目次

臨床試験一覧表（表 1） 4
1. 申請する適応症に関する比較対照試験報告書 6
1.1 SP0982 試験［発作コントロールが得られていない強直間代発作を有するてんかん患者を対象とするラコサミド併用療法における有効性及び安全性を評価する多施設共同、二重盲検、無作為化、プラセボ対照、並行群間比較試験］（5.3.5.1.1：評価資料） 6
2. 非対照試験報告書 652
2.1 EP0012 試験［発作コントロールが得られていない強直間代発作を有するてんかん患者を対象とするラコサミド併用療法における安全性及び有効性を評価する多施設共同、非盲検、長期継続投与試験、第 2 回中間報告］（5.3.5.2.4：評価資料） 652
2.2 SP0961 試験［発作コントロールが得られていない強直間代発作を有するてんかん患者を対象とするラコサミド併用療法における安全性を検討する非盲検、パイロット試験］（5.3.5.2.2：参考資料） 1312
2.3 SP0962 試験［発作コントロールが得られていない強直間代発作を有するてんかん患者を対象とするラコサミド投与における安全性及び発作回数を検討する非盲検、長期継続投与試験］（5.3.5.2.3：参考資料） 1496

略語及び名称一覧表

略語（略称）	内容
ALP	Alkaline phosphatase：アルカリホスファターゼ
ALT	Alanine aminotransferase：アラニンアミノトランスフェラーゼ
AST	Aspartate aminotransferase：アスパラギン酸アミノトランスフェラーゼ
BMI	Body mass index：体格指数
BRIEF	Behavior Rating Inventory of Executive Function：実行機能に関する行動評価尺度
BRIEF-P	Behavior Rating Inventory of Executive Function-Preschool Version : 実行機能に関する行動評価尺度-幼児版
CBCL	Child Behavior Checklist：子どもの行動チェックリスト
CIOMS	Council for International Organizations of Medical Science : 国際医学団体協議会
CL_{CR}	Creatinine clearance：クレアチニンクリアランス
C-SSRS	Columbia Suicide Severity Rating Scale：コロンビア自殺評価スケール
CT	Computed tomography：コンピュータ断層撮影
EQ-5D-3L	3-Level EuroQol-5 Dimension：EuroQol による 5 項目 3 段階
FAS	Full Analysis Set：最大の解析対象集団
GGT	Gamma-glutamyl transferase：γ-グルタミルトランスフェラーゼ
HbA1c	Hemoglobin A1c：ヘモグロビン A1c
KM	Kaplan-Meier：－
LCM	Lacosamide：ラコサミド
MedDRA	Medical Dictionary for Regulatory Activities：ICH 国際医薬用語集
MRI	Magnetic resonance imaging：磁気共鳴画像
PedsQL	Pediatric Quality of Life Inventory：子どもの健康関連 QOL 評価
PK-PPS	Pharmacokinetics Per Protocol Set：治験実施計画書に適合した薬物動態解析対象集団
PPS	Per Protocol Set：治験実施計画書に適合した解析対象集団
PR	－：心電図上の P 波と R 波の間の時間
PT	Preferred Term：基本語
QOL	Quality of life：生活の質
QOLIE-31-P	Quality of Life in Epilepsy-31：てんかん患者用 QOL 質問票
QRS	－：心電図上の Q 波と S 波の間の時間
SOC	System Organ Class：器官別大分類
SS	Safety Set：安全性解析対象集団
ST	－：心電図上の S 波と T 波の間の部分
VAS	Visual analog scale：視覚的アナログスケール
VNS	Vagus nerve stimulation：迷走神経刺激療法

臨床試験一覧表を表 1 に示した。

表 1　臨床試験一覧表

試験の種類 (資料区分) 実施地域	試験番号	試験の目的	試験デザイン	治験薬、剤形、 用法・用量、投与経路	登録例数 [a] /完了例数	対象患者	試験期間	CTD No. 報告書の種類
申請する適応症に関する比較対照試験報告書								
第 III 相試験 （評価資料） 北米、中南米、西・中央欧州、東欧州、アジア・太平洋・その他	SP0982	有効性、安全性及び忍容性の評価	多施設共同、二重盲検、無作為化、プラセボ対照、並行群間比較	ラコサミド又はプラセボ 経口液（シロップ） 4 歳以上 18 歳未満で体重 30 kg 未満：2～12 mg/kg/日、1 日 2 回経口投与 4 歳以上 18 歳未満で体重 30 kg 以上 50 kg 未満：2～8 mg/kg/日、1 日 2 回経口投与 錠剤 4 歳以上 18 歳未満で体重 50 kg 以上又は 18 歳以上の成人：100～400 mg/日、1 日 2 回経口投与	242 例/213 例	過去に効果が認められなかった抗てんかん薬の薬剤数に関わらず、現在併用している 1～3 剤の抗てんかん薬でも発作コントロールが得られていない強直間代発作を有する 4 歳以上のてんかん患者	Prospective ベースライン期間 4 週間 増量期間 6 週間 維持期間　最長 18 週間 移行期間 4 週間又は減量期間　最長 4 週間 安全性追跡調査期間 30 日間	5.3.5.1.1 完全な報告書

a.　SP0982 試験は、無作為化例数を示した

b.　データカットオフ（2019 年 8 月 28 日）時点までの登録例数と継続例数（94 週超）を示した

表 1　臨床試験一覧表（続き）

試験の種類 (資料区分) 実施地域	試験番号	試験の目的	試験デザイン	治験薬、剤形、 用法・用量、投与経路	登録例数 [a] /完了例数	対象患者	試験期間	CTD No. 報告書の種類
非対照試験報告書								
第 III 相試験 （評価資料） アジア・太平洋・その他、東欧州、中南米、北米、西・中央欧州	EP0012	長期投与時の安全性及び有効性の評価	多施設共同、非盲検、長期継続投与	ラコサミド 経口液（シロップ） 4 歳以上 18 歳未満で体重 50 kg 未満：4～12 mg/kg/日、1 日 2 回経口投与 錠剤 4 歳以上 18 歳未満で体重 50 kg 以上：200～600 mg/日、1 日 2 回経口投与 18 歳以上の成人：200～800 mg/日、1 日 2 回経口投与	240 例/109 例 [b]	発作コントロールが得られていない強直間代発作を有する 4 歳以上のてんかん患者	治療期間 最長 5 年間 減量期間 最長 4 週間 安全性追跡調査期間 30 日間	5.3.5.2.4 第 2 回 中間報告書
第 II 相 （参考資料） 米国	SP0961	安全性の評価	多施設共同、非盲検	ラコサミド 錠剤 100～400 mg、1 日 2 回経口投与	49 例/40 例	発作コントロールが得られていない強直間代発作を有するてんかん患者	Prospective ベースライン期間 4 週間 増量期間 3 週間 維持期間 6 週間 治験終了期間 3 週間	5.3.5.2.2 完全な報告書
第 II 相 （参考資料） 米国	SP0962	長期投与時の安全性及び発作回数の評価	多施設共同、非盲検、長期継続投与	ラコサミド 錠剤 100～800 mg、1 日 2 回経口投与	39 例/29 例	発作コントロールが得られていない強直間代発作を有するてんかん患者	治療期間 56 週間 治験終了期間 最長 5 週間	5.3.5.2.3 完全な報告書

a.　SP0982 試験は、無作為化例数を示した

b.　データカットオフ（2019 年 8 月 28 日）時点までの登録例数と継続例数（94 週超）を示した

1. 申請する適応症に関する比較対照試験報告書

1.1 SP0982 試験［発作コントロールが得られていない強直間代発作を有するてんかん患者を対象とするラコサミド併用療法における有効性及び安全性を評価する多施設共同、二重盲検、無作為化、プラセボ対照、並行群間比較試験］（5.3.5.1.1：評価資料）

治験方法の概略（表 1.1-1）及び結果の要約を示した。

表 1.1-1　試験方法の概略

項目	内容
標題	発作コントロールが得られていない強直間代発作を有するてんかん患者を対象に、併用療法としてラコサミドを経口投与した時の有効性及び安全性を評価する多施設共同、二重盲検、無作為化、プラセボ対照、並行群間比較試験
開発の相	第 III 相
目的	主要目的： 過去に効果が認められなかった抗てんかん薬の薬剤数に関わらず、現在併用している 1～3 剤の抗てんかん薬でも発作コントロールが得られていない強直間代発作を有するてんかん患者を対象に、併用療法としてラコサミドを経口投与した時の有効性をプラセボと比較して評価する 副次目的： 発作コントロールが得られていない強直間代発作を有するてんかん患者を対象に、ラコサミドの安全性及び忍容性を評価する
治験デザイン	多施設共同、二重盲検、無作為化、プラセボ対照、並行群間比較
治験方法	本治験は、Prospective ベースライン期間（4 週間）、増量期間（6 週間）、維持期間（最長 18 週間）及び移行期間（4 週間）又は減量期間（最長 4 週間）並びに安全性追跡調査期間（30 日間）から構成された（最長 36 週間）。また、Prospective ベースライン期間前の 12 週間を Historical ベースライン期間とし、2 つを合わせた期間を Combined ベースライン期間（16 週間）とした。増量期間と維持期間を合わせた期間を治療期間（6～24 週間）とし、移行期間又は減量期間と安全性追跡調査期間を治験終了期間（4 週間又は最長 4 週間及び 30 日間）とした。 Prospective ベースライン期間の第 1 回来院（第−4 週）時に被験者の適格性を確認した。発作回数及び発作型分類の適格性は、Prospective ベースライン期間で収集された発作記録（例：発作日誌）で確認した。また、第 1 回来院の 2 週間後に電話調査で継続的な適格性を確認した。 Prospective ベースライン期間の完了時（第 2 回来院時）に適格性が認められた被験者を本治験に組み入れた。なお、Prospective ベースライン期間を完了し、無作為割付けに必要な強直間代発作の発現頻度の基準を除くすべての基準を満たした被験者（SP0982 試験をベースライン脱落した被験者）は、継続投与試験の EP0012 試験への参加を選択できることとし、第 2 回来院時に EP0012 試験の第 1 回来院を実施した。

表 1.1-1 試験方法の概略（続き）

項目	内容
治験方法（続き）	第 2 回来院時に、ラコサミド群又はプラセボ群のいずれかの投与群に二重盲検下で 1 : 1 の割合で無作為割付けし、Combined ベースライン期間の強直間代発作回数及び同意取得時の年齢で層別化した。第 2 回来院時に規定の評価及び治験薬の投与を開始し、増量期間に移行した。 増量期間では、維持期間の目標用量（体重 30 kg 未満の小児被験者 : 12 mg/kg/日、体重 30 kg 以上 50 kg 未満の小児被験者 : 8 mg/kg/日、体重 50 kg 以上の小児及び成人被験者 : 400 mg/日）を達成するために、忍容性に基づく用量の調整が必要な場合を除き、推奨投与スケジュールに従って治験薬を増量した。また、忍容性に応じた用量調整を可能とした。治験薬の減量又は維持は制限なく実施できることとし、いずれの場合でも増量期間中（第 6 週の少なくとも最後の 3 日間）に維持期間の最低投与量に到達することとした。最低投与量に到達しない被験者は減量期間に移行し、治験を中止した。最低投与量に到達した被験者は、維持期間に移行した。 維持期間では、増量期間の最終日の用量を維持した。維持期間中は、最低投与量が維持される限り 1 回の減量を可能とし、可能な限りメディカルモニターに相談した上で来院時又は電話調査時に減量した。減量後、忍容性に問題がある場合は、減量期間に移行し、治験を中止した。また、減量した場合は、再度増量することは不可とした。 治療期間は、以下の完了基準のいずれかに該当するまで継続した。 · 治療期間の最初の 6 週間に 2 回以上の強直間代発作が発現した場合 · 治療期間の最初の 6 週間を経過後に 2 回目の強直間代発作が発現した場合 · 24 週間の治療期間で 2 回の強直間代発作が発現しなかった場合 · 本治験で 125 イベント（2 回目の強直間代発作）が発現した場合 治療期間を 6 週間以上経過し、この期間中に 2 回目の強直間代発作が発現した場合、発作回数が 2 回未満のまま 24 週間の治療期間が完了した場合、又は本治験で 125 イベントが発現した場合（いずれか早い方）、被験者は第 10 回来院（第 24 週）又は早期中止来院において EP0012 試験への参加を選択できることとした。 EP0012 試験に参加を希望する被験者は、盲検を維持したまま移行期間へ移行し、最終来院を実施した。移行期間では、第 10 回来院又は早期中止来院から 2 週間後に電話調査を実施し、その後、治験責任医師の判断により、最終来院までの間に任意で来院を実施した。なお、治療期間中にプラセボを投与された被験者は、移行期間中に盲検下でラコサミドを漸増投与した。EP0012 試験への参加を希望しない被験者又は参加基準を満たさない被験者は、第 10 回来院後又は早期中止来院後に盲検を維持したまま減量期間へ移行し、減量完了来院及び安全性追跡調査期間を実施した。 安全性追跡調査期間では、減量完了来院から 2 週間後に安全性追跡調査来院を実施し、治験薬の最終投与から 30 日後に安全性追跡電話調査を実施した。また、本治験で 125 イベントが発現し、治験薬の投与を中止した場合は、盲検を維持したまま減量期間へ移行し、EP0012 試験の第 1 回来院と同日に減量完了来院を実施した。なお、被験者の同意が得られなかった場合を除き、EP0012 試験で安全性追跡調査期間を実施した。

表 1.1-1　試験方法の概略（続き）

項目	内容
併用薬及び併用療法	併用抗てんかん薬： 1～2 剤の非ベンゾジアゼピン系の抗てんかん薬又は 2～3 剤の抗てんかん薬（1 剤はベンゾジアゼピン系）の併用を可能とした。第 1 回来院の 28 日以上前から一定の用法・用量で使用し、Prospective ベースライン期間中及び治療期間中の変更は不可とした。ベンゾジアゼピン系薬剤の連用投与は、適応に関わらず 1 剤のみ可能とし、併用抗てんかん薬としてカウントした。 併用制限薬及び併用制限療法： 迷走神経刺激療法（VNS）：第 1 回来院の 6 ヵ月以上前に取り付けており、第 1 回来院の 28 日以上前から設定が一定に保たれている場合は、併用を可能とした。なお、治験期間中の設定変更は不可とした。 ベンゾジアゼピン系薬剤：連用投与（1 日量）は適応に関わらず可能とし、併用抗てんかん薬 1 剤としてカウントした。また、第 1 回来院の 28 日以上前から使用していた場合は、てんかんの適応症に限り頓用使用（28 日あたり 2 回まで）を可能とした。他の適応症での頓用使用は不可とした。 アンフェタミン系薬剤及び抗ヒスタミン鎮静薬：一定の用法・用量で使用する場合に限り、治験期間中の併用を可能とした。 神経遮断薬（クロザピン以外）：治験期間中の併用を可能とするが、治験責任医師は投与量を一定にするよう努めることとした。 非ベンゾジアゼピン系抗不安薬又は 1 日 1 回の睡眠薬：本治験を通じて一定の用法・用量で使用する場合に限り、併用を可能とした。 併用禁止薬： クロザピン、モノアミンオキシダーゼ A 阻害薬、バルビツール酸系薬（抗てんかん薬として使用する場合を除く）、てんかんの治療を目的で使用する植物性生薬
被験者数	計画例数：最大 250 例（各投与群 100～125 例） 無作為化例数：242 例、完了例数：213 例 安全性解析対象集団（SS）：242 例、 最大の解析対象集団（FAS）：240 例、 治験実施計画書に適合した解析対象集団（PPS）：207 例

表 1.1-1　試験方法の概略（続き）

項目	内容
被験者数（続き）	【被験者数設定の根拠】 脱落率を 15%未満と想定して、125 イベント（治療期間に 2 回目の強直間代発作が発現した被験者）を観察することでハザード比 0.56（有意水準両側 5%）を観察する 90%の検出力が得られると考えた。このハザード比は、ラモトリギンとプラセボを比較した過去の治験[(1)]から得られた生存率（プラセボ：25.4%、ラモトリギン：48.2%）を基にしている。ラモトリギンの治験で観察されたハザード比は 0.533 であったが、最近の抗てんかん薬の臨床試験で認められたプラセボ反応増加の可能性を説明するため、本治験の被験者数を推定したハザード比は 5%引き上げて 0.56 とした。この引き上げの根拠は、活性化合物がラコサミドとラモトリギンで異なること、及び本治験の有効性の主要評価項目を 2 回目の強直間代発作が発現するまでの時間にしたことである（ラモトリギンの治験では強直間代発作回数の変化率が主要評価項目であった）。 本治験は event-driven 試験であり、治験への患者登録は 125 イベントが発現するまで、又は最大 250 例の被験者が無作為割付けされるまでのいずれか早い時点まで継続した。
対象	過去に効果が認められなかった抗てんかん薬の薬剤数に関わらず、現在併用している 1～3 剤の抗てんかん薬でも発作コントロールが得られていない強直間代発作を有する 4 歳以上のてんかん患者
主な選択/除外基準	選択基準： 1)　4 歳以上の男性又は女性 2)　国際抗てんかん連盟による「てんかん発作の臨床・脳波分類（1981）」に従って強直間代発作を有するてんかんと診断された患者。30 歳より前に発症し、第 1 回来院の 24 週間以上前に確定診断されていること 3)　Combined ベースライン期間に 3 回以上の強直間代発作が認められた患者 ・　Combined ベースライン期間に 3 回以上の強直間代発作が認められること ・　Historical ベースライン期間に 2 回以上の強直間代発作が認められること ・　前述の発作が、Combined ベースライン期間の前半の 8 週間及び後半の 8 週間にそれぞれ 1 回以上認められること 4)　脳の磁気共鳴画像（MRI）検査／コンピュータ断層撮影（CT）検査が実施されている場合は、進行性異常又は部分発作に関連する可能性が高い病変の徴候が認められないこと 5)　VNS 併用の有無に関わらず、一定の用法・用量で 1～2 剤の非ベンゾジアゼピン系の抗てんかん薬、又は 2～3 剤の抗てんかん薬（1 剤はベンゾジアゼピン系）による治療を受けている患者。抗てんかん薬は第 1 回来院の 28 日以上前から用量・用法が一定に保たれていること。VNS は第 1 回来院の 6 ヵ月以上前に取り付けており、第 1 回来院の 28 日以上前から、並びに Prospective ベースライン期間中及び治療期間中に設定が一定に保たれていること

(1) French JA, Temkin NR, Hammer AE, VanLandingham KE. Time to nth seizure analysis of lamotrigine as adjunctive therapy in subjects with primary generalized tonic-clonic seizures. Epilepsia. 2007;48(S6):77-78.

表 1.1-1　試験方法の概略（続き）

項目	内容
主な選択/除外基準（続き）	6) 治験依頼者のメディカルドクターによりてんかん（3 Hz 以上の全般性棘徐波放電及び正常な背景脳波等）と一致する所見が脳波検査報告書で確認されている患者 除外基準： 1) 過去に本治験に無作為割付けされたことがある、又は過去にラコサミドの他の治験で治療群に割り付けられたことがある患者 2) 部分発作の既往がある、又は部分発作と一致する脳波所見のある患者 3) 「てんかん、てんかん症候群および関連発作性疾患の分類（1989）」に従った症候性全般てんかん（通常、強直発作を含む発作を呈するレノックス・ガストー症候群等）、Doose 症候群等の他の関連する症候群（通常、ミオクロニー脱力発作を呈する）又は焦点性及び全般性を併有するてんかんの徴候を有する患者 4) スクリーニング前 1 年以内に痙攣性てんかん重積状態の既往がある患者 5) 現在又は過去に、偽発作、転換性障害若しくはてんかん発作と混同されることがある他の非てんかん性発作を有する患者 6) 生涯において自殺企図の既往がある（実際の企図、過去に中断又は中止された企図を含む）、又は過去 6 ヵ月以内に自殺念慮が認められる患者（スクリーニング時にコロンビア自殺評価スケールの質問 4 又は質問 5 のいずれかに「はい」と回答） 7) 急性又は亜急性の進行性の中枢神経系疾患が認められる患者 8) 第 1 回来院時に、ALT、AST 若しくは ALP が基準範囲上限値の 2 倍以上、又は総ビリルビンが基準範囲上限値超（ジルベール症候群を有する場合は、基準範囲上限値の 1.5 倍以上）の患者。総ビリルビンのみが高値（基準範囲上限値超～基準範囲上限値の 1.5 倍未満）の場合は、ビリルビン分画を測定し、未診断のジルベール症候群（すなわち、直接ビリルビンが 35%未満）の可能性を特定した。 無作為割付けされた患者の ALT、AST、ALP 又は総ビリルビンのベースライン値が基準範囲上限値超の場合は、ベースライン時の診断及び／又は臨床的に意味のある高値の原因を確認し、電子症例報告書に記録した。 患者の ALT、AST 又は ALP が基準範囲上限値超でも、スクリーニング時の除外基準に抵触しない場合は、可能な限り投与開始前に再検査を実施し、臨床的に意味のある高値が更に悪化していないことを確認した。臨床的に意味のある高値が更に悪化している場合は、当該患者の組入れについてメディカルモニターと相談した。 ALT、AST 又は ALP の検査結果が除外基準を最大 25%上回っていた場合は、確認のため再検査を 1 回実施することを可能とした（再スクリーニングを含む）。 9) スクリーニング時に腎機能障害が認められる患者（CL_{CR} が 30 mL/min 未満） 10) ブルガダ症候群等の心臓チャネロパチーが判明している患者

表 1.1-1　試験方法の概略（続き）

項目	内容
主な選択/除外基準（続き）	除外基準（続き）： 11) ペースメーカー非使用時に洞不全症候群が認められる、第二度若しくは第三度房室ブロックが認められる又は他の臨床的に意味のある心電図異常が認められる患者 12) 第 1 回来院前 3 ヵ月以内に心筋梗塞の既往がある患者 13) ニューヨーク心臓協会のクラス III 又は IV に分類される心不全が認められる患者 14) 第 1 回来院前 28 日以内にモノアミンオキシダーゼ A 阻害薬、バルビツール酸系薬（てんかん以外の適応症に対する治療）又はクロザピンのいずれか 1 剤以上を定期的に服用していた患者 15) felbamate 投与による重篤な中毒（肝不全、再生不良性貧血）の既往がある患者、及び felbamate 投与が 12 ヵ月未満の患者。felbamate を第 1 回来院前に 12 ヵ月以上投与したが重篤な中毒が発現しなかった患者は登録を可能とした 16) ビガバトリンを過去 6 ヵ月に使用したことがある患者。ビガバトリンの投与歴がある場合は、ビガバトリンの投与終了後 6 ヵ月以内に視野測定試験を受けていること。視野測定試験の結果は、障害なし又は視野欠損（以下のいずれか 1 つに該当）であること ・ ビガバトリンの投与中のある時点で実施した視野測定試験の結果から変化がない ・ ビガバトリンの投与中止後まもなく実施した視野測定試験の結果から変化がない 17) ケトン食療法を受けており、第 1 回来院前 4 週間以内に変更、又は治験期間中に変更する予定のある患者
治験薬、投与量及び投与方法	被験薬： ラコサミド経口液（シロップ）10 mg/mL ラコサミド 50 mg 錠 バッチ番号：227281、241688、256412、262969、BX1012117、BX1012118、BX1012205、BX1012206、BX1013272、BX1013273、BX1013325、BX1013926、BX1014167、BX1014168、BX1014606、BX1014607、BX1014668、BX1014669、BX1013324 対照薬： プラセボ経口液（シロップ） プラセボ錠 バッチ番号：227281、241688、262969、BX1012117、BX1012205、BX1013272、BX1013325、BX1014167、BX1014606、BX1014668、BX1013324 投与量及び投与方法： 治験薬は、朝・夕 1 日 2 回、約 12 時間の間隔を空けて経口投与した。 第 2 回来院時に、被験者の年齢及び体重に基づき、4 歳以上 18 歳未満で体重が 50 kg 未満の小児被験者には経口液（シロップ）、18 歳以上の成人被験者及び体重 50 kg 以上の小児被験者には錠剤を投与した。 1 日に投与される錠剤の数が奇数の場合は、朝は低用量で夕に高用量を投与した。

表 1.1-1　試験方法の概略（続き）

<table>
<tr><th>項目</th><th>内容</th></tr>
<tr><td>治験薬、投与量及び投与方法（続き）</td><td>1)　増量期間
増量期間の治験薬の推奨投与スケジュール、忍容性に応じて用量調整した治験薬の投与量、及び第 6 週の少なくとも最後の 3 日間における治験薬の投与量を下表に示した。
第 2 回来院時にいずれかの投与群に無作為割付けした被験者に治験薬の投与を開始した。忍容性に基づく用量の調整が必要な場合を除き、推奨投与スケジュールに従って治験薬を投与した。用量を 1 段階増量した場合は、忍容性に基づく減量が必要な場合を除き、増量した用量で 7 日間以上投与を継続した後に次の用量へ増量した。減量した場合は、定常状態に到達するため、減量した用量で 3 日間以上投与を継続した後に次の用量へ増量した。
忍容性に問題がある場合は、治験薬の用量を柔軟に調整し、第 1 週の投与完了後から調整を可能とした。治験薬の減量又は維持は、治験責任医師の判断で制限なく実施できたが、第 6 週の少なくとも最後の 3 日間までに最低投与量に到達し、維持することとした。最低投与量が維持されている限り、第 6 週の最終日でも減量を可能とした。
最低投与量に到達しない被験者は減量期間に移行し、治験を中止した。最低投与量に到達した被験者は、維持期間に移行した。

治験薬の推奨投与スケジュール
<table>
<tr><th rowspan="2">体重（剤形）</th><th colspan="6">治験薬の目標用量</th></tr>
<tr><th>第 1 週</th><th>第 2 週</th><th>第 3 週</th><th>第 4 週</th><th>第 5 週</th><th>第 6 週</th></tr>
<tr><td>30 kg 未満［経口液（シロップ）］</td><td>2 mg/kg/日</td><td>4 mg/kg/日</td><td>6 mg/kg/日</td><td>8 mg/kg/日</td><td>10 mg/kg/日</td><td>12 mg/kg/日</td></tr>
<tr><td>30 kg 以上 50 kg 未満［経口液（シロップ）］</td><td>2 mg/kg/日</td><td>4 mg/kg/日</td><td>6 mg/kg/日</td><td>8 mg/kg/日</td><td>8 mg/kg/日</td><td>8 mg/kg/日</td></tr>
<tr><td>50 kg 以上及び成人被験者（錠剤）</td><td>100 mg/日</td><td>200 mg/日</td><td>300 mg/日</td><td>400 mg/日</td><td>400 mg/日</td><td>400 mg/日</td></tr>
</table>
</td></tr>
</table>

表 1.1-1　試験方法の概略（続き）

<table>
<tr><th>項目</th><th>内容</th></tr>
<tr><td>治験薬、投与量及び投与方法（続き）</td><td>
忍容性に応じて用量調整した治験薬の投与量
<table>
<tr><th rowspan="2">体重（剤形）</th><th rowspan="2">治験薬の目標用量（増量）／週 [a]</th><th colspan="2">減量調整による治験薬の減量</th><th colspan="2">減量調整後の治験薬の増量</th></tr>
<tr><th>最低投与量</th><th>最高投与量</th><th>最低投与量</th><th>最高投与量</th></tr>
<tr><td>30 kg 未満［経口液（シロップ）］</td><td rowspan="2">2 mg/kg/日</td><td rowspan="2">1 mg/kg/日</td><td rowspan="2">2 mg/kg/日</td><td rowspan="2">1 mg/kg/日</td><td rowspan="2">2 mg/kg/日</td></tr>
<tr><td>30 kg 以上 50 kg 未満［経口液（シロップ）］</td></tr>
<tr><td>50 kg 以上及び成人被験者（錠剤）</td><td>100 mg/日</td><td>50 mg/日</td><td>100 mg/日</td><td>50 mg/日</td><td>100 mg/日</td></tr>
</table>
注：50 mg ごとの減量が必要な被験者には、朝・夕で異なる用量の投与（投与量の差：50 mg 以内）を可能とした
a　以前に投与されていない用量に到達するための増量段階

第 6 週の少なくとも最後の 3 日間の治験薬の投与量
<table>
<tr><th>体重（剤形）</th><th>最低投与量</th><th>最高投与量</th></tr>
<tr><td>30 kg 未満［経口液（シロップ）］</td><td>8 mg/kg/日</td><td>12 mg/kg/日</td></tr>
<tr><td>30 kg 以上 50 kg 未満［経口液（シロップ）］</td><td>6 mg/kg/日</td><td>8 mg/kg/日</td></tr>
<tr><td>50 kg 以上及び成人被験者（錠剤）</td><td>300 mg/日</td><td>400 mg/日</td></tr>
</table>
2)　維持期間
第 6 週の少なくとも最後の 3 日間に最低投与量を投与した被験者は維持期間に移行し、増量期間の最終日の用量を維持した。最低投与量が維持される限り 1 回の減量を可能とし、可能な限りメディカルモニターに相談した上で来院時又は電話調査時に減量した。減量した場合は、再度増量することは不可とした。最低投与量で忍容性に問題がある場合は、減量期間に移行し、治験を中止した。

3)　移行期間
EP0012 試験に移行した被験者は、第 10 回来院又は早期中止来院、及び最終来院を盲検下で実施し、最終来院時に EP0012 試験の第 1 回来院を実施した。また、治験責任医師の判断で併用抗てんかん薬の調整を可能とした。なお、治療期間中にプラセボを投与された被験者は、下表に従って盲検下でラコサミドを漸増投与した。

プラセボを投与された被験者のラコサミドの投与スケジュール
<table>
<tr><th>体重（剤形）</th><th>第 1 週</th><th>第 2 週</th><th>第 3 週</th><th>第 4 週</th></tr>
<tr><td>30 kg 未満［経口液（シロップ）］</td><td>2 mg/kg/日</td><td>4 mg/kg/日</td><td>6 mg/kg/日</td><td>8 mg/kg/日</td></tr>
<tr><td>30 kg 以上 50 kg 未満［経口液（シロップ）］</td><td>2 mg/kg/日</td><td>4 mg/kg/日</td><td>6 mg/kg/日</td><td>8 mg/kg/日</td></tr>
<tr><td>50 kg 以上及び成人被験者（錠剤）</td><td>100 mg/日</td><td>200 mg/日</td><td>300 mg/日</td><td>400 mg/日</td></tr>
</table>
</td></tr>
</table>

表 1.1-1　試験方法の概略（続き）

<table>
<tr><th colspan="2">項目</th><th>内容</th></tr>
<tr><td colspan="2">治験薬、投与量及び投与方法（続き）</td><td>4)　減量期間
治験を中止した被験者若しくは EP0012 試験への参加を希望しない被験者又は参加基準を満たさない被験者は、第 10 回来院又は早期中止来院、及び減量完了来院を盲検下で実施した。減量期間では、下表に示した治験薬のスケジュールに従って減量した。医療上必要な場合は、治験の中止を決定する前に可能な限りメディカルモニターに相談した上で、緩やかな減量を可能とした。また、緊急の場合は、メディカルモニターに相談した上で、より速やかな減量を可能とした。

治験薬の減量スケジュール
<table>
<tr><th>減量開始時の治験薬の投与量</th><th>第 1 週</th><th>第 2 週</th><th>第 3 週</th><th>第 4 週</th></tr>
<tr><td>11 又は 12 mg/kg/日</td><td>9 mg/kg/日</td><td>6 mg/kg/日</td><td>4 mg/kg/日</td><td>2 mg/kg/日</td></tr>
<tr><td>9 又は 10 mg/kg/日</td><td>8 mg/kg/日</td><td>6 mg/kg/日</td><td>4 mg/kg/日</td><td>2 mg/kg/日</td></tr>
<tr><td>7 又は 8 mg/kg/日</td><td>6 mg/kg/日</td><td>4 mg/kg/日</td><td>2 mg/kg/日</td><td>—</td></tr>
<tr><td>5 又は 6 mg/kg/日</td><td>4 mg/kg/日</td><td>2 mg/kg/日</td><td>—</td><td>—</td></tr>
<tr><td>3 又は 4 mg/kg/日</td><td>2 mg/kg/日</td><td>—</td><td>—</td><td>—</td></tr>
<tr><td>2 mg/kg/日以下</td><td>—</td><td>—</td><td>—</td><td>—</td></tr>
<tr><td>350 又は 400 mg/日</td><td>300 mg/日</td><td>200 mg/日</td><td>100 mg/日</td><td>—</td></tr>
<tr><td>250 又は 300 mg/日</td><td>200 mg/日</td><td>100 mg/日</td><td>—</td><td>—</td></tr>
<tr><td>150 又は 200 mg/日</td><td>100 mg/日</td><td>—</td><td>—</td><td>—</td></tr>
<tr><td>100 mg/日</td><td>—</td><td>—</td><td>—</td><td>—</td></tr>
</table>
注：125 イベントが発現した場合は、増量期間に到達した用量に応じて減量を調整した</td></tr>
<tr><td colspan="2">投与期間</td><td>最長投与期間 28 週間
· 増量期間 6 週間
· 維持期間 最長 18 週間
· 移行期間 4 週間又は減量期間 最長 4 週間</td></tr>
<tr><td>評価項目</td><td>有効性</td><td>主要評価項目
· 治療期間における 2 回目の強直間代発作が発現するまでの時間
主な副次評価項目
· Kaplan-Meier（KM）法で算出した治療期間における強直間代発作の消失
その他の副次評価項目
· 治療期間における 1 回目の強直間代発作が発現するまでの時間</td></tr>
</table>

表 1.1-1　試験方法の概略（続き）

項目		内容
評価項目（続き）	有効性（続き）	その他の評価項目 · Combined ベースライン期間に対する治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）の 28 日あたりの強直間代発作回数の変化率 · 治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）における強直間代発作の消失割合 · Combined ベースライン期間に対する治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）の強直間代発作回数のレスポンダーレート及び 50%増悪 · Prospective ベースライン期間に対する治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）の 28 日あたりの欠神発作発現日数の変化率 · Prospective ベースライン期間に対する治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）の欠神発作発現日数のレスポンダーレート · Prospective ベースライン期間に対する治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）の 28 日あたりのミオクロニー発作発現日数の変化率 · Prospective ベースライン期間に対する治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）のミオクロニー発作発現日数のレスポンダーレート · 治療期間（最初の 6 週間、最初の 12 週間及び 24 週間）におけるすべての全般発作の消失割合 · てんかん患者用 QOL 質問票（QOLIE-31-P）のベースラインからの変化 · 子どもの健康関連 QOL 評価（PedsQL）のベースラインからの変化 · EuroQol による 5 項目 3 段階（EQ-5D-3L）QOL 評価の視覚的アナログスケール（VAS）スコアのベースラインからの変化
	安全性	主な安全性評価項目 · 被験者及び／又は介護者の自発的報告又は治験責任医師の観察により報告された有害事象 その他の安全性評価項目 · 有害事象による中止例 · 治療期間の 28 日あたりの欠神発作及びミオクロニー発作発現日数が Prospective ベースライン期間と比較して 25%以下、25%超 50%以下、50%超 75%以下及び 75%超増加した被験者の割合 · 治療期間中に新たな発作型を発現した被験者の割合 · 臨床検査値（血液学的検査、血液生化学検査、尿検査）の変化 · 12 誘導心電図の変化 · バイタルサイン（血圧及び脈拍数）、体重及び身長、並びに身体所見（神経学的検査を含む）の変化 · Achenbach の子どもの行動チェックリスト（CBCL）/1½-5 版又は 6-18 版を用いた評価（小児被験者のみ） · 実行機能に関する行動評価尺度（BRIEF／BRIEF-P）を用いた認知機能評価（小児被験者のみ）
	薬物動態	血漿中ラコサミド濃度

表 1.1-1　試験方法の概略（続き）

項目	内容
統計解析方法	解析対象集団の定義： SS：本治験に登録され、治験薬を 1 回以上投与された被験者 FAS：SS のうち、治療期間中の発作日誌の記録が 1 回以上ある被験者 PPS：FAS のうち、治療期間が 6 週間未満の被験者又は主要評価項目の解析に影響を与える治験実施計画書からの重大な逸脱（データベースロック及び盲検解除前に決定）のない被験者 有効性の解析は FAS を対象とし、安全性及び薬物動態の解析は SS を対象とした。 有効性： 主要評価項目の治療期間における 2 回目の強直間代発作が発現するまでの時間を、以下の被験者層で Cox 比例ハザード回帰モデルを用いて求めた。 ・ 層 1：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回以下の小児被験者 ・ 層 2：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回以下の成人被験者 ・ 層 3：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回超の小児及び成人被験者 ハザード比はプラセボ群を対照群として算出し、ハザード比の 95%信頼区間も算出した。また、2 回目の強直間代発作が発現するまでの時間に対する KM プロットと 2 回目の強直間代発作が発現するまでの時間の中央値及び 95%信頼区間に対する KM 推定値を示した。更に、脱落、治験実施計画書からの重大な逸脱、試験実施上のバイアスの主要評価項目への影響を評価するため、感度分析を実施した。主要評価項目が統計的に有意であった場合は、ゲートキーピング手法を用いて、主な副次評価項目を検定した。主な副次評価項目の治療期間における強直間代発作の消失、及びその他の副次評価項目の治療期間における 1 回目の強直間代発作が発現するまでの時間を、主要評価項目と同様に求めた。 安全性： 治験薬投与開始後に認められた有害事象の発現例数及び発現率を集団、投与群、年齢グループ及び期間別に求めた。治験薬投与開始後に認められた有害事象は、治験薬初回投与日から最終投与 30 日後までに認められた事象、又は治験薬初回投与日から最終投与 30 日後までに悪化した事象と定義した。 臨床検査値、バイタルサイン及び 12 誘導心電図について、測定値及びベースラインからの変化量の記述統計量を来院別に求めた。 薬物動態： 血漿中ラコサミド濃度の記述統計量を来院時別に求めた。
治験責任医師	114 名
治験実施医療機関	115 医療機関（北米、中南米、西・中央欧州、東欧州、アジア・太平洋・その他）
公表文献	なし
治験実施期間	2015 年 4 月 [redacted] 日～2019 年 6 月 [redacted] 日

1.1.1 被験者の内訳

本治験の SS での被験者の内訳及び中止理由を期間別に表 1.1-2（全集団）及び表 1.1-3（日本人集団）に示した。

全集団では、242 例が無作為化され、プラセボ群及びラコサミド群にそれぞれ 121 例が割り付けられた。このうち、213 例（88.0%）が本治験を完了し、29 例（12.0%）が本治験を中止した。投与群別では、プラセボ群 110 例（90.9%）及びラコサミド群 103 例（85.1%）が本治験を完了し、プラセボ群 11 例（9.1%）及びラコサミド群 18 例（14.9%）が本治験を中止した。

日本人集団では、30 例が無作為化され、プラセボ群に 19 例及びラコサミド群に 11 例が割り付けられた。このうち、29 例（96.7%）が本治験を完了し、1 例（3.3%）が本治験を中止した。投与群別では、プラセボ群 18 例（94.7%）及びラコサミド群 11 例（100%）が本治験を完了した。本治験を中止した被験者は、プラセボ群であった。

表 1.1-2　全集団の被験者の内訳及び中止理由：SS

Table 1.2.1
Disposition and Discontinuation Reasons
Analysis Set: Safety Set

Disposition	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Started Study	121(100)	121(100)	242(100)
Completed Study	110(90.9)	103(85.1)	213(88.0)
Discontinued	11(9.1)	18(14.9)	29(12.0)
Primary Reason for Discontinuation			
ADVERSE EVENT	4(3.3)	10(8.3)	14(5.8)
LACK OF EFFICACY	0	1(0.8)	1(0.4)
PROTOCOL VIOLATION	1(0.8)	2(1.7)	3(1.2)
LOST TO FOLLOW-UP	2(1.7)	3(2.5)	5(2.1)
CONSENT WITHDRAWN	3(2.5)	1(0.8)	4(1.7)
OTHER	1(0.8)	1(0.8)	2(0.8)

LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are relative to the number of subjects in the Safety Set.
Note: Completed study is defined as meeting any of the predetermined exit criteria or completing the 24-week Treatment Period with <2 PGTCS.
Note: Discontinuation is defined as the completion of the Early Termination Visit.
Note: Subjects SP0982-[redacted] (PBO) and SP0982-[redacted] (LCM) who completed the study are also tabulated in the AEs leading to discontinuation during the Treatment Period.
Note: Subject SP0982-[redacted] was errantly exited from the study in December 2018 with 1 PGTCS. He appears as a Completer when he should have been an Early Discontinuation.
Reference: Listing 1.2

表 1.1-2　全集団の被験者の内訳及び中止理由：SS（続き）

Table 1.2.1
Disposition and Discontinuation Reasons
Analysis Set: Safety Set

Disposition	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Started Titration Period	121(100)	121(100)	242(100)
Completed Titration Period	114(94.2)	107(88.4)	221(91.3)
Completed Titration, not continuing to Maintenance	44(36.4)	25(20.7)	69(28.5)
Completed Titration, continuing to Maintenance	70(57.9)	82(67.8)	152(62.8)
Discontinued during Titration Period	7(5.8)	14(11.6)	21(8.7)
Primary Reason for Discontinuation			
ADVERSE EVENT	2(1.7)	8(6.6)	10(4.1)
LACK OF EFFICACY	0	1(0.8)	1(0.4)
PROTOCOL VIOLATION	1(0.8)	2(1.7)	3(1.2)
LOST TO FOLLOW-UP	1(0.8)	3(2.5)	4(1.7)
CONSENT WITHDRAWN	2(1.7)	0	2(0.8)
OTHER	1(0.8)	0	1(0.4)

LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are relative to the number of subjects in the Safety Set.
Note: Completed study is defined as meeting any of the predetermined exit criteria or completing the 24-week Treatment Period with <2 PGTCS.
Note: Discontinuation is defined as the completion of the Early Termination Visit.
Note: Subjects SP0982-[redacted] (PBO) and SP0982-[redacted] (LCM) who completed the study are also tabulated in the AEs leading to discontinuation during the Treatment Period.
Note: Subject SP0982-[redacted] was errantly exited from the study in December 2018 with 1 PGTCS. He appears as a Completer when he should have been an Early Discontinuation.
Reference: Listing 1.2

表 1.1-2　全集団の被験者の内訳及び中止理由：SS（続き）

Table 1.2.1
Disposition and Discontinuation Reasons
Analysis Set: Safety Set

Disposition	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Started Maintenance Period	70(57.9)	82(67.8)	152(62.8)
Completed Maintenance Period	66(54.5)	78(64.5)	144(59.5)
Discontinued during Maintenance Period	4(3.3)	4(3.3)	8(3.3)
Primary Reason for Discontinuation			
ADVERSE EVENT	2(1.7)	2(1.7)	4(1.7)
LACK OF EFFICACY	0	0	0
PROTOCOL VIOLATION	0	0	0
LOST TO FOLLOW-UP	1(0.8)	0	1(0.4)
CONSENT WITHDRAWN	1(0.8)	1(0.8)	2(0.8)
OTHER	0	1(0.8)	1(0.4)

LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are relative to the number of subjects in the Safety Set.
Note: Completed study is defined as meeting any of the predetermined exit criteria or completing the 24-week Treatment Period with <2 PGTCS.
Note: Discontinuation is defined as the completion of the Early Termination Visit.
Note: Subjects SP0982-[redacted] (PBO) and SP0982-[redacted] (LCM) who completed the study are also tabulated in the AEs leading to discontinuation during the Treatment Period.
Note: Subject SP0982-[redacted] was errantly exited from the study in December 2018 with 1 PGTCS. He appears as a Completer when he should have been an Early Discontinuation.
Reference: Listing 1.2

表 1.1-3　日本人集団の被験者の内訳及び中止理由：SS

Table 1.2.1.1
Disposition and Discontinuation Reasons
Analysis Set: Safety Set - Japanese

Disposition	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Started Study	19(100)	11(100)	30(100)
Completed Study	18(94.7)	11(100)	29(96.7)
Discontinued	1(5.3)	0	1(3.3)
Primary Reason for Discontinuation			
ADVERSE EVENT	0	0	0
LACK OF EFFICACY	0	0	0
PROTOCOL VIOLATION	0	0	0
LOST TO FOLLOW-UP	0	0	0
CONSENT WITHDRAWN	0	0	0
OTHER	1(5.3)	0	1(3.3)

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are relative to the number of subjects in the Safety Set.
Note: Completed study is defined as meeting any of the predetermined exit criteria or completing the 24-week Treatment Period with <2 PGTCS.
Note: Discontinuation is defined as the completion of the Early Termination Visit.

Reference: Listing 1.2

表 1.1-3　日本人集団の被験者の内訳及び中止理由：SS（続き）

Table 1.2.1.1
Disposition and Discontinuation Reasons
Analysis Set: Safety Set - Japanese

Disposition	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Started Titration Period	19(100)	11(100)	30(100)
Completed Titration Period	18(94.7)	11(100)	29(96.7)
Completed Titration, not continuing to Maintenance	9(47.4)	0	9(30.0)
Completed Titration, continuing to Maintenance	9(47.4)	11(100)	20(66.7)
Discontinued during Titration Period	1(5.3)	0	1(3.3)
Primary Reason for Discontinuation			
ADVERSE EVENT	0	0	0
LACK OF EFFICACY	0	0	0
PROTOCOL VIOLATION	0	0	0
LOST TO FOLLOW-UP	0	0	0
CONSENT WITHDRAWN	0	0	0
OTHER	1(5.3)	0	1(3.3)

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are relative to the number of subjects in the Safety Set.
Note: Completed study is defined as meeting any of the predetermined exit criteria or completing the 24-week Treatment Period with <2 PGTCS.
Note: Discontinuation is defined as the completion of the Early Termination Visit.

Reference: Listing 1.2

表 1.1-3　日本人集団の被験者の内訳及び中止理由：SS（続き）

Table 1.2.1.1
Disposition and Discontinuation Reasons
Analysis Set: Safety Set - Japanese

Disposition	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Started Maintenance Period	9(47.4)	11(100)	20(66.7)
Completed Maintenance Period	9(47.4)	11(100)	20(66.7)
Discontinued during Maintenance Period	0	0	0
Primary Reason for Discontinuation			
ADVERSE EVENT	0	0	0
LACK OF EFFICACY	0	0	0
PROTOCOL VIOLATION	0	0	0
LOST TO FOLLOW-UP	0	0	0
CONSENT WITHDRAWN	0	0	0
OTHER	0	0	0

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are relative to the number of subjects in the Safety Set.
Note: Completed study is defined as meeting any of the predetermined exit criteria or completing the 24-week Treatment Period with <2 PGTCS.
Note: Discontinuation is defined as the completion of the Early Termination Visit.

Reference: Listing 1.2

1.1.2 被験者背景

1.1.2.1 人口統計学的特性及び疾患特性

本治験の SS での人口統計学的特性を表 1.1-4（全集団）及び表 1.1-5（日本人集団）に、ベースラインの疾患特性を表 1.1-6（全集団）及び表 1.1-7（日本人集団）に示した。また、本治験の登録前のてんかん発作型分類を表 1.1-8（全集団）及び表 1.1-9（日本人集団）に示し、てんかん症候群の分類を表 1.1-10（全集団）及び表 1.1-11（日本人集団）に示した。

表 1.1-4　全集団の人口統計学的特性：SS

Table 3.1.1
Demographics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Age (years)	n	121	121	242
	Mean	27.64	27.82	27.73
	SD	12.45	13.13	12.77
	Q1	19.00	19.00	19.00
	Median	25.00	25.00	25.00
	Q3	35.00	35.00	35.00
	Min	5.0	4.0	4.0
	Max	65.0	66.0	66.0

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum,
Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.1

表 1.1-4　全集団の人口統計学的特性：SS（続き）

Table 3.1.1
Demographics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Age (years) [a]				
>=4-<12	n (%)	9(7.4)	8(6.6)	17(7.0)
12-<18	n (%)	16(13.2)	16(13.2)	32(13.2)
18-<65	n (%)	95(78.5)	96(79.3)	191(78.9)
65-<85	n (%)	1(0.8)	1(0.8)	2(0.8)
>=85	n (%)	0	0	0
Age (years) [b]				
<=18	n (%)	27(22.3)	28(23.1)	55(22.7)
19-<65	n (%)	93(76.9)	92(76.0)	185(76.4)
>=65	n (%)	1(0.8)	1(0.8)	2(0.8)

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.1

表 1.1-4　全集団の人口統計学的特性：SS（続き）

Table 3.1.1
Demographics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Age stratification category based on IRT (years)				
>=4-<12	n (%)	9(7.4)	8(6.6)	17(7.0)
>=12-<18	n (%)	16(13.2)	16(13.2)	32(13.2)
>=18	n (%)	96(79.3)	97(80.2)	193(79.8)
Gender				
M	n (%)	45(37.2)	55(45.5)	100(41.3)
F	n (%)	76(62.8)	66(54.5)	142(58.7)
Weight (kg)	n	121	121	242
	Mean	72.75	70.42	71.59
	SD	22.19	21.84	22.00
	Q1	59.10	54.20	55.50
	Median	70.00	70.50	70.40
	Q3	85.40	84.00	84.90
	Min	21.1	15.8	15.8
	Max	154.3	127.4	154.3

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.1

表 1.1-4　全集団の人口統計学的特性：SS（続き）

Table 3.1.1
Demographics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Height (cm)	n	121	121	242
	Mean	164.75	165.89	165.32
	SD	12.32	15.04	13.73
	Q1	157.70	158.00	158.00
	Median	165.00	167.00	165.65
	Q3	172.70	175.00	174.70
	Min	121.0	105.0	105.0
	Max	191.5	203.2	203.2

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.1

表 1.1-4　全集団の人口統計学的特性：SS（続き）

Table 3.1.1
Demographics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
BMI (kg/m^2)	n	121	121	242
	Mean	26.47	25.09	25.78
	SD	6.78	6.21	6.52
	Q1	21.76	21.11	21.37
	Median	25.00	24.16	24.55
	Q3	30.35	28.34	29.37
	Min	14.2	14.3	14.2
	Max	47.2	50.0	50.0

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.1

表 1.1-4　全集団の人口統計学的特性：SS（続き）

Table 3.1.1
Demographics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Race				
American Indian/Alaskan Native	n (%)	1(0.8)	1(0.8)	2(0.8)
Asian	n (%)	25(20.7)	18(14.9)	43(17.8)
Black	n (%)	2(1.7)	2(1.7)	4(1.7)
Native Hawaiian or Other Pacific Islander	n (%)	0	0	0
White	n (%)	89(73.6)	97(80.2)	186(76.9)
Other/Mixed	n (%)	4(3.3)	3(2.5)	7(2.9)
Ethnicity				
Hispanic or Latino	n (%)	18(14.9)	10(8.3)	28(11.6)
Not Hispanic or Latino	n (%)	103(85.1)	111(91.7)	214(88.4)

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.1

表 1.1-5　日本人集団の人口統計学的特性：SS

Table 3.1.1.1
Demographics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Age (years)	n	19	11	30
	Mean	25.21	19.55	23.13
	SD	10.84	3.42	9.20
	Q1	17.00	17.00	17.00
	Median	24.00	20.00	21.00
	Q3	33.00	21.00	26.00
	Min	7.0	13.0	7.0
	Max	50.0	26.0	50.0

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.1

表 1.1-5　日本人集団の人口統計学的特性：SS（続き）

Table 3.1.1.1
Demographics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Age (years) [a]				
>=4-<12	n (%)	2(10.5)	0	2(6.7)
12-<18	n (%)	4(21.1)	3(27.3)	7(23.3)
18-<65	n (%)	13(68.4)	8(72.7)	21(70.0)
65-<85	n (%)	0	0	0
>=85	n (%)	0	0	0
Age (years) [b]				
<=18	n (%)	6(31.6)	4(36.4)	10(33.3)
19-<65	n (%)	13(68.4)	7(63.6)	20(66.7)
>=65	n (%)	0	0	0

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.1

表 1.1-5　日本人集団の人口統計学的特性：SS（続き）

Table 3.1.1.1
Demographics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Age stratification category based on IRT (years)				
>=4-<12	n (%)	2(10.5)	0	2(6.7)
>=12-<18	n (%)	4(21.1)	3(27.3)	7(23.3)
>=18	n (%)	13(68.4)	8(72.7)	21(70.0)
Gender				
M	n (%)	9(47.4)	4(36.4)	13(43.3)
F	n (%)	10(52.6)	7(63.6)	17(56.7)
Weight (kg)	n	19	11	30
	Mean	60.66	62.01	61.15
	SD	14.52	19.78	16.32
	Q1	55.10	48.40	52.20
	Median	59.80	53.20	59.80
	Q3	66.10	70.30	67.00
	Min	21.1	40.2	21.1
	Max	95.6	108.0	108.0

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.1

表 1.1-5　日本人集団の人口統計学的特性：SS（続き）

Table 3.1.1.1
Demographics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Height (cm)	n	19	11	30
	Mean	159.23	161.92	160.21
	SD	12.00	6.87	10.36
	Q1	154.20	154.50	154.30
	Median	162.20	162.50	162.35
	Q3	166.90	165.40	166.60
	Min	121.7	152.1	121.7
	Max	175.0	172.6	175.0

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.1

表 1.1-5　日本人集団の人口統計学的特性：SS（続き）

Table 3.1.1.1
Demographics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
BMI (kg/m^2)	n	19	11	30
	Mean	23.60	23.33	23.50
	SD	4.33	5.73	4.79
	Q1	21.29	19.69	20.92
	Median	23.37	21.87	23.10
	Q3	24.82	26.66	25.11
	Min	14.2	15.0	14.2
	Max	36.3	36.3	36.3

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.1

表 1.1-5　日本人集団の人口統計学的特性：SS（続き）

Table 3.1.1.1
Demographics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Race				
American Indian/Alaskan Native	n (%)	0	0	0
Asian	n (%)	19(100)	11(100)	30(100)
Black	n (%)	0	0	0
Native Hawaiian or Other Pacific Islander	n (%)	0	0	0
White	n (%)	0	0	0
Other/Mixed	n (%)	0	0	0
Ethnicity				
Hispanic or Latino	n (%)	0	0	0
Not Hispanic or Latino	n (%)	19(100)	11(100)	30(100)

BMI=body mass index, F=female, IRT=interactive response technology, LCM=Lacosamide, M=male, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
[a] EudraCT age categories.
[b] clinicaltrials.gov age categories.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.1

表 1.1-6　全集団のベースラインの疾患特性：SS

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Combined Baseline PGTCS categories - IRT				
<=2 per 28 days	n (%)	95(78.5)	95(78.5)	190(78.5)
>2 per 28 days	n (%)	26(21.5)	26(21.5)	52(21.5)
Combined Baseline PGTCS categories - CRF				
<=2 per 28 days	n (%)	91(75.2)	94(77.7)	185(76.4)
>2 per 28 days	n (%)	30(24.8)	27(22.3)	57(23.6)

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-6　全集団のベースラインの疾患特性：SS（続き）

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Combined Baseline PGTCS frequency per 28 days	n	121	121	242
	Mean	2.02	1.87	1.95
	SD	2.42	1.74	2.11
	Q1	1.00	1.00	1.00
	Median	1.24	1.25	1.25
	Q3	2.00	2.00	2.00
	Min	0.7	0.3	0.3
	Max	19.4	12.3	19.4

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-6　全集団のベースラインの疾患特性：SS（続き）

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Historical Baseline PGTCS frequency per 28 days	n	121	121	242
	Mean	1.71	1.66	1.68
	SD	1.76	1.39	1.58
	Q1	1.00	1.00	1.00
	Median	1.00	1.00	1.00
	Q3	2.00	2.00	2.00
	Min	0.3	0.3	0.3
	Max	14.0	9.7	14.0

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-6　全集団のベースラインの疾患特性：SS（続き）

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Prospective Baseline PGTCS frequency per 28 days	n	121	120	241
	Mean	3.00	2.51	2.76
	SD	6.42	4.14	5.40
	Q1	1.00	1.00	1.00
	Median	1.08	1.04	1.08
	Q3	2.07	2.90	2.15
	Min	0.0	0.0	0.0
	Max	53.8	30.0	53.8

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-6　全集団のベースラインの疾患特性：SS（続き）

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Time since first diagnosis (years)	n	121	121	242
	Mean	15.39	15.53	15.46
	SD	12.97	13.12	13.02
	Q1	5.94	5.56	5.59
	Median	11.26	11.42	11.32
	Q3	21.17	21.53	21.18
	Min	0.5	0.8	0.5
	Max	60.7	64.9	64.9

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-6　全集団のベースラインの疾患特性：SS（続き）

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Age at diagnosis of epilepsy (years)	n	121	121	242
	Mean	12.91	12.90	12.90
	SD	5.88	6.75	6.32
	Q1	9.00	8.33	8.71
	Median	13.24	13.22	13.23
	Q3	16.42	17.46	16.91
	Min	0.0	0.4	0.0
	Max	28.7	39.8	39.8

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-6　全集団のベースラインの疾患特性：SS（続き）

Table 3.2.1
Baseline Characteristics
Analysis Set: Safety Set

Variable	Statistic	Placebo N=121	LCM N=121	All Subjects N=242
Number of Lifetime AEDs and Benzodiazepines				
0	n (%)	70(57.9)	63(52.1)	133(55.0)
1-3	n (%)	37(30.6)	47(38.8)	84(34.7)
4-6	n (%)	13(10.7)	9(7.4)	22(9.1)
>=7	n (%)	1(0.8)	2(1.7)	3(1.2)

AEDs=antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.
Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Combined Baseline PGTCS categories - IRT				
<=2 per 28 days	n (%)	16(84.2)	9(81.8)	25(83.3)
>2 per 28 days	n (%)	3(15.8)	2(18.2)	5(16.7)
Combined Baseline PGTCS categories - CRF				
<=2 per 28 days	n (%)	15(78.9)	9(81.8)	24(80.0)
>2 per 28 days	n (%)	4(21.1)	2(18.2)	6(20.0)

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS（続き）

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Combined Baseline PGTCS frequency per 28 days	n	19	11	30
	Mean	3.18	2.14	2.80
	SD	5.03	2.23	4.20
	Q1	1.02	1.00	1.01
	Median	1.51	1.23	1.36
	Q3	2.00	1.75	2.00
	Min	0.8	0.8	0.8
	Max	19.4	6.8	19.4

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS（続き）

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Historical Baseline PGTCS frequency per 28 days	n	19	11	30
	Mean	2.18	2.00	2.11
	SD	2.92	1.78	2.53
	Q1	1.00	1.00	1.00
	Median	1.67	1.33	1.33
	Q3	2.00	2.00	2.00
	Min	0.7	1.0	0.7
	Max	14.0	6.7	14.0

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS（続き）

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Prospective Baseline PGTCS frequency per 28 days	n	19	11	30
	Mean	6.29	2.54	4.92
	SD	13.80	4.46	11.33
	Q1	1.00	0.00	1.00
	Median	1.93	1.00	1.08
	Q3	3.00	1.87	3.00
	Min	0.0	0.0	0.0
	Max	53.8	15.0	53.8

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS（続き）

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Time since first diagnosis (years)	n	19	11	30
	Mean	14.54	6.13	11.46
	SD	10.71	4.46	9.75
	Q1	6.43	2.12	3.87
	Median	13.20	6.20	9.51
	Q3	21.17	10.05	14.78
	Min	0.5	0.8	0.5
	Max	42.1	14.7	42.1

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS（続き）

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Age at diagnosis of epilepsy (years)	n	19	11	30
	Mean	11.27	13.89	12.23
	SD	4.46	4.69	4.65
	Q1	9.00	10.50	10.41
	Median	12.11	12.81	12.22
	Q3	13.24	18.29	14.35
	Min	1.7	6.6	1.7
	Max	21.0	22.3	22.3

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-7　日本人集団のベースラインの疾患特性：SS（続き）

Table 3.2.1.1
Baseline Characteristics
Analysis Set: Safety Set - Japanese

Variable	Statistic	Placebo N=19	LCM N=11	All Subjects N=30
Number of Lifetime AEDs and Benzodiazepines				
0	n (%)	2(10.5)	1(9.1)	3(10.0)
1-3	n (%)	11(57.9)	10(90.9)	21(70.0)
4-6	n (%)	6(31.6)	0	6(20.0)
>=7	n (%)	0	0	0

AEDs= antiepileptic drugs, CRF=case report form, IRT=interactive response technology, LCM=Lacosamide, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Combined Baseline includes the 16 weeks prior to randomization.
Note: Lifetime AEDs and benzodiazepines are taken in the subject's history and stopped at least 28 days prior to Visit 1.

Reference: Listings 2.1, 2.3.3

表 1.1-8　全集団のてんかん発作型分類：SS

Table 4.1.1
ILAE Seizure Classification History
Analysis Set: Safety Set

Seizure Type	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Partial onset seizures	0	1(0.8)	1(0.4)
Simple partial (IA)	0	1(0.8)	1(0.4)
Complex partial (IB)	0	0	0
Partial evolving to secondarily generalized (IC)	0	0	0
Generalized seizures	121(100)	121(100)	242(100)
Absence (IIA1)	41(33.9)	49(40.5)	90(37.2)
Atypical absence (IIA2)	2(1.7)	2(1.7)	4(1.7)
Myoclonic (IIB)	48(39.7)	46(38.0)	94(38.8)
Clonic (IIC)	2(1.7)	3(2.5)	5(2.1)
Tonic (IID)	1(0.8)	2(1.7)	3(1.2)
Tonic-clonic (IIE)	121(100)	120(99.2)	241(99.6)
Atonic (IIF)	3(2.5)	2(1.7)	5(2.1)
Unclassified epileptic seizures (III)	0	2(1.7)	2(0.8)

ILAE=International League Against Epilepsy, LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Seizures experienced at any time prior to study entry are summarized.
Reference: Listing 2.3.1

表 1.1-9　日本人集団のてんかん発作型分類：SS

Table 4.1.1.1
ILAE Seizure Classification History
Analysis Set: Safety Set - Japanese

Seizure Type	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Partial onset seizures	0	0	0
Simple partial (IA)	0	0	0
Complex partial (IB)	0	0	0
Partial evolving to secondarily generalized (IC)	0	0	0
Generalized seizures	19(100)	11(100)	30(100)
Absence (IIA1)	3(15.8)	2(18.2)	5(16.7)
Atypical absence (IIA2)	0	1(9.1)	1(3.3)
Myoclonic (IIB)	9(47.4)	5(45.5)	14(46.7)
Clonic (IIC)	0	1(9.1)	1(3.3)
Tonic (IID)	0	0	0
Tonic-clonic (IIE)	19(100)	11(100)	30(100)
Atonic (IIF)	0	0	0
Unclassified epileptic seizures (III)	0	0	0

ILAE=International League Against Epilepsy, LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: Seizures experienced at any time prior to study entry are summarized.

Reference: Listing 2.3.1

表 1.1-10　全集団のてんかん症候群の分類：SS

Table 4.2.1
Classification of Epileptic Syndrome
Analysis Set: Safety Set

Variable	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Localization related	0	0	0
Idiopathic	0	0	0
Symptomatic	0	0	0
Cryptogenic	0	0	0
Generalized idiopathic	121(100)	121(100)	242(100)
Benign neonatal familial convulsions	0	0	0
Benign neonatal convulsions	0	1(0.8)	1(0.4)
Benign myoclonic epilepsy in infancy	0	1(0.8)	1(0.4)
Childhood absence epilepsy	6(5.0)	9(7.4)	15(6.2)
Juvenile absence epilepsy	15(12.4)	13(10.7)	28(11.6)
Juvenile myoclonic epilepsy	42(34.7)	34(28.1)	76(31.4)
Epilepsy with grand mal seizures on awakening	19(15.7)	15(12.4)	34(14.0)
Other generalized idiopathic epilepsies not defined above	54(44.6)	55(45.5)	109(45.0)
Epilepsies with seizures precipitated by specific modes of activation	6(5.0)	6(5.0)	12(5.0)

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.3.2

表 1.1-10　全集団のてんかん症候群の分類：SS（続き）

Table 4.2.1
Classification of Epileptic Syndrome
Analysis Set: Safety Set

Variable	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Generalized cryptogenic or symptomatic	0	0	0
West syndrome	0	0	0
Lennox-Gastaut syndrome	0	0	0
Epilepsy with myoclonic-astatic seizures	0	0	0
Epilepsy with myoclonic absences	0	0	0
Generalized symptomatic	1(0.8)	0	1(0.4)
Non-specific etiology	0	0	0
Early myoclonic encephalopathy	0	0	0
Early infantile epileptic encephalopathy with suppression burst	0	0	0
Other symptomatic generalized epilepsies not defined above	1(0.8)	0	1(0.4)
Specific syndromes	0	0	0
Epilepsies and syndromes undetermined whether focal or generalized	0	0	0
With both generalized and focal seizures	0	0	0
Without unequivocal generalized or focal features	0	0	0
Situation-related seizures	4(3.3)	1(0.8)	5(2.1)

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set.
Reference: Listing 2.3.2

表 1.1-11　日本人集団のてんかん症候群の分類：SS

Table 4.2.1.1
Classification of Epileptic Syndrome
Analysis Set: Safety Set - Japanese

Variable	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Localization related	0	0	0
Idiopathic	0	0	0
Symptomatic	0	0	0
Cryptogenic	0	0	0
Generalized idiopathic	19(100)	11(100)	30(100)
Benign neonatal familial convulsions	0	0	0
Benign neonatal convulsions	0	0	0
Benign myoclonic epilepsy in infancy	0	0	0
Childhood absence epilepsy	0	0	0
Juvenile absence epilepsy	1(5.3)	1(9.1)	2(6.7)
Juvenile myoclonic epilepsy	8(42.1)	3(27.3)	11(36.7)
Epilepsy with grand mal seizures on awakening	8(42.1)	4(36.4)	12(40.0)
Other generalized idiopathic epilepsies not defined above	4(21.1)	4(36.4)	8(26.7)
Epilepsies with seizures precipitated by specific modes of activation	0	0	0

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.3.2

表 1.1-11　日本人集団のてんかん症候群の分類：SS（続き）

Table 4.2.1.1
Classification of Epileptic Syndrome
Analysis Set: Safety Set - Japanese

Variable	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Generalized cryptogenic or symptomatic	0	0	0
West syndrome	0	0	0
Lennox-Gastaut syndrome	0	0	0
Epilepsy with myoclonic-astatic seizures	0	0	0
Epilepsy with myoclonic absences	0	0	0
Generalized symptomatic	0	0	0
Non-specific etiology	0	0	0
Early myoclonic encephalopathy	0	0	0
Early infantile epileptic encephalopathy with suppression burst	0	0	0
Other symptomatic generalized epilepsies not defined above	0	0	0
Specific syndromes	0	0	0
Epilepsies and syndromes undetermined whether focal or generalized	0	0	0
With both generalized and focal seizures	0	0	0
Without unequivocal generalized or focal features	0	0	0
Situation-related seizures	1(5.3)	0	1(3.3)

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set.

Reference: Listing 2.3.2

1.1.2.2 抗てんかん薬

本治験の SS での本治験開始時の併用抗てんかん薬を表 1.1-12（全集団）及び表 1.1-13（日本人集団）に示した。

表 1.1-12　全集団の本治験開始時の併用抗てんかん薬：SS

Table 6.2
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
Any AED and/or Benzodiazepine	121 (100)	120 (99.2)	241 (99.6)
OTHER ANTIEPILEPTICS, N03AX	88 (72.7)	94 (77.7)	182 (75.2)
LEVETIRACETAM	48 (39.7)	55 (45.5)	103 (42.6)
LAMOTRIGINE	37 (30.6)	36 (29.8)	73 (30.2)
TOPIRAMATE	15 (12.4)	16 (13.2)	31 (12.8)
ZONISAMIDE	7 (5.8)	7 (5.8)	14 (5.8)
PERAMPANEL	3 (2.5)	2 (1.7)	5 (2.1)
PREGABALIN	2 (1.7)	2 (1.7)	4 (1.7)
FELBAMATE	1 (0.8)	0	1 (0.4)
GABAPENTIN	0	1 (0.8)	1 (0.4)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal.
Note: Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide.
Note: Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.
Reference: Listings 2.6.2, 2.6.4

表 1.1-12　全集団の本治験開始時の併用抗てんかん薬：SS（続き）

Table 6.2
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
OTHER ANTIEPILEPTICS, N03AX			
RETIGABINE	0	1 (0.8)	1 (0.4)
FATTY ACID DERIVATIVES, N03AG	67 (55.4)	59 (48.8)	126 (52.1)
VALPROATE	67 (55.4)	59 (48.8)	126 (52.1)
BENZODIAZEPINE DERIVATIVES, N03AE	23 (19.0)	20 (16.5)	43 (17.8)
CLONAZEPAM	12 (9.9)	11 (9.1)	23 (9.5)
CLOBAZAM	11 (9.1)	9 (7.4)	20 (8.3)
CARBOXAMIDE DERIVATIVES, N03AF	6 (5.0)	12 (9.9)	18 (7.4)
CARBAMAZEPINE	5 (4.1)	9 (7.4)	14 (5.8)
OXCARBAZEPINE	1 (0.8)	3 (2.5)	4 (1.7)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal.
Note: Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide.
Note: Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.
Reference: Listings 2.6.2, 2.6.4

表 1.1-12　全集団の本治験開始時の併用抗てんかん薬：SS（続き）

Table 6.2
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
BARBITURATES AND DERIVATIVES, N03AA	3 (2.5)	7 (5.8)	10 (4.1)
PHENOBARBITAL	3 (2.5)	6 (5.0)	9 (3.7)
PRIMIDONE	0	1 (0.8)	1 (0.4)
SUCCINIMIDE DERIVATIVES, N03AD	5 (4.1)	3 (2.5)	8 (3.3)
ETHOSUXIMIDE	5 (4.1)	1 (0.8)	6 (2.5)
BRIVARACETAM	0	2 (1.7)	2 (0.8)
HYDANTOIN DERIVATIVES, N03AB	4 (3.3)	3 (2.5)	7 (2.9)
PHENYTOIN	4 (3.3)	3 (2.5)	7 (2.9)
BENZODIAZEPINE DERIVATIVES, N05BA	1 (0.8)	4 (3.3)	5 (2.1)
DIAZEPAM	0	2 (1.7)	2 (0.8)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal.
Note: Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide.
Note: Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.
Reference: Listings 2.6.2, 2.6.4

表 1.1-12　全集団の本治験開始時の併用抗てんかん薬：SS（続き）

Table 6.2
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=121 n (%)	LCM N=121 n (%)	All Subjects N=242 n (%)
BENZODIAZEPINE DERIVATIVES, N05BA			
ALPRAZOLAM	0	1 (0.8)	1 (0.4)
CLOBAZAM	0	1 (0.8)	1 (0.4)
LORAZEPAM	1 (0.8)	0	1 (0.4)
BARBITURATES, PLAIN, N05CA	0	1 (0.8)	1 (0.4)
BENZOBARBITAL	0	1 (0.8)	1 (0.4)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal.
Note: Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide.
Note: Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.
Reference: Listings 2.6.2, 2.6.4

表 1.1-13　日本人集団の本治験開始時の併用抗てんかん薬：SS

Table 6.2.1.0
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set - Japanese

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
Any AED and/or Benzodiazepine	19 (100)	11 (100)	30 (100)
OTHER ANTIEPILEPTICS, N03AX	14 (73.7)	10 (90.9)	24 (80.0)
LEVETIRACETAM	7 (36.8)	5 (45.5)	12 (40.0)
LAMOTRIGINE	7 (36.8)	4 (36.4)	11 (36.7)
ZONISAMIDE	2 (10.5)	1 (9.1)	3 (10.0)
PERAMPANEL	1 (5.3)	0	1 (3.3)
TOPIRAMATE	0	1 (9.1)	1 (3.3)
FATTY ACID DERIVATIVES, N03AG	11 (57.9)	8 (72.7)	19 (63.3)
VALPROATE	11 (57.9)	8 (72.7)	19 (63.3)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1. Benzodiazepines at study entry are defined as Benzodiazepines where the start date is on or before 28 days prior to Visit 1 and the medication stopped less than 28 days prior to Visit 1 or is ongoing.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal. Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide. Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.

Reference: Listings 2.6.2, 2.6.4

表 1.1-13　日本人集団の本治験開始時の併用抗てんかん薬：SS（続き）

Table 6.2.1.0
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set - Japanese

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
BENZODIAZEPINE DERIVATIVES, N03AE	8 (42.1)	3 (27.3)	11 (36.7)
CLOBAZAM	4 (21.1)	3 (27.3)	7 (23.3)
CLONAZEPAM	4 (21.1)	0	4 (13.3)
HYDANTOIN DERIVATIVES, N03AB	2 (10.5)	0	2 (6.7)
PHENYTOIN	2 (10.5)	0	2 (6.7)
BARBITURATES AND DERIVATIVES, N03AA	1 (5.3)	0	1 (3.3)
PHENOBARBITAL	1 (5.3)	0	1 (3.3)
BENZODIAZEPINE DERIVATIVES, N05BA	0	1 (9.1)	1 (3.3)
DIAZEPAM	0	1 (9.1)	1 (3.3)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1. Benzodiazepines at study entry are defined as Benzodiazepines where the start date is on or before 28 days prior to Visit 1 and the medication stopped less than 28 days prior to Visit 1 or is ongoing.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal. Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide. Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.

Reference: Listings 2.6.2, 2.6.4

表 1.1-13　日本人集団の本治験開始時の併用抗てんかん薬：SS（続き）

Table 6.2.1.0
AEDs and Benzodiazepines at Study Entry
Analysis Set: Safety Set - Japanese

WHODD (Version SEP/2013) Chemical subgroup [Level 4] Preferred Term	Placebo N=19 n (%)	LCM N=11 n (%)	All Subjects N=30 n (%)
CARBOXAMIDE DERIVATIVES, N03AF	1 (5.3)	0	1 (3.3)
CARBAMAZEPINE	1 (5.3)	0	1 (3.3)

AED=antiepileptic drug, ATC=Anatomical Therapeutic Chemical, LCM=Lacosamide, WHODD=World Health Organization Drug Dictionary.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: AEDs at study entry are defined as AEDs where the start date is on or before 28 days prior to Visit 1 and the medication was still ongoing on the date of Visit 1. Benzodiazepines at study entry are defined as Benzodiazepines where the start date is on or before 28 days prior to Visit 1 and the medication stopped less than 28 days prior to Visit 1 or is ongoing.
Note: Phenytoin use includes phenytoin, phenytoin sodium, ethotoin, fosphenytoin, fosphenytoin sodium, and zentronal. Valproate use includes valproic acid, valproate semisodium, valproate sodium, valproate magnesium, ergenyl chrono, and valpromide. Phenobarbital included phenobarbital, phenobarbital sodium, methylphenobarbital, and primidone.

Reference: Listings 2.6.2, 2.6.4

1.1.3 有効性

1.1.3.1 主要評価項目

1.1.3.1.1 治療期間における 2 回目の強直間代発作が発現するまでの時間

本治験の FAS での治療期間（増量期間+維持期間）における 2 回目の強直間代発作が発現するまでの時間を表 1.1-14（全集団）及び表 1.1-15（日本人集団）に示し、KM 法で算出した 2 回目の強直間代発作が発現するまでの時間の推移を図 1.1-1（全集団）及び図 1.1-2（日本人集団）に示した。

全集団では、治療期間（24 週間）における 2 回目の強直間代発作の発現リスクは、プラセボ群と比較してラコサミド群で低く、統計学的に有意であった。治療期間最終時点で 2 回目の強直間代発作が発現していない KM 推定値は、プラセボ群 33.37%及びラコサミド群 55.27%であった（ハザード比：0.540、95%信頼区間：0.377～0.774、p<0.001）。また、2 回目の強直間代発作が発現するまでの時間の中央値は、プラセボ群が 77.0 日（95%信頼区間：49.0～128.0 日）であった。ラコサミド群は 50%超の被験者が治療期間に 2 回目の強直間代発作を発現しなかったため、中央値は推定できなかった。

日本人集団では、治療期間（24 週間）における 2 回目の強直間代発作の発現リスクは、プラセボ群と比較してラコサミド群で低く、治療期間最終時点で2回目の強直間代発作が発現していないKM推定値は、プラセボ群 15.79%及びラコサミド群 72.73%であった（ハザード比：0.185、95%信頼区間：0.053～0.649、p=0.008）。また、2 回目の強直間代発作が発現するまでの時間の中央値は、プラセボ群が 28.0 日（95%信頼区間：22.0～51.0 日）であった。ラコサミド群は 50%超の被験者が治療期間に 2 回目の強直間代発作を発現しなかったため、中央値は推定できなかった。

表 1.1-14　全集団の治療期間における 2 回目の強直間代発作が発現するまでの時間：FAS

Table 8.1.1
Analysis of Time to Second PGTCS (125 events)
Analysis Set: Full Analysis Set

	Placebo N=121			LCM N=118		
Timepoint	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)
1st 6 Weeks (at Day 42)	45	71	61.85	29	84	74.89
1st 12 Weeks (at Day 84)	61	53	47.74	38	70	66.46
Treatment Period (at Day 166)	76	31	33.37	49	52	55.27
KM Analysis Treatment Period						
Q1 (95% CI) - Time to Event (days)	22.0 (13.0, 29.0)			41.0 (24.0, 87.0)		
Median (95% CI) - Time to Event (days)	77.0 (49.0, 128.0)			- (144.0, -)		
Subjects Censored [a] (n, %)	45 (37.2)			69 (58.5)		
Titration - Observed Events (n, %)	46 (38.0)			29 (24.6)		
1st 12 Weeks - Observed Events (n, %)	61 (50.4)			38 (32.2)		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.

Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.

[a] Subjects who complete the Treatment Period without having a second PGTCS during the Treatment Period are censored.

If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.

[b] A Hazard Ratio <1 indicates time to second PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.

Patient SP0982-[redacted] (LCM) was randomized after the 125th event and does not appear in this analysis.

Reference: Listing 6.2.2

表 1.1-14　全集団の治療期間における 2 回目の強直間代発作が発現するまでの時間：FAS（続き）

Table 8.1.1
Analysis of Time to Second PGTCS (125 events)
Analysis Set: Full Analysis Set

	Placebo N=121			LCM N=118		
Timepoint	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)
Treatment Comparison						
LCM - Placebo						
Hazard Ratio (HR) [b]				0.540		
95% CI of HR				0.377, 0.774		
p-value				<0.001*		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a second PGTCS during the Treatment Period are censored.
If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to second PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.
Patient SP0982-[redacted] (LCM) was randomized after the 125th event and does not appear in this analysis.
Reference: Listing 6.2.2

表 1.1-15　日本人集団の治療期間における 2 回目の強直間代発作が発現するまでの時間：FAS

Table 8.1.1.1
Analysis of Time to Second PGTCS (125 events)
Analysis Set: Full Analysis Set - Japanese

	Placebo N=19			LCM N=11		
Timepoint	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)
1st 6 Weeks (at Day 42)	10	9	47.37	1	10	90.91
1st 12 Weeks (at Day 84)	15	4	21.05	1	10	90.91
Treatment Period (at Day 166)	16	3	15.79	3	8	72.73
KM Analysis Treatment Period						
Q1 (95% CI) - Time to Event (days)	15.0 (6.0, 28.0)			158.0 (32.0, -)		
Median (95% CI) - Time to Event (days)	28.0 (22.0, 51.0)			- (158.0, -)		
Subjects Censored [a] (n, %)	3 (15.8)			8 (72.7)		
Titration - Observed Events (n, %)	10 (52.6)			1 (9.1)		
1st 12 Weeks - Observed Events (n, %)	15 (78.9)			1 (9.1)		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a second PGTCS during the Treatment Period are censored. If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to second PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.

Reference: Listing 6.2.2

表 1.1-15　日本人集団の治療期間における 2 回目の強直間代発作が発現するまでの時間：FAS（続き）

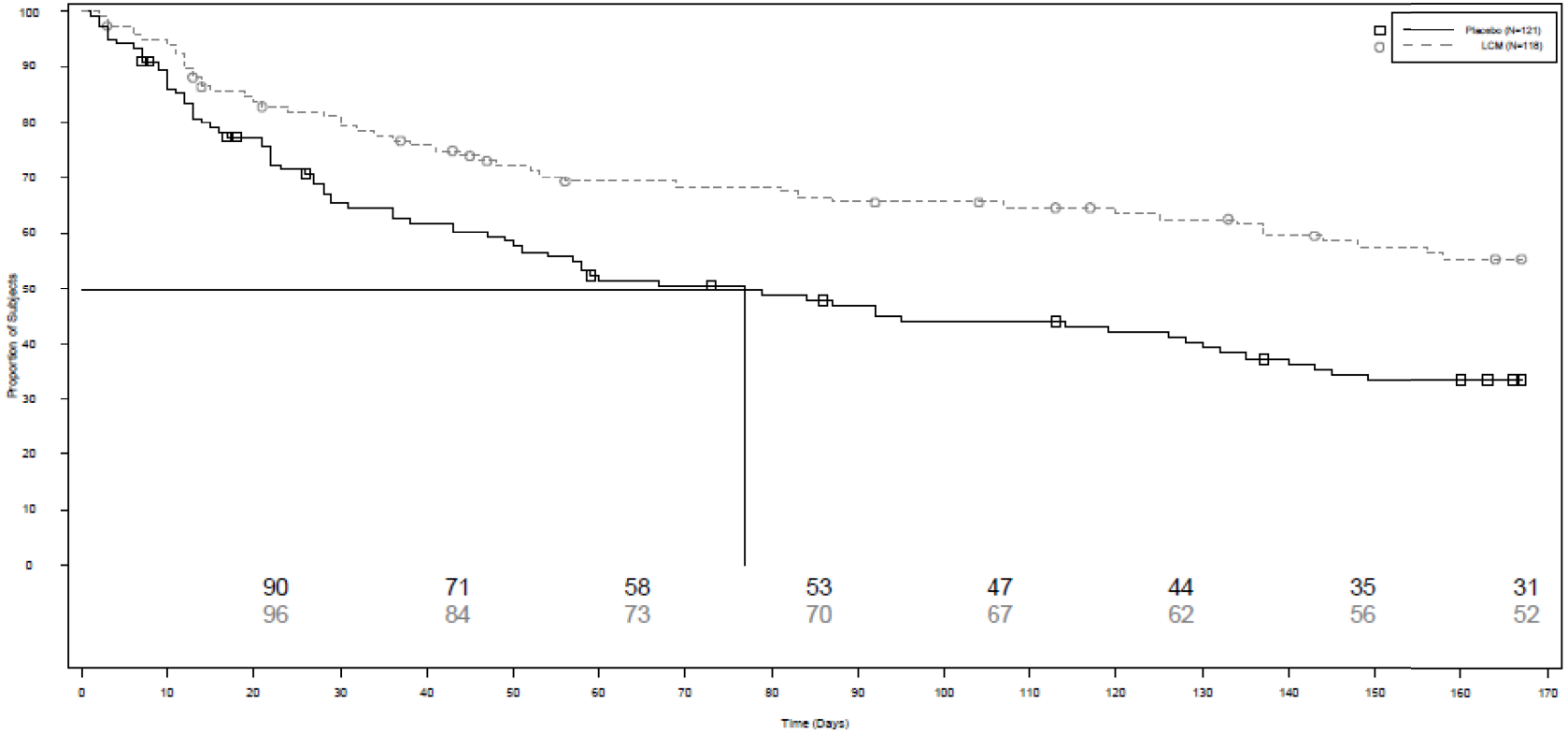
Table 8.1.1.1
Analysis of Time to Second PGTCS (125 events)
Analysis Set: Full Analysis Set - Japanese

Timepoint	Placebo N=19 Cumulative Number Of Events	Placebo N=19 Number At Risk	Placebo N=19 KM Survival Estimate (%)	LCM N=11 Cumulative Number Of Events	LCM N=11 Number At Risk	LCM N=11 KM Survival Estimate (%)
Treatment Comparison						
LCM - Placebo						
Hazard Ratio (HR) [b]				0.185		
95% CI of HR				0.053, 0.649		
p-value				0.008*		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a second PGTCS during the Treatment Period are censored. If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to second PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.

Reference: Listing 6.2.2

Figure 1.1
Kaplan-Meier Estimates for Time to Second PGTCS (125 events) During Treatment Period
Analysis Set: Full Analysis Set

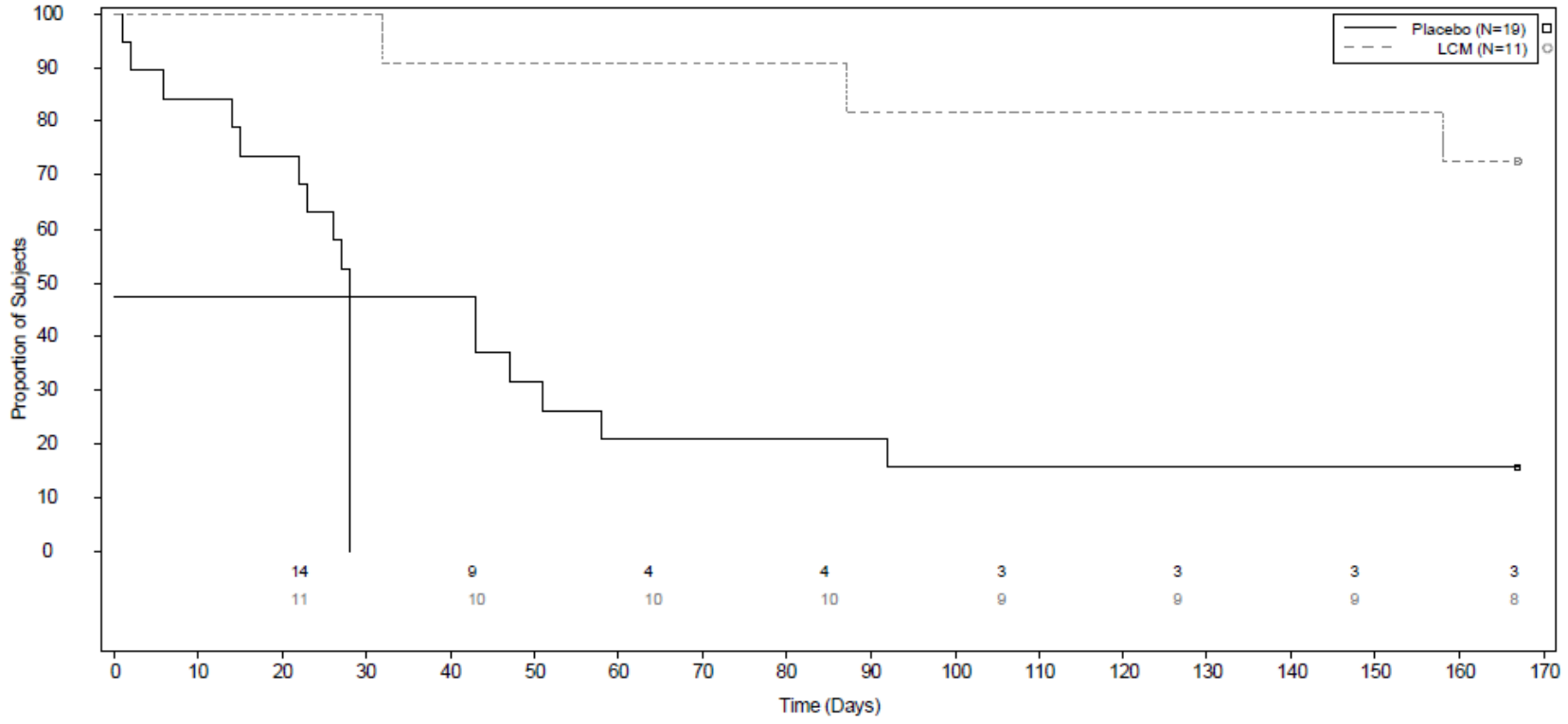


LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: The numbers represent the number of subjects at risk at the start of the final day of each 3 week period.
Note: The symbols represent censored subjects.
Note: Patient SP0982-[redacted] (LCM) was randomized after the 125th event and does not appear in this graph.
Reference: Table 8.1.1

Page 1 of 1

図 1.1-1　全集団の治療期間における 2 回目の強直間代発作が発現するまでの時間（Kaplan-Meier プロット）：FAS

Figure 1.1.1
Kaplan-Meier Estimates for Time to Second PGTCS (125 events) During Treatment Period
Analysis Set: Full Analysis Set - Japanese



LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: The numbers represent the number of subjects at risk at the start of the final day of each 3 week period.
Note: The symbols represent censored subjects.

Reference: Table 8.1.1

Page 1 of 1

図 1.1-2　日本人集団の治療期間における 2 回目の強直間代発作が発現するまでの時間（Kaplan-Meier プロット）：FAS

1.1.3.2 主な副次評価項目

1.1.3.2.1 Kaplan-Meier 法で算出した治療期間における強直間代発作の消失

本治験の FAS での治療期間（増量期間+維持期間）における強直間代発作の消失を被験者層別に表 1.1-16（全集団）及び表 1.1-17（日本人集団）に示した。

全集団では、治療期間（24 週間）に強直間代発作を消失した被験者の割合の KM 推定値（Mantel-Haenszel 法で推定）は、プラセボ群 17.2%（95%信頼区間：10.4%～24.0%）及びラコサミド群 31.3%（95%信頼区間：22.8%～39.9%）であり、統計学的に有意な差が認められた（14.1%、95%信頼区間：3.2%～25.1%、p=0.011）。また、すべての被験者層（層 1：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回以下の小児被験者、層 2：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回以下の成人被験者、層 3：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回超の小児及び成人被験者）の KM 推定値はプラセボ群と比較してラコサミド群で高かった。

日本人集団では、治療期間（24 週間）に強直間代発作を消失した被験者の割合の KM 推定値は、プラセボ群 10.5%及びラコサミド群 55.1%であり、プラセボ群と比較してラコサミド群で高かった。また、2 つの被験者層（層 2：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回以下の成人被験者、層 3：Combined ベースライン期間で 28 日あたりの強直間代発作回数が 2 回超の小児及び成人被験者）の KM 推定値はプラセボ群と比較してラコサミド群で高かった。

表 1.1-16　全集団の治療期間における強直間代発作の消失：FAS

Table 8.2.1
Proportion of Subjects With PGTC Seizure Freedom at Day 166
Analysis Set: Full Analysis Set

Parameter	Placebo N=121 n (%)	LCM N=118 n (%)	LCM - Placebo
Overall			
Number of subjects	121	118	
Number of subjects with a seizure (%)	97 (80.2)	79 (66.9)	
Number of subjects censored (%)	24 (19.8)	39 (33.1)	
KM seizure free(%) (95% CI)	17.3 (10.3, 24.3)	31.0 (22.4, 39.6)	
Stratum 1: Baseline PGTCS frequency <=2 per 28 days and Pediatric			
Number of subjects	21	21	
Number of subjects with a seizure (%)	18 (85.7)	16 (76.2)	
Number of subjects censored (%)	3 (14.3)	5 (23.8)	
KM seizure free(%) (95% CI)	14.3 (0.0, 29.3)	22.9 (4.4, 41.3)	
Stratum 2: Baseline PGTCS frequency <=2 per 28 days and Adult			
Number of subjects	74	72	
Number of subjects with a seizure (%)	56 (75.7)	46 (63.9)	
Number of subjects censored (%)	18 (24.3)	26 (36.1)	
KM seizure free(%) (95% CI)	22.3 (12.5, 32.1)	34.2 (23.0, 45.5)	

CI=Confidence interval, KM = Kaplan Meier, LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure.
*significant at 0.05 level.
[a] Estimated by extended Mantel Haenszel methods.
[b] Based on a chi-square test on 1 degree of freedom.
Patient SP0982-402-09600 (LCM) was randomized after the 125th event and does not appear in this analysis.
Baseline PGTCS Frequency from Combined Baseline and Development (Age from IRT) is calculated from IRT

Reference: Listing 6.2.7

表 1.1-16　全集団の治療期間における強直間代発作の消失：FAS（続き）

Table 8.2.1
Proportion of Subjects With PGTC Seizure Freedom at Day 166
Analysis Set: Full Analysis Set

Parameter	Placebo N=121 n (%)	LCM N=118 n (%)	LCM - Placebo
Stratum 3: Baseline PGTCS frequency >2 per 28 days			
Number of subjects	26	25	
Number of subjects with a seizure (%)	23 (88.5)	17 (68.0)	
Number of subjects censored (%)	3 (11.5)	8 (32.0)	
KM seizure free(%) (95% CI)	4.9 (0.0, 14.3)	30.0 (11.3, 48.7)	
Stratified [a]			
KM seizure free(%) (95% CI)	17.2 (10.4, 24.0)	31.3 (22.8, 39.9)	14.1 (3.2, 25.1)
Superiority of LCM vs Placebo p-value [b]			0.011*

CI=Confidence interval, KM = Kaplan Meier, LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure.
*significant at 0.05 level.
[a] Estimated by extended Mantel Haenszel methods.
[b] Based on a chi-square test on 1 degree of freedom.
Patient SP0982-402-09600 (LCM) was randomized after the 125th event and does not appear in this analysis.
Baseline PGTCS Frequency from Combined Baseline and Development (Age from IRT) is calculated from IRT

Reference: Listing 6.2.7

表 1.1-17　日本人集団の治療期間における強直間代発作の消失：FAS

Table 8.2.1.1
Proportion of Subjects With PGTC Seizure Freedom at Day 166
Analysis Set: Full Analysis Set - Japanese

Parameter	Placebo N=19 n (%)	LCM N=11 n (%)	LCM - Placebo
Overall			
Number of subjects	19	11	
Number of subjects with a seizure (%)	17 (89.5)	5 (45.5)	
Number of subjects censored (%)	2 (10.5)	6 (54.5)	
KM seizure free(%) (95% CI)	10.5 (0.0, 24.3)	54.5 (25.1, 84.0)	
Stratum 1: Baseline PGTCS frequency <=2 per 28 days and Pediatric			
Number of subjects	5	3	
Number of subjects with a seizure (%)	4 (80.0)	3 (100)	
Number of subjects censored (%)	1 (20.0)	0	
KM seizure free(%) (95% CI)	20.0 (0.0, 55.1)	0.0 (NC, NC)	

CI=Confidence interval, KM = Kaplan Meier, LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure, NC=non-calculable using the global model.
*significant at 0.05 level.
[a] Estimated by extended Mantel Haenszel methods.
[b] Based on a chi-square test on 1 degree of freedom.
Baseline PGTCS Frequency from Combined Baseline and Development (Age from IRT) is calculated from IRT.
CI (for LCM in Strata 1, Placebo in Strata 3, and stratified KM rates and difference) and p-values are not calculated because for LCM in Strata 1 and Placebo in Strata 3, all patients had a seizure; no SE could be calculated for those and for the stratified difference.

Reference: Listing 6.2.7

表 1.1-17　日本人集団の治療期間における強直間代発作の消失：FAS（続き）

Table 8.2.1.1
Proportion of Subjects With PGTC Seizure Freedom at Day 166
Analysis Set: Full Analysis Set - Japanese

Parameter	Placebo N=19 n (%)	LCM N=11 n (%)	LCM - Placebo
Stratum 2: Baseline PGTCS frequency <=2 per 28 days and Adult			
Number of subjects	11	6	
Number of subjects with a seizure (%)	10 (90.9)	1 (16.7)	
Number of subjects censored (%)	1 (9.1)	5 (83.3)	
KM seizure free(%) (95% CI)	9.1 (0.0, 26.1)	83.3 (53.5, 100.0)	
Stratum 3: Baseline PGTCS frequency >2 per 28 days			
Number of subjects	3	2	
Number of subjects with a seizure (%)	3 (100)	1 (50.0)	
Number of subjects censored (%)	0	1 (50.0)	
KM seizure free(%) (95% CI)	0.0 (NC, NC)	50.0 (0.0, 100.0)	

CI=Confidence interval, KM = Kaplan Meier, LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure, NC=non-calculable using the global model.
*significant at 0.05 level.
[a] Estimated by extended Mantel Haenszel methods.
[b] Based on a chi-square test on 1 degree of freedom.
Baseline PGTCS Frequency from Combined Baseline and Development (Age from IRT) is calculated from IRT.
CI (for LCM in Strata 1, Placebo in Strata 3, and stratified KM rates and difference) and p-values are not calculated because for LCM in Strata 1 and Placebo in Strata 3, all patients had a seizure; no SE could be calculated for those and for the stratified difference.

Reference: Listing 6.2.7

表 1.1-17　日本人集団の治療期間における強直間代発作の消失：FAS（続き）

Table 8.2.1.1
Proportion of Subjects With PGTC Seizure Freedom at Day 166
Analysis Set: Full Analysis Set - Japanese

Parameter	Placebo N=19 n (%)	LCM N=11 n (%)	LCM - Placebo
Stratified [a]			
KM seizure free(%) (95% CI)	10.5 (NC, NC)	55.1 (NC, NC)	44.7 (NC, NC)
Superiority of LCM vs Placebo p-value [b]			NC

CI=Confidence interval, KM = Kaplan Meier, LCM=Lacosamide, PBO=Placebo, PGTCS=primary generalized tonic-clonic seizure, NC=non-calculable using the global model.
*significant at 0.05 level.
[a] Estimated by extended Mantel Haenszel methods.
[b] Based on a chi-square test on 1 degree of freedom.
Baseline PGTCS Frequency from Combined Baseline and Development (Age from IRT) is calculated from IRT.
CI (for LCM in Strata 1, Placebo in Strata 3, and stratified KM rates and difference) and p-values are not calculated because for LCM in Strata 1 and Placebo in Strata 3, all patients had a seizure; no SE could be calculated for those and for the stratified difference.

Reference: Listing 6.2.7

1.1.3.3 その他の副次評価項目

1.1.3.3.1 治療期間における 1 回目の強直間代発作が発現するまでの時間

本治験の FAS での治療期間（増量期間+維持期間）における 1 回目の強直間代発作が発現するまでの時間を表 1.1-18（全集団）及び表 1.1-19（日本人集団）に示し、KM 法で算出した 1 回目の強直間代発作が発現するまでの時間の推移を図 1.1-3（全集団）及び図 1.1-4（日本人集団）に示した。

全集団では、治療期間（24 週間）における 1 回目の強直間代発作の発現リスクは、プラセボ群と比較してラコサミド群で低く、治療期間最終時点で 1 回目の強直間代発作が発現していない KM 推定値は、プラセボ群 17.27%及びラコサミド群 30.97%であった（ハザード比：0.683、95%信頼区間：0.507～0.921、p=0.012）。また、1 回目の強直間代発作が発現するまでの時間の中央値は、プラセボ群が 20.0 日（95%信頼区間：13.0～34.0 日）及びラコサミド群が 36.0 日（95%信頼区間：25.0～78.0 日）であった。

日本人集団では、治療期間（24 週間）における 1 回目の強直間代発作の発現リスクは、プラセボ群と比較してラコサミド群で低く、治療期間最終時点で1回目の強直間代発作が発現していないKM推定値は、プラセボ群 10.53%及びラコサミド群 54.55%であった（ハザード比：0.309、95%信頼区間：0.110～0.871、p=0.026）。また、1 回目の強直間代発作が発現するまでの時間の中央値は、プラセボ群が 14.0 日（95%信頼区間：7.0～34.0 日）であった。ラコサミド群は 50%超の被験者が治療期間に 1 回目の強直間代発作を発現しなかったため、中央値は推定できなかった。

表 1.1-18　全集団の治療期間における 1 回目の強直間代発作が発現するまでの時間：FAS

Table 8.3.1
Time to First PGTCS
Analysis Set: Full Analysis Set

	Placebo N=121			LCM N=118		
Timepoint (Days)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)
1st 6 Weeks (at Day 42)	78	40	34.37	64	52	44.85
1st 12 Weeks (at Day 84)	90	26	23.88	69	44	40.29
Treatment Period (at Day 166)	97	15	17.27	79	30	30.97
KM Analysis Treatment Period						
Q1 (95% CI) - Time to Event (days)	7.0 (5.0, 11.0)			9.0 (6.0, 15.0)		
Median (95% CI) - Time to Event (days)	20.0 (13.0, 34.0)			36.0 (25.0, 78.0)		
Subjects Censored [a] (n, %)	24 (19.8)			39 (33.1)		
Titration - Observed Events (n, %)	79 (65.3)			64 (54.2)		
1st 12 Weeks - Observed Events (n, %)	90 (74.4)			70 (59.3)		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a first PGTCS during the Treatment Period are censored.
If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to first PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.
Patient SP0982-[redacted] (LCM) was randomized after the 125th event and does not appear in this analysis.
Reference: Listing 6.2.6

表 1.1-18　全集団の治療期間における 1 回目の強直間代発作が発現するまでの時間：FAS（続き）

Table 8.3.1
Time to First PGTCS
Analysis Set: Full Analysis Set

	Placebo N=121			LCM N=118		
Timepoint (Days)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)
Treatment Comparison						
LCM - Placebo						
Hazard Ratio (HR) [b]				0.683		
95% CI of HR				0.507, 0.921		
p-value				0.012*		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a first PGTCS during the Treatment Period are censored.
If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to first PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.
Patient SP0982-[redacted] (LCM) was randomized after the 125th event and does not appear in this analysis.
Reference: Listing 6.2.6

表 1.1-19　日本人集団の治療期間における 1 回目の強直間代発作が発現するまでの時間：FAS

Table 8.3.1.1
Time to First PGTCS
Analysis Set: Full Analysis Set - Japanese

	Placebo N=19			LCM N=11		
Timepoint (Days)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)	Cumulative Number Of Events	Number At Risk	KM Survival Estimate (%)
1st 6 Weeks (at Day 42)	15	4	21.05	4	7	63.64
1st 12 Weeks (at Day 84)	16	3	15.79	4	7	63.64
Treatment Period (at Day 166)	17	2	10.53	5	6	54.55
KM Analysis Treatment Period						
Q1 (95% CI) - Time to Event (days)	7.0 (2.0, 14.0)			25.0 (5.0, -)		
Median (95% CI) - Time to Event (days)	14.0 (7.0, 34.0)			- (25.0, -)		
Subjects Censored [a] (n, %)	2 (10.5)			6 (54.5)		
Titration - Observed Events (n, %)	15 (78.9)			4 (36.4)		
1st 12 Weeks - Observed Events (n, %)	16 (84.2)			4 (36.4)		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a first PGTCS during the Treatment Period are censored. If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to first PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.

Reference: Listing 6.2.6

表 1.1-19　日本人集団の治療期間における 1 回目の強直間代発作が発現するまでの時間：FAS（続き）

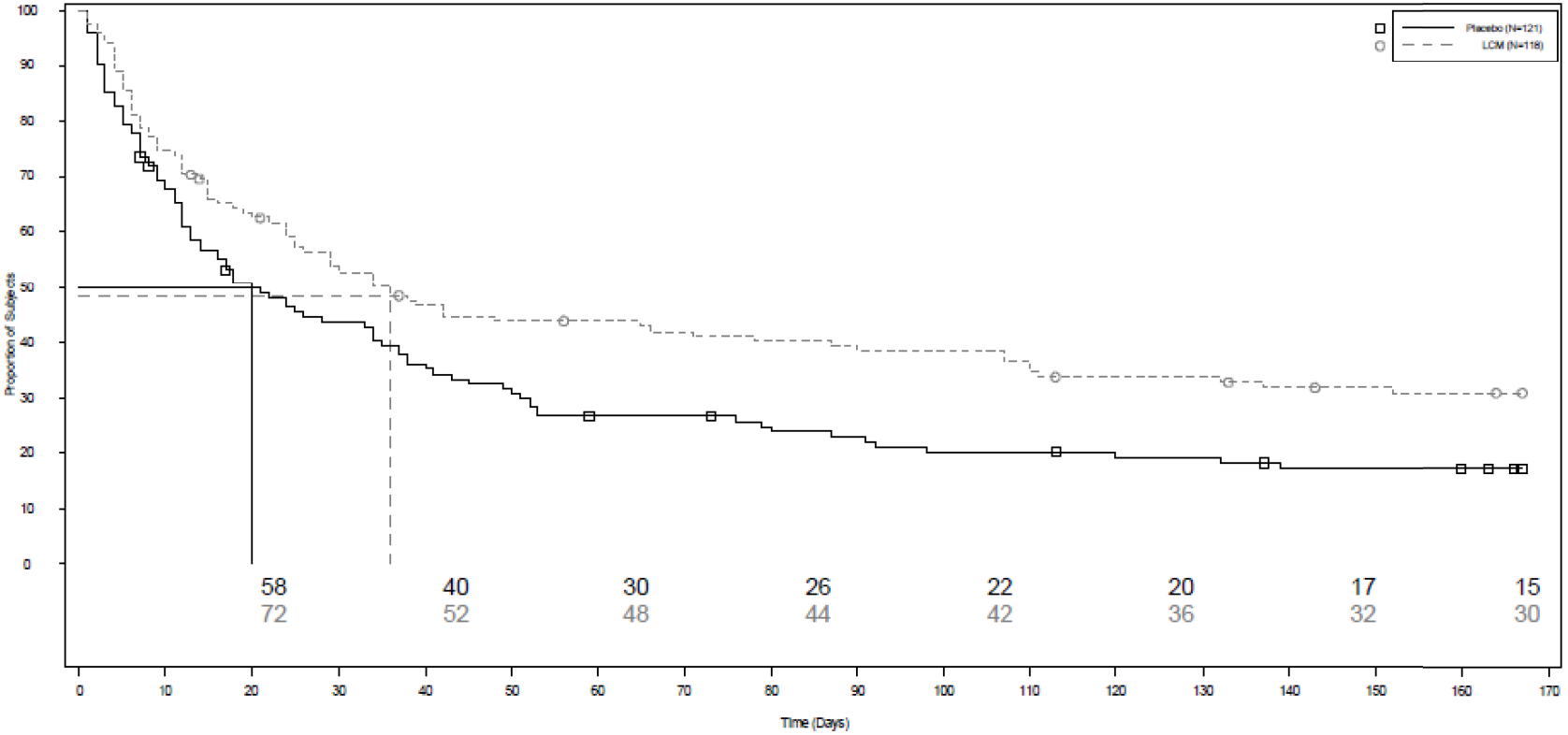
Table 8.3.1.1
Time to First PGTCS
Analysis Set: Full Analysis Set - Japanese

Timepoint (Days)	Placebo N=19 Cumulative Number Of Events	Placebo N=19 Number At Risk	Placebo N=19 KM Survival Estimate (%)	LCM N=11 Cumulative Number Of Events	LCM N=11 Number At Risk	LCM N=11 KM Survival Estimate (%)
Treatment Comparison						
LCM - Placebo						
Hazard Ratio (HR) [b]				0.309		
95% CI of HR				0.110, 0.871		
p-value				0.026*		

CI=confidence interval, KM=Kaplan-Meier, LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure, Q1=25th percentile. *significant at 0.05 level.
Note: Comparison of LCM versus Placebo is based on a Cox proportional hazards regression model with an effect for treatment, stratifying for the following combinations of subjects' Baseline PGTCS frequency and Development from IRT (<=2 per 28 days in the Combined Baseline Period and Pediatric, <=2 per 28 days in the Combined Baseline Period and Adult, >2 per 28 days in the Combined Baseline Period). The reference group is placebo.
[a] Subjects who complete the Treatment Period without having a first PGTCS during the Treatment Period are censored. If the subject's Treatment Period participation is less than 166 days, they are censored on the date of the last dose of study drug. If the subject's Treatment Period participation is greater than or equal to 166 days, they are censored as of Day 167 or the date after the 125th event.
[b] A Hazard Ratio <1 indicates time to first PGTCS is improved for LCM compared to Placebo. Wald's method is used to calculate the p-value, HR and CIs.

Reference: Listing 6.2.6

Figure 2.1
Kaplan-Meier Estimates for Time to First PGTCS During Treatment Period
Analysis Set: Full Analysis Set

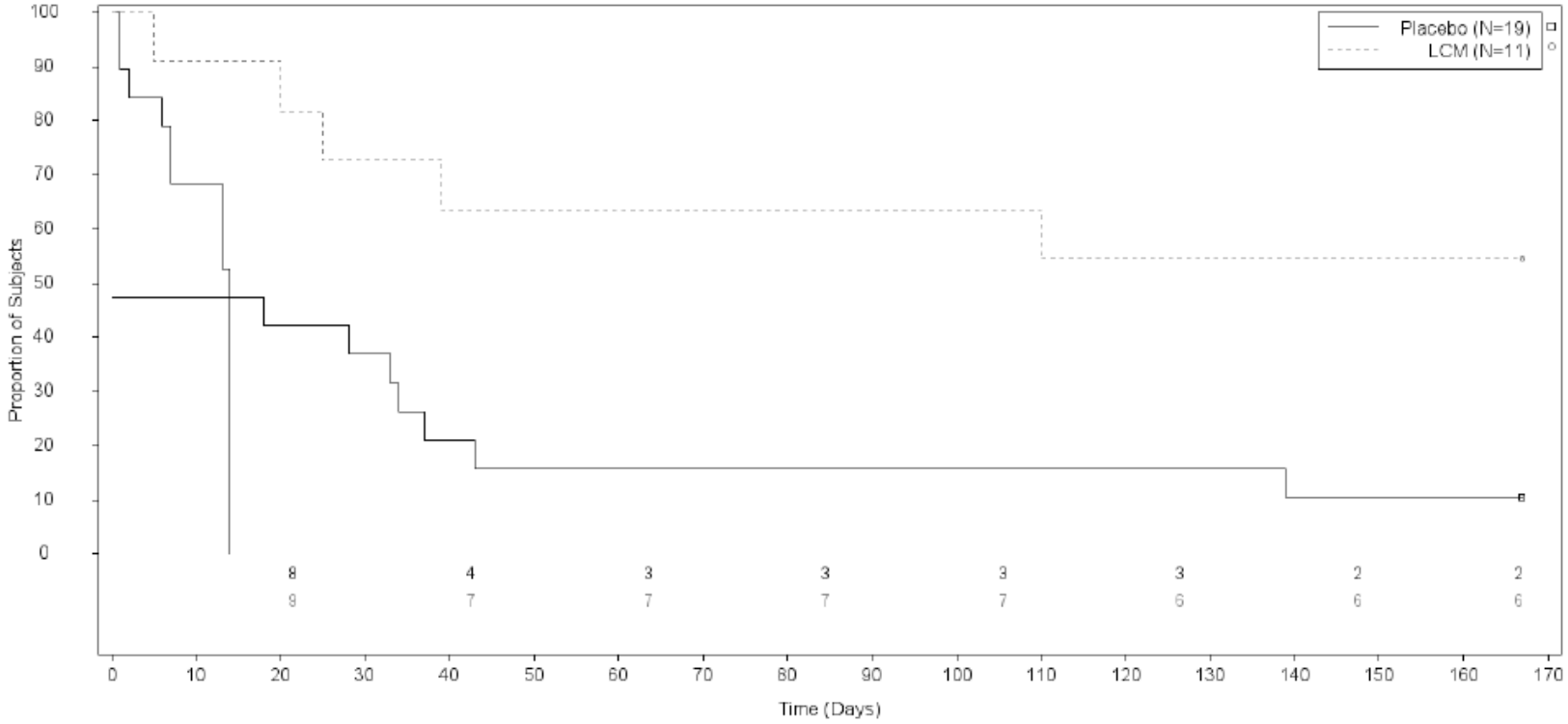


LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: The numbers represent the number of subjects at risk at the start of the final day of each 3 week period.
Note: The symbols represent censored subjects.
Note: Patient SP0982-[redacted] (LCM) was randomized after the 125th event and does not appear in this graph.
Reference: Table 8.3.1

Page 1 of 1

図 1.1-3　全集団の治療期間における 1 回目の強直間代発作が発現するまでの時間（Kaplan-Meier プロット）：FAS

Figure 2.1.1
Kaplan-Meier Estimates for Time to First PGTCS During Treatment Period
Analysis Set: Full Analysis Set - Japanese



LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: The numbers represent the number of subjects at risk at the start of the final day of each 3 week period.
Note: The symbols represent censored subjects.

Reference: Table 8.3.1

Page 1 of 1

図 1.1-4　日本人集団の治療期間における 1 回目の強直間代発作が発現するまでの時間（Kaplan-Meier プロット）：FAS

1.1.3.4 その他の有効性評価項目

1.1.3.4.1 強直間代発作回数の変化率

本治験の FAS での治療期間（増量期間+維持期間）における 28 日あたりの強直間代発作回数及び Combined ベースライン期間に対する変化率を表 1.1-20（全集団）及び表 1.1-21（日本人集団）に示した。

全集団では、Combined ベースライン期間に対する治療期間の 28 日あたりの強直間代発作回数の変化率の中央値は、プラセボ群と比較してラコサミド群で大きく、最初の 6 週間ではプラセボ群−42.71%及びラコサミド群−66.37%（以下同順）、最初の 12 週間では−55.69%及び−71.33%、24 週間では−43.24%及び−77.92%であった。

日本人集団では、Combined ベースライン期間に対する治療期間の 28 日あたりの強直間代発作回数の変化率の中央値は、プラセボ群と比較してラコサミド群で大きく、最初の 6 週間ではプラセボ群−17.78%及びラコサミド群−100.00%（以下同順）、最初の 12 週間では−2.61%及び−100.00%、24 週間では−2.61%及び−100.00%であった。

表 1.1-20　全集団の治療期間における 28 日あたりの強直間代発作回数及び Combined ベースライン期間に対する変化率：FAS

Table 8.4.1

PGTCS Frequency Observed Results and Percent Changes from Combined Baseline

Analysis Set: Full Analysis Set

Treatment Group	Observed Result							Percent Change from Combined Baseline						
Time Period	n	Mean	SD	Median	Q1, Q3	Min	Max	n	Mean	SD	Median	Q1, Q3	Min	Max
Placebo (N=121)														
Combined Baseline	121	2.02	2.42	1.24	1.00, 2.00	0.7	19.4							
Titration Period	121	2.24	7.18	0.67	0.00, 1.95	0.0	68.1	121	-20.32	113.79	-42.71	-100.00, -5.83	-100.0	715.4
First 12 Weeks	121	2.26	7.17	0.66	0.00, 1.95	0.0	68.1	121	-17.77	113.48	-55.69	-100.00, 6.73	-100.0	715.4
Treatment Period	121	2.30	7.17	0.79	0.17, 1.95	0.0	68.1	121	-14.70	113.29	-43.24	-83.53, 11.63	-100.0	715.4
LCM (N=119)														
Combined Baseline	119	1.88	1.76	1.25	1.00, 2.00	0.3	12.3							
Titration Period	119	1.43	5.00	0.64	0.00, 1.22	0.0	52.2	119	-34.28	124.28	-66.37	-100.00,-14.29	-100.0	943.6
First 12 Weeks	119	1.40	5.00	0.33	0.00, 1.22	0.0	52.2	119	-37.37	124.34	-71.33	-100.00,-20.71	-100.0	943.6
Treatment Period	119	1.40	5.00	0.17	0.00, 1.22	0.0	52.2	119	-37.49	124.26	-77.92	-100.00,-20.71	-100.0	943.6

M=maintenance, Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.

Note: Results are based upon average seizures over 28 days.

Reference: Listing 6.3.1

表 1.1-21　日本人集団の治療期間における 28 日あたりの強直間代発作回数及び Combined ベースライン期間に対する変化率：FAS

Table 8.4.1.1

PGTCS Frequency Observed Results and Percent Changes from Combined Baseline

Analysis Set: Full Analysis Set - Japanese

Treatment Group	Observed Result							Percent Change from Combined Baseline						
Time Period	n	Mean	SD	Median	Q1, Q3	Min	Max	n	Mean	SD	Median	Q1, Q3	Min	Max
Placebo (N=19)														
Combined Baseline	19	3.18	5.03	1.51	1.02, 2.00	0.8	19.4							
Titration Period	19	6.55	16.82	1.24	0.62, 3.26	0.0	68.1	19	-1.01	106.24	-17.78	-61.90, 37.60	-100.0	353.7
First 12 Weeks	19	6.69	16.77	1.24	0.86, 3.26	0.0	68.1	19	9.93	101.14	-2.61	-34.69, 37.60	-100.0	353.7
Treatment Period	19	6.71	16.76	1.24	0.86, 3.26	0.0	68.1	19	12.75	99.01	-2.61	-31.08, 37.60	-100.0	353.7
LCM (N=11)														
Combined Baseline	11	2.14	2.23	1.23	1.00, 1.75	0.8	6.8							
Titration Period	11	0.31	0.48	0.00	0.00, 0.67	0.0	1.4	11	-76.35	40.63	-100.00	-100.00, -33.33	-100.0	16.9
First 12 Weeks	11	0.22	0.42	0.00	0.00, 0.33	0.0	1.4	11	-83.20	34.77	-100.00	-100.00, -67.06	-100.0	14.0
Treatment Period	11	0.24	0.43	0.00	0.00, 0.33	0.0	1.4	11	-79.96	36.43	-100.00	-100.00, -73.49	-100.0	14.0

Max=maximum, Min=minimum, PGTCS=primary generalized tonic-clonic seizure, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Results are based upon average seizures over 28 days.

Reference: Listing 6.3.1

1.1.3.4.2 強直間代発作の消失割合

本治験の FAS での治療期間（増量期間+維持期間）における強直間代発作の消失割合を表 1.1-22（全集団）及び表 1.1-23（日本人集団）に示した。

全集団では、治療期間に強直間代発作を消失した被験者の割合は、プラセボ群と比較してラコサミド群で高く、最初の 6 週間ではプラセボ群 33.1%及びラコサミド群 44.0%（以下同順）、最初の 12 週間では 22.4%及び 38.7%、24 週間では 13.2%及び 27.5%であった。

日本人集団では、治療期間に強直間代発作を消失した被験者の割合は、最初の 6 週間ではプラセボ群 21.1%及びラコサミド群 63.6%（以下同順）、最初の 12 週間では 15.8%及び 63.6%、24 週間では 10.5%及び 54.5%であった。

表 1.1-22　全集団の治療期間における強直間代発作の消失割合：FAS

Table 8.5.3
Seizure-free Status for PGTCS
Analysis Set: Full Analysis Set

Time Period	Variable	Placebo N=121 n (%)	LCM N=119 n (%)
Titration Period	Completion of time period	114	114
	Seizure-free status	39/118 (33.1)	51/116 (44.0)
First 12 weeks of Treatment Period	Completion of time period	61	77
	Seizure-free status	26/116 (22.4)	43/111 (38.7)
24-week Treatment Period	Completion of time period	41	65
	Seizure-free status	15/114 (13.2)	30/109 (27.5)

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are based on the number of subjects in the Full Analysis Set who either have 2 PGTCS or completed the time period of interest or completed the study due to the occurrence of the 125th event.
Reference: Listing 6.2.7

表 1.1-23　日本人集団の治療期間における強直間代発作の消失割合：FAS

Table 8.5.3.1
Seizure-free Status for PGTCS
Analysis Set: Full Analysis Set - Japanese

Time Period	Variable	Placebo N=19 n (%)	LCM N=11 n (%)
Titration Period	Completion of time period	18	11
	Seizure-free status	4/19 (21.1)	7/11 (63.6)
First 12 weeks of Treatment Period	Completion of time period	4	10
	Seizure-free status	3/19 (15.8)	7/11 (63.6)
24-week Treatment Period	Completion of time period	3	9
	Seizure-free status	2/19 (10.5)	6/11 (54.5)

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are based on the number of subjects in the Full Analysis Set who either have 2 PGTCS or completed the time period of interest or completed the study due to the occurrence of the 125th event.

Reference: Listing 6.2.7

1.1.3.4.3 強直間代発作回数のレスポンダーレート及び 50%増悪

本治験の FAS での Combined ベースライン期間に対する治療期間（増量期間+維持期間）の強直間代発作回数のレスポンダーレート及び 50%増悪を表 1.1-24（全集団）及び表 1.1-25（日本人集団）に示した。

全集団では、Combined ベースライン期間に対する治療期間の強直間代発作回数の 50%及び 75%レスポンダーレートは、すべての評価時点でプラセボ群と比較してラコサミド群で高かった。50%レスポンダーレートは、最初の 6 週間ではプラセボ群 43.8%及びラコサミド群 54.6%（以下同順）、最初の 12 週間では 52.1%及び 68.9%、24 週間では 46.3%及び 68.1%であった。75%レスポンダーレートは、最初の 6 週間では 36.4%及び 47.1%、最初の 12 週間では 30.6%及び 47.1%、24 週間では 36.4%及び 57.1%であった。また、プラセボ群と比較してラコサミド群では治療期間に強直間代発作回数が 50%増悪した被験者の割合に増加は認められず、最初の 6 週間では 14.9%及び 10.1%、最初の 12 週間では 15.7%及び 10.1%、24 週間では 16.5%及び 10.1%であった。

日本人集団では、Combined ベースライン期間に対する治療期間の強直間代発作回数の 50%レスポンダーレートは、治療期間の最初の 6 週間ではプラセボ群 31.6%及びラコサミド群 72.7%（以下同順）、最初の 12 週間では 21.1%及び 90.9%、24 週間では 15.8%及び 81.8%であった。75%レスポンダーレートは、最初の 6 週間では 21.1%及び 72.7%、最初の 12 週間では 15.8%及び 72.7%、24 週間では 15.8%及び 72.7%であった。また、治療期間に強直間代発作回数が 50%増悪した被験者の割合は、いずれの評価時点もプラセボ群 15.8%で、ラコサミド群では 50%増悪した被験者はいなかった。

表 1.1-24　全集団の Combined ベースライン期間に対する治療期間の強直間代発作回数のレスポンダーレート及び 50%増悪：FAS

Table 8.5.1
Responder Status for PGTCS
Analysis Set: Full Analysis Set

Time Period	Variable	Placebo N=121 n (%)	LCM N=119 n (%)
Titration Period	50% Seizure Worsening	18 (14.9)	12 (10.1)
	50% Responder	53 (43.8)	65 (54.6)
	75% Responder	44 (36.4)	56 (47.1)
First 12 weeks of Treatment Period	50% Seizure Worsening	19 (15.7)	12 (10.1)
	50% Responder	63 (52.1)	82 (68.9)
	75% Responder	37 (30.6)	56 (47.1)
24-week Treatment Period	50% Seizure Worsening	20 (16.5)	12 (10.1)
	50% Responder	56 (46.3)	81 (68.1)
	75% Responder	44 (36.4)	68 (57.1)

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are based on the number of subjects in the Full Analysis Set.
Note: A responder is a subject experiencing >=XX% reduction in PGTCS frequency per 28 days from the Combined Baseline to the period of interest.
Note: Seizure worsening is defined as a subject experiencing >=50% increase in the PGTCS frequency per 28 days from Combined Baseline.
Reference: Listing 6.3.1

表 1.1-25　日本人集団の Combined ベースライン期間に対する治療期間の強直間代発作回数のレスポンダーレート及び 50%増悪：FAS

Table 8.5.1.1
Responder Status for PGTCS
Analysis Set: Full Analysis Set - Japanese

Time Period	Variable	Placebo N=19 n (%)	LCM N=11 n (%)
Titration Period	50% Seizure Worsening	3 (15.8)	0
	50% Responder	6 (31.6)	8 (72.7)
	75% Responder	4 (21.1)	8 (72.7)
First 12 weeks of Treatment Period	50% Seizure Worsening	3 (15.8)	0
	50% Responder	4 (21.1)	10 (90.9)
	75% Responder	3 (15.8)	8 (72.7)
24-week Treatment Period	50% Seizure Worsening	3 (15.8)	0
	50% Responder	3 (15.8)	9 (81.8)
	75% Responder	3 (15.8)	8 (72.7)

LCM=Lacosamide, PGTCS=primary generalized tonic-clonic seizure.
Note: Percentages are based on the number of subjects in the Full Analysis Set.
Note: A responder is a subject experiencing >=XX% reduction in PGTCS frequency per 28 days from the Combined Baseline to the period of interest.
Note: Seizure worsening is defined as a subject experiencing >=50% increase in the PGTCS frequency per 28 days from Combined Baseline.

Reference: Listing 6.3.1

1.1.3.4.4 欠神発作発現日数の変化率

本治験の SS での治療期間（増量期間+維持期間）における 28 日あたりの欠神発作発現日数及び Prospective ベースライン期間に対する変化率を表 1.1-26（全集団）及び表 1.1-27（日本人集団）に示した。

全集団では、Prospective ベースライン期間に対する治療期間の 28 日あたりの欠神発作発現日数の変化率の中央値は、プラセボ群と比較してラコサミド群で大きく、最初の 6 週間ではプラセボ群−11.1%及びラコサミド群−24.6%（以下同順）、最初の 12 週間では−13.3%及び−30.4%、24 週間では−15.3%及び−30.1%であった。

日本人集団では、本治験中に欠神発作を発現した被験者がラコサミド群でいなかったため、欠神発作発現日数の変化率は算出できなかった。なお、プラセボ群の Prospective ベースライン期間に対する治療期間の 28 日あたりの欠神発作発現日数の変化率の中央値は、いずれの評価時点も 24.7%であった。

表 1.1-26　全集団の治療期間における 28 日あたりの欠神発作発現日数及び Prospective ベースライン期間に対する変化率：SS

Table 8.6.2

Days with Absence Seizures Observed Results and Percent Changes from Prospective Baseline

Analysis Set: Safety Set

Treatment Group	Observed Result							Percent Change from Prospective Baseline						
Time Period	n	Mean	SD	Median	Q1, Q3	Min	Max	n	Mean	SD	Median	Q1, Q3	Min	Max
Placebo (N=42)														
Prospective Baseline	42	5.4	8.1	1.5	0.0, 7.6	0	28							
Titration Period	42	4.6	7.2	0.0	0.0, 7.3	0	27	22	-3.9	71.3	-11.1	-65.0, 20.0	-100	183
First 12 Weeks of Treatment Period	42	4.6	7.2	0.2	0.0, 7.3	0	27	22	-6.0	71.4	-13.3	-54.0, 20.0	-100	183
24-week Treatment Period	42	4.4	7.2	0.1	0.0, 6.0	0	27	22	-9.4	72.8	-15.3	-57.6, 20.0	-100	183
LCM (N=51)														
Prospective Baseline	50	5.2	8.1	0.0	0.0, 9.3	0	28							
Titration Period	49	3.9	7.1	0.0	0.0, 4.8	0	28	22	-30.5	59.4	-24.6	-80.0, -2.7	-100	155
First 12 Weeks of Treatment Period	49	3.7	6.8	0.0	0.0, 4.8	0	28	22	-35.1	59.5	-30.4	-80.0, -10.7	-100	155
24-week Treatment Period	49	3.6	6.7	0.0	0.0, 4.8	0	28	22	-36.9	60.4	-30.1	-81.3, -10.7	-100	155

M=maintenance, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation, T=Titration.
Note: Results are based upon average seizure days over 28 days for subjects who reported a history of absence seizures or an occurrence in the Combined Baseline or in the Treatment Period.
Reference: Listing 6.4

表 1.1-27　日本人集団の治療期間における 28 日あたりの欠神発作発現日数及び Prospective ベースライン期間に対する変化率：SS

Table 8.6.2.1.0

Days with Absence Seizures Observed Results and Percent Changes from Prospective Baseline

Analysis Set: Safety Set - Japanese

Treatment Group	Observed Result							Percent Change from Prospective Baseline						
Time Period	n	Mean	SD	Median	Q1, Q3	Min	Max	n	Mean	SD	Median	Q1, Q3	Min	Max
Placebo (N=3)														
Prospective Baseline	3	2.1	2.2	2.0	0.0, 4.3	0	4							
Titration Period	3	2.3	2.0	3.3	0.0, 3.7	0	4	2	24.7	53.8	24.7	-13.3, 62.8	-13	63
First 12 Weeks of Treatment Period	3	2.3	2.0	3.3	0.0, 3.7	0	4	2	24.7	53.8	24.7	-13.3, 62.8	-13	63
24-week Treatment Period	3	2.3	2.0	3.3	0.0, 3.7	0	4	2	24.7	53.8	24.7	-13.3, 62.8	-13	63
LCM (N=3)														
Prospective Baseline	3	0.0	0.0	0.0	0.0, 0.0	0	0							
Titration Period	3	0.0	0.0	0.0	0.0, 0.0	0	0	0						
First 12 Weeks of Treatment Period	3	0.0	0.0	0.0	0.0, 0.0	0	0	0						
24-week Treatment Period	3	0.0	0.0	0.0	0.0, 0.0	0	0	0						

M=maintenance, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation, T=titration.

Note: Results are based upon average seizure days over 28 days for subjects who reported a history of absence seizures or an occurrence in the Combined Baseline or in the Treatment Period.

Reference: Listing 6.4

1.1.3.4.5 欠神発作発現日数のレスポンダーレート

本治験の SS での Prospective ベースライン期間に対する治療期間（増量期間+維持期間）の欠神発作発現日数のレスポンダーレートを表 1.1-28（全集団）及び表 1.1-29（日本人集団）に示した。

全集団では、Prospective ベースライン期間に対する治療期間の欠神発作発現日数の 50%及び 75%レスポンダーレートは、すべての評価時点でプラセボ群とラコサミド群で同程度であった。50%レスポンダーレートは、最初の 6 週間ではプラセボ群 16.7%及びラコサミド群 15.7%（以下同順）、最初の 12 週間では 14.3%及び 19.6%、24 週間では 16.7%及び 19.6%であった。75%レスポンダーレートは、最初の 6 週間では 7.1%及び 13.7%、最初の 12 週間では 11.9%及び 13.7%、24 週間では 11.9%及び 17.6%であった。

日本人集団では、Prospective ベースライン期間に対する治療期間の欠神発作発現日数の 50%及び 75%レスポンダーは、いずれの評価時点もプラセボ群及びラコサミド群共に 0 例であった。

表 1.1-28　全集団の Prospective ベースライン期間に対する治療期間の欠神発作発現日数のレスポンダーレート：SS

Table 8.6.4
Responder Status and Seizure Worsening for Days with Absence Seizures
Analysis Set: Safety Set

Time Period	Variable	Placebo N=42 n (%)	LCM N=51 n (%)
Titration Period	In the time period	42	49
	50% Seizure Worsening	3/42 (7.1)	1/51 (2.0)
	50% Responder	7/42 (16.7)	8/51 (15.7)
	75% Responder	3/42 (7.1)	7/51 (13.7)
First 12 weeks of Treatment Period	In the time period	42	49
	50% Seizure Worsening	3/42 (7.1)	1/51 (2.0)
	50% Responder	6/42 (14.3)	10/51 (19.6)
	75% Responder	5/42 (11.9)	7/51 (13.7)
24-week Treatment Period	In the time period	42	49
	50% Seizure Worsening	3/42 (7.1)	1/51 (2.0)
	50% Responder	7/42 (16.7)	10/51 (19.6)
	75% Responder	5/42 (11.9)	9/51 (17.6)

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set who reported a history of absence seizures or an occurrence of absence seizures in the Combined Baseline or in the Treatment Period.
Note: A responder is a subject experiencing >=XX% reduction in the number of days with absence seizures per 28 days from the Prospective Baseline to the period of interest.
Note: Seizure worsening is defined as a subject experiencing >=50% increase in the number of days with absence seizures per 28 days from Prospective Baseline.
Reference: Listing 6.4

表 1.1-29　日本人集団の Prospective ベースライン期間に対する治療期間の欠神発作発現日数のレスポンダーレート：SS

Table 8.6.4.1.0

Responder Status and Seizure Worsening for Days with Absence Seizures

Analysis Set: Safety Set - Japanese

Time Period	Variable	Placebo N=3 n (%)	LCM N=3 n (%)
Titration Period	In the time period	3	3
	50% Seizure Worsening	1/3 (33.3)	0/3
	50% Responder	0/3	0/3
	75% Responder	0/3	0/3
First 12 weeks of Treatment Period	In the time period	3	3
	50% Seizure Worsening	1/3 (33.3)	0/3
	50% Responder	0/3	0/3
	75% Responder	0/3	0/3
24-week Treatment Period	In the time period	3	3
	50% Seizure Worsening	1/3 (33.3)	0/3
	50% Responder	0/3	0/3
	75% Responder	0/3	0/3

LCM=Lacosamide.

Note: Percentages are based on the number of subjects in the Safety Set who reported a history of absence seizures or an occurrence of absence seizures in the Combined Baseline or in the Treatment Period.

Note: A responder is a subject experiencing >=XX% reduction in the number of days with absence seizures per 28 days from the Prospective Baseline to the period of interest.

Note: Seizure worsening is defined as a subject experiencing >=50% increase in the number of days with absence seizures per 28 days from Prospective Baseline.

Reference: Listing 6.4

1.1.3.4.6 ミオクロニー発作発現日数の変化率

本治験の SS での治療期間（増量期間+維持期間）における 28 日あたりのミオクロニー発作発現日数及び Prospective ベースライン期間に対する変化率を表 1.1-30（全集団）及び表 1.1-31（日本人集団）に示した。

全集団では、Prospective ベースライン期間に対する治療期間の 28 日あたりのミオクロニー発作発現日数の変化率の中央値は、最初の 6 週間ではプラセボ群−51.8%及びラコサミド群−32.5%（以下同順）、最初の 12 週間では−65.7%及び−43.8%、24 週間では−65.7%及び−54.6%であった。

日本人集団では、Prospective ベースライン期間に対する治療期間の 28 日あたりのミオクロニー発作発現日数の変化率の中央値は、最初の 6 週間ではプラセボ群−82.9%及びラコサミド群−21.6%（以下同順）、最初の 12 週間では−82.9%及び−22.3%、24 週間では−82.9%及び−24.9%であった。

表 1.1-30　全集団の治療期間における 28 日あたりのミオクロニー発作発現日数及び Prospective ベースライン期間に対する変化率：SS

Table 8.7.2

Days with Myoclonic Seizures Observed Results and Percent Change from Prospective Baseline

Analysis Set: Safety Set

Treatment Group	Observed Result							Percent Change from Prospective Baseline						
Time Period	n	Mean	SD	Median	Q1, Q3	Min	Max	n	Mean	SD	Median	Q1, Q3	Min	Max
Placebo (N=49)														
Prospective Baseline	49	4.9	7.7	1.0	0.0, 8.3	0	28							
Titration Period	49	3.5	6.5	0.0	0.0, 4.0	0	28	25	-44.8	49.8	-51.8	-100.0, -6.7	-100	57
First 12 Weeks of Treatment Period	49	3.5	6.7	0.0	0.0, 3.7	0	28	25	-45.4	54.1	-65.7	-100.0, -7.9	-100	87
24-week Treatment Period	49	3.4	6.7	0.0	0.0, 3.6	0	28	25	-45.9	54.4	-65.7	-100.0, -7.9	-100	87
LCM (N=47)														
Prospective Baseline	47	4.8	6.9	2.0	0.0, 8.0	0	28							
Titration Period	46	4.2	6.8	0.7	0.0, 4.7	0	27	24	15.9	152.1	-32.5	-82.2, 13.5	-100	402
First 12 Weeks of Treatment Period	46	4.0	6.9	0.5	0.0, 3.8	0	28	24	8.3	144.6	-43.8	-82.2, 5.8	-100	402
24-week Treatment Period	46	3.7	6.6	0.6	0.0, 3.8	0	28	24	1.8	142.0	-54.6	-89.8, 5.8	-100	402

M=maintenance, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation, T=Titration.
Note: Results are based upon average seizure days over 28 days for subjects who reported a history of myoclonic seizures or an occurrence in the Combined Baseline or in the Treatment Period.
Reference: Listing 6.4

表 1.1-31　日本人集団の治療期間における 28 日あたりのミオクロニー発作発現日数及び Prospective ベースライン期間に対する変化率：SS

Table 8.7.2.1.0

Days with Myoclonic Seizures Observed Results and Percent Change from Prospective Baseline

Analysis Set: Safety Set - Japanese

Treatment Group	Observed Result							Percent Change from Prospective Baseline						
Time Period	n	Mean	SD	Median	Q1, Q3	Min	Max	n	Mean	SD	Median	Q1, Q3	Min	Max
Placebo (N=9)														
Prospective Baseline	9	2.8	4.1	0.0	0.0, 7.0	0	10							
Titration Period	9	1.1	2.4	0.0	0.0, 0.0	0	7	4	-73.5	34.2	-82.9	-100.0, -47.0	-100	-28
First 12 Weeks of Treatment Period	9	1.1	2.4	0.0	0.0, 0.0	0	7	4	-73.5	34.2	-82.9	-100.0, -47.0	-100	-28
24-week Treatment Period	9	1.1	2.4	0.0	0.0, 0.0	0	7	4	-73.5	34.2	-82.9	-100.0, -47.0	-100	-28
LCM (N=5)														
Prospective Baseline	5	4.8	6.6	0.0	0.0, 12.0	0	12							
Titration Period	5	3.8	6.0	0.0	0.0, 5.3	0	14	2	-21.6	48.1	-21.6	-55.6, 12.4	-56	12
First 12 Weeks of Treatment Period	5	3.8	5.9	0.0	0.0, 5.3	0	14	2	-22.3	47.8	-22.3	-56.1, 11.5	-56	12
24-week Treatment Period	5	3.6	5.9	0.0	0.0, 4.6	0	14	2	-24.9	51.5	-24.9	-61.3, 11.5	-61	12

M=maintenance, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation, T=titration.

Note: Results are based upon average seizure days over 28 days for subjects who reported a history of myoclonic seizures or an occurrence in the Combined Baseline or in the Treatment Period.

Reference: Listing 6.4

1.1.3.4.7 ミオクロニー発作発現日数のレスポンダーレート

本治験の SS での Prospective ベースライン期間に対する治療期間（増量期間+維持期間）のミオクロニー発作発現日数のレスポンダーレートを表 1.1-32（全集団）及び表 1.1-33（日本人集団）に示した。

全集団では、Prospective ベースライン期間に対する治療期間のミオクロニー発作発現日数の 50%及び 75%レスポンダーレートは、すべての評価時点でプラセボ群とラコサミド群で同程度であった。50%レスポンダーレートは、最初の 6 週間ではプラセボ群 26.5%及びラコサミド群 21.3%（以下同順）、最初の 12 週間では 26.5%及び 23.4%、24 週間では 28.6%及び 27.7%であった。75%レスポンダーレートは、最初の 6 週間では 16.3%及び 12.8%、最初の 12 週間及び 24 週間では 18.4%及び 14.9%であった。

日本人集団では、Prospective ベースライン期間に対する治療期間のミオクロニー発作発現日数の 50%レスポンダーレートは、いずれの評価時点もプラセボ群 33.3%及びラコサミド群 20.0%であった。75%レスポンダーレートは、いずれの評価時点もプラセボ群 22.2%で、ラコサミド群では 75%レスポンダーは 0 例であった。

表 1.1-32　全集団の Prospective ベースライン期間に対する治療期間のミオクロニー発作発現日数のレスポンダーレート：SS

Table 8.7.4

Responder Status and Seizure Worsening for Days with Myoclonic Seizures

Analysis Set: Safety Set

Time Period	Variable	Placebo N=49 n (%)	LCM N=47 n (%)
Titration Period	In the time period	49	46
	50% Seizure Worsening	2/49 (4.1)	4/47 (8.5)
	50% Responder	13/49 (26.5)	10/47 (21.3)
	75% Responder	8/49 (16.3)	6/47 (12.8)
First 12 weeks of Treatment Period	In the time period	49	46
	50% Seizure Worsening	2/49 (4.1)	4/47 (8.5)
	50% Responder	13/49 (26.5)	11/47 (23.4)
	75% Responder	9/49 (18.4)	7/47 (14.9)
24-week Treatment Period	In the time period	49	46
	50% Seizure Worsening	2/49 (4.1)	4/47 (8.5)
	50% Responder	14/49 (28.6)	13/47 (27.7)
	75% Responder	9/49 (18.4)	7/47 (14.9)

LCM=Lacosamide.

Note: Percentages are based on the number of subjects in the Safety Set who reported a history of myoclonic seizures or an occurrence of myoclonic seizures in the Combined Baseline or in the Treatment Period.

Note: A responder is a subject experiencing >=XX% reduction in the number of days with myoclonic seizures per 28 days from the Prospective Baseline to the period of interest.

Note: Seizure worsening is defined as a subject experiencing >=50% increase in the number of days with myoclonic seizures per 28 days from Prospective Baseline.

Reference: Listing 6.4

表 1.1-33　日本人集団の Prospective ベースライン期間に対する治療期間のミオクロニー発作発現日数のレスポンダーレート：SS

Table 8.7.4.1.0
Responder Status and Seizure Worsening for Days with Myoclonic Seizures
Analysis Set: Safety Set - Japanese

Time Period	Variable	Placebo N=9 n (%)	LCM N=5 n (%)
Titration Period	In the time period	9	5
	50% Seizure Worsening	0/9	0/5
	50% Responder	3/9 (33.3)	1/5 (20.0)
	75% Responder	2/9 (22.2)	0/5
First 12 weeks of Treatment Period	In the time period	9	5
	50% Seizure Worsening	0/9	0/5
	50% Responder	3/9 (33.3)	1/5 (20.0)
	75% Responder	2/9 (22.2)	0/5
24-week Treatment Period	In the time period	9	5
	50% Seizure Worsening	0/9	0/5
	50% Responder	3/9 (33.3)	1/5 (20.0)
	75% Responder	2/9 (22.2)	0/5

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set who reported a history of myoclonic seizures or an occurrence of myoclonic seizures in the Combined Baseline or in the Treatment Period.
Note: A responder is a subject experiencing >=XX% reduction in the number of days with myoclonic seizures per 28 days from the Prospective Baseline to the period of interest.
Note: Seizure worsening is defined as a subject experiencing >=50% increase in the number of days with myoclonic seizures per 28 days from Prospective Baseline.

Reference: Listing 6.4

1.1.3.4.8 全般発作の消失割合

本治験の SS での治療期間（増量期間+維持期間）におけるすべての全般発作の消失割合を表 1.1-34（全集団）及び表 1.1-35（日本人集団）に示した。

全集団では、治療期間にすべての全般発作を消失した被験者の割合は、最初の 6 週間ではプラセボ群 27.1%及びラコサミド群 33.6%（以下同順）、最初の 12 週間では 17.2%及び 27.9%、24 週間では 13.2%及び 21.1%であった。

日本人集団では、治療期間にすべての全般発作を消失した被験者の割合は、最初の 6 週間ではプラセボ群 21.1%及びラコサミド群 54.5%（以下同順）、最初の 12 週間では 15.8%及び 54.5%、24 週間では 10.5%及び 45.5%であった。

表 1.1-34　全集団の治療期間におけるすべての全般発作の消失割合：SS

Table 8.7.5
Seizure-free Status for All Generalized Seizure types
Analysis Set: Safety Set

Time Period	Variable	Placebo N=121 n (%)	LCM N=121 n (%)
Titration Period	Completion of time period	114	114
	Seizure-free status	32/118 (27.1)	39/116 (33.6)
First 12 weeks of Treatment Period	Completion of time period	61	77
	Seizure-free status	20/116 (17.2)	31/111 (27.9)
24-week Treatment Period	Completion of time period	41	65
	Seizure-free status	15/114 (13.2)	23/109 (21.1)

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set who either have 2 PGTCS or completed the time period of interest or completed the study due to the occurrence of the 125th event.
Reference: Listing 6.2.1

表 1.1-35　日本人集団の治療期間におけるすべての全般発作の消失割合：SS

Table 8.7.5.1
Seizure-free Status for All Generalized Seizure types
Analysis Set: Safety Set - Japanese

Time Period	Variable	Placebo N=19 n (%)	LCM N=11 n (%)
Titration Period	Completion of time period	18	11
	Seizure-free status	4/19 (21.1)	6/11 (54.5)
First 12 weeks of Treatment Period	Completion of time period	4	10
	Seizure-free status	3/19 (15.8)	6/11 (54.5)
24-week Treatment Period	Completion of time period	3	9
	Seizure-free status	2/19 (10.5)	5/11 (45.5)

LCM=Lacosamide.
Note: Percentages are based on the number of subjects in the Safety Set who either have 2 PGTCS or completed the time period of interest or completed the study due to the occurrence of the 125th event.

Reference: Listing 6.2.1

1.1.3.4.9 てんかん患者用 QOL 質問票、子どもの健康関連 QOL 評価、EuroQol による 5 項目 3 段階 QOL 評価視覚的アナログスケールスコア

全体的に、QOLIE-31-P の総スコア及び下位尺度スコア（苦痛に関する項目及び優先順位付けに関する項目を含む）、PedsQL、並びに EQ-5D-3L QOL 評価の VAS スコアのベースラインから最終来院時までの変化量は、プラセボ群及びラコサミド群のいずれも小さかった。いずれの健康に関するその他の評価項目も明らかな悪化は認められなかった。

1.1.4 安全性

1.1.4.1 曝露状況

本治験での治験薬の曝露期間を期間別に表 1.1-36（全集団）及び表 1.1-37（日本人集団）に示した。また、治験薬の 1 日投与量を表 1.1-38（全集団）及び表 1.1-39（日本人集団）に示した。

表 1.1-36　全集団の治験薬の曝露期間：SS

Table 10.1
Study Medication Duration
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Treatment	Study Medication Duration (days)		
	n	121	121
	Mean	93.74	112.32
	SD	57.73	61.18
	Q1	43.0	44.0
	Median	65.0	143.0
	Q3	167.0	169.0
	Min	7.0	1.0
	Max	176.0	176.0
	Total study medication duration (subject-years)	31.1	37.2
Titration	Study Medication Duration (days)		
	n	121	121
	Mean	41.02	40.39
	SD	7.39	7.42
	Q1	41.0	41.0
	Median	42.0	42.0
	Q3	43.0	43.0
	Min	7.0	1.0
	Max	57.0	50.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Note: Subject-years of exposure is the total treatment duration in days divided by 365.25.
Reference: Listing 5.3

表 1.1-36　全集団の治験薬の曝露期間：SS（続き）

Table 10.1
Study Medication Duration
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Maintenance	Study Medication Duration (days)		
	n	70	82
	Mean	91.46	106.18
	SD	44.01	37.55
	Q1	53.0	99.0
	Median	120.5	126.0
	Q3	127.0	127.0
	Min	3.0	13.0
	Max	134.0	135.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Note: Subject-years of exposure is the total treatment duration in days divided by 365.25.
Reference: Listing 5.3

表 1.1-37　日本人集団の治験薬の曝露期間：SS

Table 10.1.1
Study Medication Duration
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Treatment	Study Medication Duration (days)		
	n	19	11
	Mean	67.37	152.27
	SD	47.60	38.39
	Q1	43.0	169.0
	Median	45.0	169.0
	Q3	65.0	169.0
	Min	30.0	60.0
	Max	171.0	170.0
	Total study medication duration (subject-years)	3.5	4.6
Titration	Study Medication Duration (days)		
	n	19	11
	Mean	41.89	42.00
	SD	3.11	1.18
	Q1	42.0	42.0
	Median	42.0	42.0
	Q3	43.0	42.0
	Min	30.0	39.0
	Max	45.0	44.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Note: Subject-years of exposure is the total treatment duration in days divided by 365.25.

Reference: Listing 5.3

表 1.1-37　日本人集団の治験薬の曝露期間：SS（続き）

Table 10.1.1
Study Medication Duration
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Maintenance	Study Medication Duration (days)		
	n	9	11
	Mean	53.78	110.27
	SD	57.59	37.54
	Q1	7.0	125.0
	Median	23.0	127.0
	Q3	127.0	127.0
	Min	3.0	21.0
	Max	128.0	128.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Note: Subject-years of exposure is the total treatment duration in days divided by 365.25.

Reference: Listing 5.3

表 1.1-38　全集団の治験薬の 1 日投与量：SS

Table 10.5
Study Medication Daily Dosing
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Treatment	Mean Daily Dose (mg/kg/day) for Pediatrics <30 kg		
	n	2	4
	Mean	5.64	7.03
	SD	2.08	0.14
	Q1	4.2	6.9
	Median	5.6	7.0
	Q3	7.1	7.1
	Min	4.2	6.9
	Max	7.1	7.2
Treatment	Mean Daily Dose (mg/kg/day) for Pediatrics >=30 kg to <50 kg		
	n	8	6
	Mean	6.77	5.73
	SD	0.91	0.94
	Q1	6.0	5.5
	Median	7.2	5.5
	Q3	7.5	5.7
	Min	5.2	4.7
	Max	7.6	7.5

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Reference: Listings 5.1, 5.3, 2.1

表 1.1-38　全集団の治験薬の 1 日投与量：SS（続き）

Table 10.5
Study Medication Daily Dosing
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Treatment	Mean Daily Dose (mg/day) for Pediatrics >=50 kg		
	n	15	14
	Mean	313.95	330.23
	SD	78.18	53.76
	Q1	235.4	288.0
	Median	353.5	356.2
	Q3	371.6	372.9
	Min	123.1	203.4
	Max	375.7	375.0
Treatment	Mean Daily Dose (mg/day) for Adults		
	n	96	97
	Mean	303.42	298.57
	SD	62.49	78.90
	Q1	279.4	273.7
	Median	301.6	302.3
	Q3	356.7	369.4
	Min	100.0	95.0
	Max	376.3	376.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Reference: Listings 5.1, 5.3, 2.1

表 1.1-38　全集団の治験薬の 1 日投与量：SS（続き）

Table 10.5
Study Medication Daily Dosing
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Titration	Mean Daily Dose (mg/kg/day) for Pediatrics <30 kg		
	n	2	4
	Mean	5.64	5.88
	SD	2.08	1.24
	Q1	4.2	4.8
	Median	5.6	5.9
	Q3	7.1	6.9
	Min	4.2	4.6
	Max	7.1	7.0
Titration	Mean Daily Dose (mg/kg/day) for Pediatrics >=30 kg to <50 kg		
	n	8	6
	Mean	5.65	4.60
	SD	0.52	0.79
	Q1	5.2	4.0
	Median	5.7	4.4
	Q3	6.1	4.9
	Min	4.9	4.0
	Max	6.3	6.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Reference: Listings 5.1, 5.3, 2.1

表 1.1-38　全集団の治験薬の 1 日投与量：SS（続き）

Table 10.5
Study Medication Daily Dosing
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Titration	Mean Daily Dose (mg/day) for Pediatrics >=50 kg		
	n	15	14
	Mean	267.44	264.16
	SD	51.43	44.69
	Q1	235.4	214.9
	Median	290.5	289.8
	Q3	300.0	300.0
	Min	123.1	185.2
	Max	307.3	304.5
Titration	Mean Daily Dose (mg/day) for Adults		
	n	96	97
	Mean	268.02	254.74
	SD	51.14	60.68
	Q1	255.0	219.3
	Median	292.0	284.6
	Q3	300.0	298.8
	Min	100.0	95.0
	Max	318.6	317.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Reference: Listings 5.1, 5.3, 2.1

表 1.1-38　全集団の治験薬の 1 日投与量：SS（続き）

Table 10.5
Study Medication Daily Dosing
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Maintenance	Mean Daily Dose (mg/kg/day) for Pediatrics <30 kg		
	n	0	2
	Mean		8.00
	SD		0.00
	Q1		8.0
	Median		8.0
	Q3		8.0
	Min		8.0
	Max		8.0
Maintenance	Mean Daily Dose (mg/kg/day) for Pediatrics >=30 kg to <50 kg		
	n	6	5
	Mean	7.67	6.80
	SD	0.82	1.10
	Q1	8.0	6.0
	Median	8.0	6.0
	Q3	8.0	8.0
	Min	6.0	6.0
	Max	8.0	8.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Reference: Listings 5.1, 5.3, 2.1

表 1.1-38　全集団の治験薬の 1 日投与量：SS（続き）

Table 10.5
Study Medication Daily Dosing
Analysis Set: Safety Set

Period	Variable	Placebo N=121	LCM N=121
Maintenance	Mean Daily Dose (mg/day) for Pediatrics >=50 kg		
	n	11	12
	Mean	390.77	374.19
	SD	30.11	44.77
	Q1	400.0	346.8
	Median	400.0	399.0
	Q3	400.0	400.0
	Min	300.0	300.0
	Max	400.0	400.0
Maintenance	Mean Daily Dose (mg/day) for Adults		
	n	53	63
	Mean	377.70	369.77
	SD	41.26	48.53
	Q1	396.7	300.8
	Median	400.0	400.0
	Q3	400.0	400.0
	Min	300.0	196.7
	Max	400.0	400.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.
Reference: Listings 5.1, 5.3, 2.1

表 1.1-39　日本人集団の治験薬の 1 日投与量：SS

Table 10.5.1
Study Medication Daily Dosing
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Treatment	Mean Daily Dose (mg/kg/day) for Pediatrics <30 kg		
	n	1	0
	Mean	4.17	
	SD		
	Q1	4.2	
	Median	4.2	
	Q3	4.2	
	Min	4.2	
	Max	4.2	
Treatment	Mean Daily Dose (mg/kg/day) for Pediatrics >=30 kg to <50 kg		
	n	1	1
	Mean	5.72	5.48
	SD		
	Q1	5.7	5.5
	Median	5.7	5.5
	Q3	5.7	5.5
	Min	5.7	5.5
	Max	5.7	5.5

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.

Reference: Listings 5.1, 5.3, 2.1

表 1.1-39　日本人集団の治験薬の 1 日投与量：SS（続き）

Table 10.5.1
Study Medication Daily Dosing
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Treatment	Mean Daily Dose (mg/day) for Pediatrics >=50 kg		
	n	4	2
	Mean	273.46	322.34
	SD	64.90	43.73
	Q1	220.7	291.4
	Median	261.4	322.3
	Q3	326.2	353.3
	Min	217.4	291.4
	Max	353.5	353.3
Treatment	Mean Daily Dose (mg/day) for Adults		
	n	13	8
	Mean	300.96	346.75
	SD	49.12	45.15
	Q1	290.2	316.4
	Median	297.8	372.3
	Q3	310.2	373.8
	Min	175.0	273.7
	Max	374.3	375.1

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.

Reference: Listings 5.1, 5.3, 2.1

表 1.1-39　日本人集団の治験薬の 1 日投与量：SS（続き）

Table 10.5.1
Study Medication Daily Dosing
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Titration	Mean Daily Dose (mg/kg/day) for Pediatrics <30 kg		
	n	1	0
	Mean	4.17	
	SD		
	Q1	4.2	
	Median	4.2	
	Q3	4.2	
	Min	4.2	
	Max	4.2	
Titration	Mean Daily Dose (mg/kg/day) for Pediatrics >=30 kg to <50 kg		
	n	1	1
	Mean	4.88	4.13
	SD		
	Q1	4.9	4.1
	Median	4.9	4.1
	Q3	4.9	4.1
	Min	4.9	4.1
	Max	4.9	4.1

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.

Reference: Listings 5.1, 5.3, 2.1

表 1.1-39　日本人集団の治験薬の 1 日投与量：SS（続き）

Table 10.5.1
Study Medication Daily Dosing
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Titration	Mean Daily Dose (mg/day) for Pediatrics >=50 kg		
	n	4	2
	Mean	254.74	281.55
	SD	46.26	22.73
	Q1	214.8	265.5
	Median	254.0	281.5
	Q3	294.7	297.6
	Min	212.2	265.5
	Max	298.8	297.6
Titration	Mean Daily Dose (mg/day) for Adults		
	n	13	8
	Mean	283.41	263.84
	SD	33.69	43.84
	Q1	289.8	222.6
	Median	296.4	288.7
	Q3	297.7	294.0
	Min	175.0	197.6
	Max	300.0	302.3

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.

Reference: Listings 5.1, 5.3, 2.1

表 1.1-39　日本人集団の治験薬の 1 日投与量：SS（続き）

Table 10.5.1
Study Medication Daily Dosing
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Maintenance	Mean Daily Dose (mg/kg/day) for Pediatrics <30 kg		
	n	0	0
	Mean		
	SD		
	Q1		
	Median		
	Q3		
	Min		
	Max		
Maintenance	Mean Daily Dose (mg/kg/day) for Pediatrics >=30 kg to <50 kg		
	n	1	1
	Mean	6.00	8.00
	SD		
	Q1	6.0	8.0
	Median	6.0	8.0
	Q3	6.0	8.0
	Min	6.0	8.0
	Max	6.0	8.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.

Reference: Listings 5.1, 5.3, 2.1

表 1.1-39　日本人集団の治験薬の 1 日投与量：SS（続き）

Table 10.5.1
Study Medication Daily Dosing
Analysis Set: Safety Set - Japanese

Period	Variable	Placebo N=19	LCM N=11
Maintenance	Mean Daily Dose (mg/day) for Pediatrics >=50 kg		
	n	2	2
	Mean	350.00	350.00
	SD	70.71	70.71
	Q1	300.0	300.0
	Median	350.0	350.0
	Q3	400.0	400.0
	Min	300.0	300.0
	Max	400.0	400.0
Maintenance	Mean Daily Dose (mg/day) for Adults		
	n	6	8
	Mean	400.00	374.41
	SD	0.00	45.96
	Q1	400.0	347.6
	Median	400.0	400.0
	Q3	400.0	400.0
	Min	400.0	300.0
	Max	400.0	400.0

LCM=Lacosamide, Max=maximum, Min=minimum, Q1=lower quartile, Q3=upper quartile, SD=standard deviation.
Note: Study medication duration=(date of last dose during the Treatment Period - date of first dose during the Treatment Period)+1.

Reference: Listings 5.1, 5.3, 2.1

1.1.4.2 主な安全性評価項目

1.1.4.2.1 有害事象

本治験では MedDRA version 16.1 を用いて有害事象を集計した。

治験薬との因果関係は、治験責任医師が「関連なし（Not related）」又は「関連あり（Related）」のいずれかで評価し、「関連あり」の有害事象を「治験薬との因果関係が否定できない有害事象」として取り扱った。

1.1.4.2.2 有害事象発現例数の概要

本治験の治療期間（増量期間+維持期間）に認められた有害事象発現例数の概要を表 1.1-40（全集団）及び表 1.1-41（日本人集団）に示した。

全集団では、治療期間に有害事象が 175 例（72.3%）に認められた。投与群別では、プラセボ群 79 例（65.3%）及びラコサミド群 96 例（79.3%）であった。

日本人集団では、治療期間に有害事象が 24 例（80.0%）に認められた。投与群別では、プラセボ群 13 例（68.4%）及びラコサミド群 11 例（100%）であった。

表 1.1-40　全集団の有害事象発現例数の概要（治療期間）：SS

Table 11.1.1
Incidence of TEAEs During the Treatment Period - Overview
Analysis Set: Safety Set

Category	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
Any TEAEs	79 (65.3) [231]	96 (79.3) [320]	175 (72.3) [551]
Serious TEAEs	4 (3.3) [4]	8 (6.6) [14]	12 (5.0) [18]
Subject discontinuations due to TEAEs	5 (4.1) [6]	11 (9.1) [13]	16 (6.6) [19]
Drug-related TEAEs	42 (34.7) [72]	56 (46.3) [133]	98 (40.5) [205]
Severe TEAEs	3 (2.5) [3]	6 (5.0) [8]	9 (3.7) [11]
All Deaths	0	0	0
Deaths (TEAEs leading to death)	0	0	0

AE=Adverse Event, LCM=Lacosamide, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE in that category.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE in that category.
Note: An AE with missing intensity is treated as severe; an AE with missing drug relationship is treated as related.
Reference: Listing 7.2

表 1.1-41　日本人集団の有害事象発現例数の概要（治療期間）：SS

Table 11.1.1.1

Incidence of TEAEs During the Treatment Period - Overview

Analysis Set: Safety Set - Japanese

Category	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]	All Subjects N=30 n (%) [#]
Any TEAEs	13 (68.4) [32]	11 (100) [34]	24 (80.0) [66]
Serious TEAEs	0	0	0
Subject discontinuations due to TEAEs	0	0	0
Drug-related TEAEs	6 (31.6) [8]	7 (63.6) [13]	13 (43.3) [21]
Severe TEAEs	0	0	0
All Deaths	0	0	0
Deaths (TEAEs leading to death)	0	0	0

AE=Adverse Event, LCM=Lacosamide, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE in that category.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE in that category.
Note: An AE with missing intensity is treated as severe; an AE with missing drug relationship is treated as related.

Reference: Listing 7.2

1.1.4.2.3 有害事象の発現状況

本治験の治療期間（増量期間+維持期間）に認められた有害事象を表 1.1-42（全集団）及び表 1.1-43（日本人集団）に示した。また、治療期間（増量期間+維持期間）に認められた重症度別の有害事象を表 1.1-44（全集団）及び表 1.1-45（日本人集団）に示した。

全集団では、治療期間に認められた有害事象の重症度はプラセボ群及びラコサミド群のいずれも、ほとんどが軽度（プラセボ群 61.2%及びラコサミド群 62.8%）又は中等度（プラセボ群 19.0%及びラコサミド群 34.7%）であった。治療期間で最も多く認められた有害事象（SOC）は神経系障害（38.8%）で、次いで感染症および寄生虫症（19.8%）及び胃腸障害（18.2%）であった。また、最も多く認められた有害事象（PT）は傾眠（15.3%）で、次いで浮動性めまい（14.5%）及び頭痛（12.0%）であった。

プラセボ群とラコサミド群の有害事象の発現率は、以下を除いて SOC 別及び PT 別のいずれも、おおむね同程度であった。

- SOC 別の有害事象で、プラセボ群とラコサミド群の発現率に差が認められた有害事象は、神経系障害（プラセボ群 29.8%及びラコサミド群 47.9%、以下同順）、胃腸障害（15.7%及び 20.7%）、眼障害（2.5%及び 7.4%）及び耳および迷路障害（1.7%及び 7.4%）であった
- PT 別の有害事象で、プラセボ群とラコサミド群の発現率に差が認められた有害事象は、浮動性めまい（5.8%及び 23.1%）、傾眠（14.0%及び 16.5%）、頭痛（9.9%及び 14.0%）、悪心（5.8%及び 9.9%）、嘔吐（0.8%及び 5.8%）、運動失調及び注意力障害（各 0%及び 3.3%）、ミオクローヌス性てんかん（0%及び 2.5%）、回転性めまい（1.7%及び 6.6%）、並びに霧視（0.8%及び 3.3%）であった

日本人集団では、治療期間に認められた有害事象の重症度はプラセボ群及びラコサミド群のいずれも、軽度（68.4%及び 100%）であり、中等度及び高度の有害事象は認められなかった。治療期間で最も多く認められた有害事象（SOC）は神経系障害（36.7%）で、次いで胃腸障害（23.3%）、傷害、中毒および処置合併症（20.0%）及び感染症および寄生虫症（16.7%）であった。また、最も多く認められた有害事象（PT）は傾眠（30.0%）で、次いで挫傷及び鼻咽頭炎（各 13.3%）、並びに腹痛、便秘及び背部痛（各 10.0%）であった。

日本人集団の有害事象プロファイルは、全集団と同様であった。

表 1.1-42　全集団の有害事象（治療期間）：SS

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
Any TEAE	79 (65.3) [231]	96 (79.3) [320]	175 (72.3) [551]
血液およびリンパ系障害	1 (0.8) [1]	2 (1.7) [2]	3 (1.2) [3]
好酸球増加症	0	1 (0.8) [1]	1 (0.4) [1]
鉄欠乏性貧血	0	1 (0.8) [1]	1 (0.4) [1]
白血球減少症	1 (0.8) [1]	0	1 (0.4) [1]
心臓障害	3 (2.5) [4]	4 (3.3) [4]	7 (2.9) [8]
右脚ブロック	0	2 (1.7) [2]	2 (0.8) [2]
不整脈	0	1 (0.8) [1]	1 (0.4) [1]
第一度房室ブロック	0	1 (0.8) [1]	1 (0.4) [1]
洞性徐脈	2 (1.7) [3]	0	2 (0.8) [3]
頻脈	1 (0.8) [1]	0	1 (0.4) [1]
耳および迷路障害	2 (1.7) [3]	9 (7.4) [9]	11 (4.5) [12]
回転性めまい	2 (1.7) [2]	8 (6.6) [8]	10 (4.1) [10]
耳鳴	0	1 (0.8) [1]	1 (0.4) [1]
聴覚過敏	1 (0.8) [1]	0	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
内分泌障害	1 (0.8) [1]	0	1 (0.4) [1]
自己免疫性甲状腺炎	1 (0.8) [1]	0	1 (0.4) [1]
眼障害	3 (2.5) [3]	9 (7.4) [11]	12 (5.0) [14]
霧視	1 (0.8) [1]	4 (3.3) [6]	5 (2.1) [7]
複視	0	1 (0.8) [1]	1 (0.4) [1]
眼刺激	0	1 (0.8) [1]	1 (0.4) [1]
流涙増加	0	1 (0.8) [1]	1 (0.4) [1]
光視症	0	1 (0.8) [1]	1 (0.4) [1]
視力低下	0	1 (0.8) [1]	1 (0.4) [1]
結膜炎	1 (0.8) [1]	0	1 (0.4) [1]
眼部腫脹	1 (0.8) [1]	0	1 (0.4) [1]
胃腸障害	19 (15.7) [28]	25 (20.7) [47]	44 (18.2) [75]
悪心	7 (5.8) [7]	12 (9.9) [13]	19 (7.9) [20]
嘔吐	1 (0.8) [3]	7 (5.8) [11]	8 (3.3) [14]
下痢	2 (1.7) [2]	4 (3.3) [5]	6 (2.5) [7]
腹痛	2 (1.7) [2]	3 (2.5) [3]	5 (2.1) [5]
上腹部痛	2 (1.7) [2]	2 (1.7) [3]	4 (1.7) [5]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
胃腸障害			
齲歯	0	2 (1.7) [2]	2 (0.8) [2]
胃炎	1 (0.8) [5]	2 (1.7) [2]	3 (1.2) [7]
腹部不快感	0	1 (0.8) [1]	1 (0.4) [1]
下腹部痛	0	1 (0.8) [1]	1 (0.4) [1]
便秘	2 (1.7) [2]	1 (0.8) [1]	3 (1.2) [3]
口内乾燥	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
鼓腸	0	1 (0.8) [1]	1 (0.4) [1]
口の感覚鈍麻	0	1 (0.8) [1]	1 (0.4) [1]
レッチング	0	1 (0.8) [1]	1 (0.4) [1]
舌障害	0	1 (0.8) [1]	1 (0.4) [1]
根尖肉芽腫	1 (0.8) [1]	0	1 (0.4) [1]
消化不良	1 (0.8) [1]	0	1 (0.4) [1]
食中毒	1 (0.8) [1]	0	1 (0.4) [1]
胃食道逆流性疾患	1 (0.8) [1]	0	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
一般・全身障害および投与部位の状態	14 (11.6) [15]	15 (12.4) [18]	29 (12.0) [33]
疲労	6 (5.0) [6]	8 (6.6) [8]	14 (5.8) [14]
易刺激性	2 (1.7) [3]	2 (1.7) [2]	4 (1.7) [5]
発熱	0	2 (1.7) [3]	2 (0.8) [3]
無力症	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
活力増進	0	1 (0.8) [1]	1 (0.4) [1]
酩酊感	0	1 (0.8) [1]	1 (0.4) [1]
熱感	0	1 (0.8) [1]	1 (0.4) [1]
評価不能の事象	0	1 (0.8) [1]	1 (0.4) [1]
胸痛	1 (0.8) [1]	0	1 (0.4) [1]
インフルエンザ様疾患	2 (1.7) [2]	0	2 (0.8) [2]
口渇	1 (0.8) [1]	0	1 (0.4) [1]
血管穿刺部位血腫	1 (0.8) [1]	0	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
免疫系障害	1 (0.8) [1]	2 (1.7) [2]	3 (1.2) [3]
過敏症	0	1 (0.8) [1]	1 (0.4) [1]
季節性アレルギー	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
感染症および寄生虫症	23 (19.0) [32]	25 (20.7) [34]	48 (19.8) [66]
鼻咽頭炎	4 (3.3) [4]	8 (6.6) [12]	12 (5.0) [16]
インフルエンザ	2 (1.7) [2]	3 (2.5) [3]	5 (2.1) [5]
上気道感染	6 (5.0) [9]	3 (2.5) [3]	9 (3.7) [12]
咽頭扁桃炎	0	2 (1.7) [2]	2 (0.8) [2]
ウイルス性気道感染	1 (0.8) [1]	2 (1.7) [2]	3 (1.2) [3]
気管支炎	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
蜂巣炎	0	1 (0.8) [1]	1 (0.4) [1]
胃腸炎	2 (1.7) [2]	1 (0.8) [1]	3 (1.2) [3]
ウイルス性胃腸炎	0	1 (0.8) [1]	1 (0.4) [1]
膿痂疹	0	1 (0.8) [1]	1 (0.4) [1]
ライム病	0	1 (0.8) [1]	1 (0.4) [1]
爪囲炎	0	1 (0.8) [1]	1 (0.4) [1]
咽頭炎	0	1 (0.8) [1]	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
感染症および寄生虫症			
鼻炎	3 (2.5) [4]	1 (0.8) [1]	4 (1.7) [5]
副鼻腔炎	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
尿路感染	2 (1.7) [2]	1 (0.8) [1]	3 (1.2) [3]
創傷感染	0	1 (0.8) [1]	1 (0.4) [1]
膀胱炎	2 (1.7) [2]	0	2 (0.8) [2]
耳感染	1 (0.8) [1]	0	1 (0.4) [1]
口腔カンジダ症	1 (0.8) [1]	0	1 (0.4) [1]
ウイルス性上気道感染	1 (0.8) [1]	0	1 (0.4) [1]
外陰部腟カンジダ症	1 (0.8) [1]	0	1 (0.4) [1]
傷害、中毒および処置合併症	16 (13.2) [21]	11 (9.1) [18]	27 (11.2) [39]
挫傷	5 (4.1) [6]	4 (3.3) [5]	9 (3.7) [11]
上腕骨骨折	0	2 (1.7) [3]	2 (0.8) [3]
靭帯捻挫	1 (0.8) [1]	2 (1.7) [3]	3 (1.2) [4]
眼挫傷	0	1 (0.8) [1]	1 (0.4) [1]
顔面骨骨折	0	1 (0.8) [1]	1 (0.4) [1]
転倒	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
頭部損傷	2 (1.7) [2]	1 (0.8) [1]	3 (1.2) [3]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
傷害、中毒および処置合併症			
筋断裂	0	1 (0.8) [1]	1 (0.4) [1]
熱傷	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
歯牙破折	0	1 (0.8) [1]	1 (0.4) [1]
外耳道損傷	1 (0.8) [1]	0	1 (0.4) [1]
擦過傷	3 (2.5) [3]	0	3 (1.2) [3]
顔面損傷	2 (1.7) [2]	0	2 (0.8) [2]
大腿骨骨折	1 (0.8) [1]	0	1 (0.4) [1]
手骨折	1 (0.8) [1]	0	1 (0.4) [1]
交通事故	1 (0.8) [1]	0	1 (0.4) [1]
軟部組織損傷	1 (0.8) [1]	0	1 (0.4) [1]
臨床検査	11 (9.1) [21]	9 (7.4) [12]	20 (8.3) [33]
アラニンアミノトランスフェラーゼ増加	4 (3.3) [4]	4 (3.3) [4]	8 (3.3) [8]
アスパラギン酸アミノトランスフェラーゼ増加	5 (4.1) [5]	2 (1.7) [2]	7 (2.9) [7]
好酸球数増加	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
γ－グルタミルトランスフェラーゼ増加	3 (2.5) [3]	1 (0.8) [1]	4 (1.7) [4]
肝機能検査異常	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
尿中蛋白陽性	0	1 (0.8) [1]	1 (0.4) [1]
トランスアミナーゼ上昇	0	1 (0.8) [1]	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
臨床検査			
体重減少	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
血中ビリルビン増加	2 (1.7) [2]	0	2 (0.8) [2]
体温上昇	1 (0.8) [1]	0	1 (0.4) [1]
リンパ球数減少	1 (0.8) [1]	0	1 (0.4) [1]
体重増加	1 (0.8) [1]	0	1 (0.4) [1]
白血球数減少	1 (0.8) [1]	0	1 (0.4) [1]
代謝および栄養障害	7 (5.8) [7]	3 (2.5) [3]	10 (4.1) [10]
食欲減退	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
高尿酸血症	0	1 (0.8) [1]	1 (0.4) [1]
肥満	0	1 (0.8) [1]	1 (0.4) [1]
糖尿病	1 (0.8) [1]	0	1 (0.4) [1]
高クロール血症	1 (0.8) [1]	0	1 (0.4) [1]
高カリウム血症	1 (0.8) [1]	0	1 (0.4) [1]
高脂血症	1 (0.8) [1]	0	1 (0.4) [1]
高ナトリウム血症	1 (0.8) [1]	0	1 (0.4) [1]
２型糖尿病	1 (0.8) [1]	0	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
筋骨格系および結合組織障害	6 (5.0) [10]	6 (5.0) [9]	12 (5.0) [19]
四肢痛	0	2 (1.7) [2]	2 (0.8) [2]
関節痛	3 (2.5) [3]	1 (0.8) [3]	4 (1.7) [6]
背部痛	2 (1.7) [2]	1 (0.8) [1]	3 (1.2) [3]
筋骨格系胸痛	0	1 (0.8) [1]	1 (0.4) [1]
ミオキミア	0	1 (0.8) [1]	1 (0.4) [1]
変形性関節症	0	1 (0.8) [1]	1 (0.4) [1]
出血性関節症	1 (0.8) [1]	0	1 (0.4) [1]
筋肉内出血	1 (0.8) [1]	0	1 (0.4) [1]
筋痙縮	1 (0.8) [2]	0	1 (0.4) [2]
筋骨格痛	1 (0.8) [1]	0	1 (0.4) [1]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	1 (0.8) [1]	1 (0.4) [1]
脂肪腫	0	1 (0.8) [1]	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
神経系障害	36 (29.8) [51]	58 (47.9) [108]	94 (38.8) [159]
浮動性めまい	7 (5.8) [7]	28 (23.1) [36]	35 (14.5) [43]
傾眠	17 (14.0) [17]	20 (16.5) [21]	37 (15.3) [38]
頭痛	12 (9.9) [13]	17 (14.0) [19]	29 (12.0) [32]
運動失調	0	4 (3.3) [5]	4 (1.7) [5]
注意力障害	0	4 (3.3) [5]	4 (1.7) [5]
ミオクローヌス性てんかん	0	3 (2.5) [3]	3 (1.2) [3]
健忘	1 (0.8) [1]	2 (1.7) [2]	3 (1.2) [3]
平衡障害	1 (0.8) [1]	2 (1.7) [2]	3 (1.2) [3]
振戦	0	2 (1.7) [2]	2 (0.8) [2]
よだれ	0	1 (0.8) [1]	1 (0.4) [1]
大発作痙攣	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
感覚鈍麻	0	1 (0.8) [1]	1 (0.4) [1]
嗜眠	0	1 (0.8) [1]	1 (0.4) [1]
意識消失	0	1 (0.8) [1]	1 (0.4) [1]
記憶障害	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
神経系障害			
片頭痛	2 (1.7) [2]	1 (0.8) [1]	3 (1.2) [3]
錯感覚	2 (1.7) [4]	1 (0.8) [1]	3 (1.2) [5]
姿勢時振戦	0	1 (0.8) [1]	1 (0.4) [1]
鎮静	0	1 (0.8) [1]	1 (0.4) [1]
単純部分発作	0	1 (0.8) [1]	1 (0.4) [1]
会話障害	0	1 (0.8) [1]	1 (0.4) [1]
てんかん重積状態	0	1 (0.8) [1]	1 (0.4) [1]
脳血腫	1 (0.8) [1]	0	1 (0.4) [1]
体位性めまい	2 (1.7) [2]	0	2 (0.8) [2]
ミオクローヌス	1 (0.8) [1]	0	1 (0.4) [1]
精神障害	10 (8.3) [14]	12 (9.9) [14]	22 (9.1) [28]
不眠症	3 (2.5) [3]	3 (2.5) [3]	6 (2.5) [6]
不安	3 (2.5) [3]	2 (1.7) [2]	5 (2.1) [5]
自殺念慮	0	2 (1.7) [2]	2 (0.8) [2]
怒り	0	1 (0.8) [1]	1 (0.4) [1]
抑うつ気分	0	1 (0.8) [1]	1 (0.4) [1]
ディスフェミア	0	1 (0.8) [1]	1 (0.4) [1]
心因性発作	0	1 (0.8) [1]	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
精神障害			
睡眠障害	0	1 (0.8) [1]	1 (0.4) [1]
早朝覚醒型不眠症	0	1 (0.8) [1]	1 (0.4) [1]
思考異常	0	1 (0.8) [1]	1 (0.4) [1]
攻撃性	1 (0.8) [1]	0	1 (0.4) [1]
身体醜形障害	1 (0.8) [1]	0	1 (0.4) [1]
うつ病	1 (0.8) [1]	0	1 (0.4) [1]
気分変化	1 (0.8) [1]	0	1 (0.4) [1]
神経過敏	1 (0.8) [4]	0	1 (0.4) [4]
腎および尿路障害	1 (0.8) [1]	0	1 (0.4) [1]
尿失禁	1 (0.8) [1]	0	1 (0.4) [1]
生殖系および乳房障害	1 (0.8) [1]	3 (2.5) [3]	4 (1.7) [4]
月経困難症	0	1 (0.8) [1]	1 (0.4) [1]
卵巣嚢胞	0	1 (0.8) [1]	1 (0.4) [1]
子宮出血	0	1 (0.8) [1]	1 (0.4) [1]
不正子宮出血	1 (0.8) [1]	0	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
呼吸器、胸郭および縦隔障害	4 (3.3) [4]	8 (6.6) [11]	12 (5.0) [15]
咳嗽	1 (0.8) [1]	4 (3.3) [4]	5 (2.1) [5]
鼻出血	1 (0.8) [1]	2 (1.7) [2]	3 (1.2) [3]
口腔咽頭痛	0	2 (1.7) [3]	2 (0.8) [3]
鼻閉	0	1 (0.8) [1]	1 (0.4) [1]
鼻漏	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
呼吸障害	1 (0.8) [1]	0	1 (0.4) [1]
皮膚および皮下組織障害	8 (6.6) [9]	8 (6.6) [10]	16 (6.6) [19]
発疹	2 (1.7) [2]	3 (2.5) [3]	5 (2.1) [5]
そう痒症	0	2 (1.7) [2]	2 (0.8) [2]
脱毛症	1 (0.8) [1]	1 (0.8) [1]	2 (0.8) [2]
異汗性湿疹	0	1 (0.8) [1]	1 (0.4) [1]
紅斑	0	1 (0.8) [1]	1 (0.4) [1]
多汗症	0	1 (0.8) [1]	1 (0.4) [1]
顔面腫脹	0	1 (0.8) [1]	1 (0.4) [1]
ざ瘡	1 (0.8) [1]	0	1 (0.4) [1]
アトピー性皮膚炎	1 (0.8) [1]	0	1 (0.4) [1]
光線過敏性反応	1 (0.8) [2]	0	1 (0.4) [2]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-42　全集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]	All Subjects N=242 n (%) [#]
皮膚および皮下組織障害			
斑状皮疹	1 (0.8) [1]	0	1 (0.4) [1]
蕁麻疹	1 (0.8) [1]	0	1 (0.4) [1]
社会環境	1 (0.8) [1]	0	1 (0.4) [1]
閉経	1 (0.8) [1]	0	1 (0.4) [1]
血管障害	3 (2.5) [3]	4 (3.3) [4]	7 (2.9) [7]
高血圧	1 (0.8) [1]	3 (2.5) [3]	4 (1.7) [4]
潮紅	0	1 (0.8) [1]	1 (0.4) [1]
血腫	1 (0.8) [1]	0	1 (0.4) [1]
腹腔内血腫	1 (0.8) [1]	0	1 (0.4) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.
Reference: Listing 7.2

表 1.1-43　日本人集団の有害事象（治療期間）：SS

Table 11.2.1.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]	All Subjects N=30 n (%) [#]
Any TEAE	13 (68.4) [32]	11 (100) [34]	24 (80.0) [66]
心臓障害	2 (10.5) [3]	0	2 (6.7) [3]
洞性徐脈	2 (10.5) [3]	0	2 (6.7) [3]
耳および迷路障害	0	2 (18.2) [2]	2 (6.7) [2]
耳鳴	0	1 (9.1) [1]	1 (3.3) [1]
回転性めまい	0	1 (9.1) [1]	1 (3.3) [1]
眼障害	1 (5.3) [1]	0	1 (3.3) [1]
結膜炎	1 (5.3) [1]	0	1 (3.3) [1]
胃腸障害	3 (15.8) [4]	4 (36.4) [8]	7 (23.3) [12]
腹痛	1 (5.3) [1]	2 (18.2) [2]	3 (10.0) [3]
悪心	0	2 (18.2) [2]	2 (6.7) [2]
腹部不快感	0	1 (9.1) [1]	1 (3.3) [1]
便秘	2 (10.5) [2]	1 (9.1) [1]	3 (10.0) [3]
下痢	1 (5.3) [1]	1 (9.1) [1]	2 (6.7) [2]
胃炎	0	1 (9.1) [1]	1 (3.3) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.

Reference: Listing 7.2

表 1.1-43　日本人集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]	All Subjects N=30 n (%) [#]
一般・全身障害および投与部位の状態	0	1 (9.1) [1]	1 (3.3) [1]
発熱	0	1 (9.1) [1]	1 (3.3) [1]
免疫系障害	1 (5.3) [1]	0	1 (3.3) [1]
季節性アレルギー	1 (5.3) [1]	0	1 (3.3) [1]
感染症および寄生虫症	2 (10.5) [2]	3 (27.3) [6]	5 (16.7) [8]
鼻咽頭炎	1 (5.3) [1]	3 (27.3) [6]	4 (13.3) [7]
インフルエンザ	1 (5.3) [1]	0	1 (3.3) [1]
傷害、中毒および処置合併症	5 (26.3) [8]	1 (9.1) [1]	6 (20.0) [9]
挫傷	3 (15.8) [4]	1 (9.1) [1]	4 (13.3) [5]
外耳道損傷	1 (5.3) [1]	0	1 (3.3) [1]
擦過傷	1 (5.3) [1]	0	1 (3.3) [1]
靭帯捻挫	1 (5.3) [1]	0	1 (3.3) [1]
熱傷	1 (5.3) [1]	0	1 (3.3) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.

Reference: Listing 7.2

表 1.1-43　日本人集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]	All Subjects N=30 n (%) [#]
臨床検査	1 (5.3) [1]	1 (9.1) [1]	2 (6.7) [2]
尿中蛋白陽性	0	1 (9.1) [1]	1 (3.3) [1]
アスパラギン酸アミノトランスフェラーゼ増加	1 (5.3) [1]	0	1 (3.3) [1]
代謝および栄養障害	0	1 (9.1) [1]	1 (3.3) [1]
高尿酸血症	0	1 (9.1) [1]	1 (3.3) [1]
筋骨格系および結合組織障害	2 (10.5) [3]	1 (9.1) [1]	3 (10.0) [4]
背部痛	2 (10.5) [2]	1 (9.1) [1]	3 (10.0) [3]
関節痛	1 (5.3) [1]	0	1 (3.3) [1]
神経系障害	5 (26.3) [7]	6 (54.5) [7]	11 (36.7) [14]
傾眠	4 (21.1) [4]	5 (45.5) [5]	9 (30.0) [9]
浮動性めまい	0	1 (9.1) [1]	1 (3.3) [1]
頭痛	1 (5.3) [1]	1 (9.1) [1]	2 (6.7) [2]
体位性めまい	2 (10.5) [2]	0	2 (6.7) [2]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.

Reference: Listing 7.2

表 1.1-43　日本人集団の有害事象（治療期間）：SS（続き）

Table 11.2.1.1.1
Incidence of TEAEs During the Treatment Period
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]	All Subjects N=30 n (%) [#]
精神障害	0	2 (18.2) [2]	2 (6.7) [2]
不安	0	1 (9.1) [1]	1 (3.3) [1]
早朝覚醒型不眠症	0	1 (9.1) [1]	1 (3.3) [1]
腎および尿路障害	1 (5.3) [1]	0	1 (3.3) [1]
尿失禁	1 (5.3) [1]	0	1 (3.3) [1]
生殖系および乳房障害	0	1 (9.1) [1]	1 (3.3) [1]
月経困難症	0	1 (9.1) [1]	1 (3.3) [1]
呼吸器、胸郭および縦隔障害	0	2 (18.2) [2]	2 (6.7) [2]
鼻出血	0	1 (9.1) [1]	1 (3.3) [1]
口腔咽頭痛	0	1 (9.1) [1]	1 (3.3) [1]
皮膚および皮下組織障害	1 (5.3) [1]	1 (9.1) [1]	2 (6.7) [2]
発疹	0	1 (9.1) [1]	1 (3.3) [1]
ざ瘡	1 (5.3) [1]	0	1 (3.3) [1]

LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: [#] is the number of individual occurrences of the TEAE.

Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
Any TEAE	Any	79 (65.3) [231]	96 (79.3) [320]
	Mild	74 (61.2) [195]	76 (62.8) [227]
	Moderate	23 (19.0) [33]	42 (34.7) [85]
	Severe	3 (2.5) [3]	6 (5.0) [8]
血液およびリンパ系障害	Any	1 (0.8) [1]	2 (1.7) [2]
	Mild	0	2 (1.7) [2]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
好酸球増加症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class / Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
血液およびリンパ系障害			
鉄欠乏性貧血	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
白血球減少症	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0
心臓障害	Any	3 (2.5) [4]	4 (3.3) [4]
	Mild	3 (2.5) [4]	3 (2.5) [3]
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
心臓障害			
右脚ブロック	Any	0	2 (1.7) [2]
	Mild	0	2 (1.7) [2]
	Moderate	0	0
	Severe	0	0
不整脈	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
第一度房室ブロック	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
心臓障害			
洞性徐脈	Any	2 (1.7) [3]	0
	Mild	2 (1.7) [3]	0
	Moderate	0	0
	Severe	0	0
頻脈	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
耳および迷路障害	Any	2 (1.7) [3]	9 (7.4) [9]
	Mild	2 (1.7) [3]	7 (5.8) [7]
	Moderate	0	2 (1.7) [2]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
耳および迷路障害			
回転性めまい	Any	2 (1.7) [2]	8 (6.6) [8]
	Mild	2 (1.7) [2]	6 (5.0) [6]
	Moderate	0	2 (1.7) [2]
	Severe	0	0
耳鳴	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
聴覚過敏	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
内分泌障害	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
自己免疫性甲状腺炎	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
眼障害	Any	3 (2.5) [3]	9 (7.4) [11]
	Mild	3 (2.5) [3]	8 (6.6) [10]
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class / Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
眼障害			
霧視	Any	1 (0.8) [1]	4 (3.3) [6]
	Mild	1 (0.8) [1]	4 (3.3) [6]
	Moderate	0	0
	Severe	0	0
複視	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
眼刺激	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
眼障害			
流涙増加	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
光視症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
視力低下	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
眼障害			
結膜炎	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
眼部腫脹	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
胃腸障害	Any	19 (15.7) [28]	25 (20.7) [47]
	Mild	18 (14.9) [26]	19 (15.7) [32]
	Moderate	2 (1.7) [2]	7 (5.8) [13]
	Severe	0	2 (1.7) [2]

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
悪心	Any	7 (5.8) [7]	12 (9.9) [13]
	Mild	6 (5.0) [6]	8 (6.6) [8]
	Moderate	1 (0.8) [1]	4 (3.3) [4]
	Severe	0	1 (0.8) [1]
嘔吐	Any	1 (0.8) [3]	7 (5.8) [11]
	Mild	1 (0.8) [3]	5 (4.1) [7]
	Moderate	0	2 (1.7) [4]
	Severe	0	0
下痢	Any	2 (1.7) [2]	4 (3.3) [5]
	Mild	2 (1.7) [2]	3 (2.5) [3]
	Moderate	0	1 (0.8) [2]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
腹痛	Any	2 (1.7) [2]	3 (2.5) [3]
	Mild	2 (1.7) [2]	2 (1.7) [2]
	Moderate	0	0
	Severe	0	1 (0.8) [1]
上腹部痛	Any	2 (1.7) [2]	2 (1.7) [3]
	Mild	2 (1.7) [2]	2 (1.7) [3]
	Moderate	0	0
	Severe	0	0
齲歯	Any	0	2 (1.7) [2]
	Mild	0	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
胃炎	Any	1 (0.8) [5]	2 (1.7) [2]
	Mild	1 (0.8) [5]	2 (1.7) [2]
	Moderate	0	0
	Severe	0	0
腹部不快感	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
下腹部痛	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
便秘	Any	2 (1.7) [2]	1 (0.8) [1]
	Mild	2 (1.7) [2]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
口内乾燥	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
鼓腸	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
口の感覚鈍麻	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
レッチング	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
舌障害	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
根尖肉芽腫	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
消化不良	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
食中毒	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
胃腸障害			
胃食道逆流性疾患	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
一般・全身障害および投与部位の状態	Any	14 (11.6) [15]	15 (12.4) [18]
	Mild	11 (9.1) [12]	11 (9.1) [14]
	Moderate	3 (2.5) [3]	4 (3.3) [4]
	Severe	0	0
疲労	Any	6 (5.0) [6]	8 (6.6) [8]
	Mild	5 (4.1) [5]	5 (4.1) [5]
	Moderate	1 (0.8) [1]	3 (2.5) [3]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
一般・全身障害および投与部位の状態			
易刺激性	Any	2 (1.7) [3]	2 (1.7) [2]
	Mild	1 (0.8) [2]	2 (1.7) [2]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
発熱	Any	0	2 (1.7) [3]
	Mild	0	2 (1.7) [3]
	Moderate	0	0
	Severe	0	0
無力症	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
一般・全身障害および投与部位の状態			
活力増進	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
酩酊感	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
熱感	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
一般・全身障害および投与部位の状態			
評価不能の事象	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
胸痛	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
インフルエンザ様疾患	Any	2 (1.7) [2]	0
	Mild	1 (0.8) [1]	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
一般・全身障害および投与部位の状態			
口渇	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
血管穿刺部位血腫	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
免疫系障害	Any	1 (0.8) [1]	2 (1.7) [2]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
免疫系障害			
過敏症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
季節性アレルギー	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
感染症および寄生虫症	Any	23 (19.0) [32]	25 (20.7) [34]
	Mild	19 (15.7) [25]	18 (14.9) [23]
	Moderate	4 (3.3) [6]	8 (6.6) [11]
	Severe	1 (0.8) [1]	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
鼻咽頭炎	Any	4 (3.3) [4]	8 (6.6) [12]
	Mild	4 (3.3) [4]	6 (5.0) [10]
	Moderate	0	2 (1.7) [2]
	Severe	0	0
インフルエンザ	Any	2 (1.7) [2]	3 (2.5) [3]
	Mild	2 (1.7) [2]	3 (2.5) [3]
	Moderate	0	0
	Severe	0	0
上気道感染	Any	6 (5.0) [9]	3 (2.5) [3]
	Mild	5 (4.1) [6]	2 (1.7) [2]
	Moderate	1 (0.8) [3]	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
咽頭扁桃炎	Any	0	2 (1.7) [2]
	Mild	0	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0
ウイルス性気道感染	Any	1 (0.8) [1]	2 (1.7) [2]
	Mild	0	2 (1.7) [2]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
気管支炎	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
蜂巣炎	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
胃腸炎	Any	2 (1.7) [2]	1 (0.8) [1]
	Mild	0	0
	Moderate	1 (0.8) [1]	1 (0.8) [1]
	Severe	1 (0.8) [1]	0
ウイルス性胃腸炎	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
膿痂疹	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
ライム病	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
爪囲炎	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
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Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
咽頭炎	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
鼻炎	Any	3 (2.5) [4]	1 (0.8) [1]
	Mild	3 (2.5) [4]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
副鼻腔炎	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
尿路感染	Any	2 (1.7) [2]	1 (0.8) [1]
	Mild	1 (0.8) [1]	0
	Moderate	1 (0.8) [1]	1 (0.8) [1]
	Severe	0	0
創傷感染	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
膀胱炎	Any	2 (1.7) [2]	0
	Mild	2 (1.7) [2]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
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Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
耳感染	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
口腔カンジダ症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
ウイルス性上気道感染	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
感染症および寄生虫症			
外陰部腟カンジダ症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
傷害、中毒および処置合併症	Any	16 (13.2) [21]	11 (9.1) [18]
	Mild	12 (9.9) [16]	7 (5.8) [8]
	Moderate	4 (3.3) [4]	4 (3.3) [9]
	Severe	1 (0.8) [1]	1 (0.8) [1]
挫傷	Any	5 (4.1) [6]	4 (3.3) [5]
	Mild	5 (4.1) [6]	3 (2.5) [3]
	Moderate	0	1 (0.8) [2]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
傷害、中毒および処置合併症			
上腕骨骨折	Any	0	2 (1.7) [3]
	Mild	0	0
	Moderate	0	2 (1.7) [3]
	Severe	0	0
靱帯捻挫	Any	1 (0.8) [1]	2 (1.7) [3]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	1 (0.8) [2]
	Severe	0	0
眼挫傷	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
傷害、中毒および処置合併症			
顔面骨骨折	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	0
	Severe	0	1 (0.8) [1]
転倒	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
頭部損傷	Any	2 (1.7) [2]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
傷害、中毒および処置合併症			
筋断裂	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
熱傷	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
歯牙破折	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
傷害、中毒および処置合併症			
外耳道損傷	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
擦過傷	Any	3 (2.5) [3]	0
	Mild	3 (2.5) [3]	0
	Moderate	0	0
	Severe	0	0
顔面損傷	Any	2 (1.7) [2]	0
	Mild	1 (0.8) [1]	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
傷害、中毒および処置合併症			
大腿骨骨折	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	0	0
	Severe	1 (0.8) [1]	0
手骨折	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0
交通事故	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
傷害、中毒および処置合併症			
軟部組織損傷	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0
臨床検査	Any	11 (9.1) [21]	9 (7.4) [12]
	Mild	10 (8.3) [19]	6 (5.0) [8]
	Moderate	2 (1.7) [2]	3 (2.5) [4]
	Severe	0	0
アラニンアミノトランスフェラーゼ増加	Any	4 (3.3) [4]	4 (3.3) [4]
	Mild	4 (3.3) [4]	2 (1.7) [2]
	Moderate	0	2 (1.7) [2]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
臨床検査			
アスパラギン酸アミノトランスフェラーゼ増加	Any	5 (4.1) [5]	2 (1.7) [2]
	Mild	5 (4.1) [5]	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0
好酸球数増加	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
γ－グルタミルトランスフェラーゼ増加	Any	3 (2.5) [3]	1 (0.8) [1]
	Mild	2 (1.7) [2]	1 (0.8) [1]
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
臨床検査			
肝機能検査異常	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
尿中蛋白陽性	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
トランスアミナーゼ上昇	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
臨床検査			
体重減少	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
血中ビリルビン増加	Any	2 (1.7) [2]	0
	Mild	2 (1.7) [2]	0
	Moderate	0	0
	Severe	0	0
体温上昇	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
臨床検査			
リンパ球数減少	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
体重増加	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
白血球数減少	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
代謝および栄養障害	Any	7 (5.8) [7]	3 (2.5) [3]
	Mild	6 (5.0) [6]	3 (2.5) [3]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
食欲減退	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
高尿酸血症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
代謝および栄養障害			
肥満	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
糖尿病	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0
高クロール血症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
代謝および栄養障害			
高カリウム血症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
高脂血症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
高ナトリウム血症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
代謝および栄養障害			
2型糖尿病	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
筋骨格系および結合組織障害	Any	6 (5.0) [10]	6 (5.0) [9]
	Mild	6 (5.0) [9]	5 (4.1) [8]
	Moderate	1 (0.8) [1]	1 (0.8) [1]
	Severe	0	0
四肢痛	Any	0	2 (1.7) [2]
	Mild	0	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
筋骨格系および結合組織障害			
関節痛	Any	3 (2.5) [3]	1 (0.8) [3]
	Mild	3 (2.5) [3]	1 (0.8) [3]
	Moderate	0	0
	Severe	0	0
背部痛	Any	2 (1.7) [2]	1 (0.8) [1]
	Mild	2 (1.7) [2]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
筋骨格系胸痛	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
筋骨格系および結合組織障害			
ミオキミア	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
変形性関節症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
出血性関節症	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
筋骨格系および結合組織障害			
筋肉内出血	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
筋痙縮	Any	1 (0.8) [2]	0
	Mild	1 (0.8) [2]	0
	Moderate	0	0
	Severe	0	0
筋骨格痛	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
脂肪腫	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
神経系障害	Any	36 (29.8) [51]	58 (47.9) [108]
	Mild	33 (27.3) [44]	46 (38.0) [77]
	Moderate	6 (5.0) [7]	18 (14.9) [26]
	Severe	0	4 (3.3) [5]

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
浮動性めまい	Any	7 (5.8) [7]	28 (23.1) [36]
	Mild	7 (5.8) [7]	20 (16.5) [25]
	Moderate	0	9 (7.4) [9]
	Severe	0	2 (1.7) [2]
傾眠	Any	17 (14.0) [17]	20 (16.5) [21]
	Mild	15 (12.4) [15]	18 (14.9) [18]
	Moderate	2 (1.7) [2]	2 (1.7) [2]
	Severe	0	1 (0.8) [1]
頭痛	Any	12 (9.9) [13]	17 (14.0) [19]
	Mild	11 (9.1) [12]	12 (9.9) [14]
	Moderate	1 (0.8) [1]	4 (3.3) [4]
	Severe	0	1 (0.8) [1]

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
運動失調	Any	0	4 (3.3) [5]
	Mild	0	2 (1.7) [2]
	Moderate	0	3 (2.5) [3]
	Severe	0	0
注意力障害	Any	0	4 (3.3) [5]
	Mild	0	4 (3.3) [4]
	Moderate	0	1 (0.8) [1]
	Severe	0	0
ミオクローヌス性てんかん	Any	0	3 (2.5) [3]
	Mild	0	1 (0.8) [1]
	Moderate	0	2 (1.7) [2]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
健忘	Any	1 (0.8) [1]	2 (1.7) [2]
	Mild	1 (0.8) [1]	2 (1.7) [2]
	Moderate	0	0
	Severe	0	0
平衡障害	Any	1 (0.8) [1]	2 (1.7) [2]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0
振戦	Any	0	2 (1.7) [2]
	Mild	0	2 (1.7) [2]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
よだれ	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
大発作痙攣	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	1 (0.8) [1]	0
	Severe	0	0
感覚鈍麻	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
嗜眠	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
意識消失	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
記憶障害	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
片頭痛	Any	2 (1.7) [2]	1 (0.8) [1]
	Mild	2 (1.7) [2]	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
錯感覚	Any	2 (1.7) [4]	1 (0.8) [1]
	Mild	1 (0.8) [2]	1 (0.8) [1]
	Moderate	2 (1.7) [2]	0
	Severe	0	0
姿勢時振戦	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
鎮静	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
単純部分発作	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
会話障害	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
てんかん重積状態	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	0
	Severe	0	1 (0.8) [1]
脳血腫	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0
体位性めまい	Any	2 (1.7) [2]	0
	Mild	2 (1.7) [2]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
神経系障害			
ミオクローヌス	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
精神障害	Any	10 (8.3) [14]	12 (9.9) [14]
	Mild	6 (5.0) [10]	7 (5.8) [8]
	Moderate	3 (2.5) [3]	5 (4.1) [6]
	Severe	1 (0.8) [1]	0
不眠症	Any	3 (2.5) [3]	3 (2.5) [3]
	Mild	1 (0.8) [1]	3 (2.5) [3]
	Moderate	2 (1.7) [2]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
精神障害			
不安	Any	3 (2.5) [3]	2 (1.7) [2]
	Mild	2 (1.7) [2]	1 (0.8) [1]
	Moderate	1 (0.8) [1]	1 (0.8) [1]
	Severe	0	0
自殺念慮	Any	0	2 (1.7) [2]
	Mild	0	0
	Moderate	0	2 (1.7) [2]
	Severe	0	0
怒り	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
精神障害			
抑うつ気分	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
ディスフェミア	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
心因性発作	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
精神障害			
睡眠障害	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
早朝覚醒型不眠症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
思考異常	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
精神障害			
攻撃性	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
身体醜形障害	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
うつ病	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	0	0
	Severe	1 (0.8) [1]	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
精神障害			
気分変化	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
神経過敏	Any	1 (0.8) [4]	0
	Mild	1 (0.8) [4]	0
	Moderate	0	0
	Severe	0	0
腎および尿路障害	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
腎および尿路障害			
尿失禁	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
生殖系および乳房障害	Any	1 (0.8) [1]	3 (2.5) [3]
	Mild	1 (0.8) [1]	2 (1.7) [2]
	Moderate	0	1 (0.8) [1]
	Severe	0	0
月経困難症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
生殖系および乳房障害			
卵巣嚢胞	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0
子宮出血	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
不正子宮出血	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
呼吸器、胸郭および縦隔障害	Any	4 (3.3) [4]	8 (6.6) [11]
	Mild	3 (2.5) [3]	6 (5.0) [8]
	Moderate	1 (0.8) [1]	2 (1.7) [3]
	Severe	0	0
咳嗽	Any	1 (0.8) [1]	4 (3.3) [4]
	Mild	1 (0.8) [1]	4 (3.3) [4]
	Moderate	0	0
	Severe	0	0
鼻出血	Any	1 (0.8) [1]	2 (1.7) [2]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
呼吸器、胸郭および縦隔障害			
口腔咽頭痛	Any	0	2 (1.7) [3]
	Mild	0	1 (0.8) [1]
	Moderate	0	1 (0.8) [2]
	Severe	0	0
鼻閉	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
鼻漏	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
呼吸器、胸郭および縦隔障害			
呼吸障害	Any	1 (0.8) [1]	0
	Mild	0	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0
皮膚および皮下組織障害	Any	8 (6.6) [9]	8 (6.6) [10]
	Mild	7 (5.8) [7]	6 (5.0) [8]
	Moderate	2 (1.7) [2]	2 (1.7) [2]
	Severe	0	0
発疹	Any	2 (1.7) [2]	3 (2.5) [3]
	Mild	1 (0.8) [1]	3 (2.5) [3]
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
皮膚および皮下組織障害			
そう痒症	Any	0	2 (1.7) [2]
	Mild	0	2 (1.7) [2]
	Moderate	0	0
	Severe	0	0
脱毛症	Any	1 (0.8) [1]	1 (0.8) [1]
	Mild	1 (0.8) [1]	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
異汗性湿疹	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
皮膚および皮下組織障害			
紅斑	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
多汗症	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
顔面腫脹	Any	0	1 (0.8) [1]
	Mild	0	0
	Moderate	0	1 (0.8) [1]
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
皮膚および皮下組織障害			
ざ瘡	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
アトピー性皮膚炎	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
光線過敏性反応	Any	1 (0.8) [2]	0
	Mild	1 (0.8) [1]	0
	Moderate	1 (0.8) [1]	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
皮膚および皮下組織障害			
斑状皮疹	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
蕁麻疹	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
社会環境	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
社会環境			
閉経	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
血管障害	Any	3 (2.5) [3]	4 (3.3) [4]
	Mild	3 (2.5) [3]	4 (3.3) [4]
	Moderate	0	0
	Severe	0	0
高血圧	Any	1 (0.8) [1]	3 (2.5) [3]
	Mild	1 (0.8) [1]	3 (2.5) [3]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-44　全集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=121 n (%) [#]	LCM N=121 n (%) [#]
血管障害			
潮紅	Any	0	1 (0.8) [1]
	Mild	0	1 (0.8) [1]
	Moderate	0	0
	Severe	0	0
血腫	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0
腹腔内血腫	Any	1 (0.8) [1]	0
	Mild	1 (0.8) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.
Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS

Table 11.3.1

Incidence of TEAEs During the Treatment Period by Intensity

Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
Any TEAE	Any	13 (68.4) [32]	11 (100) [34]
	Mild	13 (68.4) [32]	11 (100) [34]
	Moderate	0	0
	Severe	0	0
心臓障害	Any	2 (10.5) [3]	0
	Mild	2 (10.5) [3]	0
	Moderate	0	0
	Severe	0	0
洞性徐脈	Any	2 (10.5) [3]	0
	Mild	2 (10.5) [3]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1

Incidence of TEAEs During the Treatment Period by Intensity

Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
耳および迷路障害	Any	0	2 (18.2) [2]
	Mild	0	2 (18.2) [2]
	Moderate	0	0
	Severe	0	0
耳鳴	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
回転性めまい	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1

Incidence of TEAEs During the Treatment Period by Intensity

Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
眼障害	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
結膜炎	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
胃腸障害	Any	3 (15.8) [4]	4 (36.4) [8]
	Mild	3 (15.8) [4]	4 (36.4) [8]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1

Incidence of TEAEs During the Treatment Period by Intensity

Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class / Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
胃腸障害			
腹痛	Any	1 (5.3) [1]	2 (18.2) [2]
	Mild	1 (5.3) [1]	2 (18.2) [2]
	Moderate	0	0
	Severe	0	0
悪心	Any	0	2 (18.2) [2]
	Mild	0	2 (18.2) [2]
	Moderate	0	0
	Severe	0	0
腹部不快感	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
胃腸障害			
便秘	Any	2 (10.5) [2]	1 (9.1) [1]
	Mild	2 (10.5) [2]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
下痢	Any	1 (5.3) [1]	1 (9.1) [1]
	Mild	1 (5.3) [1]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
胃炎	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
一般・全身障害および投与部位の状態	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
発熱	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
免疫系障害	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
免疫系障害			
季節性アレルギー	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
感染症および寄生虫症	Any	2 (10.5) [2]	3 (27.3) [6]
	Mild	2 (10.5) [2]	3 (27.3) [6]
	Moderate	0	0
	Severe	0	0
鼻咽頭炎	Any	1 (5.3) [1]	3 (27.3) [6]
	Mild	1 (5.3) [1]	3 (27.3) [6]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
感染症および寄生虫症			
インフルエンザ	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
傷害、中毒および処置合併症	Any	5 (26.3) [8]	1 (9.1) [1]
	Mild	5 (26.3) [8]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
挫傷	Any	3 (15.8) [4]	1 (9.1) [1]
	Mild	3 (15.8) [4]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
傷害、中毒および処置合併症			
外耳道損傷	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
擦過傷	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
靭帯捻挫	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
傷害、中毒および処置合併症			
熱傷	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
臨床検査	Any	1 (5.3) [1]	1 (9.1) [1]
	Mild	1 (5.3) [1]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
尿中蛋白陽性	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
臨床検査			
アスパラギン酸アミノトランスフェラーゼ増加	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
代謝および栄養障害	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
高尿酸血症	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
筋骨格系および結合組織障害	Any	2 (10.5) [3]	1 (9.1) [1]
	Mild	2 (10.5) [3]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
背部痛	Any	2 (10.5) [2]	1 (9.1) [1]
	Mild	2 (10.5) [2]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
関節痛	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
神経系障害	Any	5 (26.3) [7]	6 (54.5) [7]
	Mild	5 (26.3) [7]	6 (54.5) [7]
	Moderate	0	0
	Severe	0	0
傾眠	Any	4 (21.1) [4]	5 (45.5) [5]
	Mild	4 (21.1) [4]	5 (45.5) [5]
	Moderate	0	0
	Severe	0	0
浮動性めまい	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class / Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
神経系障害			
頭痛	Any	1 (5.3) [1]	1 (9.1) [1]
	Mild	1 (5.3) [1]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
体位性めまい	Any	2 (10.5) [2]	0
	Mild	2 (10.5) [2]	0
	Moderate	0	0
	Severe	0	0
精神障害	Any	0	2 (18.2) [2]
	Mild	0	2 (18.2) [2]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class / Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
精神障害			
不安	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
早朝覚醒型不眠症	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
腎および尿路障害	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1
Incidence of TEAEs During the Treatment Period by Intensity
Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
腎および尿路障害			
尿失禁	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0
生殖系および乳房障害	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
月経困難症	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1

Incidence of TEAEs During the Treatment Period by Intensity

Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
呼吸器、胸郭および縦隔障害	Any	0	2 (18.2) [2]
	Mild	0	2 (18.2) [2]
	Moderate	0	0
	Severe	0	0
鼻出血	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
口腔咽頭痛	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2

表 1.1-45　日本人集団の重症度別の有害事象（治療期間）：SS（続き）

Table 11.3.1

Incidence of TEAEs During the Treatment Period by Intensity

Analysis Set: Safety Set - Japanese

MedDRA v16.1 System Organ Class Preferred Term	Intensity	Placebo N=19 n (%) [#]	LCM N=11 n (%) [#]
皮膚および皮下組織障害	Any	1 (5.3) [1]	1 (9.1) [1]
	Mild	1 (5.3) [1]	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
発疹	Any	0	1 (9.1) [1]
	Mild	0	1 (9.1) [1]
	Moderate	0	0
	Severe	0	0
ざ瘡	Any	1 (5.3) [1]	0
	Mild	1 (5.3) [1]	0
	Moderate	0	0
	Severe	0	0

AE=Adverse Event, LCM=Lacosamide, MedDRA=Medical Dictionary for Regulatory Activities, TEAE=Treatment-emergent adverse event.
Note: n=number of subjects reporting at least one TEAE within System Organ Class/ Preferred Term.
Note: [#] is the number of individual occurrences of the TEAE.
Note: Percentages are based on the number of subjects in the Safety Set.
Note: A subject may be counted more than once according to the intensity of the TEAEs.
Note: An AE with missing intensity is treated as severe.

Reference: Listing 7.2