1.15 D2210C00008 試験（日本を含む国際共同試験，参考資料）

[M5.3.5.4 D2210C00008/STRATOS 2 Synopsis]

1.15.1 概要

表 15 概要（D2210C00008［STRATOS 2］試験）

治験実施計画書識別コード：D2210C00008

治験課題名

吸入ステロイド薬＋長時間作用性 β_2 受容体刺激薬でコントロールが不十分な喘息を有する成人および青少年患者を対象にトラロキヌマブの有効性および安全性を評価する 52 週間，多施設共同，無作為化，二重盲検，並行群間，プラセボ対照，第 3 相試験（STRATOS 2）

治験責任医師および治験実施施設

Professor Christopher Brightling, MD
本治験は 13 か国の 242 施設（カナダ［15］，チリ［6］，チェコ共和国［6］，イタリア［10］，日本［48］，メキシコ［5］，フィリピン［7］，ロシア［23］，南アフリカ［6］，台湾［3］，ウクライナ［19］，英国［10］および米国［84］）で実施された。

公表論文

Panettieri RA, Brightling C, Sjobring U, Péterffy A, Tornling G, Daoud SZ et al.
STRATOS 1 and 2: considerations in clinical trial design for a fully human monoclonal antibody in severe asthma.Clin Invest.2015;5:701-11.

治験期間

最初の被験者の組入れ日：2014 年 10 月 30 日
最後の被験者の最終来院日：2017 年 9 月 21 日

開発の相：第 3 相

目的

主要目的：
以下の 2 つの集団を対象に，トラロキヌマブ 300 mg の 2 週間隔での投与が年間喘息増悪率（AAER）に及ぼす影響をプラセボと比較して評価すること：
バイオマーカー陽性集団：SAP に規定するバイオマーカー陽性集団に対するベースライン基準を満たす，全被験者集団の中の被験者（主要集団）
全被験者：ICS＋LABA でコントロールが不十分な喘息を有する成人および青少年被験者（副次的集団）

主要な副次的目的：

- 2 つの被験者集団において，トラロキヌマブが肺機能に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが喘息症状に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが喘息特異的な健康に関連する生活の質に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが ACQ-6 で定義された喘息管理に及ぼす影響をプラセボと比較して評価すること。

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副次的目的：

- 2 つの被験者集団において，トラロキヌマブが喘息の増悪に関連するその他の評価項目に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが喘息による ER 受診，UC 受診および入院に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが投与前および BD 投与後の FEV_1 に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが健康に関連する生活の質に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが喘息による医療資源の利用および生産性の損失に及ぼす影響をプラセボと比較して評価すること。
- 2 つの被験者集団において，トラロキヌマブが喘息症状および喘息管理のその他の測定値に及ぼす影響をプラセボと比較して評価すること。
- トラロキヌマブの PK および免疫原性を評価すること。
- トラロキヌマブの安全性および忍容性を評価すること。

探索的目的：

- トラロキヌマブ投与に対する効果予測バイオマーカーとして，IL-13 の発現増加に関連する可能性のある FE_{NO} およびその他のバイオマーカーを探索的に検討すること。
- IL-13 の発現増加に関連する可能性のあるバイオマーカーのベースラインからの変化と，トラロキヌマブの臨床的有効性との相関の可能性を探索すること。
- 肺機能，症状および生活の質に関するトラロキヌマブの治療効果の発現を評価すること。
- トラロキヌマブに対するクリニカルレスポンスに影響を及ぼし，重症喘息の表現型に関する情報を提供する可能性のある，遺伝子／遺伝的変異に関する今後の探索的研究のために DNA を採取・保存すること。（任意）[a]

[a]結果は総括報告書とは別に報告する

AAER = 年間喘息増悪率，ACQ-6 = 喘息管理質問票 6，BD = 気管支拡張薬，CTR = 治験総括報告書，DNA = デオキシリボ核酸，FE_{NO} = 呼気中一酸化窒素濃度，FEV_1 = 1 秒率，PK = 薬物動態，SAP = 統計解析計画書，ICS = 吸入ステロイド薬，IL-13 = インターロイキン-13，LABA = 長時間作用性 β_2 受容体刺激薬，UC = 救急治療

方法

本治験は，コントロール不能の喘息を有し，吸入ステロイド薬（ICS；1 日の総投与量がプロピオン酸フルチカゾン乾燥粉末製剤 500 μg 以上に相当）および長時間作用性 β_2 受容体刺激薬（LABA）を投与中の喘息が増悪した既往歴のある被験者を対象にトラロキヌマブの固定用量 300 mg を 2 週間隔で（Q2W）皮下（SC）投与したときの有効性および安全性を評価した，無作為化，二重盲検，並行群間，プラセボ対照試験である。

主要解析対象集団は，試験 D2100C00007 でトラロキヌマブのベネフィットの向上が認められており、ベースラインで呼気中一酸化窒素濃度（FE_{NO}）が 37ppb 以上の部分集団であるバイオマーカー陽性集団とした。

最初の登録および組入れ基準の確認後，被験者は 4～6 週間の導入期間に入り，全ての適格性基準の評価に十分な時間をとった。適格性基準を満たした被験者を，トラロキヌマブ 300 mg またはプラセボを SC 注射にて Q2W で 52 週間の投与期間にわたって治験実施施設で投与する群に 1:1 で無作為化した。被験者は，導入期間に採取したサンプルの血清ペリオスチン濃度（16.44 ng/mL 未満，または 16.44 ng/mL 超），地域，および年齢群（成人と青少年）によって無作為化時に層別化された。

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トラロキヌマブ／プラセボの最初の投与は Week 0 に行われた。その後，Week 50 まで Q2W で投与し（合計 26 回投与），Week 52 に治験終了時来院を行った。前回の投与来院から 7 日以内に IMP を投与することはできなかった。被験者は組入れから導入期および投与期を通じて，現在処方されている ICS-LABA およびその他の喘息治療薬を変更することなく継続した。全被験者は Q2W で来院した。追跡調査来院を Week 56 および Week 72 に実施した。追跡調査期間の延長は，免疫原性を適切に評価するために設定した。

被験者の治療について盲検化された独立判定委員会（安全性の評価項目の判定委員会）が，投与期間中に発生した緊急救命室または救急治療の受診および入院の症例，ならびに全ての死亡例を評価し，そのような事象が喘息の増悪によるものであるかどうかを確認した。完全を期すため，判定委員会は，無作為化後に発現した心血管系，脳血管系および悪性腫瘍の有害事象（AE）の評価も行った。独立データ安全性モニタリング委員会を設置し，治験の安全性を評価することによって青少年被験者の利益を保護した。アナフィラキシー／過敏症の可能性がある全ての事象について，外部の臨床専門家による独立した評価を実施した。

予定被験者数および解析被験者数

合計被験者数 770 例（1 群あたり 385 例）は，治験対象集団全体およびバイオマーカー陽性の部分集団において，プラセボに対してトラロキヌマブでの年間喘息増悪率（AAER）の減少を示すのに十分なものと考えられた。

サンプルサイズは，プラセボ投与群の年間増悪率を 0.8，全被験者集団およびバイオマーカー陽性集団の形状パラメータを 0.95（過剰分散）と仮定し，必要な人年の数として算出した。サンプルサイズの計算では，全被験者集団に対する有意水準を 1%，バイオマーカー陽性集団に対する有意水準を 4%とした。

治験期間中の追跡不能率を一律 15%と仮定すると，770 例を無作為割付けすることで，投与群あたり約 355 リスク人年（subject years at risk）になると予測された。これにより，全被験者集団において，喘息増悪率の 37%減少までの効果を伴って優越性を示すことに対して 90%以上の検出力が得られると予測された。

並行群間第 3 相試験（D2210C00007）と同じ有病率を仮定し，バイオマーカー陽性集団（主要集団）に対する有意水準を 5%としたとき，被験者の 25%がバイオマーカー陽性の基準（ベースラインの FE_{NO} ≥37 ppb）を満たした場合，真の喘息増悪率の 50%減少は，80%の検出力で優越性を示すと考えられる。

診断および主要な選択基準

本治験の対象集団は，ICS-LABA ではコントロール不能なままで増悪しやすい喘息を有し，導入期間または無作為化時に 1 秒率（FEV_1）の可逆性が 12%以上かつ 200 mL 以上である成人および青少年患者（12～75 歳）とした。

治験薬

トラロキヌマブは，注射用 150 mg/mL 溶液（プレフィルドシリンジ：付属品付き，容量 1.0 mL）として提供された。プラセボは，外観を一致させた付属品付きプレフィルドシリンジ（容量 1.0 mL）として提供された。注射用トラロキヌマブ 150 mg/mL 溶液およびプラセボは，AstraZeneca の委託を受けて MedImmune が製造した。被験者をトラロキヌマブ 300 mg 投与群またはプラセボ投与群に 1:1 の割合で無作為に割り付け，Q2W で SC 注射した。

本治験では，トラロキヌマブの 3 つのロットと，プラセボの 3 つのロットを使用した。個々のロット番号およびその他の情報は，治験総括報告書に記載する。

治験薬投与期間

二重盲検下で無作為に割り付けたトラロキヌマブ 300 mg（またはプラセボ）を SC 注射により 52 週間にわたり Q2W で被験者に投与した。被験者は組入れから導入期および投与期を通じて，現在処方されている ICS-LABA およびその他の喘息治療薬を変更することなく継続した。

評価項目

治験実施計画書識別コード：D2210C00008

主要評価項目：

主要アウトカム変数：Week 52 までの AAER

主要結果尺度：AAER の減少

重要な副次的評価項目：

- 重要なアウトカム変数：投与前／BD 投与前の FEV_1 のベースラインからの変化率（重要な結果尺度：Week 52 の変化率のプラセボ投与群に対する変化率の差）
- 重要なアウトカム変数：1 日の喘息症状スコア（Asthma Daily Diary に記録された日中および夜間の合計スコア）の 2 週間平均のベースラインからの変化（重要な結果尺度：Week 52 のプラセボ投与群との平均差）
- 重要なアウトカム変数：12 歳以上の喘息管理質問票（AQLQ[S]+12）合計スコアのベースラインからの変化（重要な結果尺度：Week 52 のプラセボ投与群との平均差）
- 重要なアウトカム変数：ACQ-6 のベースラインからの変化（重要な結果尺度：Week 52 のプラセボ投与群との平均差）

副次的評価項目：

- 初回の喘息の増悪までの時間および喘息の増悪が 1 回以上認められた被験者の割合
- ER，UC の受診または入院と関連する AAER
- 投与前／BD 投与後
- EQ-5D-5L Daily Living Questionnaire
- WPAI+CIQ
- 喘息特有の資源の利用（例：予定外の受診，医師への予定外の電話連絡，他の喘息治療薬の使用）
- 救援療法の使用
- 自宅での PEF（朝と晩）
- 喘息による夜間覚醒
- PK パラメータ：C_{trough}
- 免疫原性のアウトカム変数：ADA 陽性の発現頻度およびそれらの中和能の特性評価
- AE/SAE；バイタルサイン；dECG；血液生化学検査，血液学検査および尿検査；身体検査

探索的評価項目：

- 重要なアウトカム変数：Week 52 までの AAER（重要な変数）
- その他のアウトカム変数：
  - 投与前／BD 投与前の FEV_1 のベースラインからの変化率
  - 1 日の喘息症状スコア（Asthma Daily Diary に記録された日中および夜間の合計スコア）の 2 週間平均のベースラインからの変化
  - AQLQ(S)+12 のベースラインからの変化
  - ACQ-6 のベースラインからの変化
- 評価したバイオマーカー：
  - 血中好酸球
  - FE_{NO}
  - 血清総 IgE
- 投与前／BD 投与前の FEV_1 のベースラインからの変化率および絶対変化量
- 1 日の喘息症状スコア（Asthma Daily Diary に記録された日中および夜間の合計スコア）の平均のベースラインからの変化
- AQLQ(S)+12 のベースラインからの変化
- FVC および $FEF_{25-75\%}$のベースラインからの変化率

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- ベースラインからの Clinician-Global Impression of Change（CGIC）
- DNA

AAER = 年間喘息増悪率，ADA = 抗薬物抗体，AE = 有害事象，ACQ-6 = 喘息管理質問票 6，AQLQ(S)+12 = 12 歳以上の喘息患者の生活の質に関するアンケート（標準活動版），BD = 気管支拡張薬，CGIC = 臨床全般印象度－変化，CTR = 治験総括報告書，dECG = デジタル心電図，DNA = デオキシリボ核酸，EQ-5D-5L = EuroQoL の健康に関する質問票（5 項目 5 レベル），ER = 緊急救命室，$FEF_{25-75\%}$ = 努力性肺活量の 25～75%での努力性呼気流量，FE_{NO} = 呼気中一酸化窒素濃度，FEV_1 = 1 秒率，FVC = 努力性肺活量，ICS = 吸入ステロイド薬，IgE = 免疫グロブリン E，IL-13 = インターロイキン-13，LABA = 長時間作用性 β_2 受容体刺激薬，PEF = 最大呼気流量，PK = 薬物動態，SAP = 統計解析計画書，SAE = 重篤な有害事象，UC = 救急治療，WPAI+CIQ = 労働生産性および活動障害に関する質問票+授業障害に関する質問票

統計学的手法

本治験の主要評価項目は，プラセボ Q2W と比較した，トラロキヌマブ 300 mg Q2W の Week 52 までの AAER とした。重要な副次的評価項目は，Week 52 の気管支拡張薬使用前（pre-BD）の FEV_1 のベースラインからの変化率，ならびに，Week 52 の総喘息症状スコア，12 歳以上の喘息患者の生活の質に関するアンケート（標準活動版）（AQLQ[S]+12）スコアおよび喘息管理質問票 6（ACQ-6）スコアのベースラインからの変化とした。

バイオマーカー陽性集団および全被験者集団における主要アウトカム変数および重要な副次的アウトカム変数に対し，予め規定した階層的検定法を用いた。これにより，ファミリーワイズの第一種過誤率が強力に制御された。バイオマーカー陽性集団における主要評価項目について，プラセボ Q2W と比較してトラロキヌマブ 300 mg Q2W を両側 5%の有意水準で検定した。治療効果の頑健性を評価するため，主要評価項目および重要な副次的連続評価項目について，さまざまな欠測データメカニズムの仮定に基づいて感度分析を実施した。

トラロキヌマブ 300 mg Q2W 投与群の AAER を，共変量で補正した負の二項モデルを用いてプラセボ Q2W 投与群と比較した。主要評価項目に対する治療効果の一貫性を，バイオマーカー陽性集団およびバイオマーカー陰性（ベースラインの FE_{NO} <37 ppb）集団内の異なる部分集団に渡り検討した。最大の解析対象集団[1]（FAS；全被験者）に対する部分集団解析は，FAS 集団において Week 52 で年間喘息増悪率に有意な治療効果が認められた場合にのみ実施した。重要な副次的評価項目の解析には反復測定解析を用いた。

トラロキヌマブの安全性および忍容性を，有害事象，臨床検査値，バイタルサイン，心電図（ECG）および身体所見の解析によって評価した。

[1] FAS は，無作為割付けされ，52 週間の IMP 投与を受ける可能性があり，いずれかの IMP を投与された全ての被験者と定義した。

結果の概要

治験対象集団

本治験では，被験者 1,696 例が登録され，856 例が無作為化された。無作為化された被験者のうち，849 例（99.2%）が IMP の投与を受け，7 例（0.8%）は IMP の投与を受けなかった。このうち 1 例は重複被験者であった。

無作為化された被験者 732 例（85.5%）が IMP 投与を完了した。117 例（13.7%）が IMP の投与を中止した。IMP の投与を中止した被験者の割合は，トラロキヌマブ 300 mg Q2W 投与群（61 例［14.3%］）とプラセボ Q2W 投与群（56 例［13.1%］）で同程度であった。

全体で，IMP 投与中止の理由として最も多かったものは，AE（44 例［5.1%］）および被験者による中止（42 例［4.9%］）であった。被験者による中止の報告例数は，各投与群で同程度であった。AE のため IMP の投与を中止した被験者は，トラロキヌマブ 300 mg Q2W 投与群（27 例［6.3%］）でプラセボ Q2W 投与群（17 例［4.0%］）と比べて多かった。

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無作為化された被験者 856 例のうち，バイオマーカー陽性集団への組入れ基準（ベースラインの FE_{NO} ≥37 ppb）を満たした被験者は 231 例，バイオマーカー陰性集団への組入れ基準を満たした被験者（ベースラインの FE_{NO} <37 ppb）は 612 例であった。被験者 13 例は，FE_{NO} の結果が欠測していたため，バイオマーカーの状態が「不明」であった。

FAS に含まれた，バイオマーカー陽性集団の無作為化された被験者 229 例の大半は，白人（58.5%）および女性（62.9%）であった。両投与群の平均年齢は 45.1 歳（範囲：12～75 歳）であった。18 例（7.9%）は 12 歳以上 18 歳未満（青少年），残りの被験者は成人であり，このうち 19 例（8.3%）は 65 歳以上であった。

いずれのバイオマーカー集団においても，患者背景およびベースライン疾患特性，ならびに併用薬の使用は投与群間で均衡がとれており，治験対象集団は意図した対象集団をおおむね代表するものであった。

有効性の結果

主要評価項目である，Week 52 までの AAER の減少について，バイオマーカー陽性集団においてトラロキヌマブ 300 mg Q2W ではプラセボ Q2W と比べて統計学的に有意なベネフィットまたは臨床的に意味のあるベネフィットは観察されなかった（AAER の 16%減少［95% CI：−33.71～47.01，p = 0.4656］）。バイオマーカー陽性集団について，トラロキヌマブ 300 mg Q2W 投与群内で，BD 投与前 FEV_1，BD 投与後 FEV_1，努力性肺活量，25～75%の努力性肺活量での最大呼気流量（$FEF_{25-75\%}$）のベースラインから Week 52 までの平均変化率，BD 投与前 FEV_1 のベースラインからの平均絶対変化量，および朝・夕の最大呼気流量のベースラインからの平均変化について，肺機能が改善する傾向が認められた。しかし，プラセボ効果が強かったため，トラロキヌマブ投与によりプラセボと比較して認められた肺機能パラメータの改善は，Week 52 の $FEF_{25-75\%}$ の名目上統計学的に有意な改善（p = 0.0229）を除き，統計学的に有意でも臨床的に重要でもなかった。バイオマーカー陽性集団について，トラロキヌマブ投与は，喘息症状，健康に関連する生活の質または医療経済に関連する副次的評価項目のいずれにおいても，臨床的に意味のある改善にはつながらなかった。

安全性の結果

バイオマーカー陽性集団において，平均（標準偏差）曝露期間は，トラロキヌマブ 300 mg Q2W 投与群で 335.5（78.5）日，プラセボ Q2W 投与群で 333.0（84.9）日であった。曝露期間は，バイオマーカー陰性集団の 2 投与群で同程度であった。

AE が発現した被験者の割合は，トラロキヌマブ 300 mg Q2W 投与群（72.0%）およびプラセボ Q2W 投与群（68.7%）で同程度であった。AE の多くは軽度または中等度であった。ほとんどの AE は，治験担当医師によって IMP との関連はないと判断された。

トラロキヌマブ 300 mg Q2W 投与群およびプラセボ Q2W 投与群で最も高頻度に報告された AE は，喘息（11.8% vs 14.5%），ウイルス性上気道感染（11.5% vs 12.3%），頭痛（9.4% vs 7.3%），気管支炎（8.0% vs 7.3%）および上気道感染（6.8% vs 6.9%）であった。一部の AE を報告した被験者の割合に投与群間で差が認められた。最も顕著であったのは注射部位関連事象で，トラロキヌマブ投与の被験者（65 例［15.3%］）でプラセボ投与の被験者（13 例［3.1%］）と比べて多く発現した。最も高頻度に報告された重篤な有害事象（SAE）は喘息であり，トラロキヌマブ 300 mg Q2W 投与群（4.0%）とプラセボ Q2W 投与群（5.5%）で同程度の割合の被験者で報告された。

IMP の投与中止に至った AE（DAE）が計 41 例（4.8%）で報告された。DAE が認められた被験者は，トラロキヌマブ 300 mg Q2W 投与群（27 例［6.4%］）においてプラセボ Q2W 投与群（14 例［3.3%］）のほぼ 2 倍であった。これは主に，トラロキヌマブ投与で注射部位関連事象の発現割合がより高かったためであった。トラロキヌマブ 300 mg Q2W 投与群において，注射部位関連事象は最も高頻度に報告された DAE であり，14 例で報告され，これらの被験者の大半（14 例中 13 例）で IMP との因果関係ありと判断された。プラセボ Q2W 投与群の 1 例に注射部位反応の DAE が発現し，IMP との関連ありと判断された。

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本治験期間中に 5 例の死亡が報告された。被験者 2 例は投与期間中に死亡した。バイオマーカー陰性集団において，トラロキヌマブ 300 mg Q2W 投与群の 1 例が，IMP と関連がある SAE である尿路性敗血症および IMP と関連がない SAE である心房細動により死亡した。バイオマーカー陽性集団において，プラセボ Q2W 投与群の 1 例が，IMP と関連がない SAE である喘息により死亡した。残りの 3 例はプラセボ Q2W 投与群のバイオマーカー陰性集団の被験者であり，後観察期間中に発現した IMP と関連がない SAE により死亡した。

特に注目すべき安全性に関連する AE の報告は，投与群間で均衡がとれていた。治験担当医師によりトラロキヌマブと関連ありと判断されたアナフィラキシーの症例は認められなかった。

概して，血液生化学検査および尿検査のパラメータの推移に臨床的に意味のある変化は認められなかった。血液学検査パラメータにおいて観察された唯一の変化は，治験期間中にプラセボ Q2W 投与群と比べてトラロキヌマブ 300 mg Q2W 投与群で認められた血中好酸球数のわずかな増加であったが，これは臨床的に意味がないと判断された。好酸球数の中央値は，トラロキヌマブの投与中止後に正常値に回復した。投与期間中に血中好酸球数が 1500/μL を 1 回以上上回った被験者は少なく（23 例［2.7%］），その発現頻度はトラロキヌマブ 300 mg Q2W 投与群（17 例［4.0%］）の方がプラセボ投与群（6 例［1.4%］）と比べて高かった。バイオマーカー陰性集団の 2 例で，ベースライン後の血中好酸球数が 1500/μL を上回ることに関連する，懸念すべき AE が発現した。1 例はトラロキヌマブ 300 mg Q2W 投与群で，IMP と関連がない AE として過敏性血管炎が発現した。もう 1 例はプラセボ Q2W 投与群で，IMP と関連がない SAE として好酸球性多発血管炎性肉芽腫症が発現し，IMP の投与中止に至った。Hy's Law 基準に該当した被験者はいなかった。バイタルサイン，ECG および身体検査に関連する安全性の懸念も認められなかった。

抗薬物抗体（ADA）発現頻度は，トラロキヌマブ 300 mg Q2W 投与群で 1.2%（405 例中 5 例），プラセボ Q2W 投与群で 0.8%（3/394 例）であった。トラロキヌマブ 300 mg Q2W 投与群の ADA 陽性の被験者全 5 例で，トラロキヌマブに対する中和抗体が陽性であった。

薬物動態の結果

トラロキヌマブは一貫して Week 8 頃に定常状態に達し，トラロキヌマブ反復投与後にトラロキヌマブ 300 mg Q2W 投与群で観察された累積係数は 2.4 と小さかった。青少年被験者は，成人被験者と比べて体重が低いことから，血清中トラロキヌマブ濃度が予想どおりわずかに高かった。

結論

コントロール不能の喘息を有し，ICS（1 日の総投与量がプロピオン酸フルチカゾン乾燥粉末製剤 500 μg 以上に相当），LABA および IMP を投与中に喘息が増悪した既往歴のある被験者において，以下の全般的結論を得た。

- バイオマーカー陽性集団において，トラロキヌマブ 300 mg Q2W の投与は，プラセボと比べて，主要評価項目である AAER を有意に減少させなかった。
- トラロキヌマブの忍容性は良好で，安全性プロファイルも以前観察されたものと同様に良好であった。

報告日：20[redacted] 年[redacted] 月[redacted] 日

1.15.2　安全性の評価

1.15.2.1　有害事象

1.15.2.1.1　全ての有害事象［Source: Table 11.3.2.7.1］

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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
Subjects with any AE	306 (72.0)	78.7659	290 (68.7)	74.0287
製品の問題	2 (0.5)	0.5148	2 (0.5)	0.5105
医療機器不具合	2 (0.5)	0.5148	1 (0.2)	0.2553
患者と医療機器間の不適合	0		1 (0.2)	0.2553
感染症および寄生虫症	193 (45.4)	49.6792	202 (47.9)	51.5648
ウイルス性上気道感染	50 (11.8)	12.8703	52 (12.3)	13.2741
気管支炎	34 (8.0)	8.7518	31 (7.3)	7.9134
上気道感染	29 (6.8)	7.4647	31 (7.3)	7.9134
ウイルス性気道感染	18 (4.2)	4.6333	19 (4.5)	4.8502
尿路感染	17 (4.0)	4.3759	12 (2.8)	3.0633
インフルエンザ	16 (3.8)	4.1185	15 (3.6)	3.8291
気道感染	16 (3.8)	4.1185	18 (4.3)	4.5949
副鼻腔炎	13 (3.1)	3.3463	15 (3.6)	3.8291
鼻炎	11 (2.6)	2.8315	14 (3.3)	3.5738
鼻咽頭炎	9 (2.1)	2.3166	6 (1.4)	1.5316

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
咽頭炎	7 (1.6)	1.8018	11 (2.6)	2.8080
肺炎	7 (1.6)	1.8018	8 (1.9)	2.0422
扁桃炎	7 (1.6)	1.8018	6 (1.4)	1.5316
急性副鼻腔炎	6 (1.4)	1.5444	11 (2.6)	2.8080
胃腸炎	4 (0.9)	1.0296	7 (1.7)	1.7869
口腔カンジダ症	4 (0.9)	1.0296	3 (0.7)	0.7658
喉頭炎	3 (0.7)	0.7722	3 (0.7)	0.7658
下気道感染	3 (0.7)	0.7722	3 (0.7)	0.7658
口腔ヘルペス	3 (0.7)	0.7722	2 (0.5)	0.5105
蜂巣炎	2 (0.5)	0.5148	3 (0.7)	0.7658
結膜炎	2 (0.5)	0.5148	2 (0.5)	0.5105
ウイルス性胃腸炎	2 (0.5)	0.5148	2 (0.5)	0.5105
帯状疱疹	2 (0.5)	0.5148	1 (0.2)	0.2553
レンサ球菌性咽頭炎	2 (0.5)	0.5148	0	
ウイルス性発疹	2 (0.5)	0.5148	1 (0.2)	0.2553
外陰部腟カンジダ症	2 (0.5)	0.5148	0	
外陰腟真菌感染	2 (0.5)	0.5148	1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
細菌性結膜炎	1 (0.2)	0.2574	0	
膀胱炎	1 (0.2)	0.2574	5 (1.2)	1.2764
感染性下痢	1 (0.2)	0.2574	1 (0.2)	0.2553
耳感染	1 (0.2)	0.2574	3 (0.7)	0.7658
心内膜炎	1 (0.2)	0.2574	0	
感染性腸炎	1 (0.2)	0.2574	0	
眼感染	1 (0.2)	0.2574	0	
毛包炎	1 (0.2)	0.2574	0	
皮膚真菌感染	1 (0.2)	0.2574	0	
ヘルペスウイルス感染	1 (0.2)	0.2574	0	
皮膚播種性帯状疱疹	1 (0.2)	0.2574	0	
膿痂疹	1 (0.2)	0.2574	0	
注射部位蜂巣炎	1 (0.2)	0.2574	0	
骨髄炎	1 (0.2)	0.2574	0	
外耳炎	1 (0.2)	0.2574	1 (0.2)	0.2553
急性中耳炎	1 (0.2)	0.2574	0	
咽頭扁桃炎	1 (0.2)	0.2574	4 (0.9)	1.0211

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
処置後感染	1 (0.2)	0.2574	0	
肺結核	1 (0.2)	0.2574	0	
歯髄炎	1 (0.2)	0.2574	1 (0.2)	0.2553
腎盂腎炎	1 (0.2)	0.2574	1 (0.2)	0.2553
ブドウ球菌性咽頭炎	1 (0.2)	0.2574	0	
歯感染	1 (0.2)	0.2574	1 (0.2)	0.2553
気管気管支炎	1 (0.2)	0.2574	2 (0.5)	0.5105
細菌性尿路感染	1 (0.2)	0.2574	1 (0.2)	0.2553
尿路性敗血症	1 (0.2)	0.2574	0	
ウイルス感染	1 (0.2)	0.2574	3 (0.7)	0.7658
ウイルス性咽頭炎	1 (0.2)	0.2574	2 (0.5)	0.5105
ダニ皮膚炎	0		1 (0.2)	0.2553
虫垂炎	0		1 (0.2)	0.2553
細菌性疾患キャリアー	0		1 (0.2)	0.2553
細菌性気管支炎	0		1 (0.2)	0.2553
カンジダ感染	0		1 (0.2)	0.2553
子宮頚管炎	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
慢性副鼻腔炎	0		6 (1.4)	1.5316
ウイルス性結膜炎	0		2 (0.5)	0.5105
せつ	0		2 (0.5)	0.5105
A型肝炎	0		1 (0.2)	0.2553
単純ヘルペス	0		1 (0.2)	0.2553
感染性胸水	0		1 (0.2)	0.2553
ウイルス性喉頭炎	0		1 (0.2)	0.2553
限局性感染	0		1 (0.2)	0.2553
中咽頭カンジダ症	0		1 (0.2)	0.2553
中耳炎	0		1 (0.2)	0.2553
骨盤内炎症性疾患	0		1 (0.2)	0.2553
歯周炎	0		1 (0.2)	0.2553
膿疱性皮疹	0		1 (0.2)	0.2553
レンサ球菌性尿路感染	0		1 (0.2)	0.2553
白癬感染	0		1 (0.2)	0.2553
足部白癬	0		1 (0.2)	0.2553
細菌性扁桃炎	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
歯膿瘍	0		1 (0.2)	0.2553
気管炎	0		1 (0.2)	0.2553
細菌性上気道感染	0		1 (0.2)	0.2553
水痘	0		1 (0.2)	0.2553
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.5)	0.5148	1 (0.2)	0.2553
腎血管筋脂肪腫	1 (0.2)	0.2574	0	
平滑筋腫	1 (0.2)	0.2574	0	
直腸癌	0		1 (0.2)	0.2553
血液およびリンパ系障害	13 (3.1)	3.3463	20 (4.7)	5.1054
貧血	3 (0.7)	0.7722	4 (0.9)	1.0211
白血球減少症	2 (0.5)	0.5148	3 (0.7)	0.7658
脾腫	2 (0.5)	0.5148	0	
血小板減少症	2 (0.5)	0.5148	2 (0.5)	0.5105
好酸球増加症	1 (0.2)	0.2574	0	
リンパ節症	1 (0.2)	0.2574	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
好中球減少症	1 (0.2)	0.2574	3 (0.7)	0.7658
白血球障害	1 (0.2)	0.2574	1 (0.2)	0.2553
高色素性貧血	0		1 (0.2)	0.2553
鉄欠乏性貧血	0		2 (0.5)	0.5105
白血球増加症	0		4 (0.9)	1.0211
リンパ球増加症	0		1 (0.2)	0.2553
小赤血球症	0		1 (0.2)	0.2553
好中球増加症	0		1 (0.2)	0.2553
血小板障害	0		1 (0.2)	0.2553
血小板増加症	0		2 (0.5)	0.5105
免疫系障害	7 (1.6)	1.8018	6 (1.4)	1.5316
季節性アレルギー	4 (0.9)	1.0296	2 (0.5)	0.5105
食物アレルギー	2 (0.5)	0.5148	1 (0.2)	0.2553
薬物過敏症	1 (0.2)	0.2574	1 (0.2)	0.2553
節足動物刺傷アレルギー	0		1 (0.2)	0.2553
好酸球性多発血管炎性肉芽腫症	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
内分泌障害	2 (0.5)	0.5148	2 (0.5)	0.5105
甲状腺機能低下症	2 (0.5)	0.5148	0	
甲状腺腫瘤	0		1 (0.2)	0.2553
甲状腺炎	0		1 (0.2)	0.2553
代謝および栄養障害	8 (1.9)	2.0592	17 (4.0)	4.3396
高尿酸血症	2 (0.5)	0.5148	0	
低カリウム血症	2 (0.5)	0.5148	0	
2型糖尿病	2 (0.5)	0.5148	1 (0.2)	0.2553
食欲減退	1 (0.2)	0.2574	1 (0.2)	0.2553
痛風	1 (0.2)	0.2574	1 (0.2)	0.2553
肥満	1 (0.2)	0.2574	1 (0.2)	0.2553
脱水	0		1 (0.2)	0.2553
糖尿病	0		5 (1.2)	1.2764
脂質異常症	0		1 (0.2)	0.2553
耐糖能障害	0		1 (0.2)	0.2553
高コレステロール血症	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
高血糖	0		3 (0.7)	0.7658
高脂血症	0		1 (0.2)	0.2553
低カルシウム血症	0		1 (0.2)	0.2553
ビタミンD欠乏	0		1 (0.2)	0.2553
精神障害	15 (3.5)	3.8611	18 (4.3)	4.5949
不安	8 (1.9)	2.0592	7 (1.7)	1.7869
不眠症	5 (1.2)	1.2870	5 (1.2)	1.2764
うつ病	2 (0.5)	0.5148	4 (0.9)	1.0211
不快気分	1 (0.2)	0.2574	0	
睡眠障害	1 (0.2)	0.2574	1 (0.2)	0.2553
自殺念慮	1 (0.2)	0.2574	0	
中期不眠症	0		1 (0.2)	0.2553
気分変化	0		1 (0.2)	0.2553
心的外傷後ストレス障害	0		1 (0.2)	0.2553
ストレス	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
神経系障害	63 (14.8)	16.2165	47 (11.1)	11.9978
頭痛	40 (9.4)	10.2962	32 (7.6)	8.1687
浮動性めまい	11 (2.6)	2.8315	7 (1.7)	1.7869
肋間神経痛	5 (1.2)	1.2870	1 (0.2)	0.2553
片頭痛	4 (0.9)	1.0296	2 (0.5)	0.5105
坐骨神経痛	3 (0.7)	0.7722	0	
失神	3 (0.7)	0.7722	1 (0.2)	0.2553
無嗅覚	2 (0.5)	0.5148	1 (0.2)	0.2553
頚腕症候群	2 (0.5)	0.5148	0	
神経炎	2 (0.5)	0.5148	1 (0.2)	0.2553
神経根障害	2 (0.5)	0.5148	3 (0.7)	0.7658
傾眠	2 (0.5)	0.5148	1 (0.2)	0.2553
灼熱感	1 (0.2)	0.2574	0	
意識消失	1 (0.2)	0.2574	0	
腰髄神経根障害	1 (0.2)	0.2574	0	
神経筋痛	1 (0.2)	0.2574	0	
末梢性ニューロパチー	1 (0.2)	0.2574	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
錯感覚	1 (0.2)	0.2574	0	
副鼻腔炎に伴う頭痛	1 (0.2)	0.2574	0	
血管性脳症	1 (0.2)	0.2574	0	
頚動脈瘤	0		1 (0.2)	0.2553
味覚異常	0		1 (0.2)	0.2553
根症候群	0		1 (0.2)	0.2553
緊張性頭痛	0		2 (0.5)	0.5105
振戦	0		1 (0.2)	0.2553
血管性頭痛	0		1 (0.2)	0.2553
眼障害	11 (2.6)	2.8315	14 (3.3)	3.5738
アレルギー性結膜炎	2 (0.5)	0.5148	3 (0.7)	0.7658
眼そう痒症	2 (0.5)	0.5148	2 (0.5)	0.5105
眼瞼浮腫	2 (0.5)	0.5148	1 (0.2)	0.2553
流涙増加	2 (0.5)	0.5148	0	
眼瞼炎	1 (0.2)	0.2574	0	
黄斑色素沈着	1 (0.2)	0.2574	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term
(Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
眼充血	1 (0.2)	0.2574	0	
羞明	1 (0.2)	0.2574	0	
潰瘍性角膜炎	1 (0.2)	0.2574	0	
白内障	0		3 (0.7)	0.7658
結膜出血	0		1 (0.2)	0.2553
角膜菲薄化	0		1 (0.2)	0.2553
眼乾燥	0		1 (0.2)	0.2553
眼刺激	0		1 (0.2)	0.2553
眼痛	0		1 (0.2)	0.2553
眼部腫脹	0		1 (0.2)	0.2553
眼瞼障害	0		1 (0.2)	0.2553
円錐角膜	0		1 (0.2)	0.2553
網膜剥離	0		1 (0.2)	0.2553
網膜血管障害	0		1 (0.2)	0.2553
耳および迷路障害	8 (1.9)	2.0592	12 (2.8)	3.0633
回転性めまい	4 (0.9)	1.0296	6 (1.4)	1.5316

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
耳痛	1 (0.2)	0.2574	3 (0.7)	0.7658
耳そう痒症	1 (0.2)	0.2574	0	
混合性難聴	1 (0.2)	0.2574	0	
頭位性回転性めまい	1 (0.2)	0.2574	0	
アレルギー性中耳炎	0		1 (0.2)	0.2553
片耳難聴	0		1 (0.2)	0.2553
耳閉	0		1 (0.2)	0.2553
メニエール病	0		1 (0.2)	0.2553
中耳滲出液	0		1 (0.2)	0.2553
心臓障害	17 (4.0)	4.3759	15 (3.6)	3.8291
頻脈	5 (1.2)	1.2870	8 (1.9)	2.0422
狭心症	3 (0.7)	0.7722	2 (0.5)	0.5105
心房細動	2 (0.5)	0.5148	0	
第一度房室ブロック	2 (0.5)	0.5148	0	
心不全	2 (0.5)	0.5148	1 (0.2)	0.2553
不整脈	1 (0.2)	0.2574	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
心筋症	1 (0.2)	0.2574	0	
期外収縮	1 (0.2)	0.2574	2 (0.5)	0.5105
心筋梗塞	1 (0.2)	0.2574	0	
動悸	1 (0.2)	0.2574	0	
洞性頻脈	1 (0.2)	0.2574	1 (0.2)	0.2553
上室性頻脈	1 (0.2)	0.2574	0	
発作性頻脈	1 (0.2)	0.2574	0	
不安定狭心症	0		1 (0.2)	0.2553
うっ血性心筋症	0		1 (0.2)	0.2553
慢性肺性心	0		1 (0.2)	0.2553
僧帽弁閉鎖不全症	0		1 (0.2)	0.2553
血管障害	21 (4.9)	5.4055	16 (3.8)	4.0843
高血圧	16 (3.8)	4.1185	11 (2.6)	2.8080
高血圧クリーゼ	3 (0.7)	0.7722	3 (0.7)	0.7658
静脈瘤	2 (0.5)	0.5148	0	
ほてり	1 (0.2)	0.2574	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
末梢静脈疾患	1 (0.2)	0.2574	0	
低血圧	0		2 (0.5)	0.5105
末梢動脈閉塞性疾患	0		1 (0.2)	0.2553
血栓性静脈炎	0		1 (0.2)	0.2553
呼吸器、胸郭および縦隔障害	93 (21.9)	23.9387	106 (25.1)	27.0588
喘息	50 (11.8)	12.8703	63 (14.9)	16.0821
咳嗽	9 (2.1)	2.3166	12 (2.8)	3.0633
アレルギー性鼻炎	9 (2.1)	2.3166	10 (2.4)	2.5527
口腔咽頭痛	8 (1.9)	2.0592	13 (3.1)	3.3185
発声障害	6 (1.4)	1.5444	4 (0.9)	1.0211
鼻漏	4 (0.9)	1.0296	3 (0.7)	0.7658
鼻閉	3 (0.7)	0.7722	5 (1.2)	1.2764
慢性気管支炎	2 (0.5)	0.5148	0	
鼻出血	2 (0.5)	0.5148	1 (0.2)	0.2553
咽喉刺激感	2 (0.5)	0.5148	0	
アレルギー性気管支炎	1 (0.2)	0.2574	1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
アレルギー性咳嗽	1 (0.2)	0.2574	0	
アレルギー性咽頭炎	1 (0.2)	0.2574	0	
アレルギー性呼吸器疾患	1 (0.2)	0.2574	0	
喀血	1 (0.2)	0.2574	0	
過換気	1 (0.2)	0.2574	0	
鼻粘膜潰瘍	1 (0.2)	0.2574	0	
鼻中隔潰瘍	1 (0.2)	0.2574	0	
鼻甲介肥大	1 (0.2)	0.2574	0	
咽頭感覚鈍麻	1 (0.2)	0.2574	0	
咽頭浮腫	1 (0.2)	0.2574	0	
胸膜炎	1 (0.2)	0.2574	0	
呼吸障害	1 (0.2)	0.2574	3 (0.7)	0.7658
くしゃみ	1 (0.2)	0.2574	3 (0.7)	0.7658
上気道咳症候群	1 (0.2)	0.2574	1 (0.2)	0.2553
血管運動性鼻炎	1 (0.2)	0.2574	0	
喘鳴	1 (0.2)	0.2574	5 (1.2)	1.2764
急性呼吸不全	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
アレルギー性副鼻腔炎	0		1 (0.2)	0.2553
気管支閉塞	0		1 (0.2)	0.2553
気管支痙攣	0		1 (0.2)	0.2553
慢性好酸球性副鼻腔炎	0		1 (0.2)	0.2553
呼吸困難	0		8 (1.9)	2.0422
鼻閉塞	0		1 (0.2)	0.2553
鼻茸	0		2 (0.5)	0.5105
鼻そう痒症	0		1 (0.2)	0.2553
鼻甲介異常	0		1 (0.2)	0.2553
湿性咳嗽	0		2 (0.5)	0.5105
呼吸不全	0		1 (0.2)	0.2553
睡眠時無呼吸症候群	0		1 (0.2)	0.2553
喀痰増加	0		2 (0.5)	0.5105
胃腸障害	62 (14.6)	15.9591	50 (11.8)	12.7636
下痢	17 (4.0)	4.3759	9 (2.1)	2.2974
消化不良	9 (2.1)	2.3166	7 (1.7)	1.7869

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) − date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
上腹部痛	8 (1.9)	2.0592	1 (0.2)	0.2553
胃食道逆流性疾患	7 (1.6)	1.8018	3 (0.7)	0.7658
腹痛	6 (1.4)	1.5444	7 (1.7)	1.7869
悪心	5 (1.2)	1.2870	3 (0.7)	0.7658
歯痛	5 (1.2)	1.2870	4 (0.9)	1.0211
嘔吐	5 (1.2)	1.2870	2 (0.5)	0.5105
腹部不快感	4 (0.9)	1.0296	2 (0.5)	0.5105
口内炎	3 (0.7)	0.7722	1 (0.2)	0.2553
腹部膨満	2 (0.5)	0.5148	0	
びらん性胃炎	2 (0.5)	0.5148	1 (0.2)	0.2553
根尖肉芽腫	1 (0.2)	0.2574	0	
潰瘍性大腸炎	1 (0.2)	0.2574	1 (0.2)	0.2553
齲歯	1 (0.2)	0.2574	0	
口内乾燥	1 (0.2)	0.2574	1 (0.2)	0.2553
胃潰瘍	1 (0.2)	0.2574	0	
胃炎	1 (0.2)	0.2574	2 (0.5)	0.5105
歯肉出血	1 (0.2)	0.2574	1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
痔核	1 (0.2)	0.2574	1 (0.2)	0.2553
腸管ポリープ	1 (0.2)	0.2574	0	
過敏性腸症候群	1 (0.2)	0.2574	0	
口唇腫脹	1 (0.2)	0.2574	0	
メレナ	1 (0.2)	0.2574	0	
嚥下痛	1 (0.2)	0.2574	1 (0.2)	0.2553
食道炎	1 (0.2)	0.2574	1 (0.2)	0.2553
流涎過多	1 (0.2)	0.2574	0	
歯の知覚過敏	1 (0.2)	0.2574	0	
臍ヘルニア	1 (0.2)	0.2574	2 (0.5)	0.5105
腹部圧痛	0		2 (0.5)	0.5105
後天性食道ウエッブ	0		1 (0.2)	0.2553
慢性胃炎	0		2 (0.5)	0.5105
便秘	0		1 (0.2)	0.2553
憩室	0		1 (0.2)	0.2553
鼓腸	0		1 (0.2)	0.2553
食中毒	0		3 (0.7)	0.7658

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
血便排泄	0		1 (0.2)	0.2553
裂孔ヘルニア	0		3 (0.7)	0.7658
口の感覚鈍麻	0		1 (0.2)	0.2553
鼠径ヘルニア	0		1 (0.2)	0.2553
腸出血	0		1 (0.2)	0.2553
食道潰瘍	0		1 (0.2)	0.2553
口蓋障害	0		1 (0.2)	0.2553
肝胆道系障害	6 (1.4)	1.5444	6 (1.4)	1.5316
胆道ジスキネジア	1 (0.2)	0.2574	0	
急性胆嚢炎	1 (0.2)	0.2574	0	
慢性胆嚢炎	1 (0.2)	0.2574	0	
脂肪肝	1 (0.2)	0.2574	0	
肝腫大	1 (0.2)	0.2574	1 (0.2)	0.2553
高ビリルビン血症	1 (0.2)	0.2574	0	
胆道仙痛	0		1 (0.2)	0.2553
胆嚢炎	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
胆汁うっ滞	0		1 (0.2)	0.2553
肝機能異常	0		1 (0.2)	0.2553
肝損傷	0		1 (0.2)	0.2553
皮膚および皮下組織障害	41 (9.6)	10.5536	34 (8.1)	8.6792
発疹	10 (2.4)	2.5741	4 (0.9)	1.0211
そう痒症	7 (1.6)	1.8018	5 (1.2)	1.2764
皮膚反応	5 (1.2)	1.2870	0	
蕁麻疹	5 (1.2)	1.2870	9 (2.1)	2.2974
紅斑	4 (0.9)	1.0296	1 (0.2)	0.2553
丘疹	3 (0.7)	0.7722	0	
乾癬	3 (0.7)	0.7722	0	
アレルギー性皮膚炎	2 (0.5)	0.5148	0	
湿疹	2 (0.5)	0.5148	4 (0.9)	1.0211
皮下出血	2 (0.5)	0.5148	0	
皮膚炎	1 (0.2)	0.2574	2 (0.5)	0.5105
アトピー性皮膚炎	1 (0.2)	0.2574	1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term (Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
接触皮膚炎	1 (0.2)	0.2574	5 (1.2)	1.2764
過敏性血管炎	1 (0.2)	0.2574	0	
点状出血	1 (0.2)	0.2574	0	
紅斑性皮疹	1 (0.2)	0.2574	0	
全身性皮疹	1 (0.2)	0.2574	1 (0.2)	0.2553
皮膚病変	1 (0.2)	0.2574	0	
尋常性白斑	1 (0.2)	0.2574	0	
血管浮腫	0		1 (0.2)	0.2553
皮膚嚢腫	0		1 (0.2)	0.2553
皮膚乾燥	0		2 (0.5)	0.5105
斑状出血	0		1 (0.2)	0.2553
全身性そう痒症	0		1 (0.2)	0.2553
斑状皮疹	0		1 (0.2)	0.2553
顔面腫脹	0		1 (0.2)	0.2553
筋骨格系および結合組織障害	53 (12.5)	13.6425	40 (9.5)	10.2109
関節痛	16 (3.8)	4.1185	9 (2.1)	2.2974

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term
(Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
背部痛	16 (3.8)	4.1185	11 (2.6)	2.8080
筋肉痛	7 (1.6)	1.8018	3 (0.7)	0.7658
筋骨格痛	6 (1.4)	1.5444	4 (0.9)	1.0211
四肢痛	6 (1.4)	1.5444	6 (1.4)	1.5316
変形性関節症	5 (1.2)	1.2870	3 (0.7)	0.7658
筋骨格系胸痛	4 (0.9)	1.0296	7 (1.7)	1.7869
関節炎	2 (0.5)	0.5148	2 (0.5)	0.5105
骨端症	2 (0.5)	0.5148	2 (0.5)	0.5105
腱炎	2 (0.5)	0.5148	2 (0.5)	0.5105
強直性脊椎炎	1 (0.2)	0.2574	0	
滑液包炎	1 (0.2)	0.2574	0	
線維筋痛	1 (0.2)	0.2574	0	
坐骨部痛	1 (0.2)	0.2574	0	
関節腫脹	1 (0.2)	0.2574	1 (0.2)	0.2553
四肢不快感	1 (0.2)	0.2574	0	
筋拘縮	1 (0.2)	0.2574	0	
筋痙縮	1 (0.2)	0.2574	3 (0.7)	0.7658

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
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For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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Table 11.3.2.7.1 Adverse events and event rate reported during the treatment period by System Organ Class and preferred term
(Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
筋膜疼痛症候群	1 (0.2)	0.2574	0	
頚部痛	1 (0.2)	0.2574	1 (0.2)	0.2553
骨粗鬆症	1 (0.2)	0.2574	0	
膝蓋大腿関節痛症候群	1 (0.2)	0.2574	0	
脊椎痛	1 (0.2)	0.2574	1 (0.2)	0.2553
肋軟骨炎	0		2 (0.5)	0.5105
外骨腫	0		2 (0.5)	0.5105
筋骨格硬直	0		1 (0.2)	0.2553
交感神経性後頚部症候群	0		1 (0.2)	0.2553
滑液嚢腫	0		2 (0.5)	0.5105
腱鞘炎	0		1 (0.2)	0.2553
腎および尿路障害	9 (2.1)	2.3166	10 (2.4)	2.5527
尿管結石症	2 (0.5)	0.5148	0	
血尿	1 (0.2)	0.2574	4 (0.9)	1.0211
水腎症	1 (0.2)	0.2574	0	
緊張性膀胱	1 (0.2)	0.2574	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
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(Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
頻尿	1 (0.2)	0.2574	1 (0.2)	0.2553
腎仙痛	1 (0.2)	0.2574	1 (0.2)	0.2553
腎嚢胞	1 (0.2)	0.2574	0	
腎機能障害	1 (0.2)	0.2574	0	
排尿困難	0		1 (0.2)	0.2553
腎結石症	0		1 (0.2)	0.2553
尿失禁	0		2 (0.5)	0.5105
尿路障害	0		1 (0.2)	0.2553
生殖系および乳房障害	5 (1.2)	1.2870	8 (1.9)	2.0422
子宮頚管ポリープ	1 (0.2)	0.2574	0	
月経困難症	1 (0.2)	0.2574	0	
卵巣嚢胞	1 (0.2)	0.2574	0	
子宮頚部びらん	1 (0.2)	0.2574	0	
子宮脱	1 (0.2)	0.2574	0	
外陰腟不快感	1 (0.2)	0.2574	0	
腺筋症	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
子宮付属器痛	0		1 (0.2)	0.2553
亀頭包皮炎	0		1 (0.2)	0.2553
良性前立腺肥大症	0		1 (0.2)	0.2553
膀胱瘤	0		1 (0.2)	0.2553
乳瘤	0		1 (0.2)	0.2553
過少月経	0		1 (0.2)	0.2553
子宮出血	0		1 (0.2)	0.2553
腟出血	0		2 (0.5)	0.5105
腟脱	0		1 (0.2)	0.2553
先天性、家族性および遺伝性障害	1 (0.2)	0.2574	1 (0.2)	0.2553
硬化性膵胚腫	1 (0.2)	0.2574	0	
陰嚢水瘤	0		1 (0.2)	0.2553
一般・全身障害および投与部位の状態	87 (20.5)	22.3942	39 (9.2)	9.9556
注射部位反応	23 (5.4)	5.9203	3 (0.7)	0.7658
注射部位紅斑	15 (3.5)	3.8611	0	

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(Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
発熱	8 (1.9)	2.0592	11 (2.6)	2.8080
適用部位反応	6 (1.4)	1.5444	1 (0.2)	0.2553
注射部位そう痒感	6 (1.4)	1.5444	1 (0.2)	0.2553
注射部位腫脹	5 (1.2)	1.2870	0	
末梢腫脹	5 (1.2)	1.2870	1 (0.2)	0.2553
疲労	4 (0.9)	1.0296	3 (0.7)	0.7658
注射部位疼痛	4 (0.9)	1.0296	5 (1.2)	1.2764
穿刺部位反応	4 (0.9)	1.0296	0	
無力症	3 (0.7)	0.7722	5 (1.2)	1.2764
注射部位炎症	3 (0.7)	0.7722	0	
投与部位炎症	2 (0.5)	0.5148	0	
高熱	2 (0.5)	0.5148	0	
注射部位過敏反応	2 (0.5)	0.5148	1 (0.2)	0.2553
局所反応	2 (0.5)	0.5148	0	
非心臓性胸痛	2 (0.5)	0.5148	4 (0.9)	1.0211
末梢性浮腫	2 (0.5)	0.5148	3 (0.7)	0.7658
穿刺部位紅斑	2 (0.5)	0.5148	0	

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
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(Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
投与部位硬結	1 (0.2)	0.2574	0	
投与部位そう痒感	1 (0.2)	0.2574	0	
医薬品副作用	1 (0.2)	0.2574	0	
適用部位紅斑	1 (0.2)	0.2574	1 (0.2)	0.2553
適用部位疼痛	1 (0.2)	0.2574	2 (0.5)	0.5105
適用部位発疹	1 (0.2)	0.2574	0	
胸部不快感	1 (0.2)	0.2574	0	
注射部位内出血	1 (0.2)	0.2574	1 (0.2)	0.2553
注射部位漏出	1 (0.2)	0.2574	0	
注射部位血腫	1 (0.2)	0.2574	0	
注射部位刺激感	1 (0.2)	0.2574	0	
注射部位腫瘤	1 (0.2)	0.2574	0	
注射部位蕁麻疹	1 (0.2)	0.2574	0	
ワクチン接種部位発疹	1 (0.2)	0.2574	0	
乾燥症	1 (0.2)	0.2574	0	
適用部位過敏反応	0		1 (0.2)	0.2553
埋込み部位疼痛	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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System organ class/Preferred term	Tralo 300 mg Q2W (N=425) Number (%) of subjects[a]	Tralo 300 mg Q2W (N=425) Event rate (per 100 pt years)[b]	Placebo (N=422) Number (%) of subjects[a]	Placebo (N=422) Event rate (per 100 pt years)[b]
インフルエンザ様疾患	0		1 (0.2)	0.2553
注射部位出血	0		1 (0.2)	0.2553
注射部位丘疹	0		1 (0.2)	0.2553
疼痛	0		2 (0.5)	0.5105
穿刺部位出血	0		1 (0.2)	0.2553
分泌物分泌	0		1 (0.2)	0.2553
恥骨上痛	0		1 (0.2)	0.2553
臨床検査	21 (4.9)	5.4055	18 (4.3)	4.5949
アラニンアミノトランスフェラーゼ増加	6 (1.4)	1.5444	1 (0.2)	0.2553
血圧上昇	5 (1.2)	1.2870	5 (1.2)	1.2764
アスパラギン酸アミノトランスフェラーゼ増加	3 (0.7)	0.7722	1 (0.2)	0.2553
γ－グルタミルトランスフェラーゼ増加	3 (0.7)	0.7722	1 (0.2)	0.2553
肝機能検査値上昇	2 (0.5)	0.5148	0	
血中ブドウ糖増加	1 (0.2)	0.2574	1 (0.2)	0.2553
血中免疫グロブリンE増加	1 (0.2)	0.2574	0	
体温上昇	1 (0.2)	0.2574	3 (0.7)	0.7658

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(Safety analysis set)

System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
心雑音	1 (0.2)	0.2574	0	
肝機能検査異常	1 (0.2)	0.2574	0	
好中球数増加	1 (0.2)	0.2574	0	
トランスアミナーゼ上昇	1 (0.2)	0.2574	0	
白血球数減少	1 (0.2)	0.2574	0	
白血球数増加	1 (0.2)	0.2574	0	
血中ビリルビン増加	0		1 (0.2)	0.2553
血中クレアチンホスホキナーゼ異常	0		1 (0.2)	0.2553
血中クレアチニン増加	0		1 (0.2)	0.2553
グリコヘモグロビン増加	0		2 (0.5)	0.5105
ヘモグロビン異常	0		1 (0.2)	0.2553
肝酵素上昇	0		1 (0.2)	0.2553
尿中赤血球陽性	0		1 (0.2)	0.2553
傷害、中毒および処置合併症	41 (9.6)	10.5536	38 (9.0)	9.7003
挫傷	6 (1.4)	1.5444	4 (0.9)	1.0211
靭帯捻挫	6 (1.4)	1.5444	3 (0.7)	0.7658

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
動物咬傷	4 (0.9)	1.0296	3 (0.7)	0.7658
上顆炎	2 (0.5)	0.5148	1 (0.2)	0.2553
転倒	2 (0.5)	0.5148	3 (0.7)	0.7658
肉離れ	2 (0.5)	0.5148	1 (0.2)	0.2553
処置後合併症	2 (0.5)	0.5148	0	
皮膚擦過傷	2 (0.5)	0.5148	2 (0.5)	0.5105
皮下血腫	2 (0.5)	0.5148	0	
動物による引っかき傷	1 (0.2)	0.2574	0	
節足動物咬傷	1 (0.2)	0.2574	1 (0.2)	0.2553
骨折	1 (0.2)	0.2574	0	
手骨折	1 (0.2)	0.2574	0	
熱中症	1 (0.2)	0.2574	0	
上腕骨骨折	1 (0.2)	0.2574	0	
関節脱臼	1 (0.2)	0.2574	0	
裂傷	1 (0.2)	0.2574	4 (0.9)	1.0211
四肢損傷	1 (0.2)	0.2574	2 (0.5)	0.5105
腰椎骨折	1 (0.2)	0.2574	0	

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(Safety analysis set)

	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
System organ class/Preferred term	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
半月板損傷	1 (0.2)	0.2574	0	
筋損傷	1 (0.2)	0.2574	0	
放射線関連痛	1 (0.2)	0.2574	0	
軟部組織損傷	1 (0.2)	0.2574	0	
腱断裂	1 (0.2)	0.2574	0	
歯牙破折	1 (0.2)	0.2574	3 (0.7)	0.7658
手首関節骨折	1 (0.2)	0.2574	0	
節足動物刺傷	0		1 (0.2)	0.2553
骨挫傷	0		1 (0.2)	0.2553
鎖骨骨折	0		1 (0.2)	0.2553
脳振盪	0		1 (0.2)	0.2553
擦過傷	0		1 (0.2)	0.2553
毒性物質曝露	0		1 (0.2)	0.2553
足骨折	0		1 (0.2)	0.2553
前腕骨折	0		1 (0.2)	0.2553
関節損傷	0		1 (0.2)	0.2553
靭帯断裂	0		1 (0.2)	0.2553

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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System organ class/Preferred term	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]	Number (%) of subjects[a]	Event rate (per 100 pt years)[b]
眼窩周囲血腫	0		1 (0.2)	0.2553
外傷後頚部症候群	0		1 (0.2)	0.2553
処置による疼痛	0		1 (0.2)	0.2553
橈骨骨折	0		2 (0.5)	0.5105
肋骨骨折	0		1 (0.2)	0.2553
皮膚創傷	0		1 (0.2)	0.2553
サンバーン	0		2 (0.5)	0.5105

[a] Number (%) of subjects with AEs, sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
A subject can have one or more PTs reported under a given SOC.
[b] Number of subjects with AEs divided by the total time at risk across all subjects in given treatment group, multiplied by 100.
Total time at risk will be defined as (the date of last day of IP + dosing frequency) - date of randomisation +1.
For each PT, the number and percentage of subjects reporting at least one occurrence will be presented i.e., for a subject multiple occurrences of an AE will only be counted once.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
The total duration of treatment across all subjects in Tralo 300 mg Q2W = 388.4928 years; in Placebo = 391.7399 years.
Q2W = Every 2 weeks.
MedDRA version 20.0.

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1.15.2.1.2　治験薬との因果関係が否定できない有害事象［Source: Table 11.3.2.9.1］

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
Subjects with any AE[b]	93 (21.9)	213 (50.1)	33 (7.8)	257 (60.9)
製品の問題	0	2 (0.5)	0	2 (0.5)
医療機器不具合	0	2 (0.5)	0	1 (0.2)
患者と医療機器間の不適合	0	0	0	1 (0.2)
感染症および寄生虫症	3 (0.7)	190 (44.7)	1 (0.2)	201 (47.6)
ウイルス性上気道感染	0	50 (11.8)	0	52 (12.3)
気管支炎	0	34 (8.0)	0	31 (7.3)
上気道感染	0	29 (6.8)	1 (0.2)	30 (7.1)
ウイルス性気道感染	0	18 (4.2)	0	19 (4.5)
尿路感染	0	17 (4.0)	0	12 (2.8)
インフルエンザ	0	16 (3.8)	0	15 (3.6)
気道感染	0	16 (3.8)	0	18 (4.3)
副鼻腔炎	0	13 (3.1)	0	15 (3.6)
鼻炎	0	11 (2.6)	0	14 (3.3)
鼻咽頭炎	0	9 (2.1)	0	6 (1.4)
咽頭炎	0	7 (1.6)	0	11 (2.6)
肺炎	0	7 (1.6)	0	8 (1.9)
扁桃炎	0	7 (1.6)	0	6 (1.4)
急性副鼻腔炎	0	6 (1.4)	0	11 (2.6)
胃腸炎	0	4 (0.9)	0	7 (1.7)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
口腔カンジダ症	0	4 (0.9)	0	3 (0.7)
喉頭炎	0	3 (0.7)	0	3 (0.7)
下気道感染	0	3 (0.7)	0	3 (0.7)
口腔ヘルペス	0	3 (0.7)	0	2 (0.5)
蜂巣炎	1 (0.2)	1 (0.2)	0	3 (0.7)
結膜炎	0	2 (0.5)	0	2 (0.5)
ウイルス性胃腸炎	0	2 (0.5)	0	2 (0.5)
帯状疱疹	0	2 (0.5)	0	1 (0.2)
レンサ球菌性咽頭炎	0	2 (0.5)	0	0
ウイルス性発疹	0	2 (0.5)	0	1 (0.2)
外陰部腟カンジダ症	0	2 (0.5)	0	0
外陰腟真菌感染	0	2 (0.5)	0	1 (0.2)
細菌性結膜炎	0	1 (0.2)	0	0
膀胱炎	0	1 (0.2)	0	5 (1.2)
感染性下痢	0	1 (0.2)	0	1 (0.2)
耳感染	0	1 (0.2)	0	3 (0.7)
心内膜炎	0	1 (0.2)	0	0
感染性腸炎	0	1 (0.2)	0	0
眼感染	0	1 (0.2)	0	0
毛包炎	0	1 (0.2)	0	0
皮膚真菌感染	0	1 (0.2)	0	0
ヘルペスウイルス感染	0	1 (0.2)	0	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

System organ class/Preferred term	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
	Related	Not Related	Related	Not Related
皮膚播種性帯状疱疹	0	1 (0.2)	0	0
膿痂疹	0	1 (0.2)	0	0
注射部位蜂巣炎	1 (0.2)	0	0	0
骨髄炎	0	1 (0.2)	0	0
外耳炎	0	1 (0.2)	0	1 (0.2)
急性中耳炎	0	1 (0.2)	0	0
咽頭扁桃炎	0	1 (0.2)	0	4 (0.9)
処置後感染	0	1 (0.2)	0	0
肺結核	0	1 (0.2)	0	0
歯髄炎	0	1 (0.2)	0	1 (0.2)
腎盂腎炎	0	1 (0.2)	0	1 (0.2)
ブドウ球菌性咽頭炎	0	1 (0.2)	0	0
歯感染	0	1 (0.2)	0	1 (0.2)
気管気管支炎	0	1 (0.2)	0	2 (0.5)
細菌性尿路感染	0	1 (0.2)	0	1 (0.2)
尿路性敗血症	1 (0.2)	0	0	0
ウイルス感染	0	1 (0.2)	0	3 (0.7)
ウイルス性咽頭炎	0	1 (0.2)	0	2 (0.5)
ダニ皮膚炎	0	0	0	1 (0.2)
虫垂炎	0	0	0	1 (0.2)
細菌性疾患キャリアー	0	0	0	1 (0.2)
細菌性気管支炎	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
カンジダ感染	0	0	0	1 (0.2)
子宮頚管炎	0	0	0	1 (0.2)
慢性副鼻腔炎	0	0	0	6 (1.4)
ウイルス性結膜炎	0	0	0	2 (0.5)
せつ	0	0	0	2 (0.5)
A型肝炎	0	0	0	1 (0.2)
単純ヘルペス	0	0	0	1 (0.2)
感染性胸水	0	0	0	1 (0.2)
ウイルス性喉頭炎	0	0	0	1 (0.2)
限局性感染	0	0	0	1 (0.2)
中咽頭カンジダ症	0	0	0	1 (0.2)
中耳炎	0	0	0	1 (0.2)
骨盤内炎症性疾患	0	0	0	1 (0.2)
歯周炎	0	0	0	1 (0.2)
膿疱性皮疹	0	0	0	1 (0.2)
レンサ球菌性尿路感染	0	0	0	1 (0.2)
白癬感染	0	0	0	1 (0.2)
足部白癬	0	0	0	1 (0.2)
細菌性扁桃炎	0	0	0	1 (0.2)
歯膿瘍	0	0	0	1 (0.2)
気管炎	0	0	0	1 (0.2)
細菌性上気道感染	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
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Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
水痘	0	0	0	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	2 (0.5)	0	1 (0.2)
腎血管筋脂肪腫	0	1 (0.2)	0	0
平滑筋腫	0	1 (0.2)	0	0
直腸癌	0	0	0	1 (0.2)
血液およびリンパ系障害	2 (0.5)	11 (2.6)	0	20 (4.7)
貧血	1 (0.2)	2 (0.5)	0	4 (0.9)
白血球減少症	0	2 (0.5)	0	3 (0.7)
脾腫	0	2 (0.5)	0	0
血小板減少症	0	2 (0.5)	0	2 (0.5)
好酸球増加症	1 (0.2)	0	0	0
リンパ節症	0	1 (0.2)	0	0
好中球減少症	0	1 (0.2)	0	3 (0.7)
白血球障害	0	1 (0.2)	0	1 (0.2)
高色素性貧血	0	0	0	1 (0.2)
鉄欠乏性貧血	0	0	0	2 (0.5)
白血球増加症	0	0	0	4 (0.9)
リンパ球増加症	0	0	0	1 (0.2)
小赤血球症	0	0	0	1 (0.2)
好中球増加症	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
血小板障害	0	0	0	1 (0.2)
血小板増加症	0	0	0	2 (0.5)
免疫系障害	0	7 (1.6)	0	6 (1.4)
季節性アレルギー	0	4 (0.9)	0	2 (0.5)
食物アレルギー	0	2 (0.5)	0	1 (0.2)
薬物過敏症	0	1 (0.2)	0	1 (0.2)
節足動物刺傷アレルギー	0	0	0	1 (0.2)
好酸球性多発血管炎性肉芽腫症	0	0	0	1 (0.2)
内分泌障害	0	2 (0.5)	0	2 (0.5)
甲状腺機能低下症	0	2 (0.5)	0	0
甲状腺腫瘤	0	0	0	1 (0.2)
甲状腺炎	0	0	0	1 (0.2)
代謝および栄養障害	0	8 (1.9)	0	17 (4.0)
高尿酸血症	0	2 (0.5)	0	0
低カリウム血症	0	2 (0.5)	0	0
2型糖尿病	0	2 (0.5)	0	1 (0.2)
食欲減退	0	1 (0.2)	0	1 (0.2)
痛風	0	1 (0.2)	0	1 (0.2)
肥満	0	1 (0.2)	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
脱水	0	0	0	1 (0.2)
糖尿病	0	0	0	5 (1.2)
脂質異常症	0	0	0	1 (0.2)
耐糖能障害	0	0	0	1 (0.2)
高コレステロール血症	0	0	0	1 (0.2)
高血糖	0	0	0	3 (0.7)
高脂血症	0	0	0	1 (0.2)
低カルシウム血症	0	0	0	1 (0.2)
ビタミンD欠乏	0	0	0	1 (0.2)
精神障害	0	15 (3.5)	0	18 (4.3)
不安	0	8 (1.9)	0	7 (1.7)
不眠症	0	5 (1.2)	0	5 (1.2)
うつ病	0	2 (0.5)	0	4 (0.9)
不快気分	0	1 (0.2)	0	0
睡眠障害	0	1 (0.2)	0	1 (0.2)
自殺念慮	0	1 (0.2)	0	0
中期不眠症	0	0	0	1 (0.2)
気分変化	0	0	0	1 (0.2)
心的外傷後ストレス障害	0	0	0	1 (0.2)
ストレス	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
神経系障害	6 (1.4)	57 (13.4)	3 (0.7)	44 (10.4)
頭痛	3 (0.7)	37 (8.7)	1 (0.2)	31 (7.3)
浮動性めまい	2 (0.5)	9 (2.1)	0	7 (1.7)
肋間神経痛	0	5 (1.2)	0	1 (0.2)
片頭痛	0	4 (0.9)	0	2 (0.5)
坐骨神経痛	0	3 (0.7)	0	0
失神	0	3 (0.7)	1 (0.2)	0
無嗅覚	0	2 (0.5)	0	1 (0.2)
頚腕症候群	0	2 (0.5)	0	0
神経炎	0	2 (0.5)	0	1 (0.2)
神経根障害	0	2 (0.5)	0	3 (0.7)
傾眠	2 (0.5)	0	1 (0.2)	0
灼熱感	1 (0.2)	0	0	0
意識消失	0	1 (0.2)	0	0
腰髄神経根障害	0	1 (0.2)	0	0
神経筋痛	0	1 (0.2)	0	0
末梢性ニューロパチー	0	1 (0.2)	0	0
錯感覚	0	1 (0.2)	0	0
副鼻腔炎に伴う頭痛	0	1 (0.2)	0	0
血管性脳症	0	1 (0.2)	0	0
頚動脈瘤	0	0	0	1 (0.2)
味覚異常	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
根症候群	0	0	0	1 (0.2)
緊張性頭痛	0	0	0	2 (0.5)
振戦	0	0	0	1 (0.2)
血管性頭痛	0	0	0	1 (0.2)
眼障害	2 (0.5)	9 (2.1)	2 (0.5)	12 (2.8)
アレルギー性結膜炎	0	2 (0.5)	0	3 (0.7)
眼そう痒症	0	2 (0.5)	1 (0.2)	1 (0.2)
眼瞼浮腫	1 (0.2)	1 (0.2)	0	1 (0.2)
流涙増加	0	2 (0.5)	0	0
眼瞼炎	1 (0.2)	0	0	0
黄斑色素沈着	0	1 (0.2)	0	0
眼充血	0	1 (0.2)	0	0
羞明	0	1 (0.2)	0	0
潰瘍性角膜炎	0	1 (0.2)	0	0
白内障	0	0	0	3 (0.7)
結膜出血	0	0	0	1 (0.2)
角膜菲薄化	0	0	0	1 (0.2)
眼乾燥	0	0	0	1 (0.2)
眼刺激	0	0	0	1 (0.2)
眼痛	0	0	0	1 (0.2)
眼部腫脹	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
眼瞼障害	0	0	1 (0.2)	0
円錐角膜	0	0	0	1 (0.2)
網膜剥離	0	0	0	1 (0.2)
網膜血管障害	0	0	0	1 (0.2)
耳および迷路障害	0	8 (1.9)	0	12 (2.8)
回転性めまい	0	4 (0.9)	0	6 (1.4)
耳痛	0	1 (0.2)	0	3 (0.7)
耳そう痒症	0	1 (0.2)	0	0
混合性難聴	0	1 (0.2)	0	0
頭位性回転性めまい	0	1 (0.2)	0	0
アレルギー性中耳炎	0	0	0	1 (0.2)
片耳難聴	0	0	0	1 (0.2)
耳閉	0	0	0	1 (0.2)
メニエール病	0	0	0	1 (0.2)
中耳滲出液	0	0	0	1 (0.2)
心臓障害	1 (0.2)	16 (3.8)	0	15 (3.6)
頻脈	1 (0.2)	4 (0.9)	0	8 (1.9)
狭心症	0	3 (0.7)	0	2 (0.5)
心房細動	0	2 (0.5)	0	0
第一度房室ブロック	0	2 (0.5)	0	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
心不全	0	2 (0.5)	0	1 (0.2)
不整脈	0	1 (0.2)	0	0
心筋症	0	1 (0.2)	0	0
期外収縮	0	1 (0.2)	0	2 (0.5)
心筋梗塞	0	1 (0.2)	0	0
動悸	0	1 (0.2)	0	0
洞性頻脈	0	1 (0.2)	0	1 (0.2)
上室性頻脈	0	1 (0.2)	0	0
発作性頻脈	0	1 (0.2)	0	0
不安定狭心症	0	0	0	1 (0.2)
うっ血性心筋症	0	0	0	1 (0.2)
慢性肺性心	0	0	0	1 (0.2)
僧帽弁閉鎖不全症	0	0	0	1 (0.2)
血管障害	2 (0.5)	19 (4.5)	1 (0.2)	15 (3.6)
高血圧	1 (0.2)	15 (3.5)	0	11 (2.6)
高血圧クリーゼ	0	3 (0.7)	0	3 (0.7)
静脈瘤	0	2 (0.5)	0	0
ほてり	1 (0.2)	0	0	0
末梢静脈疾患	0	1 (0.2)	0	0
低血圧	0	0	1 (0.2)	1 (0.2)
末梢動脈閉塞性疾患	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

System organ class/Preferred term	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
	Related	Not Related	Related	Not Related
血栓性静脈炎	0	0	0	1 (0.2)
呼吸器、胸郭および縦隔障害	1 (0.2)	92 (21.6)	3 (0.7)	103 (24.4)
喘息	0	50 (11.8)	0	63 (14.9)
咳嗽	0	9 (2.1)	0	12 (2.8)
アレルギー性鼻炎	0	9 (2.1)	0	10 (2.4)
口腔咽頭痛	0	8 (1.9)	2 (0.5)	11 (2.6)
発声障害	0	6 (1.4)	0	4 (0.9)
鼻漏	0	4 (0.9)	0	3 (0.7)
鼻閉	0	3 (0.7)	0	5 (1.2)
慢性気管支炎	0	2 (0.5)	0	0
鼻出血	0	2 (0.5)	0	1 (0.2)
咽喉刺激感	0	2 (0.5)	0	0
アレルギー性気管支炎	0	1 (0.2)	0	1 (0.2)
アレルギー性咳嗽	0	1 (0.2)	0	0
アレルギー性咽頭炎	0	1 (0.2)	0	0
アレルギー性呼吸器疾患	0	1 (0.2)	0	0
喀血	0	1 (0.2)	0	0
過換気	0	1 (0.2)	0	0
鼻粘膜潰瘍	0	1 (0.2)	0	0
鼻中隔潰瘍	0	1 (0.2)	0	0
鼻甲介肥大	0	1 (0.2)	0	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
[b] Each subject is counted only once within a treatment group in this overall summary.
Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
咽頭感覚鈍麻	1 (0.2)	0	0	0
咽頭浮腫	1 (0.2)	0	0	0
胸膜炎	0	1 (0.2)	0	0
呼吸障害	0	1 (0.2)	0	3 (0.7)
くしゃみ	0	1 (0.2)	0	3 (0.7)
上気道咳症候群	0	1 (0.2)	0	1 (0.2)
血管運動性鼻炎	0	1 (0.2)	0	0
喘鳴	0	1 (0.2)	1 (0.2)	4 (0.9)
急性呼吸不全	0	0	0	1 (0.2)
アレルギー性副鼻腔炎	0	0	0	1 (0.2)
気管支閉塞	0	0	0	1 (0.2)
気管支痙攣	0	0	0	1 (0.2)
慢性好酸球性副鼻腔炎	0	0	0	1 (0.2)
呼吸困難	0	0	0	8 (1.9)
鼻閉塞	0	0	0	1 (0.2)
鼻茸	0	0	0	2 (0.5)
鼻そう痒症	0	0	0	1 (0.2)
鼻甲介異常	0	0	0	1 (0.2)
湿性咳嗽	0	0	0	2 (0.5)
呼吸不全	0	0	0	1 (0.2)
睡眠時無呼吸症候群	0	0	0	1 (0.2)
喀痰増加	0	0	0	2 (0.5)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
胃腸障害	7 (1.6)	55 (12.9)	0	50 (11.8)
下痢	3 (0.7)	14 (3.3)	0	9 (2.1)
消化不良	1 (0.2)	8 (1.9)	0	7 (1.7)
上腹部痛	0	8 (1.9)	0	1 (0.2)
胃食道逆流性疾患	0	7 (1.6)	0	3 (0.7)
腹痛	0	6 (1.4)	0	7 (1.7)
悪心	1 (0.2)	4 (0.9)	0	3 (0.7)
歯痛	0	5 (1.2)	0	4 (0.9)
嘔吐	0	5 (1.2)	0	2 (0.5)
腹部不快感	0	4 (0.9)	0	2 (0.5)
口内炎	0	3 (0.7)	0	1 (0.2)
腹部膨満	1 (0.2)	1 (0.2)	0	0
びらん性胃炎	0	2 (0.5)	0	1 (0.2)
根尖肉芽腫	0	1 (0.2)	0	0
潰瘍性大腸炎	0	1 (0.2)	0	1 (0.2)
齲歯	0	1 (0.2)	0	0
口内乾燥	0	1 (0.2)	0	1 (0.2)
胃潰瘍	0	1 (0.2)	0	0
胃炎	0	1 (0.2)	0	2 (0.5)
歯肉出血	0	1 (0.2)	0	1 (0.2)
痔核	0	1 (0.2)	0	1 (0.2)
腸管ポリープ	0	1 (0.2)	0	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
過敏性腸症候群	0	1 (0.2)	0	0
口唇腫脹	0	1 (0.2)	0	0
メレナ	1 (0.2)	0	0	0
嚥下痛	0	1 (0.2)	0	1 (0.2)
食道炎	0	1 (0.2)	0	1 (0.2)
流涎過多	0	1 (0.2)	0	0
歯の知覚過敏	0	1 (0.2)	0	0
臍ヘルニア	0	1 (0.2)	0	2 (0.5)
腹部圧痛	0	0	0	2 (0.5)
後天性食道ウエッブ	0	0	0	1 (0.2)
慢性胃炎	0	0	0	2 (0.5)
便秘	0	0	0	1 (0.2)
憩室	0	0	0	1 (0.2)
鼓腸	0	0	0	1 (0.2)
食中毒	0	0	0	3 (0.7)
血便排泄	0	0	0	1 (0.2)
裂孔ヘルニア	0	0	0	3 (0.7)
口の感覚鈍麻	0	0	0	1 (0.2)
臍径ヘルニア	0	0	0	1 (0.2)
腸出血	0	0	0	1 (0.2)
食道潰瘍	0	0	0	1 (0.2)
口蓋障害	0	0	0	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
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	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
肝胆道系障害	0	6 (1.4)	2 (0.5)	4 (0.9)
胆道ジスキネジア	0	1 (0.2)	0	0
急性胆嚢炎	0	1 (0.2)	0	0
慢性胆嚢炎	0	1 (0.2)	0	0
脂肪肝	0	1 (0.2)	0	0
肝腫大	0	1 (0.2)	0	1 (0.2)
高ビリルビン血症	0	1 (0.2)	0	0
胆道仙痛	0	0	0	1 (0.2)
胆嚢炎	0	0	0	1 (0.2)
胆汁うっ滞	0	0	0	1 (0.2)
肝機能異常	0	0	1 (0.2)	0
肝損傷	0	0	1 (0.2)	0
皮膚および皮下組織障害	17 (4.0)	24 (5.6)	7 (1.7)	27 (6.4)
発疹	5 (1.2)	5 (1.2)	1 (0.2)	3 (0.7)
そう痒症	4 (0.9)	3 (0.7)	3 (0.7)	2 (0.5)
皮膚反応	4 (0.9)	1 (0.2)	0	0
蕁麻疹	1 (0.2)	4 (0.9)	1 (0.2)	8 (1.9)
紅斑	2 (0.5)	2 (0.5)	0	1 (0.2)
丘疹	0	3 (0.7)	0	0
乾癬	1 (0.2)	2 (0.5)	0	0
アレルギー性皮膚炎	1 (0.2)	1 (0.2)	0	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
湿疹	1 (0.2)	1 (0.2)	0	4 (0.9)
皮下出血	2 (0.5)	0	0	0
皮膚炎	0	1 (0.2)	0	2 (0.5)
アトピー性皮膚炎	0	1 (0.2)	0	1 (0.2)
接触皮膚炎	0	1 (0.2)	0	5 (1.2)
過敏性血管炎	0	1 (0.2)	0	0
点状出血	0	1 (0.2)	0	0
紅斑性皮疹	0	1 (0.2)	0	0
全身性皮疹	0	1 (0.2)	0	1 (0.2)
皮膚病変	1 (0.2)	0	0	0
尋常性白斑	0	1 (0.2)	0	0
血管浮腫	0	0	0	1 (0.2)
皮膚嚢腫	0	0	0	1 (0.2)
皮膚乾燥	0	0	0	2 (0.5)
斑状出血	0	0	1 (0.2)	0
全身性そう痒症	0	0	1 (0.2)	0
斑状皮疹	0	0	1 (0.2)	0
顔面腫脹	0	0	0	1 (0.2)
筋骨格系および結合組織障害	4 (0.9)	49 (11.5)	5 (1.2)	35 (8.3)
関節痛	1 (0.2)	15 (3.5)	4 (0.9)	5 (1.2)
背部痛	0	16 (3.8)	0	11 (2.6)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
筋肉痛	2 (0.5)	5 (1.2)	1 (0.2)	2 (0.5)
筋骨格痛	0	6 (1.4)	0	4 (0.9)
四肢痛	1 (0.2)	5 (1.2)	0	6 (1.4)
変形性関節症	0	5 (1.2)	0	3 (0.7)
筋骨格系胸痛	0	4 (0.9)	0	7 (1.7)
関節炎	0	2 (0.5)	0	2 (0.5)
骨端症	0	2 (0.5)	0	2 (0.5)
腱炎	0	2 (0.5)	0	2 (0.5)
強直性脊椎炎	0	1 (0.2)	0	0
滑液包炎	0	1 (0.2)	0	0
線維筋痛	0	1 (0.2)	0	0
坐径部痛	0	1 (0.2)	0	0
関節腫脹	0	1 (0.2)	0	1 (0.2)
四肢不快感	0	1 (0.2)	0	0
筋拘縮	0	1 (0.2)	0	0
筋痙縮	0	1 (0.2)	0	3 (0.7)
筋膜疼痛症候群	0	1 (0.2)	0	0
頚部痛	0	1 (0.2)	0	1 (0.2)
骨粗鬆症	0	1 (0.2)	0	0
膝蓋大腿関節痛症候群	0	1 (0.2)	0	0
脊椎痛	0	1 (0.2)	0	1 (0.2)
肋軟骨炎	0	0	0	2 (0.5)

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
外骨腫	0	0	0	2 (0.5)
筋骨格硬直	0	0	0	1 (0.2)
交感神経性後頚部症候群	0	0	0	1 (0.2)
滑液嚢腫	0	0	0	2 (0.5)
腱鞘炎	0	0	0	1 (0.2)
腎および尿路障害	0	9 (2.1)	0	10 (2.4)
尿管結石症	0	2 (0.5)	0	0
血尿	0	1 (0.2)	0	4 (0.9)
水腎症	0	1 (0.2)	0	0
緊張性膀胱	0	1 (0.2)	0	0
頻尿	0	1 (0.2)	0	1 (0.2)
腎仙痛	0	1 (0.2)	0	1 (0.2)
腎嚢胞	0	1 (0.2)	0	0
腎機能障害	0	1 (0.2)	0	0
排尿困難	0	0	0	1 (0.2)
腎結石症	0	0	0	1 (0.2)
尿失禁	0	0	0	2 (0.5)
尿路障害	0	0	0	1 (0.2)
生殖系および乳房障害	0	5 (1.2)	0	8 (1.9)
子宮頚管ポリープ	0	1 (0.2)	0	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
[a] Each subject is represented by the maximum reported causality for each SOC and PT.
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Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
MedDRA version 20.0.
Subjects with missing causality have been set to related.

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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
月経困難症	0	1 (0.2)	0	0
卵巣嚢胞	0	1 (0.2)	0	0
子宮頚部びらん	0	1 (0.2)	0	0
子宮脱	0	1 (0.2)	0	0
外陰膣不快感	0	1 (0.2)	0	0
腺筋症	0	0	0	1 (0.2)
子宮付属器痛	0	0	0	1 (0.2)
亀頭包皮炎	0	0	0	1 (0.2)
良性前立腺肥大症	0	0	0	1 (0.2)
膀胱瘤	0	0	0	1 (0.2)
乳瘤	0	0	0	1 (0.2)
過少月経	0	0	0	1 (0.2)
子宮出血	0	0	0	1 (0.2)
膣出血	0	0	0	2 (0.5)
膣脱	0	0	0	1 (0.2)
先天性、家族性および遺伝性障害	0	1 (0.2)	0	1 (0.2)
硬化性胼胝腫	0	1 (0.2)	0	0
陰嚢水瘤	0	0	0	1 (0.2)
一般・全身障害および投与部位の状態	63 (14.8)	24 (5.6)	14 (3.3)	25 (5.9)
注射部位反応	21 (4.9)	2 (0.5)	2 (0.5)	1 (0.2)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
注射部位紅斑	13 (3.1)	2 (0.5)	0	0
発熱	1 (0.2)	7 (1.6)	2 (0.5)	9 (2.1)
適用部位反応	6 (1.4)	0	1 (0.2)	0
注射部位そう痒感	4 (0.9)	2 (0.5)	1 (0.2)	0
注射部位腫脹	4 (0.9)	1 (0.2)	0	0
末梢腫脹	1 (0.2)	4 (0.9)	0	1 (0.2)
疲労	0	4 (0.9)	0	3 (0.7)
注射部位疼痛	4 (0.9)	0	4 (0.9)	1 (0.2)
穿刺部位反応	3 (0.7)	1 (0.2)	0	0
無力症	1 (0.2)	2 (0.5)	3 (0.7)	2 (0.5)
注射部位炎症	3 (0.7)	0	0	0
投与部位炎症	2 (0.5)	0	0	0
高熱	1 (0.2)	1 (0.2)	0	0
注射部位過敏反応	2 (0.5)	0	1 (0.2)	0
局所反応	2 (0.5)	0	0	0
非心臓性胸痛	0	2 (0.5)	1 (0.2)	3 (0.7)
末梢性浮腫	0	2 (0.5)	0	3 (0.7)
穿刺部位紅斑	1 (0.2)	1 (0.2)	0	0
投与部位硬結	1 (0.2)	0	0	0
投与部位そう痒感	1 (0.2)	0	0	0
医薬品副作用	0	1 (0.2)	0	0
適用部位紅斑	1 (0.2)	0	1 (0.2)	0

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
適用部位疼痛	1 (0.2)	0	1 (0.2)	1 (0.2)
適用部位発疹	1 (0.2)	0	0	0
胸部不快感	0	1 (0.2)	0	0
注射部位内出血	1 (0.2)	0	0	1 (0.2)
注射部位漏出	1 (0.2)	0	0	0
注射部位血腫	1 (0.2)	0	0	0
注射部位刺激感	1 (0.2)	0	0	0
注射部位腫瘤	1 (0.2)	0	0	0
注射部位蕁麻疹	1 (0.2)	0	0	0
ワクチン接種部位発疹	1 (0.2)	0	0	0
乾燥症	0	1 (0.2)	0	0
適用部位過敏反応	0	0	0	1 (0.2)
埋込み部位疼痛	0	0	0	1 (0.2)
インフルエンザ様疾患	0	0	0	1 (0.2)
注射部位出血	0	0	1 (0.2)	0
注射部位丘疹	0	0	1 (0.2)	0
疼痛	0	0	0	2 (0.5)
穿刺部位出血	0	0	0	1 (0.2)
分泌物分泌	0	0	0	1 (0.2)
恥骨上痛	0	0	0	1 (0.2)
臨床検査	8 (1.9)	13 (3.1)	2 (0.5)	16 (3.8)

Sorted for System Organ Class (SOC) by international order and for preferred term (PT) by decreasing frequency in subjects treated with Tralo.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
アラニンアミノトランスフェラーゼ増加	4 (0.9)	2 (0.5)	1 (0.2)	0
血圧上昇	0	5 (1.2)	0	5 (1.2)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.5)	1 (0.2)	1 (0.2)	0
γ－グルタミルトランスフェラーゼ増加	1 (0.2)	2 (0.5)	0	1 (0.2)
肝機能検査値上昇	1 (0.2)	1 (0.2)	0	0
血中ブドウ糖増加	0	1 (0.2)	0	1 (0.2)
血中免疫グロブリンE増加	0	1 (0.2)	0	0
体温上昇	1 (0.2)	0	1 (0.2)	2 (0.5)
心雑音	0	1 (0.2)	0	0
肝機能検査異常	0	1 (0.2)	0	0
好中球数増加	0	1 (0.2)	0	0
トランスアミナーゼ上昇	1 (0.2)	0	0	0
白血球数減少	0	1 (0.2)	0	0
白血球数増加	1 (0.2)	0	0	0
血中ビリルビン増加	0	0	0	1 (0.2)
血中クレアチンホスホキナーゼ異常	0	0	0	1 (0.2)
血中クレアチニン増加	0	0	0	1 (0.2)
グリコヘモグロビン増加	0	0	0	2 (0.5)
ヘモグロビン異常	0	0	0	1 (0.2)
肝酵素上昇	0	0	0	1 (0.2)
尿中赤血球陽性	0	0	0	1 (0.2)

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Includes adverse events with an onset date >= the first day of study treatment and <= (the last day of study treatment + 2 weeks).
Q2W = Every 2 weeks.
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Table 11.3.2.9.1 Adverse events reported during the treatment period, by System Organ Class, preferred term and investigator's causality assessment (Safety analysis set)

	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
傷害、中毒および処置合併症	1 (0.2)	40 (9.4)	0	38 (9.0)
挫傷	0	6 (1.4)	0	4 (0.9)
靭帯捻挫	0	6 (1.4)	0	3 (0.7)
動物咬傷	0	4 (0.9)	0	3 (0.7)
上顎炎	0	2 (0.5)	0	1 (0.2)
転倒	0	2 (0.5)	0	3 (0.7)
肉離れ	0	2 (0.5)	0	1 (0.2)
処置後合併症	1 (0.2)	1 (0.2)	0	0
皮膚擦過傷	0	2 (0.5)	0	2 (0.5)
皮下血腫	0	2 (0.5)	0	0
動物による引っかき傷	0	1 (0.2)	0	0
節足動物咬傷	0	1 (0.2)	0	1 (0.2)
骨折	0	1 (0.2)	0	0
手骨折	0	1 (0.2)	0	0
熱中症	0	1 (0.2)	0	0
上腕骨骨折	0	1 (0.2)	0	0
関節脱臼	0	1 (0.2)	0	0
裂傷	0	1 (0.2)	0	4 (0.9)
四肢損傷	0	1 (0.2)	0	2 (0.5)
腰椎骨折	0	1 (0.2)	0	0
半月板損傷	0	1 (0.2)	0	0
筋損傷	0	1 (0.2)	0	0

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	Number (%) of subjects[a]			
	Tralo 300 mg Q2W (N=425)		Placebo (N=422)	
	Assessed causality		Assessed causality	
System organ class/Preferred term	Related	Not Related	Related	Not Related
放射線関連痛	0	1 (0.2)	0	0
軟部組織損傷	0	1 (0.2)	0	0
腱断裂	0	1 (0.2)	0	0
歯牙破折	0	1 (0.2)	0	3 (0.7)
手首関節骨折	0	1 (0.2)	0	0
節足動物刺傷	0	0	0	1 (0.2)
骨挫傷	0	0	0	1 (0.2)
鎖骨骨折	0	0	0	1 (0.2)
脳振盪	0	0	0	1 (0.2)
擦過傷	0	0	0	1 (0.2)
毒性物質曝露	0	0	0	1 (0.2)
足骨折	0	0	0	1 (0.2)
前腕骨折	0	0	0	1 (0.2)
関節損傷	0	0	0	1 (0.2)
靭帯断裂	0	0	0	1 (0.2)
眼窩周囲血腫	0	0	0	1 (0.2)
外傷後頚部症候群	0	0	0	1 (0.2)
処置による疼痛	0	0	0	1 (0.2)
橈骨骨折	0	0	0	2 (0.5)
肋骨骨折	0	0	0	1 (0.2)
皮膚創傷	0	0	0	1 (0.2)
サンバーン	0	0	0	2 (0.5)

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