARDIOASPIRINE, CORDARONE, CORVATON, DAFALGAN, DALACIN [INGREDIENT: CLINDAMYCIN], DOLZAM, DUOVENT, EFFORTIL, ENOXAPARIN, GLUCOPHAGE, GLUCOSE 5% + 22.5 MG NACL +40MEQ KCL + 10 MG MGSO4 [SEVERE METABOLIC DYSFUNCTION, LACTATE RINGER + 30 MEQ KCL, LACTEOL, LANOXIN, LASIX, MAGNETOP, MAXI LASIX [CONFIRM SAME AS LASIX BUT HIGHER CONCENTRATION], MOVICOL, PERFUSALGAN, SOLUMEDROL, SPIRIVA, SPIRONOLACTONE, STEROPOTASSIUM, STILNOCT, STRUCTOKABIVEN, TEMESTA, TILCOTIL, TILDIEM, TILDIEM RETARD, ULTRA POTASSIUM, WARFARIN, XANAX, ZANTAC, ZURCALE, ZYLORIC
Adverse Events (AE) Preferred term	1. Metabolic disorder 2. Atrial fibrillation 3. Pleural effusion 4. Anaemia 5. Atrial fibrillation 6. Renal failure acute 7. Bronchitis 8. Thrombocytopenia 9. Erysipelas 10. Staphylococcus test positive
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MODERATE/YES/YES/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MODERATE/YES/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 24JUL2008 (142) - 18AUG2008 (167) 2. 24JUL2008 (142) - 25JUL2008 (143) 3. 24JUL2008 (142) - --AUG2008 (.) 4. 25JUL2008 (143) - --------- (.) 5. 26JUL2008 (144) - --------- (.) 6. 29JUL2008 (147) - 02AUG2008 (151) 7. 02AUG2008 (151) - 11AUG2008 (160) 8. 02AUG2008 (151) - 10AUG2008 (159) 9. 16AUG2008 (165) - 18AUG2008 (167)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280064004

Parameter	Value
	10. 18AUG2008 (167) - --AUG2008 (.)
Duration of AE	1. 26
	2. 2
	3. .
	4. .
	5. .
	6. 5
	7. 10
	8. 9
	9. 3
	10. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280064004

Parameter	Value
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED 4. UNCHANGED 5. IMPROVED 6. RESOLVED 7. RESOLVED 8. RESOLVED 9. RESOLVED 10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-280064004[4),1)]	ACUTE RENAL INSUFFICIENCY（PT：急性腎不全） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、代謝障害によるものであり、エノキサパリン及びアセノクマロールとの因果関係は否定できると考える。 ANEMIA（PT：出血性貧血） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280074017

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280074017/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/BELGIUM/YES
Medical history	Appendicectomy, Hypertension, Lymphadenopathy mediastinal, Myocardial infarction, Myocardial infarction, Ear infection, Renal colic, Hypoacusis, Dyslipidaemia, Tobacco poisoning
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BISOPROLOL, CARDIOASPIRINE, CRESTOR, ENOXAPARIN, PLAVIX, ZESTRIL
Adverse Events (AE) Preferred term	1. Haematuria 2. Benign prostatic hyperplasia 3. Anaemia 4. Non-small cell lung cancer 5. Metastases to central nervous system
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/NO 4. SEVERE/NO/YES/NO 5. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 08JAN2009 (16) - 21JAN2009 (29) 2. 13JAN2009 (21) - --------- (.) 3. 15JAN2009 (23) - --------- (.) 4. 22JAN2009 (30) - --------- (.) 5. 06FEB2009 (45) - --------- (.)
Duration of AE	1. 14 2. . 3. . 4. . 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. OTHER 2. NONE 3. OTHER 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 5. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280074017

Parameter	Value
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. UNCHANGED
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280084001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280084001/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/76/WHITE/BELGIUM/YES
Medical history	Back pain, Hypertension, Insomnia, Scoliosis, Venous insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BRUFEN, CALCIUM, DEXAMETHASONE, KONAKION, LASIX, NOVATEC, RIVOTRIL, STILNOCT, TEMESTA EXPIDET, TRADONAL ODIS, VITAMINE D, ZALDIAR, ZYLORIC
Adverse Events (AE) Preferred term	1. Back pain 2. Lymphoma 3. Anxiety
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 23OCT2007 (43) - --------- (.) 2. 15NOV2007 (66) - --------- (.) 3. 16NOV2007 (67) - --------- (.)
Duration of AE	1. . 2. . 3. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280084008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280084008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/57/WHITE/BELGIUM/YES
Medical history	Cholecystectomy, Diverticulum intestinal, Hepatic cirrhosis, Hepatic steatosis, Hyperlipidaemia, Hypertension, Liver transplant rejection, Liver transplant, Congenital cystic kidney disease, Osteoporosis, Pleural effusion, Dyspepsia, Postmenopause, Cerebral haemangioma, Hernial eventration
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMLOR, AUGMENTIN, CALCIUM, CELL CEPT, CIPROXINE, D CURE, EMCONCOR, ENOXAPARIN, ENOXAPARINE, EUSAPRIM, MAGNETOP, MEDROL, OMEPRAZOL, PRAVASTATINE, PROGRAFT, RAPAMUNE, XYZALL
Adverse Events (AE) Preferred term	1. Asthenia 2. Liver transplant rejection 3. Pruritus allergic 4. Diverticulum intestinal 5. Liver transplant rejection 6. Urinary tract infection 7. Pancreatic cyst 8. Hernial eventration
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/NO 8. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. --AUG2008 (.) - --------- (.) 2. 08JUN2008 (66) - 12JUN2008 (70) 3. 30JUN2008 (88) - --JUL2008 (.) 4. 14JUL2008 (102) - 25JUL2008 (113) 5. 15SEP2008 (165) - 24SEP2008 (174) 6. 24SEP2008 (174) - --OCT2008 (.) 7. 16OCT2008 (196) - 17OCT2008 (197) 8. 28OCT2008 (208) - 29OCT2008 (209)
Duration of AE	1. . 2. 5 3. . 4. 12 5. 10 6. . 7. 2 8. 2
Dose on AE onset	1.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280084008

Parameter	Value
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	6. REMEDIAL DRUG THERAPY
	7. OTHER
	8. OTHER
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280114008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280114008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/64/WHITE/BELGIUM/YES
Medical history	Meniscus lesion, Meniscus lesion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AUGMENTIN, CLEXANE, DAFALGAN, ENOXAPARIN, TARADYL
Adverse Events (AE) Preferred term	1. Dyspnoea 2. Cholecystitis acute 3. Cholelithiasis 4. Hydrocholecystis 5. Colitis 6. Hepatic steatosis 7. Insomnia 8. Gouty arthritis 9. Oedema
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/NO/NO 8. MILD/NO/NO/NO 9. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 16NOV2008 (51) - 20NOV2008 (55) 2. 01DEC2008 (66) - 12DEC2008 (77) 3. 01DEC2008 (66) - 17APR2009 (203) 4. 01DEC2008 (66) - 17APR2009 (203) 5. 01DEC2008 (66) - 12DEC2008 (77) 6. 03DEC2008 (68) - --------- (.) 7. 05DEC2008 (70) - 05DEC2008 (70) 8. 09DEC2008 (74) - 12DEC2008 (77) 9. 25FEB2009 (152) - 26FEB2009 (153)
Duration of AE	1. 5 2. 12 3. 138 4. 138 5. 12 6. . 7. 1 8. 4 9. 2

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280114008

Parameter	Value
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	3. OTHER
	4. OTHER
	5. NONE
	6. OTHER
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280114008

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-280114008[4)]	ACUTE CHOLECYSTITIS（PT：急性胆嚢炎） 治験担当医は、エノキサパリンについて、因果関係評価を行っていない。弊社は、合併症（胆嚢結石症）によるものであり、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280134004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/BELGIUM/YES
Medical history	Alcohol abuse, Arteriosclerosis coronary artery, Gastric ulcer, Gastritis, Haemochromatosis, Hypercholesterolaemia, Hypertension, Gouty arthritis, Obesity, Oesophagitis, Varicose vein
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEDOCARD, COLCHICINE, DAFALGAN, ENOXAPARIN, LOORTAN 50, NEXIAM, PLAVIX, SOTALEX, STILNOCT, TIAPRIDAL, VALIUM, VOLTAREN, WARFARIN, ZANTAC 300, ZURCALE 40
Adverse Events (AE) Preferred term	1. Haematuria 2. Haemoptysis 3. International normalised ratio abnormal 4. Liver function test abnormal 5. Gastritis 6. Oesophagitis 7. Hepatic steatosis 8. Malaise 9. Myocardial ischaemia 10. Haematemesis 11. Liver function test abnormal 12. Pancreatitis acute 13. Malaise 14. Palpitations 15. Alcohol withdrawal syndrome 16. Gout 17. Oedema peripheral 18. Epistaxis 19. Haematuria 20. International normalised ratio abnormal 21. Liver function test abnormal 22. Liver function test abnormal 23. Pancreatitis 24. Malaise 25. Vomiting 26. Alcohol withdrawal syndrome
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/YES/NO/YES 4. MODERATE/NO/YES/YES 5. MODERATE/NO/YES/YES 6. MODERATE/NO/YES/YES 7. MILD/NO/YES/YES 8. SEVERE/NO/YES/YES 9. MILD/NO/YES/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134004

Parameter	Value
	10. MILD/YES/NO/YES
	11. MODERATE/NO/NO/YES
	12. MILD/NO/NO/YES
	13. MODERATE/NO/NO/YES
	14. MILD/NO/NO/YES
	15. MODERATE/NO/NO/YES
	16. MILD/NO/NO/YES
	17. MODERATE/NO/NO/YES
	18. MILD/YES/NO/YES
	19. MILD/YES/NO/YES
	20. SEVERE/YES/NO/YES
	21. MILD/NO/NO/YES
	22. SEVERE/NO/YES/NO
	23. MODERATE/NO/YES/NO
	24. SEVERE/NO/YES/NO
	25. MILD/NO/YES/NO
	26. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 04AUG2007 (38) - --AUG2007 (.)
	2. 04AUG2007 (38) - 04AUG2007 (38)
	3. 05AUG2007 (39) - 06AUG2007 (40)
	4. 27AUG2007 (61) - 27SEP2007 (92)
	5. 27AUG2007 (61) - 31AUG2007 (65)
	6. 27AUG2007 (61) - 31AUG2007 (65)
	7. 27AUG2007 (61) - --------- (.)
	8. 27AUG2007 (61) - 31AUG2007 (65)
	9. 27AUG2007 (61) - 29AUG2007 (63)
	10. 23OCT2007 (118) - 23OCT2007 (118)
	11. 30OCT2007 (125) - 23NOV2007 (149)
	12. 30OCT2007 (125) - 13NOV2007 (139)
	13. 30OCT2007 (125) - --------- (.)
	14. 30OCT2007 (125) - 04NOV2007 (130)
	15. 02NOV2007 (128) - 04NOV2007 (130)
	16. 05NOV2007 (131) - --------- (.)
	17. 12NOV2007 (138) - --------- (.)
	18. 01DEC2007 (157) - --DEC2007 (.)
	19. 01DEC2007 (157) - --DEC2007 (.)
	20. 21DEC2007 (177) - 28DEC2007 (184)
	21. 21DEC2007 (177) - 27DEC2007 (183)
	22. 27DEC2007 (183) - 10JAN2008 (197)
	23. 27DEC2007 (183) - 30DEC2007 (186)
	24. 27DEC2007 (183) - 30DEC2007 (186)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134004

Parameter	Value
	25. 27DEC2007 (183) - 28DEC2007 (184)
	26. 28DEC2007 (184) - 30DEC2007 (186)
Duration of AE	1. .
	2. 1
	3. 2
	4. 32
	5. 5
	6. 5
	7. .
	8. 5
	9. 3
	10. 1
	11. 25
	12. 15
	13. .
	14. 6
	15. 3
	16. .
	17. .
	18. .
	19. .
	20. 8
	21. 7
	22. 15
	23. 4
	24. 4
	25. 2
	26. 3
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134004

Parameter	Value
	14.
	15.
	16.
	17.
	18.
	19.
	20.
	21.
	22.
	23.
	24.
	25.
	26.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
	20.
	21.
	22.
	23.
	24.
	25.
	26.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
	2. STUDY DRUG DISCONTINUED AND RESTARTED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134004

Parameter	Value
	3. DOSE OF STUDY DRUG REDUCED
	4. OTHER
	5. REMEDIAL DRUG THERAPY,OTHER
	6. REMEDIAL DRUG THERAPY
	7. OTHER
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. NONE
	11. OTHER
	12. OTHER
	13. NONE
	14. NONE
	15. REMEDIAL DRUG THERAPY
	16. REMEDIAL DRUG THERAPY,OTHER
	17. OTHER
	18. DOSE OF STUDY DRUG REDUCED
	19. DOSE OF STUDY DRUG REDUCED
	20. DOSE OF STUDY DRUG REDUCED,REMEDIAL DRUG THERAPY
	21. OTHER
	22. OTHER
	23. REMEDIAL DRUG THERAPY,OTHER
	24. OTHER
	25. REMEDIAL DRUG THERAPY
	26. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. IMPROVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. IMPROVED
	12. RESOLVED
	13. IMPROVED
	14. RESOLVED
	15. RESOLVED
	16. IMPROVED
	17. INSUFFICIENT FOLLOW-UP

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134004

Parameter	Value
	18. RESOLVED
	19. RESOLVED
	20. RESOLVED
	21. WORSENED
	22. RESOLVED
	23. RESOLVED
	24. RESOLVED
	25. RESOLVED
	26. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/280134010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/70/WHITE/BELGIUM/YES
Medical history	Appendicectomy, Bronchiectasis, Tobacco user, Emphysema, Reflux oesophagitis, Thrombosed varicose vein, Thrombosed varicose vein, Varicose vein operation, Varicose vein operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLCYSTEINE EG, AMUKIN, ATROVENT, AUGMENTIN, AVELOX, CISPLATINUM, CLAVUCID 875, CLEXANE, COMBIVENT, DAFALGAN, DUOVENT, EMEND, ENOXAPARIN, GEMCITABINE, GLAZIDIM, LYSOMUCIL, MEDROL, OMEPRAZOL EG, SERETIDE 50/500, SOLU MEDROL, SPIRIVA, ULTRA MG, WARFARIN
Adverse Events (AE) Preferred term	1. Epistaxis 2. Lymphadenopathy mediastinal 3. Infective exacerbation of chronic obstructive airways disease 4. Metastatic squamous cell carcinoma 5. Infective exacerbation of chronic obstructive airways disease 6. Epistaxis 7. Infective exacerbation of chronic obstructive airways disease 8. Infective exacerbation of chronic obstructive airways disease 9. Radiation pneumonitis 10. Lung infection 11. Thrombocytopenia 12. Sepsis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MILD/YES/NO/YES 7. SEVERE/NO/YES/YES 8. MODERATE/NO/NO/YES 9. SEVERE/NO/YES/NO 10. SEVERE/NO/YES/NO 11. SEVERE/NO/YES/NO 12. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 16JAN2008 (1) - 27FEB2008 (43) 2. 17JAN2008 (2) - 07FEB2008 (23) 3. 18JAN2008 (3) - 05FEB2008 (21) 4. 07FEB2008 (23) - --------- (.) 5. 02MAR2008 (47) - 10MAR2008 (55) 6. 01APR2008 (77) - --APR2008 (.) 7. 10APR2008 (86) - 06MAY2008 (112) 8. 26MAY2008 (132) - 09JUN2008 (146) 9. 10JUN2008 (147) - --------- (.)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134010

Parameter	Value
	10. 10JUN2008 (147) - 03JUL2008 (170)
	11. 14JUN2008 (151) - --------- (.)
	12. 18JUN2008 (155) - --------- (.)
Duration of AE	1. 43
	2. 22
	3. 19
	4. .
	5. 9
	6. .
	7. 27
	8. 15
	9. .
	10. 24
	11. .
	12. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Action taken	1. DOSE OF STUDY DRUG REDUCED
	2. OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 280134010

Parameter	Value
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. NONE
	12. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. WORSENED
	3. RESOLVED
	4. IMPROVED
	5. IMPROVED
	6. RESOLVED
	7. IMPROVED
	8. WORSENED
	9. UNCHANGED
	10. DEATH
	11. UNCHANGED
	12. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300064006/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/83/WHITE/NETHERLANDS/YES
Medical history	Iron deficiency anaemia, Osteoarthritis, Skin irritation, Osteoarthritis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DAKTACORT, DICLOFENAC, PARACETAMOL, UNG TRIAMCINOLON AC 1MG / G
Adverse Events (AE) Preferred term	1. Oedema peripheral 2. Chest pain 3. Haematoma 4. Fatigue 5. Dyspnoea exertional 6. Microcytic anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. --NOV2007 (.) - --------- (.) 2. --FEB2008 (.) - 05MAR2008 (189) 3. 30AUG2007 (1) - 18SEP2007 (20) 4. 11FEB2008 (166) - --------- (.) 5. 11FEB2008 (166) - 05MAR2008 (189) 6. 27FEB2008 (182) - 18MAR2008 (202)
Duration of AE	1. . 2. . 3. 20 4. . 5. 24 6. 21
Dose on AE onset	1. 2. 3. 15 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. 2. 3. . 4. . 5. . 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064006

Parameter	Value
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. IMPROVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064024

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300064024/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/67/WHITE/NETHERLANDS/YES
Medical history	Diabetes mellitus, Hypercholesterolaemia, Hypertension, Osteoporosis, Osteoarthritis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARCOXIA, DIAZEPAM, HYDROCHLOORTHIAZIDE, LISINOPRIL, METOPROLOL, MS CONTIN, NAPROXEN, OXYCONTIN, OXYNORM, PARACETAMOL, SIMVASTATINE, TOLBUTAMIDE
Adverse Events (AE) Preferred term	1. Anaemia 2. Blood alkaline phosphatase increased 3. Arthralgia 4. Duodenal ulcer 5. Constipation 6. Constipation 7. Rectal cancer 8. Abscess limb 9. Metabolic acidosis 10. Abdominal sepsis 11. Respiratory failure 12. Death
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MILD/YES/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/NO 7. SEVERE/NO/NO/NO 8. MODERATE/NO/NO/NO 9. MODERATE/NO/NO/NO 10. MODERATE/NO/NO/NO 11. MODERATE/NO/NO/NO 12. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. --JUL2008 (.) - 30JUL2008 (108) 2. 18JUN2008 (66) - --------- (.) 3. 11JUL2008 (89) - --------- (.) 4. 11JUL2008 (89) - --------- (.) 5. 12JUL2008 (90) - 15JUL2008 (93) 6. 18JUL2008 (96) - 20JUL2008 (98) 7. 25JUL2008 (103) - --------- (.) 8. 26JUL2008 (104) - 27JUL2008 (105) 9. 27JUL2008 (105) - --------- (.) 10. 27JUL2008 (105) - --------- (.) 11. 27JUL2008 (105) - --------- (.) 12. 30JUL2008 (108) - 30JUL2008 (108)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064024

Parameter	Value
Duration of AE	1. . 2. . 3. . 4. . 5. 4 6. 3 7. . 8. 2 9. . 10. . 11. . 12. 1
Dose on AE onset	1. 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg 8. 20 mg 9. 20 mg 10. 20 mg 11. 20 mg 12. 20 mg
Dose status on AE onset	1. 2. . 3. . 4. . 5. F 6. F 7. F 8. F 9. F 10. F 11. F 12. F
Action taken	1. NONE 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 4. NONE 5. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064024

Parameter	Value
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY,OTHER
	8. OTHER
	9. NONE
	10. NONE
	11. NONE
	12. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. UNCHANGED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. RESOLVED
	9. UNCHANGED
	10. UNCHANGED
	11. UNCHANGED
	12. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-300064024[3),4)]	HEMORRHAGIC ANEMIA（PT：出血性貧血） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。 ULCUS DUODENI（PT：十二指腸潰瘍） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、併用薬（非ステロイド性鎮痛薬）によるものであり、リバーロキサバンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。

1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064034

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300064034/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/60/WHITE/NETHERLANDS/YES
Medical history	Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BROOMHEXINE, CODEINE, DICLOFENAC, ENOXAPARIN, FYTOMENADION
Adverse Events (AE) Preferred term	1. Haematoma 2. Arthralgia 3. Cough 4. Vein pain 5. Cough 6. Pyrexia 7. Abdominal pain 8. Muscle haemorrhage 9. Haematoma 10. Haematoma 11. Anaemia 12. International normalised ratio increased 13. Pyrexia 14. Constipation 15. Oedema peripheral 16. Blood bilirubin increased 17. Bilirubin conjugated increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. SEVERE/YES/YES/YES 9. MODERATE/YES/NO/YES 10. MODERATE/YES/NO/YES 11. MODERATE/NO/NO/YES 12. MODERATE/YES/NO/YES 13. MILD/NO/NO/YES 14. MILD/NO/NO/YES 15. MILD/NO/NO/NO 16. MILD/NO/NO/NO 17. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 22AUG2008 (1) - 18SEP2008 (28) 2. 22AUG2008 (1) - 27AUG2008 (6)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064034

Parameter	Value
	3. 05SEP2008 (15) - 24OCT2008 (64)
	4. 24OCT2008 (64) - 24NOV2008 (95)
	5. 28DEC2008 (129) - 18JAN2009 (150)
	6. 01JAN2009 (133) - 08JAN2009 (140)
	7. 06JAN2009 (138) - 25JAN2009 (157)
	8. 12JAN2009 (144) - 16FEB2009 (179)
	9. 12JAN2009 (144) - 16FEB2009 (179)
	10. 12JAN2009 (144) - 16FEB2009 (179)
	11. 12JAN2009 (144) - --------- (.)
	12. 12JAN2009 (144) - 13JAN2009 (145)
	13. 12JAN2009 (144) - 16JAN2009 (148)
	14. 14JAN2009 (146) - 15JAN2009 (147)
	15. 17JAN2009 (149) - --------- (.)
	16. 22JAN2009 (154) - 16FEB2009 (179)
	17. 22JAN2009 (154) - 16FEB2009 (179)
Duration of AE	1. 28
	2. 6
	3. 50
	4. 32
	5. 22
	6. 8
	7. 20
	8. 36
	9. 36
	10. 36
	11. .
	12. 2
	13. 5
	14. 2
	15. .
	16. 26
	17. 26
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064034

Parameter	Value
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	9. NONE
	10. NONE
	11. NONE
	12. NONE
	13. NONE
	14. REMEDIAL DRUG THERAPY
	15. REMEDIAL DRUG THERAPY
	16. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064034

Parameter	Value
Outcome of event	17. NONE 1. RESOLVED 2. RESOLVED 3. RESOLVED 4. RESOLVED 5. RESOLVED 6. RESOLVED 7. RESOLVED 8. RESOLVED 9. RESOLVED 10. RESOLVED 11. IMPROVED 12. RESOLVED 13. RESOLVED 14. RESOLVED 15. UNCHANGED 16. RESOLVED 17. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-300064034[2)]	ANEMIA（PT：貧血） 治験担当医は、否定できると判断した。弊社は、アセノクマロール投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064038

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300064038/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/35/WHITE/NETHERLANDS/YES
Medical history	Blood alkaline phosphatase increased, Arthralgia, Biopsy cervix, Dizziness, Fatigue, Hydronephrosis, Laparotomy, Metastases to lymph nodes, Uterine cancer, Nausea, Normochromic normocytic anaemia, Palpitations, Paraesthesia, Radiotherapy, Dyspnoea, Squamous cell carcinoma of the cervix, Syncope, Vomiting, Weight decreased, Nephrostomy tube placement, Ureteral catheterisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMOXICILLINE/CLAVUL, ENOXAPARIN, LOSEC, OXYCODON, OXYCONTIN, PARACETAMOL, PRIMPERAN
Adverse Events (AE) Preferred term	1. Anaemia 2. Abdominal pain
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 01OCT2008 (13) - 11OCT2008 (23) 2. 10OCT2008 (22) - --------- (.)
Duration of AE	1. 11 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064042

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300064042/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/64/WHITE/NETHERLANDS/YES
Medical history	Articular disc disorder, Epilepsy, Hypertension, Migraine, Osteoarthritis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CAPTOPRIL, DEPAKINE, DICLOFENAC, ENOXAPARIN, FRAXODI, INFLUVAC 2008/2009, NADROPARINE, PARACETAMOL
Adverse Events (AE) Preferred term	1. Feeling hot 2. Feeling abnormal 3. Heart rate decreased 4. Alanine aminotransferase increased 5. Gastroenteritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 18OCT2008 (3) - --------- (.) 2. 18OCT2008 (3) - 01MAR2009 (137) 3. 18OCT2008 (3) - --------- (.) 4. 30OCT2008 (15) - 18DEC2008 (64) 5. 25JAN2009 (102) - 26JAN2009 (103)
Duration of AE	1. . 2. 135 3. . 4. 50 5. 2
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064042

Parameter	Value
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064066

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300064066/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/41/WHITE/NETHERLANDS/YES
Medical history	Arthroscopy, Dysmenorrhoea, Migraine
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CIPROFLOXACINE, DICLOFENAC, ENOXAPARIN, FYTOMENADION, GLUCOSE 2.5 % / NACL 0.9 %, IMIGRAN NOSESPRAY, METOPROLOL, MICROGYNON, NADROPARINE, NITROFURANTOINE, PARACETAMOL, PARACETEMOL, PETHIDINE, PRIMPERAN
Adverse Events (AE) Preferred term	1. Headache 2. International normalised ratio increased 3. Urinary tract infection 4. Haematuria 5. International normalised ratio increased 6. Paraesthesia 7. Hypoaesthesia 8. Pain in extremity 9. Sleep disorder 10. Headache 11. Dyspnoea
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/NO/YES/YES 4. MODERATE/YES/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 05FEB2009 (3) - 11FEB2009 (9) 2. 06FEB2009 (4) - 09FEB2009 (7) 3. 12FEB2009 (10) - 02MAR2009 (28) 4. 13FEB2009 (11) - 14FEB2009 (12) 5. 13FEB2009 (11) - 16FEB2009 (14) 6. 26FEB2009 (24) - 22JUN2009 (140) 7. 26FEB2009 (24) - 22JUN2009 (140) 8. 26FEB2009 (24) - 22JUN2009 (140) 9. 26FEB2009 (24) - --------- (.) 10. 01MAR2009 (27) - 01APR2009 (58) 11. 01MAR2009 (27) - 01APR2009 (58)
Duration of AE	1. 7 2. 4

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064066

Parameter	Value
	3. 19
	4. 2
	5. 4
	6. 117
	7. 117
	8. 117
	9. .
	10. 32
	11. 32
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. NONE
	8. NONE
	9. NONE
	10. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300064066

Parameter	Value
Outcome of event	11. NONE 1. RESOLVED 2. RESOLVED 3. RESOLVED 4. RESOLVED 5. RESOLVED 6. RESOLVED 7. RESOLVED 8. RESOLVED 9. UNCHANGED 10. RESOLVED 11. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/51/WHITE/NETHERLANDS/YES
Medical history	Ascites, Depression, Insomnia, Nervousness, Ovarian cancer, Salpingo-oophorectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARBOPLATIN, CITALOPRAM, DEXAMETHASON, DIAZEPAM, FLAGYL, KALIUMCHLORIDE, KEFZOL, LACTULOSE, MAALOX, MAGNESIUM OXIDE, NICORETTE PLASTER, OMEPRAZOL, OXAZEPAM, PACLITAXEL, PARACETAMOL, PRIMPERAN, SEROQUEL, TAVEGIL, TEMAZEPAM, TRIMETHOPRIM, ZOFRAN
Adverse Events (AE) Preferred term	1. Wound dehiscence 2. Ascites 3. Hypokalaemia 4. Wound dehiscence 5. Ascites 6. Cystitis 7. Constipation
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 21MAY2007 (1) - 30MAY2007 (10) 2. 21MAY2007 (1) - 30MAY2007 (10) 3. 23MAY2007 (3) - 10JUN2007 (21) 4. 31MAY2007 (11) - 15JUN2007 (26) 5. 31MAY2007 (11) - 15JUN2007 (26) 6. 11JUN2007 (22) - 14JUN2007 (25) 7. 31JUL2007 (72) - 14AUG2007 (86)
Duration of AE	1. 10 2. 10 3. 19 4. 16 5. 16 6. 4 7. 15
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg 6. 15 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074005

Parameter	Value
	7. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074018/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/NETHERLANDS/YES
Medical history	Hypertension, Prostate cancer, Type 2 diabetes mellitus, Dyslipidaemia, Gastric pH decreased
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CO DIOVAN, CRESTOR, DICLOFENAC, NOVOMIX, OMEPRAZOL, TAMSULOSINE HCI ACTAVIS RETARD, TRAMADOL
Adverse Events (AE) Preferred term	1. Urinary tract obstruction 2. Musculoskeletal pain 3. Abdominal wall cyst
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --OCT2007 (.) - --------- (.) 2. 03SEP2007 (47) - 23OCT2007 (97) 3. 18SEP2007 (62) - 21SEP2007 (65)
Duration of AE	1. . 2. 51 3. 4
Dose on AE onset	1. 2. 20 mg 3. 20 mg
Dose status on AE onset	1. 2. . 3. I
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER 3. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
Outcome of event	1. UNCHANGED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074037

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074037/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/62/WHITE/NETHERLANDS/YES
Medical history	Anaemia, Rectal cancer, Rectal cancer, Metastases to liver, Resection of rectum, Thrombocytopenia, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DIPIDOLOR, FUROSEMIDE, KALIUMCHLORIDE, NORMISON, ONDANSETRON, PARACETAMOL, SLOW-K, TELEBRIX; CONTRAST MEDIUM, TRAMAGETIC, ZOFRAN, ZOLPIDEMTARTRAAT
Adverse Events (AE) Preferred term	1. Spinal column injury 2. Wound haemorrhage 3. Inflammation of wound 4. Wound abscess
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 08OCT2007 (2) - --------- (.) 2. 13OCT2007 (7) - 15OCT2007 (9) 3. 16OCT2007 (10) - 24OCT2007 (18) 4. 28OCT2007 (22) - 06NOV2007 (31)
Duration of AE	1. . 2. 3 3. 9 4. 10
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. OTHER 2. OTHER 3. OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074037

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074043

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074043/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/28/WHITE/NETHERLANDS/YES
Medical history	Osteochondrosis, Breast disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CLEXANE, CYPROTERONE ETHYLESTRADIOL, ENOXAPARIN, IBUPROFEN, LEVONORGESTREL, PARACETAMOL, ZYBAN
Adverse Events (AE) Preferred term	1. Drug exposure during pregnancy 2. Abortion induced
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/NO/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. -----2008 (.) - 07APR2008 (155) 2. 07APR2008 (155) - 07APR2008 (155)
Duration of AE	1. . 2. 1
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. OTHER 2. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074054

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074054/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/53/WHITE/NETHERLANDS/YES
Medical history	Diabetes mellitus, Dyspnoea, Hypertension, Constipation, Uterine prolapse, Vaginal haemorrhage, Right ventricular hypertrophy, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMITRIPTYLINE, ENALAPRIL, ENOXAPARIN, HYDROCHLOROTHIAZIDE, KEFZOL, METRONIDAZOL, MOVICOLON, PRIMOLUT-N, PROVERA, SIMVASTATINE, TRIMETHOPRIM, VIT K
Adverse Events (AE) Preferred term	1. Haematoma 2. Vaginal haemorrhage 3. Haematemesis 4. Vaginal haemorrhage 5. Urinary tract infection 6. Uterine polypectomy
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/YES/NO/YES 4. MILD/YES/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 03DEC2007 (1) - --NOV2008 (.) 2. 13DEC2007 (11) - 19DEC2007 (17) 3. 25DEC2007 (23) - 25DEC2007 (23) 4. 27DEC2007 (25) - 30DEC2007 (28) 5. 15FEB2008 (75) - 20FEB2008 (80) 6. 14MAY2008 (164) - 16MAY2008 (166)
Duration of AE	1. . 2. 7 3. 1 4. 4 5. 6 6. 3
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074054

Parameter	Value
	6.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074083

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074083/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/62/WHITE/NETHERLANDS/YES
Medical history	Arthroscopy, Chorioretinitis, Chronic obstructive pulmonary disease, Hypercholesterolaemia, Female sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMOXICILLINE/CLAVULAANZUUR, CODEINE, ENOXAPARIN, ENOXAPARINE, METAMUCIL, PARACETAMOL, SALMETEROL/FLUTICASONE, SIMVASTATINE, TRAMAL
Adverse Events (AE) Preferred term	1. Liver function test abnormal 2. Thrombophlebitis migrans 3. Dyspnoea 4. Chest pain 5. Bronchitis 6. Lung adenocarcinoma 7. Thrombophlebitis migrans 8. Chorioretinitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/NO/YES/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 04FEB2008 (1) - 11JUN2008 (129) 2. 24FEB2008 (21) - 12MAR2008 (38) 3. 09MAR2008 (35) - 12MAR2008 (38) 4. 09MAR2008 (35) - 12MAR2008 (38) 5. 10MAR2008 (36) - --------- (.) 6. 12MAR2008 (38) - --------- (.) 7. 14APR2008 (71) - --------- (.) 8. 26JUN2008 (144) - 06JUL2008 (154)
Duration of AE	1. 129 2. 18 3. 4 4. 4 5. . 6. . 7. . 8. 11
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074083

Parameter	Value
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED AND RESTARTED,STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. IMPROVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074089

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074089/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/74/WHITE/NETHERLANDS/YES
Medical history	Angina pectoris, Aortic aneurysm, Chronic obstructive pulmonary disease, Diverticulitis, Myocardial infarction, Oesophageal ulcer, Osteoporosis, Pleural disorder, Pneumonia, Reflux oesophagitis, Ventricular tachycardia, Post-traumatic pain, Post-traumatic pain, Implantable defibrillator insertion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ATROVENT, AUGMENTIN, CALCI D3, CALCICHEW, CARBASALAATCALCIUM, COVERSYL, ENOXAPARIN, FOSAMAX, IPRAMOL STERI-NEB INHALOR, METOPROLOL RETARD, MOVICOLON, NATRIUM CHLORIDE 0.9 %, OMEPRAZOL, PARACETAMOL, PREDNISOLON, SERETIDE, SIMVASTATINE, TRAMADOL, TRAMAGETIC RETARD
Adverse Events (AE) Preferred term	1. Pneumonia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 07AUG2008 (178) - 13AUG2008 (184)
Duration of AE	1. 7
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074094

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074094/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/NETHERLANDS/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Prostate cancer
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 13AUG2008 (181) - --------- (.)
Duration of AE	1. .
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. F
Action taken	1. OTHER
Outcome of event	1. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074100

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074100/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/81/WHITE/NETHERLANDS/YES
Medical history	Hiatus hernia, Multiple myeloma, Osteoporosis, Prostate cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ACTRAPID, AUGMENTIN, BISACODYL, COMBIVENT, DEXAMETHASON, ENOXAPARIN, FRAXIPARINE, FRAXODI, KALIUMCHLORIDE, OMEPRAZOL, REVLIMID [M KAHLER], TAZOCIN, TRAMADOL, VITAMINE K
Adverse Events (AE) Preferred term	1. Lower respiratory tract infection 2. Blood glucose increased 3. International normalised ratio increased 4. Respiratory tract infection
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 01MAR2008 (6) - 19MAR2008 (24) 2. 01MAR2008 (6) - --------- (.) 3. 19MAR2008 (24) - 25MAR2008 (30) 4. 24MAR2008 (29) - 26MAR2008 (31)
Duration of AE	1. 19 2. . 3. 7 4. 3
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. INSUFFICIENT FOLLOW-UP 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074100

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074109

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074109/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/50/WHITE/NETHERLANDS/YES
Medical history	Anaemia, Colitis ulcerative, Diabetes mellitus, Tuberculosis, Ileocolectomy, Cervical dysplasia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID, AMOXICILLINE, BECLOMETASON/MESALAZINE, CALCI CHEW, COFACT, EPINEFRINE, FERROFUMARAAT, FRESH FROZEN PLASMA, LANTUS, MAGNESIUM SULFATE, METRONIDAZOL, NOVO SEVEN, PARACETAMOL, POTASSIUM CHLORIDE, PREDNISOLON, PROVERA, TRAMADOL
Adverse Events (AE) Preferred term	1. Arthralgia 2. Rectal haemorrhage 3. Hypokalaemia 4. Menorrhagia 5. Bursitis 6. Bronchitis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/YES/YES/YES 3. MILD/NO/NO/YES 4. MILD/YES/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --JUN2008 (.) - --------- (.) 2. 14MAR2008 (1) - 15MAR2008 (2) 3. 15MAR2008 (2) - 15MAR2008 (2) 4. 01APR2008 (19) - --MAY2008 (.) 5. 29MAY2008 (77) - 07JUN2008 (86) 6. 29MAY2008 (77) - 04JUN2008 (83)
Duration of AE	1. . 2. 2 3. 1 4. . 5. 10 6. 7
Dose on AE onset	1. 2. 15 mg 3. 15 mg 4. 15 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. 2. . 3. I 4. . 5. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074109

Parameter	Value
	6. .
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074111

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074111/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/NETHERLANDS/YES
Medical history	Anaemia, Cholecystectomy, Diverticulitis, Laparotomy, Metastases to liver, Osteoarthritis, Pancreatic carcinoma, Postmenopause, Metastasis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BUSCOPAN, CELECOXIB, HALDOL, MORFINE, OMEPRAZOL, OXAZEPAM, OXYNORM, PARACETAMOL, SANDOSTATINE
Adverse Events (AE) Preferred term	1. Pancreatic carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 05APR2008 (20) - 08APR2008 (23)
Duration of AE	1. 4
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074117

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074117/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/NETHERLANDS/YES
Medical history	Cerebrovascular accident, Depression, Diaphragmatic hernia, Pain in extremity, Hypertension, Microcytic anaemia, Multiple sclerosis, Productive cough, Reflux oesophagitis, Skin disorder, Erosive duodenitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYL CYSTEINE, ACETYLSALICYLIC ACID, AMITRIPTYLINE, AMLODIPINE, DICLOFENAC, KETOCONAZOL, METOPROLOL, MICONAZOL, OMEPRAZOL, PARACETAMOL, TEMAZEPAM
Adverse Events (AE) Preferred term	1. Cerebral haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 31AUG2008 (163) - 09SEP2008 (172)
Duration of AE	1. 10
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074126

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074126/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/79/WHITE/NETHERLANDS/YES
Medical history	Anaemia, Basal cell carcinoma, Dyspnoea, Hypercholesterolaemia, Hypertension, Gastric ulcer, Hepatic steatosis, Type 2 diabetes mellitus, Varices oesophageal
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AUGMENTIN, ENOXAPARIN, FERROFUMARAAT, HYDROCHLOORTHIAZIDE, LISINOPRIL, METFORMINE, MIXTARD 30/70, PANTOZOL, SIMVASTATINE
Adverse Events (AE) Preferred term	1. Pneumonia 2. Large cell carcinoma of the respiratory tract stage unspecified
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 18APR2008 (14) - 25APR2008 (21) 2. 24APR2008 (20) - 29MAY2008 (55)
Duration of AE	1. 8 2. 36
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074137

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074137/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/NETHERLANDS/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMOXICILLINE, AUGMENTIN, BUSCOPAN, COFACT, DIPIDOLOR, DUROGESIC, DUSPATAL, ENOXAPARIN, ENOXAPARINE, FLUIMICIL, MOVICOLON, NADROPARINE, OMEPRAZOL, PARACETAMOL, TRAMADOL, VITAMINE K
Adverse Events (AE) Preferred term	1. Oedema peripheral 2. Abdominal discomfort 3. Haemoptysis 4. Liver function test abnormal 5. Constipation 6. Colon cancer 7. Bacteraemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/NO/YES/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --AUG2008 (.) - --------- (.) 2. --MAY2008 (.) - --------- (.) 3. 15MAY2008 (25) - 28MAY2008 (38) 4. 21MAY2008 (31) - --------- (.) 5. 28MAY2008 (38) - --JUL2008 (.) 6. 24JUN2008 (65) - --------- (.) 7. 02JUL2008 (73) - 17JUL2008 (88)
Duration of AE	1. . 2. . 3. 14 4. . 5. . 6. . 7. 16
Dose on AE onset	1. 2. 3. 4. 5. 6. 7.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074137

Parameter	Value
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY,OTHER
	6. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP
	2. INSUFFICIENT FOLLOW-UP
	3. RESOLVED
	4. INSUFFICIENT FOLLOW-UP
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074142

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074142/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/78/WHITE/NETHERLANDS/YES
Medical history	Oesophageal carcinoma, Diabetes mellitus, Hypercholesterolaemia, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	COZAAR, DEPAKINE CHRONO, GLIMEPIRIDE, HYDROCHLOORTHIAZIDE, NEXIUM, OFLOXACINE, PRAVASTATINE, ULCOGANT [SUCRALFATE]
Adverse Events (AE) Preferred term	1. Pyelonephritis 2. Epilepsy 3. Anaemia 4. Anaemia 5. Haematoma 6. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/YES 4. SEVERE/YES/YES/NO 5. MILD/NO/NO/NO 6. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 24JUN2008 (51) - 05JUL2008 (62) 2. 28JUN2008 (55) - 07JUL2008 (64) 3. 04AUG2008 (92) - 11AUG2008 (99) 4. 12AUG2008 (100) - 03SEP2008 (122) 5. 01SEP2008 (120) - --------- (.) 6. 12SEP2008 (131) - 19SEP2008 (138)
Duration of AE	1. 12 2. 10 3. 8 4. 23 5. . 6. 8
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074142

Parameter	Value
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	5. NONE
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. WORSENED
	4. RESOLVED
	5. INSUFFICIENT FOLLOW-UP
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074156

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074156/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/54/WHITE/NETHERLANDS/YES
Medical history	Osteoarthritis, Hysterectomy, Vein disorder, Postmenopause, Colpocele
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DEXAMETHASON, DORMICUM, FLUTICASONPROPIONAAT, LIDOCAINE, MORPHINE, MOVICOLON, NATTERMAN MUCODYNE ADULT, PARACETAMOL, VESICARE, ZOFRAN
Adverse Events (AE) Preferred term	1. Cough 2. Vaginal haemorrhage 3. Post procedural haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 12OCT2008 (118) - 12OCT2008 (118) 2. 19NOV2008 (156) - 19NOV2008 (156) 3. 24NOV2008 (161) - 28NOV2008 (165)
Duration of AE	1. 1 2. 1 3. 5
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074161

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074161/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/52/WHITE/NETHERLANDS/YES
Medical history	Blister, Varicose vein, Inflammation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ENOXAPARIN, PARACETAMOL
Adverse Events (AE) Preferred term	1. Alanine aminotransferase increased 2. Nasopharyngitis 3. Oropharyngeal blistering 4. Subcutaneous haematoma 5. Joint sprain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 09JUL2008 (10) - 28JUL2008 (29) 2. 14JUL2008 (15) - 28JUL2008 (29) 3. 14JUL2008 (15) - 28JUL2008 (29) 4. 25AUG2008 (57) - 07SEP2008 (70) 5. 25AUG2008 (57) - 31AUG2008 (63)
Duration of AE	1. 20 2. 15 3. 15 4. 14 5. 7
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. NONE 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074161

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074172

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074172/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/61/WHITE/NETHERLANDS/YES
Medical history	Cardiac failure, Goitre, Ischiatic hernia, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ATACAND [THE INGREDIENTS ARE CANDESARTAN ALONE], ENOXAPARIN, FRAXIPARINE, FUROSEMIDE, LANOXIN, METOPROLOL, PARACETAMOL, SLOW-K, STRUMAZOL
Adverse Events (AE) Preferred term	1. Hypertension 2. Cardiac failure 3. Cardiac failure
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12AUG2008 (29) - --------- (.) 2. 05SEP2008 (53) - 15SEP2008 (63) 3. 16SEP2008 (64) - 02FEB2009 (203)
Duration of AE	1. . 2. 11 3. 140
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. IMPROVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-300074172[4)]	DECOMPENSATIO CORDIS（PT：心不全） 治験担当医は、合併症（心筋症）によるものと判断したが、エノキサパリンについては、報告事象との因果関係評価を行っていない。弊社は、合併症（甲状腺腫）によるものであり、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。

1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074191

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074191/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/58/WHITE/NETHERLANDS/YES
Medical history	Congenital great vessel anomaly, Dental implantation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BISACODYL, BISOLVON, FRAXIPARINE, GLUCOSE/NACL INFUSION, KALIUMCHLORIDE, MOVICOLON, PARACETAMOL, RECTAL ENEMA [CONTENTS PER ML :NATRIUMBIFOSFATE 160 MG, NATRIUMFOSFATE 60 MG.], TRAMADOL
Adverse Events (AE) Preferred term	1. Constipation 2. Constipation
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 20AUG2008 (2) - 22AUG2008 (4) 2. 22AUG2008 (4) - 27AUG2008 (9)
Duration of AE	1. 3 2. 6
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. WORSENED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074203

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074203/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/91/WHITE/NETHERLANDS/YES
Medical history	Anaemia, Angina pectoris, Aortic stenosis, Aortic valve replacement, Arteriosclerosis, Cervix carcinoma recurrent, Cervix carcinoma, Diabetes mellitus, Urinary tract infection, Coronary angioplasty, Coronary artery bypass
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMLODIPINE, ASCAL, CLARITROMYCINE, DOMPERIDON, ENALAPRIL, ENOXAPARIN, FERROFUMARAT, FUROSEMIDE, MONOCEDOCARD, MORFINE, OMEPRAZOL, SIMVASTATINE, TOLBUTAMIDE
Adverse Events (AE) Preferred term	1. Cervix carcinoma 2. Dermatitis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 03OCT2008 (10) - 13OCT2008 (20) 2. 03OCT2008 (10) - 12OCT2008 (19)
Duration of AE	1. 11 2. 10
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-300074203[4)]	FATAL PROGRESSION OF CERVICAL CANCER（PT：子宮頚部癌） 治験担当医は、合併症（子宮頸部癌）によるものであると判断したが、エノキサパリンとの因果関係評価は行っていない。弊社は、合併症（子宮頸部癌）によるものであり、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074223

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074223/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/30/WHITE/NETHERLANDS/YES
Medical history	Acute lymphocytic leukaemia, Dermatitis atopic, Depression, Graft versus host disease, Stem cell transplant
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CALCICHEW, ENOXAPARIN, PREDNISOLON, PROTOPIC GEL, ZELITREX
Adverse Events (AE) Preferred term	1. Folate deficiency 2. Depression 3. Traumatic haematoma 4. Cerebral toxoplasmosis 5. Hypokalaemia 6. Post procedural haemorrhage 7. Anxiety 8. Anaemia megaloblastic
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/YES/NO/YES 4. SEVERE/NO/YES/YES 5. MODERATE/NO/NO/NO 6. MILD/YES/NO/NO 7. SEVERE/NO/NO/NO 8. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. --DEC2008 (.) - --------- (.) 2. --NOV2008 (.) - --------- (.) 3. 01NOV2008 (6) - -----2008 (.) 4. 12NOV2008 (17) - 23MAR2009 (148) 5. 20NOV2008 (25) - 15JAN2009 (81) 6. 03DEC2008 (38) - --------- (.) 7. 16DEC2008 (51) - 15JAN2009 (81) 8. 22DEC2008 (57) - --------- (.)
Duration of AE	1. . 2. . 3. . 4. 132 5. 57 6. . 7. 31 8. .
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074223

Parameter	Value
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. RESOLVED
	4. DEATH
	5. RESOLVED
	6. INSUFFICIENT FOLLOW-UP
	7. RESOLVED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074227

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074227/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/77/WHITE/NETHERLANDS/YES
Medical history	Anaemia, Crohn's disease, Crohn's disease, Crohn's disease, Crohn's disease, Crohn's disease, Cystitis, Giardiasis, Hypertension, Hysterectomy, Oral candidiasis, Pancreatitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CALCI-CHEW D3, CIPROXIN, ENOXAPARIN, IMURAN, METRONIDAZOL, PANZYTRAT, PREDNISON, SELOKEEN, SLOW K, VANCOCIN
Adverse Events (AE) Preferred term	1. Leukopenia 2. Pyrexia 3. Crohn's disease 4. Pseudomembranous colitis 5. Alopecia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/YES/NO/YES
Start/stop date of event with relative date	1. --DEC2008 (.) - --------- (.) 2. 06NOV2008 (6) - 16NOV2008 (16) 3. 16NOV2008 (16) - 24NOV2008 (24) 4. 16NOV2008 (16) - 24NOV2008 (24) 5. 07DEC2008 (37) - 04JAN2009 (65)
Duration of AE	1. . 2. 11 3. 9 4. 9 5. 29
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY 5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074227

Parameter	Value
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074231

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074231/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/85/WHITE/NETHERLANDS/YES
Medical history	Chronic obstructive pulmonary disease, Dizziness, Hypertension, Osteoporosis, Polymyalgia rheumatica, Benign prostatic hyperplasia, Vitamin B12 deficiency, Transitional cell carcinoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTONEL, CALCI-CHEW, CLINDAMYCINE, COVERSYL, FLUCLOXACILLINE, FRAXIPARINE, FUROSEMIDE, HYDROCHLOORTHIAZIDE, OMNIC, PARACETAMOL, PIPERACILLINE-TAZOBACTAM, SELOKEEN ZOC, SPIRIVA, TETRACYCLINE CREME, TRIAMCINOLON CREME, VITAMIN B12
Adverse Events (AE) Preferred term	1. Skin ulcer 2. Haematuria 3. Crushing injury of trunk 4. Oedema peripheral 5. Lymphoma 6. Cellulitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. -----2009 (.) - --------- (.) 2. 11NOV2008 (5) - 11NOV2008 (5) 3. 01DEC2008 (25) - 06FEB2009 (92) 4. 28JAN2009 (83) - --------- (.) 5. 13APR2009 (158) - --------- (.) 6. 13APR2009 (158) - --------- (.)
Duration of AE	1. . 2. 1 3. 68 4. . 5. . 6. .
Dose on AE onset	1. 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. 2. . 3. . 4. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074231

Parameter	Value
	5. I
	6. I
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY,OTHER
	5. OTHER
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. INSUFFICIENT FOLLOW-UP
	5. INSUFFICIENT FOLLOW-UP
	6. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074235

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074235/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/66/WHITE/NETHERLANDS/YES
Medical history	Prostate cancer, Lymphadenectomy, Prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ENOXAPARIN, FRAXIPARINE, PARACETAMOL
Adverse Events (AE) Preferred term	1. Scar 2. Musculoskeletal pain 3. Scar
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 08JAN2009 (58) - 10JAN2009 (60) 2. 13FEB2009 (94) - --------- (.) 3. 16APR2009 (156) - 18APR2009 (158)
Duration of AE	1. 3 2. . 3. 3
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074241

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074241/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/29/WHITE/NETHERLANDS/YES
Medical history	Joint injury
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	PARACETAMOL
Adverse Events (AE) Preferred term	1. Dry skin 2. Dyspnoea
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --NOV2008 (.) - --------- (.) 2. 30JAN2009 (74) - 01FEB2009 (76)
Duration of AE	1. . 2. 3
Dose on AE onset	1. 2. 20 mg
Dose status on AE onset	1. 2. F
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300074257

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300074257/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/78/WHITE/NETHERLANDS/YES
Medical history	Bursitis, Hypothyroidism
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ARTHROTEC [DICLOFENAC SODIUM/MISOPROSTOL], ASCAL, PARACETAMOL, THYRAX, TRAMAL
Adverse Events (AE) Preferred term	1. Non-Hodgkin's lymphoma 2. Bronchitis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 03JAN2009 (7) - --------- (.) 2. 18JAN2009 (22) - --------- (.)
Duration of AE	1. . 2. .
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. F 2. F
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300084043

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300084043/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/47/WHITE/NETHERLANDS/YES
Medical history	Muscle rupture, Muscle strain
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ENOXAPARIN, PARACETAMOL
Adverse Events (AE) Preferred term	1. Haematoma 2. Haematoma 3. Hepatic enzyme increased 4. Headache 5. Pain in extremity 6. Alanine aminotransferase increased 7. Nasopharyngitis 8. Nasopharyngitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/YES/YES/YES 4. MODERATE/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 21AUG2009 (4) - 17SEP2009 (31) 2. 21AUG2009 (4) - 01SEP2009 (15) 3. 31AUG2009 (14) - 25NOV2009 (100) 4. 11NOV2009 (86) - 11NOV2009 (86) 5. 11NOV2009 (86) - 08DEC2009 (113) 6. 22DEC2009 (127) - 19JAN2010 (155) 7. 09FEB2010 (176) - 23FEB2010 (190) 8. 13MAR2010 (208) - --------- (.)
Duration of AE	1. 28 2. 12 3. 87 4. 1 5. 28 6. 29 7. 15 8. .
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300084043

Parameter	Value
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. NONE
	2. NONE
	3. OTHER
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. NONE
	7. NONE
	8. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300094006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300094006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/28/WHITE/NETHERLANDS/YES
Medical history	Arthroscopy, Eczema, Arthralgia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, DICLOFENAC, ENOXAPARIN, OMEPRAZOL, PARACETAMOL, ZALDIAR
Adverse Events (AE) Preferred term	1. Hepatic enzyme increased 2. Influenza
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 02JAN2008 (16) - 31JAN2008 (45) 2. 15FEB2008 (60) - 20FEB2008 (65)
Duration of AE	1. 30 2. 6
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-300094006[1)]	INCREASED LIVER ENZYMES（PT：肝酵素上昇） 治験担当医はアセノクマロールと報告事象との関連性があると判断した。弊社は、アセノクマロールについて、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300094033

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300094033/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/72/WHITE/NETHERLANDS/YES
Medical history	Cholecystectomy, Dizziness, Hysterectomy, Osteoarthritis, Irritable bowel syndrome, Tinnitus, Fibromyalgia, Sciatica, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BETAHISTINE, DUSPATAL RETARD, FLU VACCINATION, FLU VACCINATION (H1N1), FRAXIPARINE, PARACETAMOL, QUESTRAN
Adverse Events (AE) Preferred term	1. Myalgia 2. Myalgia 3. Nasopharyngitis 4. Diarrhoea
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 26AUG2009 (6) - 28AUG2009 (8) 2. 28AUG2009 (8) - 24OCT2009 (65) 3. 10OCT2009 (51) - 24OCT2009 (65) 4. 28OCT2009 (69) - 26NOV2009 (98)
Duration of AE	1. 3 2. 58 3. 15 4. 30
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. IMPROVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300094033

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300104013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300104013/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/NETHERLANDS/YES
Medical history	B-cell lymphoma, Hand fracture, Malaise, Constipation, Pathological fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADRIAMYCINE, AUGMENTIN, CIPROXIN, CYCLOFOSFAMIDE, DUROGESIC, FORTUM, FRAXODI, GRANISETRON, IBUPROFEN, LACTULOSE, METOCLOPRAMIDE, OXYNORM, PEGFILGRASTIM, PREDNISOLON, RITUXIMAB, VINCRISTINE, ZINACEF
Adverse Events (AE) Preferred term	1. Epistaxis 2. Febrile neutropenia 3. Prostatitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/YES/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 02OCT2007 (1) - --NOV2007 (.) 2. 11OCT2007 (10) - 15OCT2007 (14) 3. 18OCT2007 (17) - 25OCT2007 (24)
Duration of AE	1. . 2. 5 3. 8
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300104019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/300104019/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/51/WHITE/NETHERLANDS/YES
Medical history	Chronic obstructive pulmonary disease, Myocardial infarction
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BERODUAL, CALCI-CHEW D3, DI-ADRESON-F, ENOXAPARIN, FLUIMUCIL, FOSAMAX, MINISTAT, OXYGEN, OXYGEN ADMINISTRATION, PREDNISOLON, PREDNISON, SALBUTANOL, SALMETEROL-FLUTICASON, SPIRIVA RESPIMAT, SYMBICORT
Adverse Events (AE) Preferred term	1. Dyspnoea 2. Limb discomfort 3. Hypoxia 4. Contusion 5. Abdominal pain lower 6. Chronic obstructive pulmonary disease 7. Haematoma 8. Chronic obstructive pulmonary disease
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/YES/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/NO/YES/YES 7. MILD/YES/NO/YES 8. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --JAN2008 (.) - --------- (.) 2. --FEB2008 (.) - --MAR2008 (.) 3. --FEB2008 (.) - --------- (.) 4. 18JAN2008 (1) - -----2008 (.) 5. 21FEB2008 (35) - 25FEB2008 (39) 6. 25FEB2008 (39) - 03MAR2008 (46) 7. 07MAY2008 (111) - --------- (.) 8. 07MAY2008 (111) - 16MAY2008 (120)
Duration of AE	1. . 2. . 3. . 4. . 5. 5 6. 8 7. . 8. 10
Dose on AE onset	1. 2. 3.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 300104019

Parameter	Value
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. INSUFFICIENT FOLLOW-UP
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 340014010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/340014010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/77/WHITE/SWEDEN/YES
Medical history	Anxiety, Deep vein thrombosis, Gastritis, Hyperlipidaemia, Hypertension, Insomnia, Constipation, Osteoarthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLCYSTEIN, BETOLVEX, BUSPAR, CITODON, EKVACILLIN, ELOCON, ENOXAPARIN, FEMAR, FRAGMIN, FUROSEMID, INDERAL RETARD, INOLAXOL, OMEPRAZOL, PANODIL, SIMVASTATIN, SOBRIL, WARFARIN
Adverse Events (AE) Preferred term	1. Blood alkaline phosphatase increased 2. Breast cancer 3. Oedema peripheral
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12FEB2008 (1) - --------- (.) 2. 20APR2008 (69) - --------- (.) 3. 20APR2008 (69) - 15MAY2008 (94)
Duration of AE	1. . 2. . 3. 26
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-340014010[3)]	CANCER MAMMAE（PT：乳癌） 治験担当医は、偶発症であると判断したが、エノキサパリンについては、因果関係評価を行なっていない。弊社は、試験開始前から発症していたと考えられ、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 340024007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/340024007/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/65/WHITE/SWEDEN/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	FENYLEFRIN, TROPIKAMID 0,5%
Adverse Events (AE) Preferred term	1. Vitreous detachment 2. Eye haemorrhage 3. Cataract
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MODERATE/YES/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 05MAY2009 (43) - 18MAY2009 (56) 2. 05MAY2009 (43) - 18MAY2009 (56) 3. 05MAY2009 (43) - --------- (.)
Duration of AE	1. 14 2. 14 3. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. OTHER 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-340024007[1)]	VITREOUS BODY DETACHMENT（PT：硝子体剥離） 治験担当医はリバーロキサバンと報告事象との関連性があると判断した。弊社は、患者の年齢（高齢者）によるものであり、リバーロキサバンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 350024002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/350024002/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/70/WHITE/DENMARK/YES
Medical history	Hypercholesterolaemia, Hypertension, Menopause, Osteoporosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALENDRONAT, CENTYL WITH POTTASSIUM CLORIDE, PARACETAMOL, PENICILLIN, SIMVASTATIN
Adverse Events (AE) Preferred term	1. Pneumonia 2. Osteoporosis 3. Aortic valve incompetence
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 17APR2008 (22) - 28APR2008 (33) 2. 09MAY2008 (44) - 10MAY2008 (45) 3. 10MAY2008 (45) - --------- (.)
Duration of AE	1. 12 2. 2 3. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 350024003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/350024003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/59/WHITE/DENMARK/YES
Medical history	Hepatic cirrhosis, Hypercholesterolaemia, Hypertension, Myocardial ischaemia, Atrial fibrillation, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CORODIL, FURIX RETARD, KALEORID, NOVOMIX, PANTOLOC, SELOZOK, SIMVASTATIN, SPIRON [SPIRONOLACTON]
Adverse Events (AE) Preferred term	1. Melaena 2. Haematemesis 3. Bradycardia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MODERATE/YES/NO/YES 3. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 21MAY2008 (8) - 24MAY2008 (11) 2. 21MAY2008 (8) - 24MAY2008 (11) 3. 27MAY2008 (14) - 31MAY2008 (18)
Duration of AE	1. 4 2. 4 3. 5
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg
Dose status on AE onset	1. . 2. . 3. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 350024004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/350024004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/49/WHITE/DENMARK/YES
Medical history	Angina pectoris, Intervertebral disc protrusion, Tachycardia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADALAT, CENTYL, ENOXAPARIN, MAGNYL, MYONIL UNO, OXYCONTIN, PANODYL, PARACETAMOL, RIVAROXABAN, SELOZOK, WARFARIN, ZINACEF
Adverse Events (AE) Preferred term	1. Back pain 2. Oedema peripheral 3. Foot deformity
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 12AUG2008 (91) - 20AUG2008 (99) 2. 09DEC2008 (210) - 07JAN2009 (239) 3. 07APR2009 (329) - --------- (.)
Duration of AE	1. 9 2. 30 3. .
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 350024011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/350024011/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/57/WHITE/DENMARK/YES
Medical history	Gastritis, Hypertension, Bipolar I disorder, Polycythaemia, Pain
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BRUFEN, CIFROL NOS, CITALOPAM, DIOVAN, FURIX, HYDREA, MAGNYL, PANTOLOC, PINEX
Adverse Events (AE) Preferred term	1. Spontaneous haematoma 2. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES 2. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 25APR2009 (3) - 30APR2009 (8) 2. 25APR2009 (3) - 30APR2009 (8)
Duration of AE	1. 6 2. 6
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 350044002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/350044002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/DENMARK/YES
Medical history	Arteriosclerosis coronary artery, Hypertension, Myocardial infarction
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	FELODIPIN, FORTZAAR, INNOHEP, MAGNYL
Adverse Events (AE) Preferred term	1. Haematoma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 22DEC2007 (25) - 26FEB2008 (91)
Duration of AE	1. 67
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360014005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/360014005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/35/WHITE/NORWAY/YES
Medical history	Asthma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALIMEMAZINE, BUDESONID, DICLOFENAC, ESCITALOPRAM OXALATE, ESCITALOPRAMOKSALAT, INTERFERON, ZOPIKLON
Adverse Events (AE) Preferred term	1. Epilepsy 2. Tachycardia 3. Anxiety 4. Insomnia 5. Depression 6. Multiple sclerosis 7. Inflammation
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/NO/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 28AUG2008 (163) - 25SEP2008 (191) 2. 28AUG2008 (163) - --SEP2008 (.) 3. 09SEP2008 (175) - --DEC2008 (.) 4. 09SEP2008 (175) - --DEC2008 (.) 5. 09SEP2008 (175) - --DEC2008 (.) 6. 25SEP2008 (191) - --------- (.) 7. 10OCT2008 (206) - --------- (.)
Duration of AE	1. 29 2. . 3. . 4. . 5. . 6. . 7. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360014005

Parameter	Value
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360014011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/360014011/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/36/WHITE/NORWAY/YES
Medical history	Muscle spasms, Spondylolisthesis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMITRIPTYLIN, KALIUMKLORID, LEVOMEPROMAZIN, PARACETAMOL, PREGABALIN, TRAMADOL
Adverse Events (AE) Preferred term	1. Tachycardia 2. Palpitations 3. Rectal haemorrhage 4. Tendonitis 5. Myositis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/NO 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 26AUG2008 (6) - 27AUG2008 (7) 2. 03SEP2008 (14) - 08SEP2008 (19) 3. 03JAN2009 (136) - 04JAN2009 (137) 4. 25FEB2009 (189) - 11MAR2009 (203) 5. 25FEB2009 (189) - 11MAR2009 (203)
Duration of AE	1. 2 2. 6 3. 2 4. 15 5. 15
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. F 5. F
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360014011

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360014013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/360014013/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/26/WHITE/NORWAY/YES
Medical history	Post-traumatic stress disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALIMEMAZINE, OXAZEPAM, PLASMA, PROPYLPARAHYDROXYBENZOAT [NATRIUMBIKARBONAT INDIC: INTOX]
Adverse Events (AE) Preferred term	1. Depression 2. Anxiety 3. Syncope 4. Suicide attempt 5. Dyspnoea 6. Drug toxicity 7. Drug toxicity
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/NO/YES 7. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 22DEC2008 (8) - --------- (.) 2. 22DEC2008 (8) - 28DEC2008 (14) 3. 02JAN2009 (19) - 02JAN2009 (19) 4. 21JAN2009 (38) - 02FEB2009 (50) 5. 28JAN2009 (45) - 05FEB2009 (53) 6. 02FEB2009 (50) - 02FEB2009 (50) 7. 14FEB2009 (62) - 15FEB2009 (63)
Duration of AE	1. . 2. 7 3. 1 4. 13 5. 9 6. 1 7. 2
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360014013

Parameter	Value
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. OTHER
	5. NONE
	6. NONE
	7. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-360014013[1)]	MEDICAL INTOX（PT：有害事象なし） 治験担当医はリバーロキサバンと報告事象との関連性があると判断した。弊社は、患者にうつ病による自殺企図の既往があることから、リバーロキサバンとの因果関係は否定できると考える。 なお、本症例においては、具体的な有害事象は確認されていないが、患者が本剤を大量に服用し、入院治療を受けていることから、「有害事象なし」は「過量投与」と同義と判断した。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360044006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/360044006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/63/WHITE/NORWAY/YES
Medical history	Tendon rupture, Eczema, Femur fracture, Nephrolithiasis, Back pain, Muscle rupture, Osteoarthritis, Respiratory tract infection
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DAKTACORT
Adverse Events (AE) Preferred term	1. Gingival infection 2. Malignant melanoma 3. Nasopharyngitis 4. Muscle strain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --AUG2008 (.) - --AUG2008 (.) 2. 17JUN2008 (146) - 09JUL2008 (168) 3. 01JAN2009 (344) - 15JAN2009 (358) 4. 10JAN2009 (353) - --FEB2009 (.)
Duration of AE	1. . 2. 23 3. 15 4. .
Dose on AE onset	1. 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. 2. I 3. . 4. .
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 3. NONE 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360044006

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360044008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/360044008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/81/WHITE/NORWAY/YES
Medical history	Cataract, Dizziness, Hypertension, Menopause, Migraine, Osteoarthritis, Drug hypersensitivity, Peroneal nerve palsy, Urinary tract infection, Fibromyalgia, Thyroidectomy, Hip surgery, Hip surgery
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BURINEX, COZAAR, ENOXAPARIN, LACTULOSE, MAREVAN, OCTAPLAS, OFTAN EYE DROPS, PARACET, VOLTAREN [DICLOFENAC ALONE], WARFARIN, XALATAN EYE DROPS
Adverse Events (AE) Preferred term	1. Back pain 2. Nephrolithiasis 3. Constipation 4. Nasopharyngitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 15MAR2008 (23) - --------- (.) 2. 28MAR2008 (36) - 04APR2008 (43) 3. 21AUG2008 (182) - --------- (.) 4. 03JAN2009 (317) - 21JAN2009 (335)
Duration of AE	1. . 2. 8 3. . 4. 19
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. UNCHANGED 2. RESOLVED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360044008

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 360054014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/360054014/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/75/WHITE/NORWAY/YES
Medical history	Chronic obstructive pulmonary disease, Gastrectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATROVENT, MUCOMYST, SPIRIVA
Adverse Events (AE) Preferred term	1. Chronic obstructive pulmonary disease 2. Urinary retention
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/NO 2. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 20JUN2009 (107) - 23JUN2009 (110) 2. 03JUL2009 (120) - 03JUL2009 (120)
Duration of AE	1. 4 2. 1
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. F 2. F
Action taken	1. REMEDIAL DRUG THERAPY 2. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370014011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370014011/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/70/WHITE/SOUTH AFRICA/YES
Medical history	Hypothyroidism, Hysterectomy, Neuropathy peripheral
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CIPRALEX, DEPO-MEDROL, ELTROXIN, LAMICTIN
Adverse Events (AE) Preferred term	1. Nausea 2. Muscle spasms 3. Headache 4. Depression 5. Cough
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12NOV2008 (10) - 16NOV2008 (14) 2. 13NOV2008 (11) - 14NOV2008 (12) 3. 02MAR2009 (120) - 03MAR2009 (121) 4. 03MAR2009 (121) - --------- (.) 5. 04MAY2009 (183) - 25MAY2009 (204)
Duration of AE	1. 5 2. 2 3. 2 4. . 5. 22
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. NONE 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370014011

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370024006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/63/WHITE/SOUTH AFRICA/YES
Medical history	Gout, Hip fracture, Hip fracture, Peptic ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, ENOXAPARIN, FRESH FROZEN PLASMA, LOSEC, PREGAMAL, WARFARIN
Adverse Events (AE) Preferred term	1. International normalised ratio increased 2. Gastric ulcer haemorrhage 3. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 29MAY2008 (15) - 05JUN2008 (22) 2. 13JUN2008 (30) - 14JUN2008 (31) 3. 13JUN2008 (30) - 20JAN2009 (251)
Duration of AE	1. 8 2. 2 3. 222
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. DOSE OF STUDY DRUG REDUCED 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370024006[2)]	ANEMIA（PT：出血性貧血） 治験担当医は、非ステロイド性抗炎症薬の飲みすぎによるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370024010/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/18/BLACK/SOUTH AFRICA/YES
Medical history	Anaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BRUFEN, FRESH FROZEN PLASMA, OMNOPON, PANADO, PREGAMAL
Adverse Events (AE) Preferred term	1. Menorrhagia 2. Syncope
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01AUG2008 (7) - 08AUG2008 (14) 2. 03AUG2008 (9) - 03AUG2008 (9)
Duration of AE	1. 8 2. 1
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370024012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/66/BLACK/SOUTH AFRICA/YES
Medical history	Anaemia, Colostomy, Constipation, Gout, Hydronephrosis, Hypertension, Ovarian cancer, Ovarian cancer, Urinary tract infection, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALLOPURINOL, BRUFEN, CIPROBAY, CLEXANE, COVERSYL, DF118, DOXYCICLINE, DOYCYCLIN, ENOXAPARIN, FLAGYL, FRESH FROZEN PLASMA, ISOFLURANE, KEFZOL, MACRODANTIN, MORPHINE, OMNOPON, PANADO, PERFALGON, PROPOFOL, SENAKOT, SUFENTA, TORA-DOL, WARFARIN
Adverse Events (AE) Preferred term	1. Vomiting 2. Intestinal haemorrhage 3. Radius fracture 4. Ulna fracture
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/YES/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 17OCT2008 (8) - 17OCT2008 (8) 2. 19OCT2008 (10) - 02NOV2008 (24) 3. 21AUG2009 (316) - 26AUG2009 (321) 4. 21AUG2009 (316) - 26AUG2009 (321)
Duration of AE	1. 1 2. 15 3. 6 4. 6
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY,OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024012

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370024012[3)]	ANEMIA（PT：貧血） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、エノキサパリン及びワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024017

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370024017/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/28/WHITE/SOUTH AFRICA/YES
Medical history	Femur fracture, Gun shot wound
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BREVIBLOC, CLEXANE, DORMICUM, HEPARIN, ISOFLURANE, KEFZOL, LIGNOCAINE, MORPHINE, NORFLEX CO, OMNOPON, PANADO, PERFALGAN, PROPOFOL, PROSULF, SPASMEND, SUFENTA, TRACRIUM, VOLUVEN, WARFARIN
Adverse Events (AE) Preferred term	1. Arterial thrombosis limb
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 31MAR2009 (2) - 08APR2009 (10)
Duration of AE	1. 9
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370024018/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/38/BLACK/SOUTH AFRICA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, ENOXAPARIN, LOSEC, PANADO, PANTOLOC, UNFRACTIONATED HEPARIN, VOLTAREN, WARFARIN
Adverse Events (AE) Preferred term	1. Haematemesis 2. Gynaecomastia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 17APR2009 (2) - 30APR2009 (15) 2. 02SEP2009 (140) - 09NOV2009 (208)
Duration of AE	1. 14 2. 69
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370024018[2)]	HEMATEMESIS（PT：吐血） 治験担当医は、合併症（胃潰瘍）によるものであり、否定できると判断した。弊社は、エノキサパリン及びワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370024021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370024021/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/53/BLACK/SOUTH AFRICA/YES
Medical history	Cardiac failure, Cervix carcinoma, Gangrene, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BASCOPAN, CYCLOKAPRON, LASIX, MORPHINE SYRUP, MST CONTINUS, OMNOPON, PANADO, PLENISH-K, THIAMINE
Adverse Events (AE) Preferred term	1. Abdominal pain 2. Vaginal haemorrhage 3. Cervix carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/YES/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 09JUN2009 (6) - 09JUN2009 (6) 2. 22JUN2009 (19) - --------- (.) 3. 27JUN2009 (24) - 27JUN2009 (24)
Duration of AE	1. 1 2. . 3. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. F
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 3. NONE
Outcome of event	1. RESOLVED 2. INSUFFICIENT FOLLOW-UP 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370044001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370044001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/80/WHITE/SOUTH AFRICA/YES
Medical history	Oedema peripheral, Asthma, Cardiovascular disorder, Constipation, Hiatus hernia, Hysterectomy, Lung infiltration, Pulmonary tuberculosis, Pulmonary tuberculosis, Adverse drug reaction
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AGIOLAX, ATROVENT, AVELON, BETHAMETHASONE, CEPACAINE PRN, COMBIVENT, DULCOLAX [BISACODYL], DUPHALAC [LACTULOSE], ENOXAPARIN, ETHAMBUTAMOL, INH, LACSON, LANSOLOC, MAXOLON, MORPHINE, MOVICOL, MYPRODOL, PZA, SEREPAX, STEMITIL, TAVANIC, VIT BCO, VIT K, WARFARIN
Adverse Events (AE) Preferred term	1. Nausea 2. International normalised ratio increased 3. Lung neoplasm malignant 4. Insomnia 5. Lung neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 03MAY2008 (2) - 15MAY2008 (14) 2. 05MAY2008 (4) - 11MAY2008 (10) 3. 09MAY2008 (8) - 18JUN2008 (48) 4. 30MAY2008 (29) - 23JUN2008 (53) 5. 19JUN2008 (49) - 24JUN2008 (54)
Duration of AE	1. 13 2. 7 3. 41 4. 25 5. 6
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370044001

Parameter	Value
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. WORSENED
	4. RESOLVED
	5. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054019/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/75/WHITE/SOUTH AFRICA/YES
Medical history	Hypertension, Pain in extremity, Angina unstable, Hyperlipidaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATORVASTATIN, CALCIUM C VITA, DICLOHEXAL TOPICAL GEL, DILTIAZEM HCL, DISPRIN CV, ENOXAPARIN, MAGNESIT, MULTIVITAMINS, TRIAMHEXAL, WARFARIN
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Angina unstable
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 05SEP2008 (53) - 06FEB2009 (207) 2. 12SEP2008 (60) - 17OCT2008 (95)
Duration of AE	1. 155 2. 36
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054026

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054026/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/40/BLACK/SOUTH AFRICA/YES
Medical history	Baker's cyst excision
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DIPRIVAN, ENOXAPARIN, PARACETAMOL, PARACETAMOL,DEXROPROPOXYPHENE,DIPHENHYDRAMINE,CAFFEINE, PENICILLIN/CLAVULANIC ACID, PETHIDINE, RAPIFEN, RAYZON, WARFARIN, ZOLPIDEM
Adverse Events (AE) Preferred term	1. Anal abscess
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 27DEC2008 (123) - 30DEC2008 (126)
Duration of AE	1. 4
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054037

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054037/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/39/WHITE/SOUTH AFRICA/YES
Medical history	Fibula fracture, Tibia fracture, Skin ulcer, Osteosynthesis, Osteosynthesis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALFENTANIL, AMOXIL,CLAVULANIC ACID, CELECOXIB, CIPROFLOXACIN, ENOXAPARIN, ESOMEPRAZOLE, GRANISETRON, MIDAZOLAM, MORPHINE SULPHATE, MORPHINE,PAPAVERINE,CODEINE [COLLECTIVELY THIS IS CALLED OMNOPON AND DOSAGE IS A, PARACETAMOL,DEXTROPROPOXYPHENE,DIPHENHYDRAMINE,CAFFEINE, PARECOXIB, PREGABALIN, PROPOFOL, TRAMADOL, TRAMAL, WARFARIN, ZOLPIDEM
Adverse Events (AE) Preferred term	1. Neuropathy peripheral 2. Postoperative wound infection 3. Dyspepsia 4. Haemorrhoidal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 23DEC2008 (52) - --------- (.) 2. 24JAN2009 (84) - 05MAY2009 (185) 3. 26FEB2009 (117) - --------- (.) 4. 02MAY2009 (182) - 05MAY2009 (185)
Duration of AE	1. . 2. 102 3. . 4. 4
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. OTHER
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. RESOLVED 3. INSUFFICIENT FOLLOW-UP

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054037

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054040

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054040/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/44/BLACK/SOUTH AFRICA/YES
Medical history	Arthralgia, Arthroscopy, Haemoglobin decreased, Menorrhagia, Uterine polyp, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALFENTANIL, CIPROFLOXACIN, DICLOFENAC SODIUM, FEROUS SULPHATE-FE REPLACEMENT, FLAGYL, HAEMOFER, LIDOCAINE, MIDAZOLAM, NORETHISTERONE, PARACETAMOL/DEXTROPROPOXYPHENE/DIPHENHYDRAMINE/CAFFEINE, ZOLPIDEM
Adverse Events (AE) Preferred term	1. Dyspepsia 2. Menorrhagia 3. Back pain 4. Urinary tract infection 5. Menorrhagia 6. Muscle spasms
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 20NOV2008 (2) - 20NOV2008 (2) 2. 21NOV2008 (3) - 21NOV2008 (3) 3. 16DEC2008 (28) - 03JAN2009 (46) 4. 29DEC2008 (41) - 03JAN2009 (46) 5. 03MAR2009 (105) - 04MAR2009 (106) 6. 02MAY2009 (165) - 08MAY2009 (171)
Duration of AE	1. 1 2. 1 3. 19 4. 6 5. 2 6. 7
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054040

Parameter	Value
	6. .
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370054040[2)]	MENORRHAGIA（PT：月経過多） 治験担当医は、合併症（ポリープ）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054044

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054044/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/SOUTH AFRICA/YES
Medical history	Hypertension, Back pain, Pain in extremity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATENOLOL, CAFFEINE,PARACETMOL,ASPIRIN(GRANDPA POWDER), CITALOPRAM HYDROBROMIDE, COLCHICINE, DEXTROPRPPOXYPHENE/PARACETAMOL, DIPRIVAN, DORMICUM, ENOXAPARIN, ESOMEPRAZOLE, FERROUS SULPHATE, GABAPENTIN, IMOVANE, KLEAN PREP, KYTRIL, MOVICOL, PERINDOPRIL, PREGABALIN, RAPIFEN, RAYZON, THIAMINE, TRAMAL, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Depression 2. Rectal haemorrhage 3. Haemoglobin decreased 4. Duodenal ulcer 5. Haemorrhoids 6. Gout
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 23DEC2008 (3) - 16JUL2009 (208) 2. 11FEB2009 (53) - 22FEB2009 (64) 3. 14FEB2009 (56) - 22FEB2009 (64) 4. 15FEB2009 (57) - 20MAR2009 (90) 5. 16FEB2009 (58) - 16FEB2009 (58) 6. 20FEB2009 (62) - --------- (.)
Duration of AE	1. 206 2. 12 3. 9 4. 34 5. 1 6. .
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054044

Parameter	Value
	5.
	6.
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	3. OTHER
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370054044[2)]	RECTAL BLEEDING（PT：直腸出血） 治験担当医は、併用薬（抗炎症剤）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、本剤との因果関係を完全には否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054071

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054071/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/66/WHITE/SOUTH AFRICA/YES
Medical history	Chronic obstructive pulmonary disease, Cardiac failure congestive, Hyperlipidaemia, Hypertension, Osteoarthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DUOLIN NEBS, ENOXAPARIN, ESOMEPRAZOLE, LASIX, LISINOPRIL, LOVACHOL, MELOXICAM, PANTALOC, SLOW K, SLOW MAG, SLOW-K, SOLUCORTEF, SYNAP FORTE, THEOPHYLLINE, TRAMACET, TREPILINE, TRI-PLEN, TRITACE, VENTOLIN, WARFARIN
Adverse Events (AE) Preferred term	1. Joint effusion 2. Respiratory tract infection 3. Bronchospasm 4. Hypertensive heart disease 5. Pleural fibrosis 6. Dyspnoea exertional 7. Nausea 8. Vomiting 9. Hypertension 10. Thrombophlebitis 11. Oedema peripheral
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12MAY2009 (21) - 02MAR2010 (315) 2. 26MAY2009 (35) - 30MAY2009 (39) 3. 26MAY2009 (35) - 29MAY2009 (38) 4. 26MAY2009 (35) - --------- (.) 5. 26MAY2009 (35) - 26MAY2009 (35) 6. 15JUN2009 (55) - --------- (.) 7. 16JUL2009 (86) - 25AUG2009 (126) 8. 16JUL2009 (86) - 25AUG2009 (126) 9. 20JUL2009 (90) - 25AUG2009 (126) 10. 25AUG2009 (126) - 23SEP2009 (155) 11. 23SEP2009 (155) - --------- (.)
Duration of AE	1. 295 2. 5

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054071

Parameter	Value
	3. 4
	4. .
	5. 1
	6. .
	7. 41
	8. 41
	9. 37
	10. 30
	11. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. OTHER
	8. OTHER
	9. NONE
	10. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054071

Parameter	Value
Outcome of event	11. NONE 1. RESOLVED 2. RESOLVED 3. RESOLVED 4. UNCHANGED 5. RESOLVED 6. UNCHANGED 7. RESOLVED 8. RESOLVED 9. RESOLVED 10. RESOLVED 11. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054077

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054077/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/32/BLACK/SOUTH AFRICA/YES
Medical history	Muscle spasms, HIV infection, Kaposi's sarcoma, Kaposi's sarcoma, Paraesthesia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMIKACIN, BISOLVON, DUOLIN, ENOXAPARIN, KLACID, MAGNESIUM SULPHATE, STOCRIN, STOPAYNE [CAFFEINE, PARACETAMOL, CODEINE PHOSPHATE, MEPROBAMATE], SYNAP FORTE, TRAMAL, TRUVADA, VITAMIN C, WARFARIN, ZINACEF
Adverse Events (AE) Preferred term	1. Lobar pneumonia 2. Respiratory tract infection 3. Thrombocytopenia 4. Oedema peripheral
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 20JUN2009 (39) - 26JUN2009 (45) 2. 18OCT2009 (159) - 24OCT2009 (165) 3. 22OCT2009 (163) - --------- (.) 4. 14DEC2009 (216) - --------- (.)
Duration of AE	1. 7 2. 7 3. . 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. NONE 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. INSUFFICIENT FOLLOW-UP

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054077

Parameter	Value
	4. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054082

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370054082/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/55/WHITE/SOUTH AFRICA/YES
Medical history	Duodenal ulcer perforation, Rib fracture, Haemoglobin decreased, Hypertension, Hysterectomy, Laparotomy, Lung consolidation, Osteoarthritis, Tracheostomy, Angiomyolipoma, Explorative laparotomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACYCLOVIR, ADRENALINE, ATERAX, ATROVENT/BEROTEC NEBULIZER, AUGMENTIN, AVALON, BUSCOPAN, DAKTARIN GEL, DIFLUCAN, DIPRIVAN, DIXARIT, DUOLIN NEBS, ESMERON, FLAGYL, FUROSEMIDE, HEPARIN, IMDUR, INVANZ, LASIX, LIGNOCAINE, LISINOPRIL, MAXALON, MERONEM, MONOSODIUM PHOSPHATE/DISODIUM PHOSPHATE, MORPHINE, NEUPOGEN, NEXIAM, NIMBEX, OLICLINOMEL, PANTOPRAZOLE, PARACETAMOL,DEXTROPROPOXYPHENE,DIPHENHYDRAMINE,CAFFEINE, PERFALGAN, PETHIDINE, RAPIFEN, RAYZON, REUTERI, RISPERDAL, SALINE NEBS, SCOLINE, SUFENTA, TARGOCID, TRAMAL, VITAMIN B12, VOLTAREN, ZOFRAN
Adverse Events (AE) Preferred term	1. Fistula discharge 2. Abdominal pain 3. Haemoglobin decreased 4. Contusion 5. Constipation 6. Enterocutaneous fistula 7. Wound infection 8. Haemoglobin decreased 9. Nausea 10. Procedural pain 11. Anxiety 12. Mood swings 13. Headache 14. Oral candidiasis 15. Sepsis 16. Haemoglobin decreased 17. Multi-organ failure 18. Hypotension 19. Anuria
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. SEVERE/NO/YES/YES 7. MODERATE/NO/NO/YES 8. MODERATE/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054082

Parameter	Value
	11. MILD/NO/NO/YES
	12. MILD/NO/NO/YES
	13. MILD/NO/NO/YES
	14. MILD/NO/NO/YES
	15. SEVERE/NO/YES/YES
	16. MODERATE/NO/NO/YES
	17. SEVERE/NO/YES/YES
	18. SEVERE/NO/NO/YES
	19. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --OCT2009 (.) - --------- (.)
	2. 24JUL2009 (37) - 12AUG2009 (56)
	3. 26JUL2009 (39) - 30JUL2009 (43)
	4. 28JUL2009 (41) - --AUG2009 (.)
	5. 08AUG2009 (52) - 08AUG2009 (52)
	6. 31AUG2009 (75) - --------- (.)
	7. 13SEP2009 (88) - 28SEP2009 (103)
	8. 24SEP2009 (99) - 29SEP2009 (104)
	9. 26SEP2009 (101) - 26SEP2009 (101)
	10. 02OCT2009 (107) - 07OCT2009 (112)
	11. 02OCT2009 (107) - 05OCT2009 (110)
	12. 03OCT2009 (108) - 05OCT2009 (110)
	13. 03OCT2009 (108) - 05OCT2009 (110)
	14. 03OCT2009 (108) - 07OCT2009 (112)
	15. 05OCT2009 (110) - 07OCT2009 (112)
	16. 05OCT2009 (110) - 07OCT2009 (112)
	17. 06OCT2009 (111) - 07OCT2009 (112)
	18. 06OCT2009 (111) - --------- (.)
	19. 06OCT2009 (111) - 06OCT2009 (111)
Duration of AE	1. .
	2. 20
	3. 5
	4. .
	5. 1
	6. .
	7. 16
	8. 6
	9. 1
	10. 6
	11. 4
	12. 3
	13. 3

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054082

Parameter	Value
	14. 5
	15. 3
	16. 3
	17. 2
	18. .
	19. 1
Dose on AE onset	1.
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
	16. 20 mg
	17. 20 mg
	18. 20 mg
	19. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .
	13. .
	14. .
	15. .
	16. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054082

Parameter	Value
	17. .
	18. .
	19. .
Action taken	1. OTHER
	2. REMEDIAL DRUG THERAPY
	3. OTHER
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. OTHER
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. REMEDIAL DRUG THERAPY
	15. REMEDIAL DRUG THERAPY
	16. REMEDIAL DRUG THERAPY
	17. NONE
	18. REMEDIAL DRUG THERAPY
	19. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. RESOLVED
	15. DEATH
	16. RESOLVED
	17. DEATH
	18. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370054082

Parameter	Value
	19. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370064004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370064004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/68/BLACK/SOUTH AFRICA/YES
Medical history	Hypertension, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPHANE, ADALAT XL, COVERSYL (PERINDOPRIL), ENOXAPARIN, GLUCOPHAGE, HCTZ, PROTAPHANE, SLOW K, WARFARIN
Adverse Events (AE) Preferred term	1. Vitreous haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 17APR2008 (50) - 28AUG2008 (183)
Duration of AE	1. 134
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370064004[2)]	VITREOUS HAEMORRHAGE（PT：硝子体出血） 治験担当医は、合併症（糖尿病及び高血圧症）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370064007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370064007/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/74/WHITE/SOUTH AFRICA/YES
Medical history	Diarrhoea, Gastroenteritis, Scoliosis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CIPROBAY, ENOXAPARIN, FLAGYL, LOSEC, SLOW-K, WARFARIN
Adverse Events (AE) Preferred term	1. Hepatic enzyme increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 07APR2008 (31) - 13MAY2008 (67)
Duration of AE	1. 37
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. NONE
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370064007[2)]	RAISED LIVER ENZYMES（PT：肝酵素上昇） 治験担当医は、ワルファリンとの因果関係を否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370064016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370064016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/25/BLACK/SOUTH AFRICA/YES
Medical history	HIV infection, Pulmonary tuberculosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BACTRIM, DOXYPHENE, ENOXAPARIN, PYRIDOCINE, RIFAFOUR, WARFARIN
Adverse Events (AE) Preferred term	1. Respiratory distress
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 20OCT2008 (5) - -----2009 (.)
Duration of AE	1. .
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370074003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370074003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/54/WHITE/SOUTH AFRICA/YES
Medical history	Fatigue, Fibroma, Insomnia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FRESH FROZEN PLASMA, MYPAID, PERFALGAN, RAYZON, VITATHION, WARFARIN, ZOPIVANE
Adverse Events (AE) Preferred term	1. Therapeutic agent toxicity 2. Haematuria 3. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/YES/YES 2. MODERATE/NO/NO/YES 3. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 22MAY2008 (10) - 24MAY2008 (12) 2. 22MAY2008 (10) - 24MAY2008 (12) 3. 24MAY2008 (12) - 29MAY2008 (17)
Duration of AE	1. 3 2. 3 3. 6
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. DOSE OF STUDY DRUG REDUCED 2. NONE 3. DOSE OF STUDY DRUG REDUCED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. WORSENED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-370074003[4),3),4)]	MACROSCOPIC HEMATURIA（PT：血尿） 治験担当医はエノキサパリンについて、報告事象との因果関係評価を行っていない。弊社は、エノキサパリンについて、時間的関連性が認められないことから、因果関係を否定できると考える。 WARFARIN TOXICITY（PT：各種物質毒性） 治験担当医はエノキサパリンについて、報告事象との因果関係評価を行っていない。弊社は、ワルファリン投与との時間的関連性から、因果関係は否定できないと考えるが、エノキサパリンについては、時間的関連性が認められないことから、因果関係を否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370084002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370084002/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/SOUTH AFRICA/YES
Medical history	Colitis, Hypertension, Migraine, Gastrooesophageal reflux disease, Porphyria, Type 2 diabetes mellitus, Fluid retention
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASACOL, CAPTOMAX, CLEXANE, DIAGLUCIDE, EPILIM 200MG, LANZOR, LASIX, PLENISH K
Adverse Events (AE) Preferred term	1. Sinusitis 2. Intestinal obstruction 3. Thrombosis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 18APR2008 (10) - 17JUL2008 (100) 2. 17MAY2008 (39) - 20MAY2008 (42) 3. 02NOV2008 (208) - 19NOV2008 (225)
Duration of AE	1. 91 2. 4 3. 18
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. F
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED AND RESTARTED 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370104001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370104001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/81/WHITE/SOUTH AFRICA/YES
Medical history	Asthma, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, SYMBICORD TURBUHAL, SYNAP FORTE, WARFARIN
Adverse Events (AE) Preferred term	1. Myocardial infarction
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 24DEC2008 (43) - 24DEC2008 (43)
Duration of AE	1. 1
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. NONE
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370154002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370154002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/37/BLACK/SOUTH AFRICA/YES
Medical history	HIV test positive, Hypertension, Aortic valve disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	3TC, ADALAT XL, ALDACTONE [SPIRONOLACTONE], AMOXIL, ATENOLOL, AUGMENTIN, AZT, BACTRIM (TRIMETHOPRIM +SULFAMETHOXAZOLE), COVERSYL, DOXYPHENE, EFAVIRENZ (STOCRIN), ENOXAPARIN, LASIX, MULTIVITAMINS, NORVASC, PHARMAPRESS(ENALAPRIL MALEATE), WARFARIN
Adverse Events (AE) Preferred term	1. Aortic valve disease 2. Cardiac failure congestive 3. Cardiac failure congestive 4. Aortic valve disease 5. Cardiac failure congestive
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/YES/YES 4. SEVERE/NO/YES/NO 5. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 26NOV2008 (202) - --------- (.) 2. 26NOV2008 (202) - 09DEC2008 (215) 3. 05JAN2009 (242) - --------- (.) 4. 17MAR2009 (313) - 27MAR2009 (323) 5. 17MAR2009 (313) - 27MAR2009 (323)
Duration of AE	1. . 2. 14 3. . 4. 11 5. 11
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY,OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370154002

Parameter	Value
Outcome of event	5. REMEDIAL DRUG THERAPY 1. IMPROVED 2. IMPROVED 3. IMPROVED 4. IMPROVED 5. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 370154011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/370154011/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/38/BLACK/SOUTH AFRICA/YES
Medical history	Cor pulmonale, Pulmonary hypertension, Right ventricular failure, Tuberculosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATENOLOL, DOXEFENE, LASIX, SLOW K
Adverse Events (AE) Preferred term	1. Right ventricular failure 2. Skin ulcer 3. Right ventricular failure
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 18MAY2009 (132) - 08JUN2009 (153) 2. 02JUN2009 (147) - --------- (.) 3. 01AUG2009 (207) - --------- (.)
Duration of AE	1. 22 2. . 3. .
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380024003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380024003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/57/WHITE/CZECH REPUBLIC/YES
Medical history	Diabetes mellitus, Hyperlipidaemia, Back pain, Meningitis, Myocardial infarction, Varicose vein operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID, BETALOC ZOK, ENOXAPARIN, ENOXAPARINE, GLUCOPHAGE, GLYVENOL, NADROPARIN, SIMVACARD, WARFARIN
Adverse Events (AE) Preferred term	1. Colon cancer 2. Colon cancer
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 12JUN2008 (150) - 07JAN2009 (359) 2. 27JUN2008 (165) - --------- (.)
Duration of AE	1. 210 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/CZECH REPUBLIC/YES
Medical history	Hypertension, Inguinal hernia repair, Inguinal hernia repair, Transurethral prostatectomy, Renal failure chronic, Paraparesis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AKTIFERRIN TBL., AMBROBENE GTT, AMBROBENE SIR., ATROVENT SPR., BACLOFEN, CLEXANE, COXTRAL, DETRALEX, DIPIDOLOR, ENOXAPARIN, KALIUM CHLORATUM, KANAVIT GTT, MONOSAN, NOVALGIN, TRALGIT, UNASYN AMP., WARFARIN
Adverse Events (AE) Preferred term	1. Congenital cystic kidney disease 2. Bladder diverticulum 3. Femoral neck fracture 4. Anaemia 5. Bronchitis 6. Angina unstable
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 11OCT2007 (2) - --------- (.) 2. 11OCT2007 (2) - --------- (.) 3. 20DEC2007 (72) - 23APR2008 (197) 4. 20DEC2007 (72) - 08APR2008 (182) 5. 01JAN2008 (84) - 31JAN2008 (114) 6. 10FEB2008 (124) - 10FEB2008 (124)
Duration of AE	1. . 2. . 3. 126 4. 111 5. 31 6. 1
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044002

Parameter	Value
	5.
	6.
Action taken	1. NONE
	2. NONE
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/72/WHITE/CZECH REPUBLIC/YES
Medical history	Back pain, Gastritis, Hemiparesis, Hypertension, Inguinal hernia repair, Renal cyst, Cerebrovascular accident, Transient ischaemic attack, Urinary incontinence, Cholelithiasis, Renal failure chronic, Venous thrombosis limb
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALGIFEN NEO GTT, ANOPYRIN TBL., CLEXANE, DETRALEX TBL., ENALAPRIL TBL., ENOXAPARIN, GLYVENOL CPS., HELICID CPS., MAGNESII LACTICI TBL., MEDRIN TBL., QUAMATEL TBL., TRALGIT AMP., WARFARIN
Adverse Events (AE) Preferred term	1. Contusion 2. Tooth disorder 3. Jaw cyst
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 05MAR2008 (111) - 08MAR2008 (114) 2. 07MAY2008 (174) - 19MAY2008 (186) 3. 12MAY2008 (179) - 19MAY2008 (186)
Duration of AE	1. 4 2. 13 3. 8
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. OTHER 3. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044022/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/52/WHITE/CZECH REPUBLIC/YES
Medical history	Exostosis, Drug hypersensitivity, Menstruation irregular, Epicondylitis, Iodine allergy, Breast disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARTHRONA 1000-S TBL.-D-GLUCOSAMIN SULFAT, DEGAN INJ., DEGAN TBL., ESSENTIALE FORTE N CPS., GLYVENOL CPS., HELICID CPS., HELICID INJ.
Adverse Events (AE) Preferred term	1. Dyspepsia 2. Liver function test abnormal 3. Liver function test abnormal
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/YES/YES/YES 3. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 24JAN2008 (2) - 26JAN2008 (4) 2. 25JAN2008 (3) - 31MAR2008 (69) 3. 31MAR2008 (69) - 17APR2008 (86)
Duration of AE	1. 3 2. 67 3. 18
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
Outcome of event	1. RESOLVED 2. WORSENED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044036

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044036/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/47/WHITE/CZECH REPUBLIC/YES
Medical history	Colon cancer, Ascites, Diabetes mellitus, Drug hypersensitivity, Hepatic steatosis, Hypertriglyceridaemia, Ileostomy, Ileus, Hepatectomy, Obesity, Ovarian cyst, Pelvic adhesions, Uterine leiomyoma, Bone pain, Proctocolectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AVANDAMET 2MG/1000MG TBL, DETRALEX TBL, FASTUM GEL, GLYVENOL 400MG TBL, MAGNOSOLV POR GRA SOL, MOVALIS 15 MG TBL, MYOLASTAN 50 MG TBL, MYOLASTAN 50MG TBL, STOPANGIN ORM GGR
Adverse Events (AE) Preferred term	1. Metrorrhagia 2. Aspartate aminotransferase increased 3. Alanine aminotransferase increased 4. Gamma-glutamyltransferase increased 5. Cervicobrachial syndrome 6. Nasopharyngitis 7. Venous insufficiency 8. Metrorrhagia 9. Anaemia 10. Nasopharyngitis 11. Methylenetetrahydrofolate reductase polymorphism
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/YES/NO/YES 4. MILD/YES/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MODERATE/NO/NO/YES 9. MODERATE/YES/YES/YES 10. MILD/NO/NO/NO 11. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 11APR2008 (3) - 19APR2008 (11) 2. 14APR2008 (6) - 10JUL2008 (93) 3. 14APR2008 (6) - 23APR2008 (15) 4. 14APR2008 (6) - 07OCT2008 (182) 5. 02JUL2008 (85) - --------- (.) 6. 04JUL2008 (87) - 09JUL2008 (92) 7. 03SEP2008 (148) - --------- (.) 8. 07OCT2008 (182) - 09OCT2008 (184) 9. 07OCT2008 (182) - 09OCT2008 (184) 10. 28OCT2008 (203) - 05NOV2008 (211) 11. 31OCT2008 (206) - --------- (.)
Duration of AE	1. 9

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044036

Parameter	Value
	2. 88
	3. 10
	4. 177
	5. .
	6. 6
	7. .
	8. 3
	9. 3
	10. 9
	11. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. F
	11. F
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	2. NONE
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY,OTHER
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY,OTHER
	9. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044036

Parameter	Value
	10. NONE
	11. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. INSUFFICIENT FOLLOW-UP
	6. RESOLVED
	7. UNCHANGED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044041

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044041/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/48/WHITE/CZECH REPUBLIC/YES
Medical history	Back pain, Contusion, Hypertension, Deep vein thrombosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AGEN, ANOPYRIN, BETADINE UNG, CEFOTAXIM, CLEXANE, DEGAN, DORSIFLEX, GLYVENOL, HELICID, HELICID TBL, IALUGEN PLUS CRM, IALUGEN PLUS CRM., IBALGIN 400 MG TBL, NOVALGIN, OFLOXIN, PLAVIX TBL, PRESTARIUM NEO, QUAMATEL, TENSIOMIN TBL, TRALGIT, WARFARIN TBL
Adverse Events (AE) Preferred term	1. Skin ulcer 2. Peripheral ischaemia 3. Anaemia 4. Peripheral ischaemia 5. Urinary tract infection 6. Skin ulcer
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 21OCT2008 (141) - 20FEB2009 (263) 2. 29JAN2009 (241) - --------- (.) 3. 13FEB2009 (256) - --------- (.) 4. 13FEB2009 (256) - 26FEB2009 (269) 5. 23FEB2009 (266) - 09MAR2009 (280) 6. 16APR2009 (318) - --------- (.)
Duration of AE	1. 123 2. . 3. . 4. 14 5. 15 6. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. I 4. I 5. I

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044041

Parameter	Value
	6. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY,OTHER
	3. NONE
	4. REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044058

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044058/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/65/WHITE/CZECH REPUBLIC/YES
Medical history	Anaemia, Back pain, Abdominal hernia, Gastric ulcer, Hyperlipidaemia, Hypertension, Nephrolithiasis, Osteoporosis, Benign prostatic hyperplasia, Renal colic, Respiratory tract infection, Rheumatoid arthritis, Spinal compression fracture, Synovectomy, Foot operation, Cataract operation, Venous insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACIDUM FOLICUM TBL., ALFA D3 CPS., APO-OME CPS., ARAVA TBL., BONVIVA TBL., CEFOTAXIM INJ., CLARITHROMYCIN TBL., CLEXANE INJ., DETRALEX TBL., ECOBEC SPR., ESSENTIALE F CPS., FORADIL, GINGIUM TBL., INSPRA TBL., KCL INJ., LYRICA TBL., MEDROL TBL., METOTHREXAT TBL., MUCOSOLVAN SOL., NACL INJ., PARALEN TBL., PLAZMALYTE SOL., PRESTARIUM NEO TBL., SORTIS TBL., TRAMAL RET. CPS., ZINNAT TBL., ZOXON TBL.
Adverse Events (AE) Preferred term	1. Congenital cystic kidney disease 2. Asthma 3. Diarrhoea 4. Respiratory tract infection 5. Dehydration 6. Renal failure acute 7. Bronchopneumonia 8. Liver function test abnormal 9. Epistaxis 10. Nasopharyngitis 11. Peripheral sensorimotor neuropathy 12. Antiphospholipid syndrome
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MODERATE/YES/YES/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MODERATE/NO/NO/YES 12. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 03SEP2008 (2) - --------- (.) 2. 04SEP2008 (3) - --------- (.) 3. 03NOV2008 (63) - 08NOV2008 (68) 4. 03NOV2008 (63) - 08NOV2008 (68) 5. 08NOV2008 (68) - 10NOV2008 (70) 6. 08NOV2008 (68) - 10NOV2008 (70) 7. 08NOV2008 (68) - 04DEC2008 (94)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044058

Parameter	Value
	8. 08NOV2008 (68) - 01DEC2008 (91)
	9. 23DEC2008 (113) - 31DEC2008 (121)
	10. 23DEC2008 (113) - 31DEC2008 (121)
	11. 14JAN2009 (135) - --------- (.)
	12. 29JAN2009 (150) - --------- (.)
Duration of AE	1. .
	2. .
	3. 6
	4. 6
	5. 3
	6. 3
	7. 27
	8. 24
	9. 9
	10. 9
	11. .
	12. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044058

Parameter	Value
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED AND RESTARTED
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	8. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	9. NONE
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. NONE
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. RESOLVED
	4. WORSENED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. UNCHANGED
	12. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-380044058[1)]	ELEVATION LFT（PT：肝機能検査異常） 治験担当医はリバーロキサバンと報告事象との関連性があると判断した。弊社は、リバーロキサバン投与と報告事象発現との間に時間的関連性がないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044060

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044060/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/52/WHITE/CZECH REPUBLIC/YES
Medical history	Cervix carcinoma, Urinary tract infection, Ectopic pregnancy, Hypertension, Urinary incontinence, Uterine cancer, Uterine cancer, Uterine cancer, Anaemia, Liver disorder, Varicose vein operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALGIFEN NEO, CLEXANE, DETRALEX, DITROPAN, ENOXAPARIN, ESSENTIALE FORTE N, GLYVENOL, LACTULOSE SYRUP, NITROFURANTOIN, TARKA, TENAXUM, TENORETIC, TRIPRIM, VERAPAMIL AL 240 RETARD, WARFARIN
Adverse Events (AE) Preferred term	1. Haemangioma of liver 2. Alanine aminotransferase increased 3. Aspartate aminotransferase increased 4. Gamma-glutamyltransferase increased 5. Constipation 6. Genital pain 7. Nasopharyngitis 8. Arthralgia 9. Hydronephrosis 10. Hydronephrosis 11. Renal failure acute 12. International normalised ratio increased 13. Gamma-glutamyltransferase increased 14. Cervix carcinoma 15. Hypotension 16. Anaemia 17. Renal failure acute 18. Pyelonephritis 19. International normalised ratio increased 20. Liver disorder
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/YES/YES 10. MODERATE/NO/NO/YES 11. MODERATE/NO/NO/YES 12. MODERATE/YES/NO/YES 13. MILD/NO/NO/YES 14. SEVERE/NO/YES/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044060

Parameter	Value
	15. MILD/NO/NO/YES
	16. MODERATE/NO/NO/YES
	17. MODERATE/NO/YES/YES
	18. MODERATE/NO/NO/YES
	19. MODERATE/YES/NO/YES
	20. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 09SEP2008 (6) - --------- (.)
	2. 09SEP2008 (6) - 19SEP2008 (16)
	3. 09SEP2008 (6) - 19SEP2008 (16)
	4. 09SEP2008 (6) - 19SEP2008 (16)
	5. 01JAN2009 (120) - 27APR2009 (236)
	6. 07JAN2009 (126) - 13JUL2009 (313)
	7. 29MAR2009 (207) - 04APR2009 (213)
	8. 13APR2009 (222) - 04AUG2009 (335)
	9. 17JUN2009 (287) - 01JUL2009 (301)
	10. 17JUN2009 (287) - 11SEP2009 (373)
	11. 23JUN2009 (293) - 11AUG2009 (342)
	12. 23JUN2009 (293) - 30JUN2009 (300)
	13. 09JUL2009 (309) - --------- (.)
	14. 13JUL2009 (313) - --------- (.)
	15. 04AUG2009 (335) - 11AUG2009 (342)
	16. 11AUG2009 (342) - 21SEP2009 (383)
	17. 11AUG2009 (342) - --------- (.)
	18. 11AUG2009 (342) - 18SEP2009 (380)
	19. 12AUG2009 (343) - 13AUG2009 (344)
	20. 30SEP2009 (392) - --------- (.)
Duration of AE	1. .
	2. 11
	3. 11
	4. 11
	5. 117
	6. 188
	7. 7
	8. 114
	9. 15
	10. 87
	11. 50
	12. 8
	13. .
	14. .
	15. 8

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044060

Parameter	Value
	16. 42
	17. .
	18. 39
	19. 2
	20. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
	20.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044060

Parameter	Value
	17.
	18.
	19.
	20.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. NONE
	9. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	10. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	11. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	12. STUDY DRUG DISCONTINUED AND RESTARTED
	13. NONE
	14. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	15. OTHER
	16. OTHER
	17. REMEDIAL DRUG THERAPY
	18. REMEDIAL DRUG THERAPY
	19. REMEDIAL DRUG THERAPY
	20. NONE
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. WORSENED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. WORSENED
	12. RESOLVED
	13. UNCHANGED
	14. UNCHANGED
	15. RESOLVED
	16. RESOLVED
	17. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044060

Parameter	Value
	18. RESOLVED
	19. RESOLVED
	20. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-380044060[4)]	RENAL INSUFFICIENCY（PT：腎不全） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、合併症（慢性尿路感染）や子宮頸部癌に対する化学療法によるものであり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044074

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044074/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/38/WHITE/CZECH REPUBLIC/YES
Medical history	Inguinal hernia repair, Drug hypersensitivity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, DETRALEX, ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Gene mutation 2. Pregnancy 3. Abortion
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/NO
Start/stop date of event with relative date	1. 23FEB2009 (92) - --------- (.) 2. 25MAY2009 (183) - 29MAY2009 (187) 3. 29MAY2009 (187) - 29MAY2009 (187)
Duration of AE	1. . 2. 5 3. 1
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. NONE 2. OTHER 3. OTHER
Outcome of event	1. UNCHANGED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044090

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044090/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/66/WHITE/CZECH REPUBLIC/YES
Medical history	Urticaria, Chronic tonsillitis, Pneumoconiosis, Benign prostatic hyperplasia, Hypertension, Phlebitis superficial, Varicose vein, Meniscus operation, Prostate cancer, Hydrocele operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANDROCUR 100 POR TBL NOB, ANDROCUR- 50 POR TBL NOB, AUGMENTIN 1 G TBL FLM, BETADINE LIQ, CLEXANE 100 MG INJ SOL, CLEXANE INJ SOL, COVEREX 4MG TBL, DHC CONTINUS 60MG POR TBL RET, ENDIARON POR TBL FLM [CLOROXINUM (AA 250MG/ 1 TBL)], ENDIARON POR TBL FLM [CLOROXINUM], ENOXAPARIN, ENTEROL POR CPS DUR [SACCHAROMYCES BOULARDII SICCATUS,LACTOS MONOHYD,MAGN STEARA, FRAXIPARINE INJ SOL 0.4 ML, FYZIOLOGICKÝ ROZTOK INF SOL, GLYVENOL 400MG CPS, GUAJACURAN 5% INJ SOL, IMODIUM POR CPS DUR, LOMIR SRO TBL, MESOCAIN 1% INJ SOL, NEUROL 0.25 POR TBL NOB [ALPRAZOLAMUM], PEROXID VODÍKU 3% COO DRM SOL, PRESTARIUM NEO POR TBL FLM, REASEC POR TBL NOB, SMECTA POR PLV SUS, SUPRACAIN 4% INJ SOL, TRAMAL RETARD TABLETY 100 POR TBL, TRAMAL TOBOLKY 50MG POR CPS DUR, WARFARIN
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Hepatic steatosis 3. Renal cyst 4. Adrenal adenoma 5. Metastases to abdominal cavity 6. Diabetes mellitus 7. Prostate cancer metastatic 8. Musculoskeletal pain 9. Periodontitis 10. Nocturia 11. Anxiety 12. Diarrhoea 13. Methylenetetrahydrofolate reductase polymorphism 14. Gene mutation
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/NO/NO/NO

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044090

Parameter	Value
	14. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 29MAR2009 (3) - 03APR2009 (8)
	2. 02APR2009 (7) - --------- (.)
	3. 02APR2009 (7) - --------- (.)
	4. 08APR2009 (13) - --------- (.)
	5. 08APR2009 (13) - 15JUL2009 (111)
	6. 21MAY2009 (56) - --------- (.)
	7. 13JUL2009 (109) - 19OCT2009 (207)
	8. 01AUG2009 (128) - 04SEP2009 (162)
	9. 29SEP2009 (187) - 07OCT2009 (195)
	10. 01DEC2009 (250) - --------- (.)
	11. 03JAN2010 (283) - 31JAN2010 (311)
	12. 03JAN2010 (283) - 09FEB2010 (320)
	13. 18FEB2010 (329) - --------- (.)
	14. 18FEB2010 (329) - --------- (.)
Duration of AE	1. 6
	2. .
	3. .
	4. .
	5. 99
	6. .
	7. 99
	8. 35
	9. 9
	10. .
	11. 29
	12. 38
	13. .
	14. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044090

Parameter	Value
	13.
	14.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	6. NONE
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	8. REMEDIAL DRUG THERAPY,OTHER
	9. REMEDIAL DRUG THERAPY,OTHER
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. NONE
	14. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. UNCHANGED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. UNCHANGED
	11. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044090

Parameter	Value
	12. RESOLVED
	13. UNCHANGED
	14. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044108

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380044108/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/26/WHITE/CZECH REPUBLIC/YES
Medical history	Alanine aminotransferase increased, Joint sprain, Joint sprain, Blood bilirubin increased, Gamma-glutamyltransferase increased, Tobacco poisoning
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE 0.8ML INJ SOL, ENOXAPARIN, ESSENTIALE FORTE N POR CPS, FLAVOBION POR TBL, GLYVENOL 400 CPS, NOVALGIN TABLETY POR TBL, PARALEN 500 POR TBL, WARFARIN, ZINNAT 500 MG POR TBL
Adverse Events (AE) Preferred term	1. Aspartate aminotransferase increased 2. Alanine aminotransferase increased 3. Aspartate aminotransferase increased 4. Methylenetetrahydrofolate reductase polymorphism 5. Methylenetetrahydrofolate reductase polymorphism
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 17JUL2009 (4) - 12AUG2009 (30) 2. 20JUL2009 (7) - 19AUG2009 (37) 3. 26AUG2009 (44) - 07SEP2009 (56) 4. 03DEC2009 (143) - --------- (.) 5. 03DEC2009 (143) - --------- (.)
Duration of AE	1. 27 2. 31 3. 13 4. . 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. OTHER 4. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380044108

Parameter	Value
Outcome of event	5. NONE 1. RESOLVED 2. RESOLVED 3. RESOLVED 4. UNCHANGED 5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380054006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380054006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/70/WHITE/CZECH REPUBLIC/YES
Medical history	Back pain, Hypercholesterolaemia, Urinary incontinence, Varicose vein, Osteoarthritis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APO-DICLO TBL, BUSCOPAN, ENOXAPARIN, GLYVENOL, LANZUL TBL, LIPOHEXAL 250MG RETARD, SILYMARIN, TIAPRIDAL TBL, TRAMAL, UNASYN, VESICARE TBL, WARFARIN
Adverse Events (AE) Preferred term	1. Biliary colic
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 15DEC2008 (181) - 22DEC2008 (188)
Duration of AE	1. 8
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380054015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380054015/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/65/WHITE/CZECH REPUBLIC/YES
Medical history	Anaemia macrocytic, Arteriosclerosis, Coronary artery disease, Hepatitis A, Hypertension, Peptic ulcer, Prostate cancer, Tuberculosis, Liver disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APO-OME (OMEPRAZOLE), DETRALEX, FAKTU [POLICRESULEN, CINCHOCAIN HYDROCHLORIDE], PRESTARIUM NEO
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Large intestine carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 09APR2009 (16) - 03MAY2009 (40) 2. 06MAY2009 (43) - --------- (.)
Duration of AE	1. 25 2. .
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. F
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/68/WHITE/CZECH REPUBLIC/YES
Medical history	Anaemia, Hypertension, Hyperuricaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENAP, ENOXAPARIN, KANAVIT, LOKREN, PURINOL [ALLOPURINOL], WARFARIN
Adverse Events (AE) Preferred term	1. International normalised ratio increased 2. International normalised ratio increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/YES/YES 2. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 20FEB2008 (16) - 22FEB2008 (18) 2. 07MAY2008 (93) - 08MAY2008 (94)
Duration of AE	1. 3 2. 2
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064005/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/47/WHITE/CZECH REPUBLIC/YES
Medical history	Anaemia, Crohn's disease, Menopause, Migraine, Ileectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTIVELLE, AVRAZOR, CINARIZIN, CIPHIN, ENOXAPARIN, IMURAN, PENTASA, PREDNISON, WARFARIN, ZOLOFT
Adverse Events (AE) Preferred term	1. Crohn's disease 2. Crohn's disease 3. Intestinal infarction 4. Abdominal abscess 5. Depression 6. Culture throat positive 7. Pneumothorax traumatic 8. Cellulitis 9. Dermatitis allergic 10. Central venous catheterisation 11. Methylenetetrahydrofolate reductase polymorphism
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/NO 3. MODERATE/NO/NO/NO 4. MODERATE/NO/YES/NO 5. MODERATE/NO/NO/NO 6. MILD/NO/NO/NO 7. MODERATE/NO/YES/NO 8. MODERATE/NO/NO/NO 9. SEVERE/NO/NO/NO 10. MILD/NO/NO/NO 11. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 29FEB2008 (11) - 14MAR2008 (25) 2. 06MAY2008 (78) - 02SEP2008 (197) 3. 12MAY2008 (84) - 12MAY2008 (84) 4. 26MAY2008 (98) - 20JUN2008 (123) 5. 08JUN2008 (111) - 02SEP2008 (197) 6. 09JUN2008 (112) - 23JUN2008 (126) 7. 22JUL2008 (155) - 28JUL2008 (161) 8. 23JUL2008 (156) - 05AUG2008 (169) 9. 25JUL2008 (158) - 29JUL2008 (162) 10. 12AUG2008 (176) - 02SEP2008 (197) 11. 19AUG2008 (183) - --------- (.)
Duration of AE	1. 15 2. 120 3. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064005

Parameter	Value
	4. 26
	5. 87
	6. 15
	7. 7
	8. 14
	9. 5
	10. 22
	11. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	2. OTHER
	3. REMEDIAL DRUG THERAPY,OTHER
	4. REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. OTHER
	7. OTHER
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. NONE
	11. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064005

Parameter	Value
Outcome of event	1. IMPROVED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064017

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064017/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/44/WHITE/CZECH REPUBLIC/YES
Medical history	Cholelithiasis, Nephrolithiasis, Renal aplasia, Urinary tract infection, Lower limb fracture, Hepatitis B antigen positive
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXIKLAV, AUGMENTIN, LANZUL
Adverse Events (AE) Preferred term	1. Urinary tract infection 2. Congenital urethral anomaly
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07JUL2008 (34) - 12JUL2008 (39) 2. 12AUG2008 (70) - --------- (.)
Duration of AE	1. 6 2. .
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064019/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/37/WHITE/CZECH REPUBLIC/YES
Medical history	Wrist fracture, Quadriplegia, Tendon injury, Tibia fracture, Urinary tract infection, Spinal column injury
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCINUM, CIPLOX, DETRALEX
Adverse Events (AE) Preferred term	1. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 29JUN2009 (370) - 01JUL2009 (372)
Duration of AE	1. 3
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. F
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064020/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/43/WHITE/CZECH REPUBLIC/YES
Medical history	Diabetes mellitus, Glioblastoma, Hepatic steatosis, Hypertension, Pneumonia, Cholelithiasis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BETALOC, FORTECORTIN, PRESTARIUM NEO
Adverse Events (AE) Preferred term	1. Glioblastoma 2. Transaminases increased 3. Grand mal convulsion
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/YES/YES 3. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 13JAN2009 (201) - 27JAN2009 (215) 2. 27JAN2009 (215) - 19FEB2009 (238) 3. 15FEB2009 (234) - 23FEB2009 (242)
Duration of AE	1. 15 2. 24 3. 9
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. F
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064022/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/CZECH REPUBLIC/YES
Medical history	Anaemia, Pulmonary tuberculosis, Silicosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALGIFEN, AUGMENTIN, BATRAFEN, BERODUAL, COTRIMOXAZOL AL, ENOXAPARIN, EUPHYLLIN [EUPHYLLIN=THEOPHYLLINE], FRAXIPARIN, HELICID, TRAMAL, WARFARIN
Adverse Events (AE) Preferred term	1. Fungal skin infection 2. Jugular vein thrombosis 3. Oesophageal ulcer 4. Lung neoplasm 5. Lung neoplasm
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 20AUG2008 (1) - 12MAR2009 (205) 2. 02SEP2008 (14) - 17SEP2008 (29) 3. 09SEP2008 (21) - 17OCT2008 (59) 4. 13OCT2008 (55) - 05NOV2008 (78) 5. 06NOV2008 (79) - --------- (.)
Duration of AE	1. 205 2. 16 3. 39 4. 24 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY,OTHER 5. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064022

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. IMPROVED
	5. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064023/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/74/WHITE/CZECH REPUBLIC/YES
Medical history	Appendicectomy, Diabetes mellitus, Hypertension, Menopause, Tibia fracture, Umbilical hernia repair, Thyroidectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXYKLAV, APO ATENOL, AVRAZOR, CARDILOPIN, CLEXANE, DOLMINA [DOLMINA=DICLOFENACUM NATRICUM], ENOXAPARIN, GENTAMYCIN, STILNOX, TARKA, WARFARIN
Adverse Events (AE) Preferred term	1. Ovarian cancer 2. Incision site infection
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 26AUG2008 (5) - 18FEB2009 (181) 2. 02FEB2009 (165) - 31MAR2009 (222)
Duration of AE	1. 177 2. 58
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/CZECH REPUBLIC/YES
Medical history	Appendicectomy, Hypertension, Gastroenteritis salmonella
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AGEN, AMBROBENE, ATROPIN, AUGMENTIN, CEFAZOLIN, ENOXAPARIN, FRAXIPARIN, HELICID, LORISTA, MORPHIN, TRAMAL, WARFARIN
Adverse Events (AE) Preferred term	1. Aortic aneurysm 2. Aortic aneurysm
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/NO 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 23SEP2008 (1) - 26FEB2009 (157) 2. 27FEB2009 (158) - 11MAR2009 (170)
Duration of AE	1. 157 2. 13
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064028/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/82/WHITE/CZECH REPUBLIC/YES
Medical history	Arthralgia, Spinal fracture, Hypertension, Menopause, Osteoporosis, Urinary tract infection, Cerebrosclerosis, Pneumonia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CALTRATE PLUS, ENELBIN, ETOPHYLLIN, OMEPRAZOL, PREDNISON, RHEFLUIN
Adverse Events (AE) Preferred term	1. Cerebral arteriosclerosis 2. Pleural effusion 3. Hepatic cancer metastatic 4. Cerebral arteriosclerosis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 21NOV2008 (14) - 02DEC2008 (25) 2. 24NOV2008 (17) - --------- (.) 3. 28NOV2008 (21) - 10DEC2008 (33) 4. 03DEC2008 (26) - --------- (.)
Duration of AE	1. 12 2. . 3. 13 4. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg
Dose status on AE onset	1. . 2. . 3. F 4. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. NONE 3. NONE 4. NONE
Outcome of event	1. IMPROVED 2. INSUFFICIENT FOLLOW-UP 3. DEATH

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064028

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064034

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064034/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/CZECH REPUBLIC/YES
Medical history	Bronchopneumonia, Haemorrhoids, Inguinal hernia repair, Rib fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXIKLAV, ATROPIN, DOLSIN, ENOXAPARIN, ENTIZOL, FRAXIPARINE, METRONIDAZOL, VERAL, WARFARIN
Adverse Events (AE) Preferred term	1. Appendicitis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 08JUN2009 (49) - 18JUN2009 (59)
Duration of AE	1. 11
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064035

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380064035/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/71/WHITE/CZECH REPUBLIC/YES
Medical history	Bronchiectasis, Femur fracture, Hypertension, Prostate cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARDILOPIN, DOXYCYCLIN, ENOXAPARIN, FRAXIPARINE, HYDROCHLOROTHIAZID, KLACID SR, MICARDIS, WARFARIN
Adverse Events (AE) Preferred term	1. Bronchitis 2. Bronchitis 3. Prostate cancer 4. Non-cardiac chest pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01JUL2009 (34) - 08JUL2009 (41) 2. 27AUG2009 (91) - 09SEP2009 (104) 3. 06OCT2009 (131) - 13OCT2009 (138) 4. 15OCT2009 (140) - 15OCT2009 (140)
Duration of AE	1. 8 2. 14 3. 8 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380064035

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380074015/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/70/WHITE/CZECH REPUBLIC/YES
Medical history	Arteriosclerosis, Cholecystectomy, Diabetes mellitus, Inguinal hernia repair, Bladder neoplasm, Urostomy, Colorectostomy, Bladder neoplasm surgery
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACID ACETYLSALICYLIC, CILKANOL, DETRALEX, ENELBIN RET, GLIMEPIRID, HYLAK, OLTAR, REASEC
Adverse Events (AE) Preferred term	1. Blood alkaline phosphatase increased 2. Diarrhoea 3. Carcinoembryonic antigen increased 4. Hepatic steatosis 5. Pyelocaliectasis 6. Lymphadenopathy 7. Pelvic neoplasm 8. Adrenal adenoma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. SEVERE/NO/YES/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 04APR2008 (0) - --------- (.) 2. 06APR2008 (2) - 07APR2008 (3) 3. 18APR2008 (14) - --------- (.) 4. 24APR2008 (20) - --------- (.) 5. 24APR2008 (20) - --------- (.) 6. 24APR2008 (20) - --------- (.) 7. 19MAY2008 (45) - --------- (.) 8. 19MAY2008 (45) - --------- (.)
Duration of AE	1. . 2. 2 3. . 4. . 5. . 6. . 7. . 8. .
Dose on AE onset	1. 2. 15 mg 3. 15 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074015

Parameter	Value
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. OTHER
	8. NONE
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. UNCHANGED
	4. UNCHANGED
	5. UNCHANGED
	6. UNCHANGED
	7. UNCHANGED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380074018/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/84/WHITE/CZECH REPUBLIC/YES
Medical history	Diabetes mellitus, Hypertension, Insomnia, Menopause, Renal stone removal, Osteoarthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARTRILOM, CILKANOL, ENOXAPARIN, GLIMEPIRID, HYPNOGEN, TENORMIN, TRITACE, WARFARIN
Adverse Events (AE) Preferred term	1. Hypercoagulation 2. Cholelithiasis 3. Renal failure chronic 4. Sudden death
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 16APR2008 (1) - --------- (.) 2. 12MAY2008 (27) - --------- (.) 3. 12MAY2008 (27) - --------- (.) 4. 27JUL2008 (103) - 27JUL2008 (103)
Duration of AE	1. . 2. . 3. . 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. NONE 3. NONE 4. NONE
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074018

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380074025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/54/WHITE/CZECH REPUBLIC/YES
Medical history	Postmenopause, Venous insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACID ACETYLSALICYLIC, AUGMENTIN, CARBIMAZOL, CARDILAN, CILKANOL, CIPHIN, CLEXANE, DETRALEX, ENOXAPARIN, FROZEN PLASMA, KANAVIT, PROPYCIL, SIMEPAR, THYROZOL, TRAMAL, VASOCARDIN, WARFARIN
Adverse Events (AE) Preferred term	1. Hyperthyroidism 2. Epistaxis 3. Ear haemorrhage 4. International normalised ratio increased 5. Hepatic steatosis 6. Cystitis 7. Nephrolithiasis 8. Haemorrhagic anaemia 9. Pyelonephritis acute 10. International normalised ratio increased 11. Blood alkaline phosphatase increased 12. Pyelonephritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/YES/YES/YES 3. SEVERE/YES/YES/YES 4. SEVERE/YES/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/YES/NO/YES 11. MODERATE/NO/NO/YES 12. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 11JUL2008 (32) - --------- (.) 2. 09OCT2008 (122) - 15OCT2008 (128) 3. 09OCT2008 (122) - 15OCT2008 (128) 4. 13OCT2008 (126) - 15OCT2008 (128) 5. 14OCT2008 (127) - --------- (.) 6. 15OCT2008 (128) - 21OCT2008 (134) 7. 15OCT2008 (128) - --------- (.) 8. 15OCT2008 (128) - 22OCT2008 (135) 9. 15OCT2008 (128) - 21OCT2008 (134) 10. 04MAR2009 (268) - 06MAR2009 (270) 11. 27MAR2009 (291) - --------- (.)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074025

Parameter	Value
	12. 01APR2009 (296) - 01APR2009 (296)
Duration of AE	1. .
	2. 7
	3. 7
	4. 3
	5. .
	6. 7
	7. .
	8. 8
	9. 7
	10. 3
	11. .
	12. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074025

Parameter	Value
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. REMEDIAL DRUG THERAPY
	10. STUDY DRUG DISCONTINUED AND RESTARTED
	11. NONE
	12. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED
	7. UNCHANGED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. UNCHANGED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-380074025[4),4)]	BLEEDING FROM THE EARS（PT：耳出血） 治験担当医はエノキサパリンとの因果関係評価を行っていない。弊社は、時間的関連性が認められないことから、因果関係は否定できると考える。 NASAL BLEEDING（PT：鼻出血） 治験担当医はエノキサパリンとの因果関係評価を行っていない。弊社は、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074035

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380074035/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/66/WHITE/CZECH REPUBLIC/YES
Medical history	Bronchitis, Hypertension, Inguinal hernia repair, Umbilical hernia repair, Venous insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AGEN, BETALOC SR, CILKANOL, ENOXAPARIN, FORADIL, PRESTARIUM NEO, PULMICORT, WARFARIN
Adverse Events (AE) Preferred term	1. Haematochezia 2. Haemorrhoids 3. Colon cancer 4. Metastases to liver 5. Hepatic steatosis 6. Diverticulum intestinal
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 20FEB2009 (120) - 24FEB2009 (124) 2. 02MAR2009 (130) - --------- (.) 3. 02MAR2009 (130) - 14OCT2009 (356) 4. 04MAR2009 (132) - 09DEC2009 (412) 5. 04MAR2009 (132) - --------- (.) 6. 10MAR2009 (138) - 14OCT2009 (356)
Duration of AE	1. 5 2. . 3. 227 4. 281 5. . 6. 219
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380074035

Parameter	Value
Action taken	1. OTHER
	2. NONE
	3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	4. OTHER
	5. NONE
	6. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-380074035[2)]	ENTERORRHAGIA（PT：腸出血） 治験担当医は、合併症（内痔核、大腸憩室）によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380084002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380084002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/CZECH REPUBLIC/YES
Medical history	Gun shot wound, Hypertension, Renal cyst, Cholelithiasis, Bone pain, Cataract operation, Cataract operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATORIS, DETRALEX, ENAP H, ENOXAPARIN, FRAXIPARIE, HEPRIN, ISUPREL, PRESTARIUM, RHEFLUIN, WARFARIN
Adverse Events (AE) Preferred term	1. Factor V Leiden mutation 2. Amnesia 3. Cerebral atrophy 4. Ventricular tachycardia 5. Ventricular tachycardia 6. Hypercholesterolaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/YES/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 27OCT2008 (3) - --------- (.) 2. 11MAY2009 (199) - 11MAY2009 (199) 3. 03JUN2009 (222) - --------- (.) 4. 21JUL2009 (270) - 21JUL2009 (270) 5. 02AUG2009 (282) - 04AUG2009 (284) 6. 03AUG2009 (283) - --------- (.)
Duration of AE	1. . 2. 1 3. . 4. 1 5. 3 6. .
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380084002

Parameter	Value
Action taken	1. NONE
	2. OTHER
	3. NONE
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380094016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380094016/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/73/WHITE/CZECH REPUBLIC/YES
Medical history	Aortic valve stenosis, Bladder cancer, Myocardial ischaemia, Chronic obstructive pulmonary disease, Hyperlipidaemia, Hypertension, Peripheral ischaemia, Renal cancer, Cerebrovascular accident, Renal failure chronic, Rheumatic heart disease, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALDACTON [SPIRONOLACTONE], ANOPYRIN, BETALOC, DIAPREL, DOPAMIN, ENELBIN, FURON, FUROSEMID, MONOSAN, PENTOXYFYLLIN, SIMGAL, TRITACE, VEROSPIRON, ZOREM
Adverse Events (AE) Preferred term	1. Nephrogenic anaemia 2. Cardiac failure
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 25OCT2008 (2) - --------- (.) 2. 24NOV2008 (32) - 27NOV2008 (35)
Duration of AE	1. . 2. 4
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. UNCHANGED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380094038

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380094038/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/73/WHITE/CZECH REPUBLIC/YES
Medical history	Anaemia, Nervous system disorder, Colon cancer, Spine malformation, Lung lobectomy, Atrial fibrillation, Lung cancer metastatic, Traumatic haematoma, Toxic neuropathy, Metastases to central nervous system, Chemotherapy, Epilepsy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMPICILIN, CARBOSORB, CIPHIN, ENDIARON [CHLOROXINE], FORTECORTIN, HELICID, KALIUM CHLORATUM, NEUROTOP, VEROGALID SR, VITAMIN B 12
Adverse Events (AE) Preferred term	1. Enterocolitis bacterial 2. General physical health deterioration 3. Bronchopneumonia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 11FEB2009 (3) - 20FEB2009 (12) 2. 21OCT2009 (255) - --------- (.) 3. 16DEC2009 (311) - 19DEC2009 (314)
Duration of AE	1. 10 2. . 3. 4
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 380094053

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/380094053/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/74/WHITE/CZECH REPUBLIC/YES
Medical history	Diabetes mellitus, Haemorrhoids, Hepatitis non-A non-B, Hepatitis alcoholic, Skin neoplasm excision, Intervertebral disc disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, ESSENTIALE, GLUCOPHAGE, NADROPARIN, SPOFAX
Adverse Events (AE) Preferred term	1. Rectal cancer
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 08JUL2009 (7) - 07AUG2009 (37)
Duration of AE	1. 31
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. I
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390014002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/ISRAEL/YES
Medical history	Cataract, Femur fracture, Tobacco user
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANTI-TETANUS VACCINE, OXYCODONE
Adverse Events (AE) Preferred term	1. Contusion 2. Skin laceration
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 10NOV2007 (11) - 11NOV2007 (12) 2. 10NOV2007 (11) - 11NOV2007 (12)
Duration of AE	1. 2 2. 2
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390014004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/35/WHITE/ISRAEL/YES
Medical history	Tobacco user, Obesity, Factor V Leiden mutation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DORMICUM [MIDAZOLAM], ENALADEX, ENOXAPARIN, HYDROCORTISONE, LANTON, MICROPIRIN, NORMITEN, OPTALGIN, PHENERGAN, STUNARONE, VABEN, WARFARIN
Adverse Events (AE) Preferred term	1. Lipoma 2. Vertigo 3. Drug eruption 4. Abdominal pain 5. Dyspnoea 6. Vertigo 7. Anxiety 8. Chest pain 9. Dizziness 10. Hypertension 11. Headache 12. Paraesthesia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/YES/YES 6. MILD/NO/YES/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/YES/YES 10. MILD/NO/NO/YES 11. MILD/NO/YES/YES 12. MILD/NO/NO/YES
Start/stop date of event with relative date	1. -----2008 (.) - 14AUG2008 (267) 2. 23NOV2007 (2) - 23NOV2007 (2) 3. 24NOV2007 (3) - 25NOV2007 (4) 4. 24NOV2007 (3) - 25NOV2007 (4) 5. 04DEC2007 (13) - 06DEC2007 (15) 6. 04DEC2007 (13) - 06DEC2007 (15) 7. 04JAN2008 (44) - 04JAN2008 (44) 8. 04JAN2008 (44) - 04JAN2008 (44) 9. 21JAN2008 (61) - 24JAN2008 (64) 10. 21JAN2008 (61) - --------- (.) 11. 21JAN2008 (61) - 24JAN2008 (64) 12. 21JAN2008 (61) - 24JAN2008 (64)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014004

Parameter	Value
Duration of AE	1. .
	2. 1
	3. 2
	4. 2
	5. 3
	6. 3
	7. 1
	8. 1
	9. 4
	10. .
	11. 4
	12. 4
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Action taken	1. OTHER
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014004

Parameter	Value
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. OTHER
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. NONE
	12. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. IMPROVED
	11. RESOLVED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390014021/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/76/WHITE/ISRAEL/YES
Medical history	Angina pectoris, Anxiety, Cerebrovascular accident, Constipation, Dizziness, Fall, Hyperlipidaemia, Hypertension, Insomnia, Myocardial infarction, Varicose vein, Vertigo, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, BETISTINE, BONDORMIN, ENOXAPARIN, FUSID, IKAPRESS, LAXATIVE, LOPRESSOR OROS, LORIVAN, NOVITROPAN, SIMOVIL, WARFARIN
Adverse Events (AE) Preferred term	1. Urinary incontinence 2. Haematoma 3. Pulmonary oedema 4. Pulmonary oedema 5. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/YES/YES 5. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 30APR2008 (8) - --------- (.) 2. 07JUN2008 (46) - 20JUN2008 (59) 3. 28AUG2008 (128) - 28AUG2008 (128) 4. 29AUG2008 (129) - 02SEP2008 (133) 5. 09NOV2008 (201) - 11NOV2008 (203)
Duration of AE	1. . 2. 14 3. 1 4. 5 5. 3
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. NONE 4. REMEDIAL DRUG THERAPY 5. OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014021

Parameter	Value
Outcome of event	1. IMPROVED 2. RESOLVED 3. WORSENED 4. RESOLVED 5. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390014025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/75/WHITE/ISRAEL/YES
Medical history	Anaemia, Bladder neoplasm, Cholecystectomy, Hypertension, Urinary tract infection, Retinal detachment, Retinal detachment, Syncope, Urinary bladder excision, Prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BICARBONATE [SODIUM BICARBONATE], ENOXAPARIN, MOXYPEN, PENEDIL, SLOW FE, WARFARIN
Adverse Events (AE) Preferred term	1. General physical health deterioration 2. Dyspnoea 3. Dyspnoea 4. Post procedural haemorrhage 5. Dyspnoea 6. Metastases to lung 7. Metastases to liver
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/YES/NO/NO 5. SEVERE/NO/NO/NO 6. SEVERE/NO/YES/NO 7. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 13SEP2008 (104) - --------- (.) 2. 05OCT2008 (126) - 12OCT2008 (133) 3. 13OCT2008 (134) - 23OCT2008 (144) 4. 16OCT2008 (137) - 16OCT2008 (137) 5. 24OCT2008 (145) - --------- (.) 6. 29OCT2008 (150) - 02NOV2008 (154) 7. 29OCT2008 (150) - 02NOV2008 (154)
Duration of AE	1. . 2. 8 3. 11 4. 1 5. . 6. 5 7. 5
Dose on AE onset	1. 2. 3. 4. 5. 6. 7.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014025

Parameter	Value
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. NONE
	3. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. WORSENED
	3. WORSENED
	4. RESOLVED
	5. UNCHANGED
	6. DEATH
	7. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390014026

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390014026/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/74/WHITE/ISRAEL/YES
Medical history	Anaemia, Cataract, Renal failure chronic, Gastritis, Hypercholesterolaemia, Hypertension, Pruritus, Postpartum hypopituitarism, Weight decreased, Colon adenoma, Intervertebral disc disorder, Ligament rupture, Gastritis atrophic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALTRATE AND VIT D, ELTROXIN, ENOXAPARIN, KEFLEX, LIPITOR, OCSAAR, OXYCONTIN, PREDNISONE, TELFAST, WARFARIN
Adverse Events (AE) Preferred term	1. Oedema peripheral 2. Skin laceration 3. Back pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --JUL2008 (.) - --------- (.) 2. 16SEP2008 (98) - 17SEP2008 (99) 3. 05NOV2008 (148) - --------- (.)
Duration of AE	1. . 2. 2 3. .
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390024001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390024001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/76/WHITE/ISRAEL/YES
Medical history	Breast cancer, Essential hypertension, Hyperlipidaemia, Hypothyroidism, Insomnia, Obesity, Varicose vein, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, ELTROXIN, ENOXAPARIN, METFORMINE, NOVONORM, SIMVASTATIN, SPIRONOLACTONE, VABEN, VERAPRESS, WARFARIN
Adverse Events (AE) Preferred term	1. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 16SEP2007 (11) - 19SEP2007 (14)
Duration of AE	1. 4
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. OTHER
Outcome of event	1. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390024003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390024003/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/48/WHITE/ISRAEL/YES
Medical history	Anaemia, Oophorectomy bilateral, Breast cancer metastatic, Nausea, Cardiac tamponade, Ovarian cancer metastatic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DUPHALAC [CONTEINS; GALACTOSE+ LACTULOSE], FUSID, NOVOLAX [NOVOLAX, TRIMA- OSMOTIC LAXATIVE, LACTITOLE MONOHYDRATE. INDICATION IS, OPTALGIN, PARAFFIN OIL, PRAMIN, XELODA, ZOMERA
Adverse Events (AE) Preferred term	1. Lymphoedema 2. Constipation
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 30SEP2007 (24) - 02OCT2007 (26) 2. 30SEP2007 (24) - 01OCT2007 (25)
Duration of AE	1. 3 2. 2
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390024014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390024014/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/ISRAEL/YES
Medical history	Anaemia, Lung neoplasm malignant, Unevaluable event, Bundle branch block right, Pathological fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, CARDILOC, FOSIDE, GEMZAR, LIPITOR, SLOW K, STILNOX, TRITACE
Adverse Events (AE) Preferred term	1. Acute coronary syndrome
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 20MAR2008 (17) - 27MAR2008 (24)
Duration of AE	1. 8
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. I
Action taken	1. OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390034008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/ISRAEL/YES
Medical history	Cellulitis, Drug hypersensitivity, Gout, Hypertension, Peripheral vascular disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALFALFA, ALLORIL, ASPIRIN, LOSEC, NORMITEN, OPTALGIN, REVENOL, TRITACE, VMM
Adverse Events (AE) Preferred term	1. Gastric cancer 2. Pneumonia 3. Alanine aminotransferase increased 4. Gastrointestinal disorder postoperative 5. Cellulitis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/NO 3. MILD/NO/NO/NO 4. SEVERE/NO/YES/NO 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 06JAN2008 (6) - --------- (.) 2. 20JAN2008 (20) - 30JAN2008 (30) 3. 28JAN2008 (28) - 03FEB2008 (34) 4. 31JAN2008 (31) - 22FEB2008 (53) 5. 14FEB2008 (45) - 22FEB2008 (53)
Duration of AE	1. . 2. 11 3. 7 4. 23 5. 9
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg
Dose status on AE onset	1. F 2. F 3. F 4. F 5. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 2. REMEDIAL DRUG THERAPY 3. NONE 4. REMEDIAL DRUG THERAPY,OTHER 5. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034008

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390034009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/58/WHITE/ISRAEL/YES
Medical history	Cellulitis, Hypertension, Menopause, Obesity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACAMOL, CAPOTEN, CEFAMEZIN [CEFAZOLIN SODIUM], CONCOR, ENALADEX, ENOXAPARIN, KEFLEX, NEOBLOC, WARFARIN
Adverse Events (AE) Preferred term	1. Hypertension 2. Leukocytosis 3. Pulmonary infarction 4. Cellulitis 5. Hepatic neoplasm malignant 6. Pleural effusion 7. Headache 8. Hypertension 9. Colonic polyp 10. Haemorrhoids
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/NO 8. MILD/NO/NO/NO 9. MILD/NO/NO/NO 10. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 02JAN2008 (1) - 08JAN2008 (7) 2. 03JAN2008 (2) - --------- (.) 3. 03JAN2008 (2) - --------- (.) 4. 04JAN2008 (3) - --------- (.) 5. 08JAN2008 (7) - 22FEB2008 (52) 6. 09JAN2008 (8) - --------- (.) 7. 14JAN2008 (13) - 14JAN2008 (13) 8. 15JAN2008 (14) - 15JAN2008 (14) 9. 15JAN2008 (14) - --------- (.) 10. 15JAN2008 (14) - --------- (.)
Duration of AE	1. 7 2. . 3. . 4. . 5. 46 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034009

Parameter	Value
	7. 1
	8. 1
	9. .
	10. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. NONE
	10. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. IMPROVED
	5. DEATH
	6. UNCHANGED
	7. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034009

Parameter	Value
	8. RESOLVED
	9. UNCHANGED
	10. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390034011/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/78/WHITE/ISRAEL/YES
Medical history	Microcytic anaemia, Anxiety, Arrhythmia, Hysterectomy, Colon cancer, Drug hypersensitivity, Colectomy, Monarthritis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARDILOC, ENOXAPARIN, ENSURE, FOLIC ACID, LOSEC, MORPHINE, OPTALGIN, OXYCOD, TRAMADEX, TRAMAL, VANCOMYCIN, WARFARIN, XEFO
Adverse Events (AE) Preferred term	1. Endocarditis staphylococcal 2. Epistaxis 3. Leukocytosis 4. Haemoglobin decreased 5. International normalised ratio increased 6. Haemoglobin decreased 7. Hypocalcaemia 8. Hypophosphataemia 9. Cough
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/NO 7. MILD/NO/NO/NO 8. MILD/NO/NO/NO 9. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 11FEB2008 (4) - 23MAR2008 (45) 2. 11FEB2008 (4) - 11FEB2008 (4) 3. 11FEB2008 (4) - 25FEB2008 (18) 4. 13FEB2008 (6) - 17FEB2008 (10) 5. 16FEB2008 (9) - 19FEB2008 (12) 6. 19FEB2008 (12) - 13MAY2008 (96) 7. 20FEB2008 (13) - 27FEB2008 (20) 8. 24FEB2008 (17) - 28FEB2008 (21) 9. 26FEB2008 (19) - 07MAR2008 (29)
Duration of AE	1. 42 2. 1 3. 15 4. 5 5. 4 6. 85 7. 8 8. 5

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034011

Parameter	Value
	9. 11
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED
	3. NONE
	4. OTHER
	5. NONE
	6. OTHER
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034011

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390034015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/ISRAEL/YES
Medical history	Drug hypersensitivity, Back pain, Chronic myeloid leukaemia, Gastritis, Haemoglobin decreased, Hypertriglyceridaemia, Osteoarthritis, Polyneuropathy, Complex regional pain syndrome, Knee arthroplasty, Umbilical hernia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALLORIL, ENOXAPARIN, ETOPAN, GLIVEC, LOSEC, OPTALGIN, OXYCONTIN, RESPRIM, SEDURAL, SILVEROL, SKIN BETACORTEN, STOPIT, TRIBEMIN, WARFARIN
Adverse Events (AE) Preferred term	1. Decubitus ulcer 2. Blister 3. Petechiae 4. Diarrhoea 5. Decubitus ulcer 6. Pyrexia 7. Dysuria 8. Medical device complication 9. Gingival bleeding
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/YES/YES 9. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 09MAY2008 (1) - 18MAY2008 (10) 2. 11MAY2008 (3) - --------- (.) 3. 13MAY2008 (5) - 16MAY2008 (8) 4. 14MAY2008 (6) - 18MAY2008 (10) 5. 15MAY2008 (7) - 18MAY2008 (10) 6. 04JUN2008 (27) - 06JUN2008 (29) 7. 04JUN2008 (27) - 11JUN2008 (34) 8. 02JUL2008 (55) - 04JUL2008 (57) 9. 11AUG2008 (95) - 11AUG2008 (95)
Duration of AE	1. 10 2. . 3. 4 4. 5 5. 4 6. 3 7. 8

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034015

Parameter	Value
	8. 3
	9. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY,OTHER
	9. NONE
Outcome of event	1. RESOLVED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034015

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390034016/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/53/WHITE/ISRAEL/YES
Medical history	Appendicectomy, Gilbert's syndrome, Lymphoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Pruritus 2. Pyrexia 3. Diarrhoea 4. Abdominal pain upper 5. Vomiting 6. Alanine aminotransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/YES/NO/YES 6. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. --JUN2008 (.) - --------- (.) 2. --JAN2009 (.) - --JAN2009 (.) 3. 25JUN2008 (1) - 01JUL2008 (7) 4. 25JUN2008 (1) - 26JUN2008 (2) 5. 25JUN2008 (1) - 25JUN2008 (1) 6. 25NOV2008 (154) - 12APR2009 (292)
Duration of AE	1. . 2. . 3. 7 4. 2 5. 1 6. 139
Dose on AE onset	1. 2. 3. 15 mg 4. 15 mg 5. 15 mg 6. 20 mg
Dose status on AE onset	1. 2. 3. . 4. . 5. . 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034016

Parameter	Value
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. OTHER
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390034025/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/71/WHITE/ISRAEL/YES
Medical history	Arthralgia, Cataract, Depression, Hypercholesterolaemia, Hypertension, Hysterectomy, Spinal osteoarthritis, Deep vein thrombosis, Parkinson's disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACAMOL, AVILAC, CLEXANE, CLONEX, DERMACOMBIN, EVITOL, GLYCERINE SUPPS, KEMADRIN, LEVOPAR, LYRICA, PK- MERZ, PK-MERZ, REQUIP, SIMOVIL, STILNOX, VIEPAX, XENAZINE
Adverse Events (AE) Preferred term	1. Decubitus ulcer 2. Confusional state 3. Haematoma 4. Parkinson's disease 5. Constipation 6. Hypotension 7. Urinary tract infection
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/YES/NO/YES 4. SEVERE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --JUL2009 (.) - --------- (.) 2. 28NOV2008 (30) - 28NOV2008 (30) 3. 12FEB2009 (106) - 01MAR2009 (123) 4. 12AUG2009 (287) - --------- (.) 5. 17AUG2009 (292) - 17AUG2009 (292) 6. 21AUG2009 (296) - 22AUG2009 (297) 7. 21AUG2009 (296) - 25AUG2009 (300)
Duration of AE	1. . 2. 1 3. 18 4. . 5. 1 6. 2 7. 5
Dose on AE onset	1. 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390034025

Parameter	Value
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. F
	7. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. STUDY DRUG DISCONTINUED PERMANENTLY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390044001/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/79/WHITE/ISRAEL/YES
Medical history	Microcytic anaemia, Arthralgia, Atrial fibrillation, Cataract, Blindness, Cholelithiasis, Cardiac failure congestive, Depression, Endophthalmitis, Hyperlipidaemia, Hypertension, Hypertriglyceridaemia, Hypoalbuminaemia, Arthropathy, Mental disorder due to a general medical condition, Otitis media chronic, Peptic ulcer, Postmenopause, Constipation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AEROVENT, CARTIA [ACETYLSALICYLIC ACID], DERALIN, ELATROL, ENALAPRIL, FLEXOTIDE NEBULES, FUSID, IKACOR, LANOXINE, LANTON, LASIX, LAXADIN, LOSEC, NORMITEN, NYSTATIN READY MIX, ORBENIL, OXYCOD, OXYCONTIN, ROCEPHIN, SIMOVIL
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Cellulitis 3. Pneumonia 4. Sudden cardiac death
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 08NOV2007 (4) - 08NOV2007 (4) 2. 11NOV2007 (7) - 14NOV2007 (10) 3. 11NOV2007 (7) - 14NOV2007 (10) 4. 18DEC2007 (44) - 18DEC2007 (44)
Duration of AE	1. 1 2. 4 3. 4 4. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044001

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390044003/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/86/WHITE/ISRAEL/YES
Medical history	Abdominal pain upper, Normochromic normocytic anaemia, Depression, Coeliac disease, Constipation, Viral hepatitis carrier, Hepatitis C antibody positive, Hypertension, Insomnia, Weight decreased, Mesenteric vein thrombosis, Nausea, Osteoporosis, Pancreatic cyst, Pancreatitis chronic, Peptic ulcer, Renal failure, Splenic vein thrombosis, Thrombocytopenia, Portal vein thrombosis, Vitamin B12 deficiency, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BROTIZOLAM, CALTRATE [CALCIUM CARBONATE, VITAMIN D], LAEVOLAC, MAALOX [ALUMINIUM HYDROXIDE + MAGNESIUM HYDROXIDE], NORIT, OMEPRADEX, OXYCONTIN, PANCREASE, PAPAVERIN, PRAMIN, VABEN, VASODIP, VITAMIN B12, XANAX, ZANTAC
Adverse Events (AE) Preferred term	1. Abdominal pain 2. Acute prerenal failure 3. Epistaxis 4. Periorbital haematoma 5. Fall
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 14APR2008 (21) - 15APR2008 (22) 2. 14APR2008 (21) - 15APR2008 (22) 3. 18APR2008 (25) - 18APR2008 (25) 4. 18APR2008 (25) - 05MAY2008 (42) 5. 18APR2008 (25) - 18APR2008 (25)
Duration of AE	1. 2 2. 2 3. 1 4. 18 5. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044003

Parameter	Value
	3. NONE
	4. NONE
	5. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390044004/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/70/WHITE/ISRAEL/YES
Medical history	Normochromic normocytic anaemia, Blindness unilateral, Nephrolithiasis, Cellulitis, Cellulitis, Constipation, Depression, Erysipelas, Hyperlipidaemia, Hypertension, Hypokalaemia, Nephrectomy, Obesity, Onychomycosis, Osteoarthritis, Renal failure, Bundle branch block right, Sciatica, Type 2 diabetes mellitus, Mitral valve calcification, Aortic dilatation, Lymphostasis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID, CARTIA, ENALADEX, GLUBEN, GLUCOPHAGE, LIQUID PARAFFIN, OPTALGIN, SEROXAT, VASODIP
Adverse Events (AE) Preferred term	1. Peripheral artery aneurysm 2. Bradycardia 3. Angiosarcoma 4. Pneumonia 5. Atelectasis 6. Tachycardia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. SEVERE/NO/NO/NO 3. MODERATE/NO/YES/NO 4. MODERATE/NO/NO/NO 5. MODERATE/NO/NO/NO 6. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 19AUG2008 (7) - 09SEP2008 (28) 2. 25AUG2008 (13) - 25AUG2008 (13) 3. 25AUG2008 (13) - --------- (.) 4. 25AUG2008 (13) - 13SEP2008 (32) 5. 27AUG2008 (15) - 09SEP2008 (28) 6. 29AUG2008 (17) - 29AUG2008 (17)
Duration of AE	1. 22 2. 1 3. . 4. 20 5. 14 6. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg 6. 15 mg
Dose status on AE onset	1. . 2. F 3. F

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044004

Parameter	Value
	4. F
	5. F
	6. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY,OTHER
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390044006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/72/WHITE/ISRAEL/YES
Medical history	Angina pectoris, Carotid artery stenosis, Cerebrovascular accident, Folate deficiency, Hemiparesis, Haemolytic anaemia, Hyperlipidaemia, Hypertension, Inguinal hernia repair, Insomnia, Iron deficiency, Leg amputation, Myocardial infarction, Peripheral vascular disorder, Cerebrovascular accident, Carotid artery occlusion, Arterial bypass operation, Arterial bypass operation, Intervertebral discitis, Fungal infection
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BONDORMIN, CARTIA, CEFAMEZIN, CEFORAL, CIPROGIS, CLAVAMOX, CLEXAN, CLONEX, DERALIN, DUPHALAC [IT CONTAINS : LACTULOSE], ENALADEX, ENOXAPARIN, FOLIC ACID, FRESH FROZEN PLASMA, HEPARIN, LAEVOLAC, LIPITOR, NORMITEN, OMEPRADEX, OPTALGIN, OSMOADALAT, OXYCOD, OXYCONTIN, PLAVIX, PREDNISONE, SIMOVIL, SLOW FE, UROKINASE, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Constipation 2. Overdose 3. Urticaria 4. Cellulitis 5. Cellulitis 6. Cellulitis 7. Arteriosclerosis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 01DEC2008 (2) - 15DEC2008 (16) 2. 11DEC2008 (12) - 16DEC2008 (17) 3. 31DEC2008 (32) - --------- (.) 4. 01FEB2009 (64) - 08MAR2009 (99) 5. 08MAR2009 (99) - 11MAR2009 (102) 6. 11MAR2009 (102) - --------- (.) 7. 22APR2009 (144) - 27APR2009 (149)
Duration of AE	1. 15 2. 6 3. . 4. 36 5. 4 6. . 7. 6
Dose on AE onset	1. 2.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044006

Parameter	Value
	3.
	4.
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. WORSENED
	5. IMPROVED
	6. UNCHANGED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390044007/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/ISRAEL/YES
Medical history	Renal failure acute, Microcytic anaemia, Asthma, Bladder neoplasm, Constipation, Chronic obstructive pulmonary disease, Deep vein thrombosis, Tobacco user, Hyperkalaemia, Hypertension, Hyperthyroidism, Hypertriglyceridaemia, Urostomy, Iron deficiency, Hepatic enzyme abnormal, Peptic ulcer, Peritonitis, Urinary bladder excision, Catheterisation cardiac, Hypergammaglobulinaemia, Hydronephrosis, Urostomy, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACAMOL, AEROVENT, AHISTON, ALBUMIN, AMINOPHYLLINE, ATACAND [CANDESARTAN CILEXETIL], AUGMENTIN, BUDICORT, CALCIUM GLUCONATE, CAPOTEN, CARTIA, CONTROLOC, CORDIL, DILATAM, DORMICUM, FLAGYL, FLUCONAZOLE, FORADIL, FRESH FROZEN PLASMA, FUSID, GLUBEN, HALIDOL, HEPARIN, KCL, LIPITOR, LOSEC, MACRODANTIN, MAGNESIUM SULPHATE, MORPHINE, NORADRENALINE, NORMOPRESAN, NUMBON, OLICLINOMEL, OPTALGIN, PENBRITIN, PHENERGAN, PRAMIN, REGULAR INSULIN, ROCEPHIN, SYNACTHEN [TETRACOSACTIDE HEXAACETATE], THEOTARD, TRAMAL, ULTIVA, VANCOMYCIN, VITAMIN K, ZINACEF
Adverse Events (AE) Preferred term	1. Viral infection 2. Intestinal perforation 3. Peritonitis 4. Sepsis 5. Viral infection
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 03JUL2009 (10) - 06JUL2009 (13) 2. 20JUL2009 (27) - 29JUL2009 (36) 3. 20JUL2009 (27) - 06AUG2009 (44) 4. 20JUL2009 (27) - 29JUL2009 (36) 5. 09NOV2009 (139) - 10NOV2009 (140)
Duration of AE	1. 4 2. 10 3. 18 4. 10 5. 2
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390044007

Parameter	Value
	4. .
	5. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390054006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/82/WHITE/ISRAEL/YES
Medical history	Cataract, Renal failure chronic, Hypertension, Hypertriglyceridaemia, Hypothyroidism, Malignant melanoma, Bladder cancer, Peripheral vascular disorder, Suprapubic prostatectomy, Transient ischaemic attack, Transitional cell carcinoma, Hypopharyngeal neoplasm, Hernia repair, Inguinal hernia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DISOTHIAZIDE, ELTROXIN, ENALADEX, MICROPIRIN
Adverse Events (AE) Preferred term	1. Femoral artery occlusion 2. Peripheral arterial occlusive disease
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 12DEC2007 (35) - 30DEC2007 (53) 2. 12DEC2007 (35) - 30DEC2007 (53)
Duration of AE	1. 19 2. 19
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY 2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390054008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/59/WHITE/ISRAEL/YES
Medical history	Diabetes mellitus, Hyperlipidaemia, Peripheral vascular disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CEFAZOLIN, CIPROXIN, ENOXAPARIN, GASTRO, GLUCOPHAGE, MICROPIRIN, NPH INSULIN, OXOPURIN, REGULAR INSULIN, SIMVASTATIN, ZANTAC
Adverse Events (AE) Preferred term	1. Peripheral vascular disorder 2. Postoperative wound infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 28JAN2008 (63) - -----2008 (.) 2. 20MAY2008 (176) - 02JUN2008 (189)
Duration of AE	1. . 2. 14
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390054012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/ISRAEL/YES
Medical history	Diabetes mellitus, Dizziness, Nephrolithiasis, Osteoporosis, Polymyositis, Bile duct stone, Postmenopause, Oesophageal hypomotility
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALTRATE + VIT D, ENOXAPARIN, FOSALAN, LANTON, METFORMIN, METHOTREXATE, PRAMIN, PREDNISONE, REGULAR INSULIN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. International normalised ratio increased 2. International normalised ratio increased 3. International normalised ratio increased 4. International normalised ratio increased 5. International normalised ratio increased
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/YES/NO/YES 3. MILD/YES/NO/YES 4. MILD/YES/YES/YES 5. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 27FEB2008 (13) - 28FEB2008 (14) 2. 13MAR2008 (28) - 15MAR2008 (30) 3. 30MAR2008 (45) - 01APR2008 (47) 4. 19MAY2008 (95) - 23MAY2008 (99) 5. 23DEC2008 (313) - 31DEC2008 (321)
Duration of AE	1. 2 2. 3 3. 3 4. 5 5. 9
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED 3. STUDY DRUG DISCONTINUED AND RESTARTED 4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 5. STUDY DRUG DISCONTINUED AND RESTARTED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054012

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-390054012[1)]	ELEVATED INR（PT：国際標準比増加） 治験担当医は、エノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投薬終了 9 日後に発現していることから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390054016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/55/WHITE/ISRAEL/YES
Medical history	Hypothyroidism, Normochromic normocytic anaemia, Debridement, Postmenopause, Haemangioma removal, Cerebral haemangioma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEPHAZOLIN, CEPHORAL, CIPROXIN, DANTOIN, ELTROXIN, ENOXAPARIN, RULID, TARIVID, WARFARIN
Adverse Events (AE) Preferred term	1. Cellulitis 2. Cellulitis 3. Drug eruption
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 25APR2008 (17) - 29APR2008 (21) 2. 30APR2008 (22) - -----2008 (.) 3. 01MAY2008 (23) - 05MAY2008 (27)
Duration of AE	1. 5 2. . 3. 5
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390054020/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/29/WHITE/ISRAEL/YES
Medical history	Eclampsia, Secondary hypogonadism, Ovarian torsion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Chest pain 2. Anxiety 3. Musculoskeletal pain 4. Aspartate aminotransferase increased 5. Alanine aminotransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/NO 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 27JUL2008 (4) - 27JUL2008 (4) 2. 02AUG2008 (10) - 02AUG2008 (10) 3. 11AUG2008 (19) - 12AUG2008 (20) 4. 10SEP2008 (49) - 16OCT2008 (85) 5. 10SEP2008 (49) - 16OCT2008 (85)
Duration of AE	1. 1 2. 1 3. 2 4. 37 5. 37
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg
Dose status on AE onset	1. . 2. . 3. F 4. F 5. F
Action taken	1. NONE 2. NONE 3. REMEDIAL DRUG THERAPY 4. NONE 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390054020

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390064009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390064009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/78/WHITE/ISRAEL/YES
Medical history	Accident, Anaemia, Renal failure chronic, Diabetes mellitus, Hypercholesterolaemia, Hypertension, Lymphadenopathy, Bladder cancer, Metastases to lung, Sleep disorder, Thrombocytopenia, Urinary bladder excision, Nephrostomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, ATENOLOL, CEFTRIAXONE, CEFUROXIME, CISPLASTIN, DEXAMETAZONE, DEXAMOL, ENOXAPARIN, FUROSEMIDE, GEMCITABINE, LORAZEPAM, METOCLOPRAMIDE, OMEPRAZOLE, SIMVASTATIN, SLOW FE, WARFARIN
Adverse Events (AE) Preferred term	1. Accident 2. Urinary tract infection 3. Urinary tract infection 4. Accident 5. Contusion 6. Anaemia 7. Pyrexia 8. Haematoma 9. Accident 10. Alanine aminotransferase increased 11. Aspartate aminotransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/YES/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/NO 11. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 21AUG2008 (46) - 21AUG2008 (46) 2. 21AUG2008 (46) - 25AUG2008 (50) 3. 25AUG2008 (50) - 01SEP2008 (57) 4. 02SEP2008 (58) - 02SEP2008 (58) 5. 02SEP2008 (58) - 07SEP2008 (63) 6. 03SEP2008 (59) - 09SEP2008 (65) 7. 05SEP2008 (61) - 09SEP2008 (65) 8. 17NOV2008 (134) - 27NOV2008 (144) 9. 17NOV2008 (134) - 17NOV2008 (134) 10. 29JAN2009 (207) - --------- (.) 11. 29JAN2009 (207) - --------- (.)
Duration of AE	1. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390064009

Parameter	Value
	2. 5
	3. 8
	4. 1
	5. 6
	6. 7
	7. 5
	8. 11
	9. 1
	10. .
	11. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390064009

Parameter	Value
	10. NONE
	11. NONE
Outcome of event	1. RESOLVED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. UNCHANGED
	11. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390084001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390084001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/76/WHITE/ISRAEL/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALGOLYSIN, ENOXAPARIN, FRESH FROZEN PLASMA, LOSEC, SEDURAL, WARFARIN
Adverse Events (AE) Preferred term	1. Melaena 2. Dysuria 3. Duodenitis 4. Oesophagitis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 07FEB2008 (144) - 10FEB2008 (147) 2. 08FEB2008 (145) - 18FEB2008 (155) 3. 10FEB2008 (147) - --------- (.) 4. 10FEB2008 (147) - --------- (.)
Duration of AE	1. 4 2. 11 3. . 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390084001

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-390084001[1)]	MELENA（PT：メレナ） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投与と報告事象発現との時間的関連性がないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390084003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390084003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/60/WHITE/ISRAEL/YES
Medical history	Anaemia, Arthralgia, Asthma, Cholecystectomy, Diabetes mellitus, Herpes zoster, Hyperlipidaemia, Hyperparathyroidism, Hypertension, Hypothyroidism, Arthralgia, Pulmonary fibrosis, Menopause, Pulmonary hypertension, Knee arthroplasty, Vaginal haemorrhage, Fibromyalgia, Meniscus lesion, Coronary angioplasty, Polypectomy, Thyroidectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADRIAMYCIN, ADRYAMYCIN, AUGMENTIN, CYCLOPHOPHAMID, DERALIN, DEXACORT, ELATROLET, ELTROXIN, ENOXAPARIN, IFOSFAMID, IFOSFAMIDE, IFOSPHAMID, IFOSPHAMIDE, INSULIN HOMOLOG, INSULIN MIXTARD, LOSEC, MESNA, MOTILIUM, NEULASTIN, PRAMIN, PREDNISONE, SETRON, SLOW FE, TAGMENT, TRACLEER, TRITACE, VASOLIP, VIT -D, WARFARIN, ZANDIEX, ZINATT
Adverse Events (AE) Preferred term	1. Endometrial cancer 2. Bronchitis 3. Cellulitis 4. Endometrial cancer 5. Endometrial cancer 6. Metastases to liver 7. Chest pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 17AUG2009 (57) - 10OCT2009 (111) 2. 21SEP2009 (92) - 28SEP2009 (99) 3. 30SEP2009 (101) - 04OCT2009 (105) 4. 08OCT2009 (109) - 18OCT2009 (119) 5. 11OCT2009 (112) - --FEB2010 (.) 6. 18NOV2009 (150) - --------- (.) 7. 02DEC2009 (164) - 04DEC2009 (166)
Duration of AE	1. 55 2. 8 3. 5 4. 11 5. . 6. . 7. 3
Dose on AE onset	1. 2. 3.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390084003

Parameter	Value
	4.
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	5. REMEDIAL DRUG THERAPY,OTHER
	6. NONE
	7. NONE
Outcome of event	1. WORSENED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390094003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390094003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/27/WHITE/ISRAEL/YES
Medical history	Anorexia nervosa, Hand fracture, Rhinoplasty, Anxiety disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLONEX, ENOXAPARIN, LOSEC, OPTALGIN, SERTRALINE, VABEN, WARFARIN, XANAX
Adverse Events (AE) Preferred term	1. Sudden hearing loss 2. Sudden hearing loss
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/NO 2. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 27MAY2009 (184) - 03JUN2009 (191) 2. 04JUN2009 (192) - --------- (.)
Duration of AE	1. 8 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. NONE
Outcome of event	1. IMPROVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/69/WHITE/ISRAEL/YES
Medical history	Hyperlipidaemia, Hypertension, Hypothyroidism, Breast cancer, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALPHA D3, ASPIRIN, BONDORMIN, CALTRATE [CALCIUM CARBONATE, VITAMIN D], ELTROXIN, ENOXAPARIN, FEMARA, LANTON, MOXYVIT, OCSAAR, SIMVASTATIN, WARFARIN
Adverse Events (AE) Preferred term	1. Otitis externa 2. Transient ischaemic attack
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 02MAY2008 (296) - 08MAY2008 (302) 2. 05JUN2008 (330) - 08JUN2008 (333)
Duration of AE	1. 7 2. 4
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104015/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/78/WHITE/ISRAEL/YES
Medical history	Hypercholesterolaemia, Myocardial infarction, Coronary angioplasty
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CORDIL, ENALADEX, LOPRESOR, MICROPIRIN, MONONIT, PLAVIX, SIMVASTATIN, VABEN
Adverse Events (AE) Preferred term	1. Chest pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 08NOV2007 (31) - 12NOV2007 (35)
Duration of AE	1. 5
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104018/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/51/WHITE/ISRAEL/YES
Medical history	Hyperlipidaemia, Hypertension, Myocardial infarction, Coronary angioplasty, Myocardial ischaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, CARDILOC, COUMADIN, DISOTHIAZIDE, ENALADEX, LOSEC, PLAVIX, SIMOVIL, TRITACE
Adverse Events (AE) Preferred term	1. Cough 2. Hypertension
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 16NOV2007 (19) - 18NOV2007 (21) 2. 02DEC2007 (35) - 03DEC2007 (36)
Duration of AE	1. 3 2. 2
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104020/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/82/WHITE/ISRAEL/YES
Medical history	Hypercholesterolaemia, Hypertension, Myocardial infarction, Myocardial ischaemia, Percutaneous coronary intervention
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARTIA [ACETYLSALICYLIC ACID], NORMITEN, PLAVIX, SIMOVIL, TRIBEMIN, TROMBIN, VITAMIN E
Adverse Events (AE) Preferred term	1. Chest pain 2. Vascular pseudoaneurysm 3. Malaise 4. Chest pain 5. Chest pain 6. Chest pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/YES/YES 4. MILD/NO/YES/YES 5. MILD/NO/YES/YES 6. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 18NOV2007 (4) - 18NOV2007 (4) 2. 22NOV2007 (8) - 06DEC2007 (22) 3. 16DEC2007 (32) - 17DEC2007 (33) 4. 01JAN2008 (48) - 02JAN2008 (49) 5. 04JAN2008 (51) - 06JAN2008 (53) 6. 09JAN2008 (56) - 21JAN2008 (68)
Duration of AE	1. 1 2. 15 3. 2 4. 2 5. 3 6. 13
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. . 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104020

Parameter	Value
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. NONE
	6. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104042

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104042/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/26/WHITE/ISRAEL/YES
Medical history	Anaemia, Joint sprain, Arthralgia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALCIUM, CIPROXIN, DALAGIS 1%, DOXIBIOTIC, ENOXAPARIN, FOLIC ACID, LOSEC, NAXYN, PLAQUENIL, PREDINSONE, PREDNISONE, WARFARIN
Adverse Events (AE) Preferred term	1. Rash 2. Arthritis 3. Arthritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/YES 3. MILD/NO/YES/YES
Start/stop date of event with relative date	1. --AUG2008 (.) - --AUG2008 (.) 2. 31JUL2008 (10) - 01AUG2008 (11) 3. 03AUG2008 (13) - 06AUG2008 (16)
Duration of AE	1. . 2. 2 3. 4
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104045

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104045/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/34/WHITE/ISRAEL/YES
Medical history	Bronchitis chronic, Drug abuse, Hepatic steatosis, Hepatitis C, Palpitations, Tobacco user
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CONTROLOC, COUMADIN, METHADONE, SLOW K
Adverse Events (AE) Preferred term	1. Presyncope
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 19NOV2008 (7) - 20NOV2008 (8)
Duration of AE	1. 2
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. NONE
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104058

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390104058/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/55/WHITE/ISRAEL/YES
Medical history	Essential hypertension, Diabetic retinopathy, Hyperlipidaemia, Optic ischaemic neuropathy, Obesity, Osteoarthritis, Peripheral vascular disorder, Pancreatitis relapsing, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CEFAMEZIN VIAL [CEFAZOLIN SODIUM], CIPROFLOXACIN, DIOVAN, ENOXAPARIN, GLUCOMIN, INSULIN HUMALOG MIX, LAEVOLAC, MICROPIRIN, NOPAN, OMEPRADEX, SIMVACOR, SOL OPTALGIN, VASODIP, WARFARIN
Adverse Events (AE) Preferred term	1. Pancreatitis 2. Pancreatitis acute 3. Cellulitis 4. Diabetic foot 5. Localised infection 6. Arteriosclerosis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/YES/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 25MAR2009 (34) - 30MAR2009 (39) 2. 11MAY2009 (81) - 22MAY2009 (92) 3. 20MAY2009 (90) - 31MAY2009 (101) 4. 23JUN2009 (124) - 28JUN2009 (129) 5. 11JUL2009 (142) - 18JUL2009 (149) 6. 16AUG2009 (178) - --------- (.)
Duration of AE	1. 6 2. 12 3. 12 4. 6 5. 8 6. .
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390104058

Parameter	Value
	5.
	6.
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 390114006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/390114006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/64/WHITE/ISRAEL/YES
Medical history	Benign prostatic hyperplasia, Arteriogram coronary, Hyperlipidaemia, Myocardial ischaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARTIA, LIPITOR, NORMITEN
Adverse Events (AE) Preferred term	1. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 07SEP2008 (18) - 17SEP2008 (28)
Duration of AE	1. 11
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400014012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400014012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/41/WHITE/AUSTRALIA/YES
Medical history	Asthma, Uterine leiomyoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FERROGRADUMET, KEFLEX, PRIMOLUT [NORETHISTERONE], VENTOLIN, VITAMIN C, WARFARIN
Adverse Events (AE) Preferred term	1. Hepatic enzyme increased 2. Hepatic enzyme increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/YES/YES/YES
Start/stop date of event with relative date	1. 13MAR2008 (2) - 08APR2008 (28) 2. 09MAY2008 (59) - 12JUN2008 (93)
Duration of AE	1. 27 2. 35
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-400014012[1),2)]	ELEVATED LIVER ENZYMES LEVEL（PT：肝酵素上昇）2 事象有 1）治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、投薬終了 7 週間後に発現していることから、エノキサパリンとの因果関係は否定できると考える。 2）治験担当医は、エノキサパリンと報告事象との因果関係を否定できると判断した。弊社は、投薬開始 2 日後に発現していることからエノキサパリンとの因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400024005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400024005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/63/UNCODABLE/AUSTRALIA/YES
Medical history	Lower respiratory tract infection, Constipation, Irritable bowel syndrome, Multiple myeloma, Nausea, Oesophagitis, Paraplegia, Spinal cord compression, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACIMAX, COLOXYL [DOCUSATE SODIUM], DITROPAN, KEFLEX
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Mouth ulceration 3. Humerus fracture
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MILD/NO/NO/NO 3. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 04JAN2008 (43) - 23JAN2008 (62) 2. 21MAY2008 (181) - 27MAY2008 (187) 3. 28MAY2008 (188) - 05JUN2008 (196)
Duration of AE	1. 20 2. 7 3. 9
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. F 3. F
Action taken	1. NONE 2. NONE 3. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400024021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400024021/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/41/WHITE/AUSTRALIA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Hepatic enzyme increased
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 06FEB2009 (8) - 16FEB2009 (18)
Duration of AE	1. 11
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. NONE
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-400024021[1)]	INCREASED LIVER ENZYMES（PT：肝酵素上昇） 治験担当医はワルファリンと報告事象との関連性があると判断した。弊社は、ワルファリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400024025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400024025/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/43/WHITE/AUSTRALIA/YES
Medical history	Back pain
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CLEXANE, ENDONE, NUROFEN PLUS, PANADEINE FORTE, VALIUM
Adverse Events (AE) Preferred term	1. Sciatica 2. Sciatica 3. Menorrhagia 4. Feeling abnormal 5. Induced abortion haemorrhage 6. Post procedural haemorrhage 7. Post abortion haemorrhage 8. Skin haemorrhage 9. Oedema peripheral 10. Contusion
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/NO/YES 8. MODERATE/NO/NO/YES 9. MILD/YES/NO/YES 10. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 06APR2009 (14) - 27APR2009 (35) 2. 27APR2009 (35) - 27APR2009 (35) 3. 01JUN2009 (70) - --JUL2009 (.) 4. 03JUL2009 (102) - 20JUL2009 (119) 5. 21JUL2009 (120) - 22JUL2009 (121) 6. 21JUL2009 (120) - 24SEP2009 (185) 7. 24SEP2009 (185) - 22OCT2009 (213) 8. 05NOV2009 (227) - 06NOV2009 (228) 9. 21JAN2010 (304) - 22JAN2010 (305) 10. 25MAR2010 (367) - 01APR2010 (374)
Duration of AE	1. 22 2. 1 3. . 4. 18 5. 2 6. 66

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400024025

Parameter	Value
	7. 29
	8. 2
	9. 2
	10. 8
Dose on AE onset	1. 15 mg
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. I
	6. I
	7. .
	8. .
	9. .
	10. F
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED
	3. NONE
	4. STUDY DRUG DISCONTINUED AND RESTARTED
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. OTHER
	7. NONE
	8. NONE
	9. NONE
	10. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED
	7. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400024025

Parameter	Value
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400034002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/92/WHITE/AUSTRALIA/YES
Medical history	Anxiety, Colonic polyp, Hypercholesterolaemia, Hypertension, Dyspepsia, Inguinal hernia, Myocardial ischaemia, Myocardial infarction, Peptic ulcer, Peripheral vascular disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, ATENOLOL, CLOPIDOGREL, COVERSYL, ENOXAPARIN, LANSOPRAZOLE, LIPITOR, MAXOLON, MYLANTA [SIMETHICONE, MG(OH)2, AL(OH)3 GEL, NA SACCHARIN, & HYDROXYBENZOATES.], PANAMAX, PRAZOSIN, TRIMETHOPRIM
Adverse Events (AE) Preferred term	1. Hand fracture 2. Dementia 3. Abdominal discomfort 4. Diarrhoea 5. Food poisoning 6. Contusion 7. Wound haemorrhage 8. Headache 9. Acute myocardial infarction 10. Urinary tract infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. SEVERE/NO/YES/YES 10. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. --JUL2008 (.) - --------- (.) 2. --JUL2008 (.) - --------- (.) 3. 19AUG2007 (13) - 21AUG2007 (15) 4. 19AUG2007 (13) - 21AUG2007 (15) 5. 27JAN2008 (174) - 31JAN2008 (178) 6. 20FEB2008 (198) - 05MAR2008 (212) 7. 24APR2008 (262) - 24APR2008 (262) 8. 28MAY2008 (296) - 07JUL2008 (336) 9. 29JUL2008 (358) - 02AUG2008 (362) 10. 29JUL2008 (358) - 01AUG2008 (361)
Duration of AE	1. . 2. . 3. 3 4. 3

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034002

Parameter	Value
	5. 5
	6. 15
	7. 1
	8. 41
	9. 5
	10. 4
Dose on AE onset	1.
	2.
	3. 15 mg
	4. 15 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
Dose status on AE onset	1.
	2.
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034002

Parameter	Value
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400034014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/40/WHITE/AUSTRALIA/YES
Medical history	Asthma, Diabetes mellitus, Gastrooesophageal reflux disease, Hypercholesterolaemia, Drug hypersensitivity, Vertigo, Bipolar disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DIABEX, EFEXOR, EFEXOR XR, ENOXAPARIN, LIPITOR, LOSEC, METFORMIN, OMEPRAZOLE, SEROQUEL, STILNOX, WARFARIN
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Depression
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 18APR2008 (18) - --------- (.) 2. 11JUN2008 (72) - 03JUL2008 (94)
Duration of AE	1. . 2. 23
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400034028/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/62/WHITE/AUSTRALIA/YES
Medical history	Hypertension, Lung neoplasm malignant
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, CEFTRIXONE, COLOXYL & SENNA, COVERSYL PLUS, DEXAMETHASONE, ENDONE, ENOXAPARIN, GRANISETRON, MAXALON, MORPHINE, NUROFEN, PARACETAMOL, RULIDE, VENTOLIN, WARFARIN
Adverse Events (AE) Preferred term	1. Dyspnoea 2. Lung neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/NO 2. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 17FEB2009 (174) - 24FEB2009 (181) 2. 18MAR2009 (203) - 18MAR2009 (203)
Duration of AE	1. 8 2. 1
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. RESOLVED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034031

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400034031/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/86/WHITE/AUSTRALIA/YES
Medical history	Glaucoma, Hypertension, Pancreatic carcinoma, Rotator cuff syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMLODIPINE, AMPICILLIN, AUGMENTIN DUO FORTE, COLOXYL [DOCUSATE NA, NA BENZOATE], DEXAMETHASONE, GENTAMICIN, GRANISETRON, HALOPERDOL, MAXALON, METOPROLOL, METRONIDAZOLE, MIDAZOLAM, MORPHINE, NILSTAT, NOZINAM, OMEPRAZOLE, PARACETAMOL, SENOKOT, TEMAZEPAM, TIMENTIN
Adverse Events (AE) Preferred term	1. Cholangitis 2. Nausea 3. Vomiting 4. Pancreatic carcinoma 5. Gastrooesophageal reflux disease 6. Oral candidiasis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 28OCT2008 (7) - 03NOV2008 (13) 2. 04NOV2008 (14) - --------- (.) 3. 04NOV2008 (14) - --------- (.) 4. 17NOV2008 (27) - 29NOV2008 (39) 5. 23NOV2008 (33) - 28NOV2008 (38) 6. 26NOV2008 (36) - 28NOV2008 (38)
Duration of AE	1. 7 2. . 3. . 4. 13 5. 6 6. 3
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034031

Parameter	Value
	5. .
	6. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. DEATH
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034045

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400034045/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/80/WHITE/AUSTRALIA/YES
Medical history	Fluid retention, Gastrooesophageal reflux disease, Hypercholesterolaemia, Hypertension, Osteoarthritis, Type 2 diabetes mellitus, Postmenopause, Cataract operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALPHAPRESS, ASPIRIN, ENOXAPARIN, FRUSEMIDE, MAXIDEX, NORVASC, PANADOL OSTEO, RANITIDINE, SIMVASTATIN, STEMEZINE, TEMAZEPAM, TEVETEN, TOBREX OPHTHALMIC, TRIMETHOPRIM, WARFARIN
Adverse Events (AE) Preferred term	1. Food poisoning
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 26APR2009 (33) - 29APR2009 (36)
Duration of AE	1. 4
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034056

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400034056/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/58/WHITE/AUSTRALIA/YES
Medical history	Gastrooesophageal reflux disease, Soft tissue injury
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXYCILLIN & CLAVULANIC ACID, ATROVENT, CEFOXITIN, CEFTRIAXONE, COLOXYL+SENNA, DIAZEPAM, ENOXAPARIN, FENTANYL PATCH, GASTROGEL, HEPARIN, METOCLOPROMIDE, METRONIDAZOLE, MORPHINE, NEXIUM, OXYCODONE, PANADOL, PEPPERMINT WATER, RULIDE, TIMENTIN, TRAMADOL, VENTOLIN
Adverse Events (AE) Preferred term	1. Pneumonia 2. Colon cancer 3. Haemorrhoids 4. Rectal polyp 5. Colonic polyp 6. Diverticulum intestinal 7. Dyspnoea 8. Abdominal discomfort 9. Abdominal distension
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 07AUG2009 (2) - 17AUG2009 (12) 2. 13AUG2009 (8) - 04NOV2009 (91) 3. 08SEP2009 (34) - --------- (.) 4. 08SEP2009 (34) - --------- (.) 5. 08SEP2009 (34) - --------- (.) 6. 08SEP2009 (34) - --------- (.) 7. 02DEC2009 (119) - 04DEC2009 (121) 8. 15JAN2010 (163) - --JAN2010 (.) 9. 15JAN2010 (163) - --JAN2010 (.)
Duration of AE	1. 11 2. 84 3. . 4. . 5. . 6. . 7. 3

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034056

Parameter	Value
	8. .
	9. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. OTHER
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY,OTHER
	8. NONE
	9. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. UNCHANGED
	5. UNCHANGED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400034056

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400054010/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/64/WHITE/AUSTRALIA/YES
Medical history	Atelectasis, Brain neoplasm benign, Brain neoplasm benign, Hypercholesterolaemia, Hypertension, Pneumonia, Post herpetic neuralgia, Herpes zoster, Postmenopause, Gastrooesophageal reflux disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANGININE, ASPIRIN, ATORVASTATIN, CEPHAZOLIN, DROPERIDOL, ENOXAPARIN, IVC FILTER, METARAMINOL, MORPHINE, OXYCODONE, PARACETAMOL, PICOLAX, RAMIPRIL, RANITIDINE, TINIDAZOLE, TROPISETRON
Adverse Events (AE) Preferred term	1. Ovarian mass 2. Chest pain 3. Uterine polyp 4. Uterine leiomyoma 5. Operative haemorrhage 6. Nausea 7. Chest pain 8. Anxiety
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 06AUG2008 (14) - 14AUG2008 (22) 2. 15AUG2008 (23) - 17AUG2008 (25) 3. 15AUG2008 (23) - 22AUG2008 (30) 4. 15AUG2008 (23) - 22AUG2008 (30) 5. 18AUG2008 (26) - 18AUG2008 (26) 6. 19AUG2008 (27) - 20AUG2008 (28) 7. 07NOV2008 (107) - 07NOV2008 (107) 8. 07NOV2008 (107) - 07NOV2008 (107)
Duration of AE	1. 9 2. 3 3. 8 4. 8 5. 1 6. 2 7. 1 8. 1
Dose on AE onset	1. 15 mg 2. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054010

Parameter	Value
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1. .
	2. I
	3. I
	4. I
	5. I
	6. I
	7. .
	8. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400054016/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/34/WHITE/AUSTRALIA/YES
Medical history	Anxiety, Asthma, Depression, Migraine
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	FOLIC ACID, PANADEINE FORTE, SERETIDE, VENTOLIN
Adverse Events (AE) Preferred term	1. Folate deficiency 2. Thrombocytopenia 3. Hepatic steatosis 4. Cholelithiasis 5. Haematoma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 25NOV2008 (1) - --------- (.) 2. 17DEC2008 (23) - 28JAN2009 (65) 3. 24DEC2008 (30) - --------- (.) 4. 24DEC2008 (30) - --------- (.) 5. 11JUL2009 (229) - 20JUL2009 (238)
Duration of AE	1. . 2. 43 3. . 4. . 5. 10
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. F
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY 3. NONE 4. NONE 5. NONE
Outcome of event	1. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054016

Parameter	Value
	2. RESOLVED
	3. UNCHANGED
	4. UNCHANGED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054026

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400054026/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/66/WHITE/AUSTRALIA/YES
Medical history	Alcohol abuse, Blood alkaline phosphatase increased, Blood bilirubin increased, Cellulitis, Chronic obstructive pulmonary disease, Gamma-glutamyltransferase increased, Prostate cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEFAZOLIN, ENOXAPARIN, FENTANYL, LIGNOCAINE SPRAY, MIDAZOLAM, MYLICON SPRAY, WARFARIN
Adverse Events (AE) Preferred term	1. Catheter site infection 2. Oesophageal carcinoma 3. Gastric ulcer 4. Malnutrition 5. Blood alkaline phosphatase increased 6. Contusion 7. Dizziness 8. Venous thrombosis limb 9. Hypotension 10. Escherichia sepsis 11. Lobar pneumonia 12. Dizziness 13. Hypovolaemia 14. Atrial fibrillation 15. Aspartate aminotransferase increased 16. Alanine aminotransferase increased 17. Acute hepatic failure 18. Pleural effusion 19. Blood bilirubin increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/NO 8. MODERATE/NO/NO/NO 9. SEVERE/NO/YES/NO 10. SEVERE/NO/YES/NO 11. SEVERE/NO/YES/NO 12. MODERATE/NO/NO/NO 13. MODERATE/NO/NO/NO 14. MODERATE/NO/NO/NO 15. MODERATE/NO/NO/NO 16. MODERATE/NO/NO/NO

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054026

Parameter	Value
	17. SEVERE/NO/YES/NO
	18. MODERATE/NO/NO/NO
	19. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 05AUG2009 (13) - 11AUG2009 (19)
	2. 05AUG2009 (13) - --------- (.)
	3. 19AUG2009 (27) - --------- (.)
	4. 19AUG2009 (27) - --------- (.)
	5. 19AUG2009 (27) - --------- (.)
	6. 01OCT2009 (70) - --------- (.)
	7. 09OCT2009 (78) - 20OCT2009 (89)
	8. 09OCT2009 (78) - --------- (.)
	9. 16OCT2009 (85) - --------- (.)
	10. 27OCT2009 (96) - 29OCT2009 (98)
	11. 27OCT2009 (96) - --------- (.)
	12. 27OCT2009 (96) - --------- (.)
	13. 27OCT2009 (96) - --------- (.)
	14. 27OCT2009 (96) - --------- (.)
	15. 27OCT2009 (96) - --------- (.)
	16. 27OCT2009 (96) - --------- (.)
	17. 27OCT2009 (96) - --------- (.)
	18. 27OCT2009 (96) - --------- (.)
	19. 28OCT2009 (97) - --------- (.)
Duration of AE	1. 7
	2. .
	3. .
	4. .
	5. .
	6. .
	7. 12
	8. .
	9. .
	10. 3
	11. .
	12. .
	13. .
	14. .
	15. .
	16. .
	17. .
	18. .
	19. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054026

Parameter	Value
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054026

Parameter	Value
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. NONE
	7. NONE
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. NONE
	13. NONE
	14. REMEDIAL DRUG THERAPY
	15. REMEDIAL DRUG THERAPY
	16. REMEDIAL DRUG THERAPY
	17. REMEDIAL DRUG THERAPY
	18. NONE
	19. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. UNCHANGED
	5. UNCHANGED
	6. UNCHANGED
	7. RESOLVED
	8. UNCHANGED
	9. UNCHANGED
	10. DEATH
	11. UNCHANGED
	12. UNCHANGED
	13. UNCHANGED
	14. UNCHANGED
	15. UNCHANGED
	16. UNCHANGED
	17. UNCHANGED
	18. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400054026

Parameter	Value
	19. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-400054026[4)]	ACUTE GASTRIC ULCERS（PT：胃潰瘍） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、合併症（食道癌）によるものであり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400064004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400064004/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/20/UNCODABLE/AUSTRALIA/YES
Medical history	Cardiolipin antibody positive, Lower respiratory tract infection, Depression, Hyperlipidaemia, Systemic lupus erythematosus, Antiphospholipid antibodies positive
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXYCILLIN-CLAVULANIC ACID, ATORVASTATIN, ENOXAPARIN, KETOCONAZOLE SHAMPOO, OMEPRAZOLE, PARACETAMOL, PLAQUENIL (HYDROXYCHLOROQUINE), PREDNISOLONE
Adverse Events (AE) Preferred term	1. Mononeuritis 2. Headache 3. Arthralgia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 06DEC2007 (98) - 10DEC2007 (102) 2. 06DEC2007 (98) - 10DEC2007 (102) 3. 06DEC2007 (98) - 10DEC2007 (102)
Duration of AE	1. 5 2. 5 3. 5
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400064016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400064016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/26/WHITE/AUSTRALIA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CELEBREX, COLOXYL & SENNA, DICLOXACILLIN, ENOXAPARIN, MORPHINE, OXYCODONE, OXYCONTIN, PARACETAMOL, UNFRACTIONATED HEPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Thrombophlebitis superficial 2. Constipation 3. Hepatic enzyme increased
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 27MAR2008 (11) - 01APR2008 (16) 2. 28MAR2008 (12) - 01APR2008 (16) 3. 31MAR2008 (15) - 08APR2008 (23)
Duration of AE	1. 6 2. 5 3. 9
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400064029

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400064029/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/82/WHITE/AUSTRALIA/YES
Medical history	Colon cancer, Colostomy, Decubitus ulcer, Dementia, Femoral neck fracture, Hypertension, Incisional hernia repair, Knee arthroplasty, Large intestine perforation, Myocardial infarction, Myocardial infarction, Type 2 diabetes mellitus, Penile ulceration, Wound dehiscence, Renal impairment
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATENOLOL, ENOXAPARIN, FENTANYL, HEPARIN INFUSION, METOPROLOL, MULTIVITAMIN, PARACETAMOL, TEMAZEPAM, WARFARIN
Adverse Events (AE) Preferred term	1. Penis carcinoma 2. International normalised ratio fluctuation 3. Insomnia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 30MAY2009 (145) - 22JUN2009 (168) 2. 04JUN2009 (150) - 05JUN2009 (151) 3. 10JUN2009 (156) - 10JUN2009 (156)
Duration of AE	1. 24 2. 2 3. 1
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. OTHER 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400074025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400074025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/37/WHITE/AUSTRALIA/YES
Medical history	Asthma, Nephrolithiasis, Juvenile arthritis, Poor dental condition
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CELEBREX, ENOXAPARIN, FOLIC ACID, IOSCAN, METHOTREXATE, PAMIDRONATE, PANADEINE FORTE, PREDNISONE, SOMAC, SYMBICORT, WARFARIN
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Dyspnoea 3. Oedema peripheral 4. Juvenile arthritis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 16JUL2008 (1) - 26AUG2008 (42) 2. 08AUG2008 (24) - --------- (.) 3. 08AUG2008 (24) - --------- (.) 4. 09DEC2008 (147) - 19DEC2008 (157)
Duration of AE	1. 42 2. . 3. . 4. 11
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. OTHER 3. OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400074025

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400084009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400084009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/39/WHITE/AUSTRALIA/YES
Medical history	Joint injury, Cholecystectomy, Gastrooesophageal reflux disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, ESOMEPRAZOLE, WARFARIN
Adverse Events (AE) Preferred term	1. Alanine aminotransferase increased 2. Aspartate aminotransferase increased 3. Abdominal pain 4. Diarrhoea 5. Dyspepsia 6. Abdominal distension 7. Weight increased 8. Diarrhoea 9. Arthralgia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 20JUN2008 (15) - 28JUL2008 (53) 2. 20JUN2008 (15) - 07JUL2008 (32) 3. 29JUN2008 (24) - 02SEP2008 (89) 4. 29JUN2008 (24) - 02SEP2008 (89) 5. 01AUG2008 (57) - 10OCT2008 (127) 6. 17SEP2008 (104) - --------- (.) 7. 17SEP2008 (104) - --------- (.) 8. 05OCT2008 (122) - --------- (.) 9. 22OCT2008 (139) - 01NOV2008 (149)
Duration of AE	1. 39 2. 18 3. 66 4. 66 5. 71 6. . 7. . 8. . 9. 11

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400084009

Parameter	Value
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. OTHER
	2. OTHER
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. NONE
	9. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. UNCHANGED
	8. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400084009

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-400084009[2)]	RAISED ALT（PT：アラニンアミノトランスフェラーゼ増加） 治験担当医は、併用薬によるものであり、否定できると判断した。弊社は、エノキサパリン及びワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400094008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400094008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/66/ASIAN/AUSTRALIA/YES
Medical history	Asthma, Periarthritis, Gastrooesophageal reflux disease, Lethargy, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXYL, CENTRUM MULTIVITAMIN, ENOXAPARIN, FERROGRADUMET, IRON TABLETS, RANITIDINE, WARFARIN
Adverse Events (AE) Preferred term	1. Ascites 2. Iron deficiency 3. Upper respiratory tract infection 4. Pancreatic carcinoma metastatic
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/NO/YES 2. MODERATE/NO/NO/NO 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. --MAY2008 (.) - --------- (.) 2. 08FEB2008 (1) - --------- (.) 3. 15FEB2008 (8) - 22FEB2008 (15) 4. 12MAY2008 (95) - 23JUN2008 (137)
Duration of AE	1. . 2. . 3. 8 4. 43
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400094008

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400094031

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400094031/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/22/WHITE/AUSTRALIA/YES
Medical history	Ligament rupture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Periorbital haematoma
	2. Conjunctival haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES
	2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 09JUL2009 (168) - 14JUL2009 (173)
	2. 09JUL2009 (168) - 31JUL2009 (190)
Duration of AE	1. 6
	2. 23
Dose on AE onset	1.
	2.
Dose status on AE onset	1.
	2.
Action taken	1. OTHER
	2. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-400094031[2)]	RIGHT SUBCONJUNCTIVAL BLEED（PT：結膜出血） 治験担当医は、暴行を受けたことによるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400124003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400124003/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/81/WHITE/AUSTRALIA/YES
Medical history	Renal failure acute, Blood cholesterol increased, Hypertension, Myocardial infarction, Nausea, Urinary tract infection, Vomiting
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, MAXOLON, MOBIC, RAMIPRIL, SLOW K, STEMETIL, TEMAZEPAM, TRIMETHOPRIM, ZANTAC
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Blood potassium decreased 3. Cognitive disorder 4. Nausea 5. Vomiting
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 29JUL2007 (4) - 31JUL2007 (6) 2. 29JUL2007 (4) - 29JUL2007 (4) 3. 30JUL2007 (5) - --------- (.) 4. 30JUL2007 (5) - --AUG2007 (.) 5. 30JUL2007 (5) - --AUG2007 (.)
Duration of AE	1. 3 2. 1 3. . 4. . 5. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED PERMANENTLY 4. REMEDIAL DRUG THERAPY 5. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400124003

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. INSUFFICIENT FOLLOW-UP
	4. IMPROVED
	5. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400124028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400124028/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/AUSTRALIA/YES
Medical history	Cardiomyopathy, Cholecystectomy, Hypertension, Transurethral prostatectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BICOR, CHLORPROMEZINE, COVERSYL, ENOXAPARIN, HYDROZOLE CREAM, MERSYNDOL, PANADEINE FORTE, PANADOL, PARACETAMOL & CODEINE PHOSPHATE, RULIDE, TOPAMAX, WARFARIN
Adverse Events (AE) Preferred term	1. Headache 2. Lethargy 3. Contusion 4. Fungal skin infection 5. Diarrhoea 6. IIIrd nerve paresis 7. Headache 8. Tooth fracture 9. Bronchitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/YES/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --SEP2008 (.) - 15MAY2009 (294) 2. --SEP2008 (.) - 17OCT2008 (84) 3. 26JUL2008 (1) - 08AUG2008 (14) 4. 28JUL2008 (3) - 30NOV2008 (128) 5. 30JUL2008 (5) - 01AUG2008 (7) 6. 08NOV2008 (106) - 15MAY2009 (294) 7. 08NOV2008 (106) - --NOV2008 (.) 8. 16APR2009 (265) - 28APR2009 (277) 9. 18JUN2009 (328) - 23JUN2009 (333)
Duration of AE	1. . 2. . 3. 14 4. 126 5. 3 6. 189 7. . 8. 13

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400124028

Parameter	Value
	9. 6
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400124028

Parameter	Value
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-400124028[4)]	MILD STROKE IN OPTIC NERVE（PT：視神経梗塞） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、偶発症であり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400154008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400154008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/40/WHITE/AUSTRALIA/YES
Medical history	Iron deficiency, Rectal haemorrhage, Rheumatoid arthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FOLIC ACID, HYDROCORTISONE, IRON, LORATADINE, METHOTREXATE, NEXIUM, PREDNISONE, WARFARIN
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Wound haemorrhage 3. Contusion 4. Contusion 5. Menorrhagia 6. Contusion 7. Menorrhagia 8. Contusion 9. Menorrhagia 10. Menorrhagia 11. Autoimmune thrombocytopenia 12. Epistaxis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/YES/NO/YES 6. MILD/NO/NO/YES 7. MILD/YES/NO/YES 8. MILD/NO/NO/YES 9. MILD/YES/NO/YES 10. MILD/YES/NO/YES 11. SEVERE/NO/YES/YES 12. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 17OCT2008 (1) - --------- (.) 2. 29OCT2008 (13) - 29OCT2008 (13) 3. 01NOV2008 (16) - --NOV2008 (.) 4. 01NOV2008 (16) - --NOV2008 (.) 5. 09NOV2008 (24) - 16NOV2008 (31) 6. 01DEC2008 (46) - --JAN2009 (.) 7. 11DEC2008 (56) - 18DEC2008 (63) 8. 12DEC2008 (57) - --DEC2008 (.) 9. 01JAN2009 (77) - -----2009 (.) 10. 22FEB2009 (129) - --------- (.) 11. 18MAY2009 (214) - --------- (.) 12. 08JUL2009 (265) - 08JUL2009 (265)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400154008

Parameter	Value
Duration of AE	1. .
	2. 1
	3. .
	4. .
	5. 8
	6. .
	7. 8
	8. .
	9. .
	10. .
	11. .
	12. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400154008

Parameter	Value
	6. NONE
	7. NONE
	8. NONE
	9. NONE
	10. NONE
	11. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	12. OTHER
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. UNCHANGED
	11. IMPROVED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400174005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400174005/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/AUSTRALIA/YES
Medical history	Arthralgia, Back pain, Depression, Gout, Hypertension, Myalgia, Drug hypersensitivity, Peptic ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENDEP, ENOXAPARIN, PANADEINE FORTE, PANADOL, VOLTAREN, WARFARIN
Adverse Events (AE) Preferred term	1. Back pain 2. Muscle spasms 3. Syncope 4. Excoriation 5. Excoriation
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 27SEP2007 (8) - 22NOV2007 (64) 2. 27SEP2007 (8) - 22JAN2008 (125) 3. 27SEP2007 (8) - 28SEP2007 (9) 4. 02OCT2007 (13) - 22NOV2007 (64) 5. 11OCT2007 (22) - 22NOV2007 (64)
Duration of AE	1. 57 2. 118 3. 2 4. 52 5. 43
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. NONE 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400174005

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400204011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400204011/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/63/WHITE/AUSTRALIA/YES
Medical history	Epilepsy, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, ENOXAPARIN, HEPARIN SODIUM, MAGNESIUM SULPHATE, METACLOPRAMIDE, METOPROLOL, PANADEINE, PANADOL, PERINDOPRIL, SOTALOL, TEGRETOL, WARFARIN, ZOFRAN
Adverse Events (AE) Preferred term	1. Contusion 2. Rash 3. Lung adenocarcinoma 4. Atrial fibrillation 5. Nausea 6. Vomiting 7. Ischaemic stroke 8. Headache 9. Catheter site haemorrhage 10. Cardiac valve vegetation 11. Catheter site haemorrhage 12. Constipation 13. Dizziness 14. Headache 15. Vomiting 16. Cardiac arrest
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. SEVERE/NO/YES/YES 8. MODERATE/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/NO/YES/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/NO 13. SEVERE/NO/YES/NO 14. MODERATE/NO/NO/NO 15. MILD/NO/NO/NO 16. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 14MAY2009 (15) - --------- (.) 2. 15MAY2009 (16) - 15MAY2009 (16) 3. 26MAY2009 (27) - --------- (.) 4. 01JUN2009 (33) - 03JUN2009 (35)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400204011

Parameter	Value
	5. 01JUN2009 (33) - --------- (.)
	6. 01JUN2009 (33) - 01JUN2009 (33)
	7. 02JUN2009 (34) - --------- (.)
	8. 02JUN2009 (34) - 02JUN2009 (34)
	9. 04JUN2009 (36) - 04JUN2009 (36)
	10. 04JUN2009 (36) - --------- (.)
	11. 04JUN2009 (36) - 04JUN2009 (36)
	12. 06JUN2009 (38) - 06JUN2009 (38)
	13. 28JUN2009 (60) - --------- (.)
	14. 28JUN2009 (60) - --------- (.)
	15. 28JUN2009 (60) - 28JUN2009 (60)
	16. 29JUN2009 (61) - 29JUN2009 (61)
Duration of AE	1. .
	2. 1
	3. .
	4. 3
	5. .
	6. 1
	7. .
	8. 1
	9. 1
	10. .
	11. 1
	12. 1
	13. .
	14. .
	15. 1
	16. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400204011

Parameter	Value
	14.
	15.
	16.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
Action taken	1. NONE
	2. NONE
	3. OTHER
	4. REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	8. REMEDIAL DRUG THERAPY,OTHER
	9. NONE
	10. NONE
	11. NONE
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. REMEDIAL DRUG THERAPY
	15. REMEDIAL DRUG THERAPY
	16. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. INSUFFICIENT FOLLOW-UP
	4. RESOLVED
	5. IMPROVED
	6. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400204011

Parameter	Value
	7. UNCHANGED
	8. RESOLVED
	9. RESOLVED
	10. UNCHANGED
	11. RESOLVED
	12. RESOLVED
	13. UNCHANGED
	14. UNCHANGED
	15. RESOLVED
	16. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214010/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/81/WHITE/AUSTRALIA/YES
Medical history	Anaemia, Angina pectoris, Bone graft, Constipation, Depression, Hip arthroplasty, Hypercholesterolaemia, Hypokalaemia, Hypothyroidism, Knee arthroplasty, Knee arthroplasty, Nausea, Osteoarthritis, Spinal laminectomy, Hip arthroplasty, Ostectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXYCILLIN, AMOXYCILLIN,POTASSIUM CLAVULANATE, AMPHOTERICIN B LOZENGE, AMPICILLIN, CALCIUM CARBONATE,CHOLECALCIFEROL, CARDIZEM, CEFTRIAXONE, CELEBREX, COLOXYL [BISACODYL AND DOCUSATE SODIUM], DIAZEPAM, DOXEPIN, ENOXAPARIN, FERROUS SULPHATE, FERROUS SULPHATE,SODIUM ASCORBATE, FRESH FROZEN PLASMA, GENTAMYCIN, LACTULOSE, LIPITOR, MAXOLON, MORPHINE, NYSTATIN, ONDANSETRON, OXYCODONE, PANADEINE FORTE, PANADOL, PANADOL [PARACETAMOL ALONE], PETHIDINE, POOLED PLATELETS, POTASSIUM CHLORIDE, SOMAC, STEMETIL, TEMAZEPAM, THYROXINE, TRAMADOL, VANCOMYCIN, VOLTAREN, WARFARIN, ZOLOFT
Adverse Events (AE) Preferred term	1. Femur fracture 2. Contusion 3. Lower respiratory tract infection 4. Urinary tract infection 5. Operative haemorrhage 6. Constipation 7. Postoperative wound infection 8. Mouth ulceration
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/YES/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 27JUL2007 (3) - 23OCT2007 (91) 2. 01AUG2007 (8) - 17SEP2007 (55) 3. 09AUG2007 (16) - 16AUG2007 (23) 4. 29AUG2007 (36) - 07SEP2007 (45) 5. 08SEP2007 (46) - 10SEP2007 (48) 6. 08SEP2007 (46) - 26SEP2007 (64) 7. 12SEP2007 (50) - 06OCT2007 (74) 8. 14SEP2007 (52) - 21OCT2007 (89)
Duration of AE	1. 89 2. 48 3. 8 4. 10

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214010

Parameter	Value
	5. 3
	6. 19
	7. 25
	8. 38
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. OTHER
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214010

Parameter	Value
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214017

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214017/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/74/WHITE/AUSTRALIA/YES
Medical history	Arthroscopy, Burkitt's lymphoma, Coronary artery disease, Diverticulitis, Emphysema, Gastrooesophageal reflux disease, Hiatus hernia, Hypercholesterolaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AGAROL, ASPIRIN, CEFTRIAXONE, CIPROXIN, COLOXYL WITH SENNA, FLAGYL, FLEET ENEMA, GLYCERINE SUPPOSITORIES, LACTULOSE, LIPIDIL, LIPITOR, MAXOLON, MORPHINE, NEXIUM, PANADOL, PANADOL SUPPOSITORIES, PANADOL [PARACETAMOL ALONE], PANTOPRAZOLE, PEPPERMINT WATER, PETHIDINE, SPIRIVA, TEMAZEPAM
Adverse Events (AE) Preferred term	1. Scratch 2. Gastrooesophageal reflux disease 3. Abdominal pain 4. Abdominal pain lower 5. Exfoliative rash 6. Constipation 7. Pancreatitis 8. Pyrexia 9. Pneumonia 10. Insomnia 11. Flatulence 12. Back pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --FEB2008 (.) - --FEB2008 (.) 2. 24OCT2007 (2) - 28NOV2007 (37) 3. 29NOV2007 (38) - 30NOV2007 (39) 4. 19DEC2007 (58) - 19DEC2007 (58) 5. 18FEB2008 (119) - 08MAY2008 (199) 6. 16APR2008 (177) - 22APR2008 (183) 7. 17APR2008 (178) - 26APR2008 (187) 8. 17APR2008 (178) - 22APR2008 (183) 9. 19APR2008 (180) - 26APR2008 (187)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214017

Parameter	Value
	10. 20APR2008 (181) - 25APR2008 (186)
	11. 21APR2008 (182) - 21APR2008 (182)
	12. 25APR2008 (186) - 25APR2008 (186)
Duration of AE	1. .
	2. 36
	3. 2
	4. 1
	5. 81
	6. 7
	7. 10
	8. 6
	9. 8
	10. 6
	11. 1
	12. 1
Dose on AE onset	1.
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. .
	12. .
Action taken	1. OTHER
	2. DOSE OF STUDY DRUG REDUCED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214017

Parameter	Value
	3. NONE
	4. NONE
	5. OTHER
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214027

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214027/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/75/WHITE/AUSTRALIA/YES
Medical history	Asthma, Benign prostatic hyperplasia, Cellulitis, Chronic obstructive pulmonary disease, Cardiac failure congestive, Diverticulitis, Hypokalaemia, Microcytic anaemia, Spinal osteoarthritis, Osteoarthritis, Osteoporosis, Nephrolithiasis, Knee arthroplasty, Stent placement, Ureteral stent insertion, Ureteral stent removal, Melanoma recurrent
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMILORIDE, ASPIRIN, AUGMENTIN DUO FORTE TABLETS (AMOXYCILLIN TRIHYDRATE; POTASSIUM CLAVULANATE), BECLOMETHASONE DIPROPIONATE, CALCIUM CARBONATE, CEFACLOR, CEFEPIME HYDROCHLORIDE, CEFTAZIDIME PENTAHYDRATE, CEFTRIAXONE SODIUM, CEPHALEXIN, CHLORAMPHENICOL, CIPROFLOXACIN HYDROCHLORIDE, COVERSYL, DURO -K SR (POTASSIUM CHLORIDE), ERGOCALCIFEROL, FLUCLOXACILLIN SODIUM, FOSAMAX, FRUSEMIDE, GENTAMICIN SULFATE, MAGNESIUM ASPARTATE (SUPPLEMENT), MOMETASONE FUROATE, PARACETAMOL, PREDNISOLONE ACETATE, ROXITHROMYCIN, SALBUTAMOL SULFATE, SERETIDE, TEMEZEPAM, THEOPHYLLINE, TIOTROPIUM BROMIDE, VANCOMYCIN HYDROCHLORIDE
Adverse Events (AE) Preferred term	1. Chronic obstructive pulmonary disease 2. Contusion 3. Epistaxis 4. Infective exacerbation of chronic obstructive airways disease 5. Wound haemorrhage 6. Chronic obstructive pulmonary disease 7. Chronic obstructive pulmonary disease 8. Conjunctivitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/YES/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 08FEB2008 (2) - 16FEB2008 (10) 2. 13FEB2008 (7) - 05MAR2008 (28) 3. 27FEB2008 (21) - --------- (.) 4. 04MAR2008 (27) - 08MAR2008 (31) 5. 10MAY2008 (94) - --------- (.) 6. 02JUN2008 (117) - 07JUN2008 (122) 7. 15JUN2008 (130) - 30JUN2008 (145) 8. 20JUN2008 (135) - 26JUN2008 (141)
Duration of AE	1. 9 2. 22 3. . 4. 5

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214027

Parameter	Value
	5. .
	6. 6
	7. 16
	8. 7
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY,OTHER
	5. OTHER
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. IMPROVED
	6. RESOLVED
	7. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214027

Parameter	Value
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214029

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214029/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/81/WHITE/AUSTRALIA/YES
Medical history	Coronary artery disease, Hypercholesterolaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, ATORVASTATIN CALCIUM, ENOXAPARIN, RAMIPRIL, WARFARIN
Adverse Events (AE) Preferred term	1. Haematoma 2. Muscle spasms
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 28FEB2008 (7) - 10APR2008 (49) 2. 03JUN2008 (103) - 02AUG2008 (163)
Duration of AE	1. 43 2. 61
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214030

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214030/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/AUSTRALIA/YES
Medical history	Asthma, Atrial fibrillation, Basal cell carcinoma, Hypertension, Osteoarthritis, Bundle branch block left, Prostatism, Umbilical hernia repair, Upper respiratory tract infection, Gastrointestinal motility disorder, Hyperlipidaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALFENTANIL HYDROCHLORIDE, AMIODARONE HYDROCHLORIDE, AMPICILLIN SODIUM, ASPIRIN, ATENOLOL, CEFTRIAXONE SODIUM, CENTRUM MULTIVITAMIN CAPSULES, CEPHALEXIN, CEPHALOTHIN SODIUM, CODEINE FORTE, DICLOXACILLIN SODIUM, ESOMEPRAZOLE MAGNESIUM TRIHYDRATE, GENTAMICIN SULFATE, GLUCOSAMINE, HEPARIN SODIUM, KETAMINE HYDROCHLORIDE, LOPERAMIDE HYDROCHLORIDE SIMETHICONE, METARAMINOL TARTRATE, METOCLOPRAMIDE HYDROCHLORIDE, METRONIDAZOLE, MIDAZOLAM HYDROCHLORIDE, MORPHINE SULFATE, ONDANSETRON HYDROCHLORIDE, PARACETAMOL, PARECOXIB SODIUM, PROPOFOL, QUINIDINE BISULFATE, TRAMADOL HYDROCHLORIDE, VECURONIUM BROMIDE
Adverse Events (AE) Preferred term	1. Frequent bowel movements 2. Rectal haemorrhage 3. Colorectal cancer 4. Hypotension 5. Nail infection 6. Localised infection 7. Ileostomy closure 8. Incisional hernia repair 9. Incisional hernia repair 10. Lobar pneumonia 11. Nausea 12. Intestinal dilatation 13. Wound haemorrhage 14. Contusion 15. Wound infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/YES/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/NO/YES/YES 11. MILD/NO/NO/YES 12. MODERATE/NO/YES/YES 13. MILD/NO/NO/YES 14. MILD/YES/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214030

Parameter	Value
	15. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --APR2008 (.) - 17SEP2008 (202)
	2. 01MAR2008 (2) - 31MAR2008 (32)
	3. 12MAR2008 (13) - 31MAR2008 (32)
	4. 31MAR2008 (32) - 31MAR2008 (32)
	5. 25JUN2008 (118) - 07JUL2008 (130)
	6. 25JUN2008 (118) - 07JUL2008 (130)
	7. 18AUG2008 (172) - 18AUG2008 (172)
	8. 18AUG2008 (172) - 18AUG2008 (172)
	9. 18AUG2008 (172) - 18AUG2008 (172)
	10. 19AUG2008 (173) - 22AUG2008 (176)
	11. 19AUG2008 (173) - 25AUG2008 (179)
	12. 20AUG2008 (174) - 22AUG2008 (176)
	13. 01SEP2008 (186) - 16SEP2008 (201)
	14. 01SEP2008 (186) - 16SEP2008 (201)
	15. 01SEP2008 (186) - 11SEP2008 (196)
Duration of AE	1. .
	2. 31
	3. 20
	4. 1
	5. 13
	6. 13
	7. 1
	8. 1
	9. 1
	10. 4
	11. 7
	12. 3
	13. 16
	14. 16
	15. 11
Dose on AE onset	1.
	2. 15 mg
	3. 15 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214030

Parameter	Value
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. I
	5. .
	6. .
	7. I
	8. I
	9. I
	10. I
	11. I
	12. I
	13. .
	14. .
	15. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	8. OTHER
	9. OTHER
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. NONE
	13. NONE
	14. NONE
	15. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214030

Parameter	Value
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. RESOLVED
	15. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214062

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214062/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/81/WHITE/AUSTRALIA/YES
Medical history	Aortic stenosis, Renal failure chronic, Hypercholesterolaemia, Iron deficiency anaemia, Plantar fasciitis, Myalgia, Gastrooesophageal reflux disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CHOLECALCIFEROL, COVERSYL, DIAZEPAM, ENDONE, ENOXAPARIN, GAVISCON, GLYCOPREP, LACTULOSE, LOSEC, MORPHINE, OXYCODONE HYDROCHLORIDE, PANADEINE FORTE, PARACETAMOL, PICOLAX, PRAVACHOL, PREDINISOLONE, PREDNISOLONE, SENNOSIDES A AND B, TRAMADOL HYDROCHLORIDE, WARFARIN, ZINC SUPPLEMENT WITH VITAMIN C & MAGNESIUM
Adverse Events (AE) Preferred term	1. Contusion 2. Contusion 3. Wound haemorrhage 4. Arthralgia 5. Back pain 6. Sacroiliitis 7. Spinal compression fracture 8. Colon cancer 9. Osteoporosis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/YES/YES 8. MODERATE/NO/YES/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 09APR2009 (1) - --------- (.) 2. 17APR2009 (9) - --------- (.) 3. 10JUN2009 (63) - 08JUL2009 (91) 4. 15JUN2009 (68) - 21JUL2009 (104) 5. 15JUN2009 (68) - 21JUL2009 (104) 6. 15JUN2009 (68) - --------- (.) 7. 22JUL2009 (105) - 31AUG2009 (145) 8. 23JUL2009 (106) - 31AUG2009 (145) 9. 28JUL2009 (111) - --------- (.)
Duration of AE	1. . 2. . 3. 29 4. 37 5. 37 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214062

Parameter	Value
	7. 41
	8. 40
	9. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	8. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	9. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214062

Parameter	Value
	9. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 400214067

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/400214067/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/84/WHITE/AUSTRALIA/YES
Medical history	Circumcision, Transurethral prostatectomy, Seborrhoeic dermatitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BEROCCA MULTIVITAMIN & MINERAL, FISH OIL CAPSULES, GARLIC TABLETS, SORBOLENE CREAM
Adverse Events (AE) Preferred term	1. Seborrhoeic dermatitis 2. Lymphoma cutis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 07SEP2009 (21) - 07NOV2009 (82) 2. 12JAN2010 (148) - --------- (.)
Duration of AE	1. 62 2. .
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014032

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440014032/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/49/WHITE/AUSTRIA/YES
Medical history	Psoriasis, Radius fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ANTIPYRETIC THERAPY [HOSPITAL DISCHARGE LETTER="ANTIPYRETIC THERAPY], BUSCOPAN COMPOSITUM (HYOSCIN-N-BUTYLBROMID + METAMIZOL), CALCIPOT D3 (VITAMIN D3 + CALCIUM), CARBO MEDICINALIS, ENOXAPARIN, HELOPANFLAT, LEFAXIN, LOVENOX, PANTOLOC, PROTON PUMP INHIBITOR, PYRALVEX [HYDROYANTHRAZEN DERIVATIVES, SALICYLIC ACID], XANOR
Adverse Events (AE) Preferred term	1. Muscle spasms 2. Headache 3. Panic attack 4. Dehydration 5. Flatulence 6. Diarrhoea 7. Abdominal pain upper 8. Nausea 9. Abdominal pain upper 10. Gingivitis 11. Traumatic haematoma 12. Gastroenteritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/YES/NO/YES 12. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 18JUL2008 (8) - 18JUL2008 (8) 2. 04AUG2008 (25) - 04AUG2008 (25) 3. 27AUG2008 (48) - 27AUG2008 (48) 4. 27AUG2008 (48) - 27AUG2008 (48) 5. 27AUG2008 (48) - 10SEP2008 (62) 6. 03SEP2008 (55) - 06SEP2008 (58) 7. 03SEP2008 (55) - 10SEP2008 (62) 8. 01OCT2008 (83) - 27OCT2008 (109) 9. 01OCT2008 (83) - 27OCT2008 (109)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014032

Parameter	Value
	10. 07OCT2008 (89) - 10OCT2008 (92)
	11. 31OCT2008 (113) - 05NOV2008 (118)
	12. 04JAN2009 (178) - 05JAN2009 (179)
Duration of AE	1. 1
	2. 1
	3. 1
	4. 1
	5. 15
	6. 4
	7. 8
	8. 27
	9. 27
	10. 4
	11. 6
	12. 2
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Action taken	1. NONE
	2. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014032

Parameter	Value
	3. REMEDIAL DRUG THERAPY
	4. OTHER
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. NONE
	12. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014076

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440014076/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/48/WHITE/AUSTRIA/YES
Medical history	Asthma, Hypertension, Hypokalaemia, Osteoporosis, Type 2 diabetes mellitus, Bacterial infection
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMARYL, AMLODIPIN, APREDNISOLON, BERODUAL (FENOTEROL + IPRATROPIUMBROMID), DIPRIVAN, ELOMEL, ELOMEL ISOTON, ELOZELL SPEZIAL, FLOXAPEN, FOSAMAX, GLUCOSE-PHOSPHAT, KALIORAL [POTASSIUM CITRATE, POTASSIUM HYDROGENCARBONATE, CITRIC ACID], KALIUMCHLORID, KCL, LOVENOX, MARCOUMAR, MEXALEN, NOVALGIN, PANTOLOC, PAPERTIN, PARKEMED, PASPERTIN, PERFALGAN, RINGERLOESUNG, RINGERLOSUNG, SERETIDE, SINGULAIR, SOLU DACORTIN, SOLU-DACORTIN, SUCRALAN, SULTANOL, TARDYFERON, TAVANIC, TRAMAL, UNIFYL RETARD, VENA CAVA FILTER, VOLTAREN, XYLOCAIN SPRAY [LIDOCAINE ALONE], ZOLDEM
Adverse Events (AE) Preferred term	1. Pyrexia 2. Vaginal haemorrhage 3. Adenomyosis 4. Anaemia 5. Sleep disorder 6. Nausea 7. Anaemia 8. Pyrexia 9. Sepsis 10. Pyrexia 11. Vomiting 12. Nausea 13. Oesophageal candidiasis 14. Vertigo 15. Nasopharyngitis 16. Vertigo 17. Vertigo 18. Gastritis 19. Oesophagitis 20. Nausea
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/YES/YES/YES 3. MILD/NO/NO/YES 4. SEVERE/YES/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MILD/NO/NO/YES 11. MODERATE/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014076

Parameter	Value
	12. MILD/NO/NO/YES
	13. MILD/NO/NO/YES
	14. MILD/NO/NO/YES
	15. MILD/NO/NO/YES
	16. MODERATE/NO/YES/YES
	17. MILD/NO/NO/YES
	18. MILD/NO/NO/YES
	19. MILD/NO/NO/YES
	20. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 21AUG2009 (5) - 21AUG2009 (5)
	2. 21AUG2009 (5) - 28AUG2009 (12)
	3. 21AUG2009 (5) - 28AUG2009 (12)
	4. 21AUG2009 (5) - 28AUG2009 (12)
	5. 26AUG2009 (10) - 29AUG2009 (13)
	6. 28AUG2009 (12) - 31AUG2009 (15)
	7. 29AUG2009 (13) - --------- (.)
	8. 31AUG2009 (15) - 03SEP2009 (18)
	9. 31AUG2009 (15) - 09SEP2009 (24)
	10. 22SEP2009 (37) - 24SEP2009 (39)
	11. 25SEP2009 (40) - 01DEC2009 (107)
	12. 25SEP2009 (40) - 12FEB2010 (180)
	13. 23OCT2009 (68) - 17DEC2009 (123)
	14. 15NOV2009 (91) - 01DEC2009 (107)
	15. 23NOV2009 (99) - 29NOV2009 (105)
	16. 01DEC2009 (107) - 07DEC2009 (113)
	17. 08DEC2009 (114) - 15FEB2010 (183)
	18. 17DEC2009 (123) - --------- (.)
	19. 17DEC2009 (123) - --------- (.)
	20. 07MAR2010 (203) - --------- (.)
Duration of AE	1. 1
	2. 8
	3. 8
	4. 8
	5. 4
	6. 4
	7. .
	8. 4
	9. 10
	10. 3
	11. 68
	12. 141

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014076

Parameter	Value
	13. 56
	14. 17
	15. 7
	16. 7
	17. 70
	18. .
	19. .
	20. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 15 mg
	9. 15 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
	16. 20 mg
	17. 20 mg
	18. 20 mg
	19. 20 mg
	20. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. I
	6. I
	7. I
	8. I
	9. I
	10. .
	11. .
	12. .
	13. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014076

Parameter	Value
	14. .
	15. .
	16. .
	17. .
	18. .
	19. .
	20. F
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	3. OTHER
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. NONE
	14. NONE
	15. NONE
	16. NONE
	17. NONE
	18. NONE
	19. NONE
	20. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. IMPROVED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. WORSENED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440014076

Parameter	Value
	15. RESOLVED
	16. IMPROVED
	17. RESOLVED
	18. UNCHANGED
	19. UNCHANGED
	20. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440034004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440034004/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/62/WHITE/AUSTRIA/YES
Medical history	Chronic obstructive pulmonary disease, Hyperthyroidism, Hysterectomy, Osteoporosis, Hyperlipidaemia, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTONEL, AEROCEF, AEROCORTIN, AEROMUC, AUGMENTIN, COMBIVENT, DICLOBENE, DIFLUCAN, LOVENOX, PARKEMED, PRONERV, SIMVASTATIN, THIAMAZOL
Adverse Events (AE) Preferred term	1. Epiglottitis 2. Infective exacerbation of chronic obstructive airways disease 3. Pyrexia 4. Oral candidiasis 5. Leukopenia 6. Basedow's disease 7. Diarrhoea 8. Large intestine perforation 9. Ascites 10. Pyloric stenosis 11. Metastases to peritoneum 12. Vomiting 13. Abdominal pain 14. Ovarian cancer 15. Gastric ulcer haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/NO/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/NO/NO 8. SEVERE/NO/YES/NO 9. SEVERE/NO/NO/NO 10. SEVERE/NO/NO/NO 11. SEVERE/NO/YES/NO 12. SEVERE/NO/NO/NO 13. SEVERE/NO/NO/NO 14. SEVERE/NO/YES/NO 15. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. --NOV2007 (.) - 05DEC2007 (61) 2. 12OCT2007 (7) - 26OCT2007 (21) 3. 27NOV2007 (53) - 05DEC2007 (61) 4. 27NOV2007 (53) - 04DEC2007 (60) 5. 27NOV2007 (53) - 03DEC2007 (59)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440034004

Parameter	Value
	6. 04APR2008 (182) - 10APR2008 (188)
	7. 18APR2008 (196) - --------- (.)
	8. 20APR2008 (198) - 22APR2008 (200)
	9. 20APR2008 (198) - --------- (.)
	10. 20APR2008 (198) - --------- (.)
	11. 20APR2008 (198) - --------- (.)
	12. 20APR2008 (198) - 20APR2008 (198)
	13. 20APR2008 (198) - --------- (.)
	14. 20APR2008 (198) - --------- (.)
	15. 22APR2008 (200) - --------- (.)
Duration of AE	1. .
	2. 15
	3. 9
	4. 8
	5. 7
	6. 7
	7. .
	8. 3
	9. .
	10. .
	11. .
	12. 1
	13. .
	14. .
	15. .
Dose on AE onset	1.
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
	15. 20 mg
Dose status on AE onset	1.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440034004

Parameter	Value
	2. .
	3. .
	4. .
	5. .
	6. .
	7. F
	8. F
	9. F
	10. F
	11. F
	12. F
	13. F
	14. F
	15. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. NONE
	6. OTHER
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY,OTHER
	9. NONE
	10. NONE
	11. NONE
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. NONE
	15. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. DEATH
	9. UNCHANGED
	10. UNCHANGED
	11. UNCHANGED
	12. WORSENED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440034004

Parameter	Value
	13. INSUFFICIENT FOLLOW-UP
	14. UNCHANGED
	15. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440034025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440034025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/49/WHITE/AUSTRIA/YES
Medical history	Hypertension, Phimosis, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CONCOR, DIABETEX, DIPIDOLOR, ENOXAPARIN, OPTINEM, PRAXITEN
Adverse Events (AE) Preferred term	1. Phimosis 2. Post procedural haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 01DEC2008 (5) - 12FEB2009 (78) 2. 19FEB2009 (85) - 26FEB2009 (92)
Duration of AE	1. 74 2. 8
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702- 440034025[2)]	POST SURGICAL BLEEDING（PT：処置後出血） 治験担当医は、合併症（包茎）に対する処置によるものであり、否定できると判断した。弊社は、アセノクマロール及びエノキサパリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440044016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440044016/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/43/WHITE/AUSTRIA/YES
Medical history	Thrombophlebitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BETAHISTIN, MEXALEN, NASIVIN, OSPEN, PEVARYL CREME, VACCINATION INFLUENZA
Adverse Events (AE) Preferred term	1. Tinnitus 2. Limb discomfort 3. Factor V Leiden mutation 4. Factor II mutation 5. Paraesthesia 6. Limb discomfort 7. Limb discomfort 8. Fungal skin infection 9. Influenza like illness 10. Contusion 11. Pharyngitis 12. Rhinitis 13. Pharyngitis 14. Limb discomfort
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/YES/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/NO/NO/YES 14. MILD/NO/NO/NO
Start/stop date of event with relative date	1. --NOV2008 (.) - 11DEC2008 (267) 2. 25MAR2008 (6) - 25MAR2008 (6) 3. 08APR2008 (20) - --------- (.) 4. 08APR2008 (20) - --------- (.) 5. 11APR2008 (23) - 12APR2008 (24) 6. 14APR2008 (26) - 14APR2008 (26) 7. 10JUL2008 (113) - 14JUL2008 (117) 8. 20AUG2008 (154) - 23AUG2008 (157)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440044016

Parameter	Value
	9. 25SEP2008 (190) - 09OCT2008 (204)
	10. 04NOV2008 (230) - 05NOV2008 (231)
	11. 20NOV2008 (246) - 30NOV2008 (256)
	12. 02FEB2009 (320) - 05FEB2009 (323)
	13. 02FEB2009 (320) - 05FEB2009 (323)
	14. 05APR2009 (382) - 09APR2009 (386)
Duration of AE	1. .
	2. 1
	3. .
	4. .
	5. 2
	6. 1
	7. 5
	8. 4
	9. 15
	10. 2
	11. 11
	12. 4
	13. 4
	14. 5
Dose on AE onset	1.
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
	13. 20 mg
	14. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440044016

Parameter	Value
	8. .
	9. .
	10. .
	11. .
	12. .
	13. .
	14. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. REMEDIAL DRUG THERAPY
	9. NONE
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
	14. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. UNCHANGED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440044016

Parameter	Value
	14. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440054004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440054004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/82/WHITE/AUSTRIA/YES
Medical history	Cardiac failure, Hypertension, Renal failure chronic, Venous insufficiency
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AEROMUC, CENIPRES, DAFLON - FLAVONOID, DIOSMIN, HESPERIDIN, ENOXAPARIN, FLUDEX, FURON, IRENAT, LOVENOX, MAXIPIME, METOHEXAL, PASPERTIN, PERFALGAN, PLAVIX, RAMIPRIL, SELOKEN PLUS, SIMVASTATIN, SORTIS, TAVANIC, THIAMAZOL, THROMBO ASS, TRITACE PLUS
Adverse Events (AE) Preferred term	1. Renal failure chronic 2. Dyslipidaemia 3. Nasopharyngitis 4. Acute myocardial infarction 5. Chest pain 6. Troponin increased 7. Vaginal haemorrhage 8. Hyperlipidaemia 9. Pneumonia 10. Nausea 11. Pyrexia 12. Chronic obstructive pulmonary disease 13. Uterine cancer
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/YES/NO/YES 8. MODERATE/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/NO 13. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 05NOV2007 (85) - --------- (.) 2. 05NOV2007 (85) - --------- (.) 3. 05NOV2007 (85) - 10NOV2007 (90) 4. 06NOV2007 (86) - 07DEC2007 (117) 5. 06NOV2007 (86) - 07DEC2007 (117) 6. 06NOV2007 (86) - 07DEC2007 (117) 7. 07NOV2007 (87) - --NOV2007 (.) 8. 09NOV2007 (89) - --------- (.)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440054004

Parameter	Value
	9. 11NOV2007 (91) - 26NOV2007 (106)
	10. 11NOV2007 (91) - 11NOV2007 (91)
	11. 11NOV2007 (91) - 11NOV2007 (91)
	12. 07DEC2007 (117) - --------- (.)
	13. 18DEC2007 (128) - --------- (.)
Duration of AE	1. .
	2. .
	3. 6
	4. 32
	5. 32
	6. 32
	7. .
	8. .
	9. 16
	10. 1
	11. 1
	12. .
	13. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440054004

Parameter	Value
	11.
	12.
	13.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. NONE
	7. STUDY DRUG DISCONTINUED PERMANENTLY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. OTHER
Outcome of event	1. UNCHANGED
	2. IMPROVED
	3. WORSENED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. UNCHANGED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. UNCHANGED
	13. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440054027

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440054027/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/75/WHITE/AUSTRIA/YES
Medical history	Anaemia, Carotid artery stenosis, Erysipelas, Goitre, Pruritus, Drug hypersensitivity, Benign prostatic hyperplasia, Renal cyst, Osteopenia, Phlebitis, Dyslipidaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ALNA RETARD, AVELOX, CODIDOL, DIBONDRIN, ENOXAPARIN, KONAKION, LOVENOX, MAXI KALZ, MEXALEN, PRAVASTATIN, PROPOFOL, THROMBO-ASS, VIT D3
Adverse Events (AE) Preferred term	1. Concussion 2. Wound haemorrhage 3. Rib fracture 4. Haematoma 5. Traumatic haematoma 6. Colonic polyp 7. Hiatus hernia 8. Gastrointestinal tract mucosal discolouration
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/YES/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/YES/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 05NOV2008 (14) - 06NOV2008 (15) 2. 05NOV2008 (14) - 05NOV2008 (14) 3. 05NOV2008 (14) - 23FEB2009 (124) 4. 05NOV2008 (14) - 05DEC2008 (44) 5. 05NOV2008 (14) - 05DEC2008 (44) 6. 22JAN2009 (92) - 11FEB2009 (112) 7. 23JAN2009 (93) - --------- (.) 8. 23JAN2009 (93) - --------- (.)
Duration of AE	1. 2 2. 1 3. 111 4. 31 5. 31 6. 21 7. . 8. .
Dose on AE onset	1. 2. 3.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440054027

Parameter	Value
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. NONE
	2. OTHER
	3. NONE
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. OTHER
	6. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	7. NONE
	8. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-440054027[2)]	HEMATOMA LEFT OLECRANON（PT：血腫） 治験担当医は、自転車事故によるものであり、否定できると判断した。弊社は、アセノクマロール投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440064002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/86/WHITE/AUSTRIA/YES
Medical history	Actinic keratosis, Aortic arteriosclerosis, Appendicectomy, Spinal osteoarthritis, Cholecystectomy, Coronary artery disease, Dysthymic disorder, Emphysema, Goitre, Hypertension, Mixed hyperlipidaemia, Myocardial infarction, Transurethral prostatectomy, Benign prostatic hyperplasia, Renal failure, Hiccups, Tonsillectomy, Tuberculosis, Hypoacusis, Pancreas lipomatosis, Kidney fibrosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AXURA, ENOXAPARIN, EPINEPHRINE, GLADEM, NEOSTRATA FACE-GEL [VITAMINE B5 AND HYALURONIC ACID], NEUROBION FORTE [CYANOCOBALAMIN; PYRIDOXIN HYDROCHLORID; THIAMIN DISULFID], TRILEPTAL, TRITTICO, VICARD, XYLONEST
Adverse Events (AE) Preferred term	1. Actinic keratosis 2. Dyspnoea 3. Fall 4. Dementia 5. Chondrocalcinosis 6. Basal cell carcinoma 7. Squamous cell carcinoma of skin 8. Basal cell carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/NO/YES 8. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 03OCT2007 (1) - --------- (.) 2. 06OCT2007 (4) - 07OCT2007 (5) 3. 06OCT2007 (4) - 06OCT2007 (4) 4. 16OCT2007 (14) - --------- (.) 5. 23NOV2007 (52) - 25NOV2007 (54) 6. 20MAR2008 (170) - 21MAR2008 (171) 7. 20MAR2008 (170) - 20MAR2008 (170) 8. 21MAR2008 (171) - --------- (.)
Duration of AE	1. . 2. 2 3. 1 4. . 5. 3 6. 2 7. 1 8. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064002

Parameter	Value
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. NONE
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED
	6. IMPROVED
	7. RESOLVED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440064006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/AUSTRIA/YES
Medical history	Bronchitis chronic, Hypertension, Pneumonia, Tonsillectomy, Tobacco abuse
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLCYSTEINE, BUSCOPAN, DORMICUM [MIDAZOLAM.], ELOMEL ISOTON, FENTANYL, IRENAT, PRAXITEN, PROPOFOL, XYLOCAIN [LIDOCAIN]
Adverse Events (AE) Preferred term	1. Peripheral arterial occlusive disease 2. Cholelithiasis 3. Aortic aneurysm 4. Lung neoplasm 5. Emphysema 6. Aortic arteriosclerosis 7. Pancreas lipomatosis 8. Lipoma 9. Diverticulum intestinal 10. Dolichocolon 11. Faecaloma 12. Spinal osteoarthritis 13. Lung neoplasm 14. Lymphadenopathy mediastinal
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/NO/YES/YES 14. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 18MAR2008 (7) - --------- (.) 2. 19MAR2008 (8) - --------- (.) 3. 19MAR2008 (8) - --------- (.) 4. 19MAR2008 (8) - 10JUN2008 (91) 5. 19MAR2008 (8) - --------- (.) 6. 19MAR2008 (8) - --------- (.) 7. 27MAR2008 (16) - --------- (.) 8. 27MAR2008 (16) - --------- (.)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064006

Parameter	Value
	9. 27MAR2008 (16) - --------- (.)
	10. 27MAR2008 (16) - --------- (.)
	11. 27MAR2008 (16) - 01APR2008 (21)
	12. 27MAR2008 (16) - --------- (.)
	13. 10JUN2008 (91) - --------- (.)
	14. 14AUG2008 (156) - --------- (.)
Duration of AE	1. .
	2. .
	3. .
	4. 84
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. 6
	12. .
	13. .
	14. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 15 mg
	9. 15 mg
	10. 15 mg
	11. 15 mg
	12. 15 mg
	13. 20 mg
	14. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064006

Parameter	Value
	8. .
	9. .
	10. .
	11. .
	12. .
	13. I
	14. .
Action taken	1. NONE
	2. NONE
	3. NONE
	4. STUDY DRUG DISCONTINUED AND RESTARTED
	5. NONE
	6. NONE
	7. NONE
	8. NONE
	9. NONE
	10. NONE
	11. NONE
	12. NONE
	13. STUDY DRUG DISCONTINUED AND RESTARTED,STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
	14. NONE
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. UNCHANGED
	4. RESOLVED
	5. UNCHANGED
	6. UNCHANGED
	7. UNCHANGED
	8. UNCHANGED
	9. UNCHANGED
	10. UNCHANGED
	11. RESOLVED
	12. UNCHANGED
	13. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064006

Parameter	Value
	14. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440064009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/41/WHITE/AUSTRIA/YES
Medical history	Appendicectomy, Caesarean section, Gastritis, Duodenal ulcer, Gastric ulcer, Autoimmune thyroiditis, Hypertriglyceridaemia, Spinal osteoarthritis, Thrombocytopenia, Tonsillectomy, Uterine leiomyoma, Intervertebral disc protrusion, Obesity, Gastrooesophageal reflux disease, Tobacco abuse
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BUSCOPAN, CIPROXIN, CYMBALTA, DAFLON [DIOSMIN, HESPERIDIN], DIPIDOLOR, ENOXAPARIN, FORLAX, LOVENOX, MAGNOSOLV, NEODOLPASSE, NEXIUM, NOVALGIN, NOVOTHYRAL, PANTOLOC, PARKEMED, PASPERTIN, PERFALGAN, ZOFRAN
Adverse Events (AE) Preferred term	1. Nausea 2. Headache 3. Nasopharyngitis 4. Dermatitis contact 5. Reflux oesophagitis 6. Cervicobrachial syndrome 7. Vertigo 8. Cyst 9. Blepharochalasis 10. Blepharochalasis 11. Cholecystitis 12. Cholecystitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/YES/YES 11. MILD/NO/NO/YES 12. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 29APR2008 (7) - 29APR2008 (7) 2. 29APR2008 (7) - 29APR2008 (7) 3. 14MAY2008 (22) - 18MAY2008 (26) 4. 14MAY2008 (22) - 28MAY2008 (36) 5. 19MAY2008 (27) - 28JUL2008 (97) 6. 26MAY2008 (34) - 13JUN2008 (52) 7. 08AUG2008 (108) - 10AUG2008 (110) 8. 16SEP2008 (147) - --------- (.) 9. 01NOV2008 (193) - 12JAN2009 (265)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064009

Parameter	Value
	10. 12JAN2009 (265) - 13JAN2009 (266)
	11. 04MAR2009 (316) - 11MAR2009 (323)
	12. 12MAR2009 (324) - 16MAR2009 (328)
Duration of AE	1. 1
	2. 1
	3. 5
	4. 15
	5. 71
	6. 19
	7. 3
	8. .
	9. 73
	10. 2
	11. 8
	12. 5
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064009

Parameter	Value
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. NONE
	9. STUDY DRUG DISCONTINUED AND RESTARTED
	10. OTHER
	11. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	12. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. UNCHANGED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/440064019/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/46/WHITE/AUSTRIA/YES
Medical history	Fibroadenoma of breast, Hypothyroidism, Anal abscess, Anal abscess, Spinal osteoarthritis, Umbilical hernia, Ligament rupture, Thyroidectomy, Obesity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ANEXATE, BUSCOPAN, COLONORM, ENOXAPARIN, LOVENOX, MARVELON, MEXALEN, MIDAZOLOAM, OMEPRALAN, THYREX, XYLOCAIN 2% GEL [LIDOCAIN HCL,METHYL 4-HYDROXYBENZOAT,PROPYL-4-HYDROXYBENZOAT,HY
Adverse Events (AE) Preferred term	1. Haemangioma of liver 2. Renal cyst 3. Headache 4. Colonic polyp 5. Hiatus hernia 6. Reflux oesophagitis 7. Gastritis 8. Anal skin tags 9. Haemorrhoids 10. Fibroma
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/YES/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 13FEB2009 (4) - --------- (.) 2. 13FEB2009 (4) - --------- (.) 3. 15FEB2009 (6) - 17FEB2009 (8) 4. 13MAY2009 (93) - 15MAY2009 (95) 5. 14MAY2009 (94) - --------- (.) 6. 14MAY2009 (94) - --------- (.) 7. 14MAY2009 (94) - --------- (.) 8. 14MAY2009 (94) - --------- (.) 9. 14MAY2009 (94) - --------- (.) 10. 14MAY2009 (94) - --------- (.)
Duration of AE	1. . 2. . 3. 3 4. 3

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064019

Parameter	Value
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED AND RESTARTED
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. NONE
	10. NONE
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 440064019

Parameter	Value
	6. UNCHANGED
	7. UNCHANGED
	8. UNCHANGED
	9. UNCHANGED
	10. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460014001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460014001/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/56/WHITE/HUNGARY/YES
Medical history	Metastases to bone, Breast cancer, Cardiac failure, Diverticulum intestinal, Colonic fistula, Drug dependence, Haemorrhoids, Hypertension, Vertigo, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANDAXIN, BETALOC, BETASERC, BONDRONAT, CONTRAMAL, EUNOCTIN, FUROSEMID, KALDYUM
Adverse Events (AE) Preferred term	1. Blood alkaline phosphatase increased 2. Gastrointestinal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/NO 2. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 25OCT2007 (1) - --------- (.) 2. 03NOV2007 (10) - 12NOV2007 (19)
Duration of AE	1. . 2. 10
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460014009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460014009/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/HUNGARY/YES
Medical history	Hypertension, Lipids increased, Skin ulcer, Varicose vein, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALPROSTAPINT, AUGMENTIN DUO, COVEREX COMB, FUROSEMID, KALIUM, NORMODIPIN, QUAMATEL, SORTIS, TRENTAL, VENORUTON FORTE
Adverse Events (AE) Preferred term	1. Cardiac failure 2. Peripheral arterial occlusive disease 3. Wound infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 04DEC2008 (16) - --------- (.) 2. 30MAR2009 (132) - 07APR2009 (140) 3. 07APR2009 (140) - 11MAY2009 (174)
Duration of AE	1. . 2. 9 3. 35
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. I 3. I
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 3. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460034014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460034014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/77/WHITE/HUNGARY/YES
Medical history	Osteoarthritis, Bronchitis chronic, Cardiomyopathy, Cholecystectomy, Coronary artery disease, Hypertension, Osteoporosis, Pneumonia, Renal cyst, Thoracic vertebral fracture
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ADEXOR MR, AMILORID COMP, ASPIRIN PROTECT, AUGMENTIN, AUGMENTIN DUO, CEDAX, CONTRAMAL, ENOXAPARIN, FUROSEMID, KALDYUM, KONAKION, LISONORM, MESULID, NEBILET, NITROMINT TTS 5, OMEPRAZOL HEXAL, PANADOL, SERETIDE, THEOSPIREX, XANAX
Adverse Events (AE) Preferred term	1. International normalised ratio increased 2. Pneumonia 3. Erysipelas
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/YES/YES 3. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 08AUG2008 (16) - 15AUG2008 (23) 2. 09AUG2008 (17) - 15AUG2008 (23) 3. 30NOV2008 (130) - 05DEC2008 (135)
Duration of AE	1. 8 2. 7 3. 6
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,INFUSION RATE OF STUDY DRUG REDUCED 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460034014

Parameter	Value
	3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460044013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460044013/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/46/WHITE/HUNGARY/YES
Medical history	Caesarean section, Caesarean section, Pyrexia, Menstruation irregular, Nervousness, Nervousness, Suicide attempt, Suicide attempt, Female sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	DETRALEX (DIOSMIN, HESPERIDINE), QUAMATEL (FAMOTIDINE), RIVOTRIL (CLONAZEPAM), TISASEN (SENNA GLYCOSIDES)
Adverse Events (AE) Preferred term	1. Constipation 2. Hypoaesthesia oral 3. Vaginal haemorrhage 4. Ovarian cyst 5. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/YES/YES/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 27MAR2008 (2) - 27MAR2008 (2) 2. 27JUN2008 (94) - 28JUN2008 (95) 3. 10SEP2008 (169) - 25SEP2008 (184) 4. 19SEP2008 (178) - --------- (.) 5. 19SEP2008 (178) - --------- (.)
Duration of AE	1. 1 2. 2 3. 16 4. . 5. .
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. OTHER 4. NONE 5. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460044013

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460044025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460044025/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/52/WHITE/HUNGARY/YES
Medical history	Hypertension, Dysmenorrhoea, Hyperkeratosis, Furuncle, Furuncle, Furuncle, Dyspepsia, Insomnia, Rhinitis allergic, Tinnitus, Uterine leiomyoma, Wrist surgery, Postmenopause, Uterine cervix ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANDAXIN (MEPROBAMATE), BISOPROLOL (BISOPROLOL), C-VITAMIN (ASCORBIC ACID), CLARITINE AKUT (LORATADINE), DUOPRIL (FOSINOPRIL +HYDROCHLOROTHIAZIDE), NORCOLUT (NORETHISTERONE), RUTASCORBIN (RUTOSIDE + ASCORBIC ACID), XANAX (ALPRAZOLAM)
Adverse Events (AE) Preferred term	1. Dyspnoea 2. Cough 3. Chest pain 4. Anxiety 5. Postmenopausal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 28SEP2008 (10) - 30SEP2008 (12) 2. 28SEP2008 (10) - 30SEP2008 (12) 3. 28SEP2008 (10) - 30SEP2008 (12) 4. 28SEP2008 (10) - 30SEP2008 (12) 5. 02DEC2008 (75) - 25DEC2008 (98)
Duration of AE	1. 3 2. 3 3. 3 4. 3 5. 24
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY,OTHER 3. OTHER 4. REMEDIAL DRUG THERAPY,OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460044025

Parameter	Value
Outcome of event	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 1. RESOLVED 2. RESOLVED 3. RESOLVED 4. RESOLVED 5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-460044025[2)]	POSTMENOPAUSAL VAGINAL BLEEDING（PT：閉経後出血） 治験担当医は、合併症（高血圧症、月経困難症、手術）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460044028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460044028/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/67/WHITE/HUNGARY/YES
Medical history	Angina pectoris, Appendicectomy, Dyspepsia, Benign prostatic hyperplasia, Nephrolithiasis, Myocardial ischaemia, Nervousness, Osteoarthritis, Osteoarthritis, Phlebitis superficial, Tibia fracture, Varicose vein, Osteoarthritis, Hip surgery, Limb injury
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANDAXIN (MEPROBAMATE), CATAFLAM (DICLOFENAC), NEXIUM (EZOMEPRASOLE), NITRODUR TTS (GLICERYL TRINITRATE), PREDUCTAL MR (TRIMETAZIDINE), QUAMATEL (FAMOTIDINE), RIVOTRIL (CLONAZEPAM)
Adverse Events (AE) Preferred term	1. Angina unstable 2. Chest pain 3. Dyspepsia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 18NOV2008 (8) - 19NOV2008 (9) 2. 24NOV2008 (14) - 11DEC2008 (31) 3. 25NOV2008 (15) - 09MAR2009 (119)
Duration of AE	1. 2 2. 18 3. 105
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460054001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460054001/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/58/WHITE/HUNGARY/YES
Medical history	Hypertension, Non-Hodgkin's lymphoma, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATENOLOL, CHLORTALIDON, CLEXANE
Adverse Events (AE) Preferred term	1. Dizziness 2. Metastases to central nervous system 3. Metastases to lymph nodes
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 27NOV2007 (15) - --------- (.) 2. 30NOV2007 (18) - --------- (.) 3. 02JAN2008 (51) - --------- (.)
Duration of AE	1. . 2. . 3. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460054011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460054011/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/58/WHITE/HUNGARY/YES
Medical history	Depression, Diabetes mellitus, Hypertension, Gastrooesophageal reflux disease, Myocardial ischaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ADEXOR MR, BETALOC ZOK, CIFRAN, DALACIN C, ENOXAPARIN, FRAXIPARINE, INSULIN LANTUS, INSULIN NOVORAPID, LISONORM, MIZAPIN, VASILIP, VENORUTON FORTE
Adverse Events (AE) Preferred term	1. Abscess limb
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 30APR2008 (100) - 27MAY2008 (127)
Duration of AE	1. 28
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460054022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460054022/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/76/WHITE/HUNGARY/YES
Medical history	Atrial fibrillation, Cholecystectomy, Gastrooesophageal reflux disease, Hypertension, Menopause, Cataract operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BETALOC ZOK, DIGOXIN, ENOXAPARIN, LOSEC, TRITACE
Adverse Events (AE) Preferred term	1. Metastases to liver 2. Metastases to lung 3. Metastases to lymph nodes 4. Ovarian cancer metastatic
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/YES/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 07OCT2008 (34) - --------- (.) 2. 30OCT2008 (57) - --------- (.) 3. 30OCT2008 (57) - --------- (.) 4. 14NOV2008 (72) - --------- (.)
Duration of AE	1. . 2. . 3. . 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. NONE 3. NONE 4. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460054022

Parameter	Value
	4. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460064008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/66/WHITE/HUNGARY/YES
Medical history	Angina pectoris, Appendicectomy, Benign prostatic hyperplasia, Renal failure chronic, Diabetes mellitus, Hepatic steatosis, Hip arthroplasty, Hyperlipidaemia, Hypertension, Renal cyst, Subdural haematoma, Calculus ureteric, Post thrombotic syndrome, Periarthritis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMLOZEK, CARDURA XL, CLEXANE, CONCOR, ENOXAPARIN, FUROSEMID, HUMALOG MIX, KALDYUM, MERCKFORMIN, NITROMINT AEROSOL, PREDUCTAL MR, PRITOR PLUS, PROSTAMOL UNO, SICOR
Adverse Events (AE) Preferred term	1. Haematuria 2. Nephrolithiasis 3. Calculus urinary 4. Cardiac failure
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01MAR2008 (17) - 03MAR2008 (19) 2. 02MAR2008 (18) - --------- (.) 3. 12MAR2008 (28) - 12MAR2008 (28) 4. 01JUN2008 (109) - --------- (.)
Duration of AE	1. 3 2. . 3. 1 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064008

Parameter	Value
	4. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-460064008[2)]	MACROSCOPIC HEMATURIA（PT：血尿） 治験担当医は合併症（腎結石、尿路結石）によるものとして、ワルファリンと報告事象との関連性はないと判断した。弊社は、報告事象発現との時間的関連性から、ワルファリンとの因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460064019/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/55/WHITE/HUNGARY/YES
Medical history	Tendon injury, Angina pectoris, Appendicectomy, Cholecystectomy, Collagen disorder, Depression, Foot fracture, Gastrooesophageal reflux disease, Gestational diabetes, Hiatus hernia, Hypertension, Hysterectomy, Muscle atrophy, Panic disorder, Sjogren's syndrome, Tendon rupture, Tonsillectomy, Intervertebral disc disorder, Intervertebral disc operation, Intervertebral disc operation, Haemorrhoid operation, Haemorrhoid operation, Hypercholesterolaemia, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AMARYL, APOFAMOTIDIN, ASPIRIN PROTECT, CLEXANE, CONCOR, CONDROSULF, CONTRAMAL, CONTROLOC, DECHOLEST [ATORVASTATINE, THE INDICATION IS HYPERCHOLESTERINAEMIA], DICLOFENAC-RATIOFARM GEL, ENOXAPARIN, FRONTIN, FUROSEMID, HUMULIN N INSULIN, HUMULIN-N, KALIUM-R, LANTUS INSULIN, MIANSERIN-MERCK, NEODOLPASSE, NITRODERM TTS 5 TRANSDERMAL PATCH, NOACID, QUAMATEL, SEROTOR, TEARS NATURALE, TENOX [THE INGRIDIENT OF TENOX IS AMLODIPINE], TRITACE, TRITACE HCT
Adverse Events (AE) Preferred term	1. Urine ketone body present 2. Phlebitis superficial 3. Adenomatous polyposis coli 4. Diverticulum intestinal 5. Melanosis coli 6. Hyperhomocysteinaemia 7. Back pain 8. Arthralgia 9. Osteoarthritis 10. Osteoarthritis 11. Spinal osteoarthritis 12. Foot deformity 13. Back pain 14. Intervertebral disc protrusion 15. Intervertebral disc protrusion 16. Arthralgia 17. Synovial cyst 18. Cartilage injury 19. Arthralgia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064019

Parameter	Value
	10. MILD/NO/NO/YES
	11. MILD/NO/NO/YES
	12. MILD/NO/NO/YES
	13. MODERATE/NO/NO/YES
	14. MODERATE/NO/NO/YES
	15. SEVERE/NO/YES/YES
	16. MODERATE/NO/NO/YES
	17. MILD/NO/NO/YES
	18. SEVERE/NO/YES/YES
	19. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 06NOV2008 (4) - 07NOV2008 (5)
	2. 01DEC2008 (29) - 08DEC2008 (36)
	3. 02DEC2008 (30) - --------- (.)
	4. 02DEC2008 (30) - --------- (.)
	5. 02DEC2008 (30) - --------- (.)
	6. 05DEC2008 (33) - --------- (.)
	7. 21JAN2009 (80) - 05MAR2009 (123)
	8. 21JAN2009 (80) - 24AUG2009 (295)
	9. 02FEB2009 (92) - --------- (.)
	10. 02FEB2009 (92) - --------- (.)
	11. 02FEB2009 (92) - --------- (.)
	12. 02FEB2009 (92) - --------- (.)
	13. 05MAR2009 (123) - --------- (.)
	14. 11MAR2009 (129) - 30MAR2009 (148)
	15. 30MAR2009 (148) - 10APR2009 (159)
	16. 24AUG2009 (295) - 01SEP2009 (303)
	17. 24AUG2009 (295) - --------- (.)
	18. 29AUG2009 (300) - 01SEP2009 (303)
	19. 01SEP2009 (303) - --------- (.)
Duration of AE	1. 2
	2. 8
	3. .
	4. .
	5. .
	6. .
	7. 44
	8. 216
	9. .
	10. .
	11. .
	12. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064019

Parameter	Value
	13. .
	14. 20
	15. 12
	16. 9
	17. .
	18. 4
	19. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
	17.
	18.
	19.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064019

Parameter	Value
	16.
	17.
	18.
	19.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. NONE
	6. NONE
	7. NONE
	8. NONE
	9. NONE
	10. REMEDIAL DRUG THERAPY
	11. NONE
	12. NONE
	13. REMEDIAL DRUG THERAPY
	14. STUDY DRUG DISCONTINUED AND RESTARTED
	15. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	16. STUDY DRUG DISCONTINUED AND RESTARTED
	17. NONE
	18. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	19. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. UNCHANGED
	5. UNCHANGED
	6. UNCHANGED
	7. WORSENED
	8. WORSENED
	9. UNCHANGED
	10. UNCHANGED
	11. UNCHANGED
	12. UNCHANGED
	13. UNCHANGED
	14. WORSENED
	15. RESOLVED
	16. IMPROVED
	17. UNCHANGED
	18. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064019

Parameter	Value
	19. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460064021/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/21/WHITE/HUNGARY/YES
Medical history	Conjunctival oedema, Haemoglobin increased, Mitral valve prolapse, Thermal burn, Spina bifida
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALGOPYRIN, AZI SANDOZ, BETALOC, FUROSEMIDE, KALIUM-R, MEXALEN, NEOMYCIN EYE DROPS, NO-SPA, NOVOPYRIN, RUTASCORBIN
Adverse Events (AE) Preferred term	1. Joint sprain 2. Influenza 3. Epstein-Barr virus infection 4. Pyrexia 5. Platelet count increased 6. Haemorrhagic ovarian cyst 7. Ovarian cyst
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/YES/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 26JAN2009 (24) - 26FEB2009 (55) 2. 21FEB2009 (50) - 25FEB2009 (54) 3. 21FEB2009 (50) - 09JUL2009 (188) 4. 21FEB2009 (50) - 23FEB2009 (52) 5. 08APR2009 (96) - 09DEC2009 (341) 6. 07AUG2009 (217) - 12AUG2009 (222) 7. 07AUG2009 (217) - 25JAN2010 (388)
Duration of AE	1. 32 2. 5 3. 139 4. 3 5. 246 6. 6 7. 172
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064021

Parameter	Value
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-460064021[2)]	HAEMORRHAGIC LEFT OVARIAN CYST（PT：出血性卵巣嚢胞） 治験担当医は、合併症（卵巣嚢胞）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460064022/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/73/WHITE/HUNGARY/YES
Medical history	Drug hypersensitivity, Diabetes mellitus, Diphtheria, Drug hypersensitivity, Hypertension, Hypertriglyceridaemia, Mastitis, Nephrolithiasis, Phlebitis superficial, Pleurisy, Postmenopause, Hypercholesterolaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID INSULIN, AMARYL, AMOXICILLIN-B, CONTRAMAL, CORENITEC, DECHOLEST, DIAPREL MR, DICLAC, ESTULIC, FROMILID, HRI GARLIC CATARRH ET RHINITIS, HRI-VITALION VITAMINS, LANTUS INSULIN, METFORMIN, NOACID, NORMODIPINE, SIMVOR, TALLITON
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Hypertension 3. Lymph node palpable 4. Diarrhoea 5. Fibrocystic breast disease 6. Helicobacter gastritis 7. Factor V Leiden mutation 8. Back pain 9. Spinal osteoarthritis 10. Intervertebral disc disorder 11. Back pain
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. --FEB2009 (.) - 20MAR2009 (73) 2. 07JAN2009 (1) - 13JAN2009 (7) 3. 07JAN2009 (1) - --------- (.) 4. 10JAN2009 (4) - 22MAR2009 (75) 5. 13JAN2009 (7) - --------- (.) 6. 12MAR2009 (65) - 11MAY2009 (125) 7. 07MAY2009 (121) - --------- (.) 8. 15MAY2009 (129) - --------- (.) 9. 12NOV2009 (310) - --------- (.) 10. 12NOV2009 (310) - --------- (.) 11. 21JAN2010 (380) - --------- (.)
Duration of AE	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064022

Parameter	Value
	2. 7
	3. .
	4. 72
	5. .
	6. 61
	7. .
	8. .
	9. .
	10. .
	11. .
Dose on AE onset	1.
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
Dose status on AE onset	1.
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .
	11. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. NONE
	9. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064022

Parameter	Value
	10. NONE
	11. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED
	7. UNCHANGED
	8. IMPROVED
	9. UNCHANGED
	10. UNCHANGED
	11. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064027

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460064027/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/30/WHITE/HUNGARY/YES
Medical history	Tendonitis, Alanine aminotransferase increased, Ankle fracture, Appendicectomy, Tendon sheath lesion excision, Hyperuricaemia, Rhinitis seasonal, Hepatic steatosis, Contusion, Hypercholesterolaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, CIPROBAY, CLEXANE, ENOXAPARIN, MESULID, NOLICIN, QUAMATEL, XYZAL
Adverse Events (AE) Preferred term	1. Calculus ureteric 2. Hyperchlorhydria 3. Haematuria 4. Contusion 5. Myalgia 6. Rotator cuff syndrome 7. Synovitis 8. Alanine aminotransferase increased 9. Muscle contractions involuntary 10. Hypertransaminasaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/NO 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/YES/NO/NO
Start/stop date of event with relative date	1. 19MAR2009 (1) - 16JUN2009 (90) 2. 28MAR2009 (10) - --------- (.) 3. 01APR2009 (14) - 22JAN2010 (310) 4. 15SEP2009 (181) - 08OCT2009 (204) 5. 15SEP2009 (181) - 08MAR2010 (355) 6. 15OCT2009 (211) - 08MAR2010 (355) 7. 15OCT2009 (211) - 08MAR2010 (355) 8. 10NOV2009 (237) - 16FEB2010 (335) 9. 11DEC2009 (268) - --------- (.) 10. 16FEB2010 (335) - --------- (.)
Duration of AE	1. 90 2. . 3. 297 4. 24 5. 175

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064027

Parameter	Value
	6. 145
	7. 145
	8. 99
	9. .
	10. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED AND RESTARTED
	8. NONE
	9. NONE
	10. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064027

Parameter	Value
	7. RESOLVED
	8. WORSENED
	9. UNCHANGED
	10. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460064028/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/55/WHITE/HUNGARY/YES
Medical history	Appendicitis, Cerebral atrophy, Chronic obstructive pulmonary disease, Pancreatitis chronic, Depression, Hepatic steatosis, Gastric ulcer perforation, Gastrooesophageal reflux disease, Hypertension, Osteoarthritis, Orchidectomy, Pulmonary tuberculosis, Raynaud's phenomenon, Post thrombotic syndrome, Colitis collagenous, Deep vein thrombosis, Lacunar infarction, Hepatic steatosis, Myocardial ischaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMLIPIN, ASTRIX, COAPROVEL, CONCOR, CORDARONE, KREON, LEGALON, PARIET, PREDUCTAL MR, RYTMONORM, SORTIS, XANAX, ZYLORAM
Adverse Events (AE) Preferred term	1. Syncope 2. Atrial fibrillation 3. Atrioventricular block second degree 4. Atrial fibrillation
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/YES/YES 3. MILD/NO/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 01AUG2009 (132) - 01AUG2009 (132) 2. 01AUG2009 (132) - 01AUG2009 (132) 3. 04AUG2009 (135) - --------- (.) 4. 28SEP2009 (190) - --------- (.)
Duration of AE	1. 1 2. 1 3. . 4. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. NONE 4. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460064028

Parameter	Value
	4. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460094010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460094010/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/62/WHITE/HUNGARY/YES
Medical history	Appendicitis, Hypertension, Cardiac failure
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APADEX, ATORIS, CLEXANE, DORMICUM [MIDAZOLAM], EUNOCTIN, IMMUNISATION FOR INFLUENSA, TARKA, ZINNAT
Adverse Events (AE) Preferred term	1. Mixed hyperlipidaemia 2. Synovial cyst 3. Calculus ureteric 4. Urinary tract infection 5. Insomnia 6. Dental caries
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/NO 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 10APR2008 (1) - --------- (.) 2. 28APR2008 (19) - --------- (.) 3. 28MAY2008 (49) - 03JUN2008 (55) 4. 02JUN2008 (54) - 07JUN2008 (59) 5. 02JUN2008 (54) - 03JUN2008 (55) 6. 14NOV2008 (219) - 14NOV2008 (219)
Duration of AE	1. . 2. . 3. 7 4. 6 5. 2 6. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg
Dose status on AE onset	1. . 2. . 3. I 4. I 5. I 6. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460094010

Parameter	Value
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. STUDY DRUG DISCONTINUED AND RESTARTED
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460094025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460094025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/80/WHITE/HUNGARY/YES
Medical history	Osteoarthritis, Depression, Hypertension, Menopause, Osteoporosis, Cerebrovascular accident
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ASASANTIN, CLEXANE, ENOXAPARIN, KETODEX, NUBAIN, PARETIN, PENTOXYL, TRAMADOL, TRIASYN
Adverse Events (AE) Preferred term	1. Femoral neck fracture
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 29JAN2009 (72) - 13FEB2009 (87)
Duration of AE	1. 16
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460094046

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460094046/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/HUNGARY/YES
Medical history	Osteoarthritis, Chronic obstructive pulmonary disease, Diabetes mellitus, Erysipelas, Hypertension, Cerebrovascular accident, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ACTRAPID INSULINE, ALGOPYRIN, AUGMENTIN, BENURON, CARDILOPIN, CHINOTAL, COVEREX AS, COVEREX-AS, DEMALGONIL, DETRALEX, ENOXAPARIN, FRUCTOSOL INFUSION, FURON, KALIUM, KCL, MEFORAL, MESULID, MOVALIS, MYDETON, NATRIUM HEPARIN, NO-SPA, NOACID, NUBAIN, RINGER-LACTATE INFUSION, TEGRETOL CR, TENAXUM, THEOSPIREX, TISASEN, TRAMADOL, ZINACEF
Adverse Events (AE) Preferred term	1. Peripheral embolism 2. Pneumonia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 08JUL2009 (5) - 21JUL2009 (18) 2. 13AUG2009 (41) - 22AUG2009 (50)
Duration of AE	1. 14 2. 10
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460104008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460104008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/66/WHITE/HUNGARY/YES
Medical history	Anaemia, Crohn's disease, Hypertension, Arterial stenosis limb, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ASTRIX, ATORVASTATIN HEXAL, BUDENOFALK, COVEREX AS, DETRALEX, ENOXAPARIN, INFUSION SALSOL, KALIUM CHLORIDE, SALAZOPYRIN EN, SALOFALK [MESALAZINE], SUPPLIN, TALLITON, TRENTAL
Adverse Events (AE) Preferred term	1. Crohn's disease 2. Platelet count decreased 3. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 30DEC2008 (33) - 28FEB2009 (93) 2. 30DEC2008 (33) - 24JAN2009 (58) 3. 22JAN2009 (56) - 24JAN2009 (58)
Duration of AE	1. 61 2. 26 3. 3
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 2. NONE 3. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460104010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460104010/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/59/WHITE/HUNGARY/YES
Medical history	Bronchitis chronic, Hypertension, Lung neoplasm
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APADEX, EXFORGE, FRONTIN, FUROSEMID, NEBILET, TALLITON, TALLITON (CARVEDIOL)
Adverse Events (AE) Preferred term	1. Lung neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 08FEB2009 (23) - 18FEB2009 (33)
Duration of AE	1. 11
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-460104010[4),4),4)]	FATAL ACUTE ENDOCARDITIS（PT：急性心内膜炎） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、病勢進行によるものであり、リバーロキサバンとの因果関係は否定できると考える。 FATAL DISSEMINATION INTRAVASCULAR COAGULATION SYNDROME（PT：播種性血管内凝固） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、腫瘍随伴性の合併症であり、リバーロキサバンとの因果関係は否定できると考える。 FATAL INSUFFICIENTIA CARDIORESPIRATORICA（PT：心肺不全） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、病勢進行によるものであり、リバーロキサバンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。

1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460104014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460104014/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/81/WHITE/HUNGARY/YES
Medical history	Asthma, Carotid artery stenosis, Cataract, Cerebral infarction, Hip arthroplasty, Hypertension, Open angle glaucoma, Trigeminal neuralgia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CARDURA XL, CONCOR, DETRALEX, ENOXAPARIN, EXFORGE, FRONTIN, FURON, INJ. CLEXANE, KALDYUM, MEFORAL, NOACID, OCULOGUTTA HUMASOLAMID, TALLITON, TEGRETOL CR 200, THEOSPIREX
Adverse Events (AE) Preferred term	1. Hypertension 2. Type 2 diabetes mellitus
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12SEP2009 (150) - 23SEP2009 (161) 2. 17SEP2009 (155) - --------- (.)
Duration of AE	1. 12 2. .
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460104016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460104016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/85/WHITE/HUNGARY/YES
Medical history	Breast cancer, Arteriosclerosis, Hypertension, Myocardial ischaemia, Arteriosclerosis obliterans
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BETALOC ZOK, ENOXAPARIN, HYZAAR, NORMODIPINE, RYTMONORM, SYNCUMAR
Adverse Events (AE) Preferred term	1. Atrial fibrillation 2. Sick sinus syndrome
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 06DEC2009 (187) - 06DEC2009 (187) 2. 15DEC2009 (196) - 23DEC2009 (204)
Duration of AE	1. 1 2. 9
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460104021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/460104021/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/HUNGARY/YES
Medical history	Breast cancer, Diabetes mellitus, Hypertension, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALGOPYRIN, AMLOZEK, GLINDIA, GLUCOBAY, INSULIN ACTRAPID, MEGLUCON, SALSOL 0.9% [WATER, NACL], TALLITON, TAXOL, XELODA
Adverse Events (AE) Preferred term	1. Breast cancer metastatic 2. Haemoptysis 3. Hypoglycaemia 4. Metastatic neoplasm
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 01AUG2009 (15) - --------- (.) 2. 01AUG2009 (15) - 06AUG2009 (20) 3. 30OCT2009 (105) - 30OCT2009 (105) 4. 27NOV2009 (133) - 30NOV2009 (136)
Duration of AE	1. . 2. 6 3. 1 4. 4
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. NONE 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 460104021

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500014009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/500014009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/53/WHITE/BRAZIL/YES
Medical history	Anxiety, Body mass index decreased, Crohn's disease, Insomnia, Labyrinthitis, Lactose intolerance, Nephrolithiasis, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AZATHIOPRINE, CALCIUM, CIPROFLOXAXIN, COLECALCIFEROL, DIMETICONE, ENOXAPARIN, FLUCONAZOLE, FLUOXETINE, INFLIXIMAB, METRONIDAZOLE, PARACETAMOL, PLASM, PREDNISONE, RANITIDINE, WARFARIN
Adverse Events (AE) Preferred term	1. Plantar fasciitis 2. Anaemia 3. Crohn's disease 4. Oesophageal candidiasis 5. Crohn's disease 6. Phlebitis 7. Crohn's disease 8. Phlebitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MODERATE/NO/YES/NO 8. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 23JUL2009 (21) - --DEC2009 (.) 2. 02SEP2009 (62) - --------- (.) 3. 02SEP2009 (62) - 08SEP2009 (68) 4. 04SEP2009 (64) - 18SEP2009 (78) 5. 27NOV2009 (148) - 04DEC2009 (155) 6. 01DEC2009 (152) - 10DEC2009 (161) 7. 04JAN2010 (186) - 12JAN2010 (194) 8. 24JAN2010 (206) - --------- (.)
Duration of AE	1. . 2. . 3. 7 4. 15 5. 8 6. 10 7. 9 8. .
Dose on AE onset	1. 2.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500014009

Parameter	Value
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500024005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/500024005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/72/BLACK/BRAZIL/YES
Medical history	Anaemia, Hysterectomy, Constipation, Uterine cancer, Blindness unilateral
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Generalised oedema 2. Anaemia 3. Hypoalbuminaemia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 15FEB2009 (164) - 27FEB2009 (176) 2. 03MAR2009 (180) - --------- (.) 3. 03MAR2009 (180) - --------- (.)
Duration of AE	1. 13 2. . 3. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. NONE 2. OTHER 3. OTHER
Outcome of event	1. RESOLVED 2. UNCHANGED 3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500024008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/500024008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/56/WHITE/BRAZIL/YES
Medical history	Hypertension, Ischaemic stroke
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CAPTOPRIL, WARFARIN
Adverse Events (AE) Preferred term	1. Pulmonary embolism 2. Nausea 3. Anxiety 4. Pancreatic carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/NO 3. MILD/NO/NO/NO 4. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 21FEB2009 (44) - 24MAR2009 (75) 2. 23MAR2009 (74) - 24MAR2009 (75) 3. 23MAR2009 (74) - 23MAR2009 (74) 4. 24MAR2009 (75) - --------- (.)
Duration of AE	1. 32 2. 2 3. 1 4. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. F 2. F 3. F 4. F
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. DEATH 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500024008

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500034023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/500034023/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/83/WHITE/BRAZIL/YES
Medical history	Chronic obstructive pulmonary disease, Hypercholesterolaemia, Hypertension, Inguinal hernia, Meningitis, Myasthenia gravis, Pneumonia, Squamous cell carcinoma of skin, Squamous cell carcinoma of skin, Lumbar vertebral fracture, Prostatic operation, Prostatic operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATROVENT, BUDECORT, CALCORT, CALTRATE [CALCIUM CARBONATE, COLECALCIFEROL], CENTRUM, CLAVULIN, DEFLAZACORT, FLUIMICIL, FLUIR, LEUKERAN, LEVOFLOXACINO, LOSARTAN, MESTINON, MIFLASONA, MYTELASE, OMEPRAZOLE, PAMELOR, ROCALTROL, SIMVASTATIN
Adverse Events (AE) Preferred term	1. Bronchopneumonia 2. Dizziness 3. Tremor 4. Rectal haemorrhage 5. Haemoptysis 6. Tracheobronchitis 7. Fall 8. Pneumonia 9. Hyperglycaemia 10. Pyrexia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/YES/NO/YES 5. MODERATE/YES/NO/YES 6. SEVERE/NO/YES/YES 7. SEVERE/NO/NO/YES 8. SEVERE/NO/YES/NO 9. MILD/NO/NO/NO 10. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 21SEP2009 (25) - 30SEP2009 (34) 2. 12OCT2009 (46) - 12OCT2009 (46) 3. 12OCT2009 (46) - 12OCT2009 (46) 4. 01NOV2009 (66) - 01NOV2009 (66) 5. 10DEC2009 (105) - 12DEC2009 (107) 6. 10DEC2009 (105) - 12DEC2009 (107) 7. 24JAN2010 (150) - 24JAN2010 (150) 8. 28FEB2010 (185) - 07MAR2010 (192) 9. 01MAR2010 (186) - 01MAR2010 (186) 10. 01MAR2010 (186) - 01MAR2010 (186)
Duration of AE	1. 10 2. 1 3. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500034023

Parameter	Value
	4. 1
	5. 3
	6. 3
	7. 1
	8. 8
	9. 1
	10. 1
Dose on AE onset	1. 20 mg
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. F
	9. F
	10. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500034023

Parameter	Value
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500084005

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/500084005/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/WHITE/BRAZIL/YES
Medical history	Anaemia, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CAFFEINE, CEFTRIAXONE, CLARITHROMYCIN, DEXAMETASONA, DIPIRONA, FUROSEMIDE, KETOPROFEN, MICOSTATIN, N-ACETYLCYSTEINE, OMEPRAZOL, PLASIL, TAZOCIN, TRAMADOL
Adverse Events (AE) Preferred term	1. Pyrexia 2. Pneumonia 3. Dermatitis 4. Pleural effusion 5. Breast cancer 6. Pleural effusion 7. Nausea 8. Haemoptysis 9. Pleural effusion 10. Tachycardia 11. Alanine aminotransferase increased 12. Aspartate aminotransferase increased 13. Oral candidiasis 14. Respiratory failure
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MILD/NO/NO/YES 14. SEVERE/NO/NO/YES
Start/stop date of event with relative date	1. 21JAN2009 (4) - 21JAN2009 (4) 2. 21JAN2009 (4) - --------- (.) 3. 21JAN2009 (4) - --------- (.) 4. 22JAN2009 (5) - 22JAN2009 (5) 5. 22JAN2009 (5) - 11FEB2009 (25) 6. 23JAN2009 (6) - --------- (.) 7. 26JAN2009 (9) - 30JAN2009 (13) 8. 28JAN2009 (11) - 28JAN2009 (11)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500084005

Parameter	Value
	9. 28JAN2009 (11) - --------- (.)
	10. 02FEB2009 (16) - --------- (.)
	11. 02FEB2009 (16) - --------- (.)
	12. 02FEB2009 (16) - --------- (.)
	13. 06FEB2009 (20) - --------- (.)
	14. 10FEB2009 (24) - --------- (.)
Duration of AE	1. 1
	2. .
	3. .
	4. 1
	5. 21
	6. .
	7. 5
	8. 1
	9. .
	10. .
	11. .
	12. .
	13. .
	14. .
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 15 mg
	9. 15 mg
	10. 15 mg
	11. 15 mg
	12. 15 mg
	13. 15 mg
	14. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500084005

Parameter	Value
	8. .
	9. .
	10. .
	11. .
	12. .
	13. .
	14. F
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. OTHER
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. OTHER
	10. NONE
	11. NONE
	12. NONE
	13. REMEDIAL DRUG THERAPY
	14. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. INSUFFICIENT FOLLOW-UP
	4. WORSENED
	5. DEATH
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED
	9. UNCHANGED
	10. UNCHANGED
	11. UNCHANGED
	12. UNCHANGED
	13. INSUFFICIENT FOLLOW-UP

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500084005

Parameter	Value
	14. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500114001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/500114001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/76/WHITE/BRAZIL/YES
Medical history	Abdominal pain, Anaemia, Arrhythmia, Breast neoplasm, Cervix carcinoma, Diverticulitis, Oesophagitis, Gastritis, Hiatus hernia, Hypertension, Leukocytosis, Lymphoedema, Lymphopenia, Bladder cancer, Nausea, Renal neoplasm, Diarrhoea
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AAS, ACFOL, BUSCOPAN COMPOSTO, CIPROFLOXACIN, CITONEURIN, CODEINE PHOSPHATE+PARACETAMOL, CODEINE PHOSPHATO+PARACETAMOL, DERMODEX, DIVELOL, ENOXAPARIN, LASIX, LOSEC, NOVALGINA, PLASIL, RENITEC, WARFARIN, ZOFRAN
Adverse Events (AE) Preferred term	1. Pain in extremity 2. Hypovitaminosis 3. Cough 4. Therapeutic agent toxicity 5. Pulmonary embolism 6. Gingival bleeding
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/YES/YES/YES 5. SEVERE/NO/YES/NO 6. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 06SEP2008 (4) - 06SEP2008 (4) 2. 11SEP2008 (9) - --------- (.) 3. 11SEP2008 (9) - --------- (.) 4. 17SEP2008 (15) - --------- (.) 5. 20SEP2008 (18) - 20SEP2008 (18) 6. 20SEP2008 (18) - 20SEP2008 (18)
Duration of AE	1. 1 2. . 3. . 4. . 5. 1 6. 1
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 500114001

Parameter	Value
	4.
	5.
	6.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. UNCHANGED
	4. UNCHANGED
	5. DEATH
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-500114001[1)]	CUMARIC POISONING（PT：各種物質毒性） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、アセノクマロールとの関連性は否定できないが、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540014003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540014003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/64/ASIAN/CHINA/YES
Medical history	Gout, Renal cyst
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, DALTEPARIN, ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Liver function test abnormal 2. Melaena 3. Upper gastrointestinal haemorrhage 4. Duodenal ulcer 5. Haemorrhagic anaemia 6. Gastritis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/NO/YES 3. SEVERE/YES/YES/NO 4. SEVERE/NO/YES/NO 5. MODERATE/NO/YES/NO 6. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 21AUG2008 (13) - 01SEP2008 (24) 2. 25AUG2008 (17) - 29AUG2008 (21) 3. 28AUG2008 (20) - 29AUG2008 (21) 4. 28AUG2008 (20) - 25SEP2008 (48) 5. 28AUG2008 (20) - 25SEP2008 (48) 6. 01SEP2008 (24) - --------- (.)
Duration of AE	1. 12 2. 5 3. 2 4. 29 5. 29 6. .
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540014003

Parameter	Value
Action taken	1. OTHER
	2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED PERMANENTLY
	6. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-540014003[1),2)]	BLEEDING OF UPPER GASTROINTESTINAL TRACT（PT：上部消化管出血） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。 HEMORRHAGIC ANEMIA（PT：出血性貧血） 治験担当医はワルファリン/アセノクマロールと報告事象との関連性がないと判断した。弊社は、ワルファリン/アセノクマロール投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024004/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/51/ASIAN/CHINA/YES
Medical history	Diabetes mellitus, Pulmonary tuberculosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	EXTRACT OF GINKGO BILOBA LEAVES
Adverse Events (AE) Preferred term	1. Haemoptysis 2. Pulmonary mass
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 13JUL2008 (3) - 13JUL2008 (3) 2. 14JUL2008 (4) - --------- (.)
Duration of AE	1. 1 2. .
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. F 2. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY 2. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024013/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/75/ASIAN/CHINA/YES
Medical history	Hypertension, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	10%CALCIUM GLUCONATE INJECTION, AESCUVEN FORTE, AVELOX, BENZYLPENICILLIN, BETALOC, CEFUROXIME SODIUM, CEFUROXINE, CLARITYNE, DIHYDROCHLOROTHIAZIDE, FAMOTIDINE, FUROSEMIDE, METOCLOPRAMIDE, MIRABILITE, NIMODIPINE, POTASSIUM CHLORIDE SUSTAINED-RELEASE TABLETS, SPIRONLACTONE
Adverse Events (AE) Preferred term	1. Abdominal distension 2. Hypersensitivity 3. Pneumonia 4. Pneumonia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/YES/YES 4. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 11OCT2008 (5) - 17OCT2008 (11) 2. 16OCT2008 (10) - 17OCT2008 (11) 3. 17DEC2008 (72) - 30DEC2008 (85) 4. 03FEB2009 (120) - 17FEB2009 (134)
Duration of AE	1. 7 2. 2 3. 14 4. 15
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. I
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024013

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024023/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/81/ASIAN/CHINA/YES
Medical history	Cerebral infarction, Colon cancer, Cholelithiasis, Hypertension, Myocardial infarction, Coronary artery disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, DAHUANG SODIUM BICARBON [CONTAINS DAHUANG(TCM), SODIUM BICARBONATE, OLEUM MENTHA, DOXIFLURIDINE CAPSULES, EXTRACT OF GINKGO BILOBA LEAVES, FUROSEMIDE, HYDROCHLOROTHIAZIDE, KANGSAIDI CAPSULE(TCM), NIMODIPINE TABLETS, PROPAFENONE HYDROCHLORIDE, SPIRONOLACTONUM
Adverse Events (AE) Preferred term	1. Hepatic mass
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 22JAN2009 (3) - --------- (.)
Duration of AE	1. .
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. NONE
Outcome of event	1. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/86/ASIAN/CHINA/YES
Medical history	Anaemia, Bronchitis, Constipation, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, AMBROXOL, AMBROXOL HYDROCHLORIDE FOR INJECTION, CEFUROXIME SODIUM, COMPOUND GLYCYRRHIZA ORAL SOLUTION, ENOXAPARIN, EXTRACT OF GINKGO BILOBA LEAVES, FAMOTIDINE, FERROUS SUCCINATE, FUROSEMIDE, GLYCERINE ENEMA, MIRABILITE, PHENOLPHTHALEIN, SPIRONOLACTONUM, TONGMAIHUASHUAN CAPSULE(CTM) [TREATMENT OF DEEP VEIN THROMBOSIS], VITAMIN K1, WARFARIN
Adverse Events (AE) Preferred term	1. Occult blood 2. Upper gastrointestinal haemorrhage 3. Intestinal mass 4. Hypertension
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/NO/YES/NO 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 15FEB2009 (3) - 20FEB2009 (8) 2. 20FEB2009 (8) - 20FEB2009 (8) 3. 27FEB2009 (15) - --------- (.) 4. 12MAR2009 (28) - 12MAR2009 (28)
Duration of AE	1. 6 2. 1 3. . 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY,OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024025

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024030

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024030/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/87/ASIAN/CHINA/YES
Medical history	Anaemia, Joint arthroplasty, Atrial fibrillation, Cerebral infarction, Coronary artery disease, Femur fracture, Hypoproteinaemia, Axillary mass, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUMIN, CEFUROXINE SODIUM, DEXAMETHASONE, DIAZEPAM, ENOXAPARIN, HYDROCHLOROTHIAZIDE, METOCLOPRAMIDE, NOVAMIN, SPIRONOLACTONE, VITAMIN K1, WARFARIN
Adverse Events (AE) Preferred term	1. Blood alkaline phosphatase increased 2. Abdominal distension 3. Prothrombin time prolonged 4. Intestinal haemorrhage 5. Metabolic acidosis 6. Hyperbilirubinaemia 7. Hyponatraemia 8. Oliguria 9. Pyrexia 10. Platelet count decreased 11. Hyponatraemia 12. Metabolic acidosis 13. Multi-organ failure
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/NO 2. MILD/NO/NO/YES 3. MODERATE/YES/NO/YES 4. MODERATE/YES/NO/YES 5. SEVERE/NO/NO/YES 6. MODERATE/YES/NO/YES 7. SEVERE/NO/NO/YES 8. MODERATE/NO/NO/NO 9. MILD/NO/NO/NO 10. SEVERE/YES/NO/NO 11. SEVERE/NO/NO/NO 12. SEVERE/NO/NO/NO 13. SEVERE/YES/YES/NO
Start/stop date of event with relative date	1. 10MAR2009 (1) - --------- (.) 2. 11MAR2009 (2) - 13MAR2009 (4) 3. 14MAR2009 (5) - 15MAR2009 (6) 4. 17MAR2009 (8) - --------- (.) 5. 17MAR2009 (8) - 18MAR2009 (9) 6. 17MAR2009 (8) - --------- (.) 7. 17MAR2009 (8) - 18MAR2009 (9) 8. 19MAR2009 (10) - --------- (.)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024030

Parameter	Value
	9. 20MAR2009 (11) - 20MAR2009 (11)
	10. 20MAR2009 (11) - --------- (.)
	11. 20MAR2009 (11) - 22MAR2009 (13)
	12. 20MAR2009 (11) - --------- (.)
	13. 23MAR2009 (14) - 23MAR2009 (14)
Duration of AE	1. .
	2. 3
	3. 2
	4. .
	5. 2
	6. .
	7. 2
	8. .
	9. 1
	10. .
	11. 3
	12. .
	13. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024030

Parameter	Value
	11.
	12.
	13.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP
	2. RESOLVED
	3. RESOLVED
	4. UNCHANGED
	5. RESOLVED
	6. INSUFFICIENT FOLLOW-UP
	7. RESOLVED
	8. UNCHANGED
	9. RESOLVED
	10. INSUFFICIENT FOLLOW-UP
	11. RESOLVED
	12. INSUFFICIENT FOLLOW-UP
	13. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-540024030[1)]	FATAL MULTIPLE ORGAN FAILURE（PT：多臓器不全） 治験担当医はエノキサパリン及びワルファリンと報告事象との関連性があると判断した。弊社は、患者の治療拒否が主因であり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

被験者番号：11702-540024030

死亡に至るまでの経過

被験者は 87 歳、アジア人女性。2009 年 3 月 10 日に深部静脈血栓症と診断され、同日エノキサパリン（90mg）／用量調節ワルファリンの投与を開始した。

2009 年 3 月 14 日、被験者はプロトロンビン時間延長（PT 延長）を呈し、本事象により被験者の治験は中止された。治験責任（分担）医師は、本事象の重症度は中等度で、治験薬との因果関係は「あり」と判断した。同日、APTT（活性化部分トロンボプラスチン時間）が 75.70 秒まで延長した。本事象に対して phytomenadione が投与された。2009 年 3 月 15 日、治験薬の投与は中止された。同日、APTT は基準値まで戻り（40.30 秒）、本事象は回復した。

2009 年 3 月 17 日、被験者は腸出血（出血：胃腸出血）を発現した。本事象は非重篤な有害事象として報告された。治験責任（分担）医師は、本事象の重症度は中等度で、治験薬との因果関係は「あり」と判断した。2009 年 3 月 10 日ヘモグロビン値は 8.8g/dL であったが、2009 年 3 月 17 日及び 3 月 20 日には 7.6g/dL に低下した。2009 年 3 月 20 日、供血者の濃厚赤血球が輸血された（200mL×1 回）。本事象に対して famotidine 及び omeprazole が投与された。

CIAC は、非重篤な事象である腸出血（出血：胃腸出血）を「重大な出血事象」と判定した。

2009 年 3 月 20 日、被験者は血小板数減少（血小板減少）を発現した。治験責任（分担）医師は、本事象を非重篤な事象として報告し、重症度は高度で、治験薬との因果関係は「あり」と判断した。被験者の血小板数は、2009 年 3 月 10 日は基準値内（260×10^9/L）であり、3 月 17 日に低下はしたが依然基準値内（105×10^9/L）であったが、2009 年 3 月 20 日に 32×10^9/L に減少した。

2009 年 3 月 23 日、被験者は多臓器不全（多臓器不全）を発現した。本事象により被験者は死亡に至ったため重篤な事象とされた。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「あり」と判断した。また、主に被験者が積極的な治療や検査を拒否したことから消化管出血が起こり、そのカスケード反応の結果として、多臓器不全が発現したと判断した。多臓器不全には、心不全、呼吸器不全の他に、代謝性アシドーシス、低ナトリウム血症、発熱（その他の非重篤な有害事象として報告）、臨床検査値異常（血小板数減少 32×10^9/L など）が含まれた。被験者は衰弱し、血圧は 70/50mmHg まで低下、心拍数も 65bpm から 0bpm（心停止）まで低下した。多臓器不全（多臓器不全）に対する治療として dopamine が投与された。2009 年 3 月 23 日、本事象により被験者は死亡に至った。剖検は実施されなかった。

CIAC は死亡原因を出血と判定した。

Laboratory Parameter	**Normal Range**	**Date**	**Result**	**Date**	**Result**	**Date**	**Result**
Hemoglobin	11.0-17.0 g/dL	10 Mar 2009	**8.8 g/dL (L)**	20 Mar 2009	**7.6 g/dL (L)**	17 Mar 2010	**7.6 g/dL (L)**
Platelets	100-400 giga/L	10 Mar 2009	260 giga/L	20 Mar 2009	**32 giga/L (L)**	17 Mar 2010	105 giga/L
Alkaline Phosphatase	36-118 U/L	10 Mar 2009	**319 U/L (H)**	17 Mar 2009	**285 U/L (H)**		

Laboratory Parameter	Normal Range	Date	Result	Date	Result	Date	Result
Amylase	28-100 U/L	10 Mar 2009	**12 U/L (L)**	17 Mar 2009	**20 U/L (L)**		
Bilirubin, Direct	0.10-0.32 mg/dL	10 Mar 2009	**0.38 mg/dL (H)**	17 Mar 2009	**1.58 mg/dL (H)**		
Bilirubin, Total	0.22-1.28 mg/dL	10 Mar 2009	0.69 mg/dL	17 Mar 2009	**2.17 mg/dL (H)**		
SGOT/AST	11-37 U/L	10 Mar 2009	28 U/L	17 Mar 2009	27 U/L		
SGPT/ALT	8-43 U/L *Local: 0-75 U/L	10 Mar 2009	10 U/L*	10 Mar 2009	**6 U/L (L)**	17 Mar 2009	13 U/L
Prothrombin Time (PT)		10 Mar 2009	**19.90 S (H)**				
PT Ratio		10 Mar 2009	**0.49 (L)**				
PT, INR	0.9-1.2	10 Mar 2009	**1.8 (H)**				

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024033

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024033/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/75/ASIAN/CHINA/YES
Medical history	Anaemia, Cholangitis, Hypothyroidism, Choledochoenterostomy, Choledocholithotomy, Bile duct T-tube insertion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE TABLETS, ANISODAMINE, CEFTRIAXONE, CEFUROXIME SODIUM, DANNING TABLETS (TCM), ENOXAPARIN, EXTRACT OF GINKGO BILOBA LEAVES, GABEXATE MESILATE, GLYCERINE ENEMA, HYDROCHLOROTHIAZIDE, LACTULOSE ORAL SOLUTION, LEVOTHYROXIN SODIUM, MAREN CAPSULE, MOXIFLOXACIN HYDROCHLORIDE TABLETS, OMEPRAZOLE, POTASSIUM CHLORIDE, SHUDAN MIXTURE [HIRUDIN, ROOTS OF CHINESE ANGELICA & SALVIA MILTRORRHIZA, ETC.], SPIRONOLACTONE, TONGMAIHUASHUAN CAPSULE [VIRGATE+CAPILLARY WORMWOOD,DESMODIUM,CHINESE RHUBARB ET, WARFARIN
Adverse Events (AE) Preferred term	1. Cholangitis 2. Constipation 3. Jaundice cholestatic 4. Hepatic failure
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 16APR2009 (9) - 17APR2009 (10) 2. 16APR2009 (9) - 21APR2009 (14) 3. 26APR2009 (19) - --------- (.) 4. 30MAY2009 (53) - 31MAY2009 (54)
Duration of AE	1. 2 2. 6 3. . 4. 2
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024033

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024036

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540024036/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/61/ASIAN/CHINA/YES
Medical history	Bronchitis chronic, Hypertension, Inguinal hernia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	?-GLOBULIN [GAMMA-GLOBULIN], AESCUVEN FORTE, AMBROXOL, AMBROXOL HYDROCHLORIDE FOR INJECTION, AMLODIPINE BESYLATE, ANISODAMINE, AZTREONAM, CEFMINOX SODIUM, CEFOTAXIME SODIUM FOR INJECTION, CEFUROXIME SODIUM, CITRULLI DEGELATINATUM [CHINESE HERB: CALABASH, WATERMELON PEEL, GLAUBER`S SALT., COMPOUND METHOXYPHENAMINE CAPSULES, DIPROPHYLLINE, DOMPERIDONE, ERYTHROPOIETIN, EXTRACT OF GINKGO BILOBA LEAVES, FAMOTIDINE, FERROIDS, FLURBIPROFEN AXETIL INJECTION, FRAXIPARINE, GLYCERINE ENEMA, HEMOCOAGULASE FOR INJECTION, HUMAN SERUM ALBUMIN, HYDROCHLOROTHIAZIDE, IMIPENEM-CILASTATIN SODIUM, INDOMETHACIN SUPPOSITORIES, JAVA BRUCEA FRUIT FAT EMULSIONS INJECTION, LACTULOSE, LEUCOGEN, METOCLOPRAMIDE, MIRABILITE, MYRTOL STANDARDIZED ENTERIC CAPSULES, NETILMICIN, NIFEDIPINE, NITRAZEPAMUM, NYSTATINDIHYDRATE, PHENERGAN, PHENOLPHTHALEIN TABLETS, RECOMBINANT HUMAN GRANULOCYTE COLONY STIMULATING FACTOR INJECTION, REDUCED GLUTATHIONE FOR INJECTION (TAD), RESERPINE, SCOPOLAMINE, SELENIOUS YEAST TABLETS, SHENG MAI YIN (TCM), SPIRONOLACTONE, SULPERAZONE, TRAMAL, TRIMEBUTINE MALEATE TABLETS, VANCOCIN
Adverse Events (AE) Preferred term	1. Lung neoplasm malignant 2. Leukopenia 3. Deficiency anaemia 4. Pyrexia 5. Hepatic function abnormal
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 19MAY2009 (21) - --------- (.) 2. 20MAY2009 (22) - 29JUN2009 (62) 3. 10JUN2009 (43) - --------- (.) 4. 14JUN2009 (47) - 21JUN2009 (54) 5. 15JUN2009 (48) - 29JUN2009 (62)
Duration of AE	1. . 2. 41 3. . 4. 8 5. 15
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540024036

Parameter	Value
	5. 20 mg
Dose status on AE onset	1. .
	2. .
	3. I
	4. I
	5. I
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540034001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540034001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/52/ASIAN/CHINA/YES
Medical history	Duodenal ulcer, Menopause, Productive cough
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AN YUAN HE JI [EXPECTORANT HERBAL PREPARATION], ENOXAPARIN, MUCOSOLVAN, WARFARIN, YAN YAN FANG [EXPECTORANT HERBAL PREPARATION]
Adverse Events (AE) Preferred term	1. Lung neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 21JAN2009 (7) - 10FEB2009 (27)
Duration of AE	1. 21
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540034007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540034007/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/52/ASIAN/CHINA/YES
Medical history	Cervix carcinoma, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, ALPROSTADIL, ATENADON, BATROXOBIN-TOBISHI, DEXTRAN-40, ENOXAPARIN, GLYCERINEENEMA, LI TI NENG [HERBAL PREP. FOR IMMUNITY ENHANCEMENT], WARFARIN
Adverse Events (AE) Preferred term	1. Cervix carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 22MAY2009 (80) - 22MAY2009 (80)
Duration of AE	1. 1
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540044003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540044003/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/64/ASIAN/CHINA/YES
Medical history	Carcinoembryonic antigen increased, Coronary artery disease, Menopause, Upper respiratory tract infection, Tumour marker increased
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AIDI INJECTION (TCM), AMBROXOL HYDROCHLORIDE TABLETS, AMOXICILLIN, BETA-BLOCKER, CARBOPLATIN INJECTION, CEFIXIME CAPSULE, CIMETIDINE TABLETS, COMPOUND PLATYCODON TABLETS(TRADITIONAL CHINESE MEDICINE), DACTYLICAPNOS RAT TABLET(TCM), DEXAMETHASONE ACETATE TABLETS, DIAZEPAM, GANMAOQINGRECHONGJI(TRADITIONAL CHINESE MEDICINE), GRANISETRON HYDROCHLORIDE INJECTION, IRESSA, KANG LAITE INJECTION(TCM), LOW MOLECULAR DEXTRAN, METOCLOPRAMIDE, NAFCILLIN SODIUM, ONDANSETRON HYDROCHLORIDE TABLETS, PACLITAXEL INJECTION, RECOMBINANT HUMAN GRANULOCYTE COLONY STIMULATING FACTOR, SHEN LIAN CAPSULE, THYMOPENTIN, XINHUANGPIAN(TRADITIONAL CHINESE MEDICINE), ZONG'ANHEJI(TRADITIONAL CHINESE MEDICINE)
Adverse Events (AE) Preferred term	1. Lung cancer metastatic
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 09JAN2009 (24) - --------- (.)
Duration of AE	1. .
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. I
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540044007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540044007/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/59/ASIAN/CHINA/YES
Medical history	Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, ALPROSTADIL FAT EMULSIOM, CALTRATE [CALCIUM,VITAMIN D], CARBAZOCHROME SODIUM SULFONATE, CARVEDILOL, CEFOTIAM HYDROCHLORIDE, CEFOTIAM HYDROCHLRIDE, CHLORPHENIRAMINE, CINEPAZIDE MALEATE, DALTEPARIN SODIUM, DIAZEPAM, DOMPERIDONE, ENALAPRIL MALEATE, ENOXAPARIN, ENOXAPARIN SUDIUM, ERYTHROPOIETINL, FELODIPINE SUSTAIND, GUSHUKANGKELI(CHINESE TRADIONAL MEDICINE), ISOSORBIDE MONONITRATE, METHYLPREDNISOLONE, METOPROLOL TARTRATE, OMEPRAZOLE, SODIUM AESCINATE, SODIUM BICARBONATE, TERAZOSIN HYDROCHLORIDE, TORASEMIDE, TRIMETAZIDINE HYDROCHLORIDE, ULINASTAIN, WARFARIN, XIN QING NING(CHINESE TRADITIONAL MEDCINE), XUEBIJING(CHINESE TRADIONAL MEDCINE)
Adverse Events (AE) Preferred term	1. Dyspepsia 2. Rash 3. Intervertebral disc protrusion 4. Coronary artery disease 5. Retroperitoneal fibrosis 6. Restlessness 7. Nephrogenic anaemia 8. Pyrexia 9. Dizziness
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 20FEB2009 (1) - 06MAR2009 (15) 2. 22FEB2009 (3) - 06MAR2009 (15) 3. 03MAR2009 (12) - --------- (.) 4. 05MAR2009 (14) - --------- (.) 5. 21MAR2009 (30) - --------- (.) 6. 26MAR2009 (35) - 17APR2009 (57) 7. 27MAR2009 (36) - --------- (.) 8. 02APR2009 (42) - 04APR2009 (44) 9. 21APR2009 (61) - 21APR2009 (61)
Duration of AE	1. 15 2. 13

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540044007

Parameter	Value
	3. .
	4. .
	5. .
	6. 23
	7. .
	8. 3
	9. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. NONE
	9. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. IMPROVED
	5. IMPROVED
	6. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540044007

Parameter	Value
	7. IMPROVED
	8. RESOLVED
	9. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540064016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/62/ASIAN/CHINA/YES
Medical history	Anaemia, Hypertension, Metastases to liver, White blood cell count increased
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE TABLETS, BAILING CAPSULE(TCM), CAPTOPRIL TABLETS, CLINDAMYCIN HYDROCHIORIDE LNJECTION, COMPOUND CODEINE PHOSPHATE SYRUP, COMPOUND DANSHEN DRIPPING PILL(TCM), DIAZEPAMTABLETS, EFLOXACIN INJECTION, ENOXAPARIN, ESTAZOLAM TABLETS, FELODIPINE SUSTAINED RELEASE TABLETS, FERROUS SACCHAROSE INJECTION, FUROSEMIDE INJECTION, GINKGO LEAF EXTRACT AND DIPYRIDAMOLE INJECTION(TCM) [TREATMENT OF DEEP VEIN THRO, GLUCUROLACTONE TABLETS, KUDIEZI INJECTION(TCM) [TREATNENT OF DEEP VEIN THROMBOSIS], LOBELINE HYDROCHLORIDE INJECTION, MELILOTUS EXTRACT TABLETS, METOPROLOL TARTRATE TABLETS, MOTILIUM TABLETS, NUODIKANG CAPSULES, PANCREATIC KININOGENASE TABLETS, REDUCED GLUTATHIONE FOR INJECTION, SODIUM FUSIDATE FOR INJECTION, TRIAZOLAM TABLETS, VITAMIN K1, WARFARIN
Adverse Events (AE) Preferred term	1. Blood alkaline phosphatase increased 2. Cough 3. Tachycardia 4. Pyrexia 5. Petechiae 6. Insomnia 7. Abdominal distension 8. Malnutrition 9. Metastases to liver
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/YES/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MODERATE/NO/NO/YES 9. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 27FEB2009 (1) - --------- (.) 2. 06MAR2009 (8) - --------- (.) 3. 06MAR2009 (8) - --------- (.) 4. 09MAR2009 (11) - 13MAR2009 (15) 5. 11MAR2009 (13) - --------- (.) 6. 13MAR2009 (15) - --------- (.) 7. 21MAR2009 (23) - --------- (.) 8. 21MAR2009 (23) - --------- (.) 9. 27MAR2009 (29) - 19APR2009 (52)
Duration of AE	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064016

Parameter	Value
	2. .
	3. .
	4. 5
	5. .
	6. .
	7. .
	8. .
	9. 24
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. DOSE OF STUDY DRUG REDUCED
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. UNCHANGED
	4. RESOLVED
	5. UNCHANGED
	6. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064016

Parameter	Value
	7. IMPROVED
	8. UNCHANGED
	9. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540064018/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/24/ASIAN/CHINA/YES
Medical history	Caesarean section, Cervix carcinoma, Hysterectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AIDI INJECTION, BICYCLOL TABLETS, CARBOPLATIN INJECTION, CHUANQING STERILE POWDER FOR INJECTION(TCM), COMETIDINE INJECTION, DEXAMETHASONE SODIUM PHOSPHATE INJECTION, DEXAMETHASONE TABLETS, DIPHENHYDRAMINE HYDROCHLORIDE INJECTION, GINKGO LEAF EXTRACT AND DIPYRIDAMOLE INJECTION(TCM) [TREATMENT OF DEEP VEIN THRO, JIANPIYISHENKELI (TCM), PACLITAXEL INJECTION, TRIPISETRON HYDROCHLORIDE INJECTION, UBENIMEX CAPSULES, WARFARIN
Adverse Events (AE) Preferred term	1. Dermatitis allergic 2. Dyspnoea 3. Metastatic neoplasm 4. Metastatic neoplasm
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MODERATE/YES/NO/YES 3. SEVERE/NO/NO/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 21MAR2009 (11) - 31MAR2009 (21) 2. 21MAR2009 (11) - 31MAR2009 (21) 3. 27MAY2009 (78) - 06JUL2009 (118) 4. 06JUL2009 (118) - --------- (.)
Duration of AE	1. 11 2. 11 3. 41 4. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. I
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. STUDY DRUG DISCONTINUED AND RESTARTED 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. WORSENED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064018

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064024

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540064024/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/74/ASIAN/CHINA/YES
Medical history	Anaemia, Hypertension, Hip arthroplasty
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, FERROUS SACCHAROSE INJECTION, GINKGO DIPYRIDOLUM INJECTION(TCM), LIGUSTRAZINE HYDROCHLORIDE FOR INJECTION(TCM), PIPERACILLIN SODIUM AND TAZOBACTAM SODIUM FOR INJECTION, WARFARIN
Adverse Events (AE) Preferred term	1. Rectal cancer 2. Haematochezia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 16APR2009 (1) - --------- (.) 2. 17APR2009 (2) - 29MAY2009 (44)
Duration of AE	1. . 2. 43
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER 2. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. UNCHANGED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064035

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540064035/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/51/ASIAN/CHINA/YES
Medical history	Anaemia, Contusion, Carotid artery stenosis, Hypokalaemia, Intracranial aneurysm, Leukopenia, Menopause, Myocarditis, Intracranial aneurysm, Subarachnoid haemorrhage, Traumatic brain injury
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE TABLETS, CALCIUM DOBESILATE CAPSULES, COMPOUND NAPROXEN SUPPOSITORIES, EL ASPIRIN ENTERIC-COATED TABLETS, ENOXAPARIN, FOLIC ACID TABLETS, GINKGO DIPYRIDOLUM INJECTION(TCM), LEUCOGEN TABLETS, LIGUSTRAZINE HYDROCHLORIDE FOR INJECTION(TCM), MAYINGLONG(TCM), SULFOTANSHINONE SODIUM INJECTION(TCM), TRIMEBUTINE MALEATE TABLETS, WARFARIN
Adverse Events (AE) Preferred term	1. Conjunctival haemorrhage 2. Haemorrhoids
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 22JUN2009 (29) - 30JUN2009 (37) 2. 05JUL2009 (42) - 26JUL2009 (63)
Duration of AE	1. 9 2. 22
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540064044

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540064044/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/67/ASIAN/CHINA/YES
Medical history	Diabetes mellitus, Hypertension, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACARBOSE, AESCUVEN FORTE TABLETS, AZTREONAM FOR INJECTION, BETAHISTINE HYDROCHLORIDE TABLETS, ENOXAPARIN, LIGUSTRAZINE HYDROCHLORIDE FOR INJECTION(TCM), LORAZEPAM TABLETS, MELILOTUS EXTRACT TABLETS, SHUXUENING INJECTION(TCM), SHUXUETONG INJECTION (TCM), WARFARIN
Adverse Events (AE) Preferred term	1. Dyspnoea 2. Depression
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --DEC2009 (.) - --------- (.) 2. 10SEP2009 (58) - --------- (.)
Duration of AE	1. . 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540074002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/54/ASIAN/CHINA/YES
Medical history	Nephritis, Back injury, Hypokalaemia, Upper respiratory tract infection, Ovarian neoplasm
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, ALANYL-L-GLUTAMINE, AMBROXOL, ANISODAMINE, ATROVENT INHALER SOLUTION, AZITHROMYCIN, CALTRATE D, CARBAZOCHROME SODIUM SULFONATE, CARBOPLATIN, CHYMOTRYPSIN, CIMETIDINE, DEMETHYL CATHARIDINE, DEXAMETHASONE, DEXTROMETHORPHAN HYDROBROMIDE, DIAZEPAM, DIPHENHYDRAMINE, ENOXAPARIN, FERROUS SUCCINATE, FILGRASTIM, FUFANG LUHUI JIAONANG(CHINESE TRADITION MEDICINE, GANMAO QINGRE KELI(CHINESE TRADITIONAL MEDICINE), GLYCERIN ENEMA, GRANOCYTE, INTEFEN, KABIVENTM PI, KALIUM CITRICUM, LOSEC, MAGNESIUM SULFATE, MAGNESIUM SULPHURICUM, MAREN RUNCHANG WAN(CHINESE TRADITION MEDICINE), MAREN RUNCHANG WAN(CHINESE TRADITION MEDICINE), METHYCOBAL, METRONIDAZOLE, OFLOXACIN, ONDANSETRON, PACLITAXEL, PIFU KANG XIYE(CHINESE TRADITION MEDICINE), POTASSIUM CHLORIDE, RECOMBINANT HUMAN GRANULOCYTE COLONY-STIMULATING FACTOR INJECTION, TRAMADOL, UBENIMEX, VIT B6, VIT C, WARFARIN, XIHUANG JIEDU JIAONANG [CHINESE TRAD MED. CHINESE DR PRESCRIBES FOR PATIENTS WIT, ZHENGZHI FUZHENG JIAONANG [CHINESE TRAD MED. CHINESE DR PRESCRIBES FOR PATIENTS, ZONGAN HEJI(CHINESE TRADIOTIONAL MEDICINE)
Adverse Events (AE) Preferred term	1. Haematuria 2. Conjunctival haemorrhage 3. Blood bilirubin increased 4. Bilirubin conjugated increased 5. Ovarian cancer recurrent 6. Epistaxis 7. Intestinal obstruction
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MILD/YES/NO/YES 7. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 08OCT2008 (75) - --------- (.) 2. 19DEC2008 (147) - 21DEC2008 (149) 3. 22DEC2008 (150) - 22JAN2009 (181) 4. 22DEC2008 (150) - 22JAN2009 (181) 5. 03FEB2009 (193) - --------- (.) 6. 15MAR2009 (233) - 20MAR2009 (238) 7. 11MAY2009 (290) - 14MAY2009 (293)
Duration of AE	1. . 2. 3 3. 32

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074002

Parameter	Value
	4. 32
	5. .
	6. 6
	7. 4
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. DOSE OF STUDY DRUG REDUCED
	2. STUDY DRUG DISCONTINUED AND RESTARTED
	3. NONE
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	6. DOSE OF STUDY DRUG REDUCED
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. IMPROVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540074003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/46/ASIAN/CHINA/YES
Medical history	Rectal cancer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, ASPRIN, CALCIUM FOLINATE, DIAZEPAM, FLUOROURACIL, FUFANG LUHUI JIAONANG (CHINESE TRADITIONAL MEDICINE), GLYCERINE ENEMA, GRANISETRON, HEPARIN, KAFLAN, MECOBALAMIN, MORPHINE SULFATE, ONDANSETRON, OXALIPLATIN, PAMIDRONATE DISODIUM-NEPTUNUS, PETHIDINE HYDROCHLORIDE, POTASSIUM ASPARTATE AND MAGNESIUM ASPARTATE, PROMETHAZINE, TRAMADOL HYDROCHLORIDE, TYLENOL [PARACETAMOL], VIT B CO, VIT B1, XELODA
Adverse Events (AE) Preferred term	1. Rectal cancer recurrent 2. Haematochezia
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 19AUG2008 (16) - 20DEC2008 (139) 2. 18SEP2008 (46) - 18SEP2008 (46)
Duration of AE	1. 124 2. 1
Dose on AE onset	1. 15 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE
Outcome of event	1. DEATH 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540074004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/74/ASIAN/CHINA/YES
Medical history	Asthma, Depression, Diabetes mellitus, Hypertension, Lumbar spinal stenosis, Vena cava filter insertion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADALAT GITS, AESCUVEN FORTE, AMBROXOL HYDROCHLORIDE, AMINOPHYLLINE, ASPIRIN, BACILLUS LICHENIFORMIS CAPSULES, BIFID TRIPLE VIABLE CASULE, BUDESONIDE, CALCIUM GLUCONATE, CHLORPHENAMINE MALEATE, CIPRAMIL, CLEXANE, CLONAZEPAM, COMBIVENT, COMPOUND DIAZEPAM, DRIED YEAST, EFEXOR XR, ENOXAPARIN, ESTAZOLAM, FORLAX, GLYCERINE ENEMA, IPRATROPIUM BROMIDE, LACIDOPHILIN, LEVOFLOXACIN, LORAZEPAM, METOPROLOL, MIRTAZAPINE, MOTILIUM, NOVORAPID, POTASSIUM CHLORIDE INJECTION, SEROQUEL, SOLU-MEDROL, TERBUTALINE SULFATE, TRAMADOL HYDROCHLORIDE, VENLAFAXINE, VIT B6, VITAMINE C INJECTION, WARFARIN, ZYRTEC
Adverse Events (AE) Preferred term	1. Rash 2. Asthma 3. Asthma 4. Cholecystitis acute 5. Asthma 6. Respiratory failure 7. Septic shock
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/YES/YES 4. SEVERE/NO/YES/NO 5. SEVERE/NO/YES/NO 6. SEVERE/NO/YES/NO 7. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 04SEP2008 (4) - 06SEP2008 (6) 2. 05SEP2008 (5) - 08SEP2008 (8) 3. 08SEP2008 (8) - 13SEP2008 (13) 4. 11SEP2008 (11) - --------- (.) 5. 13SEP2008 (13) - --------- (.) 6. 14SEP2008 (14) - 14SEP2008 (14) 7. 14SEP2008 (14) - 14SEP2008 (14)
Duration of AE	1. 3 2. 4 3. 6 4. . 5. . 6. 1 7. 1
Dose on AE onset	1. 2.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074004

Parameter	Value
	3.
	4.
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. OTHER
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. IMPROVED
	3. WORSENED
	4. WORSENED
	5. WORSENED
	6. DEATH
	7. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540074011/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/80/ASIAN/CHINA/YES
Medical history	Atrial fibrillation, Hypertension, Osteoarthritis, Cerebrovascular accident, Knee arthroplasty, Lung infection, Cervicobrachial syndrome, Peripheral arterial occlusive disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETYLCYSTEINE, ADALAT GITS, AESCUVEN FORTE, BETALOC, CEFUROXIME, CELECOXIB, CHYMOTRYPSIN, CRISPIN MELANATE, DICLOFENAC, EL ASPIRIN, ENOXAPARIN, GLUCOSAMINE HYDROCHLORIDE CAPSULES, GLYCERIN ENEMA, HEPARINOID, LOXOPROFEN, METHYCOBAL, PROSTAGLANDIN E1, ROCEPHIN, VIT B1, WARFARIN, ZONG AN HE JI(CHINESE TRADITIONAL MEDICINE)
Adverse Events (AE) Preferred term	1. Paronychia 2. Paronychia 3. Osteoarthritis 4. Rash generalised
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 13FEB2009 (12) - 17FEB2009 (16) 2. 17FEB2009 (16) - 04MAR2009 (31) 3. 22FEB2009 (21) - --------- (.) 4. 28MAR2009 (55) - 27APR2009 (85)
Duration of AE	1. 5 2. 16 3. . 4. 31
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
Outcome of event	1. WORSENED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074011

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540074015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/71/ASIAN/CHINA/YES
Medical history	Diabetes mellitus, Joint effusion, Hydronephrosis, Hypertension, Menopause, Pneumonia, Calculus ureteric
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADALAT GITS, AESCUVEN FORTE, BACILLUS LICHENIFORMIS CAPSULES, BIFID TRIPLE VIABLE, DIMETHYLDIGUANIDE, ENOXAPARIN, GLYCERINE ENEMA, HIRUDOID, MAREN RUNCHANG WAN(CHINESE TRADITIONAL MEDINE), MOXIFLXACIN, NOVOLIN, SHUANG GUA YI HUO SU (CHINESE TRADITIONAL MEDICINE), WARFARIN
Adverse Events (AE) Preferred term	1. Arthritis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 08SEP2009 (184) - 21SEP2009 (197)
Duration of AE	1. 14
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540074023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540074023/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/56/ASIAN/CHINA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Hepatic neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 21MAY2009 (11) - 04OCT2009 (147)
Duration of AE	1. 137
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540104016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540104016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/59/ASIAN/CHINA/YES
Medical history	Hypertension, Hysterectomy, Varicose vein
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CAPTOPRIL TABLETS, DOMPERIDONE TABLETS, ENOXAPARIN, FELODIPINE SUSTAIND-RELEASE TABLETS, IMIDAPRIL HYDROCHLORIDE TABLETS, WARFARIN
Adverse Events (AE) Preferred term	1. Conjunctival haemorrhage 2. Dyspepsia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 15JUL2009 (9) - --------- (.) 2. 17JUL2009 (11) - 17JUL2009 (11)
Duration of AE	1. . 2. 1
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. DOSE OF STUDY DRUG REDUCED 2. REMEDIAL DRUG THERAPY
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540114001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540114001/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/26/ASIAN/CHINA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Gingival bleeding 2. Aspartate aminotransferase increased 3. Alanine aminotransferase increased 4. Alanine aminotransferase increased 5. Fatigue
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MILD/YES/NO/YES 4. MODERATE/YES/YES/YES 5. MILD/YES/NO/NO
Start/stop date of event with relative date	1. 14FEB2009 (31) - 14FEB2009 (31) 2. 11OCT2009 (270) - 23NOV2009 (313) 3. 11OCT2009 (270) - 15OCT2009 (274) 4. 15OCT2009 (274) - 23NOV2009 (313) 5. 26OCT2009 (285) - 09NOV2009 (299)
Duration of AE	1. 1 2. 44 3. 5 4. 40 5. 15
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. F
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 3. NONE 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 5. OTHER
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540114001

Parameter	Value
	2. RESOLVED
	3. WORSENED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540114002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540114002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/61/ASIAN/CHINA/YES
Medical history	Hypertension, Menopause, Cholelithiasis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE, AMLODIPINE BESYLATE TABLETS, ENALAPRIL, ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Dizziness 2. Ischaemic stroke
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/NO 2. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 25FEB2010 (376) - 26FEB2010 (377) 2. 25FEB2010 (376) - --------- (.)
Duration of AE	1. 2 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. NONE
Outcome of event	1. RESOLVED 2. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540114003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540114003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/53/ASIAN/CHINA/YES
Medical history	Diabetes mellitus, Bone pain
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AZLOCILLIN SODIUM, ENOXAPARIN, GLICLAZIDE, INDOMETACIN, LACTULOSE, MORPHINE SULFATE, NADROPARIN, PANTOPRAZOLE, PETHIDINE HYDROCHLORIDE, PHENOLPHTHALEIN, RECOMBINANT HUMAN INSULIN, SOMEDON [AMINOPYRINE, PHENACETIN,CAFFEINE, PHENOBARBITAL/LUMBER VERTEBRAE PAIN.], TALCID, TRAMADOL HYDROCHLORIDE, VB1, VB12, WARFARIN
Adverse Events (AE) Preferred term	1. Retroperitoneal neoplasm
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 08APR2009 (5) - 22JUL2009 (110)
Duration of AE	1. 106
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540134004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540134004/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/44/ASIAN/CHINA/YES
Medical history	Gamma-glutamyltransferase increased, Hypertension, Menopause, Drug hypersensitivity, Cholelithiasis, Systemic lupus erythematosus, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACARBOSE TABLETS, ALDACTONE [SPIRONOLACTONE], ALPHA-D3, ANISODAMINE, CALCITONIN, D-CAL [NOT SURE IF D-CALSOR. ENGLISH NAME IS D-CAL. IS KIND OF CALCIUM TABLET.], DEXAMETHASONE, DICLOFENAC SODIUM SUPPOSITORIES, DIHYDROCHLOROTHIAZIDE, EXACIN, FUFANG ZAOFAN WAN (CHINESE MEDICINE), INSULIN, JIANPISHENGXUE JIAONANG (CHINESE MEDICINE) [HERBAL PREP TO TREAT SYSTEMIC LUPUS], LASIX, METHYLPREDNISOLONE TABLETS, NOVOLIN 30R, NOVOLIN 50R, NOVOLIN N, NOVOLIN R, POTASSIUM CHLORIDE SUSTAINEDRELEASE TABLETS, PREDNISONE ACETATE TABLET, THYMOPOLYPEPTIDES INJECTION, XINDING [EXTRACTIVE FROM CHINESE HERBS TO HELP PATIENT'S CIRCULATION BETTER], XUESHUANTONG (CHINESE MEDICINE), XUESHUANTONG [EXTRACTIVE FROM CHINESE HERBS TO HELP PATIENT'S CIRCULATION BETTER
Adverse Events (AE) Preferred term	1. Systemic lupus erythematosus 2. Systemic lupus erythematosus 3. Cyanosis 4. Gamma-glutamyltransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/YES/NO/YES 4. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 02SEP2008 (7) - 08SEP2008 (13) 2. 08SEP2008 (13) - 18SEP2008 (23) 3. 10FEB2009 (168) - 15FEB2009 (173) 4. 19FEB2009 (177) - --------- (.)
Duration of AE	1. 7 2. 11 3. 6 4. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540134004

Parameter	Value
Outcome of event	4. NONE 1. WORSENED 2. RESOLVED 3. RESOLVED 4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540134019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540134019/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/63/ASIAN/CHINA/YES
Medical history	
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, ETHYLENEDIAMINE DIACETURATE, MANNITE, MONOSIALOTETRAHEXOSYLGANGLIOSIDE SODIUM, SHENXIONG(CHINESE MEDICINE) [HERBAL PREP TO TREAT DVT], URAPIDIL HYDROCHLORIDE, WARFARIN, XUESHUANTONG(CHINESE MEDICINE) [TREATMENT OF DEEP VEIN THROMBOSIS]
Adverse Events (AE) Preferred term	1. Alanine aminotransferase increased 2. Cerebral haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 07MAR2009 (10) - 15MAR2009 (18) 2. 29APR2009 (63) - 29APR2009 (63)
Duration of AE	1. 9 2. 1
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号：11702-540134019

死亡に至るまでの経過

被験者は 63 歳、アジア人男性。2009 年 2 月 23 日に深部静脈血栓症と診断され、2009 年 2 月 26 日にエノキサパリン（120mg）／用量調節ワルファリンの投与を開始した。

2009 年 4 月 29 日、被験者は脳出血（出血：脳出血）を発現した。本事象により被験者は死亡に至ったため重篤とされた。本事象により被験者の治験は中止された。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「あり」と判断した。被験者は左半身不随、意識清明、構語障害、左手足の麻痺、及び口角の歪みを呈した。2009 年 4 月 29 日、PT-INR 3.56。CT スキャンにより大脳基底核及び視床に約 5×4cm 大の血腫が認められた。2009 年 4 月 29 日、本事象により治験薬の投与は中止された。本事象に対する治療として複数薬剤が投与された。同日、被験者は脳出血により死亡に至った。剖検は実施されなかった。

CIAC は、脳出血（出血：脳出血）を「重大な出血事象」とみなし、死亡原因を重大な出血と判定した。

Laboratory Parameter	Normal Range	Date	Result	Date	Result	Date	Result
Hemoglobin	12.0-16.0 g/dL	25 Feb 2009	15.4 g/dL				
Platelets	100-300 giga/L	25 Feb 2009	162 giga/L				
Alkaline Phosphatase	35-123 U/L	25 Feb 2009	**138 U/L (H)**	15 Mar 2009	123 U/L		
		07 Mar 2009	**152 U/L (H)**	26 Mar 2009	114 U/L		
Amylase	28-100 U/L	25 Feb 2009	53 U/L	15 Mar 2009	57 U/L		
Bilirubin, Direct	0.10-0.32 mg/dL	25 Feb 2009	0.12 mg/dL	26 Mar 2009	**<0.10 mg/dL (L)**		
Bilirubin, Total	0.22-1.28 mg/dL	25 Feb 2009	0.47 mg/dL	15 Mar 2009	0.29 mg/dL		
		07 Mar 2009	0.49 mg/dL	26 Mar 2009	0.46 mg/dL		
SGOT/AST	11-39 U/L	25 Feb 2009	35 U/L	15 Mar 2009	26 U/L		
		07 Mar 2009	**65 U/L (H)**	26 Mar 2009	27 U/L		
SGPT/ALT	8-45 U/L *Local: 0-40 U/L	25 Feb 2009	**51 U/L (H)***	07 Mar 2009	**125 U/L (H)**	26 Mar 2009	27 U/L
		25 Feb 2009	43 U/L	15 Mar 2009	39 U/L		

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540134023

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540134023/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/55/ASIAN/CHINA/YES
Medical history	Blood alkaline phosphatase increased, Gamma-glutamyltransferase increased, Menopause, White blood cell count increased
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AESCUVEN FORTE TABLETS, ANTISTERONE, DENGZHANXIXIN(CHINESE MEDICINE), DEXAMETHASONE, DIHYDROCHLOROTHIAZIDE, LASIX, PHENERGAN, SHENXIONG (CHINESE MEDICINE) [IT WAS ABSTRACTION OF SALVIA MILTIORRHIZA AND RHIZ, SHENXIONG(CHINESE MEDICINE) [IT WAS ABSTRACTION OF SALVIA MILTIORRHIZA AND RHIZO, XIAOSHUANTONGLUOJIAONANG (CHINESE MEDICINE) [RHIZOMA LIGUSTICI WALLICHII, SALVIA, XINDING (CHINESE MEDICINE) [YES, IT IS HEBRAL PREPARATION], XUESHUANGTONG(CHINESE MEDICINE) [TREATMENT OF DEEP VEIN THROMBOSIS]
Adverse Events (AE) Preferred term	1. Hypersensitivity 2. Blood alkaline phosphatase increased 3. Hepatic neoplasm malignant
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/YES/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 10MAR2009 (8) - 12MAR2009 (10) 2. 28MAR2009 (26) - 01APR2009 (30) 3. 01APR2009 (30) - --------- (.)
Duration of AE	1. 3 2. 5 3. .
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. WORSENED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540134023

Parameter	Value
	3. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540194006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540194006/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/72/ASIAN/CHINA/YES
Medical history	Bronchitis, Central nervous system neoplasm, Hypertension, Meningioma, Pleural effusion
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMBROXOL, CLEXANE, FRAXIPARINE, NIMODIPINE, WARFARIN
Adverse Events (AE) Preferred term	1. Intervertebral disc protrusion 2. Intra-abdominal haematoma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/NO 2. MODERATE/NO/YES/NO
Start/stop date of event with relative date	1. 04SEP2009 (72) - --------- (.) 2. 05SEP2009 (73) - 18SEP2009 (86)
Duration of AE	1. . 2. 14
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. F 2. F
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540194008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/540194008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/53/ASIAN/CHINA/YES
Medical history	Anaemia, Appendicectomy, Constipation, Hypokalaemia, Hysterectomy, Uterine leiomyoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	GLYCEROL ENEMA, POLYETHYLENE GLYCOL, POTASSIUM CHLORIDE SUSTAINED-RELEASE TABLETSL
Adverse Events (AE) Preferred term	1. Animal bite 2. Rectal haemorrhage 3. Intestinal obstruction 4. Contusion 5. Haematuria
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/NO 2. MODERATE/NO/YES/NO 3. MODERATE/NO/YES/NO 4. MILD/NO/NO/NO 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 09NOV2009 (111) - 09NOV2009 (111) 2. 22NOV2009 (124) - 03DEC2009 (135) 3. 22NOV2009 (124) - 03DEC2009 (135) 4. 22NOV2009 (124) - 03DEC2009 (135) 5. 22NOV2009 (124) - 24NOV2009 (126)
Duration of AE	1. 1 2. 12 3. 12 4. 12 5. 3
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. F 2. F 3. F 4. F 5. F
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY,OTHER 4. NONE 5. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 540194008

Parameter	Value
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550014003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/61/ASIAN/INDONESIA/YES
Medical history	Coronary artery disease, Haemorrhoids, Hypertension, Type 2 diabetes mellitus, Renal failure chronic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARDIUM, TEBOKAN
Adverse Events (AE) Preferred term	1. Cardiac disorder
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. --MAR2008 (.) - --------- (.)
Duration of AE	1. .
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. NONE
Outcome of event	1. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550014004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/32/ASIAN/INDONESIA/YES
Medical history	Acquired immunodeficiency syndrome, Anaemia, Brain abscess, Hepatitis C, Hepatic enzyme increased, Hypoalbuminaemia, Hypokalaemia, Oral candidiasis, Allergy to arthropod bite, Cerebral toxoplasmosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANUSOL SUPP [ZINC OXIDE, BISMUTH SUBGALLATE, BALSAM PERU, BISMUTH OXIDE], ARDIUM, BETAMETHASONE VALERATE, CEFTRIAXON, CLINDAMYCIN, COTRIMOXAZOLE, CURCUMA, DEXAMETHASONE, DOMPERIDONE, DUVIRAL, EFAVIRENZ, ENOXAPARIN, FAKTU [POLICRESULEN & CINCHOCAINE HCL], FOLIC ACID, HIVIRAL, KSR, LAXADINE SYRUP, LESICHOL, MYCOSTATIN, NACL 0.9%, NEW DIATAB, NYSTATIN, OMEPRAZOLE, PARACETAMOL, PHENYTOIN, PIRIMETAMIN, RANITIDIN, SISTENOL, STAVIR, WARFARIN
Adverse Events (AE) Preferred term	1. Haemorrhoids 2. Pyrexia 3. Diarrhoea 4. Pneumonia 5. Hypokalaemia 6. Hyponatraemia 7. Pyrexia 8. Gastroenteritis 9. Dengue fever 10. Oral candidiasis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MODERATE/NO/NO/YES 9. MODERATE/NO/YES/YES 10. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 07DEC2008 (19) - --------- (.) 2. 12DEC2008 (24) - 17DEC2008 (29) 3. 12DEC2008 (24) - 16DEC2008 (28) 4. 14DEC2008 (26) - -----2008 (.) 5. 14DEC2008 (26) - --------- (.) 6. 15DEC2008 (27) - --------- (.) 7. 25FEB2009 (99) - 28FEB2009 (102) 8. 27FEB2009 (101) - -----2009 (.) 9. 28FEB2009 (102) - 07MAR2009 (109) 10. 28FEB2009 (102) - 06MAR2009 (108)
Duration of AE	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014004

Parameter	Value
	2. 6
	3. 5
	4. .
	5. .
	6. .
	7. 4
	8. .
	9. 8
	10. 7
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED
	2. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014004

Parameter	Value
	3. RESOLVED
	4. RESOLVED
	5. .
	6. .
	7. WORSENED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550014009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/66/ASIAN/INDONESIA/YES
Medical history	Cataract, Cervix carcinoma stage III, Cardiac failure congestive, Hypertension, Hypoalbuminaemia, Hyponatraemia, Pneumonia, Vitiligo, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AZITHROMYCIN, BETABLOK, CAPTOPRIL, CEFIXIME, CEFTRIAXONE, DOMPERIDONE, ENOXAPARIN, LASIX, NACL CAPSULE, NEW DIATABS, OMEPRAZOLE, PARACETAMOL, SANGOBION, SUCRALFAT, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Haematuria 3. Sinus arrhythmia 4. Haematoma 5. Ecchymosis 6. Iron deficiency anaemia 7. Conjunctival haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/YES/YES/YES 3. MILD/NO/YES/YES 4. MILD/YES/NO/YES 5. MILD/YES/NO/YES 6. MILD/YES/NO/YES 7. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 14MAY2009 (10) - 14MAY2009 (10) 2. 27MAY2009 (23) - 01JUN2009 (28) 3. 05AUG2009 (93) - 14OCT2009 (163) 4. 14OCT2009 (163) - 28OCT2009 (177) 5. 14OCT2009 (163) - 28OCT2009 (177) 6. 14OCT2009 (163) - --------- (.) 7. 19NOV2009 (199) - 26NOV2009 (206)
Duration of AE	1. 1 2. 6 3. 71 4. 15 5. 15 6. . 7. 8
Dose on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014009

Parameter	Value
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	3. NONE
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	6. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	7. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. IMPROVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550014010/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/31/ASIAN/INDONESIA/YES
Medical history	Alanine aminotransferase increased, Anaemia, Pulmonary tuberculosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BISOLVON, CEFIXIME, CEFTRIAXONE, CODEIN, DOMPERIDONE, FLUIMUCYL, INH, LESICHOL, NACL, NORMAL SALINE, OMEPRAZOLE, VENTOLIN, VITAMIN K
Adverse Events (AE) Preferred term	1. Haemoptysis 2. Pulmonary tuberculosis 3. Haemoptysis 4. Pneumonia 5. Pulmonary tuberculosis 6. Tachycardia 7. Haemoptysis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/YES/YES/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/NO 6. MODERATE/NO/NO/NO 7. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 15JUN2009 (7) - 15JUN2009 (7) 2. 22JUN2009 (14) - 01JUL2009 (23) 3. 27JUN2009 (19) - 27JUN2009 (19) 4. 27JUN2009 (19) - 01JUL2009 (23) 5. 01JUL2009 (23) - --------- (.) 6. 17SEP2009 (101) - --------- (.) 7. 04NOV2009 (149) - 06NOV2009 (151)
Duration of AE	1. 1 2. 10 3. 1 4. 5 5. . 6. . 7. 3
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg 6. 15 mg 7. 15 mg
Dose status on AE onset	1. I

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014010

Parameter	Value
	2. .
	3. .
	4. .
	5. F
	6. F
	7. F
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. INSUFFICIENT FOLLOW-UP
	6. UNCHANGED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-550014010[3)]	HEMOPTYSIS（PT：気道出血） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550014012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/28/ASIAN/INDONESIA/YES
Medical history	Aplastic anaemia, Hydronephrosis, Hyperuricaemia, Hypoalbuminaemia, Hypocoagulable state, Hyponatraemia, Leukopenia, Non-Hodgkin's lymphoma, Pneumonia, Sepsis, Thrombocytopenia, Feeding disorder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMBROXOL, BISOLVON, CEFTAZIDIM, COMBIVENT, ENOXAPARIN, FLUCONAZOLE, GENTAMYCIN, LEUKOKINE [RECOMB. HUMAN GRANULOCYT COLONY STIM. FACTOR. TREAT FEBRILE NEUTROPEN, LEVOFLOXACIN, PARACETAMOL, PREDNISONE, RANITIDIN, SODIUM CHLORIDE, SODIUM CHLORIDE CAPSULE, WARFARIN
Adverse Events (AE) Preferred term	1. Haematoma 2. Neutropenia 3. Febrile neutropenia 4. Ecchymosis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/YES/NO 3. MODERATE/NO/NO/YES 4. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 19JUN2009 (1) - --------- (.) 2. 19JUN2009 (1) - 24JUN2009 (6) 3. 20JUN2009 (2) - 23JUN2009 (5) 4. 21JUN2009 (3) - --------- (.)
Duration of AE	1. . 2. 6 3. 4 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. OTHER
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550014012

Parameter	Value
	4. INSUFFICIENT FOLLOW-UP

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550024001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550024001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/42/ASIAN/INDONESIA/YES
Medical history	Cervix carcinoma, Hysterectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BLEOCYN, CYSPLATIN, ENOXAPARIN, VINBLASTIN, WARFARIN
Adverse Events (AE) Preferred term	1. Haematuria 2. Anaemia 3. Cervix carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/NO 2. SEVERE/NO/YES/NO 3. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 01JAN2008 (87) - --------- (.) 2. 31MAR2008 (177) - --------- (.) 3. 05APR2008 (182) - 05APR2008 (182)
Duration of AE	1. . 2. . 3. 1
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. OTHER 2. REMEDIAL DRUG THERAPY,OTHER 3. NONE
Outcome of event	1. UNCHANGED 2. IMPROVED 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/66/ASIAN/INDONESIA/YES
Medical history	Abdominal neoplasm, Rhabdomyosarcoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	SELOXY, TRAMADOL
Adverse Events (AE) Preferred term	1. Rhabdomyosarcoma
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 26OCT2007 (16) - 26OCT2007 (16)
Duration of AE	1. 1
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. NONE
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/72/ASIAN/INDONESIA/YES
Medical history	Menopause, Pneumonia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CRAVIT, ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Haematoma 2. Chest pain 3. Dyspnoea 4. Pulmonary embolism 5. Tachypnoea
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/NO/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/YES/YES 5. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 26OCT2007 (8) - 26OCT2007 (8) 2. 14NOV2007 (27) - --------- (.) 3. 14NOV2007 (27) - --------- (.) 4. 14NOV2007 (27) - 14NOV2007 (27) 5. 14NOV2007 (27) - --------- (.)
Duration of AE	1. 1 2. . 3. . 4. 1 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. STUDY DRUG DISCONTINUED PERMANENTLY 5. NONE
Outcome of event	1. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034003

Parameter	Value
	2. UNCHANGED
	3. UNCHANGED
	4. DEATH
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/19/ASIAN/INDONESIA/YES
Medical history	Anaemia, Neoplasm malignant, Hypoalbuminaemia, Hypocalcaemia, Ovarian cancer, Underweight
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUMIN, CEALB, CEFOTAXIM, ENOXAPARIN, FRESH FROZEN PLASMA, GLYCERYL GUAIACOLATE, RANITIDINE, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Haematochezia 2. Anaemia 3. Pneumonia 4. Haematochezia 5. Pulmonary sepsis 6. Septic shock
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/YES/YES/YES 2. MODERATE/YES/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/YES/YES/YES 5. SEVERE/NO/YES/YES 6. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 02NOV2007 (7) - 07NOV2007 (12) 2. 03NOV2007 (8) - --------- (.) 3. 20NOV2007 (25) - 24NOV2007 (29) 4. 21NOV2007 (26) - --------- (.) 5. 23NOV2007 (28) - --------- (.) 6. 24NOV2007 (29) - 24NOV2007 (29)
Duration of AE	1. 6 2. . 3. 5 4. . 5. . 6. 1
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034004

Parameter	Value
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 2. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 3. REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 5. REMEDIAL DRUG THERAPY 6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. WORSENED 4. UNCHANGED 5. WORSENED 6. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-550034004[1)]	HEMATOCHEZIA（PT：血便排泄） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては時間的関連性が認められないため、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034006/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/65/ASIAN/INDONESIA/YES
Medical history	Cardiac failure congestive, Cough, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CODIPRONT, CRAVIT, ESCOVIT [LECITHIN,VIT B1,VIT B2,VIT B6,VIT B12,NICOTINAMIDE,VITE 20,BETA CAROTEN, FLUIMUCIL, MOVICOX, PREDNISON, RAMIXAL, RETAPHYL, SALBUTAMOL
Adverse Events (AE) Preferred term	1. Transient ischaemic attack 2. Pneumonia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 28MAR2008 (2) - 28MAR2008 (2) 2. 09APR2008 (14) - 15APR2008 (20)
Duration of AE	1. 1 2. 7
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. .
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034007

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034007/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/55/ASIAN/INDONESIA/YES
Medical history	Cervix carcinoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, TORADOL 30 MG, WARFARIN
Adverse Events (AE) Preferred term	1. Gingival bleeding 2. Vaginal haemorrhage 3. Cervix carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MODERATE/YES/YES/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 21APR2008 (20) - 23APR2008 (22) 2. 21APR2008 (20) - 23APR2008 (22) 3. 31JUL2008 (121) - 31JUL2008 (121)
Duration of AE	1. 3 2. 3 3. 1
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. STUDY DRUG DISCONTINUED AND RESTARTED 3. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. RESOLVED 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-550034007[1),1)]	GINGIVAL BLEEDING（PT：歯肉出血） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投与と報告事象発現との時間的関連性がないことから、エノキサパリンとの因果関係は否定できると考える。 VAGINAL BLEEDING（PT：膣出血） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリン投与と報告事象発現との時間的関連性がないことから、エノキサパリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/48/ASIAN/INDONESIA/YES
Medical history	Anaemia, Hepatomegaly, Hypoalbuminaemia, Liver abscess, Pleural effusion, Myocardial ischaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPILETS, CEFTRIAXON, METRONIDAZOLE
Adverse Events (AE) Preferred term	1. Hepatic neoplasm malignant 2. Ascites 3. Nausea 4. Hypocalcaemia 5. Haematuria 6. Pneumonia 7. Decubitus ulcer
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MODERATE/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/NO 7. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 15MAY2008 (11) - 04JUL2008 (61) 2. 15MAY2008 (11) - --------- (.) 3. 17MAY2008 (13) - --------- (.) 4. 24MAY2008 (20) - --------- (.) 5. 25MAY2008 (21) - 26MAY2008 (22) 6. 31MAY2008 (27) - 17JUN2008 (44) 7. 18JUN2008 (45) - --------- (.)
Duration of AE	1. 51 2. . 3. . 4. . 5. 2 6. 18 7. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg 6. 15 mg 7. 15 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034008

Parameter	Value
	2. .
	3. .
	4. F
	5. F
	6. F
	7. F
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH
	2. UNCHANGED
	3. IMPROVED
	4. IMPROVED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034011

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034011/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/45/ASIAN/INDONESIA/YES
Medical history	Anaemia, Diabetes mellitus, Hypertension, Diabetic ulcer
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALDAZID, ASCARDIA, BEROTEC, CAPTOPRIL, CEFADROXIL, CLINDAMICYN, GLICERYL GUAICOLATE, GLUCODEX, GLURENORM, HIDROCORTISON CREAM, LANTUS, LORATADIN, MEFENAMIC ACID, MORPHIN SULPHATE, RANITIDIN
Adverse Events (AE) Preferred term	1. Urticaria 2. Anaemia 3. Cough 4. Pneumonia 5. Hypoglycaemic coma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 27JUN2008 (14) - 30JUN2008 (17) 2. 30JUN2008 (17) - 04JUL2008 (21) 3. 07JUL2008 (24) - 08JUL2008 (25) 4. 09JUL2008 (26) - 15JUL2008 (32) 5. 17JUL2008 (34) - 17JUL2008 (34)
Duration of AE	1. 4 2. 5 3. 2 4. 7 5. 1
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. . 5. .
Action taken	1. REMEDIAL DRUG THERAPY 2. OTHER 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY 5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034011

Parameter	Value
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. WORSENED
	4. RESOLVED
	5. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034012

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034012/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/49/ASIAN/INDONESIA/YES
Medical history	Anaemia, Aortic valve incompetence, Cardiac failure congestive, Diabetes mellitus, Hypertension, Hypoalbuminaemia, Hypocalcaemia, Hypomagnesaemia, Menopause, Mitral valve incompetence, Pleural effusion, Pulmonary tuberculosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTRAPID, AMBROXOL, ASAM MEFENAMAT, ASPAR, ASPILET, CACO3, ENOXAPARIN, ETHAMBUTOL, GLIMEPIRID, INH, NOPERTEN, PIRAZINAMID, RIFAMPICIN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Ear haemorrhage 2. Haematochezia 3. Pleural effusion 4. Death
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. MODERATE/NO/YES/YES 4. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 18JUN2008 (5) - 18JUN2008 (5) 2. 19JUN2008 (6) - 19JUN2008 (6) 3. 09AUG2008 (57) - --------- (.) 4. 15NOV2008 (155) - 15NOV2008 (155)
Duration of AE	1. 1 2. 1 3. . 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034012

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034013/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/69/ASIAN/INDONESIA/YES
Medical history	Anaemia, Hypoalbuminaemia, Pneumonia, Tuberculosis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMBROXOL, CEALB, CEFTRIAXON, PARACETAMOL, RANITIDIN, TRAMADOL
Adverse Events (AE) Preferred term	1. Vomiting 2. Pneumonia
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 12JUL2008 (2) - 14JUL2008 (4) 2. 20JUL2008 (10) - 20JUL2008 (10)
Duration of AE	1. 3 2. 1
Dose on AE onset	1. 15 mg 2. 15 mg
Dose status on AE onset	1. . 2. F
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/60/ASIAN/INDONESIA/YES
Medical history	Anaemia, Cardiomegaly, Congenital hypothyroidism, Diabetes mellitus, Hypertension, Hypoalbuminaemia, Hypokalaemia, Menopause, Cerebrovascular accident
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPAR K, CEFTRIAXON, CIPROFLOXACIN, DOBUTAMIN, DOPAMIN, ENOXAPARIN, METRONIDAZOLE, NACL, OMEPRAZOL, RANITIDIN, RENAPAR, VASCON, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Conjunctival haemorrhage 2. Ischaemic stroke 3. Sepsis 4. Bronchopneumonia 5. Haematemesis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. SEVERE/NO/YES/YES 3. SEVERE/NO/YES/YES 4. SEVERE/NO/YES/YES 5. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 18SEP2008 (24) - 20SEP2008 (26) 2. 14OCT2008 (50) - --------- (.) 3. 14OCT2008 (50) - 16OCT2008 (52) 4. 14OCT2008 (50) - --------- (.) 5. 15OCT2008 (51) - --------- (.)
Duration of AE	1. 3 2. . 3. 3 4. . 5. .
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY 5. NONE

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034015

Parameter	Value
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. DEATH
	4. UNCHANGED
	5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034017

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034017/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/39/ASIAN/INDONESIA/YES
Medical history	Anaemia, Hypoalbuminaemia, Hypocalcaemia, Hyponatraemia, Osteomyelitis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACTONEL, AMOXICILLYN, CACO3, CEFOTAXIME, CIPROFLOXACIN, ETHAMBUTOL, INH, KETOROLAC, LANSOPRAZOLE, MELOXICAM, METRONIDAZOLE, NACL, PARACETAMOL, PIRAZINAMID, RANITIDINE, RIFAMPICIN, TRAMADOL, TRANEXAMIC ACID
Adverse Events (AE) Preferred term	1. Haematuria 2. Gastritis erosive 3. Duodenal ulcer 4. Decubitus ulcer 5. Pathological fracture 6. Bone tuberculosis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 08SEP2008 (6) - 14SEP2008 (12) 2. 11SEP2008 (9) - -----2009 (.) 3. 11SEP2008 (9) - -----2009 (.) 4. 12SEP2008 (10) - -----2009 (.) 5. 15SEP2008 (13) - --------- (.) 6. 14OCT2008 (42) - --------- (.)
Duration of AE	1. 7 2. . 3. . 4. . 5. . 6. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg 5. 15 mg 6. 20 mg
Dose status on AE onset	1. . 2. I 3. I 4. I 5. I

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034017

Parameter	Value
	6. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. IMPROVED
	6. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034018/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/33/ASIAN/INDONESIA/YES
Medical history	Anaemia, Cervix carcinoma, Hyponatraemia, Sterilisation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEFTRIAXON, KCL, KETOROLAC, METOCLOPERAMIDE, NA DICLOFENAC, NACL, PLATOSIN (CISPLATIN)
Adverse Events (AE) Preferred term	1. Urinary tract infection 2. Hypochloraemia 3. Hypokalaemia 4. Renal failure 5. Hypertension 6. Metastases to liver 7. Metastases to lymph nodes
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/NO/YES/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 28OCT2008 (1) - 10NOV2008 (14) 2. 29OCT2008 (2) - 03NOV2008 (7) 3. 14NOV2008 (18) - 05DEC2008 (39) 4. 22MAR2009 (146) - 11APR2009 (166) 5. 28MAR2009 (152) - --------- (.) 6. 28MAR2009 (152) - --------- (.) 7. 28MAR2009 (152) - --------- (.)
Duration of AE	1. 14 2. 6 3. 22 4. 21 5. . 6. . 7. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg
Dose status on AE onset	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034018

Parameter	Value
	2. .
	3. .
	4. .
	5. F
	6. F
	7. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. DEATH
	5. UNCHANGED
	6. UNCHANGED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034019/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/63/ASIAN/INDONESIA/YES
Medical history	Colorectal cancer stage III, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	5 FU, ATIVAN, ONDANCETRON, RESCOVULIN
Adverse Events (AE) Preferred term	1. Colorectal cancer
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 16FEB2009 (32) - 07MAR2009 (51)
Duration of AE	1. 20
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034021

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034021/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/58/ASIAN/INDONESIA/YES
Medical history	Anaemia, Multiple myeloma, Respiratory tract infection
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BONEFOS, CEFOTAXIM, DIFLAMAT, DUROGESIC PATCH, HAES STERILE, INPEPSA SYRUP, MORPHINE SULFATE, MOTILIUM, NEUROBION 5000, SULPHAS ATROPHIN, THALIDOMIDE, TOPLEXIL SYRUP [OXOMEMAZINE, GUAIFENESIN], TORADOL, VOMCERAN
Adverse Events (AE) Preferred term	1. Back pain 2. Hypercalcaemia 3. Hiccups 4. Haematemesis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 04MAY2009 (59) - --------- (.) 2. 04MAY2009 (59) - --------- (.) 3. 08MAY2009 (63) - 08MAY2009 (63) 4. 11MAY2009 (66) - 11MAY2009 (66)
Duration of AE	1. . 2. . 3. 1 4. 1
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. REMEDIAL DRUG THERAPY 2. NONE 3. REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034021

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号：11702-550034021

死亡に至るまでの経過

被験者は 58 歳、アジア人男性。2009 年 3 月 7 日、深部静脈血栓症と診断され、同日リバーロキサバン（30mg）の投与を開始した。

2009 年 5 月 4 日、被験者は背部痛（背部痛）を発現した。本事象により入院に至ったため重篤とされた。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「なし」と判断した。外傷の病歴はなく、嘔吐もなかった。治験責任（分担）医師は、本事象を併発症の多発性骨髄腫に関連するものと判断した。本事象により治験薬は変更されなかった。本事象に対して、Toradol、Morphine Sulfate 及び Durogesic Patch による治療が行われた。また、被験者は入院中に高カルシウム血症及びしゃっくりを発現した（いずれも非重篤な事象として報告）。背部痛（背部痛）の最終転帰は継続中及び不変と報告された。

2009 年 5 月 11 日、被験者は吐血（吐血）を発現した。本事象により入院期間が延長し、また被験者は死亡に至ったため、本事象は重篤とされた。本事象により被験者の治験は中止された。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「あり」と判断した。被験者は 2009 年 3 月以降貧血の病歴を有していた。治験開始前、被験者は 2009 年 3 月 9 日と 3 月 11 日にそれぞれ 2 回ずつ濃厚赤血球 200mL の輸血を受けた。2009 年 5 月 4 日以降、被験者は背部痛のため入院していた。入院中、被験者は吐血及び出血性ショックを発現した。5 月 11 日午前 1：30、血圧が上昇したが、意識あり。酸素飽和度は 93%、心拍数は 129bpm。午前 5：00、依然意識あり。午前 6：25、吐血（約 500mL）、心拍数減少、酸素飽和度 71%。蘇生処置が取られ、救急処置室に収容。午前 6：50、昏睡状態、心拍数が更に減少、最大散瞳。午前 7：00、死亡を確認。治験責任（分担）医師は、吐血は、NSAID（非ステロイド性抗炎症薬）及びステロイドの使用による胃出血に起因すると判断したが、胃カメラによる出血の確認は行わなかった。被験者は 2009 年 3 月 7 日から 3 月 10 日まで Diflamat（NSAID）、2009 年 5 月 4 日から 5 月 10 日まで Toradol（NSAID）による治療を受けていた。また、2008 年 8 月以降は併発症の多発性骨髄腫に対する Melphalan 及び Medixon による治療を 28 日毎に 10 サイクル繰り返し受けていた。2009 年 5 月 10 日、本事象により治験薬の投与は中止された。吐血に対する治療として、Haes Sterile 及び Cefotaxim が投与された。2009 年 5 月 11 日、本事象により被験者は死亡に至った。死亡診断書に記載された死亡原因は出血性ショックであった。剖検は実施されなかった。

CIAC は、吐血（吐血）を「重大な出血事象」とし、死亡原因を吐血と判定した。

Laboratory Parameter	Normal Range	Date	Result	Date	Result	Date	Result
Hemoglobin	13.0-16.0 g/dL	06 Mar 2009	**8.2 g/dL (L)**	28 Apr 2009	15.6 g/dL		
Platelets	150-450 giga/L *Local: 150-400 giga/L	06 Mar 2009	**108 giga/L (L)**	28 Apr 2009	**112 giga/L (L)***		
Alkaline Phosphatase	35-123 U/L	07 Mar 2009	47 U/L	08 Apr 2009	55 U/L		
		21 Mar 2009	43 U/L	07 May 2009	51 U/L		
Amylase	28-100 U/L	07 Mar 2009	**193 U/L (H)**				

Laboratory Parameter	Normal Range	Date	Result	Date	Result	Date	Result
Bilirubin, Direct	0.10-0.32 mg/dL	21 Mar 2009	0.10 mg/dL	08 Apr 2009	**<0.10 mg/dL (L)**	07 May 2009	0.11 mg/dL
Bilirubin, Total	0.22-1.28 mg/dL	07 Mar 2009	0.27 mg/dL	08 Apr 2009	0.23 mg/dL		
		21 Mar 2009	0.35 mg/dL	07 May 2009	0.40 mg/dL		
SGOT/AST	11-39 U/L	07 Mar 2009	23 U/L	08 Apr 2009	22 U/L		
		21 Mar 2009	24 U/L	07 May 2009	15 U/L		
SGPT/ALT	8-45 U/L *Local: 30-65 U/L	06 Mar 2009	30 U/L*	21 Mar 2009	21 U/L	07 May 2009	12 U/L
		07 Mar 2009	28 U/L	08 Apr 2009	26 U/L		
Prothrombin Time (PT)		07 Mar 2009	**16.80 S (H)**	07 May 2009	**27.60 S (H)**		
PT Ratio		07 Mar 2009	**0.66 (L)**	07 May 2009	**0.29 (L)**		
PT, INR	0.9-1.2	07 Mar 2009	**1.3 (H)**	07 May 2009	**2.7 (H)**		

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034022

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034022/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/41/ASIAN/INDONESIA/YES
Medical history	Cervix carcinoma stage III, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ANTACID, SULFAS FEROSUM, VITAMIN B COMPLEX
Adverse Events (AE) Preferred term	1. Cervix carcinoma stage III
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 02JUL2009 (111) - 02AUG2009 (142)
Duration of AE	1. 32
Dose on AE onset	1. 20 mg
Dose status on AE onset	1. .
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034026

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034026/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/56/ASIAN/INDONESIA/YES
Medical history	Anaemia, Cellulitis, Constipation, Hypoalbuminaemia, Hyponatraemia, Menopause, Nausea, Thrombocytosis, Vomiting
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ADRENALIN, ASPIRIN, CIPROFLOXACIN, ENOXAPARIN, HAES STERILE 6%, NACL 0.9%, PARACETAMOL, RANITIDINE, SULFAS ATROPIN, TRANEXAMAT ACID, VASCON, WARFARIN
Adverse Events (AE) Preferred term	1. Ascites 2. Hydronephrosis 3. Hypokalaemia 4. Pyrexia 5. Haematemesis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. SEVERE/YES/YES/YES
Start/stop date of event with relative date	1. 21APR2009 (1) - --------- (.) 2. 21APR2009 (1) - --------- (.) 3. 28APR2009 (8) - --------- (.) 4. 28APR2009 (8) - 30APR2009 (10) 5. 30APR2009 (10) - 30APR2009 (10)
Duration of AE	1. . 2. . 3. . 4. 3 5. 1
Dose on AE onset	1. 2. 3. 4. 5.
Dose status on AE onset	1. 2. 3. 4. 5.
Action taken	1. NONE 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY 5. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続き）

Subject ID: 550034026

Parameter	Value
	2. UNCHANGED
	3. UNCHANGED
	4. RESOLVED
	5. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-550034026[1),3),4)]	FATAL HEMATEMESIS PROFUSE（PT：吐血） 治験担当医はエノキサパリンと報告事象との関連性があると判断した。弊社は、エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。 FATAL HEMORRHAGIC SHOCK（PT：出血性ショック） 治験担当医はエノキサパリン及びワルファリンと報告事象の因果関係評価を行っていない。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。エノキサパリンについては、時間的関連性が認められないことから、因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

被験者番号：11702-550034026

死亡に至るまでの経過

被験者は 56 歳、アジア人女性。2009 年 4 月 17 日に深部静脈血栓症と診断され、2009 年 4 月 21 日にエノキサパリン（120mg）／用量調節ワルファリンの投与を開始した。

2009 年 4 月 30 日、被験者は吐血（出血：大量吐血）を発現した。本事象により被験者は死亡に至ったため重篤とされた。治験責任（分担）医師は、本事象の重症度は高度で、治験薬との因果関係は「あり」と判断した。被験者は 2009 年 4 月以降貧血の病歴を有していた。2009 年 4 月 20 日、ヘモグロビン値が低下した（7.5g/dL）。2009 年 4 月 23 日、8.0g/dL に回復。2009 年 4 月 25 日、濃厚赤血球 400mL を輸血。2009 年 4 月 30 日、ヘモグロビン値は 11.0g/dL まで上昇するも依然基準値を下回った。被験者は大量に吐血し（約 600mL）、血圧は 70/60mmHg、心拍数は 100bpm となり、循環血液量減少性ショックに陥った。吐血に対して複数薬剤が投与された。本事象により治験薬は変更されなかった。2009 年 4 月 30 日、本事象により被験者は死亡に至った。剖検は実施されなかった。

CIAC は吐血（出血：大量吐血）を「重大な出血事象」とみなし、死亡原因を吐血と判定した。

Laboratory Parameter	Normal Range	Date	Result	Date	Result	Date	Result
Hemoglobin	12.0-16.0 g/dL	20 Apr 2009	**7.5 g/dL (L)**	23 Apr 2009	**8.0 g/dL (L)**	30 Apr 2009	**11.0 g/dL (L)**
Platelets	140-440 giga/L	20 Apr 2009	**592 giga/L (H)**	23 Apr 2009	**742 giga/L (H)**	30 Apr 2009	**725 giga/L (H)**
Alkaline Phosphatase	36-118 U/L	20 Apr 2009	**240 U/L (H)**				
Amylase	28-100 U/L	20 Apr 2009	**23 U/L (L)**				
Bilirubin, Direct	0.10-0.32 mg/dL	20 Apr 2009	0.13 mg/dL				
Bilirubin, Total	0.22-1.28 mg/dL	20 Apr 2009	0.43 mg/dL				
SGOT/AST	11-37 U/L	20 Apr 2009	13 U/L				
SGPT/ALT	8-43 U/L *Local: 5-40 U/L	20 Apr 2009	23 U/L*	20 Apr 2009	17 U/L		
Prothrombin Time (PT)		20 Apr 2009	**18.40 S (H)**				
PT Ratio		20 Apr 2009	**0.55 (L)**				
PT, INR	0.9-1.2	20 Apr 2009	**1.6 (H)**				

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550034027

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034027/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/47/ASIAN/INDONESIA/YES
Medical history	Anaemia, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALBUMIN, AMPICILLIN, ASPILET, B COMPLEX, CAPTOPRIL, CIPROFLOXACIN, DEXTROMETHORPHAN, FOLAVIT, FOLIC ACID, HEMOBION, NA DICLOFENAC, NACL 0.9%, ONDANSETRON, PARACETAMOL
Adverse Events (AE) Preferred term	1. Ascites 2. Ovarian cyst 3. Hypoalbuminaemia 4. Urinary tract infection 5. Pleural effusion 6. Melaena 7. Melaena 8. Hypokalaemia 9. Systemic inflammatory response syndrome
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/YES/NO/YES 7. MILD/NO/NO/NO 8. SEVERE/NO/YES/NO 9. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 30JUL2009 (100) - --------- (.) 2. 31JUL2009 (101) - --------- (.) 3. 08AUG2009 (109) - --------- (.) 4. 11AUG2009 (112) - 18AUG2009 (119) 5. 01OCT2009 (163) - --------- (.) 6. 10OCT2009 (172) - 15OCT2009 (177) 7. 23OCT2009 (185) - --------- (.) 8. 27OCT2009 (189) - --------- (.) 9. 28OCT2009 (190) - 28OCT2009 (190)
Duration of AE	1. . 2. . 3. . 4. 8 5. . 6. 6 7. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550034027

Parameter	Value
	8. .
	9. 1
Dose on AE onset	1. 20 mg
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. F
	8. F
	9. F
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY,OTHER
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. STUDY DRUG DISCONTINUED AND RESTARTED
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. UNCHANGED
	3. IMPROVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED
	7. INSUFFICIENT FOLLOW-UP
	8. INSUFFICIENT FOLLOW-UP

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550034027

Parameter	Value
	9. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550034028

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550034028/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/77/ASIAN/INDONESIA/YES
Medical history	Anaemia, Diarrhoea, Hypertension, Menopause, Pneumonia, Urinary tract infection
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEFOTAXIM, CRAVIT, ENOXAPARIN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Haematuria 2. Haematoma 3. Septic shock
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MILD/YES/NO/YES 3. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 03MAY2009 (4) - 03MAY2009 (4) 2. 03MAY2009 (4) - 04MAY2009 (5) 3. 08MAY2009 (9) - 09MAY2009 (10)
Duration of AE	1. 1 2. 2 3. 2
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 3. NONE
Outcome of event	1. RESOLVED 2. RESOLVED 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550044010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550044010/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/63/ASIAN/INDONESIA/YES
Medical history	Anaemia, Cellulitis, Diabetes mellitus, Abdominal pain upper, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACRAN, AMIKIN, CIPROFLOXACIN, FLAGYL, FOSMICIN, LANSOPRAZOL, MELOXICAM, NOVOMIX, PARACETAMOL, PELASTIN, PLETAAL, PROLIC, SIMVASTATIN
Adverse Events (AE) Preferred term	1. Pyrexia 2. Abscess 3. Anaemia 4. Abdominal pain upper
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 20SEP2008 (9) - 23SEP2008 (12) 2. 20SEP2008 (9) - 07NOV2008 (57) 3. 23SEP2008 (12) - 23SEP2008 (12) 4. 11OCT2008 (30) - 16OCT2008 (35)
Duration of AE	1. 4 2. 49 3. 1 4. 6
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 15 mg
Dose status on AE onset	1. . 2. . 3. I 4. I
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 3. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550044010

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550044014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550044014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/69/ASIAN/INDONESIA/YES
Medical history	Anaemia, Asthma, Femur fracture, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMIKACIN, AMINOPHYLLINE, AVELOX, CERADOLAN, CODIPRONT EXPECTORAN, ENOXAPARIN, FLIXOTIDE, HEMOBION, HIDONAC, INPEPSA, KETOROLAC, NEXIUM, NOVALGIN, ORADEXON, QUIBRON TSR, RANTIN, SANGOBION, SISTENOL, TRIPANZYM, ULSIKUR, VENTOLIN, VENTOLIN EXPECTORANT, WARFARIN, ZALDIAR
Adverse Events (AE) Preferred term	1. Bronchitis 2. Asthma 3. Anaemia 4. Shock 5. Subileus 6. Flatulence 7. Stress ulcer
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. SEVERE/NO/YES/NO 5. MODERATE/NO/NO/NO 6. MILD/NO/NO/NO 7. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 30DEC2008 (5) - 21JAN2009 (27) 2. 01JAN2009 (7) - 21JAN2009 (27) 3. 06JAN2009 (12) - --------- (.) 4. 03APR2009 (99) - 04APR2009 (100) 5. 03APR2009 (99) - --------- (.) 6. 03APR2009 (99) - --------- (.) 7. 03APR2009 (99) - --------- (.)
Duration of AE	1. 23 2. 21 3. . 4. 2 5. . 6. . 7. .
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550044014

Parameter	Value
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. IMPROVED
	4. DEATH
	5. UNCHANGED
	6. UNCHANGED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-550044014[4)]	SUBILEUS CAUSED BY STRESS ULCER（PT：ストレス潰瘍） 治験担当医は報告事象との因果関係評価を行っていない。弊社は、合併症（ストレス）によるものであり、クマジンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550044015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550044015/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/70/ASIAN/INDONESIA/YES
Medical history	Asthma, Hypertension, Myocardial infarction, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BETASERC, BLOREC, CRESTOR, IMDUR, METHYCOBAL, METHYCOBALT, NOOTROPIL, NORVASK, PARIET, PLAVIX, PULMO TIMELET, RANTIN
Adverse Events (AE) Preferred term	1. Vertigo
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 16JAN2009 (12) - 23JAN2009 (19)
Duration of AE	1. 8
Dose on AE onset	1. 15 mg
Dose status on AE onset	1. .
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 550044016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/550044016/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/66/ASIAN/INDONESIA/YES
Medical history	Diabetes mellitus, Diabetic gangrene, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	APIDRA, CLOPIDOGREL, ENOXAPARIN, LANTUS, MEROPENEM, METRONIDAZOLE, NEXIUM, NOVALGIN, WARFARIN
Adverse Events (AE) Preferred term	1. Sepsis 2. Multi-organ failure
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 09JAN2009 (2) - --------- (.) 2. 11JAN2009 (4) - 11JAN2009 (4)
Duration of AE	1. . 2. 1
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. UNCHANGED 2. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 560014009

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/560014009/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/ASIAN/KOREA (SOUTH)/YES
Medical history	Anaemia, Cellulitis, Diabetes mellitus, Pyrexia, Alcoholism, Intestinal mass, Diabetic foot
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ARESTAL, BISCAN N POWDER [BACILLUS LICHENIFORMIS. PROPHYLAXIS FOR DIARRHEA], CERADOLAN, COPOLANG CAP(POLYSACCHARIDE-K), ENOXAPARIN, FULURIDINE CAP(DOXIFLURIDINE), GASPYLOR CAP, GASTER, KEROLA [KETOROLAC TROMETHAMINE], SMECTA SUSP [DIOCTAHEDRAL SMECTITE], SOLETON, SUPRAX CAP, TRANSAMIN-S, TRIZELE, VITAMIN K1, WARFARIN, ZENOCEF
Adverse Events (AE) Preferred term	1. Rectal cancer 2. Haematochezia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 02JAN2009 (3) - 12JAN2009 (13) 2. 10JAN2009 (11) - 12JAN2009 (13)
Duration of AE	1. 11 2. 3
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 2. NONE
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-560014009[1)]	HEMATOCHEZIA（PT：血便排泄） 治験担当医はワルファリンと報告事象との関連性があると判断した。弊社は、時間的関連性が認められないことから、ワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 580044008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/580044008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/61/WHITE/SWITZERLAND/YES
Medical history	Hypertension, Hypothyroidism, Migraine
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, BELOC, COVERSUM, DAFALGAN(PARACETAMOL), ELTROXIN, ENOXAPARIN, FLAGYL(METRONIDAZOLE), NEXIUM(ESOMEPRAZOLE), ROCEPHINE(CEFTRIAXONE), TRYPTIZOL, VITARUBIN(CYANOCOBALAMINE)
Adverse Events (AE) Preferred term	1. Dyspepsia 2. Abdominal discomfort
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 29MAR2008 (4) - 01APR2008 (7) 2. 10APR2008 (16) - 15APR2008 (21)
Duration of AE	1. 4 2. 6
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 580044024

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/580044024/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/64/WHITE/SWITZERLAND/YES
Medical history	Crohn's disease, Hypokalaemia, Ileus, Pouchitis, Normochromic normocytic anaemia, Normochromic normocytic anaemia, Haemoglobin decreased, Diarrhoea
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALCIMAGON D3, CEFUROXIME, FERINJECT(FERRIC CRABOXYMALTOSE COMPLEX…), FLAGYL, IMUREK, METAMUCIL (PSYLLIUM), OMEPRAZOLE, PENTASA(MESALAZINE), POTASSIUM EFFERVESCENT: K+, PREDNISONE
Adverse Events (AE) Preferred term	1. Diarrhoea 2. Syncope 3. Normochromic normocytic anaemia 4. Osteopenia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/NO 2. MILD/NO/NO/NO 3. MODERATE/NO/YES/NO 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 30SEP2009 (101) - --------- (.) 2. 09OCT2009 (110) - 09OCT2009 (110) 3. 13OCT2009 (114) - --------- (.) 4. 23OCT2009 (124) - --------- (.)
Duration of AE	1. . 2. 1 3. . 4. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. F 2. F 3. F 4. F
Action taken	1. NONE 2. NONE 3. REMEDIAL DRUG THERAPY,OTHER 4. NONE
Outcome of event	1. UNCHANGED 2. RESOLVED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 580044024

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 580114001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/580114001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/49/WHITE/SWITZERLAND/YES
Medical history	Hyperuricaemia, Polyarteritis nodosa, Sleep apnoea syndrome, Metabolic syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, ALLOPUR, AUGMENTIN, AZAREK, CALCIMAGON D3, ENOXAPARIN, LASIX, LISITRIL, OMED, PREDNISONE
Adverse Events (AE) Preferred term	1. Cellulitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 28JUL2008 (50) - 11AUG2008 (64)
Duration of AE	1. 15
Dose on AE onset	1.
Dose status on AE onset	1.
Action taken	1. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 580124001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/580124001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/65/WHITE/SWITZERLAND/YES
Medical history	Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACENOCOUMAROL, AZICLAV, DAFALGAN, ENOXAPARIN, FRAXIPARINE FORTE, HYGROTON, LIQUEMIN, NOVALGIN, OLMETEC PLUS, OPTIFEN, PANTOZOL, XEFO
Adverse Events (AE) Preferred term	1. Bronchitis 2. Ankle fracture 3. Ligament injury 4. Procedural pain 5. Drug resistance 6. Post procedural swelling 7. Cough
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. SEVERE/NO/YES/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. MODERATE/YES/NO/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 18FEB2009 (9) - 25FEB2009 (16) 2. 26SEP2009 (229) - 09OCT2009 (242) 3. 26SEP2009 (229) - 09OCT2009 (242) 4. 30SEP2009 (233) - 07NOV2009 (271) 5. 04OCT2009 (237) - --------- (.) 6. 06OCT2009 (239) - 07NOV2009 (271) 7. 22JAN2010 (347) - 28FEB2010 (384)
Duration of AE	1. 8 2. 14 3. 14 4. 39 5. . 6. 33 7. 38
Dose on AE onset	1. 2. 3. 4. 5. 6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 580124001

Parameter	Value
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. REMEDIAL DRUG THERAPY
	2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	3. STUDY DRUG DISCONTINUED AND RESTARTED
	4. REMEDIAL DRUG THERAPY
	5. STUDY DRUG DISCONTINUED PERMANENTLY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600024003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/600024003/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/55/ASIAN/INDIA/YES
Medical history	Diabetes mellitus, Dysmenorrhoea
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ATORVASTATIN, CALCIUM CITRATE USP, CEFUROXIME, CHOLECALCIFEROL, CYANOCOBALAMINE I.P., GLICLAZIDE, IBUPROFEN, INSULIN, LORNOXICAM, MEFENAMIC ACID,PARACETAMOL IP, METFORMIN HYDROCHLORIDE, METHYLCOBALAMINE, PANTOCID, PIOGLITAZONE, RABEPRAZOLE, SERRATIOPEPTIDASE, VIT E
Adverse Events (AE) Preferred term	1. Blood homocysteine increased 2. Dyspnoea 3. Furuncle 4. Oedema 5. Tetany 6. Dyspnoea 7. Oedema peripheral 8. Oedema
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/YES/YES/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/NO 8. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 23JUL2008 (5) - 07AUG2008 (20) 2. 02AUG2008 (15) - 18AUG2008 (31) 3. 18AUG2008 (31) - 22AUG2008 (35) 4. 16SEP2008 (60) - 17OCT2008 (91) 5. 30SEP2008 (74) - 30OCT2008 (104) 6. 17OCT2008 (91) - 13NOV2008 (118) 7. 04FEB2009 (201) - --------- (.) 8. 04FEB2009 (201) - --------- (.)
Duration of AE	1. 16 2. 17 3. 5 4. 32 5. 31 6. 28 7. . 8. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600024003

Parameter	Value
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. F
	8. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. REMEDIAL DRUG THERAPY
	6. NONE
	7. NONE
	8. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600024003

Parameter	Value
	8. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-600024003[5)]	TETANY（PT：テタニー） 治験担当医はリバーロキサバンと報告事象との関連性があると判断した。しかしながら、ドイツ安全性部門は、合併症（副甲状腺機能低下による神経症）の可能性があるため、リバーロキサバンとの因果関係は否定できると評価している。弊社は、リバーロキサバン投与と報告事象発現の時間経過および治験担当医の評価を考慮した場合、リバーロキサバンとの因果関係を完全には否定できないが、合併症による可能性が高いと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600104002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/600104002/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/38/ASIAN/INDIA/YES
Medical history	Large intestine perforation, Hernia diaphragmatic repair, Gastrointestinal gangrene, Jejunostomy refashioning, Gastrectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BRO-ZEDEX, CALCIMAX [VITAMIN SUPP.: CALCIUM CARBONATE], INJ. PANTOCID, LACTULOSE, MAGNEX, POTKLOR, SUCRALFATE, SYP. ARYSTOZYME, SYP. DEXORANGE FORTE, TAB. PANTOCID, TAB.OFLOX, ZINCOVIT
Adverse Events (AE) Preferred term	1. Enterocutaneous fistula 2. Cough 3. International normalised ratio increased 4. Respiratory tract infection 5. Incision site abscess 6. Hypoproteinaemia 7. Enterocutaneous fistula 8. Metabolic encephalopathy 9. Sepsis 10. Enterocutaneous fistula 11. Multi-organ failure
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/YES/YES 5. MODERATE/NO/YES/YES 6. MODERATE/NO/YES/YES 7. MODERATE/NO/YES/YES 8. SEVERE/NO/YES/YES 9. SEVERE/NO/YES/YES 10. SEVERE/NO/YES/YES 11. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 19JUL2008 (9) - 13AUG2008 (34) 2. 21JUL2008 (11) - 25JUL2008 (15) 3. 21JUL2008 (11) - 22JUL2008 (12) 4. 15SEP2008 (67) - 16OCT2008 (98) 5. 15SEP2008 (67) - 16OCT2008 (98) 6. 15SEP2008 (67) - --------- (.) 7. 11OCT2008 (93) - 18OCT2008 (100) 8. 19OCT2008 (101) - 23OCT2008 (105) 9. 19OCT2008 (101) - 23OCT2008 (105) 10. 19OCT2008 (101) - --------- (.)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600104002

Parameter	Value
	11. 19OCT2008 (101) - 23OCT2008 (105)
Duration of AE	1. 26
	2. 5
	3. 2
	4. 32
	5. 32
	6. .
	7. 8
	8. 5
	9. 5
	10. .
	11. 5
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. F
	9. F
	10. F
	11. F
Action taken	1. OTHER
	2. REMEDIAL DRUG THERAPY
	3. STUDY DRUG DISCONTINUED AND RESTARTED
	4. REMEDIAL DRUG THERAPY
	5. OTHER
	6. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600104002

Parameter	Value
	7. OTHER
	8. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	9. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	10. STUDY DRUG DISCONTINUED PERMANENTLY
	11. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. WORSENED
	8. DEATH
	9. DEATH
	10. UNCHANGED
	11. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600104003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/600104003/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/28/ASIAN/INDIA/YES
Medical history	Guillain-Barre syndrome, Hemiparesis, Hip arthroplasty, Postoperative wound infection, Vascular pseudoaneurysm
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTINE, AZEE, BECOZINC, FEFOL, FUCIDIN CREAM, INJ. CEFAZOLIN, INJ. CIPLOX, INJ. CLEXANE, INJ. MAGNEX, INJ. PANTOCID, INJ. TRAMADOL, PARACETAMOL, SUPRADYN, TAB. CIPLOX, TAB. CLOPILET A, TAB. LINEZOLID, TAB. PANTOCID, TAB. PARACETAMOL, TAB. TRAMADOL, ZOVIRAX
Adverse Events (AE) Preferred term	1. Infective aneurysm 2. Infective aneurysm 3. Herpes zoster 4. Rectal haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/YES/YES
Start/stop date of event with relative date	1. 22JUL2008 (2) - 24JUL2008 (4) 2. 24JUL2008 (4) - 19SEP2008 (61) 3. 31AUG2008 (42) - 10SEP2008 (52) 4. 14SEP2008 (56) - 17SEP2008 (59)
Duration of AE	1. 3 2. 58 3. 11 4. 4
Dose on AE onset	1. 15 mg 2. 15 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. . 4. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY,OTHER 3. REMEDIAL DRUG THERAPY 4. NONE
Outcome of event	1. WORSENED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600104003

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-600104003[2)]	BLEEDING PER RECTUM（PT：下部消化管出血） 治験担当医は、無治療で本剤継続中に回復していることから、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 600104006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/600104006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/48/ASIAN/INDIA/YES
Medical history	Bone operation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CAP. MOX [AMOXYCILLIN], CAP. PROXYVON, ENOXAPARIN, PANTOCID, SUPRADYN, SYP. LINCTUSCODEINE, TAB PANTOCID, TAB. ALPRAX, TAB. PANTOCID, WARFARIN
Adverse Events (AE) Preferred term	1. Gingival bleeding 2. Haematemesis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/YES/YES/YES
Start/stop date of event with relative date	1. 26MAR2009 (107) - 04MAY2009 (146) 2. 02MAY2009 (144) - 06MAY2009 (148)
Duration of AE	1. 40 2. 5
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. OTHER 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 610014002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/610014002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/84/ASIAN/TAIWAN/YES
Medical history	Benign prostatic hyperplasia, Cellulitis, Diabetes mellitus, Hypertension, Cerebrovascular accident, Ischaemic stroke, Renal cell carcinoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACETAMINOPHEN, ADALAT, AMARYL, ATENOLOL, AUGMENTIN, CAPOTEN, CEFA, CLEXANE, D10 W, DEMEROL, DEXTROSE AND ELECTROLYTE SOLUTION, DEXTROSE MONOHYDRATE ,NACL, DOLCOL, DULCOLAX [BISACODYL], FOXATE, GLUCOPHAGE, HARNALIDGE, LASIX, MGO, NORVASC, OXACILLIN, OXBU, SALINE, TAITA NO. 5, TETANUS TOXOID, TETRACYCLINE OPH OINT 1% 5 G/TUBE, TINTEN, UNASYN, VESICARE, VOREN
Adverse Events (AE) Preferred term	1. Constipation 2. Bradycardia 3. Somnolence 4. High frequency ablation 5. Pyrexia 6. Urinary tract infection 7. Decreased appetite 8. Somnolence 9. Traumatic haemorrhage 10. Urinary tract infection 11. Hypoglycaemia 12. Renal abscess
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/YES/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/YES/YES 10. MILD/NO/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 21AUG2009 (5) - 21AUG2009 (5) 2. 23AUG2009 (7) - 23AUG2009 (7) 3. 17NOV2009 (93) - --------- (.) 4. 18NOV2009 (94) - 18NOV2009 (94) 5. 01DEC2009 (107) - 04DEC2009 (110) 6. 03DEC2009 (109) - 11DEC2009 (117)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 610014002

Parameter	Value
	7. 03DEC2009 (109) - 07DEC2009 (113)
	8. 03DEC2009 (109) - 04DEC2009 (110)
	9. 05FEB2010 (173) - 19FEB2010 (187)
	10. 06FEB2010 (174) - 14FEB2010 (182)
	11. 06FEB2010 (174) - 06FEB2010 (174)
	12. 12FEB2010 (180) - 18FEB2010 (186)
Duration of AE	1. 1
	2. 1
	3. .
	4. 1
	5. 4
	6. 9
	7. 5
	8. 2
	9. 15
	10. 9
	11. 1
	12. 7
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
	12. 20 mg
Dose status on AE onset	1. .
	2. .
	3. I
	4. I
	5. .
	6. .
	7. .
	8. .
	9. .
	10. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 610014002

Parameter	Value
	11. .
	12. F
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. NONE
	4. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. NONE
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY,OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. UNCHANGED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 650014001

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/650014001/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/54/ASIAN/HONGKONG/YES
Medical history	Anaemia, Breast cancer, Uterine polyp, Hypokalaemia, Uterine leiomyoma, Radical hysterectomy
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALENDRONATE SODIUM, CALPEROS D3, ENOXAPARIN, FERROUS SULPHATE, HIRUDOID CREAM, LETROZOLE, SYRUP POTASSIUM, TAMOXIFEN, TINZAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Syncope 2. Osteoporosis
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 14SEP2009 (21) - 15SEP2009 (22) 2. 29SEP2009 (36) - --------- (.)
Duration of AE	1. 2 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/660014002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/67/ASIAN/MALAYSIA/YES
Medical history	Duodenal ulcer, Septic shock
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CLEXANE, ENOXAPARIN, MAXOLON, MULTIVITAMIN, PANTOPRAZOLE, PARACETAMOL, POTASSIUM CHLORIDE, SLOW K, TRAMADOL, WARFARIN
Adverse Events (AE) Preferred term	1. Hypokalaemia 2. Headache 3. Inguinal hernia, obstructive 4. Hypokalaemia 5. Hypokalaemia 6. Rash pruritic
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 27JUN2008 (1) - 04JUL2008 (8) 2. 26AUG2008 (61) - 25SEP2008 (91) 3. 09SEP2008 (75) - 29OCT2008 (125) 4. 09OCT2008 (105) - 10OCT2008 (106) 5. 23OCT2008 (119) - --------- (.) 6. 15DEC2008 (172) - 05JAN2009 (193)
Duration of AE	1. 8 2. 31 3. 51 4. 2 5. . 6. 22
Dose on AE onset	1. 2. 3. 4. 5. 6.
Dose status on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014002

Parameter	Value
	5.
	6.
Action taken	1. REMEDIAL DRUG THERAPY
	2. NONE
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/660014006/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/52/ASIAN/MALAYSIA/YES
Medical history	Asthma, Hyperlipidaemia, Hypertension, Myocardial ischaemia, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, BENADRYL, CLOXACILLIN, COMBIVENT, ENOXAPARIN, ENOXAPARIN 1.0MG/KG TWICE DAILY, ETHAMBUTOL, FRUSEMIDE, GABAPENTIN, GLICLAZIDE, GLYCERYL TRINITRATE, ISONIAZID, METFORMIN, NEUROBION, PIRITON, PYRAZINAMIDE, PYRIDOXINE, RIFAMPICIN, SALBUTAMOL, WARFARIN
Adverse Events (AE) Preferred term	1. Pulmonary tuberculosis 2. Upper respiratory tract infection 3. Neuralgia 4. Neuralgia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 01AUG2008 (3) - --------- (.) 2. 23AUG2008 (25) - 02SEP2008 (35) 3. 09SEP2008 (42) - 15SEP2008 (48) 4. 16SEP2008 (49) - --------- (.)
Duration of AE	1. . 2. 11 3. 7 4. .
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014006

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/660014008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/44/ASIAN/MALAYSIA/YES
Medical history	Oedema peripheral
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEFUROXIME SODIUM, CLEXANE, DICLOFENAC 1% EMULGEL, DICLOFENAC SODIUM, DIPHENHYDRAMINE HCI EXPECTORANT, ENOXAPARIN, FERROUS FUMARATE, FOLIC ACID, HYOSCINE N-BUTYLBROMIDE, IM VOLTAREN, MELOXICAM, PARACETAMOL, TAB CEFUROXIME, TRAMADOL, WARFARIN
Adverse Events (AE) Preferred term	1. Cough 2. Menorrhagia 3. Viral infection 4. Hypoaesthesia 5. Synovitis 6. Dizziness 7. Synovitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/YES/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 16DEC2008 (14) - 16DEC2008 (14) 2. 24DEC2008 (22) - 30DEC2008 (28) 3. 01FEB2009 (61) - 02FEB2009 (62) 4. 10FEB2009 (70) - 08APR2009 (127) 5. 05MAR2009 (93) - 26APR2009 (145) 6. 08APR2009 (127) - 08APR2009 (127) 7. 26APR2009 (145) - --------- (.)
Duration of AE	1. 1 2. 7 3. 2 4. 58 5. 53 6. 1 7. .
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014008

Parameter	Value
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	6. OTHER
	7. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. IMPROVED
	6. RESOLVED
	7. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014010

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/660014010/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/77/ASIAN/MALAYSIA/YES
Medical history	Anaemia, Diabetes mellitus, Gout, Hyperlipidaemia, Hypertension, Osteoarthritis, Postmenopause, Thalassaemia trait, Lymph node cancer metastatic
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALLUPURINOL, CLOXACILLIN SODIUM, DEXAMETHASONE, EPREX, FERROUS FUMARATE, FOLIC ACID, LOSARTAN, LOVASTATIN, MAXOLON, METFORMIN, PARACETAMOL, PLASMA, RANITIDINE, SYRUP MORPHINE, VITAMIN B COMPLEX
Adverse Events (AE) Preferred term	1. Cervix cancer metastatic 2. Anaemia 3. Anaemia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 23JUL2009 (71) - 06NOV2009 (177) 2. 23JUL2009 (71) - 24JUL2009 (72) 3. 09OCT2009 (149) - 09OCT2009 (149)
Duration of AE	1. 107 2. 2 3. 1
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED 3. REMEDIAL DRUG THERAPY
Outcome of event	1. DEATH 2. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 660014010

Parameter	Value
	3. IMPROVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-660014010[2),2)]	WORSENING OF ANAEMIA（PT：貧血）2事象有 1）治験担当医は、合併症（貧血）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。 2）治験担当医は、合併症（貧血）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/670014002/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/72/ASIAN/PHILIPPINES/YES
Medical history	Anaemia, Aortic arteriosclerosis, Salpingo-oophorectomy bilateral, Cholelithiasis, Hypertension, Hysterectomy, Postmenopause, Ovarian cancer metastatic, Paraneoplastic syndrome
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXICILLIN, CALTRATE PLUS, CEFALEXIN, COMBIZAR (LOSARTAN PLUS HYDROCHLOROTHIAZIDE, DAFLON [DIOSMIN + HESPERIDIN], DICLOFENAC SODIUM, DOLO-NEUROBION [VITAMIN SUPPLEMENT: PARACETAMOL, VIT B1, VIT B6, VIT B12], DOXORUBICIN, ENERVON C, ENOXAPARIN, FERROUS SULFATE, HEPAVIT, HOLOXAN, LYRICA, LYSOZYME CHLORIDE, MEFENAMIC ACID, METATHIONE, NEVRAMIN, NORVASC, PLASIL, TEGAFUR, TRIHEMIC, VITAMIIN C, VITAMIN E, WARFARIN
Adverse Events (AE) Preferred term	1. Haematoma 2. Haematuria 3. Upper respiratory tract infection 4. Cough 5. Ovarian cancer 6. Pain 7. Blood alkaline phosphatase increased 8. Post procedural haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/YES/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. SEVERE/NO/YES/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 18MAY2008 (61) - 19JUN2008 (93) 2. 11JUN2008 (85) - 11JUN2008 (85) 3. 25AUG2008 (160) - 30AUG2008 (165) 4. 23OCT2008 (219) - 02NOV2008 (229) 5. 21NOV2008 (248) - 20MAY2009 (428) 6. 04DEC2008 (261) - 04DEC2008 (261) 7. 12FEB2009 (331) - ---------- (.) 8. 15APR2009 (393) - 15APR2009 (393)
Duration of AE	1. 33 2. 1 3. 6 4. 11 5. 181 6. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014002

Parameter	Value
	7. .
	8. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
Action taken	1. NONE
	2. DOSE OF STUDY DRUG REDUCED
	3. NONE
	4. REMEDIAL DRUG THERAPY
	5. OTHER
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. OTHER
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. DEATH
	6. RESOLVED
	7. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014002

Parameter	Value
	8. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014018

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/670014018/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/75/ASIAN/PHILIPPINES/YES
Medical history	Allergy to animal, Cardiac failure congestive, Coronary artery disease, Food allergy, Haematoma, Hypoalbuminaemia, Wound infection, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASA, ATORVASTATIN, CLOPIDOGREL, DIGOXIN, DIOSMIN + HESPERIDIN, ENOXAPARIN, FUROSEMIDE, ISOSORBIDE DINITRATE, KETOROLAC, SIMVASTATIN, UNASYN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Atrial fibrillation 2. Ischaemic stroke 3. Sepsis 4. Cardiac arrest
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. SEVERE/YES/YES/YES 3. SEVERE/NO/YES/NO 4. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 09MAY2009 (4) - --------- (.) 2. 07JUN2009 (33) - --------- (.) 3. 16JUN2009 (42) - --------- (.) 4. 16JUN2009 (42) - 16JUN2009 (42)
Duration of AE	1. . 2. . 3. . 4. 1
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED PERMANENTLY,OTHER 3. NONE 4. NONE
Outcome of event	1. UNCHANGED 2. UNCHANGED 3. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014018

Parameter	Value
	4. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-670014018[1)]	ISCHEMIC STROKE WITH COMPLETE VASCULAR（PT：虚血性脳卒中） 治験担当医はエノキサパリン及びワルファリンと報告事象との関連性があると判断した。弊社は、合併症（心房細動、動脈硬化）によるものであり、エノキサパリン及びワルファリンとの因果関係は否定できると考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/670014020/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/92/ASIAN/PHILIPPINES/YES
Medical history	Aortic arteriosclerosis, Haematochezia, Chest X-ray abnormal, Cough, Abdominal pain upper, Hypertension, Hysterectomy, Mitral valve stenosis, Phlebitis, Postmenopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMINO VITA GEL [VITS A, D3, E, B1, B2, B6 = VITAMIN SUPPLEMENT], AMINOLEBAN, APPETENS, BENADRYL, CEFUROXIME, CENTRUM, DIOSMIN+ HESPERIDIN, ESOMEPRAZOLE, FUROSEMIDE, HYDROCORTISONE, INSERTION OF CAVAL FILTER, LACIPIL, LACTULOSE, MOBIC, PARACETAMOL, PREDNISONE, VOLTAREN GEL
Adverse Events (AE) Preferred term	1. Gastrointestinal haemorrhage 2. Haemorrhoids 3. Constipation 4. Haematoma 5. Melaena 6. Lymphoma 7. Aortic arteriosclerosis 8. Scoliosis 9. Spinal cord compression 10. Oesophagogastroduodenoscopy 11. Osteoarthropathy 12. Pyrexia 13. Urinary tract infection 14. Cough 15. Melaena 16. Gastrointestinal haemorrhage 17. Lymphoma 18. Hypokalaemia 19. Blood bilirubin increased 20. Constipation 21. Hyperkalaemia 22. Pneumonia 23. Respiratory tract infection 24. Gastrointestinal haemorrhage 25. Anaemia 26. Anaemia 27. Anaemia 28. Cardio-respiratory arrest
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
	4. MILD/NO/NO/YES
	5. MILD/YES/NO/YES
	6. MODERATE/NO/YES/YES
	7. MODERATE/NO/NO/YES
	8. MODERATE/NO/NO/YES
	9. MODERATE/NO/NO/YES
	10. MILD/NO/NO/YES
	11. MILD/NO/NO/YES
	12. MILD/NO/NO/YES
	13. MILD/NO/NO/YES
	14. MILD/NO/NO/YES
	15. MILD/NO/NO/YES
	16. MODERATE/YES/YES/YES
	17. SEVERE/NO/YES/NO
	18. MILD/NO/NO/NO
	19. MILD/NO/NO/NO
	20. MILD/NO/NO/NO
	21. MILD/NO/NO/NO
	22. MODERATE/NO/NO/NO
	23. MILD/NO/NO/NO
	24. SEVERE/NO/YES/NO
	25. MODERATE/NO/NO/NO
	26. SEVERE/NO/NO/NO
	27. SEVERE/NO/NO/NO
	28. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 26JUL2009 (3) - 03SEP2009 (42)
	2. 26JUL2009 (3) - --------- (.)
	3. 26JUL2009 (3) - 29JUL2009 (6)
	4. 27JUL2009 (4) - 02AUG2009 (10)
	5. 30JUL2009 (7) - 30JUL2009 (7)
	6. 31JUL2009 (8) - 11OCT2009 (80)
	7. 31JUL2009 (8) - --------- (.)
	8. 31JUL2009 (8) - --------- (.)
	9. 31JUL2009 (8) - --------- (.)
	10. 01AUG2009 (9) - 01AUG2009 (9)
	11. 06AUG2009 (14) - --------- (.)
	12. 06AUG2009 (14) - 08AUG2009 (16)
	13. 06AUG2009 (14) - 28OCT2009 (97)
	14. 19AUG2009 (27) - 24AUG2009 (32)
	15. 28SEP2009 (67) - 28SEP2009 (67)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
	16. 07OCT2009 (76) - 16OCT2009 (85)
	17. 12OCT2009 (81) - --------- (.)
	18. 26OCT2009 (95) - 29OCT2009 (98)
	19. 27OCT2009 (96) - --------- (.)
	20. 30OCT2009 (99) - 30OCT2009 (99)
	21. 30OCT2009 (99) - 30OCT2009 (99)
	22. 01NOV2009 (101) - --------- (.)
	23. 01NOV2009 (101) - 10DEC2009 (140)
	24. 06NOV2009 (106) - 11NOV2009 (111)
	25. 18NOV2009 (118) - 22NOV2009 (122)
	26. 25NOV2009 (125) - 27NOV2009 (127)
	27. 07DEC2009 (137) - --------- (.)
	28. 29DEC2009 (159) - 29DEC2009 (159)
Duration of AE	1. 40
	2. .
	3. 4
	4. 7
	5. 1
	6. 73
	7. .
	8. .
	9. .
	10. 1
	11. .
	12. 3
	13. 84
	14. 6
	15. 1
	16. 10
	17. .
	18. 4
	19. .
	20. 1
	21. 1
	22. .
	23. 40
	24. 6
	25. 5
	26. 3
	27. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
	28. 1
Dose on AE onset	1. 15 mg
	2. 15 mg
	3. 15 mg
	4. 15 mg
	5. 15 mg
	6. 15 mg
	7. 15 mg
	8. 15 mg
	9. 15 mg
	10. 15 mg
	11. 15 mg
	12. 15 mg
	13. 15 mg
	14. 15 mg
	15. 20 mg
	16. 20 mg
	17. 20 mg
	18. 20 mg
	19. 20 mg
	20. 20 mg
	21. 20 mg
	22. 20 mg
	23. 20 mg
	24. 20 mg
	25. 20 mg
	26. 20 mg
	27. 20 mg
	28. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. I
	6. I
	7. I
	8. I
	9. I
	10. I
	11. I

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
	12. I
	13. I
	14. I
	15. .
	16. .
	17. F
	18. F
	19. F
	20. F
	21. F
	22. F
	23. F
	24. F
	25. F
	26. F
	27. F
	28. F
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER
	2. NONE
	3. REMEDIAL DRUG THERAPY,OTHER
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	7. NONE
	8. NONE
	9. NONE
	10. NONE
	11. REMEDIAL DRUG THERAPY
	12. REMEDIAL DRUG THERAPY
	13. NONE
	14. NONE
	15. NONE
	16. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	17. REMEDIAL DRUG THERAPY,OTHER
	18. REMEDIAL DRUG THERAPY
	19. NONE
	20. REMEDIAL DRUG THERAPY
	21. REMEDIAL DRUG THERAPY
	22. REMEDIAL DRUG THERAPY
	23. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
	24. OTHER
	25. OTHER
	26. NONE
	27. NONE
	28. NONE
Outcome of event	1. RESOLVED
	2. UNCHANGED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. WORSENED
	7. UNCHANGED
	8. UNCHANGED
	9. UNCHANGED
	10. RESOLVED
	11. IMPROVED
	12. RESOLVED
	13. RESOLVED
	14. RESOLVED
	15. RESOLVED
	16. RESOLVED
	17. UNCHANGED
	18. RESOLVED
	19. INSUFFICIENT FOLLOW-UP
	20. RESOLVED
	21. RESOLVED
	22. UNCHANGED
	23. RESOLVED
	24. RESOLVED
	25. RESOLVED
	26. RESOLVED
	27. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670014020

Parameter	Value
	28. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670024008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/670024008/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/38/ASIAN/PHILIPPINES/YES
Medical history	Endometriosis, Ovarian cystectomy, Vaginal haemorrhage, Platelet count increased, Haemorrhagic anaemia, Uterine dilation and curettage
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMOXICILLIN, CIPROFLOXACIN, DICLOFENAC SODIUM, ENOXAPARIN, FERROUS SULFATE, MEFENAMIC ACID, TRAMADOL, TRANEXAMIC ACID, WARFARIN
Adverse Events (AE) Preferred term	1. Vaginal haemorrhage 2. Pain in extremity 3. Upper respiratory tract infection 4. Vaginal haemorrhage 5. Vaginal haemorrhage 6. Vaginal haemorrhage 7. Back pain 8. Fatigue 9. Urinary tract infection 10. Cervix carcinoma 11. Cervix carcinoma
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/YES/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MODERATE/NO/YES/YES 11. SEVERE/NO/YES/NO
Start/stop date of event with relative date	1. 23FEB2009 (11) - 04MAR2009 (20) 2. 04MAR2009 (20) - 04MAR2009 (20) 3. 09MAR2009 (25) - 16MAR2009 (32) 4. 18MAR2009 (34) - 18MAR2009 (34) 5. 19MAR2009 (35) - 26MAR2009 (42) 6. 12APR2009 (59) - 13APR2009 (60) 7. 24APR2009 (71) - --------- (.) 8. 26APR2009 (73) - --------- (.) 9. 26APR2009 (73) - --------- (.) 10. 27APR2009 (74) - 29JUL2009 (167) 11. 30JUL2009 (168) - 02AUG2009 (171)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670024008

Parameter	Value
Duration of AE	1. 10
	2. 1
	3. 8
	4. 1
	5. 8
	6. 2
	7. .
	8. .
	9. .
	10. 94
	11. 4
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	2. NONE
	3. DOSE OF STUDY DRUG REDUCED,REMEDIAL DRUG THERAPY
	4. NONE
	5. STUDY DRUG DISCONTINUED AND RESTARTED
	6. NONE
	7. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 670024008

Parameter	Value
	8. NONE
	9. REMEDIAL DRUG THERAPY
	10. OTHER
	11. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. UNCHANGED
	8. UNCHANGED
	9. INSUFFICIENT FOLLOW-UP
	10. WORSENED
	11. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 680024008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/680024008/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/77/ASIAN/SINGAPORE/YES
Medical history	Hypertension, Paget's disease of skin, Prostate cancer stage III, Neurilemmoma
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CEFTRIAXONE, CLARITHROMYCIN, FRUSEMIDE, NIFEDIPINE, POTASSIUM CHLORIDE
Adverse Events (AE) Preferred term	1. Insomnia 2. Exercise tolerance decreased 3. Pneumonia 4. Blood creatinine increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. SEVERE/NO/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --MAR2008 (.) - --------- (.) 2. --MAR2008 (.) - --------- (.) 3. 22APR2008 (57) - 23APR2008 (58) 4. 23APR2008 (58) - --------- (.)
Duration of AE	1. . 2. . 3. 2 4. .
Dose on AE onset	1. 2. 3. 20 mg 4. 20 mg
Dose status on AE onset	1. 2. 3. . 4. F
Action taken	1. NONE 2. REMEDIAL DRUG THERAPY 3. REMEDIAL DRUG THERAPY 4. STUDY DRUG DISCONTINUED PERMANENTLY
Outcome of event	1. INSUFFICIENT FOLLOW-UP 2. INSUFFICIENT FOLLOW-UP 3. DEATH

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 680024008

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 680024015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/680024015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/54/ASIAN/SINGAPORE/YES
Medical history	Acute myeloid leukaemia, Hyperlipidaemia, Hypertension
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, NIFEDIPINE, SIMVASTATIN, WARFARIN
Adverse Events (AE) Preferred term	1. Ovarian epithelial cancer 2. International normalised ratio increased
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 19NOV2008 (68) - --------- (.) 2. 19NOV2008 (68) - 25NOV2008 (74)
Duration of AE	1. . 2. 7
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. IMPROVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 680024019

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/680024019/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/79/ASIAN/SINGAPORE/YES
Medical history	Cough, Pyrexia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AQUEOUS CREAM [SOFT WHITE PARAFFIN], AUGMENTIN, CIPROFLOXACIN, DAFLON [DAFLON CONTAINS DIOSMIN+ HESPERIDIN], DEXTROMETHORPHAN, DIFFLAM LOZENGE, DOMPERIDONE, ENOXAPARIN, ETHAMBUTOL, ISONIAZID, LOPERAMIDE (PRN), OMEPRAZOLE, PARACETAMOL, PIRITON, PROMETHAZINE/CODEINE, PYRAZINAMIDE, PYRIDOXINE, RABEPRAZOLE, RIFAMPICIN, TAZOCIN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Dysphonia 2. Haemorrhoids 3. Dry skin 4. Diarrhoea 5. Purpura 6. Haemoptysis 7. Pulmonary tuberculosis 8. Pyrexia 9. Varicose vein
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MODERATE/YES/YES/YES 7. SEVERE/NO/YES/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES
Start/stop date of event with relative date	1. --MAR2009 (.) - --------- (.) 2. --APR2009 (.) - 05MAY2009 (126) 3. --APR2009 (.) - 06MAY2009 (127) 4. 15JAN2009 (16) - 15JAN2009 (16) 5. 03FEB2009 (35) - 03MAR2009 (63) 6. 29MAR2009 (89) - 29MAR2009 (89) 7. 31MAR2009 (91) - --------- (.) 8. 31MAR2009 (91) - 31MAR2009 (91) 9. 26MAY2009 (147) - --------- (.)
Duration of AE	1. . 2. . 3. . 4. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 680024019

Parameter	Value
	5. 29
	6. 1
	7. .
	8. 1
	9. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. NONE
	2. REMEDIAL DRUG THERAPY
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. NONE
	6. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	7. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY
	9. NONE
Outcome of event	1. IMPROVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. IMPROVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 680024019

Parameter	Value
	9. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700014004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700014004/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/69/WHITE/NEW ZEALAND/YES
Medical history	Rectal haemorrhage
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALFENTANIL, CEFUROXIME, CHLORVESCENT, CODEINE PHOSPHATE, CODIENE PHOSPHATE, CYCLIZINE, DEXTROSE, DEXTROSE WITH 30MLS KCL, ENOXAPARIN, FENTANYL, FRUSEMIDE, GENTAMYCIN, HALOPERIDOL, HARTMANS SOLUTION, METRONIDAZOLE, MIDAZOLAM, MORPHINE, MORPHINE ELIXER, MYLANTA [ALUMINIUM HYDROXIDE, MAGNESIUM HYDROXIDE AND SIMETICONE], NEOSTIGMINE METHYLSULFATE, NORMAL SALINE, ONTANSETRON, OXYNORM, PARACETAMOL, PROPOFOL, QUININE SULFATE, ROCURONIUM BROMIDE, ROPIVACAINE, SEVREDOL ELIXER [MORPHINE SULPHATE. INDICATION - PAIN RELIEF.], SLOW K, SUXAMETHONIUM CHLORIDE, THIAMINE, TRAMADOL, VICKS LOZENGES [VICKS LOZENGES - BENZOCAINE 10MGS AND MENTHOL 10MGS], WARFARIN
Adverse Events (AE) Preferred term	1. Muscle spasms 2. Abdominal pain upper 3. Alanine aminotransferase increased 4. Colonic polyp 5. Gamma-glutamyltransferase increased 6. Upper respiratory tract infection 7. Abdominal pain upper 8. Nausea 9. Intestinal haemorrhage 10. Haematuria 11. Large intestine perforation 12. Hypotension 13. Delirium 14. Rectal haemorrhage 15. Fall
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MILD/NO/NO/YES 10. MILD/NO/NO/YES 11. SEVERE/NO/YES/YES 12. MILD/NO/NO/YES

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700014004

Parameter	Value
	13. MODERATE/NO/NO/YES
	14. SEVERE/NO/YES/YES
	15. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 23MAY2008 (2) - 23MAY2008 (2)
	2. 23MAY2008 (2) - 23MAY2008 (2)
	3. 04JUN2008 (14) - 19JUN2008 (29)
	4. 17JUN2008 (27) - 12SEP2008 (114)
	5. 19JUN2008 (29) - --------- (.)
	6. 20JUN2008 (30) - 27JUN2008 (37)
	7. 04AUG2008 (75) - 19AUG2008 (90)
	8. 04AUG2008 (75) - 19AUG2008 (90)
	9. 16AUG2008 (87) - 18AUG2008 (89)
	10. 03SEP2008 (105) - 22OCT2008 (154)
	11. 12SEP2008 (114) - 22SEP2008 (124)
	12. 14SEP2008 (116) - 14SEP2008 (116)
	13. 15SEP2008 (117) - 19SEP2008 (121)
	14. 23SEP2008 (125) - 26SEP2008 (128)
	15. 23SEP2008 (125) - 23SEP2008 (125)
Duration of AE	1. 1
	2. 1
	3. 16
	4. 88
	5. .
	6. 8
	7. 16
	8. 16
	9. 3
	10. 50
	11. 11
	12. 1
	13. 5
	14. 4
	15. 1
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700014004

Parameter	Value
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
Action taken	1. REMEDIAL DRUG THERAPY
	2. REMEDIAL DRUG THERAPY
	3. NONE
	4. OTHER
	5. OTHER
	6. REMEDIAL DRUG THERAPY
	7. OTHER
	8. OTHER
	9. NONE
	10. NONE
	11. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY
	12. NONE
	13. REMEDIAL DRUG THERAPY
	14. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	15. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700014004

Parameter	Value
	3. RESOLVED
	4. RESOLVED
	5. IMPROVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. RESOLVED
	15. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-700014004[2)]	PR BLEED（PT：直腸出血） 治験担当医は、合併症の大腸ポリープに対する内視鏡的切除術によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700024004

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700024004/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/72/WHITE/NEW ZEALAND/YES
Medical history	Hypertension, Iron deficiency, Raynaud's phenomenon, Reflux oesophagitis, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CALVASC, FERROGRADUMET, INHIBACE [CILAZAPRIL MONOHYDRATE], LOSEC
Adverse Events (AE) Preferred term	1. Raynaud's phenomenon 2. Colon cancer 3. Oral herpes 4. Pyrexia 5. Nausea 6. Post procedural pneumonia 7. Post procedural infection 8. Post procedural sepsis 9. Procedural hypotension 10. Wound infection 11. Insomnia
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. SEVERE/NO/YES/YES 3. MILD/NO/NO/NO 4. MODERATE/NO/NO/NO 5. MODERATE/NO/NO/NO 6. SEVERE/NO/NO/NO 7. SEVERE/NO/NO/NO 8. SEVERE/NO/NO/NO 9. MODERATE/NO/NO/NO 10. SEVERE/NO/NO/NO 11. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 18AUG2007 (3) - --------- (.) 2. 29NOV2007 (106) - --------- (.) 3. 10FEB2008 (179) - --MAR2008 (.) 4. 11FEB2008 (180) - 14FEB2008 (183) 5. 12FEB2008 (181) - 15FEB2008 (184) 6. 12FEB2008 (181) - 20FEB2008 (189) 7. 12FEB2008 (181) - 20FEB2008 (189) 8. 12FEB2008 (181) - 20FEB2008 (189) 9. 13FEB2008 (182) - 14FEB2008 (183) 10. 14FEB2008 (183) - 08MAR2008 (206) 11. 16FEB2008 (185) - 17FEB2008 (186)
Duration of AE	1. .

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700024004

Parameter	Value
	2. .
	3. .
	4. 4
	5. 4
	6. 9
	7. 9
	8. 9
	9. 2
	10. 24
	11. 2
Dose on AE onset	1. 15 mg
	2. 20 mg
	3. 20 mg
	4. 20 mg
	5. 20 mg
	6. 20 mg
	7. 20 mg
	8. 20 mg
	9. 20 mg
	10. 20 mg
	11. 20 mg
Dose status on AE onset	1. .
	2. .
	3. F
	4. F
	5. F
	6. F
	7. F
	8. F
	9. F
	10. F
	11. F
Action taken	1. NONE
	2. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY,OTHER
	3. REMEDIAL DRUG THERAPY
	4. REMEDIAL DRUG THERAPY
	5. REMEDIAL DRUG THERAPY
	6. REMEDIAL DRUG THERAPY
	7. REMEDIAL DRUG THERAPY
	8. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700024004

Parameter	Value
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700024025

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700024025/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/75/WHITE/NEW ZEALAND/YES
Medical history	Diabetes mellitus, Hypercholesterolaemia, Hypertension, Hypothyroidism, Hysterectomy, Sciatica
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AMITRIPTYLINE, ATENOLOL, CODEINE PHOSPHATE, ENOXAPARIN, GLICLAZIDE, LIPEX, METFORMIN, THYROXINE, WARFARIN
Adverse Events (AE) Preferred term	1. Pelvic mass 2. Constipation
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 05MAR2009 (22) - 04MAY2009 (82) 2. 08MAR2009 (25) - --------- (.)
Duration of AE	1. 61 2. .
Dose on AE onset	1. 2.
Dose status on AE onset	1. 2.
Action taken	1. OTHER 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700034003/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/39/WHITE/NEW ZEALAND/YES
Medical history	Alanine aminotransferase increased
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ENOXAPARIN, WARFARIN
Adverse Events (AE) Preferred term	1. Musculoskeletal chest pain 2. Alanine aminotransferase increased 3. Rectal haemorrhage 4. Muscle tightness 5. Pain in extremity 6. Post thrombotic syndrome 7. Epistaxis 8. Post procedural haemorrhage 9. Aspartate aminotransferase increased
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/YES/YES 2. MODERATE/YES/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/YES/NO/YES 8. MILD/YES/NO/YES 9. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 13SEP2007 (8) - 14SEP2007 (9) 2. 20SEP2007 (15) - 04OCT2007 (29) 3. 26DEC2007 (112) - 21JAN2008 (138) 4. 05JAN2008 (122) - 31JAN2008 (148) 5. 05JAN2008 (122) - 31JAN2008 (148) 6. 16JAN2008 (133) - 27MAR2008 (204) 7. 02FEB2008 (150) - 02FEB2008 (150) 8. 04FEB2008 (152) - 04FEB2008 (152) 9. 27MAR2008 (204) - --------- (.)
Duration of AE	1. 2 2. 15 3. 27 4. 27 5. 27 6. 72 7. 1

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034003

Parameter	Value
	8. 1
	9. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. NONE
	5. NONE
	6. OTHER
	7. NONE
	8. NONE
	9. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034003

Parameter	Value
	9. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034014

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700034014/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/78/WHITE/NEW ZEALAND/YES
Medical history	Chronic obstructive pulmonary disease, Haemochromatosis, Haemorrhoids, Hypothyroidism, Osteoporosis, Renal colic, Type 2 diabetes mellitus
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	BONJELA [CHOLINE SALICYLATE, CETALKONIUM CL, ALCOHOL, SACCHARIN], CEPHAZOLIN, DEER VELVET, ENOXAPARIN, ETIDRONATE, FLUCLOXACILLIN, GABAPENTIN, GLICLAZIDE, IBUPROFEN, LACTULOSE, LOSEC, NYSTATIN, ONDANSETRON PRN, OSTEO 500, PANADOL, PARACETAMOL PRN, SALBUTAMOL, SALBUTAMOL PRN, THYROXINE, TRAMADOL PRN, VITAMIN K, WARFARIN
Adverse Events (AE) Preferred term	1. Thermal burn 2. Pruritus 3. Contusion 4. Fall 5. Contusion 6. Chronic obstructive pulmonary disease 7. Post procedural haemorrhage 8. Lip ulceration 9. Post procedural swelling 10. Cellulitis 11. Arthralgia 12. Haemarthrosis 13. Arthritis infective
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MODERATE/NO/NO/YES 7. MILD/NO/NO/YES 8. MILD/NO/NO/YES 9. MODERATE/NO/NO/YES 10. MILD/NO/NO/YES 11. MODERATE/NO/NO/NO 12. MODERATE/NO/YES/NO 13. MODERATE/NO/NO/NO
Start/stop date of event with relative date	1. 22AUG2008 (115) - 22SEP2008 (146) 2. 22NOV2008 (207) - 21JAN2009 (267) 3. 18JAN2009 (264) - 18MAR2009 (323) 4. 18JAN2009 (264) - 18JAN2009 (264) 5. 18JAN2009 (264) - 18MAR2009 (323)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034014

Parameter	Value
	6. 04APR2009 (340) - 04APR2009 (340)
	7. 05APR2009 (341) - 08APR2009 (344)
	8. 09APR2009 (345) - 12APR2009 (348)
	9. 09APR2009 (345) - 22APR2009 (358)
	10. 18APR2009 (354) - 30APR2009 (366)
	11. 29APR2009 (365) - 18MAY2009 (384)
	12. 30APR2009 (366) - 03MAY2009 (369)
	13. 30APR2009 (366) - 08MAY2009 (374)
Duration of AE	1. 32
	2. 61
	3. 60
	4. 1
	5. 60
	6. 1
	7. 4
	8. 4
	9. 14
	10. 13
	11. 20
	12. 4
	13. 9
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034014

Parameter	Value
	7.
	8.
	9.
	10.
	11.
	12.
	13.
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY,OTHER
	4. NONE
	5. REMEDIAL DRUG THERAPY,OTHER
	6. REMEDIAL DRUG THERAPY
	7. OTHER
	8. REMEDIAL DRUG THERAPY
	9. OTHER
	10. REMEDIAL DRUG THERAPY
	11. OTHER
	12. OTHER
	13. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034014

Parameter	Value
	13. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034016

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700034016/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/82/WHITE/NEW ZEALAND/YES
Medical history	Basal cell carcinoma, Basal cell carcinoma, Diverticulum, Sinusitis, Varicose vein, Dyslipidaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	KLEAN PREP, LIPEX, OMEPRAZOLE, PARACETAMOL, RAZENE, SODIUM HEPARIN, TRAMADOL
Adverse Events (AE) Preferred term	1. Rectal haemorrhage 2. Wheezing 3. Sinusitis 4. Post thrombotic syndrome 5. Ultrasound liver abnormal
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/YES/YES 2. MILD/NO/NO/YES 3. MILD/NO/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 20JUL2008 (6) - 24JUL2008 (10) 2. 22JUL2008 (8) - 14OCT2008 (92) 3. 28JUL2008 (14) - 01AUG2008 (18) 4. 15JAN2009 (185) - --------- (.) 5. 19JAN2009 (189) - --------- (.)
Duration of AE	1. 5 2. 85 3. 5 4. . 5. .
Dose on AE onset	1. 15 mg 2. 15 mg 3. 15 mg 4. 20 mg 5. 20 mg
Dose status on AE onset	1. . 2. I 3. . 4. . 5. F
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,OTHER 2. NONE 3. REMEDIAL DRUG THERAPY 4. OTHER

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034016

Parameter	Value
Outcome of event	5. OTHER 1. RESOLVED 2. RESOLVED 3. RESOLVED 4. UNCHANGED 5. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-700034016[2)]	RECTAL BLOOD LOSS（PT：直腸出血） 治験担当医は、合併症（憩室）によるものであり、否定できると判断した。弊社は、リバーロキサバン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034029

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700034029/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/60/WHITE/NEW ZEALAND/YES
Medical history	Colon cancer, Arthritis, Cerebrovascular accident, Congenital cystic kidney disease, Hypercholesterolaemia, Hypertension, Ileectomy, Myocardial ischaemia, Knee arthroplasty, Coronary artery bypass, Rectal haemorrhage, Colectomy, Type 2 diabetes mellitus, Anastomotic haemorrhage, Renal impairment
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, AUGMENTIN, CLEXANE, COLLOIDAL SILVER CREAM, ENOXAPARIN, FELODIPINE, FRUSEMIDE, INHIBACE [CILAZAPRIL], JOINT FORMULA, LIPITOR, METAMUCIL, METOPROLOL, MICREME H, MOXIFLOXACIN, NORMAL SALINE (0.9%), PARACETAMOL, ROXITHROMYCIN, SLOW K, SUDAFED, WARFARIN
Adverse Events (AE) Preferred term	1. Rhinorrhoea 2. Chest pain 3. Contusion 4. Nasopharyngitis 5. Skin haemorrhage 6. Wound haemorrhage 7. Diarrhoea 8. Upper respiratory tract infection 9. Sepsis 10. Pneumonia 11. Contusion
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MILD/YES/NO/YES 4. MILD/NO/NO/YES 5. MILD/NO/NO/YES 6. MILD/NO/NO/YES 7. MODERATE/NO/NO/YES 8. MODERATE/NO/NO/YES 9. MODERATE/NO/YES/YES 10. MODERATE/NO/NO/YES 11. MILD/YES/NO/YES
Start/stop date of event with relative date	1. 15APR2009 (9) - 15JUL2009 (100) 2. 20APR2009 (14) - 20APR2009 (14) 3. 19MAY2009 (43) - 01JUL2009 (86) 4. 01JUN2009 (56) - 08JUN2009 (63) 5. 20JUL2009 (105) - 20JUL2009 (105) 6. 07SEP2009 (154) - 06OCT2009 (183) 7. 15SEP2009 (162) - 17SEP2009 (164) 8. 15SEP2009 (162) - 17SEP2009 (164)

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034029

Parameter	Value
	9. 17SEP2009 (164) - 06OCT2009 (183)
	10. 17SEP2009 (164) - 06OCT2009 (183)
	11. 12NOV2009 (220) - 21NOV2009 (229)
Duration of AE	1. 92
	2. 1
	3. 44
	4. 8
	5. 1
	6. 30
	7. 3
	8. 3
	9. 20
	10. 20
	11. 10
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
Action taken	1. NONE
	2. NONE
	3. NONE
	4. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034029

Parameter	Value
	5. NONE
	6. NONE
	7. OTHER
	8. OTHER
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034030

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700034030/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/62/WHITE/NEW ZEALAND/YES
Medical history	Acute myocardial infarction, Osteoarthritis, Myocardial ischaemia, Seminoma, Musculoskeletal stiffness, Hip arthroplasty, Hip arthroplasty, Impaired fasting glucose, Dyslipidaemia, Spondylolisthesis
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, BETALOC, CILAZAPRIL, CLOPIDOGREL, DEXAMETHASONE, DICLOFENAC, ENOXAPARIN, FENTANYL, GENTAMICIN, METOPROPOL CR, MIDAZOLAM, NITROLINGUAL SPRAY PRN, ONDANSETRON, PARACETAMOL PRN, PROPOFOL, SIMVASTATIN, WARFARIN
Adverse Events (AE) Preferred term	1. Injection site haematoma 2. Haematuria 3. Bladder transitional cell carcinoma stage I 4. Epistaxis 5. Haematuria 6. Anaemia postoperative 7. Conjunctival haemorrhage
Intensity/ Relationship to study drug /SAE/TE	1. MILD/YES/NO/YES 2. MODERATE/NO/NO/YES 3. MODERATE/NO/YES/YES 4. MILD/YES/NO/YES 5. MODERATE/YES/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 17APR2009 (10) - 30APR2009 (23) 2. 21JUN2009 (75) - 29JUN2009 (83) 3. 17JUL2009 (101) - 17JUL2009 (101) 4. 23JUL2009 (107) - 01AUG2009 (116) 5. 29JUL2009 (113) - 30JUL2009 (114) 6. 11AUG2009 (126) - 02NOV2009 (209) 7. 15AUG2009 (130) - 22AUG2009 (137)
Duration of AE	1. 14 2. 9 3. 1 4. 10 5. 2 6. 84 7. 8
Dose on AE onset	1. 2. 3. 4.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700034030

Parameter	Value
	5.
	6.
	7.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
Action taken	1. NONE
	2. OTHER
	3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER
	4. NONE
	5. OTHER
	6. NONE
	7. NONE
Outcome of event	1. RESOLVED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. RESOLVED
	7. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700044006

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700044006/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/83/WHITE/NEW ZEALAND/YES
Medical history	Drug hypersensitivity, Drug hypersensitivity, Amaurosis fugax, Angina pectoris, Atrial fibrillation, Back pain, Skin neoplasm excision, Cataract, Carotid endarterectomy, Spinal osteoarthritis, Diverticulitis, Drug hypersensitivity, Drug hypersensitivity, Drug hypersensitivity, Drug hypersensitivity, Gastrooesophageal reflux disease, Hiatus hernia, Hypercholesterolaemia, Hypertension, Hyperventilation, Lumbar spinal stenosis, Meniere's disease, Productive cough, Rheumatic fever, Hemiplegia, Drug hypersensitivity
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ASPIRIN, AUGMENTIN, BETAHISTINE, BRINZOLAMIDE 1%, CHLORAMPHENICOL 0.5%, CYCLOPENTOLATE HYDROCHLORIDE 1%, DILTIAZEM, LIPITOR, LOSEC, MICREME HCREME, NORMACOL PLUS, PARADEX, PERSANTIN, POLY-TEARS, PREDNISOLONE ACETATE 1%, RAZINE [THE MEDICATION IS PROCHLORPERAZINE FOR MILD NAUSEA], TIMOLOL MALEATE 0.25%
Adverse Events (AE) Preferred term	1. Headache 2. Productive cough 3. Nasopharyngitis 4. Pain in extremity 5. Back pain 6. Somnolence 7. Vulvovaginal candidiasis 8. Hyphaema 9. Diverticulitis 10. Nausea 11. Abdominal pain 12. Nephrolithiasis 13. Oral candidiasis 14. Joint stiffness
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MODERATE/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MILD/NO/NO/YES 7. MILD/NO/NO/YES 8. MODERATE/YES/YES/YES 9. SEVERE/NO/YES/NO 10. MODERATE/NO/NO/NO 11. MODERATE/NO/NO/NO 12. MODERATE/NO/NO/NO 13. MILD/NO/NO/NO 14. MILD/NO/NO/NO

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700044006

Parameter	Value
Start/stop date of event with relative date	1. 17MAR2008 (12) - --------- (.) 2. 01JUN2008 (88) - --------- (.) 3. 06JUN2008 (93) - 30JUL2008 (147) 4. 31JUL2008 (148) - 31JUL2008 (148) 5. 18AUG2008 (166) - --------- (.) 6. 05OCT2008 (214) - 02DEC2008 (272) 7. 27OCT2008 (236) - 03NOV2008 (243) 8. 22JAN2009 (323) - 11FEB2009 (343) 9. 12FEB2009 (344) - --------- (.) 10. 12FEB2009 (344) - --------- (.) 11. 12FEB2009 (344) - --------- (.) 12. 12FEB2009 (344) - 16FEB2009 (348) 13. 13FEB2009 (345) - --------- (.) 14. 16FEB2009 (348) - --------- (.)
Duration of AE	1. . 2. . 3. 55 4. 1 5. . 6. 59 7. 8 8. 21 9. . 10. . 11. . 12. 5 13. . 14. .
Dose on AE onset	1. 15 mg 2. 20 mg 3. 20 mg 4. 20 mg 5. 20 mg 6. 20 mg 7. 20 mg 8. 20 mg 9. 20 mg 10. 20 mg 11. 20 mg 12. 20 mg

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700044006

Parameter	Value
	13. 20 mg
	14. 20 mg
Dose status on AE onset	1. .
	2. .
	3. .
	4. .
	5. .
	6. .
	7. .
	8. .
	9. F
	10. F
	11. F
	12. F
	13. F
	14. F
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. NONE
	6. NONE
	7. REMEDIAL DRUG THERAPY
	8. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
	9. REMEDIAL DRUG THERAPY
	10. REMEDIAL DRUG THERAPY
	11. REMEDIAL DRUG THERAPY
	12. NONE
	13. REMEDIAL DRUG THERAPY
	14. NONE
Outcome of event	1. IMPROVED
	2. IMPROVED
	3. RESOLVED
	4. RESOLVED
	5. UNCHANGED
	6. RESOLVED
	7. RESOLVED
	8. RESOLVED
	9. IMPROVED
	10. UNCHANGED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700044006

Parameter	Value
	11. IMPROVED
	12. RESOLVED
	13. IMPROVED
	14. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
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付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700054002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/45/WHITE/NEW ZEALAND/YES
Medical history	Atrial septal defect, Cerebrovascular accident
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	
Adverse Events (AE) Preferred term	1. Post thrombotic syndrome 2. Pyrexia 3. Facial palsy 4. Eye pruritus
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/YES/NO 4. MILD/NO/NO/NO
Start/stop date of event with relative date	1. 31AUG2007 (52) - --------- (.) 2. 25OCT2007 (107) - 26OCT2007 (108) 3. 21JUL2008 (377) - --------- (.) 4. 26JUL2008 (382) - --------- (.)
Duration of AE	1. . 2. 2 3. . 4. .
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg 4. 20 mg
Dose status on AE onset	1. . 2. . 3. F 4. F
Action taken	1. NONE 2. NONE 3. NONE 4. REMEDIAL DRUG THERAPY
Outcome of event	1. UNCHANGED 2. RESOLVED 3. IMPROVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054002

Parameter	Value
	4. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054013

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700054013/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/44/WHITE/NEW ZEALAND/YES
Medical history	Bronchitis, Insomnia, Paraplegia, Decubitus ulcer, Skin ulcer, Spinal cord injury, Pain, Hypertonic bladder
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIN, CEFOTAXIME, CEFUROXIME, CHLORVESCENT, CIPROFLOXACIN, CLARITHROMYCIN, CLEXANE, COMBIVENT INHALER, DEPO PROVERA, DIAZEPAM, ENOXAPARIN, FERROGRADUMET, FLUCLOXACILLIN, IPRATROPIUM, METRONIDAZOLE, MOBIC, MOXIFLOXACIN, NUROFEN, NUROFEN MIGRAINE TABLETS, OXYBUTYNIN, PAENUI A30 (HOMEOPATHIC MEDICATION), ROBITUSSIN ME, SALBUTAMOL, TRAMADOL SR, WARFARIN
Adverse Events (AE) Preferred term	1. Cataract 2. Nausea 3. Lower respiratory tract infection 4. Upper respiratory tract infection 5. Nasopharyngitis 6. Headache 7. Contusion 8. Pneumonia 9. Viral infection 10. Injection site haematoma 11. Influenza 12. Influenza 13. Influenza 14. Sepsis 15. Lobar pneumonia 16. Oedema peripheral
Intensity/ Relationship to study drug /SAE/TE	1. MODERATE/NO/NO/YES 2. MILD/NO/NO/YES 3. MODERATE/NO/NO/YES 4. MILD/NO/NO/YES 5. MODERATE/NO/NO/YES 6. MODERATE/NO/NO/YES 7. SEVERE/YES/NO/YES 8. SEVERE/NO/YES/YES 9. MODERATE/NO/NO/YES 10. MILD/YES/NO/YES 11. MILD/NO/NO/YES 12. MILD/NO/NO/YES 13. MODERATE/NO/NO/NO 14. SEVERE/NO/YES/NO 15. SEVERE/NO/YES/NO

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054013

Parameter	Value
	16. MILD/NO/NO/NO
Start/stop date of event with relative date	1. --JUL2008 (.) - --------- (.)
	2. 20APR2008 (5) - 23APR2008 (8)
	3. 14MAY2008 (29) - 25MAY2008 (40)
	4. 07JUN2008 (53) - 14JUN2008 (60)
	5. 18JUL2008 (94) - 22JUL2008 (98)
	6. 30JUL2008 (106) - --------- (.)
	7. 26AUG2008 (133) - 12SEP2008 (150)
	8. 26AUG2008 (133) - 04SEP2008 (142)
	9. 05SEP2008 (143) - 08SEP2008 (146)
	10. 12SEP2008 (150) - 26SEP2008 (164)
	11. 30SEP2008 (168) - 02OCT2008 (170)
	12. 03OCT2008 (171) - 06OCT2008 (174)
	13. 22OCT2008 (190) - 28OCT2008 (196)
	14. 01NOV2008 (200) - --------- (.)
	15. 01NOV2008 (200) - --------- (.)
	16. 03NOV2008 (202) - --------- (.)
Duration of AE	1. .
	2. 4
	3. 12
	4. 8
	5. 5
	6. .
	7. 18
	8. 10
	9. 4
	10. 15
	11. 3
	12. 4
	13. 7
	14. .
	15. .
	16. .
Dose on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054013

Parameter	Value
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
Dose status on AE onset	1.
	2.
	3.
	4.
	5.
	6.
	7.
	8.
	9.
	10.
	11.
	12.
	13.
	14.
	15.
	16.
Action taken	1. NONE
	2. NONE
	3. REMEDIAL DRUG THERAPY
	4. NONE
	5. NONE
	6. REMEDIAL DRUG THERAPY
	7. NONE
	8. REMEDIAL DRUG THERAPY
	9. NONE
	10. NONE
	11. NONE
	12. NONE
	13. REMEDIAL DRUG THERAPY
	14. REMEDIAL DRUG THERAPY
	15. REMEDIAL DRUG THERAPY

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054013

Parameter	Value
	16. OTHER
Outcome of event	1. UNCHANGED
	2. RESOLVED
	3. RESOLVED
	4. RESOLVED
	5. RESOLVED
	6. UNCHANGED
	7. RESOLVED
	8. RESOLVED
	9. RESOLVED
	10. RESOLVED
	11. RESOLVED
	12. RESOLVED
	13. RESOLVED
	14. UNCHANGED
	15. UNCHANGED
	16. UNCHANGED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054027

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700054027/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	MALE/73/WHITE/NEW ZEALAND/YES
Medical history	Bladder cancer, Cardiac failure congestive, Metastatic neoplasm, Gout, Hypercholesterolaemia, Hypertension, Myocardial infarction, Gastrooesophageal reflux disease, Rheumatoid arthritis, Urinary bladder excision, Myocardial ischaemia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALLOPURINOL, AUGMENTIN, CODEINE, DEEP HEAT [MENTHOL, METHYL SALICYLATE], ENOXAPARIN, FRUSEMIDE, LACTULOSE, METOPROLOL, OMEPRAZOLE, PARACETAMOL, QUINAPRIL, SIMVASTATIN, WARFARIN, ZOSTRIX
Adverse Events (AE) Preferred term	1. Nausea 2. Transient ischaemic attack 3. Upper respiratory tract infection
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES 3. MODERATE/NO/NO/YES
Start/stop date of event with relative date	1. 24FEB2009 (13) - 04MAR2009 (21) 2. 12APR2009 (60) - 14APR2009 (62) 3. 12APR2009 (60) - 16APR2009 (64)
Duration of AE	1. 9 2. 3 3. 5
Dose on AE onset	1. 2. 3.
Dose status on AE onset	1. 2. 3.
Action taken	1. NONE 2. NONE 3. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700054027

Parameter	Value
	3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 700064003

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/700064003/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/53/WHITE/NEW ZEALAND/YES
Medical history	Urinary retention, Dysuria, Heat rash, Hypertension, Urinary tract infection, Retching, Hysterectomy, Metaplasia
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ALANASE 100 AQUEOUS, AUGMENTIN 500, BENDROFLUAZIDE, CEFUROXIME, CIMETIDINE, GENTAMICIN, IMIPENEM, NORFLOXACIN
Adverse Events (AE) Preferred term	1. Urinary tract infection 2. Cystitis haemorrhagic 3. Blood urine present
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES 3. MODERATE/YES/NO/YES
Start/stop date of event with relative date	1. 15JUL2008 (39) - 30JUL2008 (54) 2. 15JUL2008 (39) - 30JUL2008 (54) 3. 15JUL2008 (39) - 14SEP2008 (100)
Duration of AE	1. 16 2. 16 3. 62
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. .
Action taken	1. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 2. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY 3. STUDY DRUG DISCONTINUED AND RESTARTED
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 710024002

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/710024002/Rivaroxaban
Sex/Age/Race/Country/Safety population	MALE/25/ASIAN/THAILAND/YES
Medical history	Hodgkin's disease
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	ACYCLOVIR, BENADRYL, BLEOMYCIN, CENTRUM, DACARBAZINE, DEXTROMETHOPHAN, DOXORUBICIN, GEMCITAMINE, IFOSFAMIDE, MESNA, METHYLPREDNISOLONE, NEUTROMAX, ONDANSETRON, PLASIL, ROPECT, VINBLASTINE, VINORELBINE
Adverse Events (AE) Preferred term	1. Cough 2. Diarrhoea 3. Septic shock
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/NO/YES 3. SEVERE/NO/YES/YES
Start/stop date of event with relative date	1. 20AUG2008 (106) - 26AUG2008 (112) 2. 25AUG2008 (111) - --------- (.) 3. 27AUG2008 (113) - 27AUG2008 (113)
Duration of AE	1. 7 2. . 3. 1
Dose on AE onset	1. 20 mg 2. 20 mg 3. 20 mg
Dose status on AE onset	1. . 2. . 3. F
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. NONE 3. STUDY DRUG DISCONTINUED PERMANENTLY,REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. UNCHANGED 3. DEATH

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 710024008

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/710024008/Rivaroxaban
Sex/Age/Race/Country/Safety population	FEMALE/53/ASIAN/THAILAND/YES
Medical history	Anaemia, Cervix carcinoma stage III, Menopause
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	CELEBREX, CISPLATIN, CLOXACILLIN, DEXAMETHASONE, FERROUS FUMARATE, LORAZEPAM, ONDANSETRON, TOLPERISONE, ULTRACET
Adverse Events (AE) Preferred term	1. Back pain 2. Cellulitis
Intensity/ Relationship to study drug /SAE/TE	1. MILD/NO/NO/YES 2. MODERATE/NO/YES/YES
Start/stop date of event with relative date	1. 03DEC2008 (115) - 04DEC2008 (116) 2. 07JAN2009 (150) - 21JAN2009 (164)
Duration of AE	1. 2 2. 15
Dose on AE onset	1. 20 mg 2. 20 mg
Dose status on AE onset	1. . 2. .
Action taken	1. REMEDIAL DRUG THERAPY 2. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 710024015

Parameter	Value
Study number/ Subject ID/ Treatment group	11702/710024015/Enoxaparin/VKA
Sex/Age/Race/Country/Safety population	FEMALE/35/ASIAN/THAILAND/YES
Medical history	Anaemia, Cerebral palsy, Epilepsy, Hypocalcaemia, Mental retardation, Non-consummation
Concomitant Medication ATC subclass (WHO-DD version 3q2005)	AUGMENTIIN, AUGMENTIN, BERODUAL FORTE, CALCIUM CARBONATE, DILANTIN, ENOXAPARIN, FBC [FE FUMARATE,VITB1,B2, B12,VITC,NIACIN,FOLIC ACID,CA PHOSPHATE TRIBASIC], FLUMUCIL, KLACID, NITRAZEPAM, PHENOBARB, TARMIFLU, TOPAMAX, VENTOLIN, VITAMIN K1, WARFARIN
Adverse Events (AE) Preferred term	1. Influenza 2. Pneumonia bacterial 3. Menorrhagia 4. Bronchitis
Intensity/ Relationship to study drug /SAE/TE	1. SEVERE/NO/YES/YES 2. SEVERE/NO/YES/YES 3. SEVERE/YES/YES/YES 4. MILD/NO/NO/YES
Start/stop date of event with relative date	1. 12JUL2009 (24) - 18JUL2009 (30) 2. 12JUL2009 (24) - 23JUL2009 (35) 3. 20SEP2009 (94) - 09OCT2009 (113) 4. 20SEP2009 (94) - 30SEP2009 (104)
Duration of AE	1. 7 2. 12 3. 20 4. 11
Dose on AE onset	1. 2. 3. 4.
Dose status on AE onset	1. 2. 3. 4.
Action taken	1. REMEDIAL DRUG THERAPY,OTHER 2. REMEDIAL DRUG THERAPY,OTHER 3. STUDY DRUG DISCONTINUED AND RESTARTED,REMEDIAL DRUG THERAPY,OTHER 4. REMEDIAL DRUG THERAPY
Outcome of event	1. RESOLVED 2. RESOLVED 3. RESOLVED

付表 2.7.6.1- 2　重篤な有害事象の叙述（試験 11702-DVT、無作為割り付け例）（続く）

Subject ID: 710024015

Parameter	Value
	4. RESOLVED

All AEs (TEAE and non-TEAE) are presented.
TE: Treatment emergent (time window: 2 days)
Relative day is calculated from the first day of study drug administration: The formula for this calculation is(onset day of AE minus medication day) plus 1 day.
Concomitant Medication: Medications that are ongoing at, or began after the start of study drug are presented.
Dose on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, dose just before the onset will be listed.
Dose status on AE onset: only rivaroxaban arm. If AE onset is during dose interruption, I will be listed. If AE onset is after treatment phase,F will be listed.
Global Biostatistics: /by-sasp/patdb/projects/597939/11702_meta/stat/prod_query30/pgms/t-p-8.sas　erjli　21MAR2013 11:30
End of table

被験者番号	因果関係判定根拠に関する治験依頼者の見解
11702-710024015[2)]	IRON DEFICIENCY ANEMIA（PT：鉄欠乏性貧血） 治験担当医は、患者の栄養不良によるものであり、否定できると判断した。弊社は、ワルファリン投与と報告事象発現との時間的関連性から、因果関係は否定できないと考える。

因果関係判定に関して、治験担当医師、Bayer HealthCare 社及びバイエル薬品の見解が異なるパターンを被験者番号 の右上に以下の番号を付与した。
1）治験担当医師が「関連あり」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
2）治験担当医師が「関連なし」、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
3）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連あり」の場合
4）治験担当医師の評価は得られておらず、Bayer HealthCare 社及びバイエル薬品（両者を弊社とする）が「関連なし」の場合
5）治験担当医師及びバイエル薬品（弊社）が「関連あり」、Bayer HealthCare 社（ドイツ安全性部門）が「関連なし」の場合

2.7.6.2 【国外試験】急性症候性肺塞栓症患者を対象とした第Ⅲ相臨床試験：試験番号 11702 EINSTEIN-PE（試験 11702-PE）［報告書番号 A53042］

参照項目：5.3.5.1.2 A53042

2.7.6.2.1 試験計画

治験の標題：急性症候性肺塞栓症患者（PE）を対象とした経口直接作用型第Xa 因子阻害薬リバーロキサバンの多施設共同、無作為化、非盲検、実薬対照、盲検下評価、並行群間比較、イベント主導型、非劣性検証、第Ⅲ相試験

治験調整医師：
Harry R. Büller, MD
Academic Medical Center, Meibergdreef 9, NL-1105 AZ Amsterdam, The Netherlands

実施医療機関：38 ヵ国 263 施設（括弧内は施設数）
アンドラ（1）、オーストラリア（23）、オーストリア（6）、ベルギー（12）、ブラジル（2）、カナダ（4）、中国（15）、チェコ共和国（7）、デンマーク（1）、エストニア（1）、フィンランド（2）、フランス（34）、ドイツ（25）、香港（2）、ハンガリー（10）、インド（1）、インドネシア（1）、アイルランド（1）、イスラエル（10）、イタリア（13）、リトアニア（2）、ラトビア（1）、マレーシア（1）、オランダ（6）、ニュージーランド（5）、ノルウェイ（3）、フィリピン（1）、ポーランド（7）、シンガポール（1）、南アフリカ（10）、韓国（4）、スペイン（8）、スウェーデン（5）、スイス（6）、台湾（3）、タイ（3）、イギリス（3）、米国（23）

公表論文：The EINSTEIN Investigators, N Engl J Med 2012;366:1287-1297

治験期間：	**開発のフェーズ**：第Ⅲ相
最初の患者の組み入れ日：2007 年 3 月 29 日 最後の患者の最終来院日：2011 年 12 月 1 日	

目的：

有効性：
症候性深部静脈血栓症（DVT）の併発の有無を問わない急性症候性肺塞栓症（PE）と確定診断された患者における静脈血栓塞栓症（VTE）の再発抑制効果について、リバーロキサバンの有効性をエノキサパリン／ビタミン K 拮抗薬（VKA：ワルファリン又は acenocoumarol）と比較検討する。

安全性：
「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」を検討する。

試験方法：

本試験は、DVT の併発の有無を問わない PE と確定診断された患者を対象とした、多施設共同、無作為化、非盲検、実薬対照、盲検下評価、並行群間比較、イベント主導型、非劣性検証の第Ⅲ相試験であった。治験薬の予定投与期間は 3、6 又は 12 ヵ月のいずれかとした。

図 2.7.6.2- 1に本試験の全般的デザイン、表 2.7.6.2- 1に本試験のスケジュールを示す。

被験者はリバーロキサバン群又はエノキサパリン／VKA 群に無作為に割り付けられた。無作為 割り付けは音声応答システム（IVRS）により行い、参加国及び予定投与期間を割り付け調整因子として用いた。

無作為割り付け前に最大 48 時間（治験実施計画書改訂 4 までは最大 36 時間）の抗凝固薬による治療は可とし、VKA 治療は単回投与のみ可とした。

無作為割り付け後、リバーロキサバン群に割り付けられた被験者には、リバーロキサバン 15mg を 1 日 2 回 3 週間経口投与し、続いてリバーロキサバン 20mg の 1 日 1 回投与を 3、6 又は 12 ヵ月まで継続した。

エノキサパリン／VKA 群に割り付けられた被験者には少なくとも 5 日間エノキサパリン 1mg/kg の 1 日 2 回皮下投与と VKA の経口投与を併用（4～5 日間）し、24 時間以上の間隔をおいて測定したプロトロンビン時間国際標準比（PT-INR）が 2 回連続で 2 以上となった後は、VKA のみの投与を 3、6 又は 12 ヵ月まで継続した。VKA の投与は PT-INR が目標とする 2.5（2.0～3.0 の範囲）になるように用量調節した。VKA としてはワルファリン又は acenocoumarol を使用可とした。

無作為に割り付けられた最初の 400 例を対象に用量確認解析を実施した。対象となった被験者に対し、試験対象として診断されたイベント（index イベント）の確定診断のために行った検査〔肺換気／肺血流スキャン（VPLS）又はスパイラル CT（sCT）〕を 3 週目（第 21 日）に再度実施した。index イベントの確定診断が肺動脈造影でなされた場合は割り付け後 36 時間以内に VPLS 又は sCT を必要とした。3 週後の VPLS 又は sCT 後に、ベースラインと 2 回目の検査結果の写しを独立中央判定委員会（CIAC）に送付し、中央判定を実施した。その肺画像検査結果から血栓像の悪化（VPLS で血管内陰影欠損、sCT で新たな陰影欠損の範囲拡大など）を確認した。

すべての VTE、出血事象及び心血管事象が疑われる事象並びに死亡は、盲検下で CIAC により判定され、判定結果に基づいて解析を行った。安全性データモニタリング委員会（DSMB）は治験期間中の被験者の安全性をモニターし、試験執行委員会に勧告を行った。

治験責任（分担）医師は、すべての被験者へのコンタクト時にコンタクトレポートを使用して、下記の評価を行った。有効性又は安全性に関するイベント発現の疑いがある被験者については確認検査を行った。

- DVT 又は PE の発現、悪化あるいは再発
- 出血事象を含む有害事象（重篤な有害事象）
- 併用薬
- リバーロキサバン投与又はエノキサパリン／VKA 投与の遵守状況及び PT-INR モニタリング

更に、試験スケジュール表に示す時点で中央臨床検査用の血液採取を行った。また、医療資源利用（HCRU）のためのデータを収集し、一部の被験者では抗凝固薬治療に関する評価尺度（ACTS）による被験者満足度アンケートを実施した。

無作為割り付けされたが治験薬の投与を受けなかった、又は治験薬投与を中止した被験者には、同意撤回、追跡不能あるいは死亡がない限り、被験者の予定投与期間の終了時に来院を設定した。

予定投与期間にかかわらず、治験薬投与後に 30 日間のフォローアップ期間を設けた。治験薬投与を中止した被験者にも同様のフォローアップ期間を設定した。本試験での治験薬投与終了後、引き続き継続投与試験である試験 11899 に移行する被験者は、30 日間のフォローアップ期間を設けず、中断なく試験 11899 に移行した。

フォローアップ期間終了時に、すべての被験者にコンタクトを取ることとした。

すべての疑わしい事象について治験薬投与期間中と同様の方法で判断した。フォローアップ期間中に発現したすべての事象は記録のみとし、正式な解析は実施しなかった。

予定投与期間は下記のリスク評価及び出血の可能性に基づき、治験責任（分担）医師が無作為割り付け時に 3、6 及び 12 ヵ月のいずれかに決定した。

下記のような一過性の危険因子を有する被験者では、多くの場合予定投与期間を 3 ヵ月とした。

- 最近の手術又は外傷
- 活動性の制限
- エストロゲン含有医薬品の使用
- 産褥期

特発性 VTE 又は下記のような永続的危険因子を有する被験者では、多くの場合予定投与期間を 6 ヵ

月又は12ヵ月とした。

- 活動性悪性腫瘍
- DVT/PEの既往
- 既知の血栓性素因（アンチトロンビンⅢ、プロテインS又はプロテインCの欠乏、血液凝固第Ⅴ因子（FaV）又はプロトロンビン遺伝子突然変異、あるいは抗リン脂質抗体）

診断と選択基準：

選択基準

(1)　症候性DVTを問わない、急性症候性PEと確定診断されたもの
(2)　試験開始前に文書及び口頭による詳細な説明を受け、文書による同意が得られたもの

除外基準

(1)　法的未成年者（治験参加国により異なる）
(2)　現在のPE治療のために、血栓除去術、下大静脈フィルター留置、又は血栓溶解剤による治療を受けているもの
(3)　PE以外のVKAの適応があるもの
(4)　無作為割り付け前に、ヘパリン〔低分子量ヘパリン（LMWH）を含む〕／フォンダパリヌクスの治療用量での投与を48時間を超えて受けた、又はVKAを2回以上投与されたもの
(5)　治験開始前30日以内にほかの薬物療法試験に参加したもの
(6)　クレアチニンクリアランス（CL_{CR}）が30mL/min未満のもの
(7)　臨床的に問題となる肝障害（例：急性肝炎、慢性の活動性肝炎、肝硬変）、又はアラニン・アミノトランスフェラーゼ（ALT）が基準値上限の3倍を超えるもの
(8)　細菌性心内膜炎を有するもの
(9)　生命予後が3ヵ月未満と考えられるもの
(10)　エノキサパリン又はVKAによる治療が禁忌となる活動性出血又は高い出血リスクを有するもの
(11)　コントロール不良の高血圧（収縮期血圧が180mmHgを超える又は拡張期血圧が110mmHgを超える）を合併しているもの
(12)　妊娠中、授乳中、又は妊娠可能な女性で適切な避妊を行わないもの
(13)　ワルファリン、acenocoumarol又はエノキサパリンの添付文書に記載されているそのほかの禁忌を有するもの
(14)　強力なチトクロームP450酵素 3A4（CYP3A4）阻害薬（例：HIVプロテアーゼ阻害薬、ケトコナゾール経口剤）、又は強力なCYP3A4誘導薬（例：リファンピシン）の投与が治験薬投与期間中に予定されているもの（治験実施計画書改訂2）

有効性の評価項目：

主要評価項目：症候性VTE〔「症候性DVT」又は「症候性PE（非致死的及び致死的）」の複合エンドポイント（ただしPEの可能性が否定できない原因不明の死亡を含む）〕

副次的評価項目：

- 症候性VTE〔「症候性DVT」、「症候性PE（非致死的）」〕又は全死亡の複合エンドポイント
- 総合有用性評価指標－1：有効性主要評価項目の各構成要素又は「重大な出血事象」の複合エンドポイント
- 総合有用性評価指標－2：有効性主要評価項目の各構成要素、「重大な出血事象」、心血管死、心筋梗塞、虚血性脳卒中又は非中枢神経系塞栓症の複合エンドポイント

安全性の評価項目：

主要評価項目：「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイント

副次的評価項目：全死亡、心血管事象及び臨床検査値

薬力学的作用の評価項目：別途報告書を作成した。

リバーロキサバンの血漿中濃度のトラフ時及びピーク時におけるプロトロンビン時間及びプロトロンビナーゼ誘発凝固時間の測定（一部の被験者のみ）

症例数：

計画時：

本試験はイベント主導型の試験であり、症候性 VTE のイベント数が目標とする 88 イベントに達する見込みを得た時点を終了とするため、症例数は症候性 VTE の発現頻度に基づく。割り付け例数は 2,930 例（各群 1,465 例）と想定された。

症例数の設定根拠

リバーロキサバンが対照薬と同じ有効性を示すと仮定して、リバーロキサバンが少なくとも対照薬に対して非劣性であることを示すためには、ハザード比の 95%信頼区間の上限が非劣性マージンの 2.0 未満となる必要があることを考慮すると、検出力 90%（両側有意水準 0.05）で検出するためには合計 88 のイベント数が必要と考えられた。大部分の再発イベントが最初のイベント後 1 ヵ月以内に起こるとの知見に基づき、VTE の再発率は 3 ヵ月で 2.5%、6 ヵ月で 3%、12 ヵ月で 3.5%と想定される。従って、有効性主要評価項目の平均発現頻度は両投与群とも 3%と推定され、これにより、少なくとも 1 群 1,465 例が必要とされることから設定した。

有効性主要評価項目の発現頻度は両投与群で 3.0%未満、すなわち治験実施計画書で規定した推定総発現頻度を下回った。この結果を受け、被験者を追加で組み入れた。

解析時：

4,843 例（組み入れ被験者数：治験実施計画書改訂 5 に伴い、用量確認解析の対象であった被験者も主要解析に含めた）

intention-to-treat（ITT）解析対象集団：4,832 例（リバーロキサバン：2,419 例、エノキサパリン／VKA：2,413 例）

安全性解析対象集団：4,817 例（リバーロキサバン：2,412 例、エノキサパリン／VKA：2,405 例）

治験実施計画書に適合した（PP）解析対象集団：4,462 例（リバーロキサバン：2,224 例、エノキサパリン／VKA：2,238 例）

解析方法：

解析対象集団

ITT 解析対象集団は、無作為割り付けされたすべての被験者とした。被験者番号と割り付けられた投与は IVRS によりデータベースに登録され、それに従って解析を行った。

安全性解析対象集団は、無作為割り付けされ、治験薬が少なくとも 1 回投与されたすべての被験者とした。被験者の解析は、実際に受けた治験薬投与に従って行われた。

ITT on Treatment 解析対象集団〔統計解析計画書（SAP）補遺で規定〕は、安全性解析対象集団の部分集団であった。無作為割り付け後に、治験薬を無作為割り付けに従って少なくとも 1 回投与されたすべての被験者とした。割り付けと異なる治験薬を投与された被験者は本解析から除外された。

PP 解析対象集団は、無作為割り付けされたすべての被験者のうち、治験実施計画書からの重大な逸脱がない被験者とした。以下の被験者は PP 解析対象集団から除外された。

- ベースライン時の PE（index イベント）が、CIAC で PE と判定されなかった被験者
- IVRS で割り付けられた治験薬投与を受けなかった、又は治験薬の投与を一回も受けなかった被験者
- SAP version 1.0 に規定された、治験薬の投与が適切に行われなかった被験者

有効性

すべての有効性の解析は ITT 解析対象集団で実施した。更に、主要評価項目の補助的解析を PP 解析対象集団及び ITT on treatment 解析対象集団で実施した。有効性評価における解析対象集団ごとの対象イベントと打ち切りまでの期間の定義を表 2.7.6.2- 2に示す。

有効性の主要解析に関して、すべての主要評価項目は、実際の投与期間にかかわらず、予定投与期間の終了まで検討された。予定投与期間の後に発現したイベントは記述するのみとし、解析には含めなかった。また、予定投与期間終了時まで、及び実際の治験薬投与終了後 30 日目までに発現したイベントについて記述した。

すべての被験者の予定投与期間における累積イベント発現率について、Kaplan-Meier 推定値により表示した。

主要解析として、有効性主要評価項目の初回イベント発現までの時間について、予定投与期間（3、6 又は 12 ヵ月）で層別化し、ベースライン時の活動性悪性腫瘍の有無で調整した Cox 比例ハザードモデルを用いて解析を行った。対照薬のエノキサパリン／VKA に対するリバーロキサバンのハザード比及び両側 95%信頼区間を算出した。このモデルに基づき、95%信頼区間の上限が 2.0 未満の場合に、リバーロキサバンはエノキサパリン／VKA に対して非劣性を示すと考えられた。

逐次的検定：

逐次的検定について次の階層を適用した。有効性主要評価項目で非劣性が示された場合、有効性主要評価項目に関する優越性について、ハザード比（リバーロキサバン／対照薬）の両側 95%信頼区間により検定を行うこととした。更に、有効性主要評価項目で非劣性が示された場合、以下のとおり閉検定手順を実施することとした。

a）安全性解析対象集団を対象とした、治験薬投与下での安全性主要評価項目に関する優越性

b）安全性解析対象集団を対象とした、治験薬投与下での「重大な出血事象」に関する優越性

共変量の影響に関する部分集団解析：

ベースラインの共変量（活動性悪性腫瘍の有無、特発性 DVT/PE、DVT/PE の既往、既知の血栓性素因、性別、年齢、体重、腎機能、肺疾患、心疾患及び無作為割り付け時の可動性、肺血流スコア、用量確認解析対象）及び有効性主要評価項目におけるほかの部分集団の影響を、治療効果の調整済みハザード比とその 95%信頼区間を算出することにより分析した。

用量確認解析：

複合エンドポイント（症候性 VTE 及び治験薬投与開始 3 週間後における無症候性肺血栓像の悪化）の発現頻度を、治験薬投与 3 週間後に肺画像検査を受けた被験者、又は 3 週間後の肺画像再検査前に症候性 VTE を発症した被験者について、対照薬群とリバーロキサバン群間で比較した。両投与群間の絶対差の片側 95%信頼区間を算出し、それが 8%を超えない場合は本試験を継続することとした。

安全性

安全性解析対象集団において、すべての安全性の解析を実施した。出血事象の解析は、治験薬投与下（無作為割り付け後から治験薬投与終了後 2 日目まで）に発現したイベントを対象とした。その

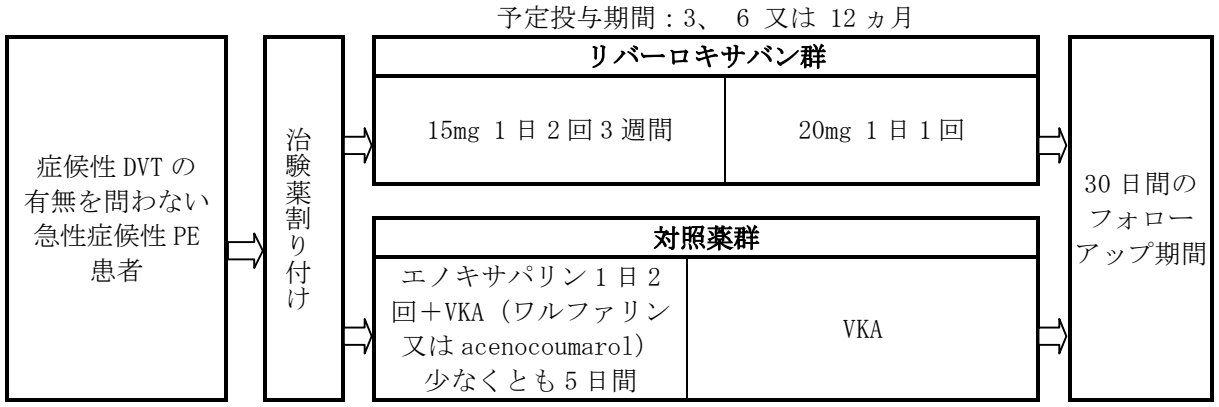
後にみられた出血事象は別途記述した。また、出血事象と死亡の解析はITT解析対象集団においても行った。

有効性及び安全性の主要解析に関して、第1種の過誤を両側0.05に維持するため、閉手順を適用し、安全性の主要解析について逐次的検定手法を用いた。有効性の主要解析において、リバーロキサバンがエノキサパリン／VKAに非劣性を示した場合、安全性主要評価項目であるイベントの発現までの時間（患者年）について、層別Cox比例ハザードモデルを用いて、有効性主要解析と同様の層及び共変量で投与群間の比較を行った。群間差が統計的に有意（両側有意水準0.05）にリバーロキサバン群で優れていた場合、「重大な出血事象」の発現までの時間のみについて同じ有意水準で検定を行うこととした。対数（部分）尤度比検定を優越性の検定に適用した。

<u>中間解析</u>

該当せず。

試験の全般的デザインを図 2.7.6.2- 1に、試験スケジュールを表 2.7.6.2- 1に示す。



DVT：深部静脈血栓症、PE：肺塞栓症、VKA：ビタミン K 拮抗薬
引用元：5.3.5.1.2 A53042/Text Figure 7-1

図 2.7.6.2- 1　試験の全般的デザイン

表 2.7.6.2- 1　試験のスケジュール

3ヵ月のコホート	スクリーニング	治験薬投与期間						フォローアップ期間
月							3	
日		1	8±1	15±1	30±7	60±7	91～98	121～128
コンタクト方法		来院	電話	来院	来院	来院	来院	来院
DVT の診断 診断のための検査	○ ○							
- 選択／除外基準の確認 [a] - VTE 危険因子 - 病歴 - 抗凝固、抗血小板療法の確認 [b] - 人口統計学的特性	○							
血小板数、Hb、aPTT、PT-INR	○[i]	出血が疑われた場合：血小板数、Hb、 aPTT、PT-INR[i] DVT / PE が疑われた場合： 血小板数、aPTT、PT-INR[i]						
ALT、クレアチニン	○[j]							
中央測定（採血） - 肝機能検査 [c,d] （全被験者） - 薬力学的検査 [e]	○ ○			○ ○	○	○ ○	○ ○	○
IVRS		○		○			○	
コンタクトレポート			○	○	○	○	○	○
HCRU			○	○	○	○	○	
ACTS [f]				○	○	○	○	
TSQM [f]					○		○	
併用薬・療法の確認 [g]	○		○	○	○	○	○	○
診断のための観察検査	○	DVT / PE、出血事象、死亡、心血管事象が疑われた場合						
対照薬群								
	[k]	エノキサパリンを少なくとも 5 日間投与						
VKA 投与（PT-INR で調整）		PT-INR は最初少なくとも 2～3 日ごと、その後少なくとも毎月測定						
リバーロキサバン群								
リバーロキサバン投与	[k]	15 mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回投与						
安全性								
(重篤な)有害事象、 出血事象、心血管事象	同意取得後に収集された事象							

表 2.7.6.2- 1　試験のスケジュール（続き）

6 ヵ月のコホート	スクリーニング	治験薬投与期間									フォローアップ期間
月							3	4	5	6	
日		1	8 ±1	15 ±1	30 ±7	60 ±7	91～98	120 ±7	150 ±7	178～185	208～215
コンタクト方法		来院	電話	来院	来院	来院	来院	LVP [h]	LVP [h]	来院	来院
DVT の診断 診断のための検査	○ ○										
- 選択／除外基準の確認 [a] - VTE 危険因子 - 病歴 - 抗凝固、抗血小板療法の確認 [b] - 人口統計学的特性	○										
血小板数、Hb、aPTT、PT-INR	○[i]	出血が疑われた場合：血小板数、Hb、 aPTT、PT-INR[i] DVT / PE が疑われた場合： 血小板数、aPTT、PT-INR[i]									
ALT、クレアチニン	○[j]										
中央測定（採血） - 肝機能検査 [c,d] （全被験者） - 薬力学的検査 [e]	○ ○			○ ○	○	○ ○	○ ○	○	○	○ ○	○
IVRS		○		○			○			○	
コンタクトレポート			○	○	○	○	○	○	○	○	○
HCRU			○	○	○	○	○	○	○	○	
ACTS [f]				○	○	○	○			○	
TSQM [f]					○		○			○	
併用薬・療法の確認 [g]	○		○	○	○	○	○	○	○	○	○
診断のための観察検査	○	DVT / PE、出血事象、死亡、心血管事象が疑われた場合									
対照薬群											
	[k]	エノキサパリンを少なくとも 5 日間投与									
VKA 投与 （PT-INR で調整）		PT-INR は最初少なくとも 2～3 日ごと、その後少なくとも毎月測定									
リバーロキサバン群											
リバーロキサバン投与	[k]	15 mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回投与									
安全性											
(重篤な)有害事象、出血事象、心血管事象	同意取得後に収集された事象										

表 2.7.6.2- 1　試験のスケジュール（続き）

12 ヵ月のコホート	スクリーニング	治験薬投与期間															フォローアップ期間
月							3	4	5	6	7	8	9	10	11	12	13
日		1	8 ±1	15 ±1	30 ±7	60 ±7	91 ～ 98	120 ±7	150 ±7	178 ～ 185	210 ±7	240 ±7	265 ～ 272	300 ±7	330 ±7	352 ～ 359	382 ～ 389
コンタクト方法		来院	電話	来院	来院	来院	来院	LVP[h]	LVP[h]	来院	LVP[h]	LVP[h]	来院	LVP[h]	LVP[h]	来院	来院
DVT の診断 診断のための検査	○ ○																
- 選択／除外基準の確認[a] - VTE 危険因子 - 病歴 - 抗凝固、抗血小板療法の確認[b] - 人口統計学的特性	○																
血小板数、Hb、aPTT、PT-INR	○[i]	出血が疑われた場合：血小板数、Hb、 aPTT、PT-INR[i] DVT / PE が疑われた場合： 血小板数、aPTT、PT-INR[i]															
ALT、クレアチニン	○[j]																
中央測定（採血） - 肝機能検査[c,d]（全被験者） - 薬力学的検査[e]	○ ○			○ ○	○	○ ○	○ ○	○	○	○ ○	○	○	○	○	○	○ ○	○
IVRS		○		○			○			○			○			○	
コンタクトレポート			○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
HCRU			○	○	○	○	○	○	○	○	○	○	○	○	○	○	
ACTS[f]				○	○	○	○			○						○	
TSQM[f]					○		○			○						○	
併用薬・療法の確認[g]	○		○	○	○	○	○	○	○	○	○	○	○	○	○	○	○
診断のための観察検査		DVT / PE、出血事象、死亡、心血管事象が疑われた場合															
対照薬群																	
	[k]	エノキサパリンを少なくとも 5 日間投与															
VKA 投与（PT-INR で調整）		PT-INR は最初少なくとも 2～3 日ごと、その後少なくとも毎月測定															
リバーロキサバン群																	
リバーロキサバン投与	[k]	15 mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回投与															
安全性																	
(重篤な)有害事象、出血事象、心血管事象	同意取得後に収集された事象																

HCRU：医療資源の利用、ACTS：抗凝固薬治療に関する評価尺度、TSQM：薬物治療の満足度に関する質問票
a：妊娠の可能性がある女性に対し妊娠検査を実施
b：無作為割り付け前 7 日以内の抗凝固、抗血小板療法

表 2.7.6.2- 1　試験のスケジュール（続き）

c：肝機能検査はビリルビン（総ビリルビン、抱合型）、ALT、AST、ALP を含む。治験薬投与期間又はフォローアップ期間に臨床的に重要な肝機能異常が発現した際に広範囲に肝機能検査を行うためベースライン時の血液検体を保管した。
d：アミラーゼ測定用採血。3 ヵ月のコホート：ベースライン時と第 3 ヵ月。6 ヵ月のコホート：ベースライン時と第 6 ヵ月。12 ヵ月のコホート：ベースライン時と第 6 及び 12 ヵ月。
e：すべての被験者を対象に治験薬投与前のスクリーニング時に薬力学的検査を実施。リバーロキサバン群のみ第 15 日に 2 回〔治験薬投与直前（トラフ状態）で 1 回、投与 2～4 時間後（ピーク状態）で 1 回〕、第 60 日及び第 6 ヵ月の治験薬投与直前のトラフ状態、及び第 3 ヵ月、12 ヵ月の治験薬投与後のピーク状態で採血する。
f：ACTS と TSQM は米国、イギリス、カナダ、ドイツ、フランス、イタリア、オランダの被験者のみ実施。
g：新たな又は継続中の治療法あるいは投与量の変更を記録する（フォローアップ期間中は抗凝固療法のみだが、イベントが発現した場合はすべての治療法）
h：LVP（Laboratory visit phone）：必ずしも来院を必要としない。中央測定（肝機能検査）のための採血を実施、コンタクトレポート及び HCRU は電話でも可。
i：血液検体は地域の検査機関で測定された。
j：ALT、クレアチニンの血液検体は被験者の適格性を確認するため地域の検査機関で測定された。
k：無作為割り付け前の抗凝固療法は最大 48 時間許容されたが、VKA は単回投与のみ許容された。
引用元：5.3.5.1.2 A53042/Text Figure 7-2

表 2.7.6.2- 2　有効性評価における解析対象集団ごとの対象イベントと打ち切りまでの期間

	ITT	ITT on treatment [a]	PP
有効性主要解析	○	×	×
対象イベント	予定投与期間（3、6 又は 12 ヵ月）の最終日までに発現したイベント。期間は、3 ヵ月では 98 日、6 ヵ月では 185 日、12 ヵ月では 359 日を最長とする。	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間に発現したイベント	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間に発現したイベント
試験を完了した被験者の打ち切り日	無作為割り付けから治験薬の最終投与時来院までの日数と、予定投与期間の日数のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間
試験を中止した被験者の打ち切り日	無作為割り付けから最後の適切なコンタクトまでの日数と、予定投与期間の日数のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間	ITT の該当期間と、記録された治験薬の最終投与日＋2 日のうち短い方の期間

ITT：intention-to-treat、PP：治験実施計画書に適合した
a：無作為割り付けされた治験薬投与を受けた期間のみを ITT on treatment 解析対象とした。
引用元：5.3.5.1.2 A53042/Text Table 7-2

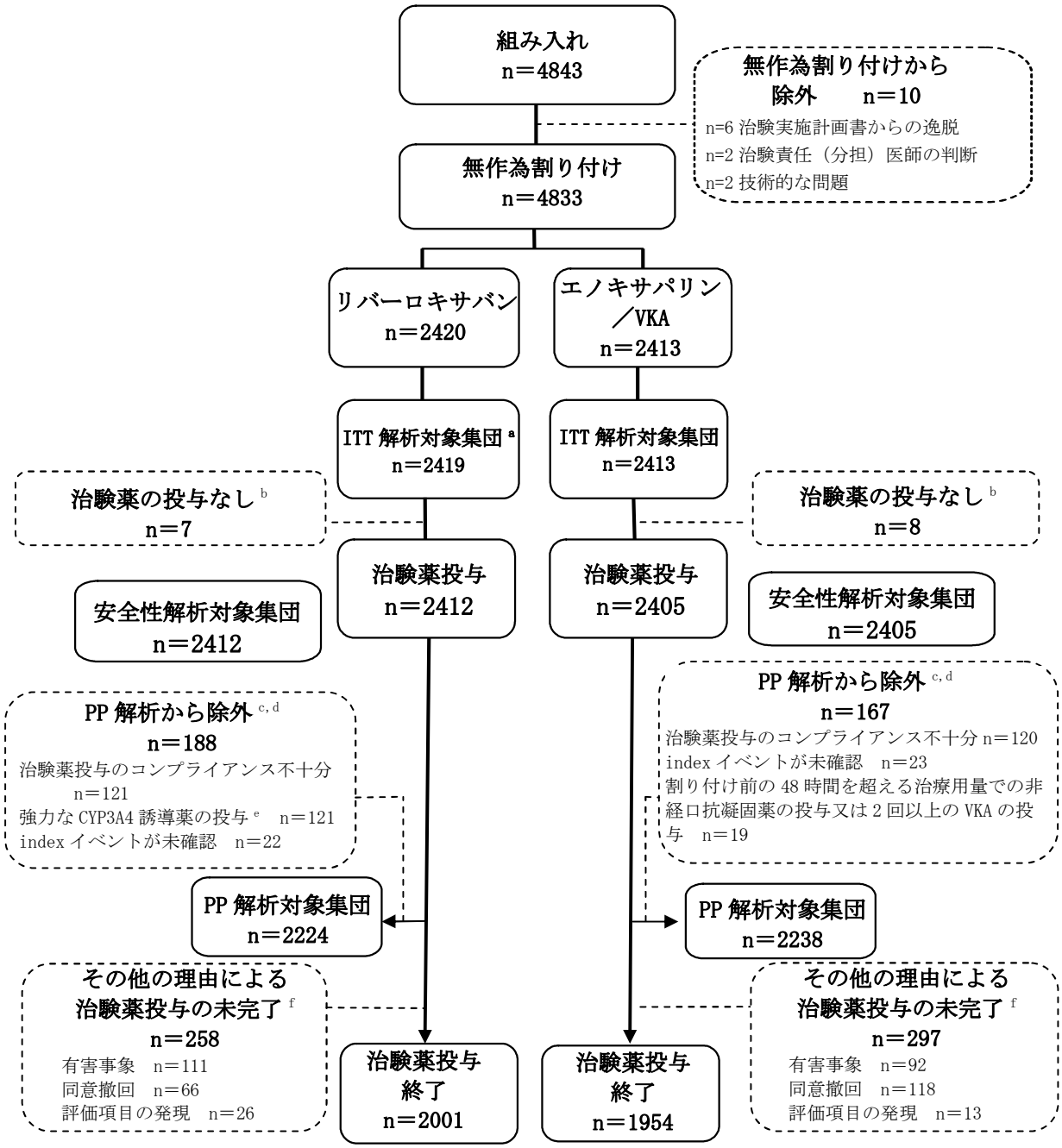
2.7.6.2.2　成績

2.7.6.2.2.1　被験者の背景

2.7.6.2.2.1.1　被験者の内訳

38 ヵ国の 263 施設で 4,843 例が組み入れられ、4,833 例〔リバーロキサバン群 2,420 例、エノキサパリンナトリウム（エノキサパリン）／VKA 群 2,413 例〕が無作為に割り付けられた。被験者の内訳を図 2.7.6.2- 2に要約する。

4,843 例の組み入れ被験者のうち、10 例が無作為割り付けされなかった。割り付けられなかった理由は、治験実施計画書からの逸脱が 6 例、治験責任（分担）医師の判断が 2 例、技術的な問題が 2 例であった。



VKA：ビタミン K 拮抗薬（acenocoumarol 又はワルファリン）、ITT：intention-to-treat 解析対象集団、PP：治験実施計画書に適合した、CYP3A4：チトクローム P450 酵素 3A4

a：被験者 660013007 は同意書の不備のため、割り付けされたが ITT 解析対象から除外された。

b：詳細情報なし

c：多く認められた理由のみ

d：各被験者で 2 つ以上の理由がある場合があるため、各理由の合計数は除外例数と合致しない。

e：治験薬投与期間に強力な CYP3A4 誘導薬を 2 日間以上投与された場合、リバーロキサバン群のみ除外とした。

f: 多く認められた理由のみ。「死亡」、「治験依頼者による試験終了の決定」、「治験責任医師による施設の試験中止」はこの図には示さなかった。

引用元：5.3.5.1.2 A53042/Table 14.1/1、Table 14.1/7、Table 14.1/8、Table 14.1/17、Table 14.1/18

図 2.7.6.2- 2　被験者の内訳

予定投与期間として 3、6 又は 12 ヵ月のいずれかの投与期間を無作為割り付け前に治験責任（分担）医師が決定した。予定投与期間別の被験者数を表 2.7.6.2- 3に示す。各予定投与期間の被験者の割合は、3 ヵ月が 5.2%、6 ヵ月が 57.4%、12 ヵ月が 37.4%であった。

表 2.7.6.2- 3　予定投与期間別の被験者数の内訳（無作為割り付けされた被験者）

予定投与期間	リバーロキサバン N=2420 (100%)	エノキサパリン／VKA N=2413 (100%)	全体 N=4833 (100%)
3 ヵ月	127 (5.2%)	122 (5.1%)	249 (5.2%)
6 ヵ月	1388 (57.4%)	1387 (57.5%)	2775 (57.4%)
12 ヵ月	905 (37.4%)	904 (37.5%)	1809 (37.4%)

VKA：ビタミン K 拮抗薬
引用元：5.3.5.1.2 A53042/Table 14.1/2

2.7.6.2.2.1.1.1　治験薬投与の完了及び未完了

すべての無作為割り付け例について、治験薬投与の完了及び未完了の内訳を表 2.7.6.2- 4に要約して示す。

すべての無作為割り付け例のうち、全体で約 82%の被験者が治験薬の投与を予定どおり完了した。両投与群の割合は同程度で、リバーロキサバン群 82.7% (2,001/2,420 例) 、エノキサパリン／VKA 群 81.0% (1,954/2,413 例) であった。本試験はイベント主導型試験であり、有効性主要評価項目の評価に必要な目標イベント発現数の 88 件に達する見込みを得た時点で組み入れを終了した。これによる試験終了（治験依頼者による試験終了の決定）は、リバーロキサバン群 5.2%、エノキサパリン／VKA 群 5.5%であった。

治験薬投与の未完了を、死亡、治験依頼者による試験終了の決定、治験責任医師による施設の試験中止、及びその他の理由による治験薬投与の未完了に区分した。その他の理由による治験薬投与の未完了で多かった理由は、有害事象〔リバーロキサバン群：111 例 (4.6%) 、エノキサパリン／VKA 群：92 例 (3.8%) 〕、同意撤回〔66 例 (2.7%) 、118 例 (4.9%) 〕、評価項目の発現〔26 例 (1.1%) 、13 例 (0.5%) 〕であった。追跡不能は、リバーロキサバン群の 8 例 (0.3%) 、エノキサパリン／VKA 群の 10 例 (0.4%) にみられた。同意撤回は投与群間で顕著に異なったが、この差は PT-INR 測定用の採血の必要性によるもので、予定投与期間 3、6 及び 12 ヵ月の 3 コホートすべてにおいて認められた (5.3.5.1.2 A53042/Table 14.1/9) 。

表 2.7.6.2- 4　治験薬投与の完了及び未完了の内訳（無作為割り付けされた被験者）

	リバーロキサバン N=2420（100%）	エノキサパリン／VKA N=2413（100%）
治験薬投与完了	2001（82.7%）	1954（81.0%）
死亡	29（ 1.2%）	21（ 0.9%）
治験依頼者による試験終了の決定[a]	125（ 5.2%）	132（ 5.5%）
治験責任医師による施設の試験中止[b]	0	1（＜0.1%）
治験薬未投与例	7（ 0.3%）	8（ 0.3%）
そのほかの理由による治験薬投与の未完了	258（10.7%）	297（12.3%）
有害事象	111（ 4.6%）	92（ 3.8%）
治験薬投与のコンプライアンス不十分	11（ 0.5%）	25（ 1.0%）
同意撤回	66（ 2.7%）	118（ 4.9%）
治療効果不十分	0	4（ 0.2%）
追跡不能	8（ 0.3%）	10（ 0.4%）
治験実施計画書からの逸脱	12（ 0.5%）	5（ 0.2%）
治験実施計画書の規定によるもの	1（＜0.1%）	3（ 0.1%）
疾患の進行又は再発	1（＜0.1%）	0
治験責任（分担）医師の判断（治験実施計画書の規定によるものではない）	7（ 0.3%）	18（ 0.7%）
評価項目の発現[c]	26（ 1.1%）	13（ 0.5%）
技術的問題[d]	3（ 0.1%）	1（＜0.1%）
被験者都合[e]	12（ 0.5%）	8（ 0.3%）

VKA：ビタミン K 拮抗薬
治験責任（分担）医師の判断による主な中止理由を示しているため、有害事象による中止の例数は、有害事象を発現しその措置として「治験薬の中止」と記録された例の数と一致しない可能性がある。
治験終了 CRF での治験責任（分担）医師の判断のため、上記理由は他の判定や解析と異なる可能性がある。
被験者 660013007 は割り付けられたが、同意書の不備のため ITT 解析から除外された。この被験者はリバーロキサバンを 3 錠服用したので、この表では治験実施計画書からの逸脱による未完了に含むこととした。
a：予定したイベント数（あらかじめ治験実施計画書で規定された）に達した後
b：実施管理上の理由
c：評価項目の発現後、治験薬投与を中止するか否かを治験責任（分担）医師が判断することとした。中止と判断された被験者のみを示す。
d：技術的理由には、リバーロキサバン群に割り付けられた被験者の「採血の静脈確保困難」、「治験薬投与継続不可」、「IRB による中止」。エノキサパリン／VKA 群に割り付けられた被験者の「スクリーニング検査の欠測」があった。
e：被験者の移転や来院の都合がつかなかった際の最終来院は治験実施計画書で計画されたものより簡単に実施された。
引用元：5.3.5.1.2 A53042/Table 14.1/8

2.7.6.2.2.1.1.2　　予定した治験薬投与期間の完了及び未完了

予定した治験薬投与期間にかかわらず、被験者が予定投与期間の来院の許容範囲のうち最短の日又はそれ以降にコンタクトレポートを作成された、来院の許容範囲の最長の日（3、6 及び 12 ヵ月について、それぞれ第 98 日、第 185 日及び第 359 日）までに有効性主要評価項目又は死

亡が判定された、若しくは治験依頼者による試験終了の決定のために終了した場合に、当該被験者は予定した治験薬投与期間を完了したこととした。

大多数の被験者（リバーロキサバン群：96.9%、エノキサパリン／VKA 群：96.1%）は、上記定義における予定した治験薬投与期間完了例であった。予定した治験薬投与期間を完了しなかった被験者における主な未完了理由は、同意撤回（リバーロキサバン群：2.1%、エノキサパリン／VKA 群：2.9%）、追跡不能（0.4% 、0.5%）、有害事象（0.2%、0.1%）、予定投与期間の終了前に治験責任（分担）医師の判断により予定投与期間を終了し試験 11899 に参加（0.2%、0.1%未満）であった（表 2.7.6.2- 5）。

表 2.7.6.2- 5　予定した治験薬投与期間の完了及び未完了の内訳（無作為割り付けされた被験者）

	リバーロキサバン N=2420（100%）	エノキサパリン／VKA N=2413（100%）
予定投与期間完了／有効性主要評価項目の発現／予定投与期間終了前に死亡／治験依頼者による試験終了の決定[a]	2346（96.9%）	2320（96.1%）
同意撤回	51（2.1%）	71（2.9%）
治験責任（分担）医師の判断により予定投与期間終了前に治験薬投与を終了し、フォローアップ期間なしで試験 11899 へ参加[b]	5（0.2%）	2（＜0.1%）
そのほかの未完了理由	18（0.7%）	20（0.8%）
有害事象	4（0.2%）	3（0.1%）
治験薬投与のコンプライアンス不十分	1（＜0.1%）	0（0.0%）
追跡不能	9（0.4%）	12（0.5%）
治験実施計画書からの逸脱	1（＜0.1%）	3（0.1%）
治験責任（分担）医師の判断（治験実施計画書の規定によるものではない）	0（0.0%）	1（＜0.1%）
評価項目の発現	0（0.0%）	1（＜0.1%）
技術的問題	1（＜0.1%）	0（0.0%）
被験者都合[c]	1（＜0.1%）	0（0.0%）
治験責任（分担）医師の判断により予定投与期間終了前に治験薬投与期間を終了	1（＜0.1%）	0（0.0%）

VKA：ビタミン K 拮抗薬

治験実施計画書に定めた最終の予定投与来院は、3 ヵ月のコホートでは第 91～98 日、6 ヵ月のコホートでは第 178～185 日、12 か月のコホートでは第 352～359 日であった。各コホートの被験者がそれぞれ第 91、178、352 日もしくはそれ以降にコンタクトレポートを作成された場合、又は各コホートの被験者がそれぞれ第 98、185、359 日以前に有効性評価項目を発現もしくは死亡した場合、又は治験依頼者が試験終了を決定した場合、被験者は予定投与期間を完了したと取り扱った。

被験者 660013007 は割り付けられたが、同意書の不備のため ITT 解析から除外された。この被験者はリバーロキサバンを 3 錠服用したので、この表では治験実施計画書からの逸脱による中止に含むこととした。

a：試験に既に組み入れられた被験者内で予定したイベント発現数（治験実施計画書で事前に規定）に到達する見込みを得た後の治験依頼者による試験終了の決定

b：治験実施計画書に規定された投与期間よりも早期に予定投与期間を終了し、その後試験 11899 に移行した全 7 例。移行期間に有効性主要評価項目を発現した被験者はいなかった。詳細は 5.3.5.1.2 A53042/Table 16.1.9.3/33 を参照。

c：来院の都合がつかなかった被験者の治験の最終来院は、治験実施計画書で計画されたものより早期に実施された。

引用元：5.3.5.1.2 A53042/Table 14.1/14

予定投与期間にかかわらず、治験薬投与後に 30 日間のフォローアップ期間を設定した。本試験では両投与群の 91%を上回る被験者がフォローアップ期間に参加し、被験者の約 89%がフォローアップ期間を完了した（5.3.5.1.2 A53042/Table 14.1/11）。予定したフォローアップ期間に参加しなかった被験者のうち、リバーロキサバン群 121 例（5.0%）、エノキサパリン／VKA 群 104 例（4.3%）は試験 11899 に参加した。フォローアップ期間を完了しなかった理由で多かったものは同意撤回と死亡であった。

2.7.6.2.2.1.2　　症例の取扱い及び解析対象集団

4,833 例（リバーロキサバン群：2,420 例、エノキサパリン／VKA 群：2,413 例）の被験者が無作為割り付けされ、そのうち 4,832 例が ITT 解析対象集団に採用された。被験者 660013007 は同意書の不備のため ITT 解析対象集団から除外された。ITT 解析対象集団のうち、リバーロキサバン群で 7 例、エノキサパリン／VKA 群で 8 例が治験薬投与に至らなかったため、安全性解析対象集団、ITT on treatment 解析対象集団、PP 解析対象集団から除外された。

無作為割り付け後に治験薬が投与された被験者（安全性解析対象集団及び ITT on treatment 解析対象集団）は 4,817 例（リバーロキサバン群：2,412 例、エノキサパリン／VKA 群：2,405 例）であった。

PP 解析対象集団には 4,462 例（リバーロキサバン群：2,224 例、エノキサパリン／VKA 群：2,238 例）が採用された。355 例（リバーロキサバン群：188 例、エノキサパリン／VKA 群：167 例）が PP 解析対象集団から除外された。除外された理由で多かったものは、治験薬投与のコンプライアンス不十分〔リバーロキサバン群：121 例（5.0%）、エノキサパリン／VKA 群：120 例（5.0%）〕、CIAC により index イベントが PE と判定されなかった〔リバーロキサバン群：22 例（0.9%）、エノキサパリン／VKA 群：23 例（1.0%）〕、投与期間中における強力なチトクローム P450 酵素 3A4（CYP3A4）誘導剤の 3 日間以上の投与〔リバーロキサバン群：29 例（1.2%）、エノキサパリン／VKA 群：0 例〕であった。治験薬投与のコンプライアンス不十分によって PP 解析対象集団から除外された被験者は、服薬率が 80%未満と算出された、又は服薬率が算出不能で服薬指導が不十分と判断されたものであった。両投与群の服薬率については 2.7.6.2.2.1.8.2に示した。

ITT 解析、安全性解析及び PP 解析対象集団の被験者数、並びに除外理由を表 2.7.6.2- 6に示す。

表 2.7.6.2- 6　各解析対象集団の内訳及び主な除外理由（無作為割り付けされた被験者）

	リバーロキサバン	エノキサパリン／VKA
無作為割り付け	2420/2420（ 100.0%）	2413/2413（100.0%）
ITT 解析対象集団	2419/2420（＞99.9%）	2413/2413（100.0%）
安全性解析対象集団	2412/2420（ 99.7%）	2405/2413（ 99.7%）
PP 解析対象集団	2224/2420（ 91.9%）	2238/2413（ 92.7%）
ITT 解析対象集団からの除外	1/2420（ ＜0.1%）	0/2413
同意書の不備	1/2420（ ＜0.1%）	0/2413
安全性解析対象集団からの除外	7/2420（ 0.3%）	8/2413（ 0.3%）
治験薬の投与なし	7/2420（ 0.3%）	8/2413（ 0.3%）
PP 解析対象集団からの除外[a]	188/2420（ 7.8%）	167/2413（ 6.9%）
治験薬投与のコンプライアンス不十分	121/2420（ 5.0%）	120/2413（ 5.0%）
治験薬の誤投与[b]	0/2420	10/2413（ 0.4%）
CIAC により index イベントが PE と判定されなかった	22/2420（ 0.9%）	23/2413（ 1.0%）
投与期間中における強力な CYP3A4 阻害薬/P-gp 阻害薬の投与	1/2420（ ＜0.1%）	0/2413
投与期間中における強力な CYP3A4 誘導薬の 3 日間以上の投与	29/2420（ 1.2%）	0/2413
投与期間中における 1 週間を超えるその他の抗凝固薬の使用（抗凝固薬の医療上の必要性がある場合を除く）	8/2420（ 0.3%）	0/2413
無作為割り付け前の 48 時間を超える治療用量での非経口抗凝固薬の投与又は 2 回以上の VKA の投与	13/2420（ 0.5%）	19/2413（ 0.8%）
index イベントのための血栓除去術治療	1/2420（ ＜0.1%）	0/2413

VKA：ビタミン K 拮抗薬、CYP3A4：チトクローム P450 3A4 分子種、P-gp：P 糖たん白、ITT：intention-to-treat、PP: 治験実施計画書に適合した
被験者は解析対象集団から複数の理由により除外される場合があった。
a：安全性解析対象集団から除外された被験者は、PP 解析対象集団からも除外された。
b：初期のエノキサパリン投与下での治験薬の誤投与
引用元：5.3.5.1.2 A53042/Table 14.1/17、Table 14.1/18

2.7.6.2.2.1.3　　人口統計学的特性

ITT 解析対象集団の人口統計学的特性を表 2.7.6.2- 7に要約して示す。

ITT 解析対象集団と安全性解析対象集団の人口統計学的特性は非常に類似したものであった。

全体として、ITT 解析対象集団の被験者背景は投与群間で類似していた。リバーロキサバン群では 54.1%、エノキサパリン／VKA 群では 51.7%の被験者が男性で、人種では白人が 66%を占めた。約 24%の被験者については、当該地域の法令により人種情報の収集が許可されなかったため、不明とされた。

年齢範囲は両投与群共に 18～97 歳であり、平均年齢はリバーロキサバン群で 57.9 歳、エノキサパリン／VKA 群で 57.5 歳であった。年齢（区分 1）の分類ではそれぞれ、18～＜40 歳が 16.9%、17.9%、40～＜60 歳が 32.8%、32.3%、60～＜75 歳が 30.6%、31.2%、≧75 歳が

19.6%、18.6%であった。年齢（区分 2）の分類では、65 歳未満が約 2/3（リバーロキサバン群：60.4%、エノキサパリン／VKA 群：61.3%）で、65 歳以上が 1/3 を占めた。

平均体重〔平均値±標準偏差（SD）〕はリバーロキサバン群で 82.9±19.2kg、エノキサパリン／VKA 群で 83.0±18.8kg、体重範囲はそれぞれ、37.4～187kg、35～220kg、平均 BMI（平均値±SD）は 28.28±5.92kg/m^2、28.37±5.74kg/m^2 、BMI 範囲は 16.3～70.8kg/m^2、12.9～63.3kg/m^2、肥満の被験者（BMI が 30kg/m^2以上と定義）は両投与群共に 31%を占めた。

リバーロキサバン群の 4 例（0.2%）及びエノキサパリン／VKA 群の 2 例（0.1%未満）は CL_{CR}（計算値）30mL/min 未満（除外基準に抵触）であった。

表 2.7.6.2- 7　人口統計学的特性（ITT 解析対象集団）

	リバーロキサバン N＝2419（100%）	エノキサパリン／VKA N=2413（100%）
性別		
男性	1309（ 54.1%）	1247（ 51.7%）
女性	1110（ 45.9%）	1166（ 48.3%）
人種		
白人	1585（ 65.5%）	1587（ 65.8%）
黒人	66（ 2.7%）	68（ 2.8%）
アジア人	163（ 6.7%）	156（ 6.5%）
アメリカンインディアン又はアラスカ先住民	0（ 0.0%）	3（ 0.1%）
ヒスパニック系	10（ 0.4%）	11（ 0.5%）
ハワイ先住民又は太平洋諸島系	4（ 0.2%）	2（ ＜0.1%）
分類不能	5（ 0.2%）	3（ 0.1%）
不明	586（ 24.2%）	583（ 24.2%）
年齢		
平均値±標準偏差（SD）	57.9±17.3	57.5±17.2
範囲	18～97	18～97
年齢（区分 1）		
18～＜40 歳	410（ 16.9%）	432（ 17.9%）
40～＜60 歳	794（ 32.8%）	779（ 32.3%）
60～＜75 歳	740（ 30.6%）	754（ 31.2%）
≧75 歳	475（ 19.6%）	448（ 18.6%）
年齢（区分 2）		
＜65 歳	1461（ 60.4%）	1479（ 61.3%）
65～75 歳	517（ 21.4%）	532（ 22.0%）
＞75 歳	441（ 18.2%）	402（ 16.7%）
体重（kg）		
欠測	2	1
平均値±SD	82.9±19.2	83.0±18.8
範囲	37.4～187	35.0～220
体重（区分）		
欠測	2（ ＜0.1%）	1（ ＜0.1%）
≦50kg	38（ 1.6%）	43（ 1.8%）
50＜～60kg	195（ 8.1%）	201（ 8.3%）
60＜～70kg	420（ 17.4%）	377（ 15.6%）
70＜～80kg	577（ 23.9%）	579（ 24.0%）
80＜～90kg	504（ 20.8%）	540（ 22.4%）
90＜～100kg	338（ 14.0%）	313（ 13.0%）
100＜～110kg	160（ 6.6%）	189（ 7.8%）
＞110kg	185（ 7.6%）	170（ 7.0%）

表 2.7.6.2- 7　人口統計学的特性（ITT 解析対象集団）（続き）

	リバーロキサバン N＝2419（100%）	エノキサパリン／VKA N=2413（100%）
BMI（kg/m²）		
N	2409	2398
平均値±SD	28.28±5.92	28.37±5.74
範囲	16.3～70.8	12.9～63.3
BMI（区分）		
欠測	10（ 0.4%）	15（ 0.6%）
＜18.5kg/m²	23（ 1.0%）	31（ 1.3%）
18.5～＜25kg/m²	697（ 28.8%）	624（ 25.9%）
25～＜30kg/m²	948（ 39.2%）	988（ 40.9%）
30～＜35kg/m²	469（ 19.4%）	493（ 20.4%）
35～＜40kg/m²	169（ 7.0%）	162（ 6.7%）
≧40kg/m²	103（ 4.3%）	100（ 4.1%）
CL_{CR}（区分）[a]		
欠測	16（ 0.7%）	10（ 0.4%）
＜30mL/min [b]	4（ 0.2%）	2（ ＜0.1%）
30～＜50mL/min	207（ 8.6%）	191（ 7.9%）
50～＜80mL/min	637（ 26.3%）	593（ 24.6%）
≧80mL/min	1555（ 64.3%）	1617（ 67.0%）

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、SD：標準偏差、BMI：body mass index（体格指数）、CL_{CR}：クレアチニンクリアランス
頻度（%）は欠測値も含めて算出した。
人種の不明は、法律上の理由による未回答である。
a：CL_{CR}は、無作為割り付け日までの直近の測定値を基に、Cockroft Gault 式を用いて算出した。
b：範囲は 16.6～29.4mL/min(リバーロキサバン群:16.6～29.1mL/min、エノキサパリン／VKA 群: 24.7 mL/min、29.4 mL/min)
引用元：5.3.5.1.2 A53042/Table 14.1/25

2.7.6.2.2.1.4　　血栓塞栓症の危険因子

頻度の高かった血栓塞栓症の危険因子は、最近の手術又は外傷、活動性の制限及びエストロゲン含有医薬品の使用からなる「一過性」危険因子と、特発性 DVT／PE、DVT／PE の既往、及び既知の血栓性素因からなる「永続的」危険因子に分類される。

最も多く報告された危険因子は特発性 DVT／PE であり、全体の被験者の約 49%で報告された。続いて DVT／PE の既往（約 20%）、最近の手術又は外傷（約 17%）、活動性の制限（約 16%）であった。活動性悪性腫瘍は約 4.6%の被験者で危険因子として報告された（表 2.7.6.2- 8）。

表 2.7.6.2- 8　血栓塞栓症の危険因子〔いずれかの投与群で 3 例（0.2%）以上：ITT 解析対象集団〕

	リバーロキサバン N=2419（100%）	エノキサパリン／VKA N=2413（100%）
特発性 DVT／PE	1196（ 49.4%）	1186（ 49.2%）
DVT／PE の既往	455（ 18.8%）	489（ 20.3%）
最近の手術又は外傷	415（ 17.2%）	398（ 16.5%）
活動性の制限	384（ 15.9%）	380（ 15.7%）
エストロゲン含有医薬品の使用	207（ 8.6%）	223（ 9.2%）
既知の血栓性素因 [a]	138（ 5.7%）	121（ 5.0%）
第Ｖ因子 Leiden 変異	60（ 43.5%）	56（ 46.3%）
抗リン脂質抗体	22（ 15.9%）	16（ 13.2%）
高ホモシステイン血症	18（ 13.0%）	15（ 12.4%）
プロテイン S 欠損症	10（ 7.2%）	15（ 12.4%）
プロテイン C 欠損症	16（ 11.6%）	9（ 7.4%）
第Ⅷ因子高値	4（ 2.9%）	6（ 5.0%）
アンチトロンビンに関するもの	4（ 2.9%）	5（ 4.1%）
活動性悪性腫瘍	114（ 4.7%）	109（ 4.5%）
肥満	95（ 3.9%）	97（ 4.0%）
ニコチン乱用	30（ 1.2%）	28（ 1.2%）
静脈炎／表在性静脈血栓症	12（ 0.5%）	17（ 0.7%）
静脈瘤	6（ 0.2%）	18（ 0.7%）
VTE の家族歴	15（ 0.6%）	7（ 0.3%）
静脈不全	7（ 0.3%）	5（ 0.2%）
産褥	6（ 0.2%）	5（ 0.2%）
炎症/感染症	5（ 0.2%）	3（ 0.1%）
その他の危険因子	10（ 0.4%）	14（ 0.6%）

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症、VTE：静脈血栓塞栓症
被験者は 2 つ以上の危険因子や血栓性素因を有する場合もあるため、合計は一致しない。
特発性 DVT／PE は治験責任（分担）医師の評価により分類された。
a：多く報告された血栓性素因を示す
b：引用表の「Antithrombin」はアンチトロンビンに関するものとした。
引用元：5.3.5.1.2 A53042/Table 14.1/37、Table 14.1/46

予定投与期間別の危険因子を表 2.7.6.2- 9に示す。

予定投与期間が 3 ヵ月のコホート（249 例、ITT 解析対象集団）では、永続的危険因子である特発性 PE、DVT／PE の既往、及び既知の血栓性素因の保有割合が最も低かった。一方、このコホートでは、一過性危険因子である最近の手術又は外傷、及び活動性の制限を伴った割合が最も高かった。活動性悪性腫瘍の保有割合は 6 及び 12 ヵ月のコホートと同様であった。

予定投与期間が 6 ヵ月のコホート（2,774 例、ITT 解析対象集団）では、3 ヵ月のコホートに比べて永続的危険因子の保有割合が高く、一過性危険因子の保有割合が低かった（エストロゲン含有医薬品の使用を除く）。

予定投与期間が 12 ヵ月のコホート（1,809 例、ITT 解析対象集団）では、3 ヵ月のコホートと比べて永続的危険因子の保有割合が高く、一過性危険因子の保有割合が低かった。予定投与期間

が 6 ヵ月のコホートと比べた場合、予定投与期間 12 ヵ月の被験者では永続的危険因子である DVT/PE の既往、及び既知の血栓性素因の保有割合が高かった。

表 2.7.6.2- 9　予定投与期間別の血栓塞栓症の危険因子（いずれかの投与群で 4%以上：ITT 解析対象集団）

	リバーロキサバン	エノキサパリン／VKA
3 ヵ月のコホート	(N=127)	(N=122)
最近の手術又は外傷	55 (43.3%)	58 (47.5%)
特発性 DVT／PE	43 (33.9%)	33 (27.0%)
活動性の制限	30 (23.6%)	37 (30.3%)
エストロゲン含有医薬品の使用	12 (9.4%)	14 (11.5%)
活動性悪性腫瘍	7 (5.5%)	6 (4.9%)
DVT／PE の既往	8 (6.3%)	3 (2.5%)
6 ヵ月のコホート	(N=1387)	(N=1387)
特発性 DVT／PE	684 (49.3%)	699 (50.4%)
最近の手術又は外傷	272 (19.6%)	259 (18.7%)
活動性の制限	254 (18.3%)	266 (19.2%)
エストロゲン含有医薬品の使用	151 (10.9%)	152 (11.0%)
DVT／PE の既往	142 (10.2%)	147 (10.6%)
活動性悪性腫瘍	68 (4.9%)	62 (4.5%)
既知の血栓性素因 [a]	65 (4.7%)	47 (3.4%)
12 か月のコホート	(N=905)	(N=904)
特発性 DVT／PE	469 (51.8%)	454 (50.2%)
DVT／PE の既往	305 (33.7%)	339 (37.5%)
活動性の制限	100 (11.0%)	77 (8.5%)
最近の手術又は外傷	88 (9.7%)	81 (9.0%)
既知の血栓性素因 [a]	72 (8.0%)	71 (7.9%)
エストロゲン含有医薬品の使用	44 (4.9%)	57 (6.3%)
肥満	42 (4.6%)	46 (5.1%)
活動性悪性腫瘍	39 (4.3%)	41 (4.5%)

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症
被験者は 2 つ以上の危険因子や血栓性素因を保有する場合もあるため、合計は一致しない。
特発性 DVT／PE は治験責任（分担）医師の評価により分類された。
a：血栓性素因の種類はコホートごとに分類されなかった。
引用元:5.3.5.1.2 A53042/Table 14.1/38

2.7.6.2.2.1.5　index イベント（PE）及び併発した DVT

ITT 解析対象集団において、ベースライン時に本試験対象として組み入れられた PE（index イベント）の CIAC による判定結果を表 2.7.6.2- 10に示す。ITT 解析対象集団の 99%の被験者が CIAC によって PE と判定された。PE ではないと判定された被験者が 0.5%で、評価不可能が 0.5%であった。

表 2.7.6.2- 10 CIAC による index イベント（PE）の判定（ITT 解析対象集団）

	リバーロキサバン群 N=2419（100%）	エノキサパリン／VKA 群 N=2413（100%）
PE が疑われる被験者	2419（ 100.0%）	2413（ 100.0%）
PE と判定	2396（ 99.0%）	2390（ 99.0%）
PE ではないと判定	11（ 0.5%）	11（ 0.5%）
評価不可能	12（ 0.5%）	12（ 0.5%）

ITT： intention-to-treat、VKA：ビタミン K 拮抗薬、PE：肺塞栓症
引用元: 5.3.5.1.2 A53042/Table 14.1/57、Table 14.1/58

また、index イベント（PE）に併発した DVT の判定結果を表 2.7.6.2- 11に示す。

表 2.7.6.2- 11 CIAC による index イベント（PE）に併発する DVT の判定（ITT 解析対象集団）

	リバーロキサバン群 N=2419（100%）	エノキサパリン／VKA 群 N=2413（100%）
DVT が疑われる被験者	691（ 28.6%）	685（ 28.4%）
DVT（近位）と判定	540（ 22.3%）	531（ 22.0%）
DVT（遠位）と判定	63（ 2.6%）	56（ 2.3%）
評価不可能	33（ 1.4%）	41（ 1.7%）
DVT ではないと判定	52（ 2.1%）	52（ 2.2%）
DVT の併発のない被験者	1728（ 71.4%）	1728（ 71.6%）

DVT：深部静脈血栓症、ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、PE：肺塞栓症
引用元: 5.3.5.1.2 A53042/Table 14.1/57、Table 14.1/58

index イベント（PE）の重症度（肺血流の欠損範囲）を肺血流スコア（0 点：全肺野で肺血流が欠損、0.75 点：大血管の 75％に欠損がない、1 点：すべてに欠損がない）を用いて表 2.7.6.2- 12に示した。算出における詳細は SAP version 1.0 に示した。

肺血流スコアは両投与群で同様であった。また、3、6 又は 12 ヵ月の予定投与期間のコホート間で肺血流スコアに大きな差はみられなかった（5.3.5.1.2 A53042/Table 14.1/121）。

表 2.7.6.2- 12 index イベント（PE）の肺血流スコア（ITT 解析対象集団）

	リバーロキサバン群 N=2419（100%）	エノキサパリン／VKA 群 N=2413（100%）
肺血流スコア		
N	2298	2299
平均値	0.81	0.81
標準偏差	0.12	0.12
最低値	0.2	0.1
最大値	1.0	1.0
0.75 点で区分		
＜0.75 点	597（ 24.7%）	576（ 23.9%）
≧0.75 点	1701（ 70.3%）	1723（ 71.4%）

ITT：intention-to-treat、 VKA：ビタミン K 拮抗薬
肺血流スコア評価は 0 点が全肺野で肺血流が欠損、1 点がすべてに欠損がないを意味する。
引用元: 5.3.5.1.2 A53042/Table 14.1/120

index イベント（PE）は、治験責任（分担）医師により報告された血栓塞栓症の危険因子により、原発性又は二次性 PE に分類された。下記の少なくとも一つの危険因子が治験責任（分担）医師により特定されれば、二次性 PE に分類し、これら以外の場合は原発性 PE と考えた。

- 最近の手術又は外傷
- 活動性の制限
- エストロゲン含有医薬品の使用
- 活動性悪性腫瘍
- 産褥

index イベント（PE）が原発性 PE とされた被験者の割合は、リバーロキサバン群では 64.7%、エノキサパリン／VKA 群では 64.3%であり、二次性 PE とされた被験者の割合はそれぞれ 35.3%、35.7%であった（表 2.7.6.2- 13）。

表 2.7.6.2- 13 index イベント（PE）の分類（ITT 解析対象集団）

	リバーロキサバン N＝2419（100%）	エノキサパリン／VKA N＝2413（100%）
原発性 PE	1566（ 64.7%）	1551（ 64.3%）
二次性 PE	853（ 35.3%）	862（ 35.7%）
最近の手術又は外傷	415（ 17.2%）	398（ 16.5%）
活動性の制限	384（ 15.9%）	380（ 15.7%）
エストロゲン含有医薬品の使用	207（ 8.6%）	223（ 9.2%）
活動性悪性腫瘍	114（ 4.7%）	109（ 4.5%）
産褥	6（ 0.2%）	5（ 0.2%）

ITT：intention-to-treat、VKA：ビタミン K 拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症
被験者は 2 つ以上の二次性 PE の危険因子を有する可能性がある。
引用元：5.3.5.1.2 A53042/Table 14.1/47

index イベント（PE）発現から無作為割り付けまでの期間：

ITT 解析対象集団における、index イベント（PE）兆候発現から無作為割り付けまでの期間の中央値（四分位範囲）はリバーロキサバン群で 4 日（2～8 日）、エノキサパリン／VKA 群で 4 日（2～9 日）であった（5.3.5.1.2 A53042/Table 14.1/102）。PP 解析対象集団においても同様であった（5.3.5.1.2 A53042/Table 14.1/108）。

また、予定投与期間別、又はベースライン時の活動性悪性腫瘍の有無別においても両投与群間で大きな差はなかった（5.3.5.1.2 A53042/Table 14.1/103、Table 14.1/104）。

2.7.6.2.2.1.6 病歴

被験者の病歴はリバーロキサバン群で 96.4%、エノキサパリン／VKA 群で 95.4%で報告された（5.3.5.1.2 A53042/Table 14.1/213）。器官別大分類別で報告が多かった病歴は血管障害（リバーロキサバン群：49.9%、エノキサパリン／VKA 群：47.0%）、外科および内科処置（42.5%、43.8%）、代謝および栄養障害（43.5%、41.6%）であった。おおむね病歴については両投与群間で差は認められず、典型的な PE 患者であった。心臓障害（20.4%、18.7%）、免疫系障害（10.3%、8.8%）において数値上わずかな差が認められた。PP 解析対象集団においても大きな差は認められなかった（5.3.5.1.2 A53042/Table 14.1/219）。

予定投与期間が 3 ヵ月のコホートにおける器官別大分類別の病歴は、全体より低い傾向がみられ、特に血管障害は両投与群共に 36%と低かった（5.3.5.1.2 A53042/Table 14.1/214）。予定投与期間が 12 ヵ月のコホートでは全体より血管障害の保有割合が高く、リバーロキサバン群で 59.0%、エノキサパリン／VKA 群で 52.2%であった。予想どおり、いくつかの合併症の保有割合はベースライン時に活動性悪性腫瘍のなかった被験者に比べ悪性腫瘍を有した被験者で高かった（5.3.5.1.2 A53042/Table 14.1/215）。

2.7.6.2.2.1.7 前治療薬及び併用薬

無作為割り付け日以前に投与された薬剤を前治療薬とみなした。治験実施計画書に従い、無作為割り付け前に LMWH を含む抗凝固薬療法（48 時間まで）が認められた（5.3.5.1.2 A53042/16.1.1）。リバーロキサバン群の 81.2%の被験者では無作為割り付け前の LMWH、未分画ヘパリン又はフォンダパリヌクスによる初期治療総期間が 2 日以内で、7.5%の被験者ではそれらによる初期治療を受けていなかった（5.3.5.1.2 A53042/Table 14.2/5）。60%を超える被験者（リバーロキサバン群：67.4%、エノキサパリン／VKA 群：66.7%）が心血管疾患治療のために併用薬の投与を受けていた。鎮痛薬を併用していた被験者の割合はリバーロキサバン群で 63.5%、エノキサパリン／VKA 群で 62.9%であった（5.3.5.1.2 A53042/Table 14.1/184）。総じて、併用薬のプロファイルには試験対象集団の合併症と整合性が認められた。

抗血栓薬を含む併用薬については投与開始・中止時刻が記録されていない。抗血栓薬の投与が治験薬投与開始日に中止された場合、あるいは治験薬投与終了日に開始された場合、併用とみなした。

安全性解析対象集団での無作為割り付けから治験薬投与終了日までの抗血栓薬（治験薬を除く）使用割合は、リバーロキサバン群で 30.6%、エノキサパリン／VKA 群で 36.1%であった（5.3.5.1.2 A53042/Table 14.1/178）。使用頻度の高い薬剤は、アセチルサリチル酸（リバーロキサバン群：14.4%、エノキサパリン／VKA 群：13.3%）、エノキサパリン（8.2%、

14.4%）及びワルファリン（4.5%、3.6%）であった。抗凝固薬は有害事象への対処又は予定手術・処置へのつなぎのため併用されたと推察された。エノキサパリン又は VKA を併用薬と治験薬のいずれに分類するかは治験責任（分担）医師が行なった分類に従った。

抗血栓薬（治験薬を除く）の使用割合は、予定投与期間が 3 ヵ月又は 6 ヵ月のコホートに比べ 12 ヵ月のコホートで高かった（3、6、12 ヵ月それぞれ、30.0%、30.3%、38.5%）（5.3.5.1.2 A53042/Table 14.1/179）。また、抗血栓薬（治験薬を除く）の使用割合はベースライン時に活動性悪性腫瘍を有した被験者で高い傾向が認められた（リバーロキサバン群：34.2%、エノキサパリン／VKA 群：41.3%）（5.3.5.1.2 A53042/Table 14.1/180）。

詳細は 5.3.5.1.2 A53042/Section 8.7.2 に示す。また、治験総括報告書作成後の併用薬に関する事後解析は 5.3.5.1.6/PH-36705 に、抗凝固薬については 5.3.5.1.7/PH-36706 に示す。

2.7.6.2.2.1.8 服薬状況

2.7.6.2.2.1.8.1 服薬期間

試験デザインがイベント主導型であったため、既に試験に組み入れられた被験者内で有効性主要評価項目の目標イベント発現数に達する見込みを得た時点で被験者の組み入れを終了した。その後、予定投与期間が 3 ヵ月のコホートは 3 ヵ月に達するまで、6 又は 12 ヵ月のコホートは 6 ヵ月に達するまで治験薬を投与することとした。その結果、予定投与期間 12 ヵ月のコホートが治験依頼者による試験終了の影響を受け、投与を完了した被験者は 3 ヵ月のコホート（86.7%）、6 ヵ月のコホート（88.0%）と比べ、12 ヵ月のコホート（71.6%）で低かった（5.3.5.1.2 A53042/Table 14.1/9）。

実際の服薬期間を表 2.7.6.2- 14に示す。安全性解析対象集団において、実際の服薬期間は、約 92%の被験者が 3 ヵ月以上、約 72%が 6 ヵ月以上、約 4%が 12 ヵ月以上であった。この実際の服薬期間に関する解析において、1 ヵ月は 30 日間で計算したため 12 ヵ月以上は 360 日間以上と規定した。一方、治験薬投与の完了・未完了の判断基準はこれとは異なり、12 ヵ月の場合は 352 日間以上治験薬投与を受けた被験者を完了と判断した。実際の服薬期間の平均値はリバーロキサバン群が 216.9 日間、エノキサパリン／VKA 群が 214.9 日間であった。両投与群の服薬期間は同程度であった。

表 2.7.6.2- 14　実際の服薬期間（安全性解析対象集団）

		リバーロキサバン N=2412（100%）	エノキサパリン／VKA N=2405（100%）
服薬期間（区分）	＜1 週間	51 （ 2.1%）	30 （ 1.2%）
	1 週間～＜1 ヵ月間	74 （ 3.1%）	87 （ 3.6%）
	1 ヵ月間～＜3 ヵ月間	49 （ 2.0%）	75 （ 3.1%）
	3 ヵ月間～＜6 ヵ月間	459 （ 19.0%）	531 （ 22.1%）
	6 ヵ月間～＜9 ヵ月間	1075 （ 44.6%）	993 （ 41.3%）
	9 ヵ月間～＜12 ヵ月間	609 （ 25.2%）	606 （ 25.2%）
	≧12 ヵ月間	95 （ 3.9%）	83 （ 3.5%）
服薬期間（日）	欠測	0	0
	中央値（IQR）	183（179～352）	182（178～351）
	平均値±SD	216.9±99.1	214.9±99.1
	範囲	1～403	1～385

IQR：四分位範囲、SD：標準偏差、VKA：ビタミン K 拮抗薬
30 日間を 1 ヵ月とした。
服薬期間（日）の計算は、日付が判明している場合、治験薬投与終了日－初回投与日＋1 とした。
治験薬の投与終了日が不明の場合、補完を行なった：治験総括報告書の SAP 補遺を参照。
引用元： 5.3.5.1.2 A53042/Table 14.2/46

2.7.6.2.2.1.8.2　服薬コンプライアンス

リバーロキサバン群については、予定投与スケジュールでの服薬率は、実際に使用された錠数を治験薬の初回処方から投与終了日までの期間における予定服薬錠数（中止した場合も含む）で除して算出した。ITT 解析対象集団において、リバーロキサバン群の全服薬率が 80%以上の被験者の割合は 94.2%であった（表 2.7.6.2- 15）。

表 2.7.6.2- 15　服薬率（リバーロキサバン群）

		ITT 解析対象集団 N＝2419 （100%）	PP 解析対象集団 N＝2224 （100%）
全服薬率	治験薬の投与なし	7 （ 0.3%）	0
	欠測	24 （ 1.0%）	0
	＜50%	31 （ 1.3%）	4 （ 0.2%）
	50～＜80%	78 （ 3.2%）	8 （ 0.4%）
	≧80%	2279 （ 94.2%）	2212 （ 99.5%）
服薬率：15mg 1 日 2 回投与期間（最初の 3 週間）	治験薬の投与なし	7 （ 0.3%）	0
	該当期間に治験薬投与なし	0	0
	欠測	19 （ 0.8%）	11 （ 0.5%）
	＜50%	78 （ 3.2%）	38 （ 1.7%）
	50～＜80%	49 （ 2.0%）	43 （ 1.9%）
	≧80%	2266 （ 93.7%）	2132 （ 95.9%）
服薬率：20mg 1 日 1 回投与期間（3、6 及び 12 ヵ月の予定投与期間終了まで）	治験薬の投与なし	7 （ 0.3%）	0
	該当期間に治験薬投与なし	110 （ 4.5%）	85 （ 3.8%）
	欠測	29 （ 1.2%）	14 （ 0.6%）
	＜50%	43 （ 1.8%）	2 （ ＜0.1%）
	50～＜80%	61 （ 2.5%）	20 （ 0.9%）
	≧80%	2169 （ 89.7%）	2103 （ 94.6%）

ITT：intention-to-treat、PP：治験実施計画書に適合した
服薬率は、実際に使用された錠数を投与期間ごとに治験薬の初回処方から投与終了日までの期間における予定服薬錠数で除して算出した。
誤投与又は部分的に治験薬投与中断があった場合、全服薬率は中止日とみなした日を基に算出したが、投与期間ごとの服薬率は算出しなかった。
引用元：5.3.5.1.2 A53042/Table 14.2/73、Table 14.2/75、Table 14.2/76、Table 14.2/78、Table 14.2/79、Table 14.2/81

エノキサパリン／VKA 群では、全服薬率が 80%以上の被験者の割合は ITT 解析対象集団では 92.3%、PP 解析対象集団では 97.5%であった（表 2.7.6.2- 16）。

表 2.7.6.2- 16　服薬率（エノキサパリン／VKA 群）

		ITT 解析対象集団 N＝2413 (100%)	PP 解析対象集団 N＝2238 (100%)
全服薬率	治験薬の投与なし	8 (0.3%)	0
	欠測	0	0
	＜50%	64 (2.7%)	35 (1.6%)
	50～＜80%	115 (4.8%)	20 (0.9%)
	≧80%	2226 (92.3%)	2183 (97.5%)
服薬率：エノキサパリン投与（治験実施計画書に従い、少なくとも 5 日間）	治験薬の投与なし	8 (0.3%)	0
	該当期間に治験薬投与なし	31 (1.3%)	28 (1.3%)
	欠測	0	0
	＜50%	24 (1.0%)	10 (0.4%)
	50～＜80%	20 (0.8%)	12 (0.5%)
	≧80%	2330 (96.6%)	2188 (97.8%)
服薬率：VKA 投与（3、6 及び 12 ヵ月間の予定投与期間中の PT-INR の測定頻度 ）	治験薬の投与なし	8 (0.3%)	0
	該当期間に治験薬投与なし	11 (0.5%)	9 (0.4%)
	欠測	18 (0.7%)	17 (0.8%)
	＜50%	15 (0.6%)	1 (＜0.1%)
	50～＜80%	99 (4.1%)	6 (0.3%)
	≧80%	2262 (93.7%)	2205 (98.5%)

ITT：intention-to-treat、PP：治験実施計画書に適合した、VKA ：ビタミン K 拮抗薬、PT-INR：プロトロンビン時間国際標準比

服薬率は下記を基に算出した。エノキサパリン投与期間が 4 日以上（5 日間の 80%以上）の被験者及びエノキサパリン投与期間が 4 日未満でも PT-INR が目標範囲内の被験者は初期のエノキサパリン投与の服薬コンプライアンスは良好と取り扱った。39 日の 80%の治験薬投与期間中に少なくとも PT-INR を 1 回測定している場合は VKA 投与の服薬コンプライアンスは良好とした。これらの期間は 1 週間重複した。

無作為割り付け前に低分子量ヘパリン/未分画ヘパリン/フォンダパリヌクスの治療を受けたがエノキサパリンの初期投与なしの被験者は「この期間中（例えば、エノキサパリン投与期間）は治験薬投与なし」として表に含んだ。VKA 投与期間中に PT-INR 測定をしなかった被験者の VKA 期間の服薬率は「欠測」として取り扱った。

引用元：5.3.5.1.2 A53042/Table 14.2/73、Table 14.2/75、Table 14.2/76、Table 14.2/78、Table 14.2/79、Table 14.2/81

2.7.6.2.2.1.8.3　PT-INR が目標範囲内に達するまでの期間

エノキサパリン／VKA 群において、VKA 投与期間中（初期の VKA 投与期間から初期の LMWH 併用投与の中止を経て VKA の投与終了まで）における PT-INR の目標範囲である 2.0～3.0 の達成度を評価した。

PT-INR が目標範囲の下限（PT-INR が 2.0）以上に達するまでの期間及び初期の LWMH 投与中止時の PT-INR を表 2.7.6.2- 17に示す。PT-INR が目標範囲に達するまでの期間は、エノキサパリン／ワルファリン群では 8.9 日、エノキサパリン／acenocoumarol 群では 5.4 日、対照群全体では 8.2 日であった。初期の LMWH 投与中止の時点において、PT-INR が目標範囲内（2.0～3.0）にあった被験者は 63.4%、2.0 を下回っていたのは 15.4%、3.0 を上回っていたのは 19.4%であった。1.8%の被験者においては、初期のエノキサパリン投与期の PT-INR 測定結果を得られなかった。

表 2.7.6.2- 17　PT-INR が目標範囲の下限（PT-INR が 2）以上に達するまでの期間及び初期の LWMH 投与中止時の PT-INR（安全性解析対象集団）

	エノキサパリン／ワルファリン (N＝1939)	エノキサパリン／acenocoumarol (N＝455)	合計 (N＝2394)
PT-INR が目標範囲の下限以上（PT-INR≧2）に達するまでの期間（無作為割り付けからの日数）			
N	1903	450	2353
欠測	36	5	41
平均値	8.9	5.4	8.2
SD	11.8	4.9	10.9
最小値	1	1	1
Q1	5.0	3.0	4.0
中央値	6.0	4.0	6.0
Q3	9.0	6.0	9.0
最大値	194	52	194
初期の LWMH 投与中止時の PT-INR			
N	1939 (100.0%)	455 (100.0%)	2394 (100.0%)
初期の LMWH 未投与	0	1 (0.2%)	1 (＜0.1%)
初期の LMWH 投与時に PT-INR 未測定	22 (1.1%)	22 (4.8%)	44 (1.8%)
＜2.0（欠測値なし）	326 (16.8%)	42 (9.2%)	368 (15.4%)
2.0～3.0	1287 (66.4%)	230 (50.5%)	1517 (63.4%)
＞3.0	304 (15.7%)	160 (35.2%)	464 (19.4%)

LMWH：低分子量ヘパリン、PT-INR：プロトロンビン時間国際標準比、SD：標準偏差、Q1：第一四分位、Q3：第三四分位
値は実測及び推定（すなわち、線形補間）された PT-INR を基にした。
引用元：5.3.5.1.2 A53042/Table 14.2/420

2.7.6.2.2.1.8.4　　PT-INR が目標範囲内であった期間割合（TTR）

VKA 投与期間中に被験者の PT-INR が目標範囲内（2.0～3.0）であった期間割合（TTR）を調整の有無別に表 2.7.6.2- 18及び表 2.7.6.2- 19に示す。調整 TTR は未調整 TTR から以下の期間を除外したため、より妥当な評価と考えられた。

- 治験責任（分担）医師による意図的な VKA 投与中断期間（CIAC 判定による）、及び VKA 投与再開後の 8 日間
- 別の抗凝固薬を追加使用した期間〔ヘパリン、フォンダパリヌクスナトリウム（フォンダパリヌクス）、その他の VKA〕
- 有効性主要評価項目又は「重大な出血事象」報告後の期間

調整 TTR の評価に関しては、心房細動患者における虚血性脳卒中の発症抑制を目的とし、偽の PT-INR を用いて検討した最近の二重盲検試験[1,2]と同様の方法を採用した。

調整 PT-INR の算出には、最終 PT-INR 観察値を投与 16 日後まで外挿した（上述の除外期間を含めない）。除外日及び PT-INR が得られない場合（実測値又は補完値）は計算に入れなかった（曝露期間から除外した）。薬剤（VKA 又は追加の抗凝固薬）は投与開始日及び終了日当日も服用したと考えた。報告された投与終了日以降に投与期間の範囲とされる期間は含めなかった（投与終了後 2 日目まで投与範囲とみなすなどは行わなかった）。

未調整 TTR、調整 TTR はそれぞれ、最初の 1 ヵ月間では 54.6%（週平均値の範囲：52.1%～57.8%）、56.6%（週平均値の範囲：53.4%～59.2%）、以降の 11 ヵ月間での月平均値の範囲は 60.0%～69.5%、61.2%～70.6%で、全体で 60%以上であった。全 VKA 投与期間の未調整 TTR、調整 TTR はそれぞれ 59.9%、62.7%であった。

予定投与期間が 3 ヵ月のコホートにおける全体の TTR（全 VKA 投与期間の未調整 TTR：52.2%、調整 TTR：56.8%）は、6 ヵ月のコホート（58.8%、61.7%）及び 12 ヵ月のコホート（62.6%、65.0%）より低く、投与期間が長くなるのに伴い被験者の TTR は上昇することが示された（5.3.5.1.2 A53042/Table 14.2/426、Table 14.2/442）。

表 2.7.6.2- 18　PT-INR が目標範囲内であった期間割合（未調整 TTR、ITT on treatment 解析対象集団、エノキサパリン／VKA 群　N＝2394）

VKA 投与期間	エノキサパリン／VKA 群 (平均)	VKA 投与期間	エノキサパリン／VKA 群 (平均)
1 週目	55.3%	1 ヵ月目	54.6%
2 週目	52.1%	2 ヵ月目	60.0%
3 週目	56.2%	3 ヵ月目	61.8%
4 週目	57.8%	4 ヵ月目	66.0%
		5 ヵ月目	66.1%
		6 ヵ月目	64.1%
		7 ヵ月目	62.9%
		8 ヵ月目	66.3%
		9 ヵ月目	68.1%
		10 ヵ月目	68.0%
		11 ヵ月目	69.5%
		12 ヵ月目	67.3%
		VKA 投与期間全体	59.9%

PT-INR：プロトロンビン時間国際標準比、ITT：intention-to-treat 、VKA ：ビタミン K 拮抗薬
VKA 投与期間は、VKA の投与開始後及び最初のエノキサパリン投与中止後から VKA の投与終了までの期間とした。
実測及び推定（全実測値による線形補間）された未調整の PT-INR を基に目標範囲内であった期間を示した。安全性解析対象集団は ITT on treatment 解析対象集団と同一である。
引用元：5.3.5.1.2 A53042/Table 14.2/425

表 2.7.6.2- 19 PT-INR が目標範囲内であった期間割合（調整 TTR、ITT on treatment 解析対象集団、エノキサパリン／VKA 群 N＝2394）

VKA 投与期間	エノキサパリン／VKA 群 (平均)	VKA 投与期間	エノキサパリン／VKA 群 (平均)
1 週目	57.4%	1 ヵ月目	56.6%
2 週目	53.4%	2 ヵ月目	61.2%
3 週目	57.8%	3 ヵ月目	63.0%
4 週目	59.2%	4 ヵ月目	67.0%
		5 ヵ月目	67.1%
		6 ヵ月目	68.3%
		7 ヵ月目	66.4%
		8 ヵ月目	67.3%
		9 ヵ月目	68.8%
		10 ヵ月目	69.0%
		11 ヵ月目	70.6%
		12 ヵ月目	68.8%
		VKA 投与期間全体	62.7%

PT-INR：プロトロンビン時間国際標準比、ITT：intention-to-treat 、VKA ：ビタミン K 拮抗薬
VKA 投与期間は、予定投与期間中の VKA の投与開始後及び最初のエノキサパリンの投与中止後から VKA の投与終了までの期間とした。
下記に該当するものを除き、VKA 投与期間中に実測及び推定（線形補間、最終観察の繰り越し）された PT-INR を基に目標範囲内であった期間を示した。
- 治験責任（分担）医師による意図的な VKA 投与中断期間（CIAC 判定による）及び VKA 投与再開後の 8 日間
- ヘパリン、フォンダパリヌクス及びその他の VKA を含む抗凝固薬を追加投与した期間
- 有効性主要評価項目又は「重大な出血事象」の報告後の期間

引用元：5.3.5.1.2 A53042/Table 14.2/441

調整 TTR は、ベースライン時に活動性悪性腫瘍を有した被験者（全期間で 57.9%）で活動性悪性腫瘍を有さなかった被験者（全期間で 62.9％）よりも低かった。（5.3.5.1.2 A53042/Table 14.2/443）。

2.7.6.2.2.1.9 用量確認解析

無作為に割り付けられた最初の被験者 400 例（リバーロキサバン群：205 例、エノキサパリン／VKA 群：195 例）を対象に用量確認解析を実施した（5.3.5.1.2 A53042/16.1.9.1）。ベースライン時とその後の肺スキャン測定を両方行なっていたのは 379 例であった。そのうち 18 例が再検査後 2 週間以内に抗凝固薬を変更した（リバーロキサバン群：4 例、エノキサパリン／VKA 群：14 例）。解析結果に基づき、独立用量確認委員会は事前に仮定したバイアス（臨床的所見ではなく、治験実施計画書に規定した肺血流スキャンの再検査結果によって、抗凝固薬が変更される）が認められるかについて評価を行った。データからは抗凝固薬の変更と肺画像の再検査との関連は認められず、医学的な理由（有害事象や PT-INR が目標範囲を下回ったための治療）に基づいて変更されたことが示された。

投与開始 3 週間後に肺画像検査を受けた被験者及び計画された 3 週間後の肺画像再検査前に症候性 VTE を発現した被験者について、「症候性 VTE の発症」又は「無症候性の血栓像の悪化」の複合エンドポイントの発現頻度を、リバーロキサバン群とエノキサパリン／VKA 群の被験者間で比較した。発現頻度は、リバーロキサバン群で 3/177 例（1.7%）、エノキサパリン／VKA 群で

1/174 例（0.6%）であった。正確な方法を用いて算出した発現頻度の実測値間の絶対差における片側 95%信頼区間の上限は 3.7%であり、事前に設定した 8.0%を上回らなかった。

独立用量確認委員会は、治験実施状況の変更は不要であり、計画どおり試験を継続するよう勧告した。

2.7.6.2.2.2　有効性の結果

2.7.6.2.2.2.1　有効性主要評価項目

2.7.6.2.2.2.1.1　有効性の主要解析

有効性主要評価項目の複合エンドポイントのイベント数が 84 件報告された時点で、目標の 88 件までの残る 4 件のイベントは既に試験に組み入れられた被験者内で達すると判断し、被験者の組み入れを中止した。組み入れを中止した時点では、追加のイベントは得られておらず、追加のイベントはその後に発現した。最終的なイベント数は 94 件であった。

ITT 解析対象集団における、予定投与期間終了時までの有効性主要評価項目である症候性 VTE〔「症候性 DVT」又は「症候性 PE（非致死的又は致死的 PE）」の複合エンドポイント（ただし PE の可能性が否定できない原因不明の死亡を含む）〕のイベント発現頻度は、リバーロキサバン群で 2.1%（50/2,419 例）、エノキサパリン／VKA 群は 1.8%（44/2,413 例）であった（表 2.7.6.2- 20）。

有効性主要評価項目の各構成要素について、ITT 解析対象集団における予定投与期間終了時までの発現頻度を以下に示す。

- PE による死亡：リバーロキサバン群で 0.1%（3/2,419 例）、エノキサパリン／VKA 群で 0.1%未満（1/2,413 例）
- 死亡理由として PE の可能性が否定できない死亡：リバーロキサバン群で 0.3%（8/2,419 例）、エノキサパリン／VKA 群で 0.2%（6/2,413 例）
- 症候性 PE 及び DVT： リバーロキサバン群で 0%、エノキサパリン／VKA 群で 0.1%未満（2/2,413 例）
- 症候性 PE のみ：リバーロキサバン群で 1.0%（23/2,419 例）、エノキサパリン／VKA 群で 0.8%（20/2,413 例）
- 症候性 DVT のみ：リバーロキサバン群で 0.7%（18/2,419 例）、エノキサパリン／VKA 群で 0.7%（17/2,413 例）

表 2.7.6.2- 20　予定投与期間終了までに発現した有効性評価項目の発現頻度（ITT 解析対象集団）

評価項目／構成要素	リバーロキサバン N=2419 (100%)	エノキサパリン／VKA N=2413 (100%)	Cox 比例ハザードモデル [a] ハザード比	95%信頼区間
有効性主要評価項目（事前に規定）	50　(2.1%)	44　(1.8%)	1.123 (p=0.0026) [b] (p=0.5737) [c]	0.749～1.684
死亡（PE）	3　(0.1%)	1（＜0.1%）		
死亡（PE の可能性が否定できない）	8　(0.3%)	6　(0.2%)		
症候性 PE 及び DVT	0	2（＜0.1%）		
症候性 PE のみ	23　(1.0%)	20　(0.8%)		
症候性 DVT のみ	18　(0.7%)	17　(0.7%)		
有効性主要評価項目（抗血栓療法の変更のみで確認したイベントを除く）（事前に規定）	46　(1.9%)	41　(1.7%)	1.108 (p=0.0030) [b] (p=0.6321) [c]	0.728～1.688
死亡（PE）	3　(0.1%)	1（＜0.1%）		
死亡（PE の可能性が否定できない）	8　(0.3%)	6 (0.2%)		
症候性 PE 及び DVT	0	2（＜0.1%）		
症候性 PE のみ	18　(0.7%)	17　(0.7%)		
症候性 DVT のみ	18　(0.7%)	17　(0.7%)		
有効性副次的評価項目（事前に規定）	97　(4.0%)	82　(3.4%)	1.156 (p=0.3333) [d]	0.862～1.552
死亡（PE）	3　(0.1%)	1（＜0.1%）		
死亡（PE の可能性が否定できない）	8　(0.3%)	6　(0.2%)		
死亡（出血事象）	5　(0.2%)	4　(0.2%)		
死亡（心血管死）	10　(0.4%)	3　(0.1%)		
死亡（その他）	32　(1.3%)	36　(1.5%)		
症候性 PE 及び DVT	0	2（＜0.1%）		
症候性 PE のみ	23　(1.0%)	20　(0.8%)		
症候性 DVT のみ	18　(0.7%)	17　(0.7%)		
総合有用性評価指標－1（事前に規定）	83　(3.4%)	96　(4.0%)	0.849 (p=0.2752) [d]	0.633～1.139
死亡（PE）	3　(0.1%)	1（＜0.1%）		
死亡（PE の可能性が否定できない）	8　(0.3%)	6　(0.2%)		
症候性 PE 及び DVT	0	2（＜0.1%）		
症候性 PE のみ	23　(1.0%)	20　(0.8%)		
症候性 DVT のみ	18　(0.7%)	17　(0.7%)		
重大な出血事象	33　(1.4%)	57　(2.4%)		

表 2.7.6.2- 20　予定投与期間終了までに発現した有効性評価項目の発現頻度（ITT 解析対象集団）（続き）

評価項目／構成要素	リバーロキサバン N=2419 (100%)	エノキサパリン／VKA N=2413 (100%)	Cox 比例ハザードモデル [a] ハザード比	95% 信頼区間
総合有用性評価指標－2（追加解析）	110　(4.5%)	115　(4.8%)	0.940 (p=0.6430) [d]	0.724～1.221
死亡（PE）	3　(0.1%)	1　(＜0.1%)		
死亡（PE の可能性が否定できない）	8　(0.3%)	6　(0.2%)		
死亡（心血管死）	10　(0.4%)	3　(0.1%)		
症候性 PE 及び DVT	0	2　(＜0.1%)		
症候性 PE のみ	23　(1.0%)	20　(0.8%)		
症候性 DVT のみ	18　(0.7%)	17　(0.7%)		
重大な出血事象	33　(1.4%)	57　(2.4%)		
STEMI	5　(0.2%)	2　(＜0.1%)		
NSTEMI	2　(＜0.1%)	11　(0.5%)		
虚血性脳卒中	11　(0.5%)	7　(0.3%)		
非中枢神経系塞栓症	6　(0.2%)	3　(0.1%)		

DVT：深部静脈血栓症、ITT：intention-to-treat、(N)STEMI：（非）ST 上昇型心筋梗塞、PE：肺塞栓症、VKA：ビタミン K 拮抗薬
発現頻度＝無作為割り付けから予定投与期間終了までにイベント発現が報告された被験者数÷該当集団の被験者数。同じ被験者に複数回のイベントが発現した場合、その被験者は複数の構成要素の対象として集計されたため、各構成要素の合計と複合エンドポイントの数が一致しない場合がある。
a：予定投与期間で層別しベースライン時の悪性腫瘍で調整（予定治療期間終了まで）
b：非劣性に関する p 値（片側）
c：優越性に関する p 値（両側）
d：名目上の p 値、多重性の調整は行わなかった。
引用元：5.3.5.1.2 A53042/Table 14.2/128、Table 14.2/361、Table 14.2/363、Table 14.2/364、Table 14.2/365、Table 14.2/366

有効性の主要解析は、予定投与期間終了までの有効性主要評価項目に対して、予定投与期間で層別化し、ベースライン時の活動性悪性腫瘍の有無で調整した Cox 比例ハザードモデルを用いた。リバーロキサバン群とエノキサパリン／VKA 群の比較では、ハザード比 1.123（95% 信頼区間：0.749～1.684）であった。信頼区間の上限が予め規定していた非劣性マージンの 2.0 を下回っており、非劣性の片側検定の p 値が 0.0026 であったことから、リバーロキサバンはエノキサパリン／VKA に対し非劣性であることが検証された。リバーロキサバンの優越性検定では、統計的有意差はみられなかった（p＝0.5737）（表 2.7.6.2- 20）。

有効性の主要解析に加え、ITT on treatment 解析対象集団の解析も実施した。ITT on treatment 解析対象集団における有効性主要評価項目の発現頻度は、リバーロキサバン群で 1.8%（44/2,412 例）、エノキサパリン／VKA 群で 1.6%（39/2,405 例）であった。層別 Cox 比例ハザードモデルによる有効性主要評価項目のハザード比は 1.115（95%信頼区間：0.725～1.717、p＝0.0040）であった（表 2.7.6.2- 21）。

PP 解析対象集団における有効性主要評価項目の発現頻度は、リバーロキサバン群で 1.7%（38/2,224 例）、エノキサパリン／VKA 群で 1.6%（36/2,238 例）であった。層別 Cox 比例ハ

ザードモデルによる有効性主要評価項目のハザード比は 1.045（95%信頼区間：0.662～1.648、p＝0.0026）であった（表 2.7.6.2- 21）。

表 2.7.6.2- 21　有効性主要評価項目の概要

解析対象集団	ITT	ITT on treatment	PP
有効性主要評価項目の発現頻度			
リバーロキサバン	50 / 2419 (2.1%)	44 / 2412 (1.8%)	38 / 2224 (1.7%)
エノキサパリン／VKA	44 / 2413 (1.8%)	39 / 2405 (1.6%)	36 / 2238 (1.6%)
Cox 比例ハザードモデルを用いた解析：リバーロキサバン vs エノキサパリン／VKA			
ハザード比	1.123	1.115	1.045
95%信頼区間	0.749～1.684	0.725～1.717	0.662～1.648
非劣性に関する p 値	0.0026	0.0040	0.0026
優越性に関する p 値	0.5737	0.6194	0.8504

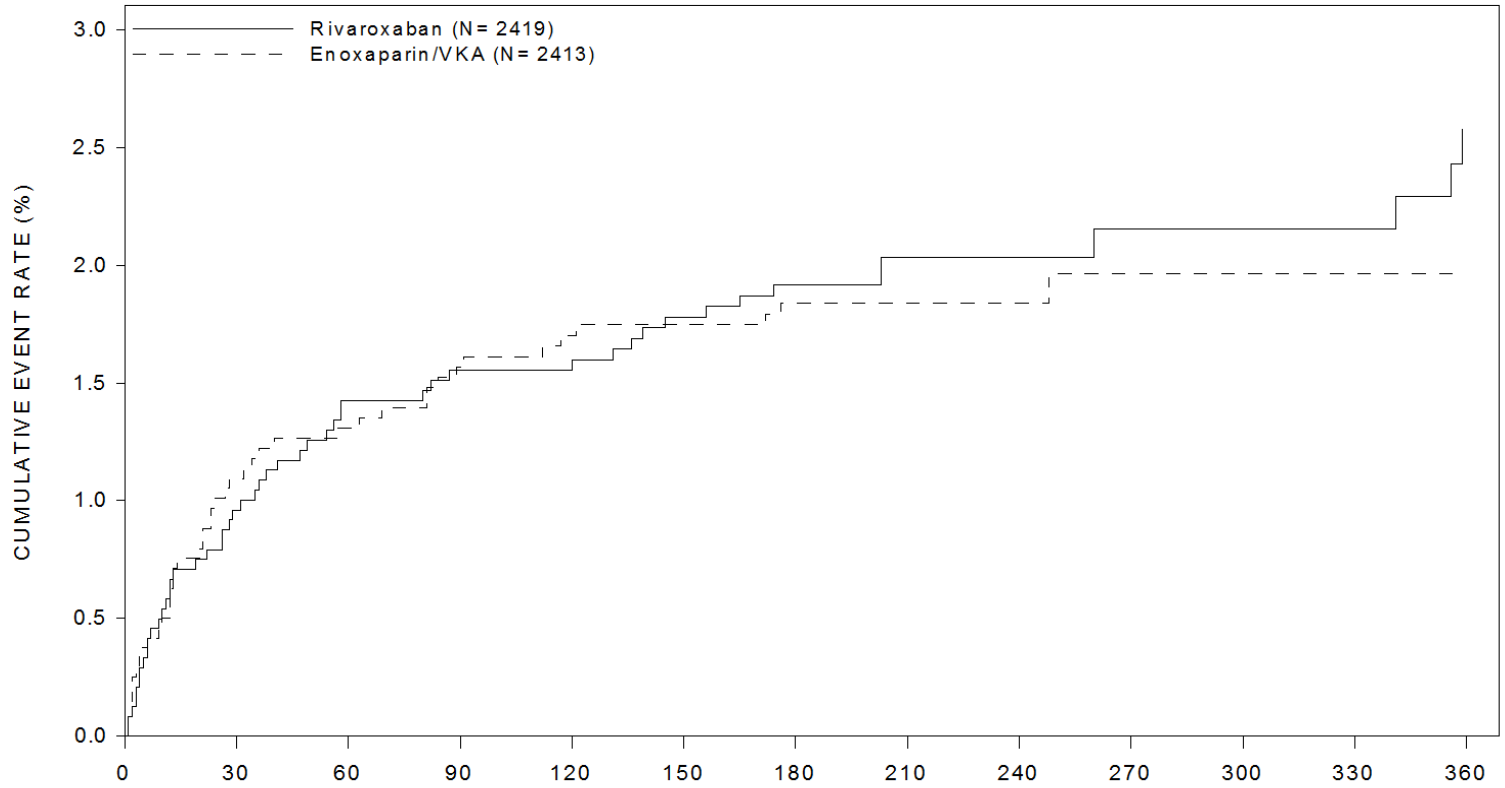
ITT：intention-to-treat、PP：治験実施計画書に適合した、VKA：ビタミン K 拮抗薬
P 値とハザード比の推定値は層別 Cox 比例ハザードモデルを用いて算出した。層調整には無作為割り付けから予定投与期間終了までのイベント（ITT 解析対象集団）又は治験薬初回投与後から治験薬投与終了後 2 日目までのイベント（ITT on treatment 解析対象集団及び PP 解析対象集団）を用いて算出した。エノキサパリン／VKA 群に対するリバーロキサバン群の対数ハザード比の推定値、標準誤差及び非劣性マージン、2.0 の対数値に基づき、非劣性に関する漸近的片側 p 値を算出した。
引用元：5.3.5.1.2 A53042/Table 14.2/128、Table 14.2/137、Table 14.2/146、Table 14.2/361、Table 14.2/380、Table 14.2/388

感度分析として、予定投与期間が 12 ヵ月のコホートに組み入れられた被験者を含む、治験実施計画書に従い治験依頼者の決定によって治験薬投与を終了した被験者を対象に、管理上の打ち切りで補正した予定投与期間終了までの有効性主要評価のイベント発現を評価した。ITT 解析対象集団で、イベントを発現した被験者はリバーロキサバン群で 2.0%（49/2,419 例）、エノキサパリン／VKA 群で 1.8%（44/2,413 例）であり、層別 Cox 比例ハザードモデルによるハザード比は 1.101 であった〔95%信頼区間：0.733～1.654、p＝0.0020（5.3.5.1.2 A53042/Table 14.2/362）〕。

ITT 解析対象集団において、Kaplan-Meier 法による有効性主要評価項目の累積イベント発現率を投与群ごとに図 2.7.6.2- 3に示す。累積イベント発現率（ITT 解析対象集団）は、無作為割り付けから第 180 日前後までは投与群間で同様であった。それ以降は、リバーロキサバン群のほうがエノキサパリン／VKA 群より数値的に高かった。第 330 日以降は、リバーロキサバン群で更に 3 件の有効性主要評価項目のイベントが発現したのに対し、エノキサパリン／VKA 群では 1 件も発現しなかった（5.3.5.1.2 A53042/Table 14.2/167）。

PP 解析対象集団において、Kaplan-Meier 法による有効性主要評価項目の累積イベント発現率は ITT 解析対象集団の結果と類似していた（5.3.5.1.2 A53042/Table 14.2/173、Figure 14.2/13）。 リバーロキサバン群とエノキサパリン／VKA 群の両投与群で、投与初期の 1 ヵ月間に有効性主要評価項目の全イベントの約 50%が発現した。6 ヵ月目以降は有効性主要評価項目の発現はほとんど認められなかった（リバーロキサバン群で 5 件、エノキサパリン／VKA 群で 1

件）（5.3.5.1.2 A53042/Table 14.2/167）。この推移パターンは、過去の文献で、抗凝固療法を受けている急性PE患者について報告されているものと類似していた[3)]。



NUMBER OF SUBJECTS AT RISK

Rivaroxaban	N=2419	N=2350	N=2321	N=2303	N=2180	N=2167	N=2063	N=837	N=794	N=785	N=757	N=725	N=672
Enoxaparin/VKA	N=2413	N=2316	N=2295	N=2273	N=2155	N=2146	N=2050	N=835	N=787	N=772	N=746	N=722	N=675

算出時点：無作為割り付け後からイベント発現又は予定投与期間終了まで
引用元：5.3.5.1.2 A53042/Figure 14.2/1

図 2.7.6.2- 3　Kaplan-Meier 法による、有効性主要評価項目の累積イベント発現率（ITT 解析対象集団）

有効性主要評価項目の各構成要素の初回イベント発現頻度を下記の時期別に解析した。

- 0～3 ヵ月　　（無作為割り付けから第 98 日までにイベント発現）
- 3～6 ヵ月　　（第 99 日から第 185 日までにイベント発現）
- 6～12 ヵ月　　（第 186 日から第 359 日までにイベント発現）

大部分のイベントは 0～3 ヵ月の期間に発現した。3～6 ヵ月の期間の発現頻度は 0～3 ヵ月の期間よりおおむね低く、6～12 ヵ月の期間の発現頻度は両投与群でおおむね 3～6 ヵ月の期間より更に低かった（5.3.5.1.2 A53042/Table 14.2/110、Table 14.2/111、Table 14.2/112）。

0～3 ヵ月の期間に関して予定投与期間が 3 ヵ月のコホートにおいて検討したところ、有効性主要評価項目のイベントを発現した被験者数はエノキサパリン／VKA 群よりリバーロキサバン群が数値的に多かった〔リバーロキサバン群 4.7%（6/127 例）、エノキサパリン／VKA 群 1.6%（2/122 例）〕。一方、予定投与期間が 6 ヵ月のコホートでは、リバーロキサバン群のほうが少なく〔リバーロキサバン群 1.4%（20/1,387 例）、エノキサパリン／VKA 群 1.6%（22/1,387 例）〕、予定投与期間が 12 ヵ月のコホートにおいても同様であった〔リバーロキサバン群 1.2%（11/905 例）、エノキサパリン／VKA 群 1.5%（14/904 例）〕（5.3.5.1.2 A53042/Table 14.2/113）。

2.7.6.2.2.2.1.2　フォローアップ期間

治験薬投与終了後 2 日目から 30 日目までの期間の有効性主要評価項目の発現頻度は、リバーロキサバン群で 0.9%（20/2,211 例）、エノキサパリン／VKA 群で 0.7%（15/2,201 例）であった（5.3.5.1.2 A53042 Table 14.2/149）。

投与終了後 3 日目から 30 日目までのフォローアップ期間についての解析も総括報告書作成後に事後解析として実施した。この 3 日目からの解析における有効性主要評価項目の発現頻度は 2 日目からの解析結果と同様であった（表 2.7.6.2- 22）。

表 2.7.6.2- 22　投与終了後 3 日目から 30 日目までの期間における有効性主要評価項目及び各構成要素の発現頻度（ITT 解析対象集団、事後解析）

評価項目／構成要素	リバーロキサバン (N=2211)	エノキサパリン／VKA (N=2201)
有効性主要評価項目	20　(0.9%)	15　(0.7%)
死亡（PE）	2（＜0.1%）	0
死亡（PE の可能性が否定できない）	0	1（＜0.1%）
症候性 PE 及び DVT	2（＜0.1%）	0
症候性 PE のみ	12　(0.5%)	11　(0.5%)
症候性 DVT のみ	5　(0.2%)	3　(0.1%)

VKA：ビタミン K 拮抗薬
発現頻度＝イベント発現数/ 該当集団の被験者数
イベント発現数＝投与終了後 3 日目から 30 日目までにイベントが発現した被験者数
フォローアップ期間に移行した被験者とは、フォローアップ期間へ移行した旨を治験責任（分担）医師により eCRF に記載された被験者、又は投与終了後 3 日目から 30 日目までに複合エンドポイントの各構成要素であるイベントの発現が判定された被験者とする。
引用元：5.3.5.1.15/PH-36762/Table 1/6

2.7.6.2.2.2.2　有効性の副次的評価項目

有効性の副次的評価項目に関する正式な検定は規定しなかったため、有効性の副次的評価項目における投与群間の比較に関し、名目上のｐ値を記述的に示した。

ITT 解析対象集団における予定投与期間終了までの有効性副次的評価項目の発現頻度を表2.7.6.2- 20に示す。一人の被験者に 2 種類以上の有効性主要評価項目の構成要素イベントが発現した場合、その被験者はそれぞれの構成要素イベントの対象として集計された。したがって、各構成要素の被験者数の合計と複合エンドポイントの被験者数が一致しない場合がある。

有効性の副次的評価項目は、症候性 VTE〔「症候性 DVT」、「症候性 PE（非致死的）」〕又は全死亡の複合エンドポイントであった。予定投与期間終了までの有効性の副次的評価項目の発現頻度は、リバーロキサバン群で 4.0％（97/2,419 例）、エノキサパリン／VKA 群で 3.4％（82/2,413 例）であった。予定投与期間で層別し、ベースライン時の悪性腫瘍の有無で調整した Cox 比例ハザードモデルによる、予定投与期間終了までのリバーロキサバンとエノキサパリン／VKA のハザード比は 1.156（95%信頼区間：0.862～1.552、p＝0.3333）であった。

総合有用性評価指標－1 の評価項目は、有効性主要評価項目の各構成要素又は「重大な出血事象」の複合エンドポイントであった。予定投与期間終了までの総合有用性評価指標－1 の発現頻度は、リバーロキサバン群で 3.4％（83/2,419 例）、エノキサパリン／VKA 群で 4.0％（96/2,413 例）であった。Cox 比例ハザードモデルによるリバーロキサバン群とエノキサパリン／VKA 群のハザード比は 0.849（95%信頼区間：0.633～1.139、p＝0.2752）であった。

総合有用性評価指標－2 の評価項目（追加解析）は、有効性主要評価項目の各構成要素、「重大な出血事象」、心血管死、心筋梗塞、虚血性脳卒中又は非中枢神経系塞栓症の複合エンドポイントであった。予定投与期間終了までの総合有用性評価指標－2 の発現頻度は、リバーロキサバン群で 4.5％（110/2,419 例）、エノキサパリン／VKA 群で 4.8％（115/2,413 例）であった。Cox 比例ハザードモデルによるリバーロキサバン群とエノキサパリン／VKA 群のハザード比は 0.940（95%信頼区間：0.724～1.221、p＝0.6430）であった。

PP 解析対象集団及び ITT on treatment 解析対象集団において、有効性の副次的評価項目の発現頻度は ITT 解析対象集団の結果と同程度であることが示された（5.3.5.1.2 A53042/Table 14.2/143、Table 14.2/146）。

2.7.6.2.2.2.3　有効性主要評価項目の部分集団解析

有効性主要評価項目において、ベースライン及び人口統計学的因子による部分集団解析の結果を表 2.7.6.2- 23及び図 2.7.6.2- 4に示す。

有効性主要評価項目の部分集団解析結果は集団全体の結果とおおむね同様であった。有効性主要評価項目に関して、リバーロキサバン群に対するエノキサパリン／VKA 群のハザード比のほとんどは 1 を超えていたが、両側 95%信頼区間はハザード比 1 を含んでいた。

DVT 又は PE の既往：

DVT 又は PE の既往を有した被験者における有効性主要評価項目の発現頻度は、リバーロキサバン群〔1.5％（7/455 例）〕のほうがエノキサパリン／VKA 群〔1.8％（9/489 例）〕より数値的に低く、ハザード比は 0.907（95%信頼区間：0.336～2.446）であった。一方、DVT 又は PE の

既往を有さなかった被験者における有効性主要評価項目の発現頻度は、リバーロキサバン群〔2.2%（43/1,964 例）〕のほうがエノキサパリン／VKA 群〔1.8%（35/1,924 例）〕より数値的に高く、ハザード比は 1.194（95%信頼区間：0.764～1.865）であった。

活動性悪性腫瘍の有無：

ベースライン時に活動性悪性腫瘍を有した被験者は、ベースライン時に活動性悪性腫瘍を有さなかった被験者と比べて VTE の発現頻度が高く（ハザード比 1.225、95%信頼区間：0.497～3.015）（5.3.5.1.2 A53042/Table 14.2/361）、文献で報告されているように、悪性腫瘍を有する患者では抗凝固薬療法中の VTE のリスクが高いことが確認された[4)]。

ベースライン時に活動性悪性腫瘍を有した被験者では、リバーロキサバン群で 2/114 例（1.8%）が VTE を発現したのに対し、エノキサパリン／VKA 群で 3/109 例（2.8%）が発現し、ハザード比は 0.649（95%信頼区間：0.108～3.894）であった。また、ベースライン時に活動性悪性腫瘍を有さなかった被験者では、リバーロキサバン群で 48/2,305 例（2.1%）に VTE が発現したのに対し、エノキサパリン／VKA 群で 41/2,304 例（1.8%）に発現し、ハザード比は 1.161（95%信頼区間：0.765～1.761）であった。

予定投与期間：

予定投与期間が 3 ヵ月のコホートにおける有効性主要評価項目の発現頻度は、リバーロキサバン群で 4.7%（6/127 例）、エノキサパリン／VKA 群で 1.6%（2/122 例）であった（5.3.5.1.2 A53042/Table 14.2/101）。一方、試験集団全体（全予定投与期間を含む）では、最初の 3 ヵ月の治験薬投与期間における有効性主要評価項目の発現頻度はリバーロキサバン群〔1.5%（37/2,419 例）〕とエノキサパリン／VKA 群〔1.6%（38/2,413 例）〕で同程度であった（5.3.5.1.2 A53042/Table 14.2/110）。

予定投与期間が 6 ヵ月のコホートでは、有効性主要評価項目の発現頻度はリバーロキサバン群で 1.9%（27/1,387 例）、エノキサパリン／VKA 群で 1.7%（24/1,387 例）であった。予定投与期間が 12 ヵ月のコホートでは、リバーロキサバン群が 1.9%（17/905 例）、エノキサパリン／VKA 群群が 2.0%（18/904 例）であった。

地域：

本試験における地域別にみた有効性主要評価項目の発現頻度を以下に示す。

- 西欧：リバーロキサバン群 1.8%（24/1,309 例）、エノキサパリン／VKA 群 1.2%（16/1,311 例）
- 東欧：リバーロキサバン群 1.4%（3/208 例）、エノキサパリン／VKA 群 1.9%（4/209 例）
- アジア：リバーロキサバン群 4.1%（6/145 例）、エノキサパリン／VKA 群 2.1%（3/142 例）
- オーストラリア及びニュージーランド：リバーロキサバン群 1.3%（4/306 例）、エノキサパリン／VKA 群 3.3%（10/307 例）
- 北米：リバーロキサバン群 2.0%（5/244 例）、エノキサパリン／VKA 群 2.9%（7/242 例）

南米ではイベントの発現が認められなかったため、交互作用の p 値は検討しなかった（5.3.5.1.2 A53042/Table 14.2/407）。

特別な被験者集団：

総括報告書作成後の事後解析として、被験者の年齢が 75 歳超、体重が 50kg 以下、もしくは CL_{CR}（計算値）が 50mL/min 未満の基準のいずれかに該当する被験者を特殊な被験者集団とし、その部分集団における有効性主要評価項目の発現頻度を検討した。CL_{CR} は Cockcroft-Gault の式を用いて算出した（5.3.5.1.2 A53042/Table 16.1.9.1/19）。

当該被験者集団における有効性主要評価項目の発現頻度は、リバーロキサバン群で 2.7%（14/510 例）、エノキサパリン／VKA 群で 3.6%（17/477 例）であったのに対し、当該被験者集団以外の被験者における発現頻度はリバーロキサバン群で 1.9%（36/1,909 例）、エノキサパリン／VKA 群で 1.4%（27/1,936 例）であった。リバーロキサバン群とエノキサパリン／VKA 群において、Cox 比例ハザードモデルによるハザード比は、当該被験者集団で 0.748（95%信頼区間：0.369～1.519）、当該被験者集団以外の被験者で 1.345（95%信頼区間：0.816～2.215）であった。

無作為割り付け前の治療：

無作為割り付け前の LMWH を含むヘパリン〔（LMW）ヘパリン〕／フォンダパリヌクスの使用は最大 48 時間まで許容された。

無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスの投与を受けなかった被験者のうち、リバーロキサバン群で 7/182 例（3.8%）、エノキサパリン／VKA 群で 6/190 例（3.2%）に有効性主要評価項目のイベントが発現し、ハザード比は 1.177（95%信頼区間：0.395～3.508）であった。無作為割り付け前に（LMW）ヘパリン／フォンダパリヌクスの投与を受けた被験者では、リバーロキサバン群で 43/2,237 例（1.9%）、エノキサパリン／VKA 群で 38/2,223 例（1.7%）に有効性主要評価項目のイベントが発現し、ハザード比は 1.117（95%信頼区間：0.722～1.729）であった。

表 2.7.6.2- 23　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）

因子	区分	リバーロキサバン	エノキサパリン／VKA	ハザード比	ハザード比の95%信頼区間		交互作用のｐ値[a]
					下限値	上限値	
年齢（区分 1）	＜60 歳	26/1204 (2.2%)	17/1211 (1.4%)	1.530	0.830	2.820	0.177
	≧60 歳	24/1215 (2.0%)	27/1202 (2.2%)	0.866	0.500	1.501	
年齢（区分 2）	＜65 歳	29/1461 (2.0%)	23/1479 (1.6%)	1.276	0.738	2.206	0.528
	65～75 歳	10/517 (1.9%)	8/532 (1.5%)	1.279	0.504	3.245	
	＞75 歳	11/441 (2.5%)	13/402 (3.2%)	0.741	0.331	1.654	
BMI	欠測	0/10 (0.0%)	1/15 (6.7%)	.	.	.	
	＜30kg/m²	39/1668 (2.3%)	32/1643 (1.9%)	1.192	0.747	1.902	0.734
	≧30kg/m²	11/741 (1.5%)	11/755 (1.5%)	1.018	0.441	2.348	
心疾患	あり	9/428 (2.1%)	10/374 (2.7%)	0.764	0.310	1.884	0.386
	なし	41/1991 (2.1%)	34/2039 (1.7%)	1.225	0.778	1.930	
（LMW）ヘパリン／フォンダパリヌクスの前治療	なし	7/182 (3.8%)	6/190 (3.2%)	1.177	0.395	3.508	N.D.
	1 日間	34/1754 (1.9%)	29/1760 (1.6%)	1.169	0.712	1.919	
	2 日間	9/460 (2.0%)	9/443 (2.0%)	0.912	0.362	2.300	
	＞2 日間	0/23 (0.0%)	0/20 (0.0%)	.	.	.	

表 2.7.6.2- 23　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

因子	区分	リバーロキサバン	エノキサパリン／VKA	ハザード比	ハザード比の95%信頼区間		交互作用のｐ値[a]
					下限値	上限値	
（LMW）ヘパリン／フォンダパリヌクスの前治療（薬理活性で補正）	なし	7/182 (3.8%)	6/190 (3.2%)	1.177	0.395	3.508	N.D.
	1日間	23/1389 (1.7%)	25/1400 (1.8%)	0.925	0.525	1.629	
	2日間	20/801 (2.5%)	13/777 (1.7%)	1.475	0.734	2.968	
	＞2日間	0/47 (0.0%)	0/46 (0.0%)	.	.	.	
indexイベントの病因	原発性DVT／PE	32/1566 (2.0%)	29/1551 (1.9%)	1.074	0.649	1.775	0.817
	二次性DVT／PE	18/853 (2.1%)	15/862 (1.7%)	1.194	0.602	2.369	
特殊な被験者集団[b]	いいえ	36/1909 (1.9%)	27/1936 (1.4%)	1.345	0.816	2.215	0.188
	はい	14/510 (2.7%)	17/477 (3.6%)	0.748	0.369	1.519	
地域	西ヨーロッパ	24/1309 (1.8%)	16/1311 (1.2%)	1.503	0.798	2.829	N.D.
	東ヨーロッパ	3/208 (1.4%)	4/209 (1.9%)	0.753	0.169	3.366	
	オーストラリア／ニュージーランド	4/306 (1.3%)	10/307 (3.3%)	0.407	0.127	1.302	
	南米	0/8 (0.0%)	0/10 (0.0%)	.	.	.	
	北米	5/244 (2.0%)	7/242 (2.9%)	0.669	0.211	2.119	
	アジア	6/145 (4.1%)	3/142 (2.1%)	1.897	0.473	7.601	
	イスラエル	3/78 (3.8%)	1/75 (1.3%)	.	.	.	
	南アフリカ	5/121 (4.1%)	3/117 (2.6%)	1.564	0.374	6.545	

表 2.7.6.2- 23　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

因子	区分	リバーロキサバン	エノキサパリン／VKA	ハザード比	ハザード比の95%信頼区間		交互作用のp値[a]
					下限値	上限値	
index イベント	DVT のみ	0/3 (0.0%)	0/3 (0.0%)	.	.	.	N.D.
	DVT を伴う PE	16/603 (2.7%)	9/587 (1.5%)	1.737	0.767	3.935	
	DVT を伴わない PE	34/1793 (1.9%)	35/1803 (1.9%)	0.968	0.604	1.553	
	CIAC で PE 判定なし	0/20 (0.0%)	0/20 (0.0%)	.	.	.	
予定投与期間	3 ヵ月	6/127 (4.7%)	2/122 (1.6%)	2.909	0.587	14.414	0.440
	6 ヵ月	27/1387 (1.9%)	24/1387 (1.7%)	1.116	0.644	1.933	
	12 ヵ月	17/905 (1.9%)	18/904 (2.0%)	0.939	0.484	1.822	
既知の血栓性素因	あり	2/138 (1.4%)	2/121 (1.7%)	.	.	.	0.815
	なし	48/2281 (2.1%)	42/2292 (1.8%)	1.136	0.751	1.719	
（LMW）ヘパリン/フォンダパリヌクスの割り付け前の治療	なし	7/182 (3.8%)	6/190 (3.2%)	1.177	0.395	3.508	0.960
	あり	43/2237 (1.9%)	38/2223 (1.7%)	1.117	0.722	1.729	
ベースライン時の活動性悪性腫瘍	なし	48/2305 (2.1%)	41/2304 (1.8%)	1.161	0.765	1.761	0.504
	あり	2/114 (1.8%)	3/109 (2.8%)	0.649	0.108	3.894	
ベースライン時の活動性の制限	あり	10/384 (2.6%)	8/380 (2.1%)	1.143	0.449	2.907	0.831
	なし	40/2035 (2.0%)	36/2033 (1.8%)	1.095	0.698	1.718	
血栓塞栓症の危険因子数	なし	27/1138 (2.4%)	23/1119 (2.1%)	1.126	0.646	1.965	0.971
	1 つ	11/891 (1.2%)	11/922 (1.2%)	1.022	0.443	2.358	
	2 つ以上	12/390 (3.1%)	10/372 (2.7%)	1.140	0.492	2.640	

表 2.7.6.2- 23　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

因子	区分	リバーロキサバン	エノキサパリン／VKA	ハザード比	ハザード比の95%信頼区間		交互作用のｐ値 [a]
					下限値	上限値	
用量確認解析の実施	なし	44/2214 (2.0%)	41/2218 (1.8%)	1.063	0.694	1.626	0.426
	あり	6/205 (2.9%)	3/195 (1.5%)	1.875	0.469	7.498	
DVT／PE の既往	あり	7/455 (1.5%)	9/489 (1.8%)	0.907	0.336	2.446	0.512
	なし	43/1964 (2.2%)	35/1924 (1.8%)	1.194	0.764	1.865	
肺疾患	あり	16/627 (2.6%)	13/608 (2.1%)	1.179	0.567	2.453	0.849
	なし	34/1792 (1.9%)	31/1805 (1.7%)	1.094	0.672	1.780	
人種	不明	14/586 (2.4%)	5/583 (0.9%)	2.822	1.016	7.838	N.D.
	白人	26/1585 (1.6%)	32/1587 (2.0%)	0.802	0.478	1.345	
	黒人	2/66 (3.0%)	2/68 (2.9%)	.	.	.	
	アジア人	8/163 (4.9%)	5/156 (3.2%)	1.470	0.480	4.501	
	アメリカンインディアン又はアラスカ先住民	0/0 (0.0%)	0/3 (0.0%)	.	.	.	
	ヒスパニック	0/10 (0.0%)	0/11 (0.0%)	.	.	.	
	ハワイ先住民又は太平洋諸島系	0/4 (0.0%)	0/2 (0.0%)	.	.	.	
	分類不能	0/5 (0.0%)	0/3 (0.0%)	.	.	.	
index イベントの肺血流量（区分）	欠測	0/121 (0.0%)	1/114 (0.9%)	.	.	.	
	＜0.75	10/597 (1.7%)	8/576 (1.4%)	1.198	0.472	3.037	0.907
	≧0.75	40/1701 (2.4%)	35/1723 (2.0%)	1.142	0.725	1.797	

表 2.7.6.2- 23　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

因子	区分	リバーロキサバン	エノキサパリン／VKA	ハザード比	ハザード比の95%信頼区間		交互作用のｐ値 [a]
					下限値	上限値	
index イベントの肺血流量（最低値）	欠測	0/121 (0.0%)	1/114 (0.9%)	.	.	.	
	肺血流欠損最低値	5/309 (1.6%)	4/299 (1.3%)	1.152	0.309	4.294	0.964
	＞肺血流欠損最低値	45/1989 (2.3%)	39/2000 (2.0%)	1.155	0.752	1.773	
index イベントの肺血流スコア（三分位値）	欠測	0/121 (0.0%)	1/114 (0.9%)	.	.	.	
	第 1 三分位	16/751 (2.1%)	11/723 (1.5%)	1.417	0.657	3.055	0.817
	第 2 三分位	16/737 (2.2%)	16/756 (2.1%)	1.005	0.503	2.010	
	第 3 三分位	18/810 (2.2%)	16/820 (2.0%)	1.131	0.577	2.220	
腎機能：CL_{CR}	欠測	1/16 (6.3%)	1/10 (10.0%)	.	.	.	
	≧80mL/min	30/1555 (1.9%)	22/1617 (1.4%)	1.410	0.813	2.445	0.311
	50～＜80mL/min	12/637 (1.9%)	16/593 (2.7%)	0.684	0.324	1.447	
	＜50mL/min	7/211 (3.3%)	5/193 (2.6%)	1.247	0.395	3.937	
性別	男性	25/1309 (1.9%)	21/1247 (1.7%)	1.120	0.627	2.001	0.999
	女性	25/1110 (2.3%)	23/1166 (2.0%)	1.123	0.638	1.979	

表 2.7.6.2- 23　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

因子	区分	リバーロキサバン	エノキサパリン／VKA	ハザード比	ハザード比の95%信頼区間		交互作用のp値[a]
					下限値	上限値	
体重（区分1）	欠測	0/2 (0.0%)	0/1 (0.0%)	.	.	.	
	＜90kg	35/1657 (2.1%)	31/1655 (1.9%)	1.118	0.690	1.813	0.966
	≧90kg	15/760 (2.0%)	13/757 (1.7%)	1.154	0.549	2.426	
体重（区分2）	欠測	0/2 (0.0%)	0/1 (0.0%)	.	.	.	
	＜50kg	1/22 (4.5%)	1/29 (3.4%)	.	.	.	0.846
	≧50kg	49/2395 (2.0%)	43/2383 (1.8%)	1.124	0.746	1.693	
体重（区分3）	欠測	0/2 (0.0%)	0/1 (0.0%)	.	.	.	
	≦70kg	17/653 (2.6%)	10/621 (1.6%)	1.606	0.735	3.508	0.442
	＞70～90kg	20/1081 (1.9%)	24/1119 (2.1%)	0.865	0.477	1.566	
	＞90kg	13/683 (1.9%)	10/672 (1.5%)	1.289	0.565	2.940	

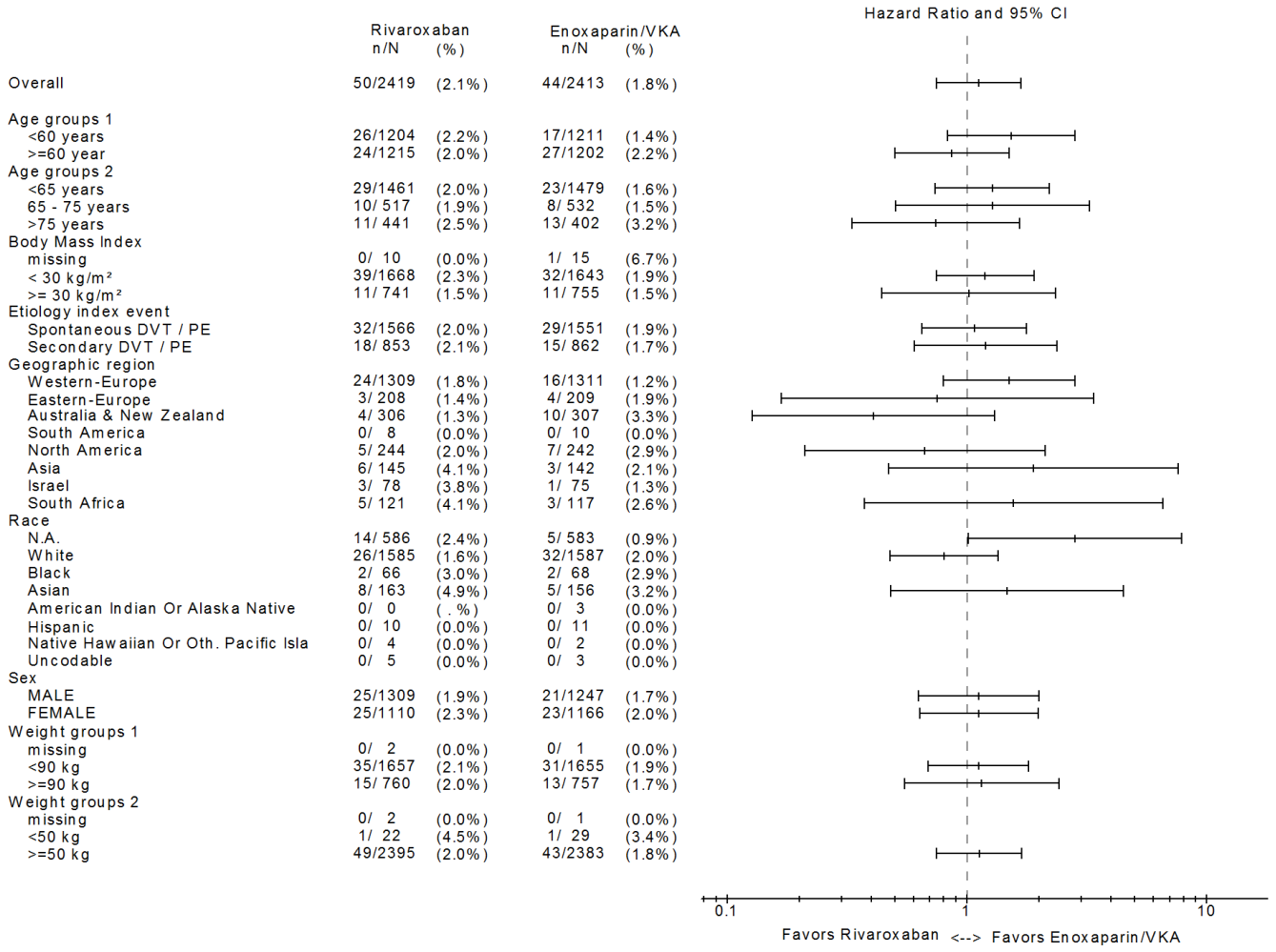
ITT：intention-to-treat、VKA：ビタミンK拮抗薬、DVT：深部静脈血栓症、PE：肺塞栓症、（LMW）ヘパリン：LMWHを含むヘパリン、LMWH：低分子量ヘパリン、CL_{CR}：クレアチニンクリアランス、ND：部分集団の少なくとも1つのカテゴリで1つの投与群内にイベントの発現はなかったため、交互作用のp値は算出しなかった。

層別Cox比例ハザードモデルを用いた解析はカテゴリに少なくとも5事象あるときのみ実施した。予定投与期間で層別化し、ベースライン時の活動性悪性腫瘍の有無を共変量として各モデルに含めた。ベースライン時の悪性腫瘍の有無別の解析では、この共変量はモデルに含めなかった。予定投与期間別の解析では、層としてモデルに含めなかった。

a：交互作用項に対するp値は投与群、投与群と部分集団の交互作用、ベースライン時の活動性悪性腫瘍の有無を含めたモデルで計算された。交互作用に対するp値は、ベースライン及び人口統計学的特性に関する記録が欠測のものを除いて算出された。

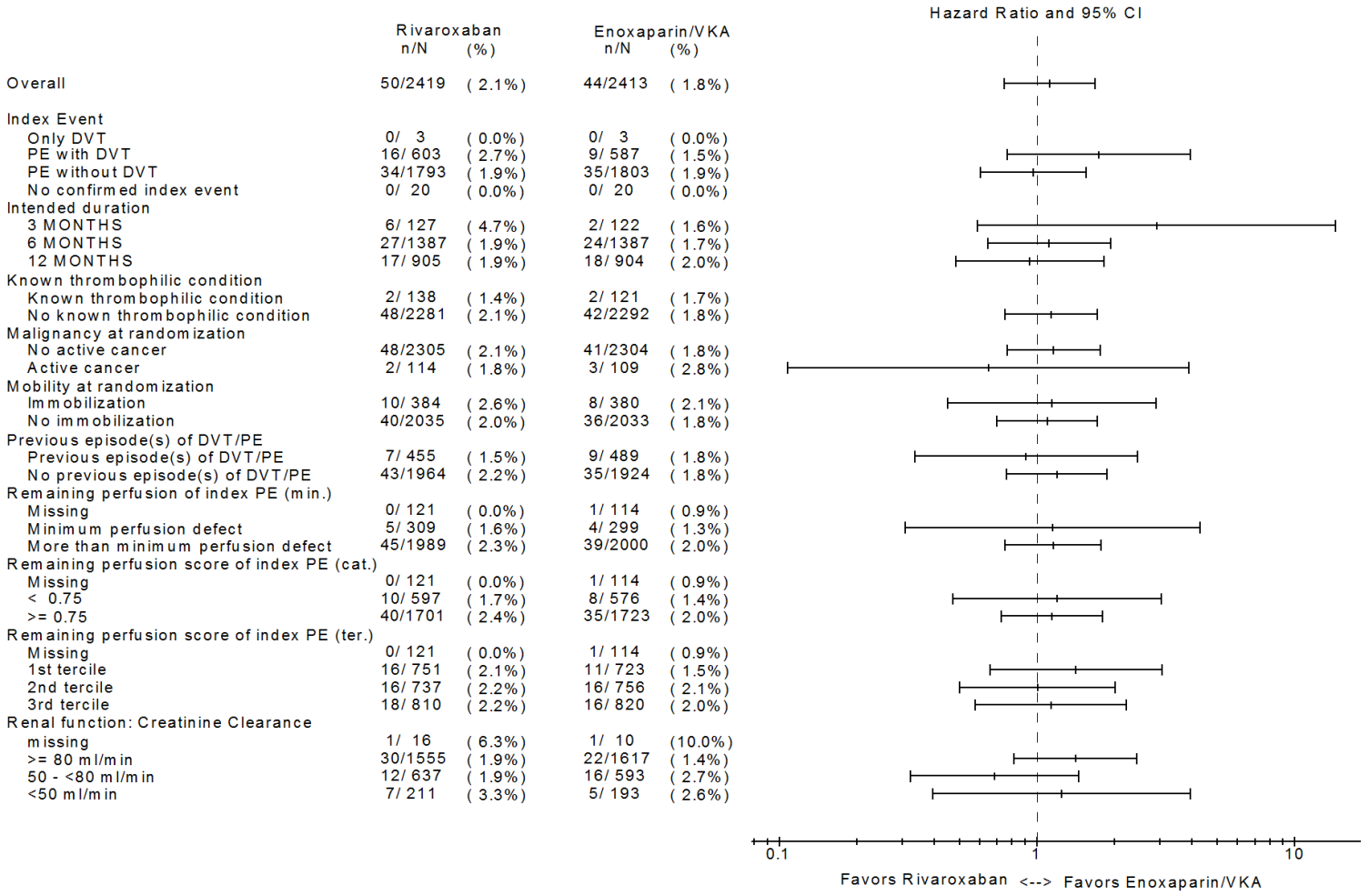
b：被験者の年齢が75歳超、体重が50kg以下もしくはCL_{CR}が50mL/min未満のいずれかに該当する場合を特殊な被験者集団とした。

引用元：5.3.5.1.2 A53042/Table 14.2/407



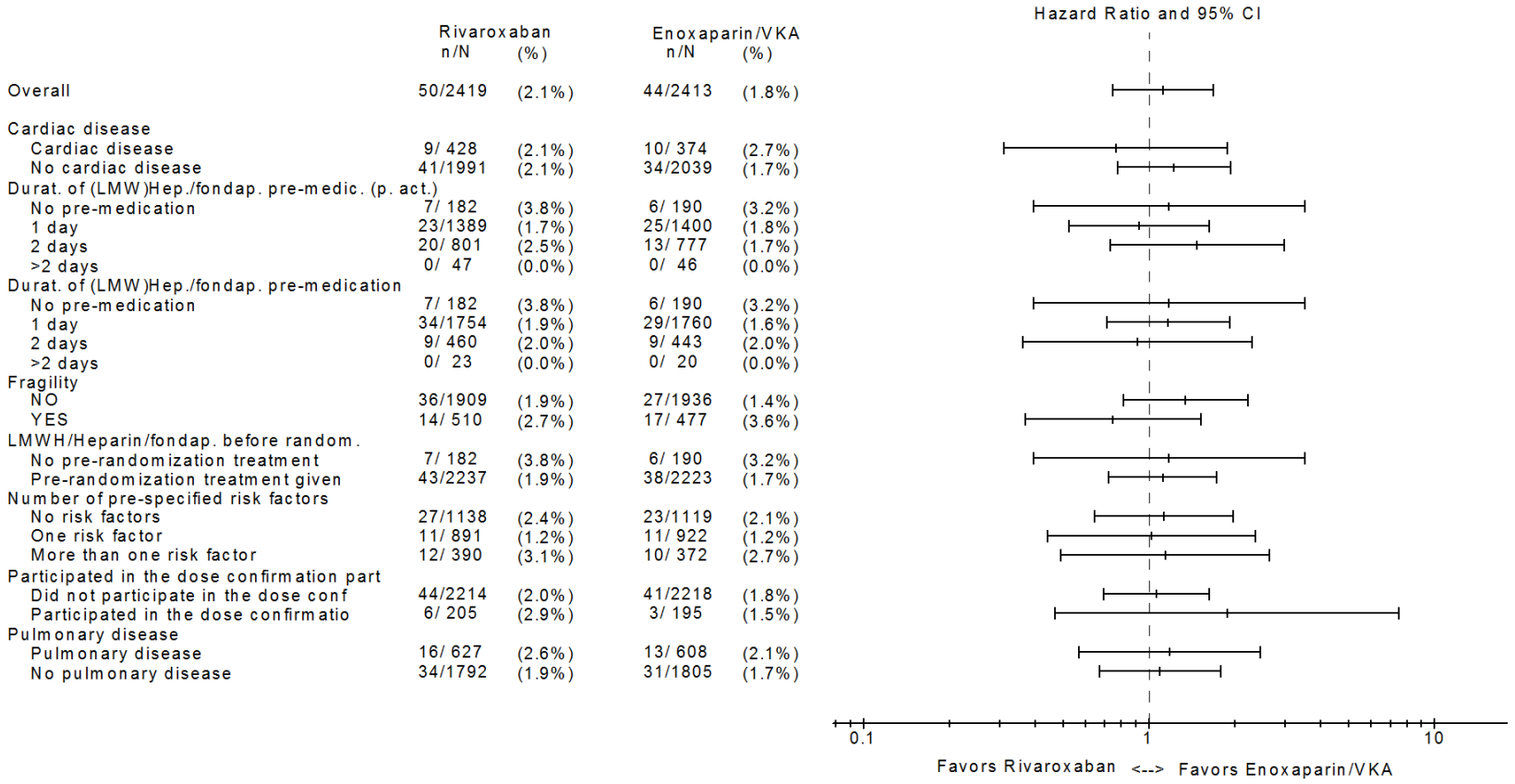
引用元：5.3.5.1.2 A53042/Figure 14.2/389

図 2.7.6.2- 4　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）



引用元：5.3.5.1.2 A53042/Figure 14.2/390

図 2.7.6.2- 4　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）



引用元：5.3.5.1.2 A53042/Figure 14.2/391

図 2.7.6.2- 4　有効性主要評価項目のベースライン及び人口統計学的因子別解析（ITT 解析対象集団）（続き）

対照薬の種類による解析（ワルファリン対 acenocoumarol）：

本試験では、acenocoumarol とワルファリンのいずれかを使用した被験者の部分集団ごとに解析を行った。ワルファリンの部分集団には、ワルファリンのみを投与した施設を含めた。acenocoumarol の部分集団には、acenocoumarol のみを投与した施設を含めた。有効性主要評価項目の構成要素の発現頻度を VKA 療法の種類ごとに要約した（5.3.5.1.2 A53042/Table 14.2/154、Table 14.2/158、Table 14.2/396、Table 14.2/400）。

ワルファリンの部分集団では、有効性主要評価項目の発現頻度は、リバーロキサバン群で 2.2%（40/1,801 例）、エノキサパリン／ワルファリン群で 1.8%（34/1,841 例）であり、ハザード比は 1.184（95%信頼区間：0.750～1.871）であった。acenocoumarol の部分集団では、有効性主要評価項目の発現頻度はリバーロキサバン群で 1.7%（6/359 例）、エノキサパリン／acenocoumarol 群で 1.7%（6/359 例）であり、ハザード比は 1.011（95%信頼区間：0.326～3.136）であった。

施設ごとの TTR：

TTR は、被験者内及び被験者間、施設内及び施設間、国内及び各国間で異なり、このことが試験の結果に影響を及ぼした可能性が考えられる。そこで、同施設内の各被験者の調整 TTR の平均値を求め、施設 TTR を算出した。エノキサパリン／VKA 群の被験者がほぼ同数となるように 3 つの部分集団に施設を分類し検討した。3 つの部分集団（エノキサパリン／VKA 群の被験者を施設 TTR＜58.7%、58.7%～67.7%、＞67.7%の 3 つに区分）による施設 TTR ごとの有効性主要評価項目の発現頻度を表 2.7.6.2- 24に示す。

施設 TTR と有効性主要評価項目の発現頻度には明らかな関係は認められなかった。

表 2.7.6.2- 24　施設 TTR 別の有効性主要評価項目の発現頻度（ITT 解析対象集団）

施設 TTR	リバーロキサバン	エノキサパリン／VKA	リバーロキサバンのエノキサパリン／VKA に対するハザード比（95%信頼区間）	交互作用の p 値
＜58.7%	17/793（2.14%）	19/802（2.37%）	0.903（0.470～1.738）	0.082
58.7%～67.7%	23/808（2.85%）	11/800（1.38%）	2.081（1.014～4.270）	
＞67.7%	9/790（1.14%）	14/807（1.73%）	0.642（0.277～1.484）	
施設 TTR が得られなかった被験者	1/28（3.57%）	0/4（0.00%）		

PT-INR：プロトロンビン時間国際標準比、ITT：intention-to-treat、TTR：PT-INR が目標範囲内（2.0～3.0）であった期間割合、VKA：ビタミン K 拮抗薬

同施設内の各被験者の調整 TTR の平均値を求め、施設 TTR を算出した。エノキサパリン／VKA 群の PT-INR が得られない施設は除外した。施設 TTR を 3 つに区分し、各施設 TTR 内の被験者数がほぼ同数となるように施設を 3 つの部分集団に分類した。各カテゴリーに 5 件以上のイベント数が認められる場合、予定投与期間で層別し、ベースライン時の活動性悪性腫瘍の有無を共変量として層別 Cox 比例ハザードモデルを用いて解析を行った。交互作用の p 値は、投与群、部分集団、投与群の部分集団及びベースライン時の活動性悪性腫瘍を共変量としたモデルを用い算出した。交互作用の p 値は、施設 TTR が得られなかった被験者を除いて算出した。

引用元：5.3.5.1.2 A53042/Table 14.2/453

2.7.6.2.2.2.4 有効性の結論

本試験では、リバーロキサバン群（15mg 1 日 2 回 3 週間投与に引き続き、20mg 1 日 1 回投与）のエノキサパリン／VKA 群に対する有効性主要評価項目における非劣性が検証された。ハザード比は 1.123（95%信頼区間：0.749～1.684；ITT 解析対象集団）であり、信頼区間の上限値は予め規定された非劣性マージンの 2.0 を下回り、非劣性の片側検定の p 値は 0.0026 であった。

有効性主要評価項目は症候性 VTE〔症候性 DVT、症候性 PE（非致死的及び致死的）〕の複合エンドポイントである。致死的 PE は、客観的な診断検査又は部検に基づく PE 、あるいは原因が特定されない死亡及び DVT/PE の可能性が否定できない死亡（原因不明の死亡）のいずれかとした。

本試験の用量確認解析に加わらなかった被験者でのリバーロキサバン群に対するエノキサパリン／VKA 群の有効性主要評価項目のハザード比は 1.063（95%信頼区間：0.694～1.626）であった。用量確認解析実施の有無（交互作用の p 値：0.426）でハザード比が異なるという成績は得られなかった。

有効性主要評価項目の発現頻度（ITT 解析対象集団）は両投与群共に 3.0%を下回った。すなわち、実際に得られた有効性主要評価項目の発現頻度は、治験実施計画書で規定した推定総発現頻度を下回った。この結果を受け、有効性主要評価項目の規定した発現数に到達させるため、さらに多くの被験者を組み入れなければならなかった。

有効性主要評価項目の結果は、その各構成要素においても同様であり、また、予め規定した部分集団である地域、予定投与期間、人口統計学的特性とベースラインの特性及び凝固状態にかかわらず一貫していた。

有効性主要評価項目において示されたリバーロキサバン群のエノキサパリン／VKA 群に対する比較結果は、すべての有効性副次評価項目においても同様に示された。

2.7.6.2.2.3 安全性の結果

2.7.6.2.2.3.1 有害事象の要約

有害事象のコード化はすべて MedDRA Version 14.1 に基づいて行なった。表 2.7.6.2- 25に安全性解析対象集団における有害事象及び治験薬投与下で発現した有害事象（TEAE）の要約を示す。本試験における「治験薬投与下」とは、無作為割り付け後から治験薬の投与終了後 2 日目までと定義した。

有害事象の発現頻度は、リバーロキサバン群で 81.2%、エノキサパリン／VKA 群で 80.2%であった。TEAE の発現頻度はリバーロキサバン群で 80.3%、エノキサパリン／VKA 群で 79.0%であった。治験薬投与終了後 3 日目以降のフォローアップ期間に発現した有害事象の発現頻度は、両投与群で同程度（13.8%）であった。

出血に関する有害事象〔以下、出血関連有害事象；治験責任（分担）医師の報告による〕を除く TEAE の発現頻度はリバーロキサバン群で 76.8%、エノキサパリン／VKA 群で 75.7%であった。治験薬投与下で発現した出血関連有害事象〔治験責任（分担）医師の報告による〕の発現頻度は、エノキサパリン／VKA 群（33.6%）とリバーロキサバン群（33.3%）で同様であった。

治験薬との因果関係が否定できない TEAE の発現頻度はエノキサパリン／VKA 群（32.6%）とリバーロキサバン群（32.2%）で同様であった。

出血関連有害事象〔治験責任（分担）医師の報告による〕を除く、治験薬との因果関係が否定できない TEAE の発現頻度は、リバーロキサバン群で 13.3%、エノキサパリン／VKA 群で 13.1%。であり、両投与群で同様であった。

死亡例（CIAC で判定）は 114 例報告された〔リバーロキサバン群：63 例（2.6%）、エノキサパリン／VKA 群：51 例（2.1%）〕。治験薬投与下での死亡例は 48 例であった〔リバーロキサバン群：28 例（1.2%）、エノキサパリン／VKA 群：20 例（0.8%）〕。

治験薬の投与中止に至った有害事象の発現頻度はリバーロキサバン群で 5.1%、エノキサパリン／VKA 群で 4.1%であった。重篤な TEAE の発現頻度は投与群間で同程度であった（リバーロキサバン群：19.5%、エノキサパリン／VKA 群：19.3%）。

表 2.7.6.2- 25　有害事象の要約（安全性解析対象集団）

有害事象	リバーロキサバン N=2412 (100%)	エノキサパリン／VKA N=2405 (100%)
AE	1959 (81.2%)	1928 (80.2%)
SAE	504 (20.9%)	497 (20.7%)
死亡（無作為割り付け後のすべての死亡）	63 (2.6%)	51 (2.1%)
治験薬投与下の死亡 [a]	28 (1.2%)	20 (0.8%)
TEAE [a]	1937 (80.3%)	1901 (79.0%)
TEAE（出血関連有害事象を除く）[a, b]	1852 (76.8%)	1821 (75.7%)
治験薬投与下の出血関連有害事象 [a, b]	802 (33.3%)	807 (33.6%)
治験薬投与終了後 3 日目以降の AE	332 (13.8%)	332 (13.8%)
治験薬との因果関係が否定できない TEAE [a]	776 (32.2%)	784 (32.6%)
治験薬との因果関係が否定できない TEAE（出血関連有害事象を除く）[a, b]	322 (13.3%)	314 (13.1%)
治験薬投与下の治験薬との因果関係が否定できない出血関連有害事象 [a, b]	579 (24.0%)	596 (24.8%)
治験薬投与終了後 3 日目以降の治験薬との因果関係が否定できない AE	33 (1.4%)	40 (1.7%)
重篤な TEAE[a]	471 (19.5%)	463 (19.3%)
重篤な TEAE（出血関連有害事象を除く）[a, b]	416 (17.2%)	406 (16.9%)
治験薬との因果関係が否定できない 重篤な TEAE [a]	112 (4.6%)	118 (4.9%)
治験薬投与終了後 3 日目以降の SAE	67 (2.8%)	75 (3.1%)
治験薬投与終了後 3 日目以降の治験薬との因果関係が否定できない SAE	1 (<0.1%)	6 (0.2%)
治験薬の投与中止に至った AE	123 (5.1%)	99 (4.1%)
入院（入院期間の延長）に至った AE	425 (17.6%)	430 (17.9%)

VKA：ビタミン K 拮抗薬、AE：有害事象、SAE：重篤な有害事象

a：TEAE とは、無作為割り付け後から治験薬投与終了後 2 日目までに発現した有害事象とした。

b：出血関連有害事象は治験責任（分担）医師による報告に基づく。

引用元：5.3.5.1.2 A53042/Table 14.3.1/1、Table 14.3.1/16、Table 14.3.1/28、Table 14.3.1/54

2.7.6.2.2.3.2　　比較的よく見られる有害事象

2.7.6.2.2.3.2.1　　治験薬投与下で発現した有害事象（TEAE）

TEAE が認められたのはリバーロキサバン群で 1,937 例（80.3%）、エノキサパリン／VKA 群で 1,901 例（79.0%）であった。TEAE の種類及び発現頻度はリバーロキサバン群とエノキサパリン／VKA 群とでおおむね同様であった。

器官別大分類別で発現頻度が高かったのは、「感染症および寄生虫症」（リバーロキサバン群：30.9%、エノキサパリン／VKA 群：30.8%）、「胃腸障害」（30.6%、27.9%）、「呼吸器、胸郭および縦隔障害」（27.2%、26.9%）、「筋骨格系および結合組織障害」（22.0%、22.7%）、「一般・全身障害および投与部位の状態」（20.8%、20.0%）、「神経系障害」（17.0%、16.2%）であった。「心臓障害」に関する TEAE の発現頻度はリバーロキサバン群で 8.6%、エノキサパリン／VKA 群で 8.2%であった（5.3.5.1.2 A53042/Table 14.3.1/18、Table 14.3.1/42）。

いずれかの投与群の発現頻度が 2%以上の TEAE を MedDRA 基本語別に表 2.7.6.2- 26に示した。全体として、TEAE の発現頻度は両投与群で同様であった。リバーロキサバン群でエノキサパリン／VKA 群より 1%以上発現頻度が高かった TEAE は、月経過多（リバーロキサバン群：3.0%、エノキサパリン／VKA 群：1.9%）、そう痒症（2.2%、1.1%）、呼吸困難（6.7%、5.7%）であった。リバーロキサバン群でエノキサパリン／VKA 群より 1%以上発現頻度が低かった TEAE は、挫傷（リバーロキサバン群：3.8%、エノキサパリン／VKA 群：5.4%）、背部痛（3.6%、5.4%）、血腫（2.4%、3.8%）、アラニン・アミノトランスフェラーゼ増加（2.2%、3.2%）、INR 増加（0.2%、3.4%）であった。

TEAE の重症度はほとんどが軽度又は中等度であり、高度のものはリバーロキサバン群で 10.8%、エノキサパリン／VKA 群で 9.5%にみられた（5.3.5.1.2 A53042/Table 14.3.1/60）。

表 2.7.6.2- 26　TEAE の発現頻度（いずれかの投与群で 2%以上、安全性解析対象集団）

MedDRA 器官別大分類／基本語	リバーロキサバン N=2412 (100%)	エノキサパリン／VKA N=2405 (100%)
全事象	1937 (80.3%)	1901 (79.0%)
血液およびリンパ系障害		
貧血	53 (2.2%)	37 (1.5%)
胃腸障害		
上腹部痛	53 (2.2%)	41 (1.7%)
便秘	139 (5.8%)	131 (5.4%)
下痢	125 (5.2%)	124 (5.2%)
歯肉出血	57 (2.4%)	76 (3.2%)
悪心	106 (4.4%)	122 (5.1%)
直腸出血	57 (2.4%)	41 (1.7%)
嘔吐	51 (2.1%)	74 (3.1%)
一般・全身障害および投与部位の状態		
無力症	51 (2.1%)	53 (2.2%)
胸痛	183 (7.6%)	185 (7.7%)
末梢性浮腫	87 (3.6%)	94 (3.9%)
疲労	66 (2.7%)	53 (2.2%)
発熱	67 (2.8%)	70 (2.9%)
感染症および寄生虫症		
気管支炎	108 (4.5%)	89 (3.7%)
インフルエンザ	58 (2.4%)	51 (2.1%)
鼻咽頭炎	181 (7.5%)	189 (7.9%)
上気道感染	48 (2.0%)	44 (1.8%)
尿路感染	93 (3.9%)	95 (4.0%)
傷害、中毒および処置合併症		
挫傷	92 (3.8%)	129 (5.4%)
臨床検査		
アラニン・アミノトランスフェラーゼ増加	52 (2.2%)	77 (3.2%)
INR 増加	6 (0.2%)	82 (3.4%)
筋骨格系および結合組織障害		
関節痛	85 (3.5%)	77 (3.2%)
背部痛	88 (3.6%)	131 (5.4%)
筋痙縮	49 (2.0%)	54 (2.2%)
四肢痛	154 (6.4%)	154 (6.4%)
神経系障害		
浮動性めまい	64 (2.7%)	86 (3.6%)
頭痛	193 (8.0%)	174 (7.2%)
精神障害		
不安	80 (3.3%)	76 (3.2%)
不眠症	67 (2.8%)	76 (3.2%)
腎および尿路障害		
血尿	72 (3.0%)	72 (3.0%)
生殖系および乳房障害		
月経過多	73 (3.0%)	45 (1.9%)

表 2.7.6.2- 26 TEAE の発現頻度（いずれかの投与群で 2%以上、安全性解析対象集団）（続き）

MedDRA 器官別大分類／基本語	リバーロキサバン N=2412（100%）	エノキサパリン／VKA N=2405（100%）
呼吸器、胸郭および縦隔障害		
咳嗽	155 (6.4%)	169 (7.0%)
呼吸困難	161 (6.7%)	136 (5.7%)
鼻出血	218 (9.0%)	197 (8.2%)
喀血	81 (3.4%)	81 (3.4%)
皮膚および皮下組織障害		
そう痒症	54 (2.2%)	27 (1.1%)
発疹	71 (2.9%)	61 (2.5%)
血管障害		
血腫	57 (2.4%)	92 (3.8%)
高血圧	111 (4.6%)	88 (3.7%)

MedDRA：ICH 国際医薬用語集、VKA：ビタミン K 拮抗薬、INR：（プロトロンビン時間）国際標準比
MedDRA version 14.1
無作為割り付けから治験薬投与終了後 2 日目までに発現した有害事象のみが含まれる。
引用元：5.3.5.1.2 A53042/Table 14.3.1/18、Table 14.3.1/43

2.7.6.2.2.3.2.2 治験薬との因果関係が否定できない TEAE

いずれかの投与群の発現頻度が 2%以上の治験薬との因果関係が否定できない TEAE を MedDRA 基本語別に表 2.7.6.2- 27に示した。

治験薬との因果関係が否定できない TEAE の発現頻度はリバーロキサバン群（32.2%）とエノキサパリン／VKA 群（32.6%）で同程度であった。基本語別でいずれかの投与群の発現頻度が 2%以上の治験薬との因果関係が否定できない TEAE は 8 事象あり、月経過多、喀血、鼻出血ではリバーロキサバン群の発現頻度がエノキサパリン／VKA 群よりも高かった（月経過多；リバーロキサバン群 2.5%、エノキサパリン／VKA 群 1.4%、喀血；リバーロキサバン群 2.6%、エノキサパリン／VKA 群 1.9%、鼻出血；リバーロキサバン群 7.2%、エノキサパリン／VKA 群 6.6%）。一方、INR 増加、歯肉出血、挫傷、血腫及び血尿ではエノキサパリン／VKA 群の発現頻度がリバーロキサバン群よりも高かった（PT-INR 増加；リバーロキサバン群 0.2%、エノキサパリン／VKA 群 3.2%、歯肉出血；リバーロキサバン群 1.9%、エノキサパリン／VKA 群 2.7%、挫傷；リバーロキサバン群 2.2%、エノキサパリン／VKA 群 3.6%、血腫；リバーロキサバン群 1.5%、エノキサパリン／VKA 群 2.8%、血尿；リバーロキサバン群 2.0%、エノキサパリン／VKA 群 2.2%）。

表 2.7.6.2- 27　治験薬との因果関係が否定できない TEAE の発現頻度（いずれかの投与群で 2%以上、安全性解析対象集団）

MedDRA 器官別大分類／基本語	リバーロキサバン N=2412 (100%)	エノキサパリン／VKA N=2405 (100%)
全事象	776 (32.2%)	784 (32.6%)
胃腸障害		
歯肉出血	46 (1.9%)	64 (2.7%)
傷害、中毒および処置合併症		
挫傷	53 (2.2%)	86 (3.6%)
臨床検査		
INR 増加	4 (0.2%)	76 (3.2%)
腎および尿路障害		
血尿	49 (2.0%)	52 (2.2%)
生殖系および乳房障害		
月経過多	61 (2.5%)	34 (1.4%)
呼吸器、胸郭および縦隔障害		
鼻出血	173 (7.2%)	159 (6.6%)
喀血	62 (2.6%)	45 (1.9%)
血管障害		
血腫	37 (1.5%)	68 (2.8%)

MedDRA：ICH 国際医薬用語集、VKA：ビタミン K 拮抗薬
MedDRA version 14.1
無作為割り付けから治験薬投与終了後 2 日目以内に発現した有害事象のみが含まれている。
引用元：5.3.5.1.2 A53042/Table 14.3.1/23、Table 14.3.1/46

2.7.6.2.2.3.2.3　治験薬投与終了後 3 日目以降に発現した有害事象

治験薬投与終了後 3 日目以降に発現した有害事象の発現頻度はリバーロキサバン群及びエノキサパリン／VKA 群共に同頻度（13.8%）であった。器官別大分類別では、エノキサパリン／VKA 群に比べリバーロキサバン群の発現頻度が数値上高かったのは、「感染症および寄生虫症」（リバーロキサバン群：3.3%、エノキサパリン／VKA 群：3.0%）並びに「臨床検査」（1.0%、0.7%）であった。エノキサパリン／VKA 群の発現頻度が数値上高かったのは「一般・全身障害および投与部位の状態」であった（2.0%、2.4%）（5.3.5.1.2 A53042/Table 14.3.1/9）。

治験薬投与終了後 3 日目以降に発現した治験薬との因果関係が否定できない有害事象の発現例数は、リバーロキサバン群で 33 例（1.4%）、エノキサパリン／VKA 群で 40 例（1.7%）であった（5.3.5.1.2 A53042/Table 14.3.1/11）。「代謝および栄養障害」（鉄欠乏 1 件）及び「筋骨格系および結合組織障害」（四肢痛 3 件）がリバーロキサバン群で認められ、一方「耳および迷路障害」（耳出血 1 件）及び「生殖系および乳房障害」（月経過多及び腟出血各 1 件、不正子宮出血 2 件）はエノキサパリン／VKA 群のみで認められた。

2.7.6.2.2.3.3　有害事象の部分集団解析

予定投与期間、性別、地域、年齢グループ及びベースライン時の活動性悪性腫瘍の有無を部分集団として、TEAE 及び出血関連有害事象〔治験責任（分担）医師の報告〕を除く TEAE の解析を行なった。

出血関連有害事象〔治験責任（分担）医師の報告〕を含む含まないにかかわらず、すべての部分集団別の TEAE の発現頻度の結果は TEAE 全体の結果と同様であった（5.3.5.1.2 A53042/Table 14.3.1/2～Table 14.3.1/6）。

予定投与期間が 3 ヵ月、6 ヵ月、12 ヵ月の各コホート間、2 つの年齢グループ（60 歳未満と 60 歳以上）間の発現頻度について顕著な差は認められなかった（5.3.5.1.2 A53042/Table 14.3.1/2、Table 14.3.1/5）。

性別では、女性で TEAE が 83.1～83.8%、出血関連有害事象〔治験責任（分担）医師の報告〕を除く TEAE が 79.8～79.9%、男性でそれぞれ 75.2～77.4%、71.9～74.1%であり、いずれも女性で高かった（5.3.5.1.2 A53042/Table 14.3.1/3）。

地域別での TEAE と出血関連有害事象〔治験責任（分担）医師の報告〕の発現頻度は、西ヨーロッパ（2,614 例）や東ヨーロッパ（416 例）が 71.3～80.6%であるのと比較し、オーストラリア/ニュージーランド（612 例）で 88.3%～93.1%と数値上高く、北アメリカで（483 例）で 62.3～68.2%と数値上低かった。南アメリカ、アジア、イスラエル、南アフリカでは被験者数が 18～283 例と少なかったため、TEAE と出血関連有害事象〔治験責任（分担）医師の報告〕の比較結果が示せなかった（5.3.5.1.2 A53042/Table 14.3.1/4）。

ベースライン時に活動性悪性腫瘍を有した被験者での TEAE はエノキサパリン／VKA 群（85.2%）と比較しリバーロキサバン群（89.5%）でわずかに高かった。しかし、表 2.7.6.2-8に示すように、ベースライン時に活動性悪性腫瘍を有する被験者数は少なかった（4.6%）。ベースライン時に活動性悪性腫瘍を有さなかった被験者での TEAE の発現頻度は、出血関連有害事象〔治験責任（分担）医師の報告〕を含む含まないにかかわらず両投与群間で同様であった（5.3.5.1.2 A53042/Table 14.3.1/6）。

2.7.6.2.2.3.4　死亡

死亡原因は CIAC によって判定された。

安全性解析対象集団において 114 例の死亡が報告された（表 2.7.6.2- 28）。死亡の発現頻度は数値上、エノキサパリン／VKA 群（2.1%、51/2,405 例）よりもリバーロキサバン群（2.6%、63/2,412 例）で高かった。CIAC 判定による死亡理由で両投与群に多かったものは、悪性腫瘍〔リバーロキサバン群: 0.9%（22/2,412 例）、エノキサパリン／VKA 群：1.0%（23/2,405 例）〕、感染症〔0.4%（9/2,412 例）、0.2%（6/2,405 例）〕、PE の可能性が否定できない原因不明の死亡〔0.3%（8/2,412 例）、0.2%（6/2,405 例）〕及び出血〔0.2%（5/2,412 例）、0.2%（4/2,405 例）〕であった。

表 2.7.6.2- 28 無作為割り付け後の死因別の死亡（安全性解析対象集団）

死因（CIAC 判定）	リバーロキサバン N=2412（100%）	エノキサパリン／VKA N=2405（100%）
全事象	63 （ 2.6%）	51 （ 2.1%）
判定なし [a]	0 （ 0.0%）	1 （ ＜0.1%）
肺塞栓症	3 （ 0.1%）	1 （ ＜0.1%）
出血	5 （ 0.2%）	4 （ 0.2%）
悪性腫瘍	22 （ 0.9%）	23 （ 1.0%）
敗血症	2 （ ＜0.1%）	0 （ 0.0%）
多臓器不全	1 （ ＜0.1%）	0 （ 0.0%）
PE の可能性が否定できない原因不明の死亡	8 （ 0.3%）	6 （ 0.2%）
心筋梗塞	2 （ ＜0.1%）	1 （ ＜0.1%）
虚血性脳卒中	2 （ ＜0.1%）	1 （ ＜0.1%）
その他の心血管事象	3 （ 0.1%）	0 （ 0.0%）
感染症	9 （ 0.4%）	6 （ 0.2%）
心不全	5 （ 0.2%）	0 （ 0.0%）
その他の心臓死	0 （ 0.0%）	1 （ ＜0.1%）
その他の呼吸不全	0 （ 0.0%）	3 （ 0.1%）
悪液質	0 （ 0.0%）	1 （ ＜0.1%）
炎症性疾患	1 （ ＜0.1%）	0 （ 0.0%）
筋萎縮性側索硬化症	0 （ 0.0%）	1 （ ＜0.1%）
多発性外傷	0 （ 0.0%）	1 （ ＜0.1%）
高齢	0 （ 0.0%）	1 （ ＜0.1%）

CIAC：中央独立判定委員会、VKA：ビタミン K 拮抗薬、PE：肺塞栓症
治験責任医師によって転帰が死亡と判断された有害事象が複数発現した被験者も含む。転帰が死亡であるすべての有害事象を含む。
a：判定なしの取り扱いは 5.3.5.1.2 A53042/Table 16.1.9.3/55、Section 16.1.9.3.b に示す。
引用元：5.3.5.1.2 A53042/Table 16.1.9.3/57、Section 16.1.9.3.b

治験薬投与下で発現した死亡例は 48 例であり、エノキサパリン／VKA 群〔0.8%（20/2,405 例）〕に比べ、リバーロキサバン群〔1.2%（28/2,412 例）〕で高かった。両投与群において死亡原因のうち頻度が高かった上位 3 つは、癌〔リバーロキサバン群：0.4%（10/2,412 例）、エノキサパリン／VKA 群：0.2%（4/2,405 例）〕、PE の可能性が否定できない原因不明の死亡〔0.3%（8/2,412 例）、0.2%（5/2,405 例）〕、感染性疾患〔0.1%未満（2/2,412 例）、0.2%（4/2,405 例）〕であった（5.3.5.1.2/A53042 Table 14.3.1/54）。

死亡例に関する詳細情報は付表 2.7.6.2- 2 に示す。

2.7.6.2.2.3.5 重篤な有害事象

2.7.6.2.2.3.5.1 重篤な TEAE

いずれかの投与群で発現頻度が器官別大分類別で 1%以上である重篤な TEAE を表 2.7.6.2- 29 に示す。

重篤な TEAE の発現頻度は、リバーロキサバン群 19.5%、エノキサパリン／VKA 群 19.3%で同程度であった。重篤な TEAE で頻度が高かった事象は、胸痛（リバーロキサバン群: 0.8%、エノ

キサパリン／VKA 群：1.1%）、貧血（0.5%、0.2%）、肺炎（0.8%、0.8%）、虚血性脳卒中（0.5%、0.2%）であった（5.3.5.1.2 A53042/Table 14.3.1/28）。

表 2.7.6.2- 29　重篤な TEAE の発現頻度（いずれかの投与群で 1%以上、安全性解析対象集団）

MedDRA 器官別大分類	リバーロキサバン N=2412 (100%)	エノキサパリン／VKA N=2405 (100%)
全事象	471 (19.5%)	463 (19.3%)
心臓障害	56 (2.3%)	58 (2.4%)
胃腸障害	55 (2.3%)	56 (2.3%)
一般・全身障害および投与部位の状態	45 (1.9%)	43 (1.8%)
感染症および寄生虫症	72 (3.0%)	69 (2.9%)
傷害、中毒および処置合併症	29 (1.2%)	35 (1.5%)
臨床検査	22 (0.9%)	31 (1.3%)
筋骨格系および結合組織障害	34 (1.4%)	37 (1.5%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	63 (2.6%)	62 (2.6%)
神経系障害	44 (1.8%)	35 (1.5%)
腎および尿路障害	19 (0.8%)	25 (1.0%)
呼吸器、胸郭および縦隔障害	74 (3.1%)	74 (3.1%)

MedDRA：ICH 国際医薬用語集、VKA：ビタミン K 拮抗薬
MedDRA version 14.1
TEAE とは、無作為割り付け後から治験薬投与終了後 2 日目までに発現した有害事象とする。
引用元：5.3.5.1.2 A53042/Table 14.3.1/28

治験薬との因果関係が否定できない重篤な TEAE の発現頻度は、エノキサパリン／VKA 群〔4.9%（118/2,405 例）〕よりリバーロキサバン群〔4.6%（112/2,412 例）〕のほうが低かった（5.3.5.1.2 A53042/Table 14.3.1/33）。器官別大分類別でリバーロキサバン群が低かったのは、「胃腸障害」〔リバーロキサバン群：24 例（1.0%）、エノキサパリン／VKA 群：31 例（1.3%）〕、「傷害、中毒および処置合併症」〔5 例（0.2%）、13 例（0.5%）〕、「筋骨格系および結合組織障害」〔1 例（＜1.0%）、10 例（0.4%）〕、「臨床検査」〔12 例（0.5%）、17 例（0.7%）〕及び「腎および尿路障害」〔8 例（0.3%）、11 例（0.5%）〕であった。これらの差に影響していた主な事象（基本語）は、メレナ（0.1%未満、0.2%）、筋肉内出血（0.1%未満、0.4%）、INR 増加（0.1%未満、0.2%）、肝機能検査異常（0.1%未満、0.2%）であった。

治験薬との因果関係が否定できない重篤な TEAE の発現頻度は、器官別大分類別の「生殖系および乳房障害」（基本語別では月経過多、不正子宮出血及び膣出血）ではリバーロキサバン群で高かった（リバーロキサバン群：0.7%、エノキサパリン／VKA 群：0.2%）。「血液およびリンパ系障害」（基本語別では貧血）でも、リバーロキサバン群で高かった〔リバーロキサバン群：7 例（0.3%）、エノキサパリン／VKA 群：2 例（0.1%未満）〕。

MedDRA 器官別大分類／基本語で分類した両投与群の治験薬との因果関係が否定できない重篤な TEAE の発現頻度の差異は、すべて 1%以下であった。

2.7.6.2.2.3.5.2 治験薬投与終了後3日目以降に発現した重篤な有害事象

治験薬投与終了後 3 日目以降に発現した重篤な有害事象の発現頻度は、リバーロキサバン群 2.8%、エノキサパリン／VKA 群 3.1%であった。投与群間の差が認められた器官別大分類は、「感染症および寄生虫症」（リバーロキサバン群：0.7%、エノキサパリン／VKA 群：0.4%）であった（5.3.5.1.2 A53042/Table 14.3.1/13）。リバーロキサバン群ではエノキサパリン／VKA 群（敗血症 0.1%未満、急性呼吸不全 0.2%）に比べ敗血症（0.2%）の発現頻度が高く、急性呼吸不全（0%）の発現頻度が低かった。他の個々の事象の発現頻度は非常に低く、投与群間の差について臨床的に意味のある評価はできなかった。

治験薬投与終了後 3 日目以降に治験薬との因果関係が否定できない重篤な有害事象が発現したのは 7 例であった〔リバーロキサバン群：1 例（0.1%未満）、エノキサパリン／VKA 群：6 例（0.2%）〕（5.3.5.1.2 A53042/Table 14.3.1/15）。リバーロキサバン群の 1 例では貧血が認められ、エノキサパリン／VKA 群では、貧血、メレナ、後腹膜出血、処置後出血、不正子宮出血、喀血及び動脈出血が認められた（5.3.5.1.2 A53042/Table 14.3.1/15）。

2.7.6.2.2.3.6 治験薬の投与中止に至った有害事象

リバーロキサバン群の 5.1%及びエノキサパリン／VKA 群の 4.1%の被験者が有害事象によって治験薬を中止した。器官別大分類別で頻度の高かった有害事象は、「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）」（リバーロキサバン群：0.8%、エノキサパリン／VKA 群：1.0%）、「胃腸障害」（0.7%、0.5%）、「呼吸器、胸郭および縦隔障害」（0.5%、0.4%）、「神経系障害」（0.5%、0.3%）、「皮膚および皮下組織障害」（0.5%、0.2%）、「傷害、中毒および処置合併症」（0.2%、0.5%）であった（表 2.7.6.2- 30）。治験薬の投与中止に至った有害事象で頻度の高い上位 5 事象は、貧血〔リバーロキサバン群：6 例（0.2%）、エノキサパリン／VKA 群：2 例（0.1%未満）〕、虚血性脳卒中〔6 例（0.2%）、0 例（0.0%）〕、直腸出血〔4 例（0.2%）、2 例（0.1%未満）〕、発疹〔4 例（0.2%）、1 例（0.1%未満）〕、胸水〔0 例（0.0%）、4 例（0.2%）〕であった（5.3.5.1.2 A53042 Table 14.3.1/35）。

表 2.7.6.2- 30　治験薬の投与中止に至った有害事象（いずれかの投与群で 5 例以上、安全性解析対象集団）

MedDRA 器官別大分類／基本語	リバーロキサバン N=2412 (100%)	エノキサパリン／VKA N=2405 (100%)
全事象	123 (5.1%)	99 (4.1%)
血液およびリンパ系障害	8 (0.3%)	6 (0.2%)
貧血	6 (0.2%)	2 (＜0.1%)
心臓障害	7 (0.3%)	5 (0.2%)
胃腸障害	18 (0.7%)	12 (0.5%)
一般・全身障害および投与部位の状態	6 (0.2%)	3 (0.1%)
傷害、中毒および処置合併症	5 (0.2%)	12 (0.5%)
臨床検査	10 (0.4%)	5 (0.2%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	19 (0.8%)	24 (1.0%)
神経系障害	12 (0.5%)	8 (0.3%)
虚血性脳卒中	6 (0.2%)	0
腎および尿路障害	5 (0.2%)	4 (0.2%)
呼吸器、胸郭および縦隔障害	11 (0.5%)	9 (0.4%)
皮膚および皮下組織障害	12 (0.5%)	5 (0.2%)

MedDRA：ICH 国際医薬用語集、VKA：ビタミン K 拮抗薬
引用元：5.3.5.1.2 A53042/Table 14.3.1/35

2.7.6.2.2.3.7　出血事象

2.7.6.2.2.3.7.1　安全性主要評価項目

本試験の安全性主要評価項目は、「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイントであった。出血事象の「治験薬投与下で発現した」とする期間の定義は、無作為割り付けから治験薬投与終了後 2 日目までとした。出血事象（疑い）は有害事象又は重篤な有害事象として報告され、CIAC により「重大な出血事象」、「重大ではないが臨床的に問題となる出血事象」、「軽微な出血事象」、又は「出血事象ではない」に分類された。

安全性解析対象集団における、治験薬投与下で初回に発現した出血事象の要約を表 2.7.6.2-31に示す。

安全性解析対象集団において、治験薬投与下で初回に発現した安全性主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイント）の発現頻度は、リバーロキサバン群 10.3％（249/2,412 例）、エノキサパリン／VKA 群 11.4％(274/2,405 例）で同様であった。

表 2.7.6.2- 31　治験薬投与下で初回に発現した安全性主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）の発現頻度の部位別内訳（安全性解析対象集団）

安全性評価項目	リバーロキサバン (N＝2412)	エノキサパリン／VKA (N＝2405)
「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」のいずれか	249 (10.3%)	274 (11.4%)
重大な出血事象	21 (0.9%)	47 (2.0%)
致死的出血事象	2 (＜0.1%)	3 (0.1%)
頭蓋内	2 (＜0.1%)	2 (＜0.1%)
後腹膜	0 (0.0%)	1 (＜0.1%)
重要な臓器の非致死的出血事象	6 (0.2%)	23 (1.0%)
頭蓋内	1 (＜0.1%)	9 (0.4%)
後腹膜	1 (＜0.1%)	5 (0.2%)
眼内	2 (＜0.1%)	2 (＜0.1%)
心臓周囲	0 (0.0%)	2 (＜0.1%)
関節内	0 (0.0%)	3 (0.1%)
肺	1 (＜0.1%)	0 (0.0%)
腹部	1 (＜0.1%)	2 (＜0.1%)
重要な臓器以外の非致死的出血事象（2g/dL 以上のヘモグロビン減少、又は 2 単位以上の輸血）	13 (0.5%)	20 (0.8%)
手術部位	0 (0.0%)	3 (0.1%)
皮膚（注射部位以外）	1 (＜0.1%)	2 (＜0.1%)
泌尿生殖器	1 (＜0.1%)	1 (＜0.1%)
消化管	6 (0.2%)	13 (0.5%)
鼻	1 (＜0.1%)	0 (0.0%)
投与/採血部位	0 (0.0%)	1 (＜0.1%)
子宮	3 (0.1%)	0 (0.0%)
肺	1 (＜0.1%)	0 (0.0%)
筋肉内	0 (0.0%)	1 (＜0.1%)
その他規定した重大な出血	0 (0.0%)	1 (＜0.1%)
直腸[a]	0 (0.0%)	1 (＜0.1%)

表 2.7.6.2- 31　治験薬投与下で初回に発現した安全性主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）の発現頻度の部位別内訳（安全性解析対象集団）（続き）

安全性評価項目	リバーロキサバン (N＝2412)		エノキサパリン／VKA (N＝2405)	
重大ではないが臨床的に問題となる出血事象	228	(9.5%)	227	(9.4%)
手術部位	4	(0.2%)	9	(0.4%)
皮膚（注射部位以外）	21	(0.9%)	33	(1.4%)
泌尿生殖器	48	(2.0%)	55	(2.3%)
消化管	37	(1.5%)	12	(0.5%)
歯肉	2	(＜0.1%)	0	(0.0%)
鼻	43	(1.8%)	39	(1.6%)
直腸	23	(1.0%)	21	(0.9%)
投与/採血部位	1	(＜0.1%)	10	(0.4%)
関節内[b]	3	(0.1%)	0	(0.0%)
気管	7	(0.3%)	6	(0.2%)
結膜	0	(0.0%)	4	(0.2%)
耳	0	(0.0%)	2	(＜0.1%)
子宮	37	(1.5%)	25	(1.0%)
咽頭	1	(＜0.1%)	0	(0.0%)
肺	2	(＜0.1%)	2	(＜0.1%)
筋肉内	0	(0.0%)	7	(0.3%)
脚	0	(0.0%)	1	(＜0.1%)
胸膜	1	(＜0.1%)	1	(＜0.1%)
胸部	0	(0.0%)	1	(＜0.1%)
甲状腺	0	(0.0%)	1	(＜0.1%)

VKA：ビタミン K 拮抗薬

被験者の初回に発現した出血事象の出血部位が 2 つ以上の場合、出血したすべての部位にカウントした。

a:当該被験者は 2g/dL を超えるヘモグロビン減少及び 2 単位を超える輸血を伴う消化管出血が発現したが、ヘモグロビン低下及び輸血情報はデータベースに入れられず、出血部位分類は「消化管」に訂正しなかった。

b:有害事象の性質によって、「重大な出血事象」と判断されなかった。

引用元：5.3.5.1.2 A53042/Table 14.3.1/63

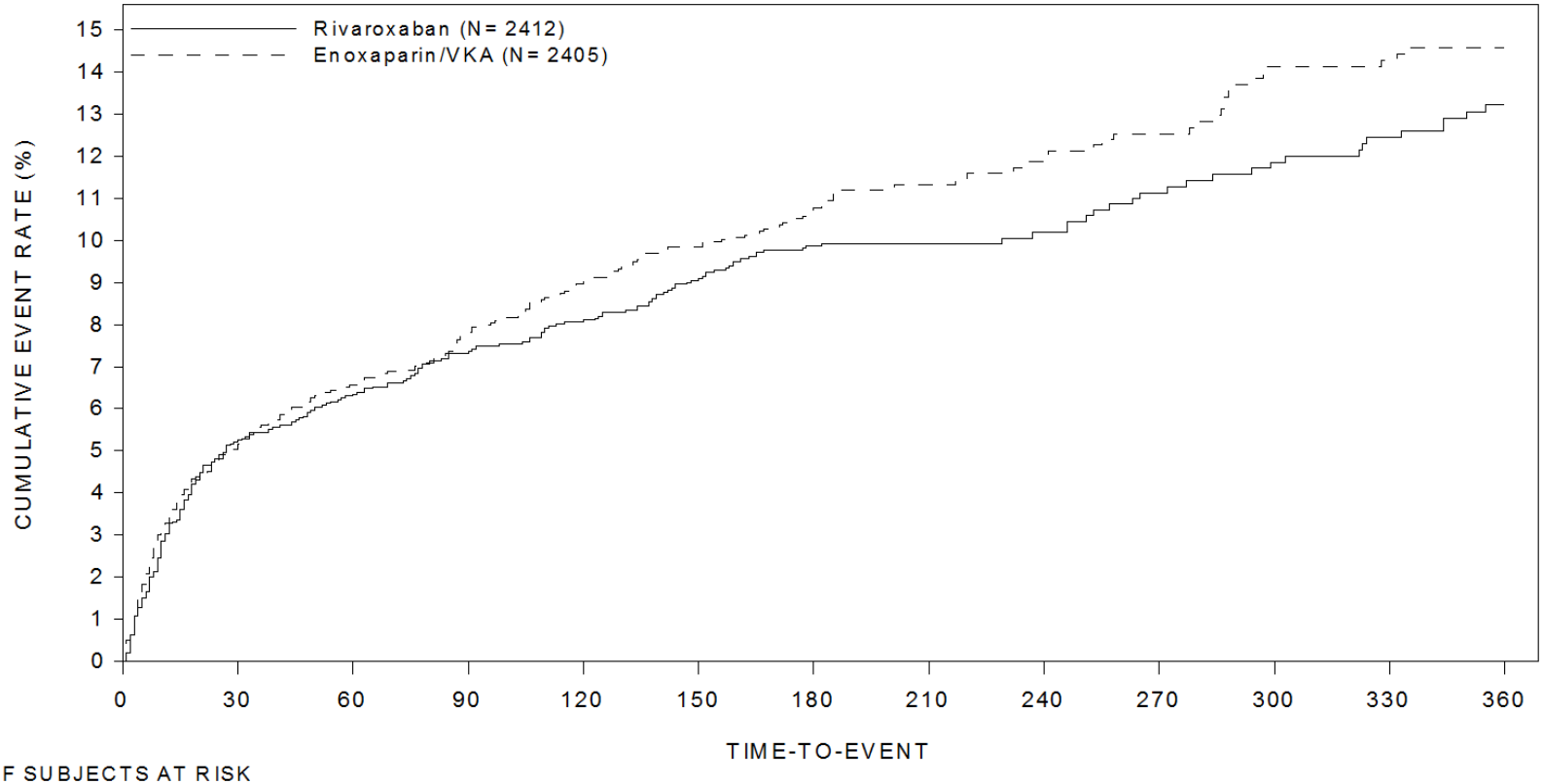
両投与群における安全性主要評価項目の発現頻度は同程度であり、ハザード比（リバーロキサバン群対エノキサパリン／VKA 群）は 0.900（95%信頼区間：0.758～1.069、優越性に関する p 値：0.2305）であった（表 2.7.6.2- 32）。

表 2.7.6.2- 32　治験薬投与下で発現した出血事象の発現頻度及び Cox 比例ハザードモデルでの解析結果（安全性解析対象集団）

評価項目	リバーロキサバン[a] (N＝2412)	エノキサパリン／VKA 群 (N＝2405)	ハザード比	95% 信頼区間	p 値[b]
安全性主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）	249 (10.3%)	274 (11.4%)	0.900	0.758～ 1.069	0.2305
重大な出血事象	26 (1.1%)	52 (2.2%)	0.493	0.308～ 0.789	0.0032
全出血事象	757 (31.4%)	774 (32.2%)			

VKA：ビタミン K 拮抗薬
p 値及びハザード比の推定値は、予定投与期間を層別因子としベースライン時の活動性悪性腫瘍の有無で調整した層別 Cox 比例ハザードモデルに基づいた。
無作為割り付けから治験薬の投与終了後 2 日目までに発現した事象。
a：リバーロキサバン投与スケジュール：15mg 1 日 2 回 3 週間、続いて 20mg 1 日 1 回
b：名目上の p 値、多重性の調整は行なわなかった。
引用元： 5.3.5.1.2 A53042/Table 14.3.1/63、Table 14.3.1/99、Table 14.3.1/132、Table 14.3.1/135

Kaplan-Meier 法による、安全性主要評価項目の出血事象の累積イベント発現率を投与群ごとに図 2.7.6.2- 5に示す。全体的に、安全性主要評価項目について、投与群間に差は認められなかった。



NUMBER OF SUBJECTS AT RISK

Rivaroxaban	N=2412	N=2183	N=2133	N=2024	N=1953	N=1913	N=1211	N=696	N=671	N=632	N=600	N=588	N=313
Enoxaparin/VKA	N=2405	N=2184	N=2115	N=1990	N=1923	N=1887	N=1092	N=687	N=660	N=620	N=589	N=574	N=251

引用元：5.3.5.1.2 A53042/Figure 14.3.1/13

図 2.7.6.2- 5　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）の Kaplan-Meier 法による累積イベント発現率（安全性解析対象集団）

2.7.6.2.2.3.7.2　　重大な出血事象

治験薬投与下の「重大な出血事象」の発現頻度はエノキサパリン／VKA 群（2.2%、52/2,405 例）よりリバーロキサバン群（1.1%、26/2,412 例）で低かった（ハザード比：0.493、95%信頼区間：0.308～0.789、優越性に関する p 値：0.0032）（表 2.7.6.2- 32）。

表 2.7.6.2- 33に示すとおり、「重大な出血事象」は、「致死的出血事象」、「重要な臓器の非致死的出血事象」及び「重要な臓器以外の非致死的出血事象」から構成された。

「致死的出血事象」、「重要な臓器の非致死的出血事象」及び「重要な臓器以外の非致死的出血事象」の区分を通して、「重大な出血事象」の発現頻度は一貫してリバーロキサバン群で低かった。両投与群共に「重大な出血事象」で最も多いのは「重要な臓器以外の非致死的出血事象」の区分に属するものであった〔リバーロキサバン群：17 例（0.3%）、エノキサパリン／VKA 群：25 例（1.0%）〕。「重大な出血事象」の発現部位で頻度が高い（両投与群合せて 6 例以上）のは、消化管〔リバーロキサバン群：9 例（0.4%）、エノキサパリン／VKA 群：16 例（0.7%）〕、頭蓋内〔1 例（0.1%未満）、9 例（0.4%）〕、後腹膜〔1 例（0.1%未満）、7 例（0.3%）〕であった。

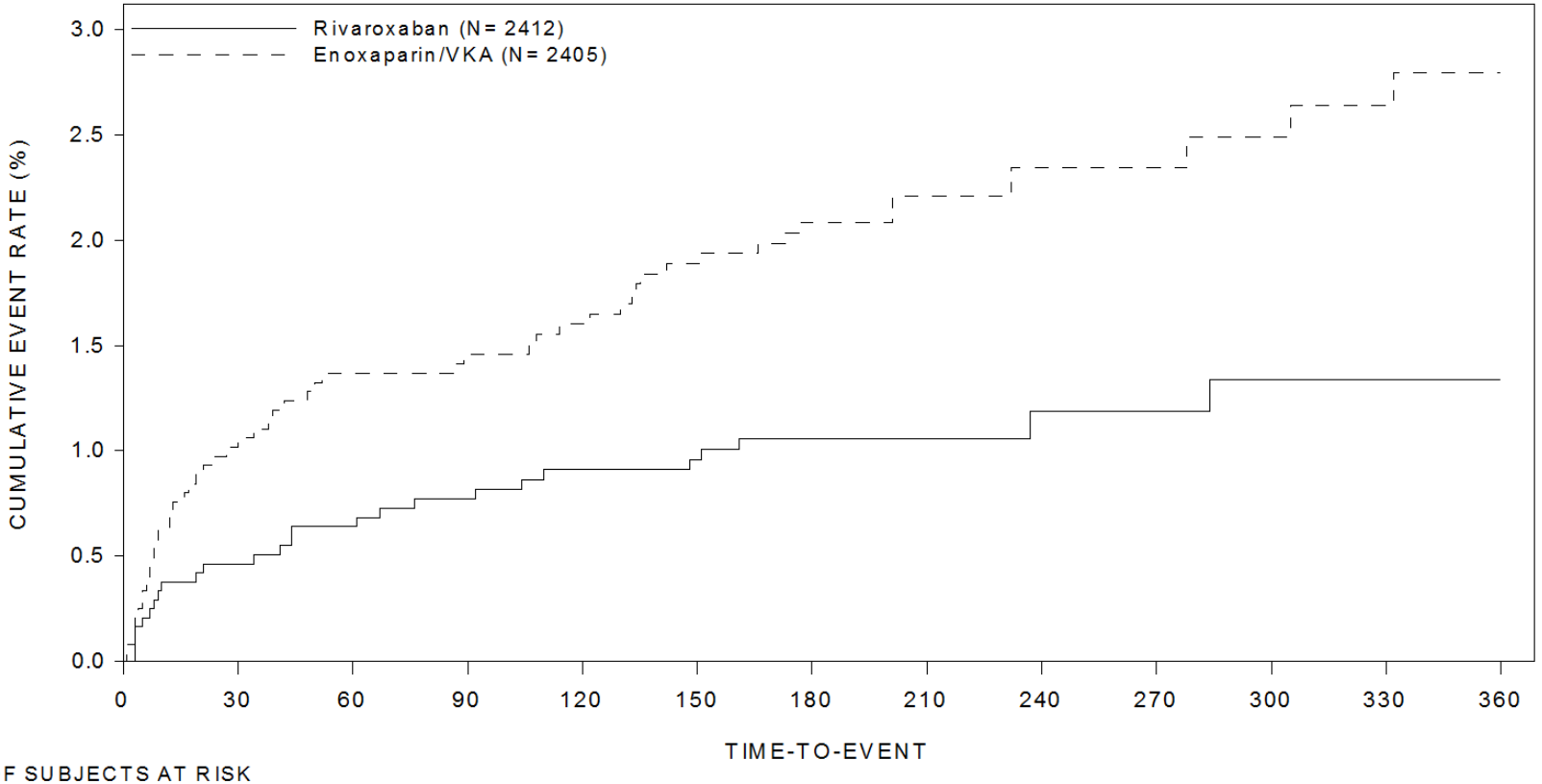
「重大な出血事象」が発現した被験者に関する叙述は 5.3.5.1.2 A53042/Section 15 に示す。

表 2.7.6.2- 33　治験薬投与下で発現した「重大な出血事象」（安全性解析対象集団）

出血事象	リバーロキサバン (N＝2412) n（%）	エノキサパリン／VKA (N＝2405) n（%）
重大な出血事象	26 （ 1.1%）	52 （ 2.2%）
- 致死的出血事象	2 （ <0.1%）	3 （ 0.1%）
頭蓋内	2 （ <0.1%）	2 （ <0.1%）
後腹膜	0 （ 0.0%）	1 （ <0.1%）
- 重要な臓器の非致死的出血事象	7 （ 0.3%）	26 （ 1.1%）
コード化されず	0 （ 0.0%）	1 （ <0.1%）
頭蓋内	1 （ <0.1%）	10 （ 0.4%）
後腹膜	1 （ <0.1%）	7 （ 0.3%）
眼内	2 （ <0.1%）	2 （ <0.1%）
心臓周囲	0 （ 0.0%）	2 （ <0.1%）
関節内	0 （ 0.0%）	3 （ 0.1%）
副腎	1 （ <0.1%）	0 （ 0.0%）
肺	1 （ <0.1%）	0 （ 0.0%）
腹部	1 （ <0.1%）	2 （ <0.1%）
- 重要な臓器以外の非致死的出血事象（Hb 減少 2 g/dL 以上及び／又は 2 単位以上の輸血）	17 （ 0.7%）	25 （ 1.0%）
手術部位	0 （ 0.0%）	3 （ 0.1%）
皮膚（注射部位以外）	1 （ <0.1%）	2 （ <0.1%）
泌尿生殖器	1 （ <0.1%）	1 （ <0.1%）
消化管	9 （ 0.4%）	16 （ 0.7%）
鼻	1 （ <0.1%）	0 （ 0.0%）
直腸	1 （ <0.1%）	0 （ 0.0%）
注射／採血部位	0 （ 0.0%）	1 （ <0.1%）
子宮	3 （ 0.1%）	0 （ 0.0%）
肺	1 （ <0.1%）	0 （ 0.0%）
筋肉内	0 （ 0.0%）	2 （ <0.1%）
腹部	0 （ 0.0%）	1 （ <0.1%）
- 他の特定された重大な出血事象	0 （ 0.0%）	1 （ <0.1%）
直腸 [a]	0 （ 0.0%）	1 （ <0.1%）

Hb：ヘモグロビン、VKA：ビタミン K 拮抗薬
治験薬投与下とは、無作為割り付けから治験薬の投与終了後 2 日目までの期間とした。 安全性解析対象集団の投与群は実投与に基づく（無作為化割り付けには基づいていない）。
a：この被験者では Hb 減少 2 g/dL 以上及び 2 単位以上の輸血を伴う消化管出血が発現したが、Hb 減少及び輸血の情報はデータベースに入力されず、また出血部位のコードも消化管に修正されなかった。
引用元： 5.3.5.1.2 A53042/Table 14.3.1/99

治験薬投与下に発現した「重大な出血事象」の累積イベント発現率を図 2.7.6.2- 6に示す。投与開始 2 週間後から投与終了まで投与群間に数値上の差が認められた。累積イベント発現率の初期の上昇はエノキサパリン群に比べリバーロキサバン群で穏やかであった。



NUMBER OF SUBJECTS AT RISK

Rivaroxaban	N=2412	N=2281	N=2248	N=2156	N=2091	N=2063	N=1317	N=761	N=735	N=700	N=669	N=659	N=350
Enoxaparin/VKA	N=2405	N=2270	N=2224	N=2116	N=2063	N=2036	N=1176	N=746	N=719	N=680	N=658	N=642	N=278

引用元： 5.3.5.1.2 A53042/Figure 14.3.1/1

図 2.7.6.2- 6　治験薬投与下で発現した「重大な出血事象」の Kaplan-Meier 法による累積イベント発現率（安全性解析対象集団）

2.7.6.2.2.3.7.3 重大ではないが臨床的に問題となる出血事象

「重大ではないが臨床的に問題となる出血事象」の発現頻度は、リバーロキサバン群で 9.5%（228/2,412 例）、エノキサパリン／VKA 群で 9.8%（235/2,405 例）で、両投与群で同程度であった（5.3.5.1.2 A53042/Table 14.3.1/99）。

報告頻度が高い出血部位でみると、リバーロキサバン群での発現頻度がより高かったのは、鼻〔リバーロキサバン群：1.9%（47/2,412 例）、エノキサパリン／VKA 群：1.7%（41/2,405 例）〕、子宮〔1.6%（38/2,412 例）、1.0%（25/2,405 例）〕、消化管〔1.6%（38/2,412 例）、0.7%（17/2,405 例）〕、直腸〔1.1%（27/2,412 例）、1.0%（24/2,405 例）〕であった。エノキサパリン／VKA 群での発現頻度がより高かったのは、泌尿生殖器〔2.2%（52/2,412 例）、2.5%（59/2,405 例）〕、皮膚（注射部位以外）〔1.0%（23/2,412 例）、1.5%（36/2,405 例）〕、注射／採血部位（0.1%未満（1/2,412 例）、0.4%（10/2,405 例）〕、筋肉内〔0%（0/2,412 例）、0.4%（9/2,405 例）〕であった。なお、CIAC が臨床所見に基づき「重大ではないが臨床的に問題となる出血事象」と判定した関節内「重要な臓器」はリバーロキサバン群で 3 件認められた。

2.7.6.2.2.3.7.4 軽微な出血事象

「重大な出血事象」及び「重大ではないが臨床的に問題となる出血事象」のいずれの基準にも合致しない臨床的な明らかな出血は CIAC により「軽微な出血事象」に分類された。

「軽微な出血事象」の発現頻度はリバーロキサバン群（25.1%）とエノキサパリン／VKA 群（25.4%）で同程度であり、発現頻度が高い出血部位は皮膚（注射部位以外）（リバーロキサバン群：9.2%、エノキサパリン／VKA 群：10.0%）、鼻（7.7%、6.9%）であった（5.3.5.1.2 A53042/Table 14.3.1/99）。投与群間の差が 1%を超えた出血事象は注射／採血部位のみであった〔1.1%（26/2,412 例）、4.0%（95/2,405 例）〕。

2.7.6.2.2.3.7.5 致死的出血

治験薬投与下に発現した出血事象のうち、致死的出血と判定されたのは 5 例であった（リバーロキサバン群：2 例、エノキサパリン／VKA 群：3 例）（表 2.7.6.2- 33）。リバーロキサバン群の 2 例（被験者 160083010 及び被験者 390013031）及びエノキサパリン／VKA 群の 2 例（被験者 160243029、被験者 160293078）では致死的な頭蓋内出血が発現した。エノキサパリン／VKA 群の 1 例（被験者 370023029）は後腹膜出血により死亡した。詳細は 5.3.5.1.2 A53042/Section 10.4.3.4.1 に示す。

なお、リバーロキサバン群の 1 例（被験者 280083032）及びエノキサパリン／VKA 群の 1 例（被験者 540193029）で致死的頭蓋内出血が発現したが、CIAC により治験薬投与下で発現した重大で非致死的な頭蓋内出血に分類され、死因は出血に分類された。詳細は 5.3.5.1.2 A53042/Section 10.4.3.4.1 に示す。

治験薬投与終了後の出血事象：治験薬投与終了後では 2 件の致死的出血が認められたが、いずれの被験者もリバーロキサバン群であった。被験者 160103012 の致死的頭蓋内出血は治験薬の投与終了後 13 日目に発現し、被験者 160153030 の下大静脈創部からの致死的心臓周囲出血（CIAC

判定による出血部位は後腹膜）は治験薬の投与終了後 3 日目に発現した。詳細は 5.3.5.1.2 A53042/Section 15 に示す。

2.7.6.2.2.3.7.6 頭蓋内出血

CIAC によって頭蓋内出血（致死的及び非致死的で重要な臓器出血）と判定された事象は 15 例にみられた（リバーロキサバン群：3 例及びエノキサパリン／VKA 群：12 例）。両投与群の頭蓋内出血の各 2 例は致死的事象であった（表 2.7.6.2- 33）。両投与群のいずれの事象も治験薬との因果関係が否定できないと判断された。

致死的頭蓋内出血 4 例：

- 外傷後の重度脳血腫 1 例：リバーロキサバン群
- 小脳内出血 1 例：リバーロキサバン群
- 頭蓋内出血 1 例：エノキサパリン／VKA 群
- 脳出血 1 例：エノキサパリン／VKA 群

他の非致死的頭蓋内出血 11 例：

- 硬膜下血腫 6 例：リバーロキサバン群 1 例、エノキサパリン／VKA 群 5 例
- 脳出血 3 例：全例エノキサパリン／VKA 群
- くも膜下出血 1 例：エノキサパリン／VKA 群
- 頭蓋内出血 1 例：エノキサパリン／VKA 群

治験薬投与終了後の事象として頭蓋内出血が 2 例あり、内訳はリバーロキサバン群 1 例（被験者 160103012）及びエノキサパリン／VKA 群 1 例（被験者 300073001）であった。頭蓋内出血が発現した被験者に関する詳細な叙述は 5.3.5.1.2 A53042/Section 15 に示す。

2.7.6.2.2.3.7.7 消化管出血

「重要な臓器以外の非致死的出血事象」のうち最もよくみられた臓器は消化管に関連するものであった。重大で非致死的な消化管（重要な臓器以外）出血の発現頻度はエノキサパリン／VKA 群（0.7%、16/2,405 例）に比べリバーロキサバン群（0.4%、9/2,412 例）で数値上低かった（表 2.7.6.2- 33）。エノキサパリン／VKA 群では 16 件すべてが治験責任（分担）医師により治験薬との因果関係が否定できないと判断され、一方リバーロキサバン群では 9 件中 6 件が治験薬との因果関係が否定できないと判断された（5.3.5.1.2 A53042/Section 10.4.3.4.1 参照）。

なお、治験薬投与下に発現した「重大ではないが臨床的に問題となる出血事象」と判定された消化管出血の発現頻度はエノキサパリン／VKA 群（0.5%、12/2,405 例）に比べリバーロキサバン群（1.5%、37/2,412 例）で高かった（表 2.7.6.2- 31）。

2.7.6.2.2.3.7.8 子宮出血

治験薬投与下に発現した「重大な出血事象」のうち、子宮出血の発現例数は、リバーロキサバン群で 3 例（被験者 140313066、被験者 400233005、被験者 460093053）、エノキサパリン／VKA 群で該当なしであった（表 2.7.6.2- 33）。ほかの 1 例（被験者 140373011）で重大な子宮出血が発現したが、治験薬投与終了後 3 日目以降の発現のため「治験薬投与下に発現」には分類されなかった（5.3.5.1.2 A53042/Table 14.3.2/5）。詳細は 5.3.5.1.2 A53042/Section 10.4.3.4.1 に示す。

全女性被験者において、すべての子宮出血の発現頻度は、リバーロキサバン群で 9.4%（104/1,105 例）、エノキサパリン／VKA 群で 6.5%（75/1,162 例）であった。また、「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の発現頻度は、リバーロキサバン群で 3.7%（41/1,105 例）、エノキサパリン／VKA 群で 2.2%（25/1,162 例）であった。

子宮出血のほとんどは 55 歳未満の被験者で観察され（リバーロキサバン群：95/104 件、エノキサパリン／VKA 群：68/75 件）、そのほとんどは治験薬との因果関係が否定できないと判断されたが（5.3.5.1.2 A53042/Table 14.3.1/27）、治験薬の投与中止に至ったものは少なかった（5.3.5.1.2 A53042/Table 14.3.1/36）。

2.7.6.2.2.3.7.9 安全性主要評価項目の部分集団解析

安全性主要評価項目（「重大な出血事象」及び「重大ではないが臨床的に問題となる出血事象」）において、性別、年齢、体重、ベースライン時の活動性悪性腫瘍の有無、予定投与期間、腎機能、施設別 VKA 投与の種類、抗凝固療法（薬理活性に基づく治療期間、治療の有無）の前治療、地域、事前に規定した危険因子、人種を含む因子を用いて部分集団解析を実施した。その結果を、図 2.7.6.2- 7、図 2.7.6.2- 8、表 2.7.6.2- 35及び 5.3.5.1.2 A53042 Table 14.3.1/142 に示す。

部分集団によっては出血事象発現例数が比較的少なく、そのためデータの判断は慎重に行なう必要がある。通常、事象の総数が 5 件を上回り両投与群共に事象が 1 件以上発現している場合に限り、ハザード比及び 95%信頼区間（漸近法に基づく）を示した。

ハザード比及び 95%信頼区間から、両投与群の安全性主要評価項目の発現頻度は事前に規定したすべての部分集団で同程度で、一貫性があることが示された。結果は以下のとおりであった：

- 活動性悪性腫瘍：ベースライン時に活動性悪性腫瘍を有する被験者での安全性主要評価項目の発現頻度は全体集団（リバーロキサバン群：10.3%、エノキサパリン／VKA 群：11.4%）に比べ、数値上リバーロキサバン群（12.3%）で高く、エノキサパリン／VKA 群（9.3%）で低かった。

- CL_{CR}：規定した 3 区分における安全性主要評価項目の発現頻度は投与群間で同程度であった。「重大な出血事象」の発現頻度は 3 区分のいずれにおいても、エノキサパリン／VKA 群に比べリバーロキサバン群が数値上低かった。

- 年齢：65 歳未満の部分集団での安全性主要評価項目の発現頻度は両投与群で同程度であった。65～75 歳及び 75 歳超の部分集団での発現頻度は、エノキサパリン／VKA 群に比べリバーロキサバン群で低かった。この不均質性は有意ではなかった（交互作用の p 値：0.39、

Gail と Simon の方法による質的交互作用の p 値：0.75）（5.3.5.1.2 A53042/Table 16.1.9.3/14）。また、「重大な出血事象」に関して、65 歳未満の部分集団での「重大な出血事象」の発現頻度は、エノキサパリン／VKA 群に比べリバーロキサバン群で数値上低かった。65～75 歳及び 75 歳超の部分集団での発現頻度は、エノキサパリン／VKA 群に比べリバーロキサバン群で数値上低かった。この交互作用は認められたが（交互作用の p 値：0.042）、Gail と Simon の方法による質的交互作用は認められなかった（p 値：0.75）（5.3.5.1.2 A53042/Table 16.1.9.3/15）。なお、リバーロキサバン群に比べエノキサパリン／VKA 群では加齢に伴う発現頻度の上昇（65～75 歳及び特に 75 歳超で）がより顕著であった。

- 特殊な被験者集団：年齢が 75 歳超、体重が 50kg 以下、もしくは CL_{CR}50mL/min 未満のいずれかに該当する被験者を特殊な被験者集団とした。この集団の安全性主要評価項目の発現頻度は、リバーロキサバン群 12.6%に対しエノキサパリン／VKA 群 16.8%である一方で、これらに該当しない被験者集団ではリバーロキサバン群 9.7%、エノキサパリン／VKA 群 10.1%であった（表 2.7.6.2- 35）。この特殊な被験者集団での「重大な出血事象」の発現頻度は、リバーロキサバン群 1.4%、エノキサパリン／VKA 群 5.0%である一方で該当しない被験者集団ではリバーロキサバン群 1.0%、エノキサパリン／VKA 群 1.5%であった（5.3.5.1.2 A53042/Table 14.3.1/142）。

- 予定投与期間：安全性主要評価項目の発現頻度はリバーロキサバン群でより低かったが、両投与群共に予定投与期間の長さに伴いわずかに上昇が認められた（3 ヵ月コホート：リバーロキサバン群 7.2%、エノキサパリン／VKA 群 10.7%、6 ヵ月コホート：それぞれ 9.3%、10.3%、12 ヵ月コホート：それぞれ 12.3%、13.2%）。

- PT-INR：エノキサパリン／VKA 群において、治験薬投与下で発現した「重大な出血事象」の発現頻度を出血事象発現時の PT-INR 別に表 2.7.6.2- 34に示す。「重大な出血事象」の数が少ないことを考慮する必要があるが、本解析から、「重大な出血事象」の発現頻度が最も低いのは PT-INR が目標範囲内の 2～3 での被験者であり（0.4%／3 人月）、一方、PT-INR が目標範囲を下回る 2.0 未満での発現頻度は 0.7%／3 人月、目標範囲を超える 3.0 超での発現頻度は更に高く、1.0%／3 人月であった。

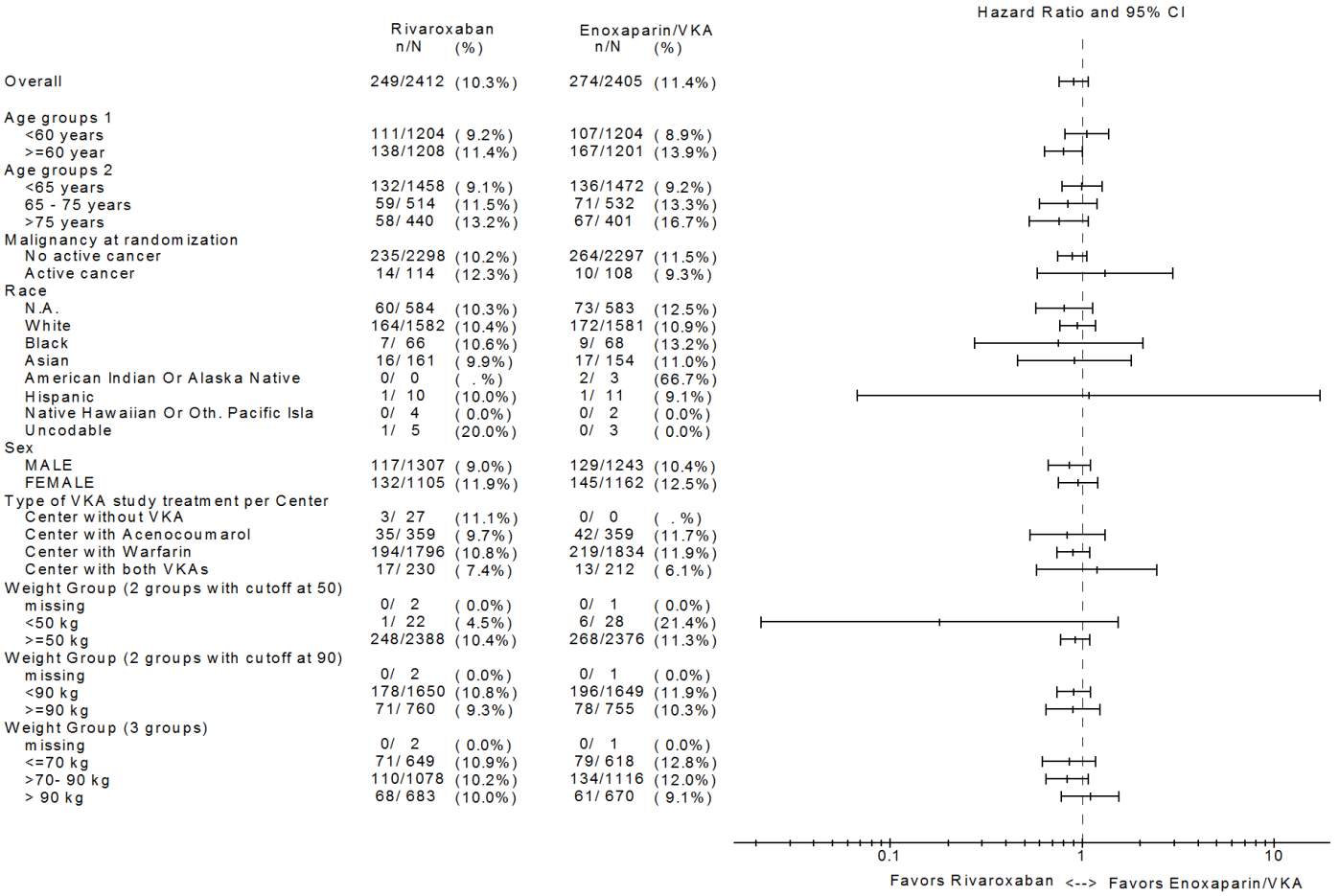
  施設 TTR は、各治験実施施設におけるエノキサパリン／VKA 群の TTR（欠測値ではない）の平均値と規定した。調整 TTR から算出した施設 TTR 値に基づき、施設をエノキサパリン／VKA 群の被験者がほぼ均等になるよう 3 つの部分集団（58.7%未満、58.7%～65.3%、65.3%を超える）に分類した。エノキサパリン／VKA 群では施設 TTR と安全性主要評価項目の発現頻度との間に関連は認められなかった（施設 TTR が 58.7%未満、58.7%～65.3%、65.3%を超える頻度はそれぞれ、10.50%、11.15%、12.56%）。3 区分におけるハザード比（リバーロキサバン：エノキサパリン／VKA）は全体でのハザード比 0.900 と同程度であった（5.3.5.1.2 A53042/Table 14.3.1/156）。

表 2.7.6.2- 34　発現時の PT-INR 別、治験薬投与下に発現した「重大な出血事象」の発現頻度（エノキサパリン/VKA 群、安全性解析対象集団）

	発現率		
PT-INR	／3 人月	発現例数／人年	1000 人年当たりの発現例数
＜2.0	0.7%	7 ／ 3107	2.3
2.0～3.0	0.4%	13 ／ 10040	1.3
＞3.0	1.0%	8 ／ 2313	3.5

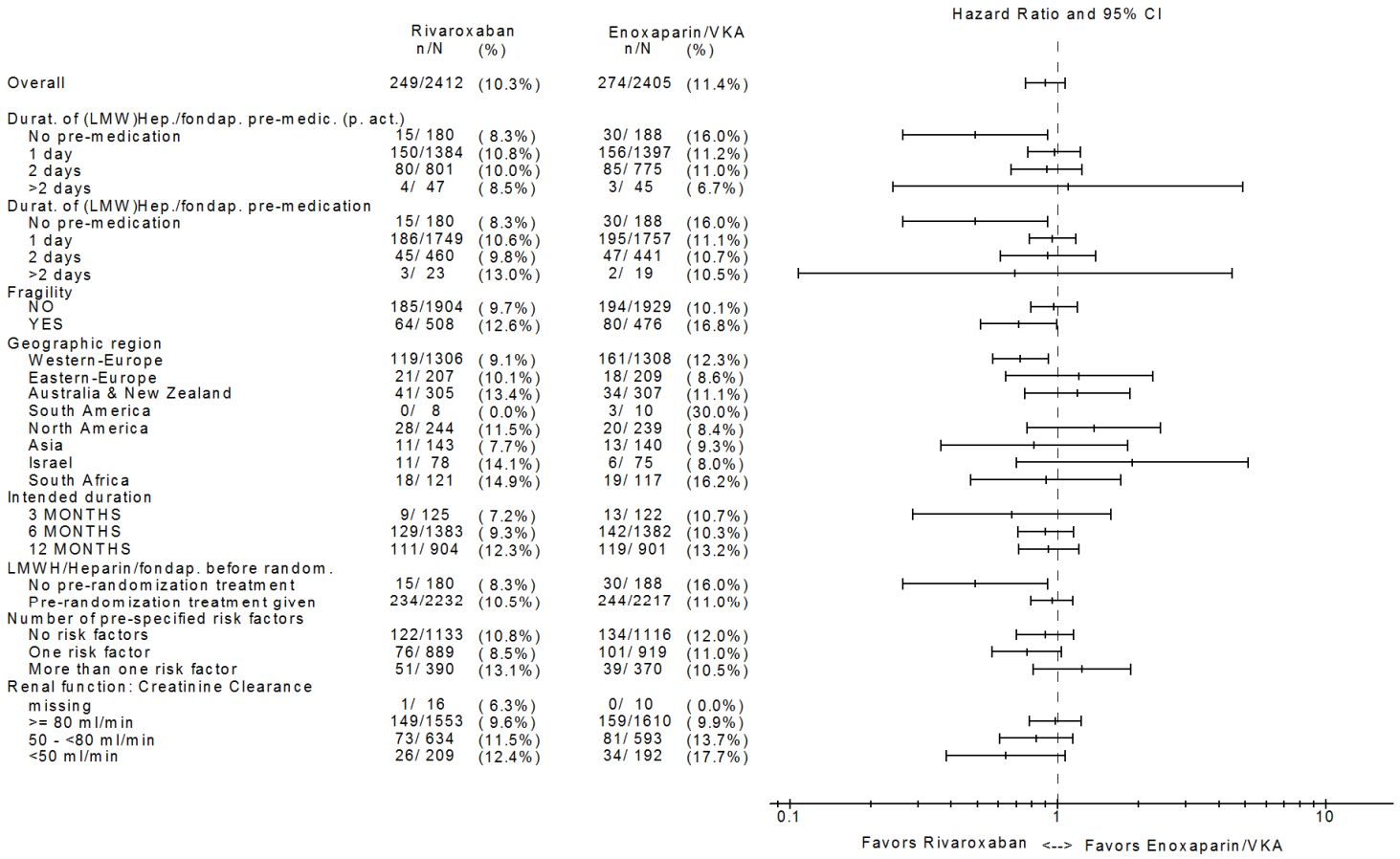
PT-INR：プロトロンビン時間国際標準比、VKA：ビタミン K 拮抗薬
低分子量ヘパリン（LMWH）の最初の投与中止日又はそれ以前に事象が発現した被験者は解析から除外した。人年は VKA 投与期間に基づく。事象発現例の VKA 投与対象期間は VKA 投与開始（VKA 開始後かつ最初の LMWH 中止後）から治験薬投与下で発現した「重大な出血事象」の初回発現（発現日含む、予定投与期間内）までとした。該当事象非発現例の対象期間は、VKA 投与開始から最終の出血連絡又は VKA 投与終了まで（期間の短い方、予定投与期間内）とした。PT-INR は事象発現日の測定値とした。測定値がない場合、直前の PT-INR（16 日以内の測定値）を使用した。
引用元： 5.3.5.1.2 A53042/Table 14.3.1/161

部分集団及び投与群間で統計学的に有意な質的交互作用は示されなかった。部分集団解析では、リバーロキサバン群においてエノキサパリン／VKA 群よりも高い出血リスクは示唆されなかった。ベースライン及び人口統計学的因子別の「重大な出血事象」のデータに関しては、総じてリバーロキサバンのほうが数値上低かった（表 2.7.6.2- 35）。



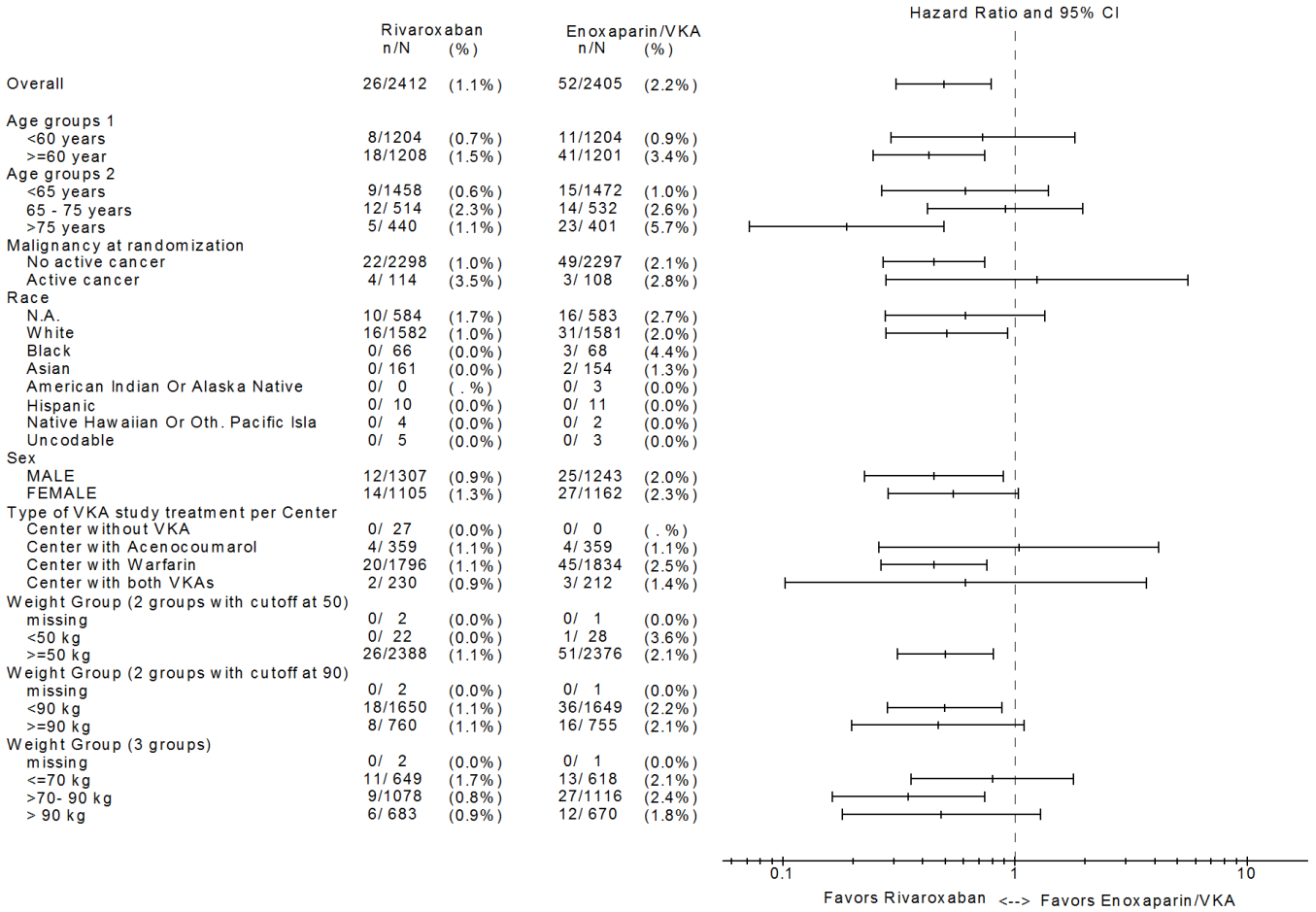
引用元： 5.3.5.1.2 A53042/Figure 14.3.1/39

図 2.7.6.2- 7　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（安全性解析対象集団）



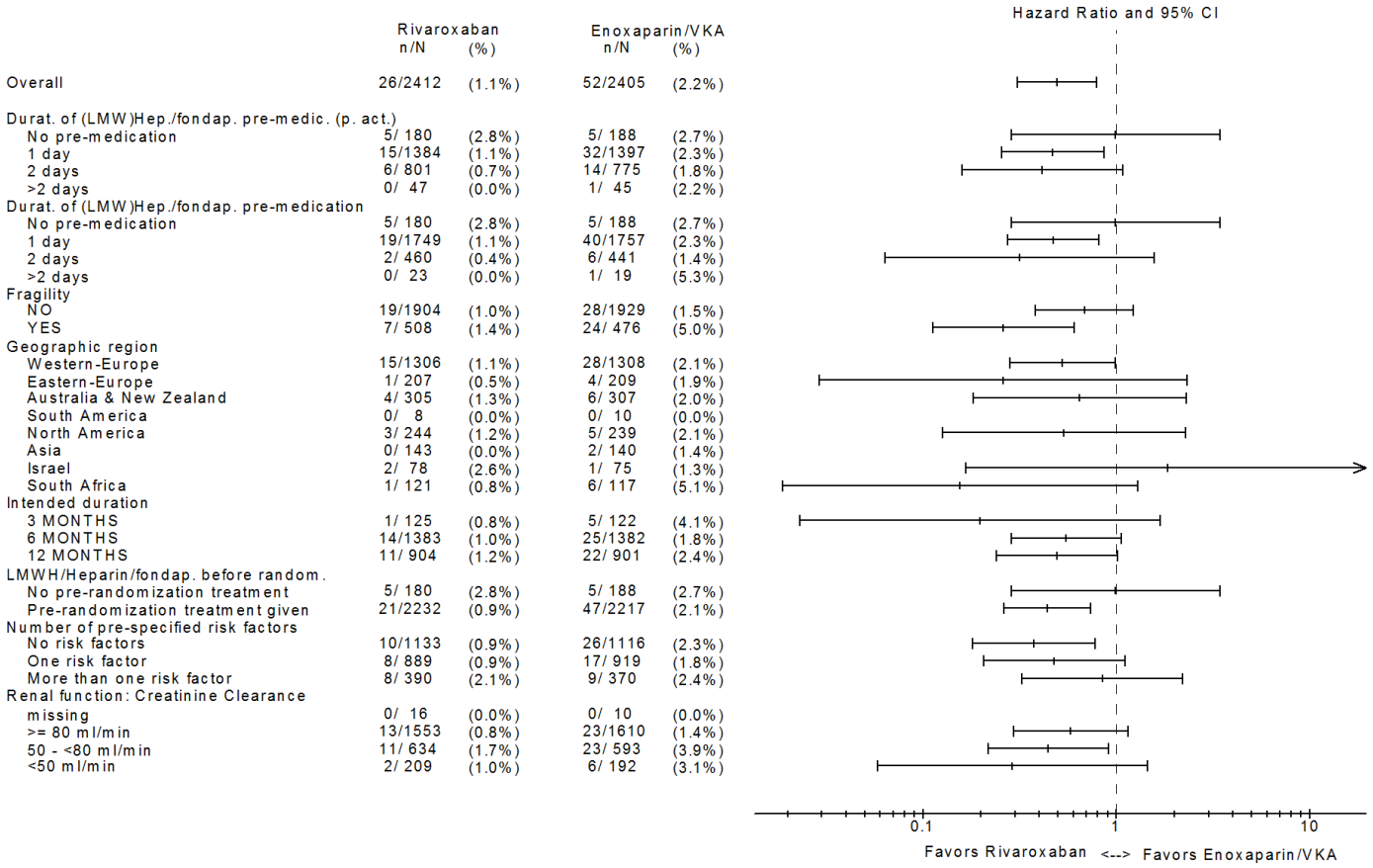
引用元： 5.3.5.1.2 A53042/Figure 14.3.1/40

図 2.7.6.2- 7　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（安全性解析対象集団）（続き）



引用元： 5.3.5.1.2 A53042/Figure 14.3.1/37

図 2.7.6.2- 8 治験薬投与下で発現した「重大な出血事象」のベースライン及び人口統計学的因子別解析（安全性解析対象集団）



引用元： 5.3.5.1.2 A53042/Figure 14.3.1/38

図 2.7.6.2- 8 治験薬投与下で発現した「重大な出血事象」のベースライン及び人口統計学的因子別解析（安全性解析対象集団）（続き）

表 2.7.6.2- 35　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（ 安全性解析対象集団）

因子	区分	発現頻度		ハザード比	ハザード比の95%信頼区間		交互作用のｐ値[a]
		リバーロキサバン	エノキサパリン/VKA		下限値	上限値	
年齢（区分1）	＜60歳	111/1204 （ 9.2%）	107/1204 （ 8.9%）	1.055	0.809	1.376	0.116
	≧60歳	138/1208 （ 11.4%）	167/1201 （ 13.9%）	0.798	0.637	1.000	
年齢（区分2）	＜65歳	132/1458 （ 9.1%）	136/1472 （ 9.2%）	0.995	0.783	1.264	0.387
	65～75歳	59/514 （ 11.5%）	71/532 （ 13.3%）	0.843	0.596	1.191	
	＞75歳	58/440 （ 13.2%）	67/401 （ 16.7%）	0.755	0.531	1.073	
予定投与期間	3ヵ月	9/125 （ 7.2%）	13/122 （ 10.7%）	0.674	0.288	1.576	0.759
	6ヵ月	129/1383 （ 9.3%）	142/1382 （ 10.3%）	0.901	0.710	1.144	
	12ヵ月	111/904 （ 12.3%）	119/901 （ 13.2%）	0.925	0.714	1.198	
活動性悪性腫瘍	なし	235/2298 （ 10.2%）	264/2297 （ 11.5%）	0.885	0.742	1.055	0.371
	あり	14/114 （ 12.3%）	10/108 （ 9.3%）	1.318	0.585	2.968	
人種	N.A.	60/584 （ 10.3%）	73/583 （ 12.5%）	0.806	0.573	1.135	ND
	白人	164/1582 （ 10.4%）	172/1581 （ 10.9%）	0.943	0.761	1.168	
	黒人	7/66 （ 10.6%）	9/68 （ 13.2%）	0.752	0.275	2.060	
	アジア人	16/161 （ 9.9%）	17/154 （ 11.0%）	0.908	0.459	1.797	
	アメリカンインディアン又はアラスカ先住民	0/0 （ 0.0%）	2/3 （ 66.7%）	.	.	.	
	ヒスパニック	1/10 （ 10.0%）	1/11 （ 9.1%）	1.080	0.067	17.305	
	ハワイ先住民又は太平洋諸島系	0/4 （ 0.0%）	0/2 （ 0.0%）	.	.	.	
	分類不能	1/5 （ 20.0%）	0/3 （ 0.0%）	.	.	.	

表 2.7.6.2- 35　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（ 安全性解析対象集団）（続き）

因子	区分	発現頻度		ハザード比	ハザード比の95%信頼区間		交互作用のｐ値[a]
		リバーロキサバン	エノキサパリン/VKA		下限値	上限値	
腎機能：CL_{CR}	欠測	1/16 (6.3%)	0/10 (0.0%)	.	.	.	.
	≧80mL/min	149/1553 (9.6%)	159/1610 (9.9%)	0.979	0.783	1.225	0.289
	50～＜80mL/min	73/634 (11.5%)	81/593 (13.7%)	0.831	0.606	1.141	
	＜50mL/min	26/209 (12.4%)	34/192 (17.7%)	0.638	0.382	1.064	
性別	男性	117/1307 (9.0%)	129/1243 (10.4%)	0.855	0.666	1.098	0.550
	女性	132/1105 (11.9%)	145/1162 (12.5%)	0.953	0.753	1.207	
体重（区分 1）	欠測	0/2 (0.0%)	0/1 (0.0%)	.	.	.	
	＜50kg	1/22 (4.5%)	6/28 (21.4%)	0.180	0.021	1.537	0.135
	≧50kg	248/2388 (10.4%)	268/2376 (11.3%)	0.917	0.771	1.089	
体重（区分 2）	欠測	0/2 (0.0%)	0/1 (0.0%)	.	.	.	
	＜90kg	178/1650 (10.8%)	196/1649 (11.9%)	0.901	0.735	1.104	0.997
	≧90kg	71/760 (9.3%)	78/755 (10.3%)	0.895	0.649	1.235	
体重（区分 3）	欠測	0/2 (0.0%)	0/1 (0.0%)	.	.	.	
	≦70kg	71/649 (10.9%)	79/618 (12.8%)	0.853	0.619	1.176	0.394
	＞70～90kg	110/1078 (10.2%)	134/1116 (12.0%)	0.834	0.648	1.074	
	＞90kg	68/683 (10.0%)	61/670 (9.1%)	1.099	0.777	1.554	

表 2.7.6.2- 35　安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」）のベースライン及び人口統計学的因子別解析（ 安全性解析対象集団）（続き）

因子	区分	発現頻度		ハザード比	ハザード比の95%信頼区間		交互作用のｐ値[a]
		リバーロキサバン	エノキサパリン/VKA		下限値	上限値	
（LMW）ヘパリン／フォンダパリヌクスの前治療	なし	15/180 （ 8.3%）	30/188 （ 16.0%）	0.492	0.264	0.915	0.043
	あり	234/2232 （ 10.5%）	244/2217 （ 11.0%）	0.951	0.794	1.137	
（LMW）ヘパリン／フォンダパリヌクスの前治療期間	なし	15/180 （ 8.3%）	30/188 （ 16.0%）	0.492	0.264	0.915	0.243
	1日間	186/1749 （ 10.6%）	195/1757 （ 11.1%）	0.956	0.782	1.169	
	2日間	45/460 （ 9.8%）	47/441 （ 10.7%）	0.917	0.609	1.381	
	＞2日間	3/23 （ 13.0%）	2/19 （ 10.5%）	0.692	0.107	4.470	
特殊な被験者集団[b]	いいえ	185/1904 （ 9.7%）	194/1929 （ 10.1%）	0.969	0.792	1.185	0.118
	はい	64/508 （ 12.6%）	80/476 （ 16.8%）	0.716	0.515	0.994	

VKA：ビタミンK拮抗薬、N.A.：利用不可能、 （LMW）ヘパリン：LMWHを含むヘパリン、CL_{CR}：クレアチニンクリアランス

ND：部分集団の少なくとも1つのカテゴリで治験薬投与中に事象の発現がなかったため、交互作用のｐ値は算出しなかった。

層別Cox比例ハザードモデルを用いた解析はカテゴリに少なくとも5事象あるときだけ実施した。予定投与期間で層別化し、ベースライン時の活動性悪性腫瘍の有無を共変量として各モデルに含めた。ベースライン時の活動性悪性腫瘍の有無別の解析においては、共変量としてモデルに含めなかった。予定投与期間毎の解析においては、層としてモデルに含めなかった。

a：交互作用に対するｐ値は投与群、投与群と部分集団の交互作用、ベースライン時の活動性悪性腫瘍の有無を含めたモデルで算出した。交互作用に対するｐ値は、ベースライン特性及び人口統計学的特性に関する記録が欠測のものを除いた。

b：被験者の年齢が75歳超、体重が50kg以下、もしくはCL_{CR}が50mL/min未満のいずれかに該当する被験者を特殊な被験者集団とした。

引用元：5.3.5.1.2 A53042/Table 14.3.1/143

2.7.6.2.2.3.7.10 出血事象に関する事後解析

本試験の治験総括報告書作成以降に出血事象に関する以下の事後解析を実施した。

2.7.6.2.2.3.7.10.1 出血事象と注目する併用薬

出血事象と注目する併用薬の解析計画の詳細及びすべての解析結果を 5.3.5.1.6/PH-36705 に示す。部分集団の中で被験者数が少ない、また出血事象の発現頻度が低いものがあることから結果は慎重に解釈する必要がある。

注目する併用薬についてベースラインの併用薬別に安全性主要評価項目（CIAC 判定による）の forest プロットを 5.3.5.1.15/PH-36762/Figure 1/2 に示す。また、ベースラインの併用薬別に「重大な出血事象」の forest プロット及び時間依存型共変量を含む併用薬別の安全性主要評価項目及び「重大な出血事象」の forest プロットを 5.3.5.1.15/PH-36762/Figure 1/1、Figure 1/3、Figure 1/4 に示す。

一般に、アセチルサリチル酸（ASA）、CYP3A4 阻害薬、クロピドグレル又はチクロピジン、非ステロイド性解熱鎮痛消炎薬（NSAID）、NSAID 及び／又は抗血小板薬、P-gp 阻害薬、PAI 又は ASA、及びスタチンの投与を受けている被験者では、これらの投与を受けていない被験者に比べ出血事象の発現頻度が高かった。しかし、エノキサパリン／VKA 群に比べリバーロキサバン群でこれらの併用薬の影響が異なることを示す徴候は認められなかった。事前に規定した併用薬の投与群と非投与群を比較した場合、「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイントに関するハザード比の 95%信頼区間に重なりが認められた。

2.7.6.2.2.3.7.10.2 治験薬投与開始後初期の出血

本試験において、リバーロキサバン群では、その試験デザインにより、最初の 21 日間は 30mg/日と、その後の期間における 20mg/日よりも高い 1 日用量が用いられた。そのため両投与群において無作為割り付け後の最初の 21 日間に発現した出血事象の解析を行なった。

第 21 日までの安全性主要評価項目の発現頻度は、リバーロキサバン群で 4.6%（110/2,412 例）、エノキサパリン／VKA 群で 4.4%（105/2,405 例）であった（5.3.5.1.15/PH-36762/Table 1/1）。22 日目から投与終了後 2 日目までの発現頻度は、リバーロキサバン群で 6.3%（139/2,218 例）、エノキサパリン／VKA 群で 7.6%（169/2,210 例）であった（5.3.5.1.15/PH-36762/Table 1/2）。

第 21 日までの「重大な出血事象」の発現頻度は、エノキサパリン／VKA 群（0.9%、21/2,405 例）に比べリバーロキサバン群（0.4%、10/2,412 例）で数値上低かった（5.3.5.1.15/PH-36762/Table 1/1）。いずれの群においても「致死的出血事象」は認められなかったが、上述の差は「非致死的で重要な臓器の出血事象」（リバーロキサバン群：3 例、エノキサパリン／VKA 群：8 例）及び「非致死的で重要な臓器以外の出血事象」（リバーロキサバン群：7 例、エノキサパリン／VKA 群：13 例）に由来するものであった。一方、22 日目から投与終了後 2 日目までの発現頻度は、リバーロキサバン群で 0.5%（11/2,218 例）、エノキサパリン／VKA 群で 1.2%（26/2,210 例）であった（5.3.5.1.15/PH-36762/Table 1/2）。

第 21 日までの「重大ではないが臨床的に問題となる出血事象」の発現頻度はエノキサパリン／VKA 群（3.5%、84/2,405 例）に比べリバーロキサバン群（4.1%、100/2,412 例）で高かった（5.3.5.1.15/PH-36762/Table 1/1）。第 22 日から投与終了後 2 日目までの発現頻度はリバーロキサバン群で 5.8%（128/2,218 例）、エノキサパリン／VKA 群で 6.5%（143/2,210 例）であった（5.3.5.1.15/PH-36762/Table 1/2）。

2.7.6.2.2.3.7.10.3 治験薬投与終了後 3 日目から 30 日目までの出血事象

治験実施計画書では、無作為割り付け後治験薬投与を受けなかった被験者又は治験薬を中止した被験者は少なくとも予定投与期間の終了時（3、6 又は 12 ヵ月目）に来院するよう規定した。また予定投与期間にかかわらず、治験薬投与後に 30 日間のフォローアップ期間を設定した。予定投与期間完了時又は中止時に治験責任（分担）医師の判断により他の抗凝固療法を行なうことが認められた。

治験薬投与終了後 3 日目から 30 日目までに発現した出血事象の要約を以下に示す（5.3.5.1.15/PH-36762/Table 1/7）。

- 全出血事象の発現頻度は、リバーロキサバン群で 2.3%、エノキサパリン／VKA 群で 2.7%であった。
- 「重大な出血事象」の発現頻度は、リバーロキサバン群で 0.3%、エノキサパリン／VKA 群で 0.4%であった。
- 「致死的出血事象」が 2 例認められたが、いずれもリバーロキサバン群に発現した（投与終了後 3 日目に発現した下大静脈創部からの心臓周囲出血（CIAC 判定による出血部位は後腹膜）1 例及び投与終了後 13 日目に発現した頭蓋内出血 1 例）。
- 「重大ではないが臨床的に問題となる出血事象」の発現頻度は、リバーロキサバン群で 0.2%、エノキサパリン／VKA 群で 0.7%であった。
- 「軽微な出血事象」の発現頻度は、両投与群共に 1.8%であった。

これらの結果から、治験薬投与終了後 3 日目から 30 日目までの両投与群の出血事象の発現頻度は同程度であることが示された。

2.7.6.2.2.3.7.10.4 複数回発現した出血事象

複数回発現した出血事象のすべての解析は治験薬投与下に限定して行なった。これらは探索的解析であった。複数回発現した出血事象は異なる手法、すなわち記述的要約、人年ごとの事象発現率、出血事象再発までの期間の解析法及び平均累積関数を用いて解析した。複数回発現した出血事象の定義は 5.3.5.1.8/PH-36707 に示す。

出血事象が 1 回だけ発現した被験者の割合は、リバーロキサバン群で 66.4%、エノキサパリン／VKA 群で 64.3%であった。「重大な出血事象」が複数回発現した被験者はリバーロキサバン群には認められず、エノキサパリン／VKA 群では 6 例（いずれも 2 回）であった。「重大ではないが臨床的に問題となる出血事象」については、リバーロキサバン群では出血事象が発現した被験者の 8.0%（20 例）で 2 件、1.6%（4 例）で 3 件の出血事象が発現し、エノキサパリン／VKA

群では 13.5%（37 例）で 2 件、0.4%（1 例）で 3 件の出血事象が発現した（5.3.5.1.8/PH-36707/Table 14.3.1/2）。治験薬投与を継続した事象発現例における発現頻度についても上述の結果と同様であった（5.3.5.1.8/PH-36707/Table 14.3.1/4）。

またこれらの結果から、Anderson-Gill モデルによる再発性出血事象に対する治療効果（すなわちハザード比）が、出血事象初回発現までの期間に関して Cox 比例ハザードモデルから得られる治療効果と実質的に差がないことが示された（5.3.5.1.8/PH-36707/Table 14.3.1/18）。

2.7.6.2.2.3.7.10.5 出血事象とプロトロンビン時間延長との関係

リバーロキサバン群の安全性解析対象集団において、Neoplastin®を用いてベースライン及びベースライン後のトラフ時かつピーク時のプロトロンビン時間を測定した（5.3.5.1.7/PH-36706 参照）。

総じて、出血事象発現例と非発現例で、ピーク時のプロトロンビン時間に明らかな差はなく、ベースラインからのプロトロンビン時間の延長が同様に認められた（5.3.5.1.7/PH-36706/Table 14.4.1/8）。

投与期間を通じたプロトロンビン時間の解析からは、時間経過（投与期間 1 年まで）に伴うリバーロキサバンの蓄積を示唆する結果は得られなかった（5.3.5.1.7/PH-36706/Figure 14.4.1/2）。また、リバーロキサバン 15mg 1 日 2 回及びリバーロキサバン 20mg 1 日 1 回投与期間中のプロトロンビン時間は想定範囲内で、リバーロキサバンの PK プロファイル（ピーク及びトラフ）を反映したものであった（5.3.5.1.7/PH-36706/Table 14.4.1/6 及び Table 14.4.1/7）。

部分集団解析も行なったが、出血事象の有無にかかわらず同様であった（5.3.5.1.7/PH-36706 参照）。

2.7.6.2.2.3.7.11 出血関連有害事象

治験責任（分担）医師の報告による治験薬投与下に発現した出血関連有害事象で、両投与群で多かった事象は、鼻出血（リバーロキサバン群：9.0%、エノキサパリン／VKA 群：8.2%）、挫傷（3.8%、5.4%）、血腫（2.4%、3.8%）であった。発現頻度が 2%を上回る出血関連有害事象のうち、リバーロキサバン群のほうが 1%以上高かったのは月経過多（3.0%、1.9%）のみであった。治験薬投与下に発現した出血関連有害事象の発現頻度を器官別大分類及び基本語別に分類した要約を表 2.7.6.2- 26に示す。

いずれかの投与群での発現頻度が 5%以上の治験薬との因果関係が否定できない TEAE（MedDRA 基本語別）は鼻出血（リバーロキサバン群：7.2%、エノキサパリン／VKA 群：6.6%）であった（表 2.7.6.2- 27）。治験薬投与下に発現した治験薬の投与中止に至った出血関連有害事象は、リバーロキサバン群 37 例（1.5%）、エノキサパリン／VKA 群 39 例（1.6%）で、個別の基本語別及び器官別大分類別での両投与群の有害事象数はすべて同程度であった（5.3.5.1.2 A53042/Table 14.3.1/36）。治験薬の投与中止に至った出血関連有害事象でよくみられたのは（いずれかの投与群で 4 例以上発現）、貧血（リバーロキサバン群：0.2%、エノキサパリン／VKA 群： 0.1%未満）、直腸出血（0.2%、0.1%未満）、小脳出血（0.1%未満、0.2%）であった。詳細は 5.3.5.1.2 A53042/Section 10.4.3.4.1 に示す。

2.7.6.2.2.3.8 心血管事象

CIAC によって心血管事象（急性冠症候群、虚血性脳卒中、一過性脳虚血発作、非中枢神経系塞栓症及び心血管死）の判定が盲検下で行なわれた。この項においては特に明記しない限り、心血管事象は CIAC により判定された事象を指す。心血管事象の定義については 5.3.5.3.7/PH-36746 に示す。

「投与中」及び「投与終了後」に発現した心血管事象の頻度について概要を表 2.7.6.2- 36に示す。「投与中」に発現した事象とは治験薬投与終了後 1 日目までに発現した事象とした。一方、「投与終了後」に発現した事象とは治験薬の投与終了後 2 日目から 30 日目までに発現した事象とした。

全体として心血管事象発現例数は少なく、急性冠症候群（ST 上昇心筋梗塞、非 ST 上昇心筋梗塞、不安定狭心症）、脳血管事象（虚血性脳卒中又は一過性脳虚血発作）、心血管死、又は非中枢神経系塞栓症について、リバーロキサバン群で「投与中」又は「投与終了後」の発現頻度は高くはなかった。

「投与中」にリバーロキサバン群の 1.5%（35/2,412 例）及びエノキサパリン／VKA 群の 1.5%（37/2,405 例）で心血管事象が発現した。致死的又は非致死的な急性冠症候群（ST 上昇心筋梗塞、非 ST 上昇心筋梗塞、不安定狭心症）の発現頻度は、リバーロキサバン群で 0.6%（15/2,412 例）、エノキサパリン／VKA 群で 0.9%（21/2,405 例）であった。致死的又は非致死的な脳血管事象（虚血性脳卒中又は一過性脳虚血発作）の発現頻度は、リバーロキサバン群で 0.5%（12/2,412 例）、エノキサパリン／VKA 群で 0.5%（13/2,405 例）であった。リバーロキサバン群では虚血性脳卒中 10 例、一過性脳虚血発作 2 例、エノキサパリン／VKA 群では虚血性脳卒中 6 例、一過性脳虚血発作 6 例の発現に加え、虚血性脳卒中として集計されず死亡とされただけの虚血性脳卒中があり、その虚血性脳卒中による死亡が 1 例あった（5.3.5.1.2 A53042/Table 14.3.1/171）。その他の心血管死（その他の血管系事象、心不全又はその他の心臓死）の発現頻度は、リバーロキサバン群で 0.1%（3/2,412 例）、エノキサパリン／VKA 群で 0.1%未満（1/2,405 例）であった。

「投与終了後」にリバーロキサバン群の 0.4%（9/2,206 例）、エノキサパリン／VKA 群の 0.1%（3/2,197 例）に心血管事象が発現した。致死的又は非致死的急性冠症候群（ST 上昇心筋梗塞、非 ST 上昇心筋梗塞、不安定狭心症）の発現頻度は、リバーロキサバン群で 0.1%（3/2,206 例）、エノキサパリン／VKA 群で 0.1%未満（2/2,197 例）であった。致死的又は非致死的脳血管事象（虚血性脳卒中又は一過性脳虚血発作）の発現頻度は、リバーロキサバン群で 0.1%未満（2/2,206 例）、エノキサパリン／VKA 群で 0.1%未満（1/2,197 例）であった。その他の心血管死（その他の血管系事象、心不全）の発現頻度は、リバーロキサバン群で 0.2%（4/2,206 例）、エノキサパリン／VKA 群で 0%であった。「投与終了後」の事象発現数はエノキサパリン／VKA 群に比べリバーロキサバン群で数値上多かった。その差はその他の心血管死の区分に起因していた。「投与中」及び「投与終了後」の双方について PE 関連死を含む心血管事象の発現頻度の解析を行なった。PE は本試験の評価項目と規定されているため、原則として有効性評価項目に分類された。しかし実際には PE は本来心血管事象であることから、事前に規定した心血管事象に加え、PE 関連死を評価するため心血管事象に加えた解析も実施した。結果、「投与中」及び「投与終了後」のいずれにおいても両投与群の発現頻度は PE を含めない場合と同程度であった（5.3.5.1.2 A53042/Table 14.3.1/168、Table 14.3.1/169）。

表 2.7.6.2- 36 「投与中」及び「投与終了後」の期間における心血管事象の発現頻度（安全性解析対象集団）

評価項目（イベント）	リバーロキサバン (N＝2412) n（%）	エノキサパリン／VKA (N＝2405) n（%）
「投与中」に発現した事象		
全心血管事象	35 (1.5%)	37 (1.5%)
全虚血性脳卒中（CIAC 判定による、死亡原因又は血管事象としての）及び一過性脳虚血発作	12 (0.5%)	13 (0.5%)
全心筋梗塞（CIAC 判定による死亡原因又は STEMI、NSTEMI としての）及び不安定狭心症	15 (0.6%)	21 (0.9%)
死亡（心血管死）	7 (0.3%)	3 (0.1%)
心筋梗塞	2 (＜0.1%)	1 (＜0.1%)
虚血性脳卒中	2 (＜0.1%)	1 (＜0.1%)
心不全	2 (＜0.1%)	0 (0.0%)
そのほかの血管事象	1 (＜0.1%)	0 (0.0%)
そのほかの心臓死	0 (0.0%)	1 (＜0.1%)
STEMI	4 (0.2%)	2 (＜0.1%)
NSTEMI	2 (＜0.1%)	10 (0.4%)
不安定狭心症	9 (0.4%)	9 (0.4%)
一過性脳虚血発作	2 (＜0.1%)	6 (0.2%)
虚血性脳卒中	10 (0.4%)	6 (0.2%)
非中枢神経系塞栓症	5 (0.2%)	3 (0.1%)
「投与終了後」（治験薬投与終了後 30 日目まで、フォローアップ期間に移行した安全性解析対象集団）に発現した事象		
	(N=2206)	(N=2197)
全心血管事象	9 (0.4%)	3 (0.1%)
全虚血性脳卒中（CIAC 判定による死亡原因又は血管事象としての）及び一過性脳虚血発作	2 (＜0.1%)	1 (＜0.1%)
全心筋梗塞（CIAC 判定による死亡原因又は STEMI、NSTEMI としての）及び不安定狭心症	3 (0.1%)	2 (＜0.1%)
死亡（心血管死）	4 (0.2%)	0 (0.0%)
心不全	2 (＜0.1%)	0 (0.0%)
そのほかの血管事象	2 (＜0.1%)	0 (0.0%)
STEMI	1 (＜0.1%)	0 (0.0%)
NSTEMI	0 (0.0%)	2 (＜0.1%)
不安定狭心症	2 (＜0.1%)	0 (0.0%)
虚血性脳卒中	2 (＜0.1%)	1 (＜0.1%)
非中枢神経系塞栓症	1 (＜0.1%)	0 (0.0%)

(N) STEMI：（非）ST 部分上昇型心筋梗塞、VKA：ビタミン K 拮抗薬

心血管事象の定義：急性冠症候群、虚血性脳卒中、一過性脳虚血発作、非中枢神経系塞栓症及び心血管死

「投与中」に発現した事象とは治験薬投与終了後 1 日目までに発現した事象とした。 「投与終了後」に発現した事象とは治験薬の投与終了後 2 日目から 30 日目までに発現した事象とした。 CIAC は心血管事象が疑われる被験者についてその事象を事前に規定した基準に基づき分類することになっていた。CIAC 判定による致死的な事象については初回の事象のみ集計した。

引用元： 5.3.5.1.2 A53042/Table 14.3.1/165、Table 14.3.1/166

心血管死：

「投与中」に発現した心血管死は 10 例で、内訳はリバーロキサバン群で 7/2,412 例（0.3%）、エノキサパリン／VKA 群で 3/2,405 例（0.1%）であった。「投与終了後」の心血管死の報告は 4 例で、内訳はリバーロキサバン群で 0.2%（4/2,206 例）、エノキサパリン／VKA 群で該当なしであった。

また、「投与中」に心血管事象が発現した 4 例は「投与終了後」に死亡した（リバーロキサバン群：被験者 160293103、被験者 400033052、被験者 160123010、エノキサパリン／VKA 群：被験者 300073113）。

リバーロキサバン群において「投与終了後」に規定期間外で心血管死が 1 例（被験者 180053017）あった（治験薬中止後 209 日目、治験薬中止理由は有害事象発現ではなく、被験者が試験のスケジュールに沿って来院できなくなったため）。被験者は循環虚脱後に死亡し、死因は心不全と判定された。

詳細は 5.3.5.1.2 A53042/Section 10.4.3.4.2 に、また被験者に関する叙述は 5.3.5.1.2 A53042/Section 15 に示す。

虚血性脳卒中：

「投与中」に発現した虚血性脳卒中は 16 例で、発現頻度はリバーロキサバン群で 0.4%（10/2,412 例）、エノキサパリン／VKA 群では 0.2%（6/2,405 例）（表 2.7.6.2- 36）であり、これに加え、虚血性脳卒中としては集計されず、死亡とされただけの虚血性脳卒中があり、その虚血性脳卒中による死亡が 1 例あった（5.3.5.1.2 A53042/Table 14.3.1/165 脚注）。これら「投与中」に発現した虚血性脳卒中のうち転帰が死亡であったのは、リバーロキサバン群で 2 例（被験者 160123010 及び被験者 400033052）、エノキサパリン／VKA 群で 1 例（被験者 280013045）であった。詳細は 5.3.5.1.2 A53042/Section 10.4.3.4.2 に示す。

「投与終了後」に発現した虚血性脳卒中は 3 例で、その内訳はリバーロキサバン群で 2/2,206 例（0.1%未満）、エノキサパリン／VKA 群で 1/2,197 例（0.1%未満）であった（表 2.7.6.2- 36）。

一過性脳虚血発作：

「投与中」に発現した一過性脳虚血発作は 8 例で、その内訳はリバーロキサバン群で 2/2,412 例（0.1%未満）、エノキサパリン／VKA 群で 6/2,405 例（0.2%）であった（表 2.7.6.2- 36）。「投与終了後」にはいずれの投与群においても一過性脳虚血発作は認められなかった。

急性冠症候群：

「投与中」に発現した急性冠症候群事象は、リバーロキサバン群で 15 例（0.6%）、エノキサパリン／VKA 群で 21 例（0.9%）であった。「投与終了後」に発現した急性冠症候群はリバーロキサバン群で 3 例（0.1%）、エノキサパリン／VKA 群で 2 例（0.1%未満）であった（表 2.7.6.2- 36）。

非中枢神経系塞栓症：

「投与中」に発現した非中枢神経系塞栓症は 8 例で、その内訳はリバーロキサバン群で 5/2,412 例（0.2%）、エノキサパリン／VKA 群で 3/2,405 例（0.1%）であった（表 2.7.6.2-

36）。「投与終了後」に発現した非中枢神経系塞栓症は 1 例で、その内訳はリバーロキサバン群で 1/2,206 例（0.1%未満）、エノキサパリン／VKA 群で 0/2,197 例であった。

2.7.6.2.2.3.9　肝臓安全性

2.7.6.2.2.3.9.1　肝臓関連臨床検査値異常

表 2.7.6.2- 37に、ベースライン後のアスパラギン酸アミノトランスフェラーゼ（AST）、ALT、アルカリフォスファターゼ（ALP）、総ビリルビン、直接ビリルビンの各臨床検査値の閾値逸脱頻度及びこれらの複数検査値の同時に基準値上限を超える増加（ALT とビリルビン、AST とビリルビン及び総ビリルビンと直接ビリルビンの組み合わせ）の発現頻度を示す。ベースライン後の期間は、無作為割り付けからそれぞれの被験者の最終観察日までとした。同時とは、同じ血液サンプルから測定された検査値のことをいう。

ベースライン後に基準値上限の 3 倍を超える ALT 増加は、リバーロキサバン群で 1.9%（45/2,351 例）、エノキサパリン／VKA 群で 3.0%（70/2,324 例）であり、リバーロキサバン群で低かった。ベースライン後に基準値上限の 5、8、10 及び 20 倍を超える ALT 増加は、リバーロキサバン群とエノキサパリン／VKA 群で同程度であった。

臨床検査でベースライン後の ALP 又は AST が増加した頻度は、リバーロキサバン群とエノキサパリン／VKA 群でおおむね同様であった（各閾値は異なる）。

総ビリルビン及び直接ビリルビンが最低閾値である基準値上限の 1.5 倍を超える増加は、エノキサパリン／VKA 群に比べリバーロキサバン群で数値上高かった。これ以外の閾値（基準値上限の 2 倍、3 倍、5 倍、8 倍を超える）については、総じて両投与群で同様であった。

無作為割り付け 14 日前から投与開始後 21 日目までに何らかのヘパリン治療を行なったリバーロキサバン群の部分集団（2,177 例）と、同期間にヘパリン治療を全く行なわなかったリバーロキサバン群の部分集団（174 例）を対象として、基準値上限の 3 倍を超える ALT 増加について追加解析を行なった。部分集団の被験者数が異なることもあり、解析からは明確な結論は導き出せなかった。しかし、データからは、基準値上限の 3 倍を超える ALT 増加の頻度に 2 部分集団間で差があることは示唆されなかった。大多数の被験者では観察された臨床検査値異常は、正常化あるいは投与前・投与継続中の観察値に回復した。

表 2.7.6.2- 37　ベースライン後の臨床検査値異常の発現頻度（中央測定、安全性解析対象集団）

期間	臨床検査値異常	リバーロキサバン群 分子/分母	%	エノキサパリン／VKA 群 分子/分母	%	リバーロキサバン群とエノキサパリン／VKA 群の差（%）	95% 信頼区間
ベースライン後	ALT＞3 x ULN 及び 総ビリルビン＞2 x ULN（同時）	2/2351	＜0.1	0/2323	0.0	0.1	-0.1～0.3
	AST＞3 x ULN 及び 総ビリルビン＞2 x ULN（同時）	2/2351	＜0.1	0/2323	0.0	0.1	-0.1～0.3
	ALT＞3 x ULN 及び 総ビリルビン＞2 x ULN 及び直接ビリルビン/総ビリルビン≧50%（同時）	2/2351	＜0.1	0/2319	0.0	0.1	-0.1～0.3
	AST＞3 x ULN 及び 総ビリルビン＞2 x ULN 及び直接ビリルビン/総ビリルビン≧50%（同時）	2/2351	＜0.1	0/2319	0.0	0.1	-0.1～0.3
	総ビリルビン＞2 x ULN 及び直接ビリルビン/総ビリルビン≧50%（同時）	3/2351	0.1	3/2319	0.1	-0.0	-0.3～0.3
	総ビリルビン＞2 x ULN 及び直接ビリルビン＞2 x ULN（同時）	9/2351	0.4	5/2319	0.2	0.2	-0.2～0.5
ベースライン後	SGOT/AST						
	＞ 3 x ULN	22/2351	0.9	21/2324	0.9	0.0	-0.5～0.6
	＞ 5 x ULN	11/2351	0.5	6/2324	0.3	0.2	-0.2～0.6
	＞ 8 x ULN	4/2351	0.2	1/2324	＜0.1	0.1	-0.1～0.4
	＞10 x ULN	3/2351	0.1	1/2324	＜0.1	0.1	-0.1～0.3
	＞20 x ULN	2/2351	＜0.1	0/2324	0.0	0.1	-0.1～0.3
ベースライン後	SGPT/ALT						
	＞ 3 x ULN	45/2351	1.9	70/2324	3.0	-1.1	-2.0～-0.2
	＞ 5 x ULN	17/2351	0.7	19/2324	0.8	-0.1	-0.6～0.4
	＞ 8 x ULN	6/2351	0.3	2/2324	＜0.1	0.2	-0.1～0.5
	＞10 x ULN	4/2351	0.2	2/2324	＜0.1	0.1	-0.2～0.4
	＞20 x ULN	1/2351	＜0.1	0/2324	0.0	0.0	-0.1～0.2

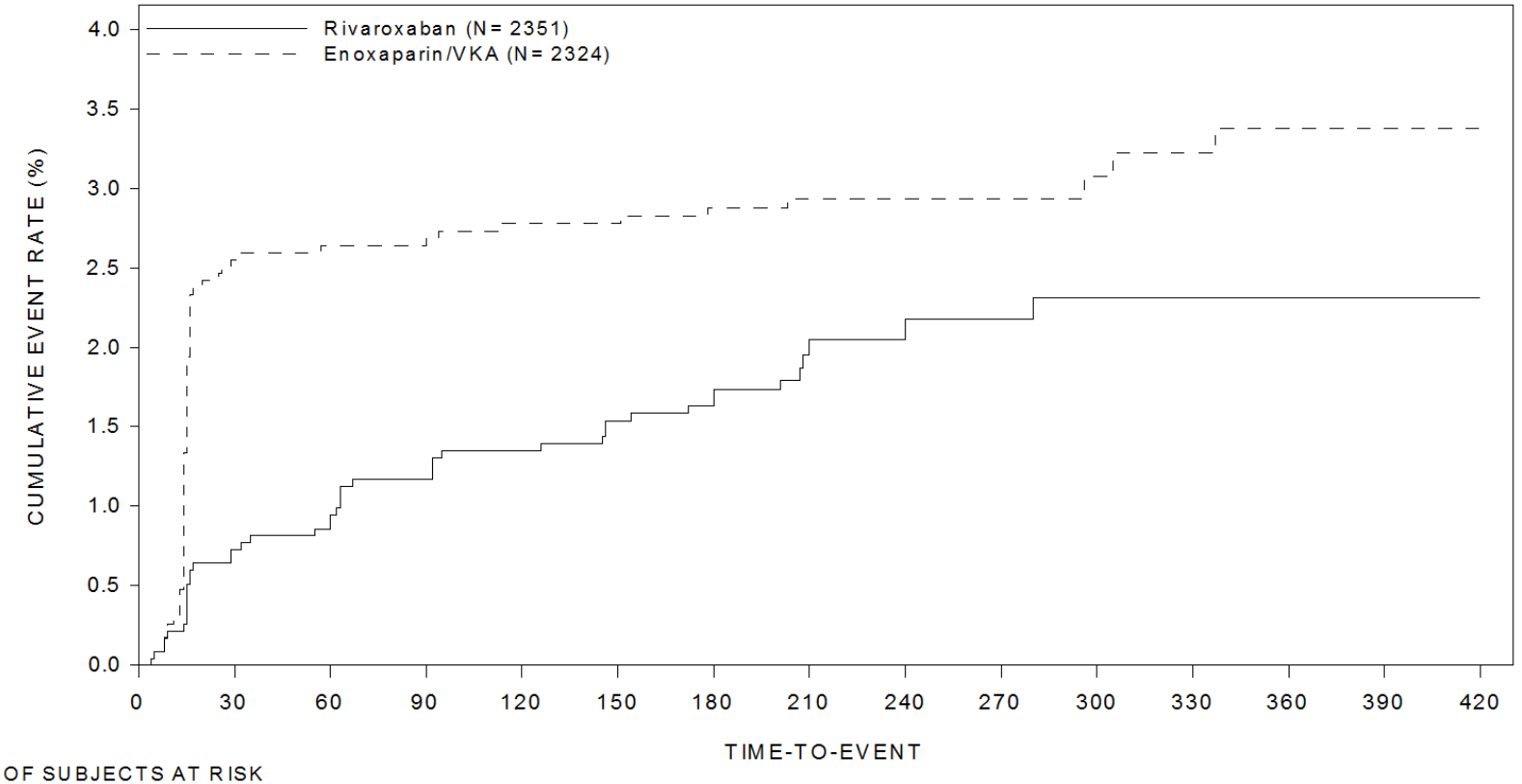
表 2.7.6.2- 37 ベースライン後の臨床検査値異常の発現頻度（中央測定、安全性解析対象集団）（続き）

期間	臨床検査値異常	リバーロキサバン群 分子/分母	%	エノキサパリン／VKA 群 分子/分母	%	リバーロキサバン群とエノキサパリン／VKA 群の差（%）	95%信頼区間
ベースライン後	ALP						
	＞ 3 x ULN	7/2352	0.3	6/2329	0.3	0.0	-0.3～0.4
	＞ 5 x ULN	3/2352	0.1	1/2329	＜0.1	0.1	-0.1～0.3
	＞ 8 x ULN	0/2352	0.0	0/2329	0.0	0.0	-0.2～0.2
	＞10 x ULN	0/2352	0.0	0/2329	0.0	0.0	-0.2～0.2
	＞20 x ULN	0/2352	0.0	0/2329	0.0	0.0	-0.2～0.2
ベースライン後	総ビリルビン						
	＞1.5 x ULN	44/2352	1.9	34/2327	1.5	0.4	-0.3～1.2
	＞ 2 x ULN	15/2352	0.6	11/2327	0.5	0.2	-0.3～0.6
	＞ 3 x ULN	5/2352	0.2	6/2327	0.3	-0.0	-0.4～0.3
	＞ 5 x ULN	1/2352	＜0.1	2/2327	＜0.1	-0.0	-0.3～0.2
	＞ 8 x ULN	0/2352	0.0	0/2327	0.0	0.0	-0.2～0.2
ベースライン後	直接ビリルビン						
	＞1.5 x ULN	72/2351	3.1	46/2319	2.0	1.1	0.2～2.0
	＞ 2 x ULN	32/2351	1.4	14/2319	0.6	0.8	0.2～1.4
	＞ 3 x ULN	12/2351	0.5	7/2319	0.3	0.2	-0.2～0.6
	＞ 5 x ULN	4/2351	0.2	4/2319	0.2	-0.0	-0.3～0.3
	＞ 8 x ULN	2/2351	＜0.1	1/2319	＜0.1	0.0	-0.2～0.3

ULN：基準値上限、VKA：ビタミン K 拮抗薬、分子：該当する検査値異常が認められた被験者数、分母：ベースライン後に該当する検査値が存在する被験者数、SGPT/ALT: アラニン・アミノトランスフェラーゼ、SGOT/AST：アスパラギン酸アミノトランスフェラーゼ、ALP：アルカリホスファターゼ
直接/総ビリルビン≧50%：直接ビリルビンの値が、総ビリルビンの少なくとも 50%であること。
信頼区間は漸近的な方法（標準化されたスコア統計量）を用いて算出した。そのため低い頻度の時は解釈に注意を要する。
ベースライン後の期間は、無作為割り付けから各被験者での最終観察日までとする。
引用元：5.3.5.1.2 A53042/Table 14.3.3/3, Table 14.3.3/9

Kaplan-Meier 法による、無作為割り付け後の ALT が基準値上限の 3 倍を超える増加（ベースライン後）の累積発現率を図 2.7.6.2- 9及び 5.3.5.1.2 A53042/Table 14.3.3/10 に示す。

エノキサパリン／VKA 群では、基準値上限の 3 倍を超える ALT 増加の過半数が投与開始から 2 週間までに認められたが、リバーロキサバン群における増加の分布は投与期間を通じてほぼ均等であった。試験の最初の 2 週間は PT-INR が目標範囲内に達するまでエノキサパリン／VKA 群の被験者に対し VKA に加えてエノキサパリン投与が行なわれた。



引用元：5.3.5.1.2 A53042/Figure 14.3.3/1

図 2.7.6.2- 9　Kaplan-Meier 法による、基準値上限の 3 倍を超える ALT 増加の累積発現率（中央測定、安全性解析対象集団）

2.7.6.2.2.3.9.2　ALTが基準値上限の3倍かつ総ビリルビンが基準値上限の2倍を超える被験者

基準値上限の3倍を超えるALT増加かつ基準値上限の2倍を超える総ビリルビン増加、基準値上限の3倍を超えるAST増加かつ基準値上限の2倍を超える総ビリルビン増加、基準値上限の3倍を超えるALT増加かつ基準値上限の2倍を超える総ビリルビン増加かつ直接ビリルビン／総ビリルビンが50%以上、及び基準値上限の3倍を超えるAST増加かつ基準値上限の2倍を超える総ビリルビン増加かつ直接ビリルビン／総ビリルビンが50%以上（中央測定による）の同時発現がリバーロキサバン群でいずれも2例認められ、一方、エノキサパリン／VKA群での発現はなかった。

中央測定及び施設測定した値による基準値上限の3倍を超えるALT増加と基準値上限の2倍を超える総ビリルビン増加の同時発現のデータでも、投与群間に特に差は認められなかった（表2.7.6.2- 38）。

表2.7.6.2- 38　基準値上限の3倍を超えるALT増加かつ基準値上限の2倍を超える総ビリルビン増加の同時発現頻度（中央測定及び施設測定、安全性解析対象集団）

発現時期	リバーロキサバン 分子 [a] / 分母 [b]		エノキサパリン／VKA 分子 [a] / 分母 [b]	
全期間 [c]	5/2404	(0.2%)	4/2399	(0.2%)
ベースライン [d]	0/2197	(0.0%)	0/2200	(0.0%)
ベースライン後 [e]	5/2355	(0.2%)	4/2327	(0.2%)
治験薬投与下に発現 [f]	4/2126	(0.2%)	2/2112	(0.1%)

VKA：ビタミンK拮抗薬

a:発現例数

b:各期間の同時発現に対しALT値及び総ビリルビン値が欠損ではない例数。同時発現とは同じ歴日の発現を指す。 同じ歴日に複数の測定値がある場合、最大値を採用。

c:スクリーニング期、ベースライン及びベースライン後の期間を含む

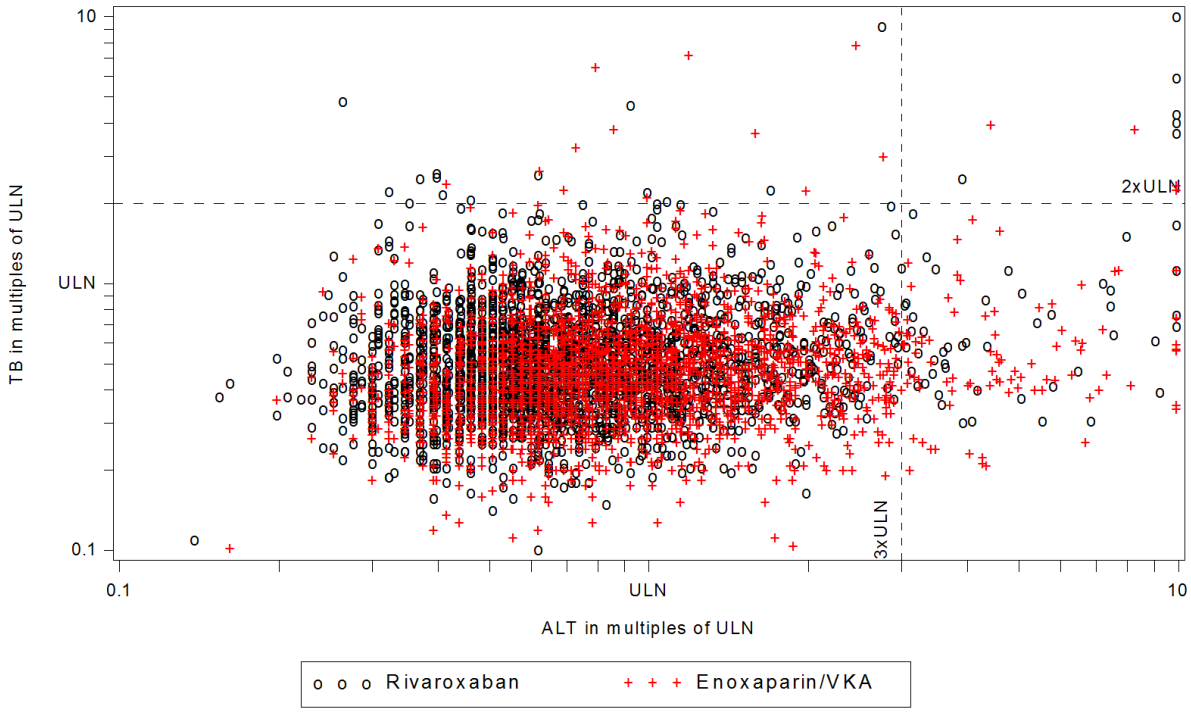
d:治験薬初回投与日もしくはその直近日（ベースライン値が欠損でない被験者）

e:治験薬投与開始後（ベースライン後の値が欠損でない被験者）

f:治験薬投与開始日から投与終了後2日目まで（ベースライン値が正常でベースライン後の値が欠損でない被験者）

引用元：5.3.5.1.2 A53042/Table 14.3.3/8

図 2.7.6.2- 10はリバーロキサバン群とエノキサパリン／VKA 群における全期間中の ALT 最高値と総ビリルビン最高値別の eDISH 散布図である。増加発現は同日の場合もあれば別々の場合もある。右上象限の 10 例は基準値上限の 3 倍を超える ALT 増加と基準値上限の 2 倍を超える総ビリルビン増加の合併例である（リバーロキサバン群：6 例、エノキサパリン／VKA 群：4 例）。このうち 9 例（リバーロキサバン群：5 例、エノキサパリン／VKA 群：4 例）は基準値上限の 3 倍を超える ALT 増加と基準値上限の 2 倍を超える総ビリルビン増加の同日（同時）発現例で、残り 1 例（リバーロキサバン群）はそれぞれの増加が別々の日（同時ではない）に発現した（5.3.5.1.2 A53042/Section 16.1.9.4）。



引用元：5.3.5.1.2 A53042/Figure 14.3.3/9

図 2.7.6.2- 10　ALT 最高値と総ビリルビン最高値別の散布図（中央測定及び施設測定に基づく随時測定値、安全性解析対象集団）

以上をまとめると、リバーロキサバン群と比較した場合にエノキサパリン／VKA 群に認められた投与初期の ALT 増加の発現頻度の上昇を除き、本試験では肝臓関連臨床検査値異常の発現に臨床的に意味のある投与群間の差は認められなかった。

中央測定び施設測定による肝臓関連臨床検査値異常の更なる解析結果を 5.3.5.1.13/PH-36755 に示す。

2.7.6.2.2.3.9.3　　肝臓関連有害事象

肝臓関連有害事象の特定には肝障害に関する MedDRA SMQ を用いた。肝障害 SMQ による肝臓関連有害事象の発現頻度を表 2.7.6.2- 39に、肝臓関連の重篤な TEAE の発現頻度を表 2.7.6.2- 40 に示す。

肝臓関連有害事象の発現頻度は、リバーロキサバン群で 8.3%（199/2,412 例）、エノキサパリン／VKA 群で 12.4%（299/2,405 例）であった。肝臓関連有害事象の大部分は臨床検査値異常であり、リバーロキサバン群で 5.3%（128/2,412 例）、エノキサパリン／VKA 群で 9.2%（222/2,405 例）であった。これらの臨床検査に関連する有害事象のうち発現頻度が高かったのはアラニン・アミノトランスフェラーゼ増加、アスパラギン酸アミノトランスフェラーゼ増加、INR 増加、肝機能検査異常であった。

表 2.7.6.2- 39　肝臓関連有害事象の発現頻度（いずれかの投与群で 0.5%以上、安全性解析対象集団）

MedDRA 器官別大分類／基本語	リバーロキサバン (N＝2412)		エノキサパリン／VKA (N＝2405)	
全事象	199	(8.3%)	299	(12.4%)
肝胆道系障害	71	(2.9%)	82	(3.4%)
肝機能異常	6	(0.2%)	12	(0.5%)
脂肪肝	41	(1.7%)	45	(1.9%)
臨床検査	128	(5.3%)	222	(9.2%)
アラニン・アミノトランスフェラーゼ増加	56	(2.3%)	78	(3.2%)
アスパラギン酸アミノトランスフェラーゼ増加	24	(1.0%)	26	(1.1%)
血中アルカリホスファターゼ増加	10	(0.4%)	12	(0.5%)
血中ビリルビン増加	11	(0.5%)	4	(0.2%)
肝酵素上昇	12	(0.5%)	8	(0.3%)
INR 増加	9	(0.4%)	85	(3.5%)
肝機能検査異常	25	(1.0%)	39	(1.6%)

VKA：ビタミン K 拮抗薬、INR：（プロトロンビン時間）国際標準比
MedDRA version 14.1
肝臓関連の有害事象は SMQ（MedDRA 標準検索式）を基に抽出した。
引用元：5.3.5.1.2 A53042/Table 14.3.1/38

肝臓関連の重篤な有害事象の発現頻度はリバーロキサバン群で 1.0%（23/2,412 例）、エノキサパリン／VKA 群で 1.5%（36/2,405 例）であった。これらの事象の大部分は臨床検査値異常（器官別大分類で「臨床検査」）であり、リバーロキサバン群で 0.7%（17/2,412 例）、エノキサパリン／VKA 群で 1.1%（27/2,405 例）であった。これらの臨床検査に関する有害事象のうち発現頻度が高かったのはアラニン・アミノトランスフェラーゼ増加、肝機能検査異常、トランスアミナーゼ上昇であった。

表 2.7.6.2- 40　肝臓関連の重篤な有害事象の発現頻度（安全性解析対象集団）

MedDRA 器官別大分類／基本語	リバーロキサバン (N＝2412) n （%）	エノキサパリン／VKA (N＝2405) n （%）
全事象	23 （ 1.0%）	36 （ 1.5%）
胃腸障害	0 （ 0.0%）	1 （ ＜0.1%）
腹水	0 （ 0.0%）	1 （ ＜0.1%）
肝胆道系障害	7 （ 0.3%）	6 （ 0.2%）
肝細胞融解性肝炎	1 （ ＜0.1%）	0 （ 0.0%）
肝不全	1 （ ＜0.1%）	2 （ ＜0.1%）
肝機能異常	0 （ 0.0%）	1 （ ＜0.1%）
肝臓痛	1 （ ＜0.1%）	0 （ 0.0%）
脂肪肝	0 （ 0.0%）	1 （ ＜0.1%）
肝炎	0 （ 0.0%）	2 （ ＜0.1%）
急性肝炎	1 （ ＜0.1%）	0 （ 0.0%）
慢性活動性肝炎	1 （ ＜0.1%）	0 （ 0.0%）
虚血性肝炎	1 （ ＜0.1%）	0 （ 0.0%）
黄疸	1 （ ＜0.1%）	0 （ 0.0%）
感染症および寄生虫症	0 （ 0.0%）	1 （ ＜0.1%）
A 型肝炎	0 （ 0.0%）	1 （ ＜0.1%）
臨床検査	17 （ 0.7%）	27 （ 1.1%）
アラニン・アミノトランスフェラーゼ増加	6 （ 0.2%）	9 （ 0.4%）
アスパラギン酸アミノトランスフェラーゼ増加	1 （ ＜0.1%）	1 （ ＜0.1%）
γ－グルタミルトランスフェラーゼ増加	0 （ 0.0%）	1 （ ＜0.1%）
肝酵素上昇	3 （ 0.1%）	1 （ ＜0.1%）
INR 異常	0 （ 0.0%）	1 （ ＜0.1%）
INR 増加	1 （ ＜0.1%）	4 （ 0.2%）
肝機能検査異常	4 （ 0.2%）	9 （ 0.4%）
トランスアミナーゼ上昇	2 （ ＜0.1%）	3 （ 0.1%）
肝超音波検査異常	1 （ ＜0.1%）	0 （ 0.0%）
代謝および栄養障害	0 （ 0.0%）	1 （ ＜0.1%）
低アルブミン血症	0 （ 0.0%）	1 （ ＜0.1%）
神経系障害	1 （ ＜0.1%）	0 （ 0.0%）
肝性脳症	1 （ ＜0.1%）	0 （ 0.0%）

VKA：ビタミン K 拮抗薬、INR：（プロトロンビン時間）国際標準比
MedDRA version 14.1
肝臓関連の有害事象は SMQ を基に抽出した。
引用元：5.3.5.1.2 A53042/Table 14.3.1/39

治験薬の投与中止に至った肝障害 SMQ 事象の発現頻度を 5.3.5.1.2 A53042/Table 14.3.1/40 に示す。全体として治験薬の投与中止に至った肝障害 SMQ 事象の発現頻度は、リバーロキサバン群で 0.5%（11/2,412 例）、エノキサパリン／VKA 群で 0.3%（7/2,405 例）であった。事象発現頻度が低いため、投与群間に明確な差を確認することはできなかった。なお、治験実施計画書に定めた肝機能検査の治験薬中止基準はリバーロキサバン群のみを対象とした。リバーロキサバン群で肝機能検査関連の中止例が多いのはそのためと考えられる。

肝障害 SMQ 事象に関する更なる解析結果を 5.3.5.1.13/PH-36755 に示す。

肝臓関連事象評価委員会の評価：

肝臓関連事象評価委員会（HEAC）は、事前に規定した肝臓に関連する以下の基準に該当する被験者について評価した。

- 死亡前 30 日以内に基準値上限の 3 倍を超える ALT の増加を伴う全死亡
- ALT が基準値上限の 3 倍を超え、かつ総ビリルビンが基準値上限の 2 倍を超える場合
  - 同時発現（同一検体の臨床検査評価で検査値増加が認められた場合）
  - 非同時発現（ALT 増加後 30 日以内に総ビリルビンが増加した場合）
- ALT が基準値上限の 8 倍を超える場合（症候性、無症候性を問わない）
- その他〔MedDRA 標準検索式（SMQ）「肝臓関連」を用いて検索した基本語に基づく〕

HEAC による評価のために送付されたデータは 36 例で（リバーロキサバン群：19 例、エノキサパリン／VKA 群：17 例）、両投与群及び個別の HEAC における被験者の選択基準について例数分布はほぼ均等であった（5.3.5.1.2 A53042/Table 16.2.7/1、Table 16.2.7/3）。

評価例の大多数は「基準値上限の 8 倍を超える ALT 増加」の区分であった（リバーロキサバン群：12 例、エノキサパリン／VKA 群：13 例）。「死亡前 30 日以内に基準値上限の 3 倍を超える ALT 増加が発現した死亡」区分の被験者は 4 例であった。内訳はリバーロキサバン群で 3 例（被験者 160183005、被験者 390043009、被験者 440013005）及びエノキサパリン／VKA 群で 1 例（被験者 400213028）であった。

データが送付された被験者のうち、いずれかの委員から治験薬との因果関係を「明らかに関連あり（definite）」判定された被験者はなかった。いずれかの委員から評価不能と判定された被験者もなかった。また、肝移植もなかった。肝臓事象関連死のうち、HEAC 委員 1 名が、治験薬との因果関係を「あるかもしれない（possibly）」）と判定した死亡例があったが、他の 2 名の委員は当該被験者を肝臓事象関連死と判定しなかった。それ以外に治験薬と関連する肝臓事象関連死とされたものはなかった（5.3.5.1.2 A53042/Section 16.4.1 参照）。

HEAC の委員のほとんどが治験薬との因果関係を「おそらく関連あり（probable）」と判定した被験者は 1 例のみであった：被験者 140163051（リバーロキサバン群）で、肝細胞性の障害を伴う基準値上限の 8 倍を超える ALT 増加が 91 日目に発現した。2 人の委員が当該事象のリバーロキサバンとの因果関係を「おそらく関連あり（probable）」と判定し、1 人の委員が因果関係を「あるかもしれない（possibly）」と判定した。委員の検討では、他に病因は確認できず、そのほかの兆候も報告はなかった。97 日目、リバーロキサバン中止後に ALT 減少が認められた。なお被験者が同意を撤回したため回復までの追跡は行なわれなかった（5.3.5.1.2 A53042/Section 16.4.1 参照）。

肝臓安全性の要約：

ベースライン後の基準値上限の 3 倍を超える ALT 増加（中央測定）は、リバーロキサバン群で 1.9%（45/2,351 例）、エノキサパリン／VKA 群で 3.0%（70/2,324 例）であった。観察された臨床検査値異常は、ほとんどの被験者で正常化あるいは投与前・投与継続中の観察値に復した。ベースライン後に ALT が基準値上限の 3 倍を超えかつ総ビリルビンが基準値上限の 2 倍を超える増加の同時発現（中央測定及び施設測定）は、リバーロキサバン群で 0.2%（5/2,355 例）、エ

ノキサパリン／VKA 群で 0.2%　(4/2,327 例）であった。本試験ではリバーロキサバンによる肝機能障害の発現は示唆されなかった。

2.7.6.2.2.3.10　そのほかの臨床検査値の評価

本試験で中央測定された肝機能検査以外の臨床検査はアミラーゼのみであった。3 又は 6 ヵ月のコホートではベースライン時及び投与終了時に、12 ヵ月のコホートではベースライン時、6 ヵ月後及び投与終了時にアミラーゼの測定を行なった。本試験においてベースライン後の上昇としてアミラーゼが基準値上限の 3 倍を超えた被験者がそれぞれの投与群で 1 例ずつ認められた（5.3.5.1.2 A53042/Table 14.3.3/3）。

2.7.6.2.2.3.11　バイタルサイン、身体的所見及び安全性に関連するほかの観察項目

バイタルサイン及び心電図は通常検査としては行なわず、そのため解析も実施しなかった。

2.7.6.2.2.3.12　安全性の結論

安全性解析対象集団は、リバーロキサバン群 2,412 例、エノキサパリン／VKA 群 2,405 例の計 4,817 例であった。出血事象の発現頻度は両投与群で同様であったが、「重大な出血事象」はリバーロキサバン群で有意に低かった。リバーロキサバン群の安全性評価では、肝機能異常及び急性冠症候群の発現頻度が増加する傾向は認められなかった。投与群間で有害事象及び死亡の発現頻度は同程度であった。

TEAE：TEAE の発現頻度は両投与群で同様であった（リバーロキサバン群：80.3%、エノキサパリン／VKA 群：79.0%）。治験薬との因果関係が否定できない TEAE の発現頻度は両投与群共に約 32%であった。留意すべきは、治験実施計画書では「症候性 DVT」及び「症候性 PE（非致死的）」は有害事象又は重篤な有害事象とはみなさないと規定したことであった。重篤な TEAE の発現頻度は両投与群共に約 19%であった。リバーロキサバン群の 5.1%、エノキサパリン／VKA 群の 4.1%の被験者は TEAE によって治験を中止した。

死亡（無作為化割り付け後の死亡）：安全性解析対象集団で死亡は 114 例であった〔リバーロキサバン群：2.6%（63/2,412 例）、エノキサパリン／VKA 群：2.1%（51/2,405 例）〕。悪性腫瘍〔リバーロキサバン群：0.9%（22/2,412 例）、エノキサパリン／VKA 群：1.0%（23/2,405 例）〕、PE の可能性が否定できない原因不明の死亡〔リバーロキサバン群：0.3%（8/2,412 例）、エノキサパリン／VKA 群：0.2%（6/2,405 例）〕及び感染症〔リバーロキサバン群：0.4%（9/2,412 例）、エノキサパリン／VKA 群：0.2%（6/2,405 例）〕の 3 つが両投与群共に死因の割合が高かった。

安全性主要評価項目：安全性主要評価項目（「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」はリバーロキサバン群 10.3%（249/2,412 例）、エノキサパリン／VKA 群 11.4%（274/2,405 例）で同様であり、ハザード比は 0.900（95%信頼区間 0.758～1.069、優越性の p 値：0.2305）であった。安全性主要評価項目で予め規定した部分集団解析では両投与群のすべての発現頻度は一貫して同様であった。CL_{CR} はリバーロキサバン群の安全性主要評価項目に影響を及ぼさなかった。

重大な出血事象：治験薬投与下の「重大な出血事象」の発現頻度はエノキサパリン／VKA 群（2.2%、52/2,405 例）に比べリバーロキサバン群（1.1%、26/2,412 例）で有意に低かった（ハザード比：0.493、95%信頼区間：0.308～0.789、優越性 p 値：0.0032）。同様に、75 歳を超えた被験者の「重大な出血事象」の発現頻度は、エノキサパリン／VKA 群よりリバーロキサバン群で低かった〔リバーロキサバン群：1.1%（5/440 例）、エノキサパリン／VKA 群：5.7%（23/401 例）、ハザード比：0.188、95%信頼区間 0.071～0.495〕。

「重大な出血事象（すべての出血事象）」を以下に示した。

- **致死的出血事象：**リバーロキサバン群 0.1%未満（2/2,412 例）、エノキサパリン／VKA 群 0.1%（3/2,405 例）。

- **重要な臓器の非致死的出血事象：**リバーロキサバン群 0.3%（7/2,412 例）、エノキサパリン／VKA 群 2.2%（26/2,405 例）。頭蓋内〔リバーロキサバン群：0.1%未満（1/2,412 例）、エノキサパリン／VKA 群：0.3%（10/2,405 例）〕、後腹膜〔リバーロキサバン群：0.1%未満（1/2,412 例）、エノキサパリン／VKA 群：0.4%（7/2,405 例）〕の発現頻度はリバーロキサバン群で低く、これ以外に投与群間の差に影響を及ぼしているものはみられなかった。

- **重要な臓器以外の非致死的出血事象（ヘモグロビン 2g/dL 以上の低下又は 2 単位以上の輸血）：**リバーロキサバン群 0.7%（17/2,412 例）、エノキサパリン／VKA 群 1.0%（25/2,405 例）。消化管〔リバーロキサバン群：0.4%（9/2,412 例）、エノキサパリン／VKA 群：0.7%（16/2,405 例）〕の発現頻度はリバーロキサバン群で低く、これ以外に投与群間の差に影響を及ぼしているものはみられなかった。

治験薬投与下で発現した頭蓋内出血：CIAC によって「重大な出血事象」と判定された治験薬投与下で発現した頭蓋内出血は 15 例あり、そのうち 4 例（各投与群 2 例）は「致死的出血事象」、11 例〔リバーロキサバン群：0.1%未満（1/2,412 例）、エノキサパリン／VKA 群：0.4%（10/2,405 例）〕は「重要な臓器の非致死的出血事象」と判定された。

治験薬投与下で発現した子宮出血：治験薬投与下で発現した子宮出血のほとんどが、治験薬投与開始時期の 55 歳以下の女性被験者で認められた。全女性被験者における発現頻度はリバーロキサバン群で 9.4%（104/1,105 例）、エノキサパリン／VKA 群で 6.5%（75/1,162 例）であった。発現した女性被験者のほとんどはそれぞれの投与を継続した。3 例（すべてリバーロキサバン群）の「重大な出血事象」を除き、ほとんどの事象は「軽微な出血事象」として分類され、全女性被験者における軽微な子宮出血の発現頻度はリバーロキサバン群で 6.8%（75/1,105 例）、エノキサパリン／VKA 群で 4.7%（55/1,162 例）であった。

心血管事象：「投与中」の心血管事象の発現頻度は、リバーロキサバン群で 1.5%（35/2,412 例）、エノキサパリン／VKA 群で 1.5%（37/2,405 例）であった。「投与終了後」の発現頻度は、リバーロキサバン群で 0.4%（9/2,206 例）、エノキサパリン／VKA 群で 0.1%（3/2,197 例）であった。急性冠症候群（ST 上昇型心筋梗塞、非 ST 上昇型心筋梗塞、不安定狭心症）、脳血管系事象（虚血性脳卒中、一過性脳虚血発作）及び非中枢神経系塞栓症の発現頻度は「投与中」、「投与終了後」にかかわらず投与群間で同様であった。各投与群で報告された心血管事象の発現頻度は 0.1%以下と極めて低く、心不全による死亡、他の心血管事象による死亡又は他の心臓死も含まれた。「投与中」、「投与終了後」にかかわらず、エノキサパリン／VKA 群よりリバーロキサバン群で心血管事象の発現数が数値上多かった。全体として本試験では「投与中」又は「投

与終了後」のリバーロキサバン群で、急性冠症候群、脳血管系事象及び非中枢神経系塞栓症の発現頻度が高くないことが示された。

肝臓安全性：ベースライン後に基準値上限の 3 倍を超える ALT 増加（中央測定）はリバーロキサバン群で 1.9%（45/2,351 例）、エノキサパリン／VKA 群で 3.0%（70/2,324 例）であった。観察された臨床検査値異常は、ほとんどの被験者で正常化又は治験薬投与前又は投与継続中の値まで回復した。ベースライン後の複数検査値の同時逸脱（ALT が基準値上限の 3 倍かつ総ビリルビンが基準値上限の 2 倍を超える同時逸脱；中央測定及び施設測定）の発現頻度はリバーロキサバン群で 0.2%（5/2,355 例）、エノキサパリン／VKA 群で 0.2%（4/2,327 例）であった。本試験結果から、リバーロキサバンに起因した肝機能障害の発現は示唆されなかった。

肝移植はなかった。肝臓事象関連死のうち、HEAC 委員 1 名が、治験薬との因果関係を「あるかもしれない（possibly）」）と判定した死亡例があったが、他の 2 名の委員は当該被験者を肝臓事象関連死と判定しなかった。それ以外に治験薬と関連する肝臓事象関連死とされたものはなかった。

2.7.6.2.3　　結論

症候性 DVT の有無を問わない急性症候性 PE 患者において、有効性主要評価項目〔症候性 VTE：症候性 DVT、症候性 PE（非致死的又は致死的）の複合エンドポイント〕のイベント発現頻度は、ITT 解析対象集団においてリバーロキサバン群で 2.1%（50/2,419 例）、エノキサパリン／VKA 群で 1.8%（44/2,413 例）で同程度であった。その結果、ハザード比は 1.123〔95%信頼区間：0.749～1.684、非劣性の p 値（片側検定；マージン 2.0）：0.0026〕であり、有効性に関して本試験の主目的であるリバーロキサバン群のエノキサパリン／VKA 群に対する非劣性が検証された。更に、CL_{CR}、性別、体重、年齢、本試験の用量確認解析対象及び種々の危険因子の影響を受けず、有効性はどの部分集団でも一貫していた。

同様に、安全性解析対象集団において、安全性主要評価項目（治験薬投与下で発現した「重大な出血事象」又は「重大ではないが臨床的に問題となる出血事象」の複合エンドポイント）について、リバーロキサバン群（10.3%、249/2,412 例）とエノキサパリン／VKA 群（11.4%、274/2,405 例）は同様の安全性プロファイルを示した。ハザード比は 0.900（95%信頼区間：0.758～1.069、優越性の p 値：0.2305）であった。安全性副次評価項目（治験薬投与下で各被験者において初回に発現した「重大な出血事象」）の発現頻度は、エノキサパリン／VKA 群（2.2%、52/2,405 例）と比べリバーロキサバン群（1.1%、26/2,412 例）で有意に低く、統計学的に優越性が示された（ハザード比：0.493、95%信頼区間 0.308～0.789、優越性の p 値：0.0032）。結果として、「重大な出血事象」を併せた臨床的に重要な有効性評価項目の発現は数値上リバーロキサバン群のほうが低かった。

本試験により、リバーロキサバン固定用量での単剤療法（最初の 3 週間は 15mg 1 日 2 回、引き続き 20mg 1 日 1 回経口投与）は、体重補正したエノキサパリン 1 日 2 回皮下投与及び PT-INR で用量調節した経口 VKA 投与の 2 剤を用いる治療法と比較し同様の有効性と安全性を示すことが示された。

2.7.6.2.4　　参考文献

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