セリンクロ錠　10mg

第 2 部（モジュール 2）：CTD の概要（サマリー）

2.7.4 臨床的安全性

大塚製薬株式会社

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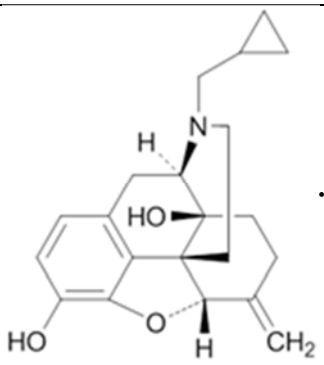
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略号一覧

略号	省略していない表現
AE	adverse event　有害事象
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
APRS	all-patients-randomised set　無作為化例
APTS	all-patients-treated set　治験薬投与例
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（肥満指数）
BRENDA	biopsychosocial evaluation report to the patient on assessment empathic understanding of the patient's situation needs collaboratively identified by the patient and treatment provider direct advice to the patient on how to meet those needs assess reaction of the patient to advice and adjust as necessary for best care
CDT	carbohydrate-deficient transferrin　炭水化物欠失トランスフェリン
%CDT	percentage CDT　炭水化物欠失トランスフェリンの割合
CI	confidence interval　信頼区間
C-SSRS	Columbia-suicide severity rating scale　コロンビア自殺評価スケール
DRL	drinking risk level　飲酒量に基づくリスクレベル
DSM	diagnostic and statistical manual of mental disorders 精神疾患の診断・統計マニュアル
DSM-IV	diagnostic and statistical manual of mental disorders fourth edition 精神疾患の診断・統計マニュアル 第 4 版
DSM-IV-TR	diagnostic and statistical manual of mental disorders fourth edition text revision 精神疾患の診断・統計マニュアル 第 4 版新訂版
ECG	electrocardiogram　心電図
eGFR	estimated glomerular filtration rate　推算糸球体濾過量
FAS	full-analysis set　最大解析対象集団
γ-GTP	gamma-glutamyl transpeptidase　γ-グルタミルトランスペプチダーゼ
HDD	heavy drinking day　多量飲酒日
IMP	investigational medicinal product　治験薬
INR	international normalized ratio for pro-thrombin time　国際標準化比
ITT	intent-to-treat
MCV	mean corpuscular volume　平均赤血球容積
MedDRA	medical dictionary for regulatory activities　ICH 国際医薬用語集
NOS	not otherwise specified

略号	省略していない表現
PCS	potentially clinically significant
QTc	QT interval corrected for heart rate　心拍数補正 QT 間隔
QTcB	QT interval as corrected by Bazett's formula　Bazett の式で補正した QT 間隔
QTcF	QT interval as corrected by Fridericia's formula　Fridericia の式で補正した QT 間隔
QTcI	QT interval as corrected by individual correction　被験者ごとに補正した QT 間隔
SMQ	standardised MedDRA queries　MedDRA 標準検索式
SD	standard deviation　標準偏差
SS	safety set　安全性解析対象集団
TAC	total alcohol consumption　総飲酒量
TEAE	treatment-emergent adverse event　治験薬投与開始後に発現した有害事象
TLFB	timeline followback
ULN	upper limit of normal　基準範囲上限

名称（由来）	構造式
ナルメフェン塩酸塩水和物（JAN） Lu AA36143	 ・HCl・$2H_2O$

2.7.4　臨床的安全性

2.7.4.1　医薬品への曝露

2.7.4.1.1　総括的安全性評価計画及び安全性試験の記述

2.7.4.1.1.1　安全性評価に用いた臨床試験

「2.7.4 臨床的安全性」（以下，本概要）でのナルメフェンの安全性評価は，DSM-IV-TR 分類に基づくアルコール依存症患者を対象とした国内の 2 試験及び海外の 3 試験の安全性成績に基づいて行った。このうち，アルコール依存症患者を対象とした国内の 2 試験を評価資料とした。また，海外のアルコール使用障害患者を対象とした 5 試験の安全性成績の概略を，安全性の参考資料として示した。そのほかに，対象に日本人を含む臨床薬理試験 2 試験を評価資料，その他の臨床薬理試験及びその他の疾患を対象とした試験を参考資料として，重要な安全性成績を示した。



図 2.7.4.1.1-1　安全性評価に用いた臨床試験

[a]：評価資料
[b]：アルコール使用障害患者：飲酒をコントロールすることが難しい患者（DSM に基づく診断ではない）

(1)　国内試験

国内では，ナルメフェンの承認申請のために，アルコール依存症患者を対象とした試験を 2 試験，健康成人を対象とした試験を 1 試験実施した。

アルコール依存症患者を対象とした 2 試験の内訳は，プラセボ対照二重盲検試験（339-14-001）と，その完了例を対象とした継続長期試験（339-14-002）であり，これら 2 試験の成績をアルコール依存症患者でのナルメフェンの安全性を評価するうえでの評価資料とした。2 試験の概略を表 2.7.4.1.1-1 に示した。プラセボ対照二重盲検試験（339-14-001）では，ナルメフェン塩酸塩 10，20 mg 又はプラセボを盲検下で（以下，各投与群をナルメフェン 10 mg 群，20 mg 群，プラセボ群と示す），継続長期試験（339-14-002）ではナルメフェン塩酸塩 20 mg を，いずれの試験でも治療期として 24 週間，飲酒のおそれがある場合に飲酒の 1～2 時間前に 1 日 1 錠を限度として頓用した。継続長期試験（339-14-002）では，24 週間の治療期終了後に 4 週間の退薬期を設け，ナルメフェン塩酸塩 20 mg 又はプラセボを盲検下で頓用して，本剤に対する依存性及び離脱症状を評価した。

健康成人を対象とした 1 試験は，日本人でのナルメフェン塩酸塩 10 mg の薬物動態及び忍容性を検討した単回投与試験（339-102-00003）である。この試験も，評価資料と位置づけた。

(2) 海外試験

海外でアルコール依存症患者を対象として実施した 3 試験の結果を，安全性の参考資料として示した。その内訳は，プラセボ対照二重盲検試験が 2 試験（12014A，12023A），プラセボ対照二重盲検長期試験が 1 試験（12013A）である。これら 3 試験の概略を表 2.7.4.1.1-2 に示した。プラセボ対照二重盲検試験（12014A，12023A）では，治療期にナルメフェン塩酸塩 20 mg 又はプラセボを盲検下で 1 日 1 錠を限度として 24 週間頓用した。治療期終了後に退薬期を設け，治療期にナルメフェン群であった被験者はナルメフェン塩酸塩 20 mg 又はプラセボを，プラセボ群であった被験者はプラセボを，盲検下で 1 日 1 錠を限度として 4 週間頓用した。プラセボ対照二重盲検長期試験（12013A）では，ナルメフェン塩酸塩 20 mg 又はプラセボを盲検下で 1 日 1 錠を限度として 52 週間頓用した。

更に，海外でアルコール使用障害患者を対象として実施した 5 試験での結果を，安全性の参考資料として示した。その内訳は，可変用量でのプラセボ対照二重盲検試験（CPH-101-0801，CPH-101-0701），プラセボ対照二重盲検試験（CPH-101-0299，CPH-101-0399），可変用量での長期試験（CPH-101-0400）である（表 2.7.4.7.2-1 参照）。

そのほかに，海外で実施した臨床薬理試験 16 試験（健康成人対象 12 試験，肝機能障害患者対象 2 試験，腎機能障害患者対象 2 試験）及びその他の疾患を対象とした試験の安全性成績のうち，日本人及び白人を対象とした薬物動態試験（13505A）を評価資料，その他の試験を参考資料とし，いずれも本概要では重要な有害事象のみを示した。

表 2.7.4.1.1-1　　アルコール依存症の国内試験一覧表

試験略名（試験番号），資料番号 （実施国） ［資料の取扱い］	試験デザイン	ナルメフェン塩酸塩 投与量及び投与方法 （いずれも経口投与）	投与期間	安全性解析対象例数
プラセボ対照二重盲検試験 （339-14-001），5.3.5.1-01 （日本） ［評価］	多施設共同，無作為化，二重盲検，プラセボ対照，並行 3 群間比較	固定用量 10，20 mg，又はプラセボ 頓用，1 日 1 回まで	24 週間	計：677 例 ナルメフェン 10 mg 群：184 例 ナルメフェン 20 mg 群：248 例 プラセボ群：245 例
継続長期試験（339-14-002）， 5.3.5.2-01 （日本） ［評価］	多施設共同，非盲検，非対照（退薬期は二重盲検，プラセボ対照），継続長期	治療期：固定用量 20 mg 退薬期：固定用量 20 mg 又はプラセボ 頓用，1 日 1 回まで	治療期 24 週間 退薬期 4 週間	計：403 例 ナルメフェン 10 mg 群からの移行例：94 例 ナルメフェン 20 mg 群からの移行例：137 例 プラセボ群からの移行例：172 例

表 2.7.4.1.1-2　　アルコール依存症の海外試験一覧表

試験略名（試験番号），資料番号 （実施国） ［資料の取扱い］	試験デザイン	ナルメフェン塩酸塩 投与量及び投与方法 （いずれも経口投与）	投与期間	安全性解析対象例数
プラセボ対照二重盲検試験（12014A），5.3.5.1-02 （オーストリア，ドイツ，フィンランド，スウェーデン） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	治療期：固定用量 20 mg 又はプラセボ 退薬期：固定用量 20 mg 又はプラセボ 頓用，1 日 1 回まで	治療期 24 週間 退薬期 4 週間	計：598 例 ナルメフェン群：302 例 プラセボ群：296 例
プラセボ対照二重盲検試験（12023A），5.3.5.1-03 （ベルギー，チェコ，スペイン，フランス，イタリア，ポーランド，ポルトガル） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	治療期：固定用量 20 mg 又はプラセボ 退薬期：固定用量 20 mg 又はプラセボ 頓用，1 日 1 回まで	治療期 24 週間 退薬期 4 週間	計：678 例 ナルメフェン群：341 例 プラセボ群：337 例
プラセボ対照二重盲検長期試験（12013A），5.3.5.1-04 （チェコ，エストニア，英国，ハンガリー，リトアニア，ラトビア，ポーランド，ロシア，スロバキア，ウクライナ） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	固定用量 20 mg 又はプラセボ 頓用，1 日 1 回まで	52 週間	計：665 例 ナルメフェン群：501 例 プラセボ群：164 例

2.7.4.1.1.2　安全性の評価

(1)　国内試験

(a)　安全性成績の提示

国内のアルコール依存症患者を対象とした 24 週間のプラセボ対照二重盲検試験（339-14-001）（以下，短期投与）の結果は，併合せず安全性成績を示した。長期投与の安全性を検討するため，継続長期試験（339-14-002）に移行した被験者（継続長期試験の安全性解析対象）を対象に，プラセボ対照二重盲検試験の治療期 24 週間と継続長期試験の治療期 24 週間での安全性成績を併合した結果を示した（以下，長期投与）。長期投与の安全性データは，ナルメフェン 10 mg 群及び 20 mg 群からの移行例（以下，ナルメフェン投与群全体からの移行例）の結果を中心に記載した。また，本剤の依存性及び離脱症状は，339-14-002 試験の退薬期及び退薬期終了後 4 週間（後観察期）での結果を示した。更に，基本語別の有害事象，副作用の解析では，339-14-001 試験の安全性解析対象のうち，339-14-001 試験又は 339-14-002 試験でナルメフェンを投与された全被験者（339-14-001 試験でナルメフェン塩酸塩 20 mg 又は 10 mg を投与された被験者，及び 339-14-001 試験でプラセボが投与され 339-14-002 試験でナルメフェンが投与された被験者）を対象に，339-14-001 試験の治療期 24 週間と，339-14-002 試験の治療期 24 週間及び退薬期 4 週間での安全性成績を併合した結果も示した。

健康成人を対象とした単回投与試験（339-102-00003）の結果は，本概要では死亡及び重篤な有害事象のみを示した。

(b)　安全性のデータセット

国内のアルコール依存症患者を対象とした試験は，いずれも治験薬を投与された被験者を安全性解析対象とした。この 2 試験のデータセットを表 2.7.4.1.1-3 に示した。

健康成人を対象とした単回投与試験（339-102-00003）は，治験薬を投与された被験者 7 例を安全性解析対象とした。

表 2.7.4.1.1-3　　安全性のデータセット：アルコール依存症の国内試験

試験略名 （試験番号）	安全性解析対象	
	ナルメフェン群	プラセボ群
プラセボ対照二重盲検試験 （339-14-001）	10 mg：184 例 20 mg：248 例	245 例
継続長期試験 [a] （339-14-002）	治療期：403 例 ナルメフェン 10 mg 群からの移行例：94 例 ナルメフェン 20 mg 群からの移行例：137 例 プラセボ群からの移行例：172 例 退薬期：172 例	治療期：－ 退薬期：171 例

[a]：継続長期試験の安全性解析対象を用いて，プラセボ対照二重盲検試験（339-14-001）の治療期 24 週間と継続長期試験（339-14-002）の治療期 24 週間での安全性成績を併合した（長期投与）。
なお，339-14-001 試験又は 339-14-002 試験でナルメフェンを投与された全被験者（339-14-001 試験でナルメフェン塩酸塩 20 mg 又は 10 mg を投与された被験者，及び 339-14-001 試験でプラセボが投与され 339-14-002 試験でナルメフェンが投与された被験者）は，604 例であった。

(c)　安全性の評価方法：アルコール依存症の国内試験（339-14-001，339-14-002）

安全性評価のための主要な試験である，国内のアルコール依存症患者を対象とした試験（339-14-001，339-14-002）で用いられた，主な安全性評価項目及び方法の概略を示した。なお，健康成人を対象とした単回投与試験（339-102-00003）で用いた安全性評価項目及び方法は，「2.7.6 個々の試験のまとめ」及び治験総括報告書に記載した。

i)　有害事象

プラセボ対照二重盲検試験（339-14-001）では，同意取得以降に発現又は悪化した事象を有害事象とした。継続長期試験（339-14-002）では，339-14-001 試験終了以降に発現又は悪化した有害事象を，この試験の有害事象とした。重症度は，軽度，中等度，高度の 3 段階で判定した。治験薬投与開始後に発現した有害事象と治験薬との関連性を，「関連性は否定できる」又は「関連性は否定できない」の 2 分類で判断した。「関連性は否定できない」と判断された有害事象を，副作用（治験薬との関連性が否定できない有害事象）とした。

治験責任医師等により報告された有害事象名は MedDRA/J version 19.0 を用いて読替えた。集計には，治験薬投与後に発現した有害事象を用いた。

- 重症度別の検討：同一被験者で同一事象が 2 回以上発現した場合，重症度の高い方を集計対象とした。
- 初回発現時期別の検討：ナルメフェンの投与開始日を起点として初回発現時期別に集計した。したがって，長期投与（339-14-001，339-14-002 併合）での初回発現時期の起点は，339-14-001 試験でナルメフェン 20 mg 群又は 10 mg 群であった被験者は，339-14-001 試験のナルメフェン投与開始日とし，339-14-001 試験でプラセボ群であった被験者は，339-14-002 試験のナルメフェン投与開始日とした。長期投与では，339-14-001 試験の治療期，339-14-002 試験の治療期及び退薬期のうち，ナルメフェンが投与された期間の有害事象を集計した。

- 内因性要因の検討：性別，年齢別（65 歳未満，65 歳以上），BMI 別（25 未満，25 以上 30 未満，30 以上）で，サブグループ解析した。
- 注目すべき有害事象の検討：以下の事象を定義し，集計した。定義は表 2.7.4.7.1-1 に示した。
  - 事故及び損傷関連有害事象
  - 痙攣関連有害事象
  - うつ病関連有害事象
  - 薬物使用障害関連有害事象
  - 薬剤に関連する肝障害，明確にアルコール関連と報告された肝障害
  - 横紋筋融解症及びミオパチー関連有害事象
  - 精神系有害事象
  - 自殺関連有害事象
  - 睡眠障害に関連する夜間の症状，睡眠障害に関連する日中の症状

ii) 臨床検査

臨床検査は，中央臨床検査機関で集中測定した。

治験薬投与後の値について，臨床的に重要な変動が認められた被験者の割合，及び薬物性肝障害に関連する臨床検査値の変動が認められた被験者の割合を求めた。基準はそれぞれ表 2.7.4.7.1-2，表 2.7.4.7.1-3 に示した。

iii) バイタルサイン（血圧，脈拍数），体重

収縮期血圧，拡張期血圧，脈拍数，及び体重を測定した。治験薬投与後の値について，臨床的に重要な変動が認められた被験者の割合を求めた（基準：表 2.7.4.7.1-4 参照）。

iv) 心電図

治験依頼者が提供した心電計を用いて，12 誘導心電図検査を実施した。心電図パラメータは心電図中央判読機関が測定した。治験薬投与後の値について，臨床的に重要な変動が認められた被験者の割合を求めた（基準：表 2.7.4.7.1-5 参照）。また，QTcB 及び QTcF について，カテゴリカル解析を行った。

v) C-SSRS

プラセボ対照二重盲検試験（339-14-001）のスクリーニング時に，ベースライン時評価（自殺関連事象及び自殺念慮の既往の評価）を行い，それ以降は継続長期試験（339-14-002）も含め，治験実施計画書で規定した時期に，前回の治験診察時以降の自殺傾向に焦点をおいたベースライン後評価を行った。

vi) 依存性調査（339-14-002 のみ）

依存性調査は，ナルメフェンに対する依存性を評価するための評価指標である。10 項目か

らなる依存性調査票 A，6 項目からなる依存性調査票 B のそれぞれの項目に対して，1（非常に）から 4（いいえ）の 4 段階で評価した。依存性調査票 A では退薬期終了時に依存性を調査し，依存性調査票 B では退薬期終了の 4 週間後に離脱症状を調査した。各質問項目について，退薬期の投与群ごとに頻度集計を行った。

(2) 海外試験

海外試験の成績は主に，欧州で提出した CTD「2.7.4 臨床的安全性」（資料番号 5.3.5.3-03）のデータを使用した。

(a) 安全性成績の提示

海外でアルコール依存症患者を対象に実施した 3 試験（12014A，12023A，12013A）の試験デザインは類似しており，特に治験薬投与開始から 6 ヵ月（24 週間）はほとんど同一のデザインであった。また，これら 3 試験の安全性成績は，互いに大きく異ならなかった。したがって，本概要では，海外のアルコール依存症患者を対象とした 3 試験（12014A，12023A，12013A）の安全性データを併合し，結果を示した（以下，アルコール依存症の海外試験併合）。更に一部の評価では，長期投与の安全性を検討するため，プラセボ対照二重盲検長期試験（12013A）単独での安全性成績も示した。

海外のアルコール使用障害患者を対象とした 5 試験（CPH-101-0801，CPH-101-0701，CPH-101-0299，CPH-101-0399，CPH-101-0400）のデザインは，投与期間，盲検化，用量などが互いに異なる。しかし，本概要では，アルコール依存症患者での安全性成績を補完するため，これら 5 試験のデータを併合し，安全性成績の概略を示した（以下，アルコール使用障害の海外試験併合）。

海外の臨床薬理試験及びその他の疾患を対象とした試験の結果は，本概要では，死亡及び重篤な有害事象を示した。更に，QTc 評価試験（BTT31-CD005），アルコールとの薬物相互作用試験（13513A），腎機能障害患者を対象とした薬物動態試験（15084A，22）及び肝機能障害患者を対象とした薬物動態試験（12417A，21）の安全性成績の要約を，それぞれ「2.7.4.4.2 心電図の評価」，「2.7.4.5.3 薬物相互作用」，「2.7.4.5.1 内因性要因」に示した。

(b) 安全性のデータセット

アルコール依存症の海外試験併合（12014A，12023A，12013A）では，無作為化例から，治験薬の服薬記録がない，かつすべての治験薬を返却した被験者を除いた被験者を治験薬投与例とし，安全性解析対象に用いた。データセットを表 2.7.4.1.1-4 に示した。

海外のプラセボ対照二重盲検試験（12014A，12023A）では，ベースライン時に DRL が Medium 以上の被験者を対象とし，プラセボ対照二重盲検長期試験（12013A）では，それに加えて Low の被験者も対象に含めて，試験を実施した。しかし，海外で製造販売承認を取得した対象は，ベースライン時及び無作為化時で DRL が High 又は Very high であった被験者（以下，DRL が High 以上であった被験者）であった。国内試験の対象は海外の製造販売承認を取得した対象と

同じ，DRL が High 以上であった被験者であり，本概要では，アルコール依存症の海外試験併合についても，DRL が High 以上であった被験者での安全性成績を中心に示した。

アルコール使用障害の海外試験併合は，すべての無作為化例を安全性解析対象とし（各総括報告書では ITT 集団と示した），その例数はナルメフェン群 689 例，プラセボ群 361 例であった。各試験の安全性解析対象は表 2.7.4.7.2-1 に示した。

表 2.7.4.1.1-4　　安全性のデータセット：アルコール依存症の海外試験

試験略名（試験番号）	安全性解析対象	
	ナルメフェン群	プラセボ群
プラセボ対照二重盲検試験（12014A）	302 例	296 例
プラセボ対照二重盲検試験（12023A）	341 例	337 例
プラセボ対照二重盲検長期試験（12013A）	501 例	164 例
計：アルコール依存症の海外試験併合	1144 例	797 例
計：DRL が High 以上であった被験者	475 例	369 例

＜資料番号 5.3.5.3-03：Panel 2，Table 10 より作成＞

(c)　安全性の評価方法：アルコール依存症の海外試験（12014A，12023A，12013A）

安全性評価のための主要な試験である，海外のアルコール依存症患者を対象とした試験（12014A，12023A，12013A）で用いられた，主な安全性評価項目及び方法の概略を示した。各安全性評価項目の実施時期は，治験実施計画書での規定に準じた。臨床検査，バイタルサイン，体重，及び心電図の評価方法は国内試験と同様であったため，本項では記載を省略した。なお, アルコール使用障害患者対象試験及び臨床薬理試験で用いた安全性評価項目及び方法は,「2.7.6 個々の試験のまとめ」及び治験総括報告書に記載した。

i)　有害事象

重症度の定義は，国内のアルコール依存症患者を対象とした試験と同様であった。治験薬との関連性は, Probable, Possible, Not related の 3 分類で判断した。このうち, Probable 又は Possible と判断された有害事象を，副作用とした。

欧州の CTD「2.7.4 臨床的安全性」では，海外のアルコール依存症患者を対象とした試験（12014A，12023A，12013A）で発現した有害事象は，MedDRA version 13.0 を用いて読替えた用語で集計した。本申請に際して，更に MedDRA/J version 19.0 を用いて読替え，再集計した。

なお，海外のアルコール使用障害患者を対象とした試験，臨床薬理試験及びその他の疾患を対象とした試験で発現した有害事象は，各総括報告書で用いられた用語で示した。海外のアルコール使用障害患者を対象とした試験の総括報告書で用いられた MedDRA version は，CPH-101-0801 と CPH-101-0701 が 5.1, CPH-101-0299 が 3.3, CPH-101-0399 が 3.1, CPH-101-0400 が 4.0 であった。本概要では MedDRA/J version 5.1 を用いて示した。

集計には，治験薬投与後に発現した有害事象を用いた。アルコール依存症の海外試験併合で

は，国内試験と同様に内因性要因（性別，年齢，BMI）及び注目すべき有害事象を検討した。注目すべき有害事象の定義は，国内試験と同様である（表 2.7.4.7.1-1 参照）。

2.7.4.1.2　全般的な曝露状況

2.7.4.1.2.1　被験者の内訳

(1)　アルコール依存症の国内試験

####### (a)　短期投与（339-14-001）

アルコール依存症の国内短期投与での被験者の内訳及び中止理由を，表 2.7.4.1.2-1 に示した。

無作為化例はナルメフェン 20 mg 群 248 例，10 mg 群 185 例，プラセボ群 245 例，治験薬投与例は 20 mg 群 248 例，10 mg 群 184 例，プラセボ群 245 例であった。中止例の割合は 20 mg 群 23.8%，10 mg 群 24.5%，プラセボ群 10.6%で，ナルメフェン各投与群でプラセボ群と比較して高かった。最も多かった中止理由はいずれの投与群でも「有害事象」であり，20 mg 群 18.1%，10 mg 群 18.5%，プラセボ群 4.5%であった。

表 2.7.4.1.2-1　　被験者の内訳及び中止理由：アルコール依存症の国内短期投与
（339-14-001，無作為化集団）

	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
Subjects	N (%)[a]	N (%)[a]	N (%)[a]	N (%)[a]	N (%)[a]
Randomized	245	248	185	433	678
Treated (SS)	245	248	184	432	677
Completed	219 (89.4)	189 (76.2)	139 (75.5)	328 (75.9)	547 (80.8)
Discontinued	26 (10.6)	59 (23.8)	45 (24.5)	104 (24.1)	130 (19.2)
Subject requested to be withdrawn from the study	9 (3.7)	10 (4.0)	8 (4.3)	18 (4.2)	27 (4.0)
Occurrence of an adverse event making continuation of trial difficult	11 (4.5)	45 (18.1)	34 (18.5)	79 (18.3)	90 (13.3)
Psychosocial therapy other than BRENDA is needed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Change in the dose of the investigational medicinal product is needed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Use of a prohibited concomitant drug and therapy	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	1 (0.1)
Discovery that the subject was enrolled in the trial despite a violation of the inclusion or exclusion criteria	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)	2 (0.3)
Suspected pregnancy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Judgment by the investigator or subinvestigator that subject withdrawal is necessary for other reasons	5 (2.0)	3 (1.2)	2 (1.1)	5 (1.2)	10 (1.5)

[a]:Percentages calculated vs number of subjects treated.
＜資料番号 5.3.5.1-01：Table 14.1.1.1-2＞

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内継続長期試験（339-14-002）の治療期での被験者の内訳及び中止理由を，表 2.7.4.1.2-2 に示した。

プラセボ対照二重盲検試験（339-14-001）を完了した被験者のうち，405 例が 339-14-002 試験に移行した。治験薬投与例は 403 例であり，このうちナルメフェン投与群全体からの移行例 231 例，プラセボ群からの移行例 172 例であった。339-14-002 試験の治療期での中止例の割合はナルメフェン投与群全体からの移行例で 9.1%，プラセボ群からの移行例で 22.7%であった。最も多かった中止理由は，ナルメフェン投与群全体からの移行例で「被験者の中止の申し出」が 5.2%，プラセボ群からの移行例で「有害事象」が 18.6%であった。ナルメフェン投与群全体からの移行例で，中止理由が「有害事象」であった被験者の割合は，3.9%であった。

339-14-002 試験の退薬期及び後観察期での被験者の内訳及び中止理由を，表 2.7.4.7.1-6 に示した。

退薬期への移行例は 343 例で，このうちナルメフェン群 172 例，プラセボ群 171 例であった。

退薬期での中止例はナルメフェン群の 1 例（0.6%）のみであり，その中止理由は「有害事象」であった。

表 2.7.4.1.2-2　被験者の内訳及び中止理由：アルコール依存症の国内継続長期試験（339-14-002）－ 治療期

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
Subjects	N (%)[a]	N (%)[a]	N (%)[a]	N (%)[a]	N (%)[a]
Advanced to study 339-14-002	172	139	94	233	405
Treated in Study 339-14-002 (SS)	172	137	94	231	403
Advanced to run-out period	133 (77.3)	126 (92.0)	84 (89.4)	210 (90.9)	343 (85.1)
Discontinued in treatment period	39 (22.7)	11 (8.0)	10 (10.6)	21 (9.1)	60 (14.9)
Subject requested to be withdrawn from the study	5 (2.9)	4 (2.9)	8 (8.5)	12 (5.2)	17 (4.2)
Occurrence of an adverse event making continuation of trial difficult	32 (18.6)	7 (5.1)	2 (2.1)	9 (3.9)	41 (10.2)
Psychosocial therapy other than BRENDA is needed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Change in the dose of the investigational medicinal product is needed	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discovery that the subject was enrolled in the trial despite a violation of the inclusion or exclusion criteria	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suspected pregnancy of female subject	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Judgment by the investigator or subinvestigator that subject withdrawal is necessary for other reasons	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)

[a]:Percentages calculated vs number of subjects treated in study 339-14-002.

＜資料番号 5.3.5.2-01：Table 14.1.1.1-2＞

(2)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合で DRL が High 以上であった被験者の内訳を，表 2.7.4.1.2-3 に示した。また，治療期の中止理由を表 2.7.4.7.2-2，退薬期の中止理由を表 2.7.4.7.2-3 に示した。

DRL が High 以上であった被験者で，無作為化例はナルメフェン群 480 例，プラセボ群 374 例，治験薬投与例はナルメフェン群 475 例，プラセボ群 369 例であった。治療期全体での中止例の割合は，ナルメフェン群 47.2%，プラセボ群 36.0%であった。最も多かった中止理由はいずれの投与群でも「被験者の中止の申し出」であり，ナルメフェン群 14.9%，プラセボ群 12.7%であった。中止理由が「有害事象」であった被験者の割合は，ナルメフェン群 13.7%，プラセボ群 5.1%であった。

アルコール依存症の海外試験併合全体で，無作為化例はナルメフェン群 1173 例，プラセボ群は 824 例，治験薬投与例はナルメフェン群 1144 例，プラセボ群 797 例であった（資料番号 5.3.5.3-03：Panel 4 参照）。治療期全体での中止例の割合は，ナルメフェン群 42.9%，プラセボ群

33.9%であった。中止理由が「有害事象」であった被験者の割合は，ナルメフェン群 10.5%，プラセボ群 3.8%であった（資料番号 5.3.5.3-03：Panel 5 参照）。

表 2.7.4.1.2-3　被験者の内訳：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

	Placebo n %	Nalmefene n %	Total n %
Patients Randomised	374	480	854
Patients Treated	369	475	844
Patients Completed	236 (64.0)	251 (52.8)	487 (57.7)
Patients Withdrawn	133 (36.0)	224 (47.2)	357 (42.3)
Efficacy Data Sets			
Full Analysis Set	364	460	824

＜資料番号 5.3.5.3-03：Table 10＞

(3)　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験併合での被験者の内訳及び中止理由を表 2.7.4.7.2-4 に示した。

アルコール使用障害の海外試験併合で，無作為化例はナルメフェン投与群 689 例，プラセボ群 361 例であった。中止例の割合はナルメフェン投与群 22.0%～46.8%，プラセボ群 37.4%で，最も多かった中止理由は，ナルメフェン 10 mg，20 mg，及び 40 mg 群では「有害事象」，5 mg 群及びプラセボ群では「追跡不能」であった。中止理由が「有害事象」であった被験者の割合は，ナルメフェン投与群 5.9%～17.0%，プラセボ群 3.0%であった。

2.7.4.1.2.2　曝露状況

(1)　アルコール依存症の国内試験

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与での治験薬の曝露状況を表 2.7.4.1.2-4，服薬状況を表 2.7.4.1.2-5 に示した。

ナルメフェン 20 mg 群 248 例，10 mg 群 184 例，プラセボ群 245 例に治験薬が投与され，ナルメフェンの曝露量は 20 mg 群で 73.0 人・年，10 mg 群で 56.7 人・年であった。

治験薬服薬日数の割合は，平均値で 20 mg 群 70.56%，10 mg 群 75.06%，プラセボ群 86.95%，中央値で 20 mg 群 85.29%，10 mg 群 88.27%，プラセボ群 95.82%であった。時期別の治験薬服薬日数の割合をみると，平均値は治療期 4 週に 20 mg 群 76.59%，10 mg 群 80.72%，プラセボ群 91.57%，治療期 24 週に 20 mg 群 78.06%，10 mg 群 78.83%，プラセボ群 85.45%であり，投与期間を通して大きく変わらなかった。中央値でも同様の結果であった（表 2.7.4.7.1-7 参照）。

表 2.7.4.1.2-4　　治験薬の曝露状況 : アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	n	PY	n	PY	n	PY	n	PY
Time in study	245	105.9	248	92.9	184	70.0	432	162.9
Exposure	244	92.6	248	73.0	182	56.7	430	129.6

Time in study = Total number of patients days (patients years [PY]) in study.

Exposure = Total number of patients days (PY) with IMP intake. Includes only patients with TLFB records.

＜資料番号 5.3.5.1-01：Table 14.1.1.3-1＞

表 2.7.4.1.2-5　　服薬状況：アルコール依存症の国内短期投与（339-14-001）

				IMP	
Treatment group	N	Summary statistics	TLFB days	Days	(%)
Placebo	244	Mean	158.4	138.6	86.95
		SD	30.6	38.8	18.29
		Min	7	1	7.7
		Median	168.0	156.0	95.82
		Max	182	175	100.0
		P10	161.0	84.0	57.89
		P25	161.0	121.5	80.73
		P75	168.0	165.0	99.41
		P90	175.0	168.0	100.00
Nalmefene 20 mg	248	Mean	136.8	107.4	70.56
		SD	57.5	63.1	31.59
		Min	1	1	1.1
		Median	164.5	139.0	85.29
		Max	176	175	100.0
		P10	14.0	2.0	17.86
		P25	161.0	45.5	43.82
		P75	168.0	161.0	98.78
		P90	174.0	168.0	100.00
Nalmefene 10 mg	182	Mean	140.3	113.7	75.06
		SD	54.2	58.6	28.35
		Min	2	1	1.8
		Median	166.0	143.0	88.27
		Max	189	176	100.0
		P10	28.0	10.0	28.57
		P25	161.0	72.0	57.14
		P75	169.0	161.0	98.82
		P90	175.0	168.0	100.00

表 2.7.4.1.2-5　　服薬状況：アルコール依存症の国内短期投与（339-14-001）（続き）

				IMP	
Treatment group	N	Summary statistics	TLFB days	Days	(%)
Nalmefene total	430	Mean	138.3	110.1	72.46
		SD	56.1	61.2	30.31
		Min	1	1	1.1
		Median	165.0	140.5	86.40
		Max	189	176	100.0
		P10	14.5	4.0	20.53
		P25	161.0	54.0	52.38
		P75	168.0	161.0	98.80
		P90	175.0	168.0	100.00

治験薬服薬日数の割合（%）= 治験薬を服薬した日数/TLFB 日数
＜資料番号 5.3.5.1-01：Table 14.1.1.3-2 より作成＞

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与での治験薬の曝露状況を表 2.7.4.1.2-6，国内継続長期試験（339-14-002）の退薬期での治験薬の曝露状況を表 2.7.4.7.1-8 に示した。また，国内長期投与及び 339-14-002 試験の退薬期での服薬状況を表 2.7.4.1.2-7 に示した。

国内長期投与で 403 例に治験薬が投与され，このうちナルメフェン投与群全体からの移行例 231 例，プラセボ群からの移行例 172 例であった。ナルメフェンの曝露量は，ナルメフェン投与群全体からの移行例では国内長期投与で 168.0 人・年，プラセボ群からの移行例では 339-14-002 試験の治療期で 51.6 人・年であった。退薬期のナルメフェンの曝露量は，ナルメフェン群で 10.0 人・年であった。

国内長期投与及び退薬期での治験薬服薬日数の割合は，平均値でナルメフェン投与群全体からの移行例 80.14%，プラセボ群からの移行例 83.45%，中央値でナルメフェン投与群全体からの移行例 91.23%，プラセボ群からの移行例 90.47%であった。時期別の治験薬服薬日数の割合をみると，平均値はナルメフェン投与群全体からの移行例で治療期 4 週に 88.57%，治療期 24 週に 79.82%，治療期 48 週に 75.92%であり，プラセボ群からの移行例で治療期 4 週に 92.90%，治療期 24 週に 87.40%，治療期 48 週に 78.36%であった。中央値でも同様の結果であった（表 2.7.4.7.1-9 参照）。

表 2.7.4.1.2-6　治験薬の曝露状況 : アルコール依存症の国内長期投与（339-14-001, 339-14-002 併合）

Overall Time in Study and Exposure in Study 339-14-001 Treatment Period

Treatment group of study 339-14-001	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	n	PY	n	PY	n	PY	n	PY
Time in study	172	79.1	137	62.7	94	43.5	231	106.2
Exposure	172	70.6	137	51.9	94	36.2	231	88.1

Overall Time in Study and Exposure in Study 339-14-002 Treatment Period

Treatment group of study 339-14-001	Placebo		Nalmefene						Total	
			20 mg		10 mg		Total			
	n	PY	n	PY	n	PY	n	PY	n	PY
Time in study	172	66.8	137	61.3	94	41.3	231	102.6	403	169.4
Exposure	172	51.6	137	48.3	94	31.6	231	79.9	403	131.5

Time in study = Total number of patients days (patients years [PY]) in study.

Exposure = Total number of patients days (PY) with IMP intake. Includes only patients with TLFB records.

＜資料番号 5.3.5.2-01：Table 14.1.1.3-1，Table 14.1.1.3-2 より作成＞

表 2.7.4.1.2-7　服薬状況 : アルコール依存症の国内長期投与（339-14-001, 339-14-002 併合）及び退薬期

Treatment group of study 339-14-001	N	Summary statistics	TLFB days	IMP	
				Days	(%)
Placebo	172	Mean	330.5	276.0	83.45
		SD	66.6	86.0	18.61
		Min	166	50	13.9
		Median	361.0	306.5	90.47
		Max	391	377	99.7
		P10	195.0	156.0	54.57
		P25	352.0	191.0	75.48
		P75	366.0	353.0	97.81
		P90	372.0	363.0	99.64
Nalmefene 20 mg	137	Mean	356.1	286.9	80.47
		SD	27.5	88.5	23.74
		Min	172	36	9.8
		Median	362.0	327.0	91.51
		Max	374	372	100.0
		P10	351.0	158.0	43.65
		P25	357.0	233.0	69.09
		P75	365.0	357.0	98.90
		P90	370.0	363.0	99.72

表 2.7.4.1.2-7　服薬状況：アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）及び退薬期（続き）

Treatment group of study 339-14-001	N	Summary statistics	TLFB days	IMP	
				Days	(%)
Nalmefene 10 mg	94	Mean	354.3	283.0	79.67
		SD	34.9	96.1	25.36
		Min	198	5	1.3
		Median	364.0	328.5	90.89
		Max	379	378	99.7
		P10	343.0	112.0	42.43
		P25	358.0	243.0	71.99
		P75	370.0	357.0	98.81
		P90	372.0	364.0	99.46
Nalmefene total	231	Mean	355.3	285.3	80.14
		SD	30.7	91.5	24.36
		Min	172	5	1.3
		Median	363.0	328.0	91.23
		Max	379	378	100.0
		P10	351.0	151.0	42.62
		P25	358.0	234.0	69.09
		P75	366.0	357.0	98.90
		P90	372.0	363.0	99.72
Total	403	Mean	344.7	281.4	81.55
		SD	50.7	89.2	22.12
		Min	166	5	1.3
		Median	363.0	319.0	90.76
		Max	391	378	100.0
		P10	259.0	153.0	46.30
		P25	358.0	209.0	71.86
		P75	366.0	356.0	98.56
		P90	372.0	363.0	99.72

治験薬服薬日数の割合（%）＝ 治験薬を服薬した日数/TLFB 日数
＜資料番号 5.3.5.3-01：Table 3.1-1 より作成＞

(2)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合で DRL が High 以上であった被験者での治験薬の曝露状況を表 2.7.4.1.2-8，治療期の服薬状況を表 2.7.4.1.2-9 に示した。

DRL が High 以上であった被験者では，ナルメフェン群 475 例，プラセボ群 369 例が治験薬投与例で，治療期と退薬期でのナルメフェンの総曝露量は 126 人・年であった。

治療期での治験薬服薬日数の割合（平均値，以下同様）は，ナルメフェン群 56.2%，プラセボ群 71.1%であり，ナルメフェン群の 25%以上の被験者で服薬日数の割合が 84.9%以上，プラセボ群の 25%以上の被験者で服薬日数の割合が 92.4%以上であった。時期別にみると，治験薬服薬日数の割合は徐々に低下し，治療期 4 週にナルメフェン群 65.7%，プラセボ群 77.0%，治療期 24 週にナルメフェン群 56.5%，プラセボ群 69.7%，治療期 52 週にナルメフェン群 46.1%，プラセボ

群 56.4%であった（表 2.7.4.7.2-5 参照）。

アルコール依存症の海外試験併合で DRL が High 以上であった被験者での退薬期の服薬状況を表 2.7.4.7.2-6 に示した。

退薬期の治験薬服薬日数の割合は，ナルメフェンーナルメフェン群（治療期，退薬期共にナルメフェンが投与された被験者，以下同様）及びナルメフェンープラセボ群（治療期にナルメフェン，退薬期にプラセボが投与された被験者，以下同様）では，プラセボープラセボ群（治療期，退薬期共にプラセボが投与された被験者，以下同様）と比較して低かった（ナルメフェンーナルメフェン群 59.3%, ナルメフェンープラセボ群 56.5%, プラセボープラセボ群 70.4%, 以下同順）。

アルコール依存症の海外試験併合全体では，ナルメフェン群 1144 例，プラセボ群 797 例が治験薬投与例で，治療期と退薬期でのナルメフェンの総曝露量は 312 人・年であった（資料番号 5.3.5.3-03：Panel 13 参照）。治療期での治験薬服薬日数の割合は，ナルメフェン群で 50.8%，プラセボ群で 62.1%であり，ナルメフェン群の 25%以上の被験者で服薬日数の割合が 81.5%以上，プラセボ群の 25%以上の被験者で服薬日数の割合が 88.7%以上であった（資料番号 5.3.5.3-03：Panel 14 参照）。

表 2.7.4.1.2-8　治験薬の曝露状況：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

	Treatment period				Run-out period					
	Placebo		Nalmefene		Placebo-Placebo		Nalmefene-Placebo		Nalmefene-Nalmefene	
	n	PY	n	PY	n	PY	n	PY	n	PY
Time in study	369	164	475	227	208	16	83	7	91	8
Exposure[a]	365	111	470	122	192	11	72	4	78	4

Time in study = total number of patient days (patient years [PY]) in the specified period

Exposure = total number of patient days (PY) with IMP intake in the specified period

[a]:Includes only patients with TLFB records.

＜資料番号 5.3.5.3-03：Panel 20＞

表 2.7.4.1.2-9　　服薬状況：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

Treatment group	Patients N	Summary statistics	TLFB days	IMP Days	IMP %
Placebo	365	Mean	157	111	71.1
		Min	5	1	2.0
		Max	448	365	100.0
		Median	168	107	75.3
		p10	35	24	33.8
		p25	113	57	55.4
		p75	175	157	92.4
		p90	222	171	98.8
Nalmefene	470	Mean	164	95	56.2
		Min	1	1	0.6
		Max	468	387	100.0
		Median	168	76	55.8
		p10	28	5	13.7
		p25	77	26	29.7
		p75	182	149	84.9
		p90	364	178	96.4

TLFB days with IMP and % days with IMP are summary statistics based on individual patient.
＜資料番号 5.3.5.3-03：Panel 21＞

(3)　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験併合では，689 例にナルメフェンが投与された。ナルメフェンの曝露量は 250 人･年であり，20 mg 以上のナルメフェンが曝露されたのは 212 人･年であった。アルコール使用障害の海外試験併合での治験薬の 1 日平均投与量及び投与期間を表 2.7.4.7.2-7 に示した。

2.7.4.1.3　　治験対象集団の人口統計学的特性及びその他の特性

2.7.4.1.3.1　アルコール依存症の国内試験

(1)　短期投与（339-14-001）

アルコール依存症の国内短期投与での人口統計学的特性及びベースライン時の体重，身長，BMI を表 2.7.4.1.3-1，ベースライン時の飲酒状況を表 2.7.4.1.3-2 に示した。

人口統計学的特性及びその他の特性は，性別を除き，ナルメフェン 20 mg 群，10 mg 群及びプラセボ群で同様であった。試験全体で，性別は男性が 68.5%，女性が 31.5%であり，投与群ごとにみると，男性が 20 mg 群 69.8%，10 mg 群 73.9%，プラセボ群 63.3%であった。平均年齢は 48.7 歳（年齢範囲 20～80 歳）であり，65 歳以上の被験者の割合は 11.7%であった。ベースライン時の HDD 数（平均値，以下同様）は 22.99 日/月，TAC は 94.58 g/日であった。

表 2.7.4.1.3-1　人口統計学的特性，ベースライン時の体重，身長，BMI：アルコール依存症の国内短期投与（339-14-001）

Characteristics		Placebo (N=245)	Nalmefene 20 mg (N=248)	Nalmefene 10 mg (N=184)	Nalmefene Total (N=432)	Total (N=677)
Age (years)	n	245	248	184	432	677
	Mean	48.1	49.0	49.1	49.1	48.7
	SD	11.4	12.1	11.9	12.0	11.8
	Min	20	20	21	20	20
	Median	48.0	49.0	50.0	49.0	49.0
	Max	77	80	78	80	80
Age categorization (n [%])	< 65	218 (89.0)	217 (87.5)	163 (88.6)	380 (88.0)	598 (88.3)
	65 <=	27 (11.0)	31 (12.5)	21 (11.4)	52 (12.0)	79 (11.7)
Sex (n [%])	Female	90 (36.7)	75 (30.2)	48 (26.1)	123 (28.5)	213 (31.5)
	Male	155 (63.3)	173 (69.8)	136 (73.9)	309 (71.5)	464 (68.5)
Body weight (kg)	n	245	248	184	432	677
	Mean	64.00	64.21	65.84	64.91	64.58
	SD	12.04	12.15	13.18	12.61	12.41
	Min	39.1	37.6	38.6	37.6	37.6
	Median	63.80	63.35	65.35	64.10	64.00
	Max	105.4	94.7	115.0	115.0	115.0
Height (cm)	n	245	248	184	432	677
	Mean	166.04	166.27	167.33	166.72	166.47
	SD	8.62	8.51	8.22	8.40	8.48
	Min	140.6	144.1	145.5	144.1	140.6
	Median	165.50	167.60	168.20	168.00	167.40
	Max	189.5	189.0	184.7	189.0	189.5
BMI (kg/m^2)[a]	n	245	248	184	432	677
	Mean	23.11	23.09	23.36	23.20	23.17
	SD	3.39	3.23	3.50	3.35	3.36
	Min	16.5	16.1	16.2	16.1	16.1
	Median	22.65	22.76	23.20	22.88	22.80
	Max	35.0	33.6	38.2	38.2	38.2
BMI categorization 1 (n [%])	< 18.5	13 (5.3)	14 (5.6)	14 (7.6)	28 (6.5)	41 (6.1)
	18.5 <= - < 25	162 (66.1)	170 (68.5)	119 (64.7)	289 (66.9)	451 (66.6)
	25 <= - < 30	63 (25.7)	56 (22.6)	41 (22.3)	97 (22.5)	160 (23.6)
	30 <= - < 40	7 (2.9)	8 (3.2)	10 (5.4)	18 (4.2)	25 (3.7)
	40 <=	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
BMI categorization 2 (n [%])	< 25	175 (71.4)	184 (74.2)	133 (72.3)	317 (73.4)	492 (72.7)
	25 <= - < 30	63 (25.7)	56 (22.6)	41 (22.3)	97 (22.5)	160 (23.6)
	30 <=	7 (2.9)	8 (3.2)	10 (5.4)	18 (4.2)	25 (3.7)

[a]:Calculated from height at screening and weight at randomized.

＜資料番号 5.3.5.1-01：Table 14.1.1.1-6 より作成＞

表 2.7.4.1.3-2　　ベースライン時の飲酒状況：アルコール依存症の国内短期投与（339-14-001，FAS）

Characteristics		Placebo (N=244)	Nalmefene 20 mg (N=242)	Nalmefene 10 mg (N=180)	Nalmefene Total (N=422)	Total (N=666)
DRL (n [%])	Low	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Medium	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
	High	127 (52.0)	135 (55.8)	93 (51.7)	228 (54.0)	355 (53.3)
	Very high	116 (47.5)	107 (44.2)	87 (48.3)	194 (46.0)	310 (46.5)
Number of HDDs (days/month)	n	244	242	180	422	666
	Mean	22.97	22.64	23.49	23.00	22.99
	SD	6.44	6.37	6.07	6.25	6.32
	Min	6.0	6.0	2.0	2.0	2.0
	Median	26.00	26.00	27.00	26.00	26.00
	Max	28.0	28.0	28.0	28.0	28.0
TAC (g/day)	n	244	242	180	422	666
	Mean	95.08	93.07	95.93	94.29	94.58
	SD	48.70	37.45	41.10	39.03	42.79
	Min	40.0	40.2	40.1	40.1	40.0
	Median	84.18	83.82	86.53	84.86	84.57
	Max	458.1	273.4	352.0	352.0	458.1

＜資料番号 5.3.5.1-01：Table 14.1.1.1-11 より作成＞

(2)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与での人口統計学的特性及びベースライン時の体重，身長，BMI を表 2.7.4.1.3-3 に示した。

性別は男性が 71.2%，女性が 28.8%であった。平均年齢は 49.4 歳（年齢範囲 21～80 歳）であり，65 歳以上の被験者の割合は 10.9%であった。

表 2.7.4.1.3-3　人口統計学的特性，ベースライン時の体重，身長，BMI：アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

Treatment group of study 339-14-001		Placebo	Nalmefene			Total
			20 mg	10 mg	Total	
Characteristics		(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Age (years)	n	172	137	94	231	403
	Mean	48.5	50.0	50.1	50.0	49.4
	SD	11.0	11.7	11.0	11.4	11.2
	Min	22	21	21	21	21
	Median	49.0	50.0	51.0	51.0	50.0
	Max	77	80	75	80	80
Age categorization (n [%])	< 65	154 (89.5)	120 (87.6)	85 (90.4)	205 (88.7)	359 (89.1)
	65 <=	18 (10.5)	17 (12.4)	9 (9.6)	26 (11.3)	44 (10.9)
Sex (n [%])	Female	64 (37.2)	33 (24.1)	19 (20.2)	52 (22.5)	116 (28.8)
	Male	108 (62.8)	104 (75.9)	75 (79.8)	179 (77.5)	287 (71.2)
Body weight (kg)	n	172	137	94	231	403
	Mean	64.54	64.56	67.76	65.86	65.30
	SD	12.12	12.40	13.55	12.95	12.60
	Min	42.6	39.2	42.0	39.2	39.2
	Median	64.40	63.20	67.55	65.40	65.00
	Max	105.4	94.7	115.0	115.0	115.0
Height (cm)	n	172	137	94	231	403
	Mean	165.82	167.69	168.66	168.09	167.12
	SD	8.35	8.17	6.85	7.66	8.03
	Min	147.1	144.1	151.5	144.1	144.1
	Median	165.20	168.50	169.20	169.10	168.00
	Max	184.5	189.0	183.3	189.0	189.0
BMI (kg/m^2)[a]	n	172	137	94	231	403
	Mean	23.38	22.81	23.69	23.17	23.26
	SD	3.45	3.21	3.84	3.50	3.47
	Min	16.8	16.5	16.2	16.2	16.2
	Median	22.94	22.48	23.54	22.80	22.88
	Max	35.0	32.4	38.2	38.2	38.2
BMI categorization 1 (n [%])	< 18.5	7 (4.1)	7 (5.1)	7 (7.4)	14 (6.1)	21 (5.2)
	18.5 <= - < 25	111 (64.5)	100 (73.0)	54 (57.4)	154 (66.7)	265 (65.8)
	25 <= - < 30	48 (27.9)	26 (19.0)	26 (27.7)	52 (22.5)	100 (24.8)
	30 <= - < 40	6 (3.5)	4 (2.9)	7 (7.4)	11 (4.8)	17 (4.2)
	40 <=	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
BMI categorization 2 (n [%])	< 25	118 (68.6)	107 (78.1)	61 (64.9)	168 (72.7)	286 (71.0)
	25 <= - < 30	48 (27.9)	26 (19.0)	26 (27.7)	52 (22.5)	100 (24.8)
	30 <=	6 (3.5)	4 (2.9)	7 (7.4)	11 (4.8)	17 (4.2)

[a]:Calculated from height at screening and weight at randomization in study 339-14-001.

Assessment time point is baseline in study 339-14-001.

＜資料番号 5.3.5.2-01：Table 14.1.1.1-7 より作成＞

2.7.4.1.3.2　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合で DRL が High 以上であった被験者での人口統計学的特性を表 2.7.4.1.3-4，ベースライン時の体重，身長，及び BMI を表 2.7.4.1.3-5，ベースライン時の飲酒状況を表 2.7.4.1.3-6 に示した。

DRL が High 以上であった被験者で，人口統計学的特性及びその他の特性は，ナルメフェン群とプラセボ群とで大きく異ならなかった。全体で，性別は男性が 68.4%，女性が 31.6%であった。平均年齢は 48.0 歳（年齢範囲 20.0～77.0 歳）であり，65 歳以上の被験者は 6.4%であった。ほとんどの被験者が白人であった（99.4%）。全体で，ベースライン時の HDD 数（平均値，以下同様）は 21.8 日/月，TAC は 104.4 g/日であった。

アルコール依存症の海外試験併合全体で，人口統計学的特性及びその他の特性は，DRL が High 以上であった被験者と大きく異ならなかった。全体で，ベースライン時の HDD 数は 17.48 日/月，TAC は 81.23 g/日であった（資料番号 5.3.5.3-03：Panel 9，Panel 10，Panel 11 参照）。

表 2.7.4.1.3-4　人口統計学的特性：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

		Placebo	Nalmefene	Total
Number of Patients		374	480	854
Age (years)	N	374	480	854
	Mean	48.4	47.7	48.0
	SD	10.8	10.9	10.9
	Min	20.0	20.0	20.0
	Max	75.0	77.0	77.0
	Median	49.0	47.0	48.0
Age group (years) n (%)	< 65 Yrs	355 (94.9)	444 (92.5)	799 (93.6)
	=> 65 Yrs	19 (5.1)	36 (7.5)	55 (6.4)
Sex n (%)	M	248 (66.3)	336 (70.0)	584 (68.4)
	F	126 (33.7)	144 (30.0)	270 (31.6)
Race n (%)	Caucasian	371 (99.2)	478 (99.6)	849 (99.4)
	Black	2 (0.5)	2 (0.4)	4 (0.5)
	Other	1 (0.3)	0 (0.0)	1 (0.1)

＜資料番号 5.3.5.3-03：Table 18＞

表 2.7.4.1.3-5　ベースライン時の体重，身長，BMI：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

		Placebo	Nalmefene	Total
Number of Patients		374	480	854
Weight (kg)	N	373	477	850
	Mean	78.1	80.0	79.1
	SD	16.0	16.9	16.5
	Min	39.2	43.0	39.2
	Max	160.0	141.0	160.0
	Median	76.1	78.4	77.6
Height (cm)	N	373	476	849
	Mean	172.2	173.9	173.2
	SD	8.7	9.0	8.9
	Min	150.0	150.0	150.0
	Max	193.0	201.1	201.1
	Median	173.0	174.0	173.0
BMI (kg/m^2)	N	373	475	848
	Mean	26.2	26.3	26.3
	SD	4.5	4.8	4.7
	Min	16.3	15.6	15.6
	Max	43.4	49.1	49.1
	Median	25.9	26.0	26.0
BMI Categories n (%)	Unknown	1 (0.3)	5 (1.0)	6 (0.7)
	< 18.5 Kg/m^2 (Underweight)	8 (2.1)	10 (2.1)	18 (2.1)
	18.5-25 Kg/m^2 (Normal)	153 (40.9)	185 (38.5)	338 (39.6)
	25-30 Kg/m^2 (Overweight)	146 (39.0)	184 (38.3)	330 (38.6)
	30-40 Kg/m^2 (Obese)	62 (16.6)	91 (19.0)	153 (17.9)
	>= 40 Kg/m^2 (Severely Obese)	4 (1.1)	5 (1.0)	9 (1.1)

＜資料番号 5.3.5.3-03：Table 19＞

表 2.7.4.1.3-6　ベースライン時の飲酒状況：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

		Placebo	Nalmefene	Total
Number of Patients		374	480	854
Number of HDDs (days/month)	N	374	480	854
	Mean	21.9	21.8	21.8
	SD	6.1	6.2	6.2
	Min	6.0	7.0	6.0
	Max	28.0	28.0	28.0
	Median	24.0	24.0	24.0
TAC (g/day)	N	374	480	854
	Mean	103.0	105.5	104.4
	SD	44.7	45.3	45.0
	Min	42.0	41.0	41.0
	Max	380.0	447.0	447.0
	Median	93.0	97.0	95.0
Drinking Risk Level n (%)	High	162 (43.3)	199 (41.5)	361 (42.3)
	Very High	212 (56.7)	281 (58.5)	493 (57.7)

＜資料番号 5.3.5.3-03：Table 21＞

2.7.4.1.3.3　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験併合での人口統計学的特性を表 2.7.4.7.2-8 に示した。

人口統計学的特性は，ナルメフェン群とプラセボ群とで大きく異ならなかった。いずれの投与群でも，性別は男性が約 75%，女性が約 25%で，平均年齢は約 48 歳，ほとんどの被験者が白人であった（約 97%）。アルコール使用障害の海外試験では，CPH-101-0801 試験では約 93%，CPH-101-0701 試験では約 77%の被験者が，DSM-IV に基づくアルコール依存症と診断された。

2.7.4.2　有害事象

2.7.4.2.1　有害事象の解析

2.7.4.2.1.1　比較的よく見られる有害事象

(1)　要約

(a)　アルコール依存症の国内試験

i)　短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した有害事象及び副作用の要約を表 2.7.4.2.1-1 に示した。

有害事象は，ナルメフェン 20 mg 群 87.9%（218/248 例），10 mg 群 84.8%（156/184 例），プラセボ群 79.2%（194/245 例）に発現した。副作用は，20 mg 群 71.0%（176/248 例），10 mg 群 71.2%（131/184 例），プラセボ群 37.1%（91/245 例）に発現した。重篤な有害事象は，20 mg 群 0.8%（2/248 例），10 mg 群 1.1%（2/184 例），プラセボ群 0.8%（2/245 例）に発現した。死亡は，10 mg 群の 1 例が報告された。投与中止に至った有害事象は，20 mg 群 18.1%（45/248 例），10 mg 群 17.9%（33/184 例），プラセボ群 4.5%（11/245 例）に発現した。

表 2.7.4.2.1-1　有害事象及び副作用の要約：アルコール依存症の国内短期投与（339-14-001）

	Placebo	Nalmefene		
		20 mg	10 mg	Total
	(N=245)	(N=248)	(N=184)	(N=432)
Subjects with TEAEs	194 (79.2)	218 (87.9)	156 (84.8)	374 (86.6)
Subjects with drug-related TEAEs	91 (37.1)	176 (71.0)	131 (71.2)	307 (71.1)
Subjects with serious TEAEs	2 (0.8)	2 (0.8)	2 (1.1)	4 (0.9)
Subjects with serious drug-related TEAEs	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Subjects with TEAEs leading to discontinuation	11 (4.5)	45 (18.1)	33 (17.9)	78 (18.1)
Subjects with drug-related TEAEs leading to discontinuation	2 (0.8)	44 (17.7)	28 (15.2)	72 (16.7)
Subjects with TEAEs result in death	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Subjects with drug-related TEAEs result in death	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Subjects with TEAEs that severity is severe	0 (0.0)	1 (0.4)	3 (1.6)	4 (0.9)
Subjects with drug-related TEAEs that severity is severe	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)

＜資料番号 5.3.5.1-01：Table 14.1.1.3-13＞

ii)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与で発現した有害事象及び副作用の要約を表 2.7.4.2.1-2 に，退薬期に発現した有害事象及び副作用の要約を表 2.7.4.2.1-3 に示した。

国内長期投与では，ナルメフェン投与群全体からの移行例で，有害事象は 90.9%（210/231 例），副作用は 75.8%（175/231 例）に発現した。重篤な有害事象は，1.3%（3/231 例）に発現

した。死亡の報告はなかった。継続長期試験（339-14-002）の治療期に，投与中止に至った有害事象は 4.3%（10/231 例）に発現した。

ナルメフェン投与群全体からの移行例での有害事象，副作用，及び重篤な有害事象の発現割合は，ナルメフェン 20 mg 群又は 10 mg 群からの移行例と大きく異ならなかった。339-14-002 試験の治療期に投与中止に至った有害事象の発現割合は，ナルメフェン投与群全体からの移行例で 4.3%（10/231 例），プラセボ群からの移行例で 18.6%（32/172 例）と，ナルメフェン投与群全体からの移行例で低かった。プラセボ群からの移行例での投与中止に至った有害事象の発現割合は，短期投与（339-14-001）の 20 mg 群で投与中止に至った有害事象の発現割合（18.1%）と大きく異ならなかった（表 2.7.4.2.1-1 参照）。

退薬期に，有害事象はナルメフェン群 17.4%（30/172 例），プラセボ群 11.7%（20/171 例）に発現した。副作用はナルメフェン群 5.8%（10/172 例），プラセボ群 5.3%（9/171 例）に発現した。重篤な有害事象はナルメフェン群 0.6%（1/172 例），プラセボ群 0.6%（1/171 例）に発現した。死亡の報告はなかった。投与中止に至った有害事象はナルメフェン群 0.6%（1/172 例）に発現し，プラセボ群での発現はなかった。

表 2.7.4.2.1-2　有害事象及び副作用の要約：アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
	n (%)	n (%)	n (%)	n (%)	n (%)
Subjects with adverse events	161 (93.6)	125 (91.2)	85 (90.4)	210 (90.9)	371 (92.1)
Subjects with drug-related adverse events	124 (72.1)	105 (76.6)	70 (74.5)	175 (75.8)	299 (74.2)
Subjects with serious adverse events	0 (0.0)	2 (1.5)	1 (1.1)	3 (1.3)	3 (0.7)
Subjects with serious drug-related adverse events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with adverse events leading to discontinuation[a]	32 (18.6)	8 (5.8)	2 (2.1)	10 (4.3)	42 (10.4)
Subjects with drug-related adverse events leading to discontinuation[a]	31 (18.0)	5 (3.6)	2 (2.1)	7 (3.0)	38 (9.4)
Subjects with adverse events result in death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with drug-related adverse events result in death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Subjects with adverse events that severity is severe	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Subjects with drug-related adverse events that severity is severe	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)

[a]：投与中止に至った有害事象は，339-14-002 試験の治療期での発現割合を示した。

＜資料番号 5.3.5.2-01：Table 14.1.1.3-61 より作成＞

表 2.7.4.2.1-3　有害事象及び副作用の要約：アルコール依存症の国内継続長期試験（339-14-002）－ 退薬期

Treatment group of run-out period	Placebo (N=171) n (%)	Nalmefene 20 mg (N=172) n (%)
Subjects with adverse events	20 (11.7)	30 (17.4)
Subjects with drug-related adverse events	9 (5.3)	10 (5.8)
Subjects with serious adverse events	1 (0.6)	1 (0.6)
Subjects with serious drug-related adverse events	1 (0.6)	0 (0.0)
Subjects with adverse events leading to discontinuation	0 (0.0)	1 (0.6)
Subjects with drug-related adverse events leading to discontinuation	0 (0.0)	1 (0.6)
Subjects with adverse events result in death	0 (0.0)	0 (0.0)
Subjects with drug-related adverse events result in death	0 (0.0)	0 (0.0)
Subjects with adverse events that severity is severe	1 (0.6)	0 (0.0)
Subjects with drug-related adverse events that severity is severe	1 (0.6)	0 (0.0)

＜資料番号 5.3.5.2-01：Table 14.1.1.3-66＞

(b)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で，有害事象は，ナルメフェン群 77.5%（368/475 例），プラセボ群 66.7%（246/369 例）に発現した（表 2.7.4.7.2-9 参照）。重篤な有害事象は，ナルメフェン群 5.5%（26/475 例），プラセボ群 3.5%（13/369 例）に発現した（表 2.7.4.2.1-16 参照）。投与中止に至った有害事象は，ナルメフェン群 16.4%（78/475 例），プラセボ群 7.0%（26/369 例）に発現した（表 2.7.4.7.2-10 参照）。

アルコール依存症の海外試験併合全体で，有害事象はナルメフェン群 74.7%（855/1144 例），プラセボ群 62.7%（500/797 例）に発現した（資料番号 5.3.5.3-01：Table 96 参照）。重篤な有害事象は，ナルメフェン群 5.0%（57/1144 例），プラセボ群 4.4%（35/797 例）に発現した（資料番号 5.3.5.3-01：Table 72 参照）。死亡は，12014A 試験でプラセボ群の 2 例，12023A 試験でナルメフェン群の 1 例，12013A 試験でナルメフェン群の 1 例が報告された（表 2.7.4.7.2-11 参照）。投与中止に至った有害事象は，ナルメフェン群 13.0%（149/1144 例），プラセボ群 5.9%（47/797 例）に発現した（資料番号 5.3.5.3-01：Table 80 参照）。

(2)　器官別大分類別有害事象

(a)　アルコール依存症の国内試験

i)　短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した器官別大分類別有害事象を表 2.7.4.2.1-4 に示した。

有害事象の発現割合が最も高かった器官別大分類は，ナルメフェン 20 mg 群及び 10 mg 群では胃腸障害でそれぞれ 51.6%（128/248 例），50.0%（92/184 例），プラセボ群では感染症およ

び寄生虫症 42.4%（104/245 例）であった。そのほかに，20 mg 群又は 10 mg 群で発現割合が 10%以上であった器官別大分類は，神経系障害，感染症および寄生虫症，一般・全身障害および投与部位の状態，精神障害，臨床検査，筋骨格系および結合組織障害であった。20 mg 群又は 10 mg 群で有害事象の発現割合が 10%以上かつプラセボ群と比較して発現割合が 2 倍以上であった器官別大分類は，胃腸障害，精神障害であった。

表 2.7.4.2.1-4　　器官別大分類別有害事象：アルコール依存症の国内短期投与（339-14-001）

	Placebo	Nalmefene		
		20 mg	10 mg	Total
	(N=245)	(N=248)	(N=184)	(N=432)
System organ class	n (%)	n (%)	n (%)	n (%)
Total number of subjects with TEAEs	194 (79.2)	218 (87.9)	156 (84.8)	374 (86.6)
血液およびリンパ系障害	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
心臓障害	4 (1.6)	16 (6.5)	11 (6.0)	27 (6.3)
耳および迷路障害	1 (0.4)	11 (4.4)	4 (2.2)	15 (3.5)
内分泌障害	1 (0.4)	1 (0.4)	2 (1.1)	3 (0.7)
眼障害	7 (2.9)	5 (2.0)	6 (3.3)	11 (2.5)
胃腸障害	51 (20.8)	128 (51.6)	92 (50.0)	220 (50.9)
一般・全身障害および投与部位の状態	34 (13.9)	55 (22.2)	24 (13.0)	79 (18.3)
肝胆道系障害	1 (0.4)	4 (1.6)	2 (1.1)	6 (1.4)
免疫系障害	0 (0.0)	4 (1.6)	2 (1.1)	6 (1.4)
感染症および寄生虫症	104 (42.4)	74 (29.8)	43 (23.4)	117 (27.1)
傷害、中毒および処置合併症	19 (7.8)	9 (3.6)	8 (4.3)	17 (3.9)
臨床検査	26 (10.6)	32 (12.9)	20 (10.9)	52 (12.0)
代謝および栄養障害	4 (1.6)	17 (6.9)	13 (7.1)	30 (6.9)
筋骨格系および結合組織障害	22 (9.0)	25 (10.1)	15 (8.2)	40 (9.3)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	53 (21.6)	100 (40.3)	63 (34.2)	163 (37.7)
精神障害	15 (6.1)	46 (18.5)	29 (15.8)	75 (17.4)
腎および尿路障害	2 (0.8)	4 (1.6)	3 (1.6)	7 (1.6)
生殖系および乳房障害	2 (0.8)	7 (2.8)	2 (1.1)	9 (2.1)
呼吸器、胸郭および縦隔障害	9 (3.7)	10 (4.0)	9 (4.9)	19 (4.4)
皮膚および皮下組織障害	7 (2.9)	18 (7.3)	10 (5.4)	28 (6.5)
血管障害	7 (2.9)	8 (3.2)	7 (3.8)	15 (3.5)
製品の問題	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-18 より作成＞

ii)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与で発現した器官別大分類別有害事象を表 2.7.4.2.1-5 に示した。

有害事象の発現割合が最も高かった器官別大分類は，ナルメフェン投与群全体からの移行例で胃腸障害 61.5%（142/231 例）であった。そのほかに，ナルメフェン投与群全体からの移行例で発現割合が 10%以上であった器官別大分類は，感染症および寄生虫症，神経系障害，一般・全身障害および投与部位の状態，臨床検査，筋骨格系および結合組織障害，精神障害であった。

表 2.7.4.2.1-5　器官別大分類別有害事象：アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
System organ class	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with adverse events	161 (93.6)	125 (91.2)	85 (90.4)	210 (90.9)	371 (92.1)
血液およびリンパ系障害	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
心臓障害	10 (5.8)	6 (4.4)	11 (11.7)	17 (7.4)	27 (6.7)
耳および迷路障害	4 (2.3)	9 (6.6)	1 (1.1)	10 (4.3)	14 (3.5)
内分泌障害	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.4)	4 (1.0)
眼障害	5 (2.9)	7 (5.1)	4 (4.3)	11 (4.8)	16 (4.0)
胃腸障害	87 (50.6)	80 (58.4)	62 (66.0)	142 (61.5)	229 (56.8)
一般・全身障害および投与部位の状態	50 (29.1)	42 (30.7)	19 (20.2)	61 (26.4)	111 (27.5)
肝胆道系障害	1 (0.6)	1 (0.7)	1 (1.1)	2 (0.9)	3 (0.7)
免疫系障害	4 (2.3)	2 (1.5)	5 (5.3)	7 (3.0)	11 (2.7)
感染症および寄生虫症	91 (52.9)	62 (45.3)	39 (41.5)	101 (43.7)	192 (47.6)
傷害、中毒および処置合併症	23 (13.4)	16 (11.7)	4 (4.3)	20 (8.7)	43 (10.7)
臨床検査	24 (14.0)	28 (20.4)	18 (19.1)	46 (19.9)	70 (17.4)
代謝および栄養障害	14 (8.1)	18 (13.1)	2 (2.1)	20 (8.7)	34 (8.4)
筋骨格系および結合組織障害	31 (18.0)	28 (20.4)	18 (19.1)	46 (19.9)	77 (19.1)
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）	3 (1.7)	2 (1.5)	0 (0.0)	2 (0.9)	5 (1.2)
神経系障害	79 (45.9)	63 (46.0)	32 (34.0)	95 (41.1)	174 (43.2)
精神障害	46 (26.7)	28 (20.4)	15 (16.0)	43 (18.6)	89 (22.1)
腎および尿路障害	1 (0.6)	2 (1.5)	3 (3.2)	5 (2.2)	6 (1.5)
生殖系および乳房障害	3 (1.7)	6 (4.4)	2 (2.1)	8 (3.5)	11 (2.7)
呼吸器、胸郭および縦隔障害	12 (7.0)	10 (7.3)	8 (8.5)	18 (7.8)	30 (7.4)
皮膚および皮下組織障害	18 (10.5)	14 (10.2)	6 (6.4)	20 (8.7)	38 (9.4)
血管障害	7 (4.1)	6 (4.4)	7 (7.4)	13 (5.6)	20 (5.0)
製品の問題	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

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＜資料番号 5.3.5.2-01：Table 14.1.1.3-31 より作成＞

(b)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で，有害事象の発現割合が最も高かった器官別大分類は，ナルメフェン群で神経系障害 43.8%（208/475 例），プラセボ群で感染症および寄生虫症 24.1%（89/369 例）であった（表 2.7.4.7.2-9 参照）。

(3) 基本語別有害事象

(a) アルコール依存症の国内試験

i) 短期投与（339-14-001）

アルコール依存症の国内短期投与で，いずれかの群で 2%以上に発現した有害事象を表 2.7.4.2.1-6 に，すべての有害事象及び副作用を表 2.7.4.7.1-10 及び表 2.7.4.7.1-11 に示した。

有害事象は，ナルメフェン 20 mg 群 87.9%（218/248 例），10 mg 群 84.8%（156/184 例），プラセボ群 79.2%（194/245 例）に発現した。

20 mg 群又は 10 mg 群で 5%以上に発現した有害事象は，悪心，鼻咽頭炎，浮動性めまい，傾眠，嘔吐，倦怠感，頭痛，不眠症，食欲減退，便秘，動悸であった。このうち，発現割合がプラセボ群の 2 倍以上であった有害事象は，悪心［20 mg 群 31.9%（79/248 例），10 mg 群 31.5%（58/184 例），プラセボ群 6.1%（15/245 例），以下同順］，浮動性めまい［20.6%（51/248 例），10.9%（20/184 例），4.1%（10/245 例）］，傾眠［15.7%（39/248 例），9.8%（18/184 例），6.9%（17/245 例）］，嘔吐［13.7%（34/248 例），8.7%（16/184 例），2.0%（5/245 例）］，倦怠感［9.7%（24/248 例），3.8%（7/184 例），3.3%（8/245 例）］，不眠症［8.1%（20/248 例），8.2%（15/184 例），0.8%（2/245 例）］，食欲減退［5.2%（13/248 例），6.0%（11/184 例），1.2%（3/245 例）］，便秘［5.2%（13/248 例），4.3%（8/184 例），0.8%（2/245 例）］，動悸［5.2%（13/248 例），3.8%（7/184 例），0.8%（2/245 例）］であった。

20 mg 群で，10 mg 群と比較して発現割合が 5%以上高かった有害事象は，浮動性めまい，傾眠，嘔吐，倦怠感であった。

副作用は，20 mg 群 71.0%（176/248 例），10 mg 群 71.2%（131/184 例），プラセボ群 37.1%（91/245 例）に発現した。

20 mg 群又は 10 mg 群で 5%以上に発現した副作用は，悪心，浮動性めまい，傾眠，嘔吐，倦怠感，頭痛，不眠症であった。このうち，発現割合がプラセボ群の 2 倍以上であった副作用は，悪心［31.0%（77/248 例），31.0%（57/184 例），4.1%（10/245 例）］，浮動性めまい［19.8%（49/248 例），10.9%（20/184 例），3.7%（9/245 例）］，傾眠［15.3%（38/248 例），9.2%（17/184 例），6.1%（15/245 例）］，嘔吐［10.9%（27/248 例），6.0%（11/184 例），0.4%（1/245 例）］，倦怠感［8.9%（22/248 例），3.8%（7/184 例），2.0%（5/245 例）］，不眠症［6.9%（17/248 例），7.1%（13/184 例），0.0%（0/245 例）］であった。

20 mg 群で，10 mg 群と比較して発現割合が 5%以上高かった副作用は，浮動性めまい，傾眠，倦怠感であった。

表 2.7.4.2.1-6　いずれかの群で 2%以上に発現した有害事象 : アルコール依存症の国内短期投与（339-14-001）

System organ class Preferred term	Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Total number of subjects with TEAEs	194 (79.2)	218 (87.9)	156 (84.8)	374 (86.6)
心臓障害	4 (1.6)	16 (6.5)	11 (6.0)	27 (6.3)
動悸	2 (0.8)	13 (5.2)	7 (3.8)	20 (4.6)
耳および迷路障害	1 (0.4)	11 (4.4)	4 (2.2)	15 (3.5)
回転性めまい	1 (0.4)	8 (3.2)	2 (1.1)	10 (2.3)
胃腸障害	51 (20.8)	128 (51.6)	92 (50.0)	220 (50.9)
腹部不快感	6 (2.4)	10 (4.0)	7 (3.8)	17 (3.9)
腹部膨満	6 (2.4)	9 (3.6)	5 (2.7)	14 (3.2)
腹痛	1 (0.4)	7 (2.8)	6 (3.3)	13 (3.0)
上腹部痛	4 (1.6)	5 (2.0)	3 (1.6)	8 (1.9)
便秘	2 (0.8)	13 (5.2)	8 (4.3)	21 (4.9)
下痢	6 (2.4)	12 (4.8)	7 (3.8)	19 (4.4)
悪心	15 (6.1)	79 (31.9)	58 (31.5)	137 (31.7)
嘔吐	5 (2.0)	34 (13.7)	16 (8.7)	50 (11.6)
一般・全身障害および投与部位の状態	34 (13.9)	55 (22.2)	24 (13.0)	79 (18.3)
疲労	4 (1.6)	10 (4.0)	5 (2.7)	15 (3.5)
異常感	2 (0.8)	6 (2.4)	5 (2.7)	11 (2.5)
倦怠感	8 (3.3)	24 (9.7)	7 (3.8)	31 (7.2)
口渇	3 (1.2)	9 (3.6)	2 (1.1)	11 (2.5)
感染症および寄生虫症	104 (42.4)	74 (29.8)	43 (23.4)	117 (27.1)
膀胱炎	2 (0.8)	0 (0.0)	4 (2.2)	4 (0.9)
鼻咽頭炎	91 (37.1)	54 (21.8)	40 (21.7)	94 (21.8)
臨床検査	26 (10.6)	32 (12.9)	20 (10.9)	52 (12.0)
血圧上昇	2 (0.8)	3 (1.2)	4 (2.2)	7 (1.6)
血中プロラクチン増加	2 (0.8)	6 (2.4)	3 (1.6)	9 (2.1)
血中トリグリセリド増加	6 (2.4)	3 (1.2)	0 (0.0)	3 (0.7)
代謝および栄養障害	4 (1.6)	17 (6.9)	13 (7.1)	30 (6.9)
食欲減退	3 (1.2)	13 (5.2)	11 (6.0)	24 (5.6)
筋骨格系および結合組織障害	22 (9.0)	25 (10.1)	15 (8.2)	40 (9.3)
関節痛	6 (2.4)	3 (1.2)	1 (0.5)	4 (0.9)
背部痛	11 (4.5)	8 (3.2)	6 (3.3)	14 (3.2)
神経系障害	53 (21.6)	100 (40.3)	63 (34.2)	163 (37.7)
浮動性めまい	10 (4.1)	51 (20.6)	20 (10.9)	71 (16.4)
味覚異常	6 (2.4)	5 (2.0)	4 (2.2)	9 (2.1)
頭痛	20 (8.2)	24 (9.7)	21 (11.4)	45 (10.4)
感覚鈍麻	3 (1.2)	5 (2.0)	3 (1.6)	8 (1.9)
傾眠	17 (6.9)	39 (15.7)	18 (9.8)	57 (13.2)
睡眠の質低下	5 (2.0)	4 (1.6)	5 (2.7)	9 (2.1)

表 2.7.4.2.1-6　いずれかの群で 2%以上に発現した有害事象：アルコール依存症の国内短期投与（339-14-001）（続き）

	Placebo	Nalmefene		
		20 mg	10 mg	Total
System organ class	(N=245)	(N=248)	(N=184)	(N=432)
Preferred term	n (%)	n (%)	n (%)	n (%)
精神障害	15 (6.1)	46 (18.5)	29 (15.8)	75 (17.4)
アルコールによる宿酔	2 (0.8)	5 (2.0)	1 (0.5)	6 (1.4)
不眠症	2 (0.8)	20 (8.1)	15 (8.2)	35 (8.1)
中期不眠症	1 (0.4)	8 (3.2)	5 (2.7)	13 (3.0)
血管障害	7 (2.9)	8 (3.2)	7 (3.8)	15 (3.5)
ほてり	3 (1.2)	3 (1.2)	4 (2.2)	7 (1.6)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-22 より作成＞

ii)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与で，プラセボ対照二重盲検試験（339-14-001）のいずれかの投与群からの移行例で 2%以上に発現した有害事象を表 2.7.4.2.1-7 に，すべての有害事象及び副作用を表 2.7.4.7.1-12 及び表 2.7.4.7.1-13 に示した。

ナルメフェン投与群全体からの移行例で，有害事象は 90.9%（210/231 例）に発現した。5%以上に発現した有害事象は，鼻咽頭炎，悪心，傾眠，浮動性めまい，嘔吐，倦怠感，頭痛，背部痛，不眠症，腹部不快感，便秘，腹部膨満，下痢であった。

副作用は，ナルメフェン投与群全体からの移行例で 75.8%（175/231 例）に発現した。5%以上に発現した副作用は，悪心，傾眠，浮動性めまい，頭痛，倦怠感，腹部不快感，不眠症，嘔吐であった。

更に，339-14-001 試験又は継続長期試験（339-14-002）でナルメフェンを投与された全被験者 604 例を対象に，339-14-001 試験の治療期 24 週間，339-14-002 試験の治療期 24 週間及び退薬期 4 週間，計 52 週間の安全性成績を併合し，ナルメフェンを投与された期間に発現した有害事象及び副作用を検討した。

ナルメフェンを投与された全期間（最大 52 週間）に，有害事象は 88.4%（534/604 例）に発現した。5%以上に発現した有害事象は，悪心，鼻咽頭炎，浮動性めまい，傾眠，嘔吐，頭痛，倦怠感，不眠症，食欲減退，腹部不快感，便秘，背部痛，動悸であった。また，副作用は 72.8%（440/604 例）に発現した。5%以上に発現した副作用は，悪心，浮動性めまい，傾眠，頭痛，嘔吐，倦怠感，不眠症，食欲減退，腹部不快感であった（資料番号 5.3.5.3-01：Table 2.1-1，Table 2.1-2 参照）。

表 2.7.4.2.1-7　いずれかの投与群からの移行例で 2%以上に発現した有害事象 : アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with adverse events	161 (93.6)	125 (91.2)	85 (90.4)	210 (90.9)	371 (92.1)
心臓障害	10 (5.8)	6 (4.4)	11 (11.7)	17 (7.4)	27 (6.7)
右脚ブロック	0 (0.0)	0 (0.0)	2 (2.1)	2 (0.9)	2 (0.5)
動悸	7 (4.1)	5 (3.6)	5 (5.3)	10 (4.3)	17 (4.2)
頻脈	2 (1.2)	0 (0.0)	3 (3.2)	3 (1.3)	5 (1.2)
耳および迷路障害	4 (2.3)	9 (6.6)	1 (1.1)	10 (4.3)	14 (3.5)
回転性めまい	2 (1.2)	6 (4.4)	1 (1.1)	7 (3.0)	9 (2.2)
眼障害	5 (2.9)	7 (5.1)	4 (4.3)	11 (4.8)	16 (4.0)
眼乾燥	2 (1.2)	1 (0.7)	2 (2.1)	3 (1.3)	5 (1.2)
胃腸障害	87 (50.6)	80 (58.4)	62 (66.0)	142 (61.5)	229 (56.8)
腹部不快感	13 (7.6)	12 (8.8)	7 (7.4)	19 (8.2)	32 (7.9)
腹部膨満	7 (4.1)	11 (8.0)	2 (2.1)	13 (5.6)	20 (5.0)
腹痛	2 (1.2)	4 (2.9)	5 (5.3)	9 (3.9)	11 (2.7)
上腹部痛	3 (1.7)	5 (3.6)	2 (2.1)	7 (3.0)	10 (2.5)
便秘	10 (5.8)	10 (7.3)	6 (6.4)	16 (6.9)	26 (6.5)
齲歯	3 (1.7)	4 (2.9)	3 (3.2)	7 (3.0)	10 (2.5)
下痢	4 (2.3)	7 (5.1)	5 (5.3)	12 (5.2)	16 (4.0)
消化不良	3 (1.7)	2 (1.5)	3 (3.2)	5 (2.2)	8 (2.0)
胃炎	2 (1.2)	1 (0.7)	2 (2.1)	3 (1.3)	5 (1.2)
悪心	46 (26.7)	50 (36.5)	32 (34.0)	82 (35.5)	128 (31.8)
歯痛	2 (1.2)	5 (3.6)	2 (2.1)	7 (3.0)	9 (2.2)
嘔吐	16 (9.3)	17 (12.4)	11 (11.7)	28 (12.1)	44 (10.9)
一般・全身障害および投与部位の状態	50 (29.1)	42 (30.7)	19 (20.2)	61 (26.4)	111 (27.5)
無力症	2 (1.2)	3 (2.2)	0 (0.0)	3 (1.3)	5 (1.2)
疲労	5 (2.9)	6 (4.4)	5 (5.3)	11 (4.8)	16 (4.0)
異常感	7 (4.1)	7 (5.1)	3 (3.2)	10 (4.3)	17 (4.2)
倦怠感	21 (12.2)	20 (14.6)	6 (6.4)	26 (11.3)	47 (11.7)
発熱	3 (1.7)	2 (1.5)	3 (3.2)	5 (2.2)	8 (2.0)
口渇	7 (4.1)	6 (4.4)	2 (2.1)	8 (3.5)	15 (3.7)
免疫系障害	4 (2.3)	2 (1.5)	5 (5.3)	7 (3.0)	11 (2.7)
季節性アレルギー	4 (2.3)	1 (0.7)	5 (5.3)	6 (2.6)	10 (2.5)
感染症および寄生虫症	91 (52.9)	62 (45.3)	39 (41.5)	101 (43.7)	192 (47.6)
膀胱炎	2 (1.2)	2 (1.5)	2 (2.1)	4 (1.7)	6 (1.5)
胃腸炎	4 (2.3)	2 (1.5)	2 (2.1)	4 (1.7)	8 (2.0)
インフルエンザ	3 (1.7)	2 (1.5)	2 (2.1)	4 (1.7)	7 (1.7)
鼻咽頭炎	76 (44.2)	51 (37.2)	34 (36.2)	85 (36.8)	161 (40.0)
傷害、中毒および処置合併症	23 (13.4)	16 (11.7)	4 (4.3)	20 (8.7)	43 (10.7)
靭帯捻挫	1 (0.6)	3 (2.2)	0 (0.0)	3 (1.3)	4 (1.0)
挫傷	5 (2.9)	2 (1.5)	0 (0.0)	2 (0.9)	7 (1.7)

表 2.7.4.2.1-7　いずれかの投与群からの移行例で 2%以上に発現した有害事象 : アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査	24 (14.0)	28 (20.4)	18 (19.1)	46 (19.9)	70 (17.4)
アラニンアミノトランスフェラーゼ増加	0 (0.0)	3 (2.2)	0 (0.0)	3 (1.3)	3 (0.7)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	3 (2.2)	1 (1.1)	4 (1.7)	5 (1.2)
血圧上昇	4 (2.3)	4 (2.9)	3 (3.2)	7 (3.0)	11 (2.7)
血中プロラクチン増加	1 (0.6)	7 (5.1)	3 (3.2)	10 (4.3)	11 (2.7)
血中トリグリセリド増加	4 (2.3)	2 (1.5)	0 (0.0)	2 (0.9)	6 (1.5)
γ－グルタミルトランスフェラーゼ増加	1 (0.6)	4 (2.9)	0 (0.0)	4 (1.7)	5 (1.2)
尿中ブドウ糖陽性	3 (1.7)	1 (0.7)	2 (2.1)	3 (1.3)	6 (1.5)
体重減少	1 (0.6)	1 (0.7)	2 (2.1)	3 (1.3)	4 (1.0)
体重増加	2 (1.2)	3 (2.2)	2 (2.1)	5 (2.2)	7 (1.7)
代謝および栄養障害	14 (8.1)	18 (13.1)	2 (2.1)	20 (8.7)	34 (8.4)
食欲減退	12 (7.0)	10 (7.3)	1 (1.1)	11 (4.8)	23 (5.7)
筋骨格系および結合組織障害	31 (18.0)	28 (20.4)	18 (19.1)	46 (19.9)	77 (19.1)
関節痛	7 (4.1)	3 (2.2)	2 (2.1)	5 (2.2)	12 (3.0)
背部痛	11 (6.4)	11 (8.0)	9 (9.6)	20 (8.7)	31 (7.7)
筋肉痛	1 (0.6)	5 (3.6)	1 (1.1)	6 (2.6)	7 (1.7)
神経系障害	79 (45.9)	63 (46.0)	32 (34.0)	95 (41.1)	174 (43.2)
浮動性めまい	31 (18.0)	23 (16.8)	10 (10.6)	33 (14.3)	64 (15.9)
体位性めまい	2 (1.2)	3 (2.2)	1 (1.1)	4 (1.7)	6 (1.5)
味覚異常	10 (5.8)	8 (5.8)	2 (2.1)	10 (4.3)	20 (5.0)
頭部不快感	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.4)	5 (1.2)
頭痛	22 (12.8)	12 (8.8)	14 (14.9)	26 (11.3)	48 (11.9)
感覚鈍麻	3 (1.7)	3 (2.2)	0 (0.0)	3 (1.3)	6 (1.5)
傾眠	24 (14.0)	29 (21.2)	11 (11.7)	40 (17.3)	64 (15.9)
睡眠の質低下	5 (2.9)	1 (0.7)	1 (1.1)	2 (0.9)	7 (1.7)
精神障害	46 (26.7)	28 (20.4)	15 (16.0)	43 (18.6)	89 (22.1)
アルコールによる宿酔	5 (2.9)	5 (3.6)	2 (2.1)	7 (3.0)	12 (3.0)
不眠症	14 (8.1)	11 (8.0)	9 (9.6)	20 (8.7)	34 (8.4)
中期不眠症	6 (3.5)	7 (5.1)	2 (2.1)	9 (3.9)	15 (3.7)
睡眠障害	5 (2.9)	1 (0.7)	1 (1.1)	2 (0.9)	7 (1.7)
早朝覚醒型不眠症	6 (3.5)	1 (0.7)	0 (0.0)	1 (0.4)	7 (1.7)
生殖系および乳房障害	3 (1.7)	6 (4.4)	2 (2.1)	8 (3.5)	11 (2.7)
勃起増強	1 (0.6)	3 (2.2)	1 (1.1)	4 (1.7)	5 (1.2)
呼吸器、胸郭および縦隔障害	12 (7.0)	10 (7.3)	8 (8.5)	18 (7.8)	30 (7.4)
鼻出血	0 (0.0)	1 (0.7)	2 (2.1)	3 (1.3)	3 (0.7)
口腔咽頭痛	2 (1.2)	4 (2.9)	2 (2.1)	6 (2.6)	8 (2.0)
皮膚および皮下組織障害	18 (10.5)	14 (10.2)	6 (6.4)	20 (8.7)	38 (9.4)
湿疹	0 (0.0)	4 (2.9)	0 (0.0)	4 (1.7)	4 (1.0)
発疹	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.4)	5 (1.2)
蕁麻疹	2 (1.2)	2 (1.5)	2 (2.1)	4 (1.7)	6 (1.5)

表 2.7.4.2.1-7　いずれかの投与群からの移行例で 2%以上に発現した有害事象 : アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
血管障害	7 (4.1)	6 (4.4)	7 (7.4)	13 (5.6)	20 (5.0)
高血圧	4 (2.3)	3 (2.2)	3 (3.2)	6 (2.6)	10 (2.5)
ほてり	3 (1.7)	1 (0.7)	3 (3.2)	4 (1.7)	7 (1.7)

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＜資料番号 5.3.5.2-01：Table 14.1.1.3-33 より作成＞

(b)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で, いずれかの群で 5%以上に発現した有害事象を表 2.7.4.2.1-8，すべての有害事象を表 2.7.4.7.2-9 に示した。

アルコール依存症の海外試験併合で，有害事象は，ナルメフェン群 77.5%（368/475 例），プラセボ群 66.7%（246/369 例）に発現した。ナルメフェン群で 10%以上に発現した有害事象は，悪心，浮動性めまい，不眠症，頭痛であった。ナルメフェン群で 5%以上に発現した有害事象のうち，発現割合がプラセボ群の 2 倍以上であった事象は，悪心［ナルメフェン群 24.2%（115/475 例），プラセボ群 6.5%（24/369 例），以下同順］，浮動性めまい［21.9%（104/475 例），6.0%（22/369 例）］，不眠症［14.5%（69/475 例），4.3%（16/369 例）］，嘔吐［8.4%（40/475 例），3.5%（13/369 例）］，睡眠障害［6.7%（32/475 例），1.1%（4/369 例）］，多汗症［5.9%（28/475 例），0.8%（3/369 例）］，食欲減退［5.7%（27/475 例），1.1%（4/369 例）］であった。

アルコール依存症の海外試験併合全体で，ナルメフェン群で 5%以上に発現した有害事象は，悪心，浮動性めまい，不眠症，頭痛，鼻咽頭炎，嘔吐，疲労，傾眠であった（資料番号 5.3.5.3-01：Table 99 参照）。

表 2.7.4.2.1-8　いずれかの群で 5%以上に発現した有害事象：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

	Placebo		Nalmefene	
Preferred Term	n	(%)	n	(%)
Number of Patients	369		475	
Patients with TEAEs	246	(66.7)	368	(77.5)
悪心	24	(6.5)	115	(24.2)
浮動性めまい	22	(6.0)	104	(21.9)
不眠症	16	(4.3)	69	(14.5)
頭痛	35	(9.5)	60	(12.6)
疲労	22	(6.0)	43	(9.1)
嘔吐	13	(3.5)	40	(8.4)
鼻咽頭炎	39	(10.6)	38	(8.0)
睡眠障害	4	(1.1)	32	(6.7)
多汗症	3	(0.8)	28	(5.9)
食欲減退	4	(1.1)	27	(5.7)
下痢	22	(6.0)	19	(4.0)
偶発的過量投与	22	(6.0)	13	(2.7)

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＜資料番号 5.3.5.3-01：Table 111 より作成＞

(c)　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験併合で，ナルメフェン群で 5%以上に発現した有害事象を表 2.7.4.7.2-12，すべての有害事象を表 2.7.4.7.2-13 に示した。なお，ナルメフェン可変用量の試験（CPH-101-0801，CPH-101-0701，CPH-101-0400）でナルメフェン群であった被験者は，ナルメフェン 20 mg 群に含めたため，用量別の検討には限界がある。

ナルメフェン群で 10%以上に発現した有害事象のうち，ナルメフェン群でプラセボ群と比較して発現割合が 5%以上高かった有害事象は，悪心，不眠症，浮動性めまい，疲労，嘔吐 NOS であった。発現した有害事象の種類や発現割合に，ナルメフェンの用量との明らかな関連性は認められなかった。

(4)　有害事象の重症度及び持続期間

(a)　アルコール依存症の国内試験

i)　短期投与（339-14-001）

アルコール依存症の国内短期投与での重症度別有害事象の発現割合は，ナルメフェン 20 mg 群では軽度 69.8%（173/248 例），中等度 17.7%（44/248 例），高度 0.4%（1/248 例），10 mg 群では軽度 64.1%（118/184 例），中等度 19.0%（35/184 例），高度 1.6%（3/184 例），プラセボ群では軽度 71.0%（174/245 例），中等度 8.2%（20/245 例），高度 0.0%（0/245 例）であり，いずれの投与群でも，有害事象のほとんどは軽度又は中等度であった。ナルメフェン各投与群で発現した高度な有害事象は，20 mg 群で悪心，嘔吐が各 1 例（同一被験者），10 mg 群で悪心，嘔吐，浮動性めまい，死亡，大腿骨骨折が各 1 例（悪心，嘔吐，浮動性めまいは同一被験者）であった。

20 mg 群又は 10 mg 群で発現割合が 5%以上かつプラセボ群の 2 倍以上であった有害事象（悪心，浮動性めまい，傾眠，嘔吐，倦怠感，不眠症，食欲減退，便秘，動悸）の重症度は，いずれもほとんどが軽度又は中等度であった（表 2.7.6.5.1-31 参照）。

また，これらの事象の持続期間別の発現割合は，悪心，浮動性めまい，嘔吐，倦怠感，不眠症，食欲減退では，いずれのナルメフェン投与群でも，持続期間は 7 日以内が最も高かった。便秘及び動悸では，20 mg 群での持続期間は 7 日以内が最も高かったが，10 mg 群では発現例数が少なく，持続期間に明らかな傾向は認められなかった。傾眠では，いずれのナルメフェン投与群でも，持続期間は 141 日以上が最も高かった（資料番号 5.3.5.1-01：Table 14.1.1.3-29 参照）。

重症度別副作用の発現割合は，20 mg 群では軽度 57.3%（142/248 例），中等度 13.3%（33/248 例），高度 0.4%（1/248 例），10 mg 群では軽度 58.2%（107/184 例），中等度 12.0%（22/184 例），高度 1.1%（2/184 例），プラセボ群では軽度 36.3%（89/245 例），中等度 0.8%（2/245 例），高度 0.0%（0/245 例）であり，いずれの投与群でも，副作用のほとんどは軽度又は中等度であった。ナルメフェン各投与群で発現した高度な副作用は，20 mg 群で悪心，嘔吐が各 1 例（同一被験者），10 mg 群で悪心，嘔吐，浮動性めまい，死亡が各 1 例（悪心，嘔吐，浮動性めまいは同一被験者）であった（表 2.7.6.5.1-33 参照）。

ii) 長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与での重症度別有害事象の発現割合は，ナルメフェン投与群全体からの移行例で軽度 71.4%（165/231 例），中等度 19.5%（45/231 例）であり，高度な有害事象の発現はなかった。なお，プラセボ群からの移行例では，継続長期試験（339-14-002）の治療期に 1.2%（2/172 例）で高度な有害事象が認められ，発現した事象は血圧上昇と浮動性めまいが各 1 例であった。

ナルメフェン投与群全体からの移行例で，発現割合が 5%以上であった有害事象（鼻咽頭炎，悪心，傾眠，浮動性めまい，嘔吐，倦怠感，頭痛，背部痛，不眠症，腹部不快感，便秘，腹部膨満，下痢）の重症度は，いずれも軽度又は中等度であった（資料番号 5.3.5.2-01：Table 14.1.1.3-29 参照）。

また，これらの事象の持続期間別の発現割合は，傾眠以外の事象では持続期間は 7 日以内が最も高く，傾眠では持続期間は 141 日以上が最も高かった（資料番号 5.3.5.2-01：Table 14.1.1.3-46 参照）。

重症度別副作用の発現割合は，ナルメフェン投与群全体からの移行例で軽度 67.1%（155/231 例），中等度 8.7%（20/231 例）であり，高度な副作用の発現はなかった。なお，プラセボ群からの移行例では，339-14-002 試験の治療期に 1.2%（2/172 例）で高度な副作用が認められ，発現した事象は血圧上昇と浮動性めまいが各 1 例であった（資料番号 5.3.5.2-01：Table 14.1.1.3-30 参照）。

(b)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合で DRL が High 以上であった被験者での重症度別有害事象の発現割合は，ナルメフェン群では軽度 18.5%（88/475 例），中等度 42.3%（201/475 例），高度 16.6%（79/475 例），プラセボ群では軽度 22.2%（82/369 例），中等度 36.6%（135/369 例），高度 7.9%（29/369 例）であった。ナルメフェン群で 2%以上に発現した高度な有害事象は，浮動性めまい 3.6%（17/475 例），悪心 3.4%（16/475 例），不眠症 2.5%（12/475 例）であった（資料番号 5.3.5.3-01：Table 114 参照）。

DRL が High 以上であった被験者のナルメフェン群で 5%以上に発現し，発現割合がプラセボ群の 2 倍以上であった有害事象（悪心，浮動性めまい，不眠症，嘔吐，睡眠障害，多汗症，食欲減退）の持続期間の中央値は，ナルメフェン群で 2.0～9.0 日であった（表 2.7.4.7.2-24 参照）。

重症度別副作用の発現割合は，ナルメフェン群では軽度 16.4%（78/475 例），中等度 34.7%（165/475 例），高度 11.6%（55/475 例），プラセボ群では軽度 20.3%（75/369 例），中等度 16.8%（62/369 例），高度 3.8%（14/369 例）であった（資料番号 5.3.5.3-01：Table 115 参照）。

アルコール依存症の海外試験併合全体での重症度別有害事象の発現割合は，ナルメフェン群では軽度 19.0%（217/1144 例），中等度 41.7%（477/1144 例），高度 14.1%（161/1144 例），プラセボ群では軽度 21.3%（170/797 例），中等度 32.1%（256/797 例），高度 9.3%（74/797 例）であった（資料番号 5.3.5.3-01：Table 103 参照）。

(5)　有害事象の発現時期

(a)　アルコール依存症の国内試験

i)　短期投与（339-14-001）

アルコール依存症の国内短期投与での初回発現時期別の有害事象を表 2.7.4.7.1-14 に示した。

初回発現時期別の有害事象の発現割合は，いずれの投与群でも初回投与後 0～6 日に最も高かった。ナルメフェン 20 mg 群での各時期の有害事象の発現割合は，0～6 日に 65.7%（163/248 例）であり，7 日以降は 0.9%～5.3%で推移した。10 mg 群での各時期の有害事象の発現割合は，0～6 日に 60.3%（111/184 例）であり，7 日以降は 1.8%～6.6%で推移した。

20 mg 群又は 10 mg 群で，0～6 日に発現割合が 5%以上であった有害事象は，悪心［20 mg 群 28.6%（71/248 例），10 mg 群 27.2%（50/184 例），プラセボ群 3.3%（8/245 例），以下同順］，浮動性めまい［18.5%（46/248 例），9.2%（17/184 例），2.9%（7/245 例）］，傾眠［12.1%（30/248 例），8.2%（15/184 例），4.1%（10/245 例）］，嘔吐［8.5%（21/248 例），4.9%（9/184 例），0.4%（1/245 例）］，頭痛［7.7%（19/248 例），7.1%（13/184 例），3.3%（8/245 例）］，不眠症［6.9%（17/248 例），7.1%（13/184 例），0.0%（0/245 例）］，倦怠感［6.9%（17/248 例），2.7%（5/184 例），1.6%（4/245 例）］であった。

更に，治験薬初回投与翌日までに発現した有害事象の検討から，いずれのナルメフェン投与群でも，有害事象の初回発現時期は，被験者の多くで治験薬の投与初日であった（資料番号

5.3.5.1-01：Table 14.1.1.3-26 参照）。

ii)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与で，ナルメフェンを投与された期間に発現した，初回発現時期別の有害事象を表 2.7.4.7.1-15 に示した。

ナルメフェン投与群全体からの移行例で，初回発現時期別の有害事象の発現割合は，初回投与後 0～84 日に 74.0%（171/231 例）と最も高く，85 日以降には低下して 85～168 日で 9.1%（21/231 例），169～252 日で 6.1%（14/231 例），253～336 日で 1.8%（4/225 例），337 日以降で 0.0%（0/214 例）と推移した。

ナルメフェンの長期投与時の安全性を検討するため，169 日以降（24 週超）に発現割合が高い有害事象に着目した。169 日以降（24 週超）に，ナルメフェン投与群全体からの移行例で初回発現時期別の発現割合が 5%以上であった有害事象は，169～252 日の鼻咽頭炎 8.7%（20/231 例）のみであった。鼻咽頭炎の初回発現時期別発現割合は投与期間の延長に伴って低下した。ナルメフェン投与群全体からの移行例で投与期間の延長に伴って発現割合が明らかに高くなる事象はなかった。

339-14-002 試験は継続長期試験であり，プラセボ対照二重盲検試験（339-14-001）で 10 mg 群であった被験者はいずれも 339-14-002 試験では 20 mg を服用したことから，10 mg から 20 mg へ増量したときの安全性を検討した。

10 mg 群からの移行例で，初回発現時期別の有害事象の発現割合は，初回投与後 0～84 日に最も高く 67.0%（63/94 例）であり，85～168 日で 11.7%（11/94 例），169～252 日で 9.6%（9/94 例），253～336 日で 2.2%（2/91 例），337 日以降で 0.0%（0/85 例）と推移し，10 mg から 20 mg へ増量後に発現割合が高くなることはなかった。

(b)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で，治験薬の初回投与翌日までに，有害事象がナルメフェン群の 47.2%（224/475 例），プラセボ群の 20.9%（77/369 例）で発現した。ナルメフェン群では，全期間で有害事象が発現した被験者の半数以上で，初回投与翌日までに有害事象が発現した。ナルメフェン群で，初回投与翌日までに 5%以上で発現した有害事象は，悪心 17.1%（81/475 例），浮動性めまい 17.5%（83/475 例），不眠症 7.8%（37/475 例），頭痛 6.7%（32/475 例），疲労 5.7%（27/475 例）であり，いずれも発現割合はプラセボ群の 2 倍以上であった（資料番号 5.3.5.3-01：Table 112 参照）。

プラセボ対照二重盲検長期試験（12013A）で，無作為化 6 ヵ月後以降に発現した有害事象を表 2.7.4.7.2-14 に示した。全般的に，52 週間のプラセボ対照二重盲検長期試験（12013A）で発現した有害事象のパターンは，24 週間のプラセボ対象二重盲検試験（12014A，12023A）と類似していた。プラセボ対照二重盲検長期試験（12013A）の後半 6 ヵ月に，新たな種類の有害事象の発現は示唆されなかった。

2.7.4.2.1.2　死亡

(1)　国内試験

アルコール依存症の国内短期投与での死亡例一覧を表 2.7.4.2.1-9 に示し，死亡例の叙述は「2.7.6.5.1.5 死亡，その他の重篤な有害事象の叙述」に示した。

アルコール依存症の国内試験では，1 例の死亡がプラセボ対照二重盲検試験（339-14-001）のナルメフェン 10 mg 群で報告された。継続長期試験（339-14-002）で，死亡の報告はなかった。

339-14-001 試験の 10 mg 群で死亡した 1 例は，[redacted] 歳，[redacted]であった。治験薬の初回投与後 168 日に死亡が確認され，死亡に至った有害事象は「死亡」（症例報告書用語 : UNKNOWN CAUSED DEATH）であった。死因が不明であり，治験薬との関連性は否定できないと判断された。

健康成人の国内単回投与試験（339-102-00003）で，死亡の報告はなかった（資料番号 5.3.3.1-01 : CT-8.4 参照）。

表 2.7.4.2.1-9　　死亡例一覧：アルコール依存症の国内短期投与（339-14-001）

Treatment group	Subject ID	Sex Age (years)	Preferred term	Days since first IMP[a] (days) Days since last IMP[b] (days) Outcome Duration[c] (days)	Causality Severity	Seriousness Action regarding IMP
Nalmefene 10 mg	[redacted]	[redacted] [redacted]	アレルギー性鼻炎	77 0 RECOVERED/RESOLVED 92	NOT RELATED MILD	N DOSE NOT CHANGED
			死亡	168 36 FATAL 1	RELATED SEVERE	Y NOT APPLICABLE

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M = man
[a]:Date of onset - date of first IMP administration
[b]:Date of onset - date of last IMP administration
[c]:Date of outcome - Date of onset + 1
＜資料番号 5.3.5.1-01：Table 14.1.1.3-79＞

(2)　海外試験

海外試験では，8 例の死亡が報告された。このうち 4 例がアルコール依存症の試験，1 例がアルコール使用障害の試験，3 例がその他の疾患を対象とした試験の被験者であった。

アルコール依存症の海外試験併合での死亡に至った有害事象一覧を，表 2.7.4.2.1-10 に示した。死亡は，ナルメフェン群で 2 例，プラセボ群で 2 例報告された。死亡に至った有害事象は，ナルメフェン群で突然死が 1 例，外傷性脳損傷が 1 例，プラセボ群で自殺既遂が 2 例であった。

ナルメフェン群で突然死した 1 例は，[redacted] 歳の[redacted]であった。治験薬初回投与後 46 日の朝に死亡が確認されたが，その前夜に問題はなかった。記録された最後の治験薬服薬は，死亡の 3 日前

であった。ベースライン時の DRL は High（TAC 91 g/日），最終来院時の DRL は Low（TAC 9 g/日）であった。被験者は 1 日に 20 本を超える喫煙があったが，そのほかに関連のある既往症はなかった。併用薬の使用はなく，死亡前の臨床検査値，バイタルサイン，及び心電図に問題は認められなかった。検死は実施されず，死因は特定されなかった。

ナルメフェン群で死亡に至った外傷性脳損傷 1 例は，自動車事故によるものであった。被験者は乗客であった。

死亡に至った有害事象は，プラセボ群での自殺既遂 1 例を除き，治験責任医師は治験薬との関連性を Not related と判断した。

アルコール使用障害の海外試験及びその他の疾患で報告された死亡に至った有害事象一覧を，表 2.7.4.7.2-11 に示した。アルコール使用障害の海外試験併合では，死亡がプラセボ群で 1 例報告された。死亡に至った有害事象は播種性癌であった。その他の疾患では死亡が 3 例報告された。死亡に至った有害事象は，長年にわたる脳卒中後の状態と腎不全による合併症（そう痒症の試験，1 mg/日），急性心筋梗塞（関節リウマチの試験，20 mg b.i.d），遠隔転移を伴う前立腺癌（間質性膀胱炎の試験，治験薬投与状況不明）であった。

表 2.7.4.2.1-10　死亡に至った有害事象一覧：アルコール依存症の海外試験併合

Study (Indication)	Treatment & dose	Patient/Sex/ Age (years)	Adverse event(s)	Time from first/ last dose to adverse event onset (Days)	Causality
12014A (alcohol dependence)	Placebo as-needed	[redacted]	自殺既遂	33/5[a]	NR
	Placebo as-needed	[redacted]	自殺既遂	30/5[a]	POS
12023A (alcohol dependence)	Nalmefene 20 mg as-needed	[redacted]	突然死	46/3	NR
12013A (alcohol dependence)	Nalmefene 20 mg as-needed	[redacted]	外傷性脳損傷	128/15	NR

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M = man; NR = not related; POS = possibly related

[a]:No information is available on IMP intake for the 5 days prior to the event.

＜資料番号 5.3.5.3-03：Panel 27 より作成＞

2.7.4.2.1.3　その他の重篤な有害事象

(1)　アルコール依存症の国内試験

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した重篤な有害事象及び副作用を表 2.7.4.2.1-11 及び表 2.7.4.2.1-12，死亡例以外の重篤な有害事象を発現した被験者一覧を表 2.7.4.7.1-16 に示した。死亡例以外の重篤な有害事象を発現した被験者の叙述は「2.7.6.5.1.5 死亡，その他の重篤な有害事象の叙述」に示した。

重篤な有害事象は，ナルメフェン 20 mg 群 0.8%（2/248 例），10 mg 群 1.1%（2/184 例），プラセボ群 0.8%（2/245 例）に発現した。

死亡以外の重篤な有害事象は，20 mg 群で慢性肝炎（症例報告書用語：CHRONIC HEPATITIS AGGRAVATED），胃腸炎が各 1 例，10 mg 群で大腿骨骨折，脊椎圧迫骨折が 1 例（同一被験者で発現），プラセボ群で出血性吻合部潰瘍，アルコール症（症例報告書用語：AGGRAVATION OF ALCOHOL DEPENDENCE）が各 1 例であった（資料番号 5.3.5.1-01：Listing 16.2.7.2 参照）。

20 mg 群の慢性肝炎，10 mg 群の大腿骨骨折，プラセボ群の出血性吻合部潰瘍は，投与中止に至った。治験薬との関連性は，20 mg 群の慢性肝炎，プラセボ群の出血性吻合部潰瘍は否定できない，その他の事象は否定できると判断された。転帰は，10 mg 群の大腿骨骨折と脊椎圧迫骨折は未回復で調査を終了し，その他の事象では回復又は軽快（回復途上）が確認された。治験薬の初回投与から発現までの日数は，20 mg 群の胃腸炎が 17 日，慢性肝炎が 41 日，10 mg 群の大腿骨骨折及び脊椎圧迫骨折が 79 日であった。

表 2.7.4.2.1-11　　重篤な有害事象：アルコール依存症の国内短期投与（339-14-001）

	Placebo	Nalmefene		
		20 mg	10 mg	Total
System organ class	(N=245)	(N=248)	(N=184)	(N=432)
Preferred term	n (%)	n (%)	n (%)	n (%)
Total number of subjects with serious TEAEs	2 (0.8)	2 (0.8)	2 (1.1)	4 (0.9)
一般・全身障害および投与部位の状態	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
死亡	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
肝胆道系障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
慢性肝炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
感染症および寄生虫症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
胃腸炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
傷害、中毒および処置合併症	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
出血性吻合部潰瘍	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
大腿骨骨折	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
精神障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
アルコール症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-33 より作成＞

表 2.7.4.2.1-12　重篤な副作用：アルコール依存症の国内短期投与（339-14-001）

	Placebo	Nalmefene		
		20 mg	10 mg	Total
System organ class	(N=245)	(N=248)	(N=184)	(N=432)
Preferred term	n (%)	n (%)	n (%)	n (%)
Total number of subjects with serious drug-related TEAEs	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
一般・全身障害および投与部位の状態	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
死亡	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
肝胆道系障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
慢性肝炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
傷害、中毒および処置合併症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
出血性吻合部潰瘍	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-34 より作成＞

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内継続長期試験（339-14-002）の治療期に発現した重篤な有害事象を表 2.7.4.2.1-13 に示した。また，退薬期に発現した重篤な有害事象及び副作用を表 2.7.4.2.1-14 及び表 2.7.4.2.1-15 に示した。死亡例以外の重篤な有害事象を発現した被験者一覧を表 2.7.4.7.1-17 に示し，叙述は「2.7.6.5.9.5 重篤な有害事象の叙述」に示した。なお，プラセボ対照二重盲検試験（339-14-001）で重篤な有害事象が発現した被験者は，いずれも 339-14-002 試験に移行しなかったため，本項では 339-14-002 試験へ移行後に発現した重篤な有害事象を示した。

339-14-002 試験の治療期に，ナルメフェン投与群全体からの移行例で重篤な有害事象は 1.3%（3/231 例）に発現した。重篤な有害事象は，胃腸炎，脱水，前立腺癌が各 1 例（胃腸炎：ナルメフェン 10 mg 群からの移行例，脱水及び前立腺癌：20 mg 群からの移行例）であった。脱水，前立腺癌は，投与中止に至った。胃腸炎，脱水，前立腺癌はいずれも，治験薬との関連性は否定できると判断され，転帰は回復又は軽快（回復途上）であった。339-14-001 試験でのナルメフェン初回投与から発現までの日数は，胃腸炎が 217 日，前立腺癌が 309 日，脱水が 321 日であった。なお，339-14-002 試験の治療期に，プラセボ群からの移行例で重篤な有害事象の発現はなかった。

退薬期に，重篤な有害事象はナルメフェン群 0.6%（1/172 例），プラセボ群 0.6%（1/171 例）に発現した。重篤な有害事象は，ナルメフェン群で血栓性脳梗塞が 1 例（339-14-001 試験のプラセボ群からの移行例），プラセボ群で器質化肺炎が 1 例（339-14-001 試験の 20 mg 群からの移行例）であった。いずれも退薬期の治験薬投与を完了した。治験薬との関連性は，ナルメフェン群の血栓性脳梗塞は否定できる，プラセボ群の器質化肺炎は否定できないと判断された。転帰は，血栓性脳梗塞は回復したが後遺症あり（軽度の麻痺），器質化肺炎は軽快（回復途上）であった。血栓性脳梗塞は，339-14-002 試験のナルメフェン初回投与後 171 日に発現した。器質化肺炎は，339-14-001 試験及び 339-14-002 試験の治療期でのナルメフェンの投与を終了し

（投与期間：338 日），退薬期のプラセボ初回投与後 18 日に発現した。

表 2.7.4.2.1-13　重篤な有害事象：アルコール依存症の国内継続長期試験（339-14-002）－ 治療期

Treatment group of study 339-14-001	Placebo	Nalmefene			Total
		20 mg	10 mg	Total	
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with serious adverse events	0 (0.0)	2 (1.5)	1 (1.1)	3 (1.3)	3 (0.7)
感染症および寄生虫症	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
胃腸炎	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
代謝および栄養障害	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
脱水	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
前立腺癌	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)

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＜資料番号 5.3.5.2-01：Table 14.1.1.3-57 より作成＞

表 2.7.4.2.1-14　重篤な有害事象：アルコール依存症の国内継続長期試験（339-14-002）－ 退薬期

Treatment group of run-out period	Placebo	Nalmefene 20 mg
System organ class	(N=171)	(N=172)
Preferred term	n (%)	n (%)
Total number of subjects with serious adverse events	1 (0.6)	1 (0.6)
神経系障害	0 (0.0)	1 (0.6)
血栓性脳梗塞	0 (0.0)	1 (0.6)
呼吸器、胸郭および縦隔障害	1 (0.6)	0 (0.0)
器質化肺炎	1 (0.6)	0 (0.0)

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＜資料番号 5.3.5.2-01：Table 14.1.1.3-62 より作成＞

表 2.7.4.2.1-15　重篤な副作用：アルコール依存症の国内継続長期試験（339-14-002）－ 退薬期

Treatment group of run-out period	Placebo	Nalmefene 20 mg
System organ class	(N=171)	(N=172)
Preferred term	n (%)	n (%)
Total number of subjects with serious drug-related adverse events	1 (0.6)	0 (0.0)
呼吸器、胸郭および縦隔障害	1 (0.6)	0 (0.0)
器質化肺炎	1 (0.6)	0 (0.0)

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＜資料番号 5.3.5.2-01：Table 14.1.1.3-63 より作成＞

(2) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した重篤な有害事象を表 2.7.4.2.1-16 に示した。

重篤な有害事象は，ナルメフェン群 5.5%（26/475 例），プラセボ群 3.5%（13/369 例）に発現した。ナルメフェン群で 2 例以上に発現した重篤な有害事象は，非心臓性胸痛，転倒，アルコール症が各 0.4%（2/475 例）であった。

アルコール依存症の海外試験併合全体で, 重篤な有害事象はナルメフェン群 5.0%（57/1144 例），プラセボ群 4.4%（35/797 例）に発現した（資料番号 5.3.5.3-01：Table 72 参照）。重篤な有害事象の一覧を表 2.7.4.7.2-15 に示した。

表 2.7.4.2.1-16　重篤な有害事象: アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with Treatment-emergent SAEs	13	(3.5)	26	(5.5)
心臓障害	0	(0.0)	1	(0.2)
心筋梗塞	0	(0.0)	1	(0.2)
眼障害	0	(0.0)	1	(0.2)
複視	0	(0.0)	1	(0.2)
胃腸障害	1	(0.3)	2	(0.4)
穿孔性胃潰瘍	0	(0.0)	1	(0.2)
急性膵炎	1	(0.3)	0	(0.0)
潰瘍性食道炎	0	(0.0)	1	(0.2)
一般・全身障害および投与部位の状態	0	(0.0)	2	(0.4)
非心臓性胸痛	0	(0.0)	2	(0.4)
肝胆道系障害	1	(0.3)	0	(0.0)
急性胆嚢炎	1	(0.3)	0	(0.0)
感染症および寄生虫症	1	(0.3)	1	(0.2)
肺炎	0	(0.0)	1	(0.2)
感染性胸水	1	(0.3)	0	(0.0)
傷害、中毒および処置合併症	4	(1.1)	7	(1.5)
アルコール中毒	1	(0.3)	1	(0.2)
転倒	1	(0.3)	2	(0.4)
大腿骨頚部骨折	0	(0.0)	1	(0.2)
腓骨骨折	1	(0.3)	1	(0.2)
頭部損傷	0	(0.0)	1	(0.2)
肋骨骨折	2	(0.5)	0	(0.0)
腱断裂	0	(0.0)	1	(0.2)
脛骨骨折	1	(0.3)	0	(0.0)
尺骨骨折	0	(0.0)	1	(0.2)
各種物質毒性	1	(0.3)	0	(0.0)
代謝および栄養障害	0	(0.0)	1	(0.2)
食欲減退	0	(0.0)	1	(0.2)

表 2.7.4.2.1-16　重篤な有害事象:アルコール依存症の海外試験併合 －DRL が High 以上であった被験者（続き）

System Organ Class Preferred Term	Placebo n	(%)	Nalmefene n	(%)
筋骨格系および結合組織障害	0	(0.0)	4	(0.8)
背部痛	0	(0.0)	1	(0.2)
四肢痛	0	(0.0)	1	(0.2)
腱炎	0	(0.0)	1	(0.2)
椎間板突出	0	(0.0)	1	(0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1	(0.3)	1	(0.2)
喉頭癌	1	(0.3)	0	(0.0)
前立腺癌 {ss}	0	(0.0)	1	(0.3)
神経系障害	2	(0.5)	4	(0.8)
浮動性めまい	1	(0.3)	1	(0.2)
てんかん	1	(0.3)	0	(0.0)
頭痛	0	(0.0)	1	(0.2)
くも膜下出血	0	(0.0)	1	(0.2)
平衡障害	0	(0.0)	1	(0.2)
精神障害	2	(0.5)	7	(1.5)
アルコール症	1	(0.3)	2	(0.4)
神経性無食欲症	0	(0.0)	1	(0.2)
不安	0	(0.0)	1	(0.2)
自殺既遂	1	(0.3)	0	(0.0)
失見当識	0	(0.0)	1	(0.2)
不眠症	0	(0.0)	1	(0.2)
悪夢	0	(0.0)	1	(0.2)
アルコール離脱症候群	0	(0.0)	1	(0.2)
呼吸器、胸郭および縦隔障害	2	(0.5)	1	(0.2)
気胸	2	(0.5)	0	(0.0)
喉頭蓋嚢胞	0	(0.0)	1	(0.2)
血管障害	1	(0.3)	0	(0.0)
動脈炎	1	(0.3)	0	(0.0)

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{ss} Sex specific

＜資料番号 5.3.5.3-01：Table 75＞

(3)　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験併合で発現した重篤な有害事象を表 2.7.4.7.2-16，重篤な有害事象の一覧を表 2.7.4.7.2-17 に示した。

重篤な有害事象はナルメフェン群 30 例，プラセボ群 14 例で発現し，いずれの投与群でも発現割合は約 4%であった。発現した重篤な有害事象は多くの器官別大分類にわたり，明らかな傾向は認められなかった。

(4)　臨床薬理試験

臨床薬理試験では，重篤な有害事象が 1 例で報告された。

Study 21 で，[redacted] 歳 [redacted] の健康成人[redacted]に，心電図異常（electrocardiogram abnormal）が認められた。重症度は軽度，治験薬との関連性は Possibly related と判断され，処置なく回復した。

(5)　その他の試験

病的賭博，ニコチン依存症患者を対象とした試験（CPH-101-0600，SP-N0406，SP-N0408）で，ナルメフェン群 357 例，プラセボ群 156 例のうち，ナルメフェン群の 7 例，プラセボ群の 2 例で重篤な有害事象が認められた。発現した重篤な有害事象の種類に，明らかな傾向は認められなかった（表 2.7.4.7.2-18 参照）。

その他の疾患を対象とした試験では，ナルメフェン群 901 例のうち，14 例（1.6%）に重篤な有害事象又は臨床的に重要な可能性がある事象が認められ，このうち 3 例は死亡例であった。4 例では肝機能検査値が高値を示した。その他の 7 例で発現した事象に明らかな傾向は認められなかった。

2.7.4.2.1.4　その他の重要な有害事象

投与中止に至った有害事象を「その他の重要な有害事象」とした。

(1)　アルコール依存症の国内試験

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，投与中止に至った有害事象を表 2.7.4.7.1-18，投与中止に至った有害事象を発現した被験者一覧を表 2.7.6.5.1-34 に示した。

投与中止に至った有害事象は，ナルメフェン 20 mg 群 18.1%（45/248 例），10 mg 群 17.9%（33/184 例），プラセボ群 4.5%（11/245 例）に発現した。

いずれのナルメフェン投与群でも，発現割合が最も高かった投与中止に至った有害事象は，悪心［20 mg 群 8.5%（21/248 例），10 mg 群 6.5%（12/184 例），以下同順］，次いで浮動性めまい［6.5%（16/248 例），4.9%（9/184 例）］であった。そのほかに，20 mg 群又は 10 mg 群で 2%以上に発現した投与中止に至った有害事象は，嘔吐，頭痛，不眠症，動悸，食欲減退であった。

初回発現時期別の投与中止に至った有害事象の発現割合は，ナルメフェン各投与群で，初回投与後 0～6 日に最も高かった。20 mg 群での各時期の有害事象の発現割合は，0～6 日に 13.7%（34/248 例）であり，7 日以降は 0.0%～1.7%で推移した。10 mg 群での各時期の有害事象の発現割合は，0～6 日に 10.9%（20/184 例）であり，7 日以降は 0.0%～2.6%で推移した。いずれのナルメフェン投与群でも，投与中止に至った有害事象の発現時期は，半数以上で初回投与後 0～6 日であった（資料番号 5.3.5.1-01：Table 14.1.1.3-38 参照）。

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内継続長期試験（339-14-002）の治療期に発現し投与中止に至った有害事象を表 2.7.4.7.1-19 に，退薬期に発現し投与中止に至った有害事象を表 2.7.4.7.1-20 に示した。投与中止に至った有害事象を発現した被験者一覧を表 2.7.6.5.9-39 に示した。なお，プラセボ対照二重盲検試験（339-14-001）で中止した被験者は 339-14-002 試験に移行しないため，339-14-001 試験で発現し中止に至った有害事象は，本項に含まれない。

339-14-002 試験の治療期にナルメフェン投与群全体からの移行例で，投与中止に至った有害事象は 4.3%（10/231 例）に発現した。2%以上に発現した投与中止に至った有害事象はなかった。

なお，339-14-002 試験の治療期に，プラセボ群からの移行例で投与中止に至った有害事象の発現割合は，18.6%（32/172 例）であった。発現割合が最も高かった投与中止に至った有害事象は，悪心 7.6%（13/172 例），次いで浮動性めまい 5.8%（10/172 例）であった。そのほかに，2%以上に発現した投与中止に至った有害事象は，頭痛，嘔吐，食欲減退であった。

退薬期に，投与中止に至った有害事象はナルメフェン群 0.6%（1/172 例）に発現し，プラセボ群での発現はなかった。

(2) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，投与中止に至った有害事象を表 2.7.4.7.2-10 に示した。

投与中止に至った有害事象は，ナルメフェン群 16.4%（78/475 例），プラセボ群 7.0%（26/369 例）に発現した。ナルメフェン群で 2%以上に発現した投与中止に至った有害事象は，浮動性めまい 5.3%（25/475 例），悪心 3.8%（18/475 例）であった。

アルコール依存症の海外試験併合全体で，投与中止に至った有害事象はナルメフェン群 13.0%（149/1144 例），プラセボ群 5.9%（47/797 例）に発現した（資料番号 5.3.5.3-01 : Table 80 参照）。

(3) アルコール使用障害の海外試験併合

アルコール使用障害の海外試験併合で発現した，投与中止に至った有害事象を表 2.7.4.7.2-19 に示した。

投与中止に至った有害事象は，ナルメフェン群 15.2%（105/689 例），プラセボ群 3.6%（13/361 例）に発現した。ナルメフェン各用量群での投与中止に至った有害事象の発現割合に，用量との明確な関連は認められなかった［5 mg 群 7.4%（5/68 例），10 mg 群 12.0%（6/50 例），20 mg 群 17.2%（78/453 例），40 mg 群 13.6%（16/118 例）］。

事象別にみると，頭痛と嘔吐を除き，各有害事象の発現割合は，各用量群で大きく異ならなかった。投与中止に至った頭痛は 20 mg 群と 40 mg 群のみで，嘔吐 NOS は 20 mg 群のみで発現した。

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

アルコール依存症の国内試験及び海外試験では，アルコール依存症患者にナルメフェンを投与する際に留意が必要な有害事象として，以下を「注目すべき有害事象」とし，集計した。定義は，表 2.7.4.7.1-1 に示した。

- 事故及び損傷関連有害事象
- 痙攣関連有害事象
- うつ病関連有害事象

- 薬物使用障害関連有害事象
- 薬剤に関連する肝障害，明確にアルコール関連と報告された肝障害
- 横紋筋融解症及びミオパチー関連有害事象
- 精神系有害事象
- 自殺関連有害事象
- 睡眠障害に関連する夜間の症状，睡眠障害に関連する日中の症状

(1) 事故及び損傷関連有害事象

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，事故及び損傷関連有害事象を表 2.7.4.2.1-17 に示した。

事故及び損傷関連有害事象はナルメフェン 20 mg 群 2.8%（7/248 例），10 mg 群 3.3%（6/184 例），プラセボ群 6.5%（16/245 例）に発現した。20 mg 群又は 10 mg 群で 2 例以上に発現した事象は，20 mg 群では転倒 0.8%（2/248 例），10 mg 群では挫傷 1.1%（2/184 例）であった。重篤と判断された 10 mg 群の大腿骨骨折と脊椎圧迫骨折の 1 例（同一被験者で発現）を除き，20 mg 群又は 10 mg 群で発現したいずれの事象も重症度は軽度又は中等度であり，投与中止に至った事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。

表 2.7.4.2.1-17　事故及び損傷関連有害事象：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with SMQ accidents and injuries	16 (6.5)	0 (0.0)	7 (2.8)	0 (0.0)	6 (3.3)	1 (0.5)	13 (3.0)	1 (0.2)
傷害、中毒および処置合併症	16 (6.5)	0 (0.0)	7 (2.8)	0 (0.0)	6 (3.3)	1 (0.5)	13 (3.0)	1 (0.2)
転倒	2 (0.8)	0 (0.0)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	1 (0.2)	1 (0.2)
足骨折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
骨折	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
熱射病	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
靭帯捻挫	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
肋骨骨折	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
脊椎圧迫骨折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)
擦過傷	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
挫傷	4 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)	2 (0.5)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
熱傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靭帯損傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部損傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.4.2.1-17　事故及び損傷関連有害事象：アルコール依存症の国内短期投与（339-14-001）（続き）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症								
耳擦過傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
外傷後頚部症候群	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-40 より作成＞

(b)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，事故及び損傷関連有害事象は，プラセボ対照二重盲検試験（339-14-001）の治療期に 2.6%（6/231 例），継続長期試験（339-14-002）の治療期に 3.9%（9/231 例）発現し，発現割合は時期により大きく異ならなかった。339-14-002 試験の治療期に発現した事象はいずれも，重症度は軽度又は中等度であり，重篤と判断された事象及び投与中止に至った事象はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-72，Table 14.1.1.3-29，表 2.7.4.2.1-13 参照）。

(c)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，事故及び損傷関連有害事象を表 2.7.4.2.1-18 に示した。

事故及び損傷関連有害事象はナルメフェン群 4.2%（20/475 例），プラセボ群 6.2%（23/369 例）に発現した。

表 2.7.4.2.1-18　事故及び損傷関連有害事象：アルコール依存症の海外試験併合 – DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	23	(6.2)	20	(4.2)
肝胆道系障害	0	(0.0)	1	(0.2)
肝損傷	0	(0.0)	1	(0.2)
傷害、中毒および処置合併症	23	(6.2)	20	(4.2)
労働災害	0	(0.0)	1	(0.2)
動物咬傷	1	(0.3)	0	(0.0)
足関節部骨折	1	(0.3)	1	(0.2)
脳振盪	1	(0.3)	0	(0.0)
転倒	8	(2.2)	9	(1.9)
大腿骨頚部骨折	0	(0.0)	1	(0.2)
腓骨骨折	2	(0.5)	1	(0.2)
足骨折	1	(0.3)	0	(0.0)
手骨折	1	(0.3)	1	(0.2)
頭部損傷	0	(0.0)	1	(0.2)
損傷	0	(0.0)	1	(0.2)
裂傷	0	(0.0)	1	(0.2)
靭帯捻挫	3	(0.8)	3	(0.6)
橈骨骨折	0	(0.0)	1	(0.2)
肋骨骨折	2	(0.5)	3	(0.6)
交通事故	0	(0.0)	1	(0.2)
硬膜下出血	0	(0.0)	1	(0.2)
腱断裂	0	(0.0)	1	(0.2)
脛骨骨折	1	(0.3)	0	(0.0)
尺骨骨折	0	(0.0)	1	(0.2)
肉離れ	2	(0.5)	0	(0.0)
挫傷	3	(0.8)	3	(0.6)
創傷	1	(0.3)	0	(0.0)
熱傷	2	(0.5)	0	(0.0)
四肢損傷	2	(0.5)	1	(0.2)
歯牙破折	0	(0.0)	1	(0.2)
四肢圧挫損傷	0	(0.0)	1	(0.2)
骨挫傷	2	(0.5)	0	(0.0)
半月板損傷	1	(0.3)	0	(0.0)

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Events captured using the MedDRA SMQ: Accident and Injuries

＜資料番号 5.3.5.3-01：Table 155＞

(2) 痙攣関連有害事象

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で，痙攣関連有害事象の発現はなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-41 参照）。

(b) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与で，痙攣関連有害事象の発現はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-73 参照）。

(c) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，痙攣関連有害事象を表 2.7.4.2.1-19 に示した。

痙攣関連有害事象はナルメフェン群 0.8%（4/475 例），プラセボ群 0.3%（1/369 例）に発現した。

表 2.7.4.2.1-19　痙攣関連有害事象：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	1	(0.3)	4	(0.8)
神経系障害	1	(0.3)	4	(0.8)
てんかん	1	(0.3)	0	(0.0)
痙攣発作	0	(0.0)	3	(0.6)
アルコール性痙攣	0	(0.0)	1	(0.2)

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Events captured using the MedDRA SMQ: Convulsions

＜資料番号 5.3.5.3-01：Table 157＞

(3) うつ病関連有害事象

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，うつ病関連有害事象を表 2.7.4.2.1-20 に示した。

うつ病関連有害事象はナルメフェン 20 mg 群 2.4%（6/248 例），10 mg 群 0.5%（1/184 例），プラセボ群 0.8%（2/245 例）に発現した。20 mg 群又は 10 mg 群で発現した事象は，20 mg 群では抑うつ気分 1.6%（4/248 例），不快気分，抑うつ症状が各 0.4%（1/248 例），10 mg 群ではう

つ病 0.5%（1/184 例）であった。いずれの事象も重症度は軽度又は中等度であり，重篤と判断された事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。投与中止に至った事象は，20 mg 群の抑うつ気分 2 例と 10 mg 群のうつ病 1 例で，いずれも回復が確認された（表 2.7.6.5.1-34 参照）。

表 2.7.4.2.1-20　うつ病関連有害事象：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with SMQ depression	2 (0.8)	1 (0.4)	6 (2.4)	2 (0.8)	1 (0.5)	1 (0.5)	7 (1.6)	3 (0.7)
精神障害	2 (0.8)	1 (0.4)	6 (2.4)	2 (0.8)	1 (0.5)	1 (0.5)	7 (1.6)	3 (0.7)
抑うつ気分	0 (0.0)	0 (0.0)	4 (1.6)	2 (0.8)	0 (0.0)	0 (0.0)	4 (0.9)	2 (0.5)
うつ病	2 (0.8)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	1 (0.2)	1 (0.2)
不快気分	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
抑うつ症状	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-42 より作成＞

(b) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，うつ病関連有害事象は，プラセボ対照二重盲検試験（339-14-001）の治療期に 0.9%（2/231 例），継続長期試験（339-14-002）の治療期に 0.4%（1/231 例）発現し，発現割合は時期により大きく異ならなかった。339-14-002 試験の治療期に発現した事象は，重症度は軽度で，非重篤と判断され，治験薬の投与に変更はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-74，Table 14.1.1.3-29，表 2.7.4.2.1-13 参照）。

(c) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，うつ病関連有害事象を表 2.7.4.2.1-21 に示した。

うつ病関連有害事象はナルメフェン群 3.6%（17/475 例），プラセボ群 2.4%（9/369 例）に発現した。

表 2.7.4.2.1-21　うつ病関連有害事象：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	9	(2.4)	17	(3.6)
精神障害	9	(2.4)	17	(3.6)
抑うつ気分を伴う適応障害	1	(0.3)	0	(0.0)
快感消失	0	(0.0)	1	(0.2)
興味の減少	0	(0.0)	2	(0.4)
抑うつ気分	2	(0.5)	7	(1.5)
うつ病	3	(0.8)	5	(1.1)
不快気分	1	(0.3)	1	(0.2)
抑うつ症状	0	(0.0)	1	(0.2)
大うつ病	3	(0.8)	0	(0.0)

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Events captured using the MedDRA sub-SMQ (Narrow Search): Depression (excl suicide and Self Injury)

＜資料番号 5.3.5.3-01：Table 159＞

(4) 薬物使用障害関連有害事象

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，薬物使用障害関連有害事象を表 2.7.4.2.1-22 に示した。

薬物使用障害関連有害事象はナルメフェン 20 mg 群 0.8%（2/248 例），10 mg 群 0.5%（1/184

例），プラセボ群 0.8%（2/245 例）に発現した。発現した事象はいずれも偶発的過量投与で，重症度はすべて軽度であり，重篤と判断された事象及び投与中止に至った事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。偶発的過量投与の詳細は，「2.7.4.5.5 過量投与」に示した。

表 2.7.4.2.1-22　薬物使用障害関連有害事象：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with SMQ drug abuse, dependence, and withdrawal	2 (0.8)	0 (0.0)	2 (0.8)	0 (0.0)	1 (0.5)	0 (0.0)	3 (0.7)	0 (0.0)
傷害、中毒および処置合併症	2 (0.8)	0 (0.0)	2 (0.8)	0 (0.0)	1 (0.5)	0 (0.0)	3 (0.7)	0 (0.0)
偶発的過量投与	2 (0.8)	0 (0.0)	2 (0.8)	0 (0.0)	1 (0.5)	0 (0.0)	3 (0.7)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-43 より作成＞

(b) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，薬物使用障害関連有害事象は，プラセボ対照二重盲検試験（339-14-001）の治療期に 0.9%（2/231 例）発現し，継続長期試験（339-14-002）の治療期に発現はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-75 参照）。

(c) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，薬物使用障害関連有害事象を表 2.7.4.2.1-23 に示した。

薬物使用障害関連有害事象はナルメフェン群 2.9%（14/475 例），プラセボ群 7.3%（27/369 例）に発現した。

表 2.7.4.2.1-23　薬物使用障害関連有害事象：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	27	(7.3)	14	(2.9)
傷害、中毒および処置合併症	27	(7.3)	13	(2.7)
偶発的過量投与	22	(6.0)	13	(2.7)
企図的過量投与	4	(1.1)	1	(0.2)
各種物質毒性	1	(0.3)	0	(0.0)
精神障害	0	(0.0)	1	(0.2)
薬物乱用	0	(0.0)	1	(0.2)

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Events captured using the MedDRA SMQ: Drug abuse, dependence, and withdrawal

＜資料番号 5.3.5.3-01：Table 161＞

(5) 肝障害

薬剤に関連する肝障害，及び明確にアルコール関連と報告された肝障害を評価した。

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，薬剤に関連する肝障害を表 2.7.4.2.1-24 に，明確にアルコール関連と報告された肝障害を表 2.7.4.2.1-25 に示した。

薬剤に関連する肝障害はナルメフェン 20 mg 群 4.4%（11/248 例），10 mg 群 2.7%（5/184 例），プラセボ群 2.4%（6/245 例）に発現した。いずれの投与群でも，MedDRA 基本語の「薬物性肝障害」の発現はなかった。20 mg 群又は 10 mg 群で 2 例以上に発現した事象は，20 mg 群ではア

ラニンアミノトランスフェラーゼ増加，γ-グルタミルトランスフェラーゼ増加が各 1.2%（3/248 例），アスパラギン酸アミノトランスフェラーゼ増加 0.8%（2/248 例），10 mg 群では血中ビリルビン増加 1.1%（2/184 例）であった。20 mg 群又は 10 mg 群で発現したいずれの事象も重症度は軽度又は中等度であった。20 mg 群の慢性肝炎 1 例が重篤と判断され，投与中止に至ったが，回復が確認された（表 2.7.6.5.1-31，表 2.7.4.7.1-16 参照）。

明確にアルコール関連と報告された肝障害は 10 mg 群 0.5%（1/184 例）に発現した。発現した事象はアルコール性肝疾患（症例報告書用語：ALCOHOLIC LIVER DISAESE WORSENING）であり，重症度は軽度で，非重篤と判断され，治験薬の投与に変更はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。

表 2.7.4.2.1-24　　薬剤に関連する肝障害：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with SMQ drug-related hepatic AEs	6 (2.4)	0 (0.0)	11 (4.4)	1 (0.4)	5 (2.7)	0 (0.0)	16 (3.7)	1 (0.2)
肝胆道系障害	1 (0.4)	0 (0.0)	4 (1.6)	1 (0.4)	1 (0.5)	0 (0.0)	5 (1.2)	1 (0.2)
慢性肝炎	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
肝硬変	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
肝機能異常	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)
脂肪肝	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
臨床検査	5 (2.0)	0 (0.0)	7 (2.8)	0 (0.0)	4 (2.2)	0 (0.0)	11 (2.5)	0 (0.0)
アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.4)	0 (0.0)	2 (0.8)	0 (0.0)	1 (0.5)	0 (0.0)	3 (0.7)	0 (0.0)
血中ビリルビン増加	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	2 (1.1)	0 (0.0)	3 (0.7)	0 (0.0)
γーグルタミルトランスフェラーゼ増加	1 (0.4)	0 (0.0)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)
肝機能検査異常	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
血中アルカリホスファターゼ増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査値上昇	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-44 より作成＞

表 2.7.4.2.1-25　明確にアルコール関連と報告された肝障害：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with SMQ alcohol-related hepatic AEs	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)
アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.2)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-45 より作成＞

(b)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，薬剤に関連する肝障害は，プラセボ対照二重盲検試験（339-14-001）の治療期に 3.5%（8/231 例），継続長期試験（339-14-002）の治療期に 1.7%（4/231 例）発現し，発現割合は時期により大きく異ならなかった。MedDRA 基本語の「薬物性肝障害」の発現はなかった。339-14-002 試験の治療期に発現した事象はいずれも，重症度は軽度であり，重篤と判断された事象はなかった。投与中止に至った事象はアスパラギン酸アミノトランスフェラーゼ増加及び γ-グルタミルトランスフェラーゼ増加（同一被験者で発現，いずれも軽度）であった（資料番号 5.3.5.2-01：Table 14.1.1.3-76，Table 14.1.1.3-29，表 2.7.4.2.1-13 参照）。

ナルメフェン投与群全体からの移行例で，明確にアルコール関連と報告された肝障害は，339-14-001 試験の治療期に 0.4%（1/231 例）発現し，339-14-002 試験の治療期に発現はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-77 参照）。

(c)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，薬剤に関連する肝障害を表 2.7.4.2.1-26 に，明確にアルコール関連と報告された肝障害を表 2.7.4.2.1-27 に示した。

薬剤に関連する肝障害はナルメフェン群 1.5%（7/475 例），プラセボ群 2.2%（8/369 例）に発現した。

明確にアルコール関連と報告された肝障害はナルメフェン群 0.2%（1/475 例），プラセボ群 0.3%（1/369 例）に発現した。

表 2.7.4.2.1-26　薬剤に関連する肝障害：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	(%)	Nalmefene n	(%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	8	(2.2)	7	(1.5)
肝胆道系障害	3	(0.8)	2	(0.4)
肝臓痛	0	(0.0)	1	(0.2)
脂肪肝	1	(0.3)	0	(0.0)
胆汁うっ滞性黄疸	1	(0.3)	0	(0.0)
肝障害	1	(0.3)	0	(0.0)
肝損傷	0	(0.0)	1	(0.2)
臨床検査	5	(1.4)	5	(1.1)
アラニンアミノトランスフェラーゼ増加	0	(0.0)	3	(0.6)
アスパラギン酸アミノトランスフェラーゼ増加	1	(0.3)	1	(0.2)
γ－グルタミルトランスフェラーゼ増加	3	(0.8)	3	(0.6)
肝酵素上昇	2	(0.5)	0	(0.0)
代謝および栄養障害	0	(0.0)	1	(0.2)
低アルブミン血症	0	(0.0)	1	(0.2)

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Events captured using the MedDRA SMQ: Drug related hepatic disorders - comprehensive search

＜資料番号 5.3.5.3-01：Table 163＞

表 2.7.4.2.1-27　明確にアルコール関連と報告された肝障害：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	(%)	Nalmefene n	(%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	1	(0.3)	1	(0.2)
肝胆道系障害	1	(0.3)	1	(0.2)
アルコール性肝炎	1	(0.3)	1	(0.2)

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Events captured using the MedDRA SMQ: Events specifically reported as alcohol-related

＜資料番号 5.3.5.3-01：Table 165＞

(6) 横紋筋融解症及びミオパチー関連有害事象

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，横紋筋融解症及びミオパチー関連有害事象を表 2.7.4.2.1-28 に示した。

横紋筋融解症及びミオパチー関連有害事象はナルメフェン 20 mg 群 2.8%（7/248 例），10 mg 群 1.6%（3/184 例），プラセボ群 1.2%（3/245 例）に発現した。いずれの投与群でも，MedDRA 基本語の「横紋筋融解症」及び「ミオパチー」の発現はなかった。20 mg 群又は 10 mg 群で発現した事象は，20 mg 群では筋肉痛 1.6%（4/248 例），筋力低下，筋骨格痛，筋骨格不快感が各 0.4%（1/248 例），10 mg 群では筋肉痛 1.1%（2/184 例），筋骨格不快感 0.5%（1/184 例）であった。いずれの事象も重症度は軽度又は中等度であり，重篤と判断された事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。投与中止に至った事象は 20 mg 群の筋力低下（中等度）の 1 例であり，回復が確認された（表 2.7.6.5.1-34 参照）。

表 2.7.4.2.1-28　横紋筋融解症及びミオパチー関連有害事象：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with SMQ rhabdomyolysis and myopathy	3 (1.2)	0 (0.0)	7 (2.8)	1 (0.4)	3 (1.6)	0 (0.0)	10 (2.3)	1 (0.2)
臨床検査	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	2 (0.8)	0 (0.0)	7 (2.8)	1 (0.4)	3 (1.6)	0 (0.0)	10 (2.3)	1 (0.2)
筋力低下	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
筋骨格痛	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
筋肉痛	1 (0.4)	0 (0.0)	4 (1.6)	0 (0.0)	2 (1.1)	0 (0.0)	6 (1.4)	0 (0.0)
筋骨格不快感	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-46 より作成＞

(b) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，横紋筋融解症及びミオパチー関連有害事象は，プラセボ対照二重盲検試験（339-14-001）の治療期に 3.0%（7/231 例），継続長期試験（339-14-002）の治療期に 2.2%（5/231 例）発現し，発現割合は時期により大きく異ならなかった。MedDRA 基本語の「横紋筋融解症」及び「ミオパチー」の発現はなかった。339-14-002 試験の治療期に発現した事象はいずれも，重症度は軽度であり，重篤と判断された事象及び投与中止に至った事象はなかった（資料番号 5.3.5.2-01 : Table 14.1.1.3-78, Table 14.1.1.3-29, 表 2.7.4.2.1-13 参照）。

(c) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，横紋筋融解症及びミオパチー関連有害事象を表 2.7.4.2.1-29 に示した。

横紋筋融解症及びミオパチー関連有害事象はナルメフェン群 1.3%（6/475 例），プラセボ群 3.0%（11/369 例）に発現した。

表 2.7.4.2.1-29　横紋筋融解症及びミオパチー関連有害事象：アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	11	(3.0)	6	(1.3)
臨床検査	2	(0.5)	0	(0.0)
血中クレアチニン増加	2	(0.5)	0	(0.0)
筋骨格系および結合組織障害	9	(2.4)	6	(1.3)
筋骨格痛	2	(0.5)	1	(0.2)
筋肉痛	7	(1.9)	4	(0.8)
筋肉疲労	0	(0.0)	1	(0.2)

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Events captured using the MedDRA SMQ: Rhabdomyolysis/Myopathy

＜資料番号 5.3.5.3-01：Table 167＞

(7) 精神系有害事象

錯乱状態，幻覚，解離などの有害事象を「精神系有害事象」として評価した。

(a) アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で，精神系有害事象の発現はなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-47 参照）。

(b)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，精神系有害事象の発現はなかった。なお，プラセボ群からの移行例で継続長期試験（339-14-002）の治療期に，精神系有害事象として幻聴が 1 例で認められた。この幻聴は，重症度は軽度で，非重篤と判断され，治験薬の投与に変更はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-79，Table 14.1.1.3-29，表 2.7.4.2.1-13 参照）。

(c)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，精神系有害事象を表 2.7.4.2.1-30 に示した。

精神系有害事象はナルメフェン群 3.6%（17/475 例），プラセボ群 0.3%（1/369 例）に発現した。

表 2.7.4.2.1-30　精神系有害事象:アルコール依存症の海外試験併合 －DRL が High 以上であった被験者

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	1	(0.3)	17	(3.6)
精神障害	1	(0.3)	17	(3.6)
錯乱状態	0	(0.0)	5	(1.1)
現実感消失	0	(0.0)	2	(0.4)
失見当識	1	(0.3)	4	(0.8)
解離	0	(0.0)	1	(0.2)
幻覚	0	(0.0)	2	(0.4)
触覚性幻覚	0	(0.0)	1	(0.2)
幻視	0	(0.0)	1	(0.2)
錯覚	0	(0.0)	1	(0.2)
思考異常	0	(0.0)	2	(0.4)

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＜資料番号 5.3.5.3-01：Table 170＞

(8)　自殺

自殺関連有害事象及び C-SSRS の評価結果を示した。なお，C-SSRS による評価は国内試験のみで実施した。

(a)　自殺関連有害事象

i)　アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，自殺関連有害事象を表 2.7.4.2.1-31 に示した。

自殺関連有害事象はナルメフェン 20 mg 群 0.4%（1/248 例），10 mg 群 0.5%（1/184 例），プラセボ群 0.4%（1/245 例）に発現した。発現した事象はいずれも自殺念慮で，重症度は軽度であり，重篤と判断された事象及び投与中止に至った事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。

表 2.7.4.2.1-31　自殺関連有害事象：アルコール依存症の国内短期投与（339-14-001）

System organ class Preferred term	Placebo (N=245)		Nalmefene 20 mg (N=248)		Nalmefene 10 mg (N=184)		Nalmefene Total (N=432)	
	Subject n (%)	Discontinue subject n (%)	Subject n (%)	Discontinue subject n (%)	Subject n (%)	Discontinue subject n (%)	Subject n (%)	Discontinue subject n (%)
Total number of subjects with SMQ AEs potentially related to suicidality	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)
精神障害	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)
自殺念慮	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-49 より作成＞

ii)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与で，自殺関連有害事象の発現はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-81 参照）。

iii)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で発現した，自殺関連有害事象を表 2.7.4.2.1-32 に示した。

自殺関連有害事象はナルメフェン群 0.2%（1/475 例），プラセボ群 1.4%（5/369 例）に発現した。

表 2.7.4.2.1-32　自殺関連有害事象：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	5	(1.4)	1	(0.2)
傷害、中毒および処置合併症	4	(1.1)	1	(0.2)
企図的過量投与	4	(1.1)	1	(0.2)
精神障害	1	(0.3)	0	(0.0)
自殺既遂	1	(0.3)	0	(0.0)

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Events captured using the MedDRA SMQ: Suicide/self-injury

＜資料番号 5.3.5.3-01：Table 174＞

(b)　C-SSRS

i)　アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与での C-SSRS に基づく治験薬投与開始後の自殺関連イベントを，表 2.7.4.2.1-33 に示した。

投与開始後に，suicidal ideation が認められた被験者の割合は，ナルメフェン 20 mg 群 0.8%（2/248 例），10 mg 群 1.1%（2/182 例），プラセボ群 1.2%（3/245 例）であった。Suicidal behavior は認められなかった。

Treatment-emergent serious suicidal ideation に該当する被験者が，20 mg 群で 1 例認められた（被験者番号 [redacted]）。この被験者では，治療期 1 週にスコア 4 の suicidal ideation が認められたが，治療期 2 週以降に suicidal ideation は認められなかった（資料番号 5.3.5.1-01：Listing 16.4.12 参照）。

表 2.7.4.2.1-33　C-SSRS：アルコール依存症の国内短期投与（339-14-001）

	Placebo			Nalmefene								
				20 mg			10 mg			Total		
	(N=245)			(N=248)			(N=184)			(N=432)		
Parameters[a]	N[b]	n[c]	(%)	N[b]	n[c]	(%)	N[b]	n[c]	(%)	N[b]	n[c]	(%)
Suicidal ideation (1-5)	245	3	(1.2)	248	2	(0.8)	182	2	(1.1)	430	4	(0.9)
Suicidal behavior (6-10)	245	0	(0.0)	248	0	(0.0)	182	0	(0.0)	430	0	(0.0)
Suicidal ideation or behavior (1-10)	245	3	(1.2)	248	2	(0.8)	182	2	(1.1)	430	4	(0.9)
Treatment-emergent suicidal ideation*[d]	245	3	(1.2)	248	2	(0.8)	182	2	(1.1)	430	4	(0.9)
Treatment-emergent serious suicidal ideation*[e]	245	0	(0.0)	248	1	(0.4)	182	0	(0.0)	430	1	(0.2)
Emergence of serious suicidal ideation*[f]	245	0	(0.0)	247	1	(0.4)	182	0	(0.0)	429	1	(0.2)
Emergence of suicidal behavior*[g]	245	0	(0.0)	248	0	(0.0)	182	0	(0.0)	430	0	(0.0)

[a]:Suicidal behavior is defined as reporting any type of suicidal behaviors (preparatory acts or behavior, aborted attempt, interrupted attempt, actual attempt, and completed suicide). Suicidal ideation is defined as reporting any type of suicidal ideation (wish to be dead, non-specific active suicidal thoughts, active suicidal ideation with any methods without intent to act, "active suicidal ideation with some intent to act, without specific plan", and active suicidal ideation with specific plan and intent).

[b]:N = Total number of subjects with C-SSRS evaluation at any post-baseline. For categories with *, N = Total number of subjects with C-SSRS evaluation at both baseline and any post-baseline.

[c]:n = Number of subjects with specified suicidal ideation/behavior at any post-baseline.

[d]:An increase in the maximum suicidal ideation score at any post-baseline from the baseline.

[e]:An increase in the maximum suicidal ideation score to 4 or 5 on the C-SSRS at any post-baseline from not having serious suicidal ideation (scores of 0-3) at the baseline.

[f]:An increase in the maximum suicidal ideation score to 4 or 5 on the C-SSRS at any post-baseline from no suicidal ideation (scores of 0) at the baseline.

[g]:The occurrence of suicidal behavior at any post-baseline from not having suicidal behavior prior to treatment.

＜資料番号 5.3.5.1-01：Table 14.1.1.3-75＞

ii)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

投与開始後にナルメフェン投与群全体からの移行例で suicidal ideation or behavior が認められた被験者の割合は，プラセボ対照二重盲検試験（339-14-001）の治療期に 0.4%（1/231 例）であり，継続長期試験（339-14-002）の治療期には認められなかった。なお，プラセボ群からの移行例でも，339-14-002 試験の治療期に suicidal ideation or behavior は認められなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-170 参照）。

(9)　睡眠障害に関連する有害事象

睡眠障害に関連する夜間の症状，及び睡眠障害に関連する日中の症状を評価した。

(a)　アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で発現した，睡眠障害に関連する夜間の症状及び睡眠障害に関連する日中の症状を，表 2.7.4.2.1-34 及び表 2.7.4.2.1-35 に示した。

睡眠障害に関連する夜間の症状はナルメフェン 20 mg 群 14.5%（36/248 例），10 mg 群 14.1%（26/184 例），プラセボ群 3.7%（9/245 例）に発現した。20 mg 群又は 10 mg 群で 2 例以上に発現した事象は，20 mg 群では不眠症 8.1%（20/248 例），中期不眠症 3.2%（8/248 例），睡眠の質低下 1.6%（4/248 例），睡眠障害 0.8%（2/248 例），10 mg 群では不眠症 8.2%（15/184 例），中期不眠症，睡眠の質低下が各 2.7%（5/184 例）であった。いずれの事象も重症度は軽度又は中等度であり，重篤と判断された事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。投与中止に至った事象は，20 mg 群 2.8%（7/248 例），10 mg 群 3.8%（7/184 例）で，いずれの投与群でも不眠症の発現割合が最も高く，20 mg 群及び 10 mg 群の不眠症各 1 例を除き，いずれも回復が確認された（表 2.7.6.5.1-34 参照）。

睡眠障害に関連する日中の症状は 20 mg 群 19.4%（48/248 例），10 mg 群 13.0%（24/184 例），プラセボ群 9.4%（23/245 例）に発現した。20 mg 群又は 10 mg 群で 2 例以上に発現した事象は，20 mg 群では傾眠 15.7%（39/248 例），疲労 4.0%（10/248 例），無力症 1.2%（3/248 例），10 mg 群では傾眠 9.8%（18/184 例），疲労 2.7%（5/184 例）であった。いずれの事象も重症度は軽度又は中等度であり，重篤と判断された事象はなかった（表 2.7.6.5.1-31，表 2.7.4.2.1-11 参照）。投与中止に至った事象は，20 mg 群 2.0%（5/248 例），10 mg 群 2.2%（4/184 例）で，10 mg 群の傾眠 1 例を除き，いずれも回復が確認された（表 2.7.6.5.1-34 参照）。

表 2.7.4.2.1-34　睡眠障害に関連する夜間の症状：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with night-time events of sleep-related disorders	9 (3.7)	0 (0.0)	36 (14.5)	7 (2.8)	26 (14.1)	7 (3.8)	62 (14.4)	14 (3.2)
神経系障害	5 (2.0)	0 (0.0)	4 (1.6)	0 (0.0)	5 (2.7)	1 (0.5)	9 (2.1)	1 (0.2)
睡眠の質低下	5 (2.0)	0 (0.0)	4 (1.6)	0 (0.0)	5 (2.7)	1 (0.5)	9 (2.1)	1 (0.2)
精神障害	4 (1.6)	0 (0.0)	32 (12.9)	7 (2.8)	21 (11.4)	6 (3.3)	53 (12.3)	13 (3.0)
初期不眠症	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)
不眠症	2 (0.8)	0 (0.0)	20 (8.1)	5 (2.0)	15 (8.2)	5 (2.7)	35 (8.1)	10 (2.3)
中期不眠症	1 (0.4)	0 (0.0)	8 (3.2)	0 (0.0)	5 (2.7)	1 (0.5)	13 (3.0)	1 (0.2)
睡眠障害	0 (0.0)	0 (0.0)	2 (0.8)	1 (0.4)	1 (0.5)	0 (0.0)	3 (0.7)	1 (0.2)
早朝覚醒型不眠症	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-50 より作成＞

表 2.7.4.2.1-35　睡眠障害に関連する日中の症状：アルコール依存症の国内短期投与（339-14-001）

	Placebo		Nalmefene					
			20 mg		10 mg		Total	
	(N=245)		(N=248)		(N=184)		(N=432)	
System organ class	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject	Subject	Discontinue subject
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with day-time events that were potentially related to sleep disturbances	23 (9.4)	0 (0.0)	48 (19.4)	5 (2.0)	24 (13.0)	4 (2.2)	72 (16.7)	9 (2.1)
一般・全身障害および投与部位の状態	7 (2.9)	0 (0.0)	13 (5.2)	1 (0.4)	5 (2.7)	2 (1.1)	18 (4.2)	3 (0.7)
無力症	3 (1.2)	0 (0.0)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)
疲労	4 (1.6)	0 (0.0)	10 (4.0)	1 (0.4)	5 (2.7)	2 (1.1)	15 (3.5)	3 (0.7)
神経系障害	17 (6.9)	0 (0.0)	40 (16.1)	4 (1.6)	18 (9.8)	1 (0.5)	58 (13.4)	5 (1.2)
鎮静	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)
傾眠	17 (6.9)	0 (0.0)	39 (15.7)	4 (1.6)	18 (9.8)	1 (0.5)	57 (13.2)	5 (1.2)
精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	1 (0.2)	1 (0.2)
無感情	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)	1 (0.2)	1 (0.2)

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＜資料番号 5.3.5.1-01：Table 14.1.1.3-51 より作成＞

(b)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，睡眠障害に関連する夜間の症状は，プラセボ対照二重盲検試験（339-14-001）の治療期に 11.3%（26/231 例），継続長期試験（339-14-002）の治療期に 6.1%（14/231 例）発現し，発現割合は 339-14-001 試験の治療期と比較して 339-14-002 試験の治療期で 5%以上低かった。339-14-002 試験の治療期に発現した事象はいずれも，重症度は軽度又は中等度であり，重篤と判断された事象はなかった。投与中止に至った事象は不眠症 1 例であり，回復が確認された（資料番号 5.3.5.2-01：Table 14.1.1.3-82，Table 14.1.1.3-29，表 2.7.4.2.1-13，表 2.7.6.5.9-39 参照）。

ナルメフェン投与群全体からの移行例で，睡眠障害に関連する日中の症状は，339-14-001 試験の治療期に 18.2%（42/231 例），339-14-002 試験の治療期に 7.4%（17/231 例）発現し，発現割合は 339-14-001 試験の治療期と比較して 339-14-002 試験の治療期で 5%以上低かった。339-14-002 試験の治療期にナルメフェン投与群全体からの移行例で発現したいずれの事象も，重症度は軽度又は中等度であり，重篤と判断された事象及び投与中止に至った事象はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-83，Table 14.1.1.3-29，表 2.7.4.2.1-13 参照）。

(c)　アルコール依存症の海外試験併合（全体）

アルコール依存症の海外試験併合全体で発現した，睡眠障害に関連する夜間の症状及び睡眠障害に関連する日中の症状を，表 2.7.4.2.1-36 及び表 2.7.4.2.1-37 に示した。

睡眠障害に関連する夜間の症状はナルメフェン群 17.8%（204/1144 例），プラセボ群 6.3%（50/797 例），睡眠障害に関連する日中の症状はナルメフェン群 16.3%（186/1144 例），プラセボ群 8.3%（66/797 例）に発現した。

表 2.7.4.2.1-36　睡眠障害に関連する夜間の症状：アルコール依存症の海外試験併合

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	797		1144	
Men	570	(71.5)	843	(73.7)
Women	227	(28.5)	301	(26.3)
Patients with TEAEs	50	(6.3)	204	(17.8)
神経系障害	0	(0.0)	4	(0.3)
睡眠の質低下	0	(0.0)	4	(0.3)
精神障害	50	(6.3)	201	(17.6)
初期不眠症	0	(0.0)	9	(0.8)
睡眠異常	0	(0.0)	1	(0.1)
睡眠障害	5	(0.6)	38	(3.3)
早朝覚醒型不眠症	1	(0.1)	2	(0.2)
中期不眠症	1	(0.1)	6	(0.5)
不眠症	43	(5.4)	153	(13.4)

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＜資料番号 5.3.5.3-01：Table 120＞

表 2.7.4.2.1-37　睡眠障害に関連する日中の症状：アルコール依存症の海外試験併合

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	797		1144	
Men	570	(71.5)	843	(73.7)
Women	227	(28.5)	301	(26.3)
Patients with TEAEs	66	(8.3)	186	(16.3)
一般・全身障害および投与部位の状態	42	(5.3)	127	(11.1)
無力症	5	(0.6)	33	(2.9)
疲労	37	(4.6)	95	(8.3)
神経系障害	28	(3.5)	74	(6.5)
過眠症	2	(0.3)	7	(0.6)
嗜眠	0	(0.0)	3	(0.3)
鎮静	3	(0.4)	5	(0.4)
傾眠	23	(2.9)	59	(5.2)
精神障害	1	(0.1)	7	(0.6)
無感情	1	(0.1)	7	(0.6)

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＜資料番号 5.3.5.3-01：Table 121＞

2.7.4.2.2　　個別有害事象の文章による説明

評価資料としたアルコール依存症の国内試験 2 試験（339-14-001，339-14-002）で認められた，死亡及びその他の重篤な有害事象の叙述は，「2.7.6 個々の試験のまとめ」及び各試験の総括報告書に示した。海外試験での死亡及びその他の重篤な有害事象の叙述は，各試験の総括報告書に示した。

2.7.4.3　臨床検査値の評価

2.7.4.3.1　アルコール依存症の国内試験

(1)　臨床検査値の経時的変化

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与で，ナルメフェン 20 mg 群，10 mg 群，及びプラセボ群でのγ-GTP のベースラインからの変化量（平均値, 以下同様）は, 治療期 12 週に−16.8 U/L, −19.2 U/L, −1.5 U/L（以下同順），治療期 24 週に−16.0 U/L，−15.4 U/L，−3.8 U/L であった。ALT のベースラインからの変化量は，治療期 12 週に−1.2 U/L，−0.3 U/L，0.5 U/L，治療期 24 週に−0.9 U/L, −0.9 U/L, 0.0 U/L であった。AST のベースラインからの変化量は, 治療期 12 週に−1.9 U/L, 0.1 U/L, 0.2 U/L，治療期 24 週に−1.0 U/L，−0.6 U/L，0.6 U/L であった。ナルメフェン各投与群で，治療期 24 週のγ-GTP，ALT，AST がベースラインと比較して低かった。

20 mg 群，10 mg 群，及びプラセボ群でのプロラクチンのベースラインからの変化量は，治療期 12 週に 1.030 μg/L，1.679 μg/L，0.404 μg/L，治療期 24 週に 0.816 μg/L，0.519 μg/L，0.233 μg/L であり，いずれの投与群でも大きな変動はなかった。

その他の臨床検査項目で，ベースラインから治療期 12 週及び 24 週への平均変化量はいずれも小さく, 特に注目すべき変化は認められなかった（資料番号 5.3.5.1-01 : Table 14.1.1.3-55, Table 14.1.1.3-56 参照）。

以上より，ナルメフェン各投与群でプラセボ群と比較して，臨床検査値に安全性上問題となる変化は認められなかった。

(b)　長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，γ-GTP のベースライン（339-14-001 試験のベースライン，以下同様）からの変化量（平均値，以下同様）は，治療期 24 週（339-14-001 試験の治療期 24 週，以下同様）に−21.8 U/L（231 例），治療期 36 週（339-14-002 試験の治療期 12 週，以下同様）に−19.3 U/L（222 例），治療期 48 週（339-14-002 試験の治療期 24 週，以下同様）に−18.8 U/L（210 例）であった。ALT のベースラインからの変化量は，治療期 24 週に−2.0 U/L（231 例），治療期 36 週に−2.5 U/L（222 例），治療期 48 週に−2.4 U/L（210 例）であった。AST のベースラインからの変化量は, 治療期 24 週に−2.2 U/L（231 例）, 治療期 36 週に−2.6 U/L（222 例），治療期 48 週に−1.6 U/L（210 例）であった。γ-GTP，ALT，AST のいずれも，治療期 24 週に認められたベースラインからの低下が，治療期 48 週まで持続した。

ナルメフェン投与群全体からの移行例でのプロラクチンのベースラインからの変化量は，治療期 24 週に 0.493 μg/L（231 例）, 治療期 36 週に 0.910 μg/L（222 例）, 治療期 48 週に 0.668 μg/L（210 例）であり，治療期 48 週を通して大きな変動はなかった。

その他の臨床検査項目で，ベースラインから治療期 48 週への平均変化量はいずれも小さく，特に注目すべき変化は認められなかった（資料番号 5.3.5.2-01 : Table 14.1.1.3-91, Table 14.1.1.3-92 参照）。

以上より，ナルメフェンの長期投与で，臨床検査値に安全性上問題となる変化は認められなかった。

(2) 臨床的に重要な臨床検査値の変動

(a) 短期投与（339-14-001）

アルコール依存症の国内短期投与での治験薬投与開始後に認められた臨床的に重要な臨床検査値の変動，及び薬物性肝障害に関連する臨床検査値の変動を，表 2.7.4.7.1-21 及び表 2.7.4.3.1-1 に示した。

肝機能に関連する臨床検査項目である γ-GTP，ALT，AST，ALP，総ビリルビン，INR の変動を検討した。投与開始後に臨床的に重要な変動が認められた被験者の割合は，ナルメフェン各投与群でプラセボ群と比較して大きく異ならなかった。

プロラクチンの高値が認められた被験者は，ナルメフェン 10 mg 群の 1 例であった。この被験者で，プロラクチンに関連する有害事象の発現はなかった。

その他の臨床検査項目でも，投与開始後に臨床的に重要な変動が認められた被験者の割合はいずれの投与群でも低く，ナルメフェン各投与群でプラセボ群と比較して，安全性上問題となる違いは認められなかった。

更に，薬物性肝障害に関連する臨床検査値の変動を検討した。いずれかの薬物性肝障害に関連する臨床検査値の変動が認められた被験者の割合は，投与群間で大きく異ならなかった。ALT 又は AST が基準範囲上限の 3 倍以上であった被験者の割合は，20 mg 群 2.0%（5/245 例），10 mg 群 1.7%（3/180 例），プラセボ群 1.7%（4/239 例）であった。このうち，ALT 又は AST が基準範囲上限の 10 倍以上であった被験者はいなかった。総ビリルビンが基準範囲上限の 2 倍以上であった被験者は，20 mg 群 2 例，10 mg 群 1 例，プラセボ群 3 例であった。ALP が基準範囲上限の 1.5 倍以上であった被験者は 20 mg 群及び 10 mg 群で各 2 例であり，プラセボ群にはいなかった。20 mg 群の 2 例が，ALT 又は AST が基準範囲上限の 3 倍以上，かつ総ビリルビンが基準範囲上限の 2 倍以上に該当した。このうち 1 例は ALP が基準範囲上限の 1.5 倍以下に該当した。なお，本試験で有害事象として報告された薬剤に関連する肝障害については，「2.7.4.2.1.5(5) 肝障害」に示した。

表 2.7.4.3.1-1　　治験薬投与開始後の，薬物性肝障害に関連する臨床検査値の変動：アルコール依存症の国内短期投与（339-14-001）

	Placebo			Nalmefene								
				20 mg			10 mg			Total		
	(N=245)			(N=248)			(N=184)			(N=432)		
Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
AST or ALT value >= 3 times ULN	239	4	(1.7)	245	5	(2.0)	180	3	(1.7)	425	8	(1.9)
AST or ALT value >= 5 times ULN	239	1	(0.4)	245	2	(0.8)	180	1	(0.6)	425	3	(0.7)
AST or ALT value >= 10 times ULN	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
AST or ALT value >= 20 times ULN	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Total bilirubin value >= 2 times ULN	239	3	(1.3)	245	2	(0.8)	180	1	(0.6)	425	3	(0.7)
ALP value >= 1.5 times ULN	238	0	(0.0)	245	2	(0.8)	180	2	(1.1)	425	4	(0.9)
AST or ALT value >= 3 times ULN, and total bilirubin value >= 2 times ULN	239	0	(0.0)	245	2	(0.8)	180	0	(0.0)	425	2	(0.5)
AST or ALT value >= 3 times ULN, and total bilirubin value >= 2 times ULN, and ALP value <= 1.5 times ULN	238	0	(0.0)	245	1	(0.4)	180	0	(0.0)	425	1	(0.2)
AST or ALT value >= 3 times ULN, and (total bilirubin value >= 2 times ULN, or INR value >= 1.5 times ULN), and ALP value <= 1.5 times ULN	238	0	(0.0)	245	1	(0.4)	180	0	(0.0)	425	1	(0.2)
Any criteria in potential drug-induced liver injury	239	7	(2.9)	245	6	(2.4)	180	6	(3.3)	425	12	(2.8)

[a]:N = number of subjects in safety set with at least one post-baseline laboratory values for the laboratory test.

[b]:n = number of subjects with post-baseline potential drug-induced liver injury for the laboratory test.

＜資料番号 5.3.5.1-01：Table 14.1.1.3-63＞

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与での治験薬投与開始後に認められた臨床的に重要な臨床検査値の変動，及び薬物性肝障害に関連する臨床検査値の変動を，表 2.7.4.7.1-22 及び表 2.7.4.3.1-2 に示した。

肝機能に関連する臨床検査項目である γ-GTP，ALT，AST，ALP，総ビリルビン，INR の変動を検討した。ナルメフェン投与群全体からの移行例で，継続長期試験（339-14-002）の治療期に臨床的に重要な変動が認められた被験者の割合が，プラセボ対照二重盲検試験（339-14-001）の治療期と比較して 5%以上高かった項目はなかった。

ナルメフェン投与群全体からの移行例で，プロラクチンの高値は認められなかった。なお，プラセボ群からの移行例で，339-14-002 試験の治療期にプロラクチンの高値が 1 例に認められた。この被験者で，有害事象として高プロラクチン血症の発現が報告され，重症度は軽度，非重篤と判断され，治験薬投与の変更はなかった。

その他の臨床検査項目でも，ナルメフェン投与群全体からの移行例で，339-14-002 試験の治療期に臨床的に重要な変動が認められた被験者の割合が，339-14-001 試験の治療期と比較して 5%以上高かった項目はなかった。以上より，ナルメフェンの長期投与で，臨床検査値に安全性上問題となる変化は認められなかった。

更に，薬物性肝障害に関連する臨床検査値の変動を検討した。ナルメフェン投与群全体からの移行例で，いずれかの薬物性肝障害に関連する臨床検査値の変動が認められた被験者の割合は 1.7%（4/231 例）であった。ナルメフェン投与群全体からの移行例で，ALT 又は AST が基準範囲上限の 3 倍以上であった被験者の割合は 1.3%（3/231 例）であった。このうち，ALT 又は AST が基準範囲上限の 10 倍以上であった被験者はいなかった。総ビリルビンが基準範囲上限の 2 倍以上であった被験者はなく，ALP が基準範囲上限の 1.5 倍以上であった被験者の割合は 0.9%（2/231 例）であった。ALT 又は AST が基準範囲上限の 3 倍以上，かつ総ビリルビンが基準範囲上限の 2 倍以上に該当した被験者はいなかった。

なお，プラセボ群からの移行例でも，ALT 又は AST が基準範囲上限の 3 倍以上，かつ総ビリルビンが基準範囲上限の 2 倍以上に該当した被験者はいなかった。

表 2.7.4.3.1-2　治験薬投与開始後の，薬物性肝障害に関連する臨床検査値の変動：アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)			Nalmefene 10 mg (N=94)			Nalmefene total (N=231)			Total (N=403)		
Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
AST or ALT value >= 3 times ULN	172	3	(1.7)	137	2	(1.5)	94	1	(1.1)	231	3	(1.3)	403	6	(1.5)
AST or ALT value >= 5 times ULN	172	2	(1.2)	137	2	(1.5)	94	0	(0.0)	231	2	(0.9)	403	4	(1.0)
AST or ALT value >= 10 times ULN	172	1	(0.6)	137	0	(0.0)	94	0	(0.0)	231	0	(0.0)	403	1	(0.2)
AST or ALT value >= 20 times ULN	172	0	(0.0)	137	0	(0.0)	94	0	(0.0)	231	0	(0.0)	403	0	(0.0)
Total bilirubin value >= 2 times ULN	172	4	(2.3)	137	0	(0.0)	94	0	(0.0)	231	0	(0.0)	403	4	(1.0)
ALP value >= 1.5 times ULN	172	1	(0.6)	137	1	(0.7)	94	1	(1.1)	231	2	(0.9)	403	3	(0.7)
AST or ALT value >= 3 times ULN, and total bilirubin value >= 2 times ULN	172	0	(0.0)	137	0	(0.0)	94	0	(0.0)	231	0	(0.0)	403	0	(0.0)
AST or ALT value >= 3 times ULN, and total bilirubin value >= 2 times ULN, and ALP value <= 1.5 times ULN	172	0	(0.0)	137	0	(0.0)	94	0	(0.0)	231	0	(0.0)	403	0	(0.0)
AST or ALT value >= 3 times ULN, and (total bilirubin value >= 2 times ULN, or INR value >= 1.5 times ULN), and ALP value <= 1.5 times ULN	172	0	(0.0)	137	0	(0.0)	94	0	(0.0)	231	0	(0.0)	403	0	(0.0)
Any criteria in potential drug-induced liver injury	172	7	(4.1)	137	2	(1.5)	94	2	(2.1)	231	4	(1.7)	403	11	(2.7)

[a]:N = number of subjects in safety set with at least one post-baseline laboratory values for the laboratory test.

[b]:n = number of subjects with post-baseline potential drug-induced liver injury for the laboratory test.

＜資料番号 5.3.5.2-01：Table 14.1.1.3- 122 より作成＞

2.7.4.3.2　アルコール依存症の海外試験併合

(1)　臨床検査値の経時的変化

アルコール依存症の海外試験併合の DRL が High 以上であった被験者で，γ-GTP，ALT，AST は，治療期 24 週に，ナルメフェン群でプラセボ群と比較してベースラインから低下し，この低下は 52 週まで持続した。γ-GTP のベースラインからの平均変化量は，治療期 24 週にナルメフェン群で−16.97 IU/L，プラセボ群で 2.00 IU/L，52 週にナルメフェン群で−20.47 IU/L，プラセボ群で 9.00 IU/L であった。治療期 24 週及び 52 週の ALT と AST は，ナルメフェン群ではベースラインから低下し，プラセボ群では上昇した。

更に，MCV，ビリルビン，直接ビリルビン，CDT，%CDT のベースラインからの平均変化量で，治療期 12 週及び 24 週に，ナルメフェン群でプラセボ群と比較して概ねベースラインからの低下が認められた。この結果は，直接ビリルビン及び CDT では 52 週まで持続し，MCV，ビリルビン，%CDT では更にナルメフェン群で低下した。

プロラクチンのベースラインからの平均変化量では，ナルメフェン群とプラセボ群とで臨床的に意味のある違いは認められなかった。

その他の臨床検査項目では，治療期 52 週までのベースラインからの平均変化量はいずれも小さく，ナルメフェン群とプラセボ群とで臨床的に意味のある違いは認められなかった（資料番号 5.3.5.3-03：Table 184 参照）。

(2)　臨床的に重要な臨床検査値の変動

アルコール依存症の海外試験併合の DRL が High 以上であった被験者での治験薬投与開始後に認められた臨床的に重要な臨床検査値の変動，及び薬物性肝障害に関連する臨床検査値の変動を，表 2.7.4.7.2-20 及び表 2.7.4.3.2-1 に示した。また，臨床的に重要な血糖，総コレステロール及びトリグリセリドの変動を表 2.7.4.7.2-21 に示した。

肝機能に関連する臨床検査項目である γ-GTP，ALT，AST，ALP，直接ビリルビン，INR の変動を検討した。投与開始後に臨床的に重要な変動が認められた被験者の割合は，γ-GTP を除く各項目で，ナルメフェン群とプラセボ群とで大きく異ならなかった。投与開始後に γ-GTP 高値が認められた被験者の割合は，ナルメフェン群でプラセボ群と比較して低かった（ナルメフェン群 8.6%，プラセボ群 16.0%，以下同順）。γ-GTP 高値が認められた被験者の割合は，ベースラインでもナルメフェン群でプラセボ群と比較して低い傾向であったが（9.7%，11.3%），投与開始後にナルメフェン群では低下が認められた（治療期 24 週：4.2%，12.0%；52 週：1.3%，17.9%）（資料番号 5.3.5.3-03：Table 199 参照）。

投与開始後に薬物性肝障害に関連する臨床検査値の変動が認められた被験者の割合をみると，ALT 又は AST が基準範囲上限の 3 倍以上であった被験者の割合は，ナルメフェン群 3.9%（16/407 例），プラセボ群 4.7%（15/322 例）であった。このうち，ALT 又は AST が基準範囲上限の 10 倍以上であった被験者はナルメフェン群の 1 例であり，基準範囲上限の 20 倍以上の被験者はいなかった。総ビリルビンが基準範囲上限の 2 倍以上であった被験者は，ナルメフェン群で 1 例，プラセボ群で 2 例であった。ALP が基準範囲上限の 1.5 倍以上であった被験者はナルメフェン群

にはなく，プラセボ群で 7 例であった。プラセボ群の 1 例が，ALT 又は AST が基準範囲上限の 3 倍以上かつ総ビリルビンが基準範囲上限の 2 倍以上に該当した。この被験者は，ALP が基準範囲上限の 1.5 倍以下には該当しなかった。

投与開始後に臨床的に重要な血糖の高値が認められた被験者の割合は，ナルメフェン群でプラセボ群と比較してわずかに高く，低値が認められた被験者の割合も，ナルメフェン群でプラセボ群と比較してわずかに高かった。臨床的に重要な総コレステロール及びトリグリセリドの高値が認められた被験者の割合は，ナルメフェン群でプラセボ群と比較して低かった。

投与開始後に臨床的に重要なプロラクチン高値が認められた被験者の割合では，ナルメフェン群でプラセボ群と比較して問題となる違いは認められなかった。

その他の臨床検査項目で，投与開始後に臨床的に重要な変動が認められた被験者の割合はいずれの投与群でも低く，ナルメフェン群でプラセボ群と比較して問題となる違いは認められなかった。

表 2.7.4.3.2-1　治験薬投与開始後の，薬物性肝障害に関連する臨床検査値の変動：アルコール依存症の海外試験併合 － DRL が High 以上であった被験者

Criterion	Placebo n (%)	Nalmefene n (%)
Number of patients	322	407
AST or ALT >= 3xULN	15 (4.7%)	16 (3.9%)
AST or ALT >= 5xULN	2 (0.6%)	7 (1.7%)
AST or ALT >= 10xULN	0 (0.0%)	1 (0.2%)
AST or ALT >= 20xULN	0 (0.0%)	0 (0.0%)
Total bilirubin >= 2xULN	2 (0.6%)	1 (0.2%)
ALP >= 1.5xULN	7 (2.2%)	0 (0.0%)
AST or ALT >= 3xULN and Total bilirubin >= 2xULN	1 (0.3%)	0 (0.0%)
AST or ALT >= 3xULN and Total bilirubin >= 2xULN and ALP <= 1.5xULN	0 (0.0%)	0 (0.0%)
AST or ALT >= 3xULN and (Total bilirubin >= 2xULN or INR >= 1.5xULN) and ALP <= 1.5xULN	0 (0.0%)	0 (0.0%)

＜資料番号 5.3.5.3-03：Table 202＞

2.7.4.3.3　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験では，各試験の臨床検査の結果から，臨床的に問題となる臨床検査値及びベースラインからの変化は認められなかった。

2.7.4.4　バイタルサイン，身体的所見及び安全性に関連する他の観察項目

2.7.4.4.1　バイタルサイン及び体重の評価

2.7.4.4.1.1　アルコール依存症の国内試験

(1)　バイタルサイン及び体重の経時的変化

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与で，バイタルサインの各項目及び体重のベースラインから治療期 12 週及び 24 週への平均変化量はいずれも小さく，ナルメフェン各投与群とプラセボ群とで大きく異ならなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-64 参照）。

(b)　長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，バイタルサインの各項目及び体重のベースライン（339-14-001 試験のベースライン）から治療期 48 週（339-14-002 試験の治療期 24 週）への平均変化量はいずれも小さく，特に注目すべき変化は認められなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-127 参照）。

(2)　臨床的に重要なバイタルサイン及び体重の変動

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与での治験薬投与開始後に認められた臨床的に重要なバイタルサイン及び体重の変動を，表 2.7.4.7.1-23 に示した。

投与開始後の臨床的に重要なバイタルサイン及び体重の変動に，ナルメフェン各投与群でプラセボ群と比較して安全性上問題となる違いは認められなかった。

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与での治験薬投与開始後に認められた臨床的に重要なバイタルサイン及び体重の変動を，表 2.7.4.7.1-24 に示した。

ナルメフェン投与群全体からの移行例で，投与開始後に臨床的に重要なバイタルサイン及び体重の変動が認められた被験者の割合が 5%以上であった項目は，体重増加 8.2%（19/231 例）及び体重減少 10.4%（24/231 例）であった。時期別にみると，継続長期試験（339-14-002）の治療期に認められた被験者の割合が，プラセボ対照二重盲検試験（339-14-001）の治療期と比較して 5%以上高かった項目は体重減少であり，339-14-001 試験の治療期に 4.8%（11/231 例），339-14-002 試験の治療期に 10.0%（23/231 例）であった。国内長期投与で，ナルメフェン投与群全体からの移行例で有害事象として報告された体重増加は 2.2%（5/231 例），体重減少は 1.3%（3/231 例）であり，重症度はいずれも軽度で，重篤と判断されたもの又は中止に至ったものはなかった（表 2.7.4.7.1-12，表 2.7.4.2.1-13，表 2.7.4.7.1-19，資料番号 5.3.5.2-01：Table 14.1.1.3-29 参照）。

2.7.4.4.1.2　アルコール依存症の海外試験併合

(1)　バイタルサイン及び体重の経時的変化

アルコール依存症の海外試験併合のDRLがHigh以上であった被験者でのバイタルサイン及び体重の変化はいずれも小さく，ナルメフェン群とプラセボ群とで臨床的に意味のある違いは認められなかった（資料番号5.3.5.3-03：Table 208～211参照）。

(2)　臨床的に重要なバイタルサイン及び体重の変動

アルコール依存症の海外試験併合のDRLがHigh以上であった被験者での治験薬投与開始後の臨床的に重要なバイタルサインの変動が認められた被験者の割合はいずれも低く，ナルメフェン群とプラセボ群とで臨床的に意味のある違いは認められなかった。体重高値が認められた被験者の割合はナルメフェン群4.9%，プラセボ群3.8%，低値が認められた被験者の割合はナルメフェン群7.5%，プラセボ群8.5%であった（資料番号5.3.5.3-03：Table 215参照）。

2.7.4.4.1.3　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験では，各試験のバイタルサインの結果から，臨床的に問題となるバイタルサイン及びベースラインからの変化は認められなかった。

2.7.4.4.2　心電図の評価

2.7.4.4.2.1　アルコール依存症の国内試験

(1)　心電図パラメータの経時的変化

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与で，心電図パラメータの各項目のベースラインから治療期12週及び24週への平均変化量はいずれも小さく，ナルメフェン各投与群とプラセボ群とで大きく異ならなかった（資料番号5.3.5.1-01：Table 14.1.1.3-66参照）。

(b)　長期投与（339-14-001，339-14-002併合）

ナルメフェン投与群全体からの移行例で，心電図パラメータの各項目のベースライン（339-14-001試験のベースライン）から治療期48週（339-14-002試験の治療期24週）への平均変化量はいずれも小さく，特に注目すべき変化は認められなかった（資料番号5.3.5.2-01：Table 14.1.1.3-136参照）。

(2)　臨床的に重要な心電図パラメータの変動

(a)　短期投与（339-14-001）

アルコール依存症の国内短期投与での治験薬投与開始後に認められた臨床的に重要な心電図パラメータの変動及びQTcの分布を，表 2.7.4.7.1-25及び表 2.7.4.7.1-26に示した。

臨床的に重要な心電図パラメータの変動で，QTcB又はQTcFが500 msec以上又はベースラ

インからの変化量が 60 msec 以上であった被験者は, QTcB がナルメフェン 20 mg 群 0.8%（2/245 例），プラセボ群 0.4%（1/238 例），QTcF が 20 mg 群 0.4%（1/245 例），10 mg 群 0.6%（1/179 例）であり，該当した被験者の割合はいずれの投与群でも低く，投与群間で大きく異ならなかった。20 mg 群の 1 例は QTcB，QTcF 共に 500 msec 以上に該当したが，ベースラインでも QTcF が 500 msec 以上であった。20 mg 群の他の 1 例と 10 mg 群の 1 例は，治療期 12 週に高値が認められたが, 24 週には低下が認められた。3 例共に, QT に関連する有害事象は認められなかった。

その他の心電図パラメータの各項目でも，ナルメフェン各投与群でプラセボ群と比較して安全性上問題となる違いは認められなかった。

(b)　長期投与（339-14-001，339-14-002 併合）

アルコール依存症の国内長期投与での治験薬投与開始後に認められた臨床的に重要な心電図パラメータの変動及び QTc の分布を，表 2.7.4.7.1-27 及び表 2.7.4.7.1-28 に示した。

ナルメフェン投与群全体からの移行例の臨床的に重要な心電図パラメータの変動で，QTcB 又は QTcF が 500 msec 以上又はベースラインからの変化量が 60 msec 以上であった被験者は，QTcB が 0.4%（1/231 例）であり，QTcF はなかった。この QTcB の 1 例はプラセボ対照二重盲検試験（339-14-001）の治療期に高値が認められた被験者であり，継続長期試験（339-14-002）で高値が認められた被験者はいなかった。なお，プラセボ投与群からの移行例の 1 例で QTcB の高値が認められた。この被験者では，プラセボが投与されていた治療期 12 週（339-14-001 試験の治療期 12 週）, 及び 20 mg が投与されていた治療期 48 週（339-14-002 試験の治療期 24 週）に QTcB の高値が認められた（資料番号 5.3.5.2-01：Table 14.1.1.3-200 参照）。

2.7.4.4.2.2　アルコール依存症の海外試験併合

(1)　心電図パラメータの経時的変化

アルコール依存症の海外試験併合の DRL が High 以上であった被験者での心電図パラメータの変化はいずれも小さく, ナルメフェン群とプラセボ群とで臨床的に意味のある違いは認められなかった（資料番号 5.3.5.3-03：Table 220，Table 221 参照）。

(2)　臨床的に重要な心電図パラメータの変動

アルコール依存症の海外試験併合の DRL が High 以上であった被験者での治験薬投与開始後に認められた臨床的に重要な心電図パラメータの変動を，表 2.7.4.7.2-22 に示した。

投与開始後の臨床的に重要な RR 間隔高値が認められた被験者の割合は, ナルメフェン群 4.1%, プラセボ群 4.6%であった。その他の心電図パラメータでは，臨床的に重要な変動が認められた被験者の割合はいずれの投与群でも低かった。

2.7.4.4.2.3　アルコール使用障害の海外試験併合

アルコール使用障害の海外試験では，各試験の心電図検査の結果から，臨床的に問題となる心電図の変化は認められなかった。

2.7.4.4.2.4　臨床薬理試験

海外で実施したQTc評価試験（BTT31-CD005）で，QTcI（被験者ごとに補正したQT）のベースラインからの平均変化量の最大値は，ナルメフェン塩酸塩20 mg/日で5.4 msec（90%CI：1.52，9.37），80 mg/日で5.6 msec（90%CI：1.61，9.52）であり，臨床的に問題となる変化は認められなかった。また，ナルメフェンの用量との明らかな関連性は認められなかった。QTcに対する作用には，ナルメフェンは，プラセボとで統計学的に有意な差は認められなかった。また，心臓の再分極に対し，ナルメフェン塩酸塩20 mg/日又は80 mg/日は，投与後いずれの時点でも，プラセボと比較して統計学的に有意な作用を示さなかった。

2.7.4.5　特別な患者集団及び状況下における安全性

2.7.4.5.1　内因性要因

アルコール依存症の国内試験及び海外試験での性別，年齢別（65 歳未満，65 歳以上），BMI 別（25 未満，25 以上 30 未満，30 以上）の有害事象を検討した。なお，アルコール依存症の海外試験併合の結果は，DRL が High 未満であった被験者も含む被験者全体での結果を示した。また，腎機能障害患者を対象とした薬物動態試験（15084A，22）及び肝機能障害患者を対象とした薬物動態試験（12417A，21）の安全性成績の要約を示し，詳細は「2.7.6 個々の試験のまとめ」に示した。

2.7.4.5.1.1　性別

(1)　アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で，性別の有害事象の発現割合はナルメフェン 20 mg 群で男性 87.3%（151/173 例），女性 89.3%（67/75 例），10 mg 群で男性 84.6%（115/136 例），女性 85.4%（41/48 例）であり，性別で大きく異ならなかった。プラセボ群での性別の有害事象の発現割合は，男性 75.5%（117/155 例），女性 85.6%（77/90 例）であった。

ナルメフェン各投与群での発現割合を事象別にみると，女性で，男性に比べて発現割合が 10%以上高かった有害事象は，20 mg 群及び 10 mg 群の嘔吐，10 mg 群の悪心，頭痛であった。これらの事象は，プラセボ群でも女性で男性に比べて発現割合が高かった。男性で，女性に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-52 参照）。

(2)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，性別の有害事象の発現割合は男性 90.5%（162/179 例），女性 92.3%（48/52 例）であり，性別で大きく異ならなかった。

ナルメフェン投与群全体からの移行例での発現割合を事象別にみると，女性で，男性に比べて発現割合が 10%以上高かった有害事象は，頭痛であった。男性で，女性に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-84 参照）。

(3)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合全体で，性別有害事象の発現割合はナルメフェン群で男性 73.7%（621/843 例），女性 77.7%（234/301 例），プラセボ群で男性 60.4%（344/570 例），女性 68.7%（156/227 例）であった。

ナルメフェン群での発現割合を事象別にみると，女性で，男性に比べて発現割合が 10%以上高かった有害事象は，悪心，浮動性めまいであった。これらの事象は，プラセボ群でも女性で男性に比べて発現割合が高かった。男性で，女性に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.3-01：Table 251 参照）。

2.7.4.5.1.2　年齢

(1)　アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で，年齢別の有害事象の発現割合はナルメフェン 20 mg 群で 65 歳未満 88.5%（192/217 例），65 歳以上 83.9%（26/31 例），10 mg 群で 65 歳未満 83.4%（136/163 例），65 歳以上 95.2%（20/21 例）であった。年齢別の検討では，各投与群での 65 歳以上の被験者数が 65 歳未満と比較して少なかったことに留意する必要があるが，各サブグループでの発現割合は 10 mg 群では 65 歳以上の方が高く，20 mg 群では年齢により大きく異ならず，一貫した傾向は認められなかった。プラセボ群での年齢別の有害事象の発現割合は，65 歳未満 79.4%（173/218 例），65 歳以上 77.8%（21/27 例）であった。

ナルメフェン各投与群での発現割合を事象別にみると，65 歳以上で，65 歳未満に比べて発現割合が 10%以上高かった有害事象は，10 mg 群の便秘であった。20 mg 群とプラセボ群では，この傾向は認められなかった。65 歳未満で，65 歳以上に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-53 参照）。

(2)　アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で，年齢別の有害事象の発現割合は 65 歳未満 91.2%（187/205 例），65 歳以上 88.5%（23/26 例）であった。年齢別の検討では，各投与群での 65 歳以上の被験者数が 65 歳未満と比較して少なかったことに留意する必要があるが，有害事象の発現割合は年齢で大きく異ならなかった。

ナルメフェン投与群全体からの移行例での発現割合を事象別にみると，65 歳未満で，65 歳以上に比べて発現割合が 10%以上高かった有害事象は，鼻咽頭炎であった。65 歳以上で，65 歳未満に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-85 参照）。

(3)　アルコール依存症の海外試験併合

アルコール依存症の海外試験併合全体で，年齢別有害事象の発現割合はナルメフェン群で 65 歳未満 74.8%（803/1074 例），65 歳以上 74.3%（52/70 例），プラセボ群で 65 歳未満 62.7%（474/756 例），65 歳以上 63.4%（26/41 例）であった。

ナルメフェン群での発現割合を事象別にみると，65 歳以上で，65 歳未満に比べて発現割合が 10%以上高かった有害事象は，浮動性めまいであった。プラセボ群ではこの傾向は認められなかった。65 歳未満で，65 歳以上に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.3-01：Table 254 参照）。

2.7.4.5.1.3　BMI

(1)　アルコール依存症の国内短期投与（339-14-001）

アルコール依存症の国内短期投与で，BMI が 30 kg/m^2 以上の被験者はナルメフェン 20 mg 群で 248 例中 8 例，10 mg 群で 184 例中 10 例と少なく，BMI が 30 kg/m^2 以上の被験者で，各有害事象の発現割合の傾向は明らかにならなかった。このため，本項では BMI が 25 kg/m^2 未満と

25 kg/m^2 以上 30 kg/m^2 未満の結果を検討した。

BMI 別の有害事象の発現割合は，20 mg 群で 25 kg/m^2 未満 87.5%（161/184 例），25 kg/m^2 以上 30 kg/m^2 未満 89.3%（50/56 例），10 mg 群で 25 kg/m^2 未満 82.7%（110/133 例），25 kg/m^2 以上 30 kg/m^2 未満 87.8%（36/41 例）であり，BMI で大きく異ならなかった。プラセボ群での BMI 別の有害事象の発現割合は, 25 kg/m^2 未満 80.0%（140/175 例）, 25 kg/m^2 以上 30 kg/m^2 未満 76.2%（48/63 例）であった。

ナルメフェン各投与群での発現割合を事象別にみると, 25 kg/m^2 以上 30 kg/m^2 未満で, 25 kg/m^2 未満に比べて 10%以上発現割合が高かった有害事象は，20 mg 群の悪心，嘔吐，頭痛であった。悪心，嘔吐は，10 mg 群とプラセボ群ではこの傾向は認められなかった。頭痛は，10 mg 群とプラセボ群でも同様に，25 kg/m^2 以上 30 kg/m^2 未満で 25 kg/m^2 未満に比べて発現割合が高かった。25 kg/m^2 未満で, 25 kg/m^2 以上 30 kg/m^2 未満に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-54 参照）。

(2) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）

ナルメフェン投与群全体からの移行例で, BMI が 30 kg/m^2 以上の被験者は 11 例と少なく, BMI が 30 kg/m^2 以上の被験者で，各有害事象の発現割合の傾向は明らかにならなかった。このため，本項では BMI が 25 kg/m^2 未満と 25 kg/m^2 以上 30 kg/m^2 未満の結果を検討した。

BMI 別の有害事象の発現割合は 25 kg/m^2 未満 91.1%（153/168 例），25 kg/m^2 以上 30 kg/m^2 未満 90.4%（47/52 例）であり，BMI で大きく異ならなかった。

ナルメフェン投与群全体からの移行例での発現割合を事象別にみると，25 kg/m^2 以上 30 kg/m^2 未満で, 25 kg/m^2 未満に比べて 10%以上発現割合が高かった有害事象は, 頭痛であった。25 kg/m^2 未満で, 25 kg/m^2 以上 30 kg/m^2 未満に比べて発現割合が 10%以上高かった有害事象はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-86 参照）。

(3) アルコール依存症の海外試験併合

アルコール依存症の海外試験併合全体で，BMI 別有害事象の発現割合はナルメフェン群で 25 kg/m^2 未満 69.1%（340/492 例），25 kg/m^2 以上 30 kg/m^2 未満 76.5%（345/451 例），30 kg/m^2 以上 84.0%（163/194 例）, プラセボ群で 25 kg/m^2 未満 63.0%（235/373 例）, 25 kg/m^2 以上 30 kg/m^2 未満 62.4%（186/298 例），30 kg/m^2 以上 62.9%（78/124 例）であった。

ナルメフェン群での発現割合を事象別にみると, サブグループ間で発現割合に 10%以上差がある有害事象はなかった（資料番号 5.3.5.3-01：Table 258 参照）。

2.7.4.5.1.4 腎機能障害

海外の腎機能障害患者を対象とした薬物動態試験 15084A では, eGFR に基づき, 軽度, 中等度, 又は高度の腎機能障害患者に，ナルメフェン塩酸塩 20 mg を単回経口投与したときの安全性及び忍容性を評価した。有害事象の発現割合は，腎機能正常群 86%（6/7 例），軽度腎機能障害群 78%（7/9 例），中等度腎機能障害群 63%（5/8 例），高度腎機能障害群 100%（8/8 例）であった。ほとんどの有害事象は軽度であり，いずれの投与群でも重篤な有害事象は認められなかった。発現割合が最も高かった有害事象は疲労（腎機能正常群 57%，軽度腎機能障害群 22%，中等度腎機能

障害群 38%，高度腎機能障害群 63%）であった。いずれの投与群でも，ナルメフェン塩酸塩 20 mg 単回経口投与の忍容性は良好であった。腎機能障害患者でのナルメフェンの曝露量の増加による安全性又は忍容性への明らかな影響は認められなかった。

海外の腎機能障害患者を対象とした薬物動態試験 22 では，末期腎臓病患者に，ナルメフェン塩酸塩 1.0 mg/回を 1～2 週間隔で 2 回，単回静脈内投与したときの安全性及び忍容性を評価した。有害事象は，投与 1 回目に 4/9 例，2 回目に 5/8 例で発現した。発現が多かった有害事象はいずれも軽度又は中等度であり，重篤な有害事象は認められなかった。ナルメフェン塩酸塩 1.0 mg を静脈内投与したときの安全性プロファイルは他の試験と異ならず，末期腎臓病患者での忍容性は良好であった。

2.7.4.5.1.5　肝機能障害

海外の肝機能障害患者を対象とした薬物動態試験 12417A では，Child-Pugh 分類に基づく軽度又は中等度の肝機能障害患者に，ナルメフェン塩酸塩 20 mg を単回経口投与したときの安全性及び忍容性を検討した。有害事象の発現割合は，肝機能正常群 63%（5/8 例），軽度肝機能障害群 88%（7/8 例），中等度肝機能障害群 75%（6/8 例）であった。ほとんどの有害事象は軽度であり，いずれの投与群でも重篤な有害事象は認められなかった。発現割合が最も高かった有害事象は疲労（肝機能正常群 50%，軽度肝機能障害群 88%，中等度肝機能障害群 0%）であった。肝機能障害患者でのナルメフェン塩酸塩 20 mg 単回経口投与の忍容性は良好であり，肝機能が正常な被験者での安全性と同様であった。

海外の肝機能障害患者を対象とした薬物動態試験 21 では，Child-Pugh 分類に基づく軽度，中等度，又は高度の肝機能障害患者に，ナルメフェン塩酸塩 2.0 mg を単回静脈内投与したときの安全性を検討した。有害事象の発現割合は，肝機能正常群 33.3%（4/12 例），軽度肝機能障害群 50.0%（2/4 例），中等度肝機能障害群 40.0%（2/5 例），高度肝機能障害群 33.3%（1/3 例）であった。すべての有害事象が軽度又は中等度であった。1 例で重篤の可能性がある有害事象（心電図異常）が報告された（「2.7.4.2.1.3(4) 臨床薬理試験」参照）。肝機能障害患者にナルメフェン塩酸塩 2.0 mg 静脈内投与の忍容性は良好であり，肝機能が正常な被験者での安全性と同様であった。

2.7.4.5.2　外因性要因

ナルメフェンの安全性について，外因性要因に関する検討はしていない。

2.7.4.5.3　薬物相互作用

In vitro のデータから，薬物相互作用の可能性は低いと考えられ，アルコールとの薬物相互作用試験（13513A）を除き，薬物相互作用を検討する臨床試験は実施しなかった。

海外のアルコールとの薬物相互作用試験（13513A）で，ナルメフェンとエタノールの併用は安全で忍容性も良好であった。発現割合が最も高かった有害事象は酩酊感であり，ナルメフェンとの併用にかかわらず，エタノールを投与された被験者で認められた。ナルメフェンとエタノールの併用投与で，ナルメフェン単独投与と比較して，傾眠，浮動性めまい及び悪心の発現割合が高かった。この結果は，アルコール依存症の海外試験併合では認められなかった（資料番号 5.3.5.3-03：Table 102 参照）。

2.7.4.5.4　　妊娠及び授乳時の使用

国内試験では，妊婦，授乳中の女性，妊娠している可能性のある女性は，除外基準に設定した。また，治験期間中に被験者の妊娠の報告はなかった。

海外試験では，ナルメフェン投与群で 2 例の妊娠が報告された。1 例はアルコール依存症患者で，20 mg の頓用期間中に妊娠した。この被験者は治験を中止し，妊娠，出産に関連する有害事象はなかった。他の 1 例は関節リウマチ患者を対象とした試験で，0.5 mg の 1 日 2 回投与期間中に妊娠した。この被験者の詳細は不明である。

2.7.4.5.5　　過量投与

アルコール依存症の国内試験（339-14-001，339-14-002）で，過量投与を MedDRA の基本語で偶発的過量投与及び企図的過量投与と定義した。プラセボ対照二重盲検試験（339-14-001）で，偶発的過量投与がナルメフェン 20 mg 群 0.8%（2/248 例），10 mg 群 0.5%（1/184 例），プラセボ群 0.8%（2/245 例）に発現し，企図的過量投与の発現はなかった（表 2.7.4.7.1-10 参照）。継続長期試験（339-14-002）で，過量投与の発現はなかった（表 2.7.4.7.1-12 参照）。国内試験で 1 日服薬量がナルメフェン塩酸塩 20 mg/日を超えた偶発的過量投与について，以下に記載した。

アルコール依存症の国内試験では，プラセボ対照二重盲検試験（339-14-001）で，20 mg/日を超える偶発的過量投与が 20 mg 群で 2 例報告された。1 例（[redacted]）は，初回投与後 11 日に 3 錠（60 mg/日）を，更に初回投与後 13 日に 2 錠（40 mg/日）を服用した。他の 1 例（[redacted]）は，初回投与後 29 日及び 30 日にそれぞれ 2 錠（40 mg/日）を服用した。いずれの被験者でも，過量投与に伴う有害事象の発現はなかった（資料番号 5.3.5.1-01：Table 14.1.1.3-87 参照）。

アルコール依存症の海外試験併合のナルメフェン群では，有害事象として企図的過量投与が 7 例，偶発的過量投与が 25 例報告された。ナルメフェンの服薬量が最も多かった被験者は，ナルメフェン塩酸塩 20 mg 錠を 1 日に 14 錠服用し，過量投与に関連する有害事象として悪心が認められた。

アルコール使用障害の海外試験併合で，ナルメフェン塩酸塩 40 mg を投与された 118 例で発現した有害事象の種類や発現割合に，20 mg 以下を投与された被験者と比較して異なるパターンは認められなかった（「2.7.4.2.1.1(3)(c) アルコール使用障害の海外試験併合」参照）。

CPH-101-0600 試験では，病的賭博患者 52 例に 100 mg/日を最大 16 週間投与した[1]。SP-N0408 試験では，ニコチン依存症患者 12 例に，2 週間の漸増投与後，80 mg/日を最大 5 週間投与した。[redacted] Studies の 1 試験（IX-318-003-EXT）では，間質性膀胱炎患者 20 例に 120 mg/日を 2 年以上投与した。QTc 評価試験（BTT31-CD005）では，健康成人 71 例に 40 mg/日を 2 日投与した後，80 mg/日を 5 日間投与した。いずれの試験でも，安全性上の懸念はなかった（資料番号 5.3.5.3-03「6.4 Overdose」参照）。

単回経口投与された最も高い用量は，オピオイド乱用歴のある被験者への 500 mg であった。血圧，心拍数，呼吸数，及び体温に変化は認められなかった[2]。

ナルメフェン塩酸塩 20 mg を超える用量を投与された他の疾患の被験者で，20 mg を頓用したアルコール依存症の被験者と比較して，異なる有害事象の発現パターンは認められなかった。

2.7.4.5.6　　薬物乱用

国内のアルコール依存症患者を対象とした継続長期試験（339-14-002）では，24 週間の治療期（全例にナルメフェン塩酸塩 20 mg 頓用）終了後，4 週間の退薬期を設けてナルメフェン塩酸塩 20 mg 又はプラセボを盲検下で頓用した。退薬期終了時に，依存性調査 A を用いてナルメフェンへの依存性を評価した。

依存性調査 A のすべての質問項目に「いいえ」と回答した被験者の割合が最も高く，プラセボ群 94.7%（162/171 例），ナルメフェン群 96.5%（165/171 例）であった。いずれかの質問項目に「少し」と回答した被験者の割合は，プラセボ群 4.7%（8/171 例），ナルメフェン群 3.5%（6/171 例）であり，投与群間で大きく異ならなかった。いずれかの質問項目に「かなり」と回答した被験者は，いずれの投与群でも認められなかった。いずれかの質問項目に「非常に」と回答した被験者がプラセボ群で 1 例認められ，ナルメフェン群では認められなかった。このプラセボ群の 1 例は，質問 8 の「段々，前程きかなくなったようですか」に対して「非常に」と回答した。依存性調査 A を用いた評価から，ナルメフェンに対する依存性は認められなかった（表 2.7.6.5.9-40 参照）。

アルコール依存症患者を対象とした国内外の臨床試験で，薬物使用障害関連有害事象を検討した結果，ナルメフェン投与群とプラセボ群とで意味のある違いは認められなかった（「2.7.4.2.1.5(4) 薬物使用障害関連有害事象」参照）。

以上，依存性調査 A を用いた評価と，薬物使用障害関連有害事象の投与群間での比較から，ナルメフェンに対する依存性の徴候は認められなかった。

2.7.4.5.7　　離脱症状及び反跳現象

(1)　アルコール依存症の国内試験

ナルメフェンの投与終了による影響を評価するため，国内のアルコール依存症患者を対象とした継続長期試験（339-14-002）では，24 週間の治療期（全例にナルメフェン塩酸塩 20 mg 頓用）終了後，4 週間の退薬期を設けてナルメフェン塩酸塩 20 mg 又はプラセボを盲検下で頓用した。また，退薬期終了後に 4 週間の後観察期を設け，ナルメフェン投与終了後の安全性を確認した。更に，後観察期終了時に，依存性調査 B を用いてナルメフェンによる離脱症状を評価した。

依存性調査 B では，退薬期にプラセボ群であった被験者 1 例が質問 4 の「あの薬を是非又のみたいですか」に対して「少し」と回答したが，その他の被験者はすべての質問項目に「いいえ」と回答した。依存性調査 B を用いた評価から，ナルメフェンによる離脱症状は認められなかった（表 2.7.6.5.9-41 参照）。

退薬期での有害事象を表 2.7.4.7.1-29 に，後観察期での有害事象を表 2.7.4.7.1-30 に示した。退薬期での有害事象の発現割合は，プラセボ群 11.7%（20/171 例），ナルメフェン群 17.4%（30/172 例）であり，プラセボ群でナルメフェン群と比較して高くなることはなかった。退薬期に，各投与群で 5%以上に発現した有害事象はなく，ナルメフェンの投与終了後に発現割合が明らかに高くなる有害事象はなかった。また，明らかにナルメフェンの離脱症状や反跳現象を疑わせる有害事象は認められなかった。後観察期に発現した有害事象からも，ナルメフェンの離脱症状又は反跳現象の徴候は認められなかった。

以上，依存性調査 B を用いた評価と，退薬期及び後観察期の有害事象の発現パターン及び投与群間での比較から，ナルメフェンの投与中止に関連した離脱症状又は反跳現象の徴候は認められなかった。

(2) アルコール依存症の海外試験

アルコール依存症患者を対象としたプラセボ対照二重盲検試験（12014A，12023A）の，退薬期での有害事象を表 2.7.4.7.2-23 に示した。退薬期での有害事象の発現割合は，ナルメフェン群からプラセボ群に移行した被験者（以下，ナルメフェンープラセボ群）で，ナルメフェン群からナルメフェン群に移行した被験者（以下，ナルメフェンーナルメフェン群）と比較してわずかに高かったが（ナルメフェンープラセボ群 16.3%，ナルメフェンーナルメフェン群 11.7%），いずれの投与群でも発現割合は低かった。ナルメフェンープラセボ群の 1 例が，有害事象により中止に至った。中止に至った有害事象は大うつ病で，家族の問題によるものであり，治験薬との関連性は Not related と判断された。有害事象の発現パターン及び投与群間での比較から，ナルメフェンの投与中止に関連した離脱症状又は反跳現象の徴候は認められなかった。

(3) アルコール使用障害の海外試験

アルコール使用障害患者を対象としたプラセボ対照二重盲検試験（CPH-101-0801）では，28 週間の治療期の後に，24 週間の退薬期を設定した。403 例中 57 例が退薬期に移行し，27 例がナルメフェンープラセボ群，30 例がナルメフェンーナルメフェン群であった。退薬期の有害事象の発現割合は，ナルメフェンーナルメフェン群（97%）と比較してナルメフェンープラセボ群（78%）で低かった。有害事象の発現パターン及び投与群間での比較から，ナルメフェンの投与中止に関連した離脱症状又は反跳現象の徴候は認められなかった。

2.7.4.5.8 自動車運転及び機械操作に対する影響又は精神機能の障害

国内，海外共に，機械操作に対する影響又は精神機能の障害の観察を目的とした，アルコール依存症患者対象試験は実施していない。また，アルコール依存症の国内試験では，自動車の運転を主たる業務とする職業に従事する患者，機械の操作，高所作業など危険を伴う職業に従事する患者は，除外基準に設定した。

事故及び損傷関連有害事象（定義：表 2.7.4.7.1-1 参照）の発現割合は，アルコール依存症の国内短期投与（339-14-001）では，ナルメフェン 20 mg 群 2.8%（7/248 例），10 mg 群 3.3%（6/184 例），プラセボ群 6.5%（16/245 例）であり，投与群間で大きく異ならなかった（表 2.7.4.2.1-17 参照）。国内長期投与（339-14-001，339-14-002 併合）では，ナルメフェン投与群全体からの移行例で投与期間の延長に伴い発現割合が明らかに高くなる傾向はなかった（「2.7.4.2.1.5(1)(b) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）」参照）。

自動車運転及び機械操作に対して影響を与える可能性のある有害事象として，睡眠障害に関連する夜間の症状及び日中の症状（定義：表 2.7.4.7.1-1 参照），更に，個別有害事象として浮動性めまい，及び注意力障害に着目した。アルコール依存症の国内短期投与（339-14-001）では，睡眠障害に関連する夜間の症状が 20 mg 群 14.5%（36/248 例），10 mg 群 14.1%（26/184 例），プラセボ群 3.7%（9/245 例），睡眠障害に関連する日中の症状が 20 mg 群 19.4%（48/248 例），10 mg 群

13.0%（24/184 例），プラセボ群 9.4%（23/245 例）に発現した。浮動性めまいが 20 mg 群 20.6%（51/248 例），10 mg 群 10.9%（20/184 例），プラセボ群 4.1%（10/245 例），注意力障害が 20 mg 群 1.6%（4/248 例），10 mg 群 0.5%（1/184 例），プラセボ群 0.0%（0/245 例）に発現した（表 2.7.4.2.1-34，表 2.7.4.2.1-35，表 2.7.4.7.1-10 参照）。国内長期投与（339-14-001，339-14-002 併合）では，ナルメフェン投与群全体からの移行例で投与期間の延長に伴い発現割合は低くなる傾向が認められた（「2.7.4.2.1.5(9)(b) アルコール依存症の国内長期投与（339-14-001，339-14-002 併合）」，表 2.7.4.7.1-12 参照）。

海外のアルコールとの薬物相互作用試験（13513A）では，識別機能の検討で最大 33 msec の反応時間の悪化が認められ，ナルメフェンの識別機能に対する作用が認められた。一般的に，この作用は血中アルコール濃度 0.2%で認められる範囲内である。

2.7.4.6　市販後データ

市販後データは，2016 年 4 月 21 日に発行された Periodic Safety Update Report（PSUR）第 5 版（集積期間：2015 年 2 月 25 日～2016 年 2 月 24 日）から，全世界の市販後の安全性情報を示した。ナルメフェンの最初の承認は，2013 年 2 月 25 日（国際誕生日）に，欧州，アイスランド，及びノルウェーで取得された。

2.7.4.6.1　推定曝露患者数

市販後データから，患者 1 人あたりナルメフェン塩酸塩 20 mg/日を 6 ヵ月投与され，服薬率 50%であったとすると，国際誕生日以降，累積で 375436 人の患者に投与されたと推定され，この曝露量は 92573 人・年に相当する。治験では，累積で 4492 人の被験者にナルメフェンが投与されたと推定された。

2.7.4.6.2　国内及び海外で報告された重篤な副作用

20[redacted]年[redacted]月[redacted]日（国際誕生日）～20[redacted]年[redacted]月[redacted]日までに報告された重篤な副作用を表 2.7.4.6.2-1 に示した。

重篤な副作用は，自発報告では 1207 件，市販後の非介入試験からの報告では 31 件であった。このうち，報告が多かった重篤な副作用は，自発報告では禁忌薬剤投与 52 件，悪心 48 件，浮動性めまい 40 件，市販後の非介入試験からの報告では入院 2 件であった。

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
Total:	1207	31
血液およびリンパ系障害		
SOC Total:	9	0
白血球減少症	2	0
リンパ球減少症	1	0
正色素性正球性貧血	1	0
汎血球減少症	1	0
血小板減少症	4	0
心臓障害		
SOC Total:	23	2
不整脈	1	0
心房細動	1	0
心不全	1	0
心肺停止	1	0
心血管障害	2	0
心筋梗塞	1	0
動悸	7	1
洞性頻脈	1	0
頻脈	7	1
心室性期外収縮	1	0
耳および迷路障害		
SOC Total:	17	0
聴覚過敏	1	0
耳鳴	3	0
回転性めまい	12	0
頭位性回転性めまい	1	0
内分泌障害		
SOC Total:	1	0
抗利尿ホルモン不適合分泌	1	0
眼障害		
SOC Total:	7	0
眼球突出症	1	0
眼痛	1	0
流涙増加	1	0
羞明	1	0
霧視	2	0
視力障害	1	0
胃腸障害		
SOC Total:	129	1
腹部不快感	1	0
腹痛	7	0
下腹部痛	2	0
上腹部痛	5	0
腹部硬直	1	0
便秘	1	0
下痢	14	0
血性下痢	1	0
口内乾燥	9	0
消化不良	1	0
放屁	1	0
胃潰瘍	1	0
胃炎	1	0
胃腸障害	2	0

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
胃腸障害		
消化器痛	1	0
歯肉出血	1	0
悪心	48	0
浮腫性膵炎	1	0
膵炎	4	0
急性膵炎	1	0
慢性膵炎	1	0
舌腫脹	1	0
嘔吐	24	1
一般・全身障害および投与部位の状態		
SOC Total:	184	1
歩行不能	1	0
アルコール相互作用	1	0
無力症	12	0
悪寒	6	0
状態悪化	3	0
泣き	1	0
死亡	3	0
疾患再発	1	0
薬効欠如	2	1
薬物相互作用	33	0
薬物不耐性	1	0
薬剤離脱症候群	33	0
顔面浮腫	1	0
疲労	15	0
異常感	17	0
冷感	3	0
酩酊感	3	0
熱感	4	0
体温変動感	1	0
口腔内泡沫	1	0
歩行障害	2	0
高熱	1	0
セルフケア障害	1	0
インフルエンザ様疾患	1	0
足のもつれ	1	0
倦怠感	22	0
疼痛	1	0
発熱	5	0
苦悶感	1	0
心突然死	1	0
突然死	1	0
温度変化不耐症	1	0
治療効果減弱	1	0
予想外の治療反応	1	0
口渇	2	0

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
肝胆道系障害		
SOC Total:	8	0
薬物性肝障害	2	0
肝臓痛	1	0
脂肪肝	1	0
肝炎	1	0
アルコール性肝炎	1	0
肝細胞損傷	1	0
黄疸	1	0
免疫系障害		
SOC Total:	4	0
アナフィラキシー反応	2	0
アナフィラキシーショック	1	0
過敏症	1	0
感染症および寄生虫症		
SOC Total:	1	0
肺感染	1	0
傷害、中毒および処置合併症		
SOC Total:	108	3
アルコール中毒	3	0
禁忌薬剤投与	52	0
挫傷	1	0
処方過誤	1	0
転倒	7	0
頭部損傷	1	1
誤用量投与	1	0
企図的過量投与	9	0
企図的製品誤用	1	0
表示された薬物－疾患相互作用による投薬	2	0
表示された薬物－薬物相互作用による投薬	1	0
投薬過誤	3	0
適応外使用	1	0
過量投与	4	0
故意の中毒	1	0
処方に基づく過少量投与	1	0
製品使用の問題	5	0
交通事故	0	1
各種物質毒性	1	0
過少量投与	5	1
誤薬投与	1	0
他の患者への薬剤誤投与	1	0
製品使用過程における誤った技法	6	0
臨床検査		
SOC Total:	23	1
アラニンアミノトランスフェラーゼ増加	1	0
アスパラギン酸アミノトランスフェラーゼ	1	0
血中アルカリホスファターゼ増加	1	0
血中ビリルビン増加	1	0
血中クレアチンホスホキナーゼ増加	2	0
血中クレアチニン増加	1	0
血中ブドウ糖	1	0
血中乳酸脱水素酵素増加	1	0
血中乳酸増加	1	0

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
Total:	1207	31
臨床検査		
血圧低下	2	0
血圧上昇	3	0
体温低下	1	0
薬物スクリーニング陽性	1	0
心電図QT延長	1	0
γーグルタミルトランスフェラーゼ増加	1	0
心拍数不整	1	0
肝酵素上昇	1	0
リパーゼ増加	1	0
肝機能検査異常	1	0
体重減少	0	1
代謝および栄養障害		
SOC Total:	16	2
食欲減退	12	1
脱水	1	0
糖尿病	0	1
低カリウム血症	1	0
低ナトリウム血症	2	0
筋骨格系および結合組織障害		
SOC Total:	42	1
関節痛	4	0
四肢不快感	2	0
筋拘縮	2	0
筋固縮	1	0
筋痙縮	16	0
筋緊張	1	0
筋攣縮	1	0
筋力低下	2	0
筋肉痛	10	0
四肢痛	1	0
横紋筋融解症	1	0
全身性エリテマトーデス	1	1
神経系障害		
SOC Total:	214	8
味覚消失	1	0
アカシジア	2	0
意識変容状態	1	0
健忘	6	0
失語症	3	0
運動失調	4	1
平衡障害	8	0
灼熱感	2	1
認知障害	1	0
昏睡	5	0
協調運動異常	1	0
意識レベルの低下	3	1
注意力障害	4	0
浮動性めまい	40	1
体位性めまい	1	0
構語障害	5	0
味覚異常	1	0

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
Total:	1207	31
神経系障害		
ジスキネジア	5	0
起立障害	1	0
ジストニア	4	0
てんかん	2	0
顔面不全麻痺	1	0
全身性強直性間代性発作	1	0
しかめ面	1	0
頭痛	16	0
過眠症	1	0
感覚鈍麻	6	0
筋緊張低下	2	0
思考散乱	1	0
意識消失	6	1
記憶障害	1	0
精神的機能障害	1	0
単麻痺	1	0
運動機能障害	2	0
筋痙直	1	0
ミオクロニーてんかん	1	0
ミオクローヌス	4	0
錯感覚	11	1
麻痺	2	0
不全麻痺	1	0
嗅覚錯誤	1	0
睡眠の質低下	1	0
精神運動亢進	1	0
精神運動機能障害	1	0
下肢静止不能症候群	1	0
鎮静	2	0
痙攣発作	9	0
傾眠	8	1
会話障害	4	0
昏迷	1	0
失神	3	1
強直性痙攣	1	0
一過性脳虚血発作	1	0
振戦	20	0
精神障害		
SOC Total:	319	6
異常行動	1	0
無為	1	0
攻撃性	5	0
激越	12	0
アルコール乱用	0	1
アルコール症	3	0
アルコール離脱症候群	6	0
怒り	1	0
快感消失	1	0
不安	19	0
不安障害	1	0
むちゃ飲み	1	0

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
Total:	1207	31
精神障害		
歯ぎしり	2	0
自殺既遂	4	0
錯乱状態	25	0
白日夢	1	0
譫妄	7	1
振戦譫妄	2	1
妄想	2	0
離人症	3	0
抑うつ気分	3	0
うつ病	6	0
抑うつ症状	2	0
現実感消失	2	0
失見当識	5	0
解離	6	0
解離性障害	3	0
解離性同一性障害	1	0
薬物乱用	1	0
高揚状態	1	0
感情的苦悩	1	0
多幸気分	3	0
恐怖	1	0
死の恐怖	2	0
罪責感	1	0
誇大的態度	1	0
幻覚	20	0
幻聴	8	0
混合性幻覚	4	0
共感覚性幻覚	1	0
幻視	17	0
殺人念慮	1	0
軽躁	0	1
非論理的思考	1	0
錯覚	1	0
精神障害		
衝動制御障害	1	0
不相応な情動	3	0
不眠症	30	1
故意の自傷行為	1	0
易刺激性	3	0
リビドー亢進	1	0
気力低下	1	0
リビドー消失	0	1
躁病	2	0
精神障害	1	0
消極的思考	2	0
悪夢	4	0
強迫性障害	1	0
パニック発作	3	0
妄想症	3	0
被害妄想	2	0
人格変化	1	0

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
Total:	1207	31
精神障害		
パーソナリティ障害	1	0
精神的機能代償不全	1	0
精神運動制止遅滞	1	0
精神病性障害	8	0
落ち着きのなさ	5	0
自尊心低下	1	0
睡眠障害	6	0
体感幻覚	1	0
身体表現性神経障害	1	0
自殺行為	2	0
自殺念慮	20	0
自殺企図	4	0
精神活動過多	1	0
思考異常	2	0
離脱症候群	17	0
腎および尿路障害		
SOC Total:	8	0
急性腎不全	1	0
着色尿	1	0
排尿困難	1	0
血尿	1	0
腎機能障害	1	0
尿失禁	2	0
尿路閉塞	1	0
生殖系および乳房障害		
SOC Total:	9	1
勃起不全	1	1
勃起増強	3	0
性器感覚鈍麻	1	0
持続勃起症	4	0
呼吸器、胸郭および縦隔障害		
SOC Total:	16	0
咳嗽	1	0
呼吸困難	5	0
労作性呼吸困難	1	0
過換気	1	0
喉頭浮腫	1	0
誤嚥性肺炎	2	0
呼吸停止	1	0
呼吸窮迫	1	0
呼吸不全	1	0
くしゃみ	1	0
頻呼吸	1	0
皮膚および皮下組織障害		
SOC Total:	53	1
血管浮腫	5	0
冷汗	1	0
アレルギー性皮膚炎	1	0
斑状出血	1	0
紅斑	3	0
多汗症	24	1

表 2.7.4.6.2-1　20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日に報告された市販後の重篤な副作用（続き）

MedDRA SOC/PT	Spontaneous, including competent authorities (Worldwide) and literature	Non Interventional post-marketing study and reports from other solicited sources
	Serious	Serious
	Cumulative	Cumulative
Total:	1207	31
皮膚および皮下組織障害		
寝汗	2	0
そう痒症	2	0
紫斑	2	0
発疹	3	0
全身性皮疹	1	0
斑状皮疹	1	0
斑状丘疹状皮疹	1	0
麻疹様発疹	1	0
皮膚熱感	1	0
中毒性皮疹	1	0
蕁麻疹	2	0
血管性紫斑病	1	0
社会環境		
SOC Total:	4	2
日常生活動作障害者	1	0
寝たきり	2	0
運動不能	0	1
運転能力障害者	1	0
治療非遵守	0	1
外科および内科処置		
SOC Total:	0	2
入院	0	2
血管障害		
SOC Total:	12	0
循環虚脱	1	0
血腫	1	0
ほてり	3	0
高血圧	2	0
高血圧クリーゼ	3	0
低血圧	1	0
蒼白	1	0

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＜資料番号 5.3.6-01：Appendix III より作成＞

2.7.4.7　付録

2.7.4.7.1　国内試験の図表

表 2.7.4.7.1-1　　注目すべき有害事象の定義

関連有害事象	定義
事故及び損傷関連有害事象	[SMQ] 20000135/事故および損傷/Accidents and injuriesで抽出される事象
痙攣関連有害事象	[SMQ] 20000079/痙攣/Convulsionsで抽出される事象
うつ病関連有害事象	[SMQ] 20000167/うつ病（自殺／自傷を除く）/Depression (excl suicide and self injury) で抽出される事象。narrow searchとする。
薬物使用障害関連有害事象	[SMQ] 20000100/薬物乱用、依存および離脱/Drug abuse, dependence and withdrawal で抽出される事象
薬剤に関連する肝障害	[SMQ] 20000006/薬剤に関連する肝障害－包括的検索/Drug related hepatic disorders - comprehensive search で抽出される事象
明確にアルコール関連と報告された肝障害	[SMQ] 20000017/明確にアルコール関連と報告された肝障害/Hepatic disorders specifically reported as alcohol-relatedで抽出される事象
横紋筋融解症及びミオパチー関連有害事象	[SMQ] 20000002/横紋筋融解症／ミオパチー/Rhabdomyolysis/myopathy で抽出される事象
自殺関連有害事象	[SMQ] 20000037/自殺／自傷/ Suicide/self injuryで抽出される事象

表 2.7.4.7.1-1　　注目すべき有害事象の定義（続き）

関連有害事象	定義		
精神系有害事象	以下の基本語とする。		
	10010305	錯乱状態	Confusional state
	10063033	うつ病性妄想	Depressive delusion
	10012245	替え玉妄想	Delusion of replacement
	10012244	関連妄想	Delusion of reference
	10012241	誇大妄想	Delusion of grandeur
	10015134	色情妄想	Erotomanic delusion
	10023164	嫉妬妄想	Jealous delusion
	10041317	身体妄想	Somatic delusion
	10034702	被害妄想	Persecutory delusion
	10012239	妄想	Delusion
	10012250	妄想性障害、誇大型	Delusional disorder, grandiose type
	10012252	妄想性障害、混合型	Delusional disorder, mixed type
	10012249	妄想性障害、色情型	Delusional disorder, erotomanic type
	10012251	妄想性障害、嫉妬型	Delusional disorder, jealous type
	10012255	妄想性障害、詳細不明	Delusional disorder, unspecified type
	10012254	妄想性障害、身体型	Delusional disorder, somatic type
	10053195	妄想性障害、被害型	Delusional disorder, persecutory type
	10012258	妄想知覚	Delusional perception
	10012295	アルツハイマー型認知症、妄想を伴う	Dementia of the Alzheimer's type, with delusions
	10076429	混合型妄想	Mixed delusion
	10077805	離人感・現実感消失障害	Depersonalisation/derealisation disorder
	10012422	現実感消失	Derealisation
	10013395	失見当識	Disorientation
	10013457	解離	Dissociation
	10062824	共感覚性幻覚	Hallucination, synaesthetic
	10020928	覚醒時幻覚	Hypnopompic hallucination
	10019063	幻覚	Hallucination
	10019072	幻嗅	Hallucination, olfactory
	10019075	幻視	Hallucination, visual
	10019070	幻聴	Hallucination, auditory

表 2.7.4.7.1-1　　注目すべき有害事象の定義（続き）

関連有害事象	定義		
精神系有害事象	10019071	幻味	Hallucination, gustatory
	10019074	触覚性幻覚	Hallucination, tactile
	10062684	体感幻覚	Somatic hallucination
	10020927	入眠時幻覚	Hypnagogic hallucination
	10019079	混合性幻覚	Hallucinations, mixed
	10021403	錯覚	Illusion
	10048294	精神状態変化	Mental status changes
	10049986	術後精神状態変化	Mental status changes postoperative
	10033864	妄想症	Paranoia
	10012355	依存性パーソナリティ障害	Dependent personality disorder
	10020155	演技性パーソナリティ障害	Histrionic personality disorder
	10003865	回避的パーソナリティ障害	Avoidant personality disorder
	10006034	境界性パーソナリティ障害	Borderline personality disorder
	10029901	強迫性パーソナリティ障害	Obsessive-compulsive personality disorder
	10028712	自己愛性パーソナリティ障害	Narcissistic personality disorder
	10034723	小児のパーソナリティ障害	Personality disorder of childhood
	10034721	パーソナリティ障害	Personality disorder
	10039651	統合失調型パーソナリティ障害	Schizotypal personality disorder
	10039624	統合失調質パーソナリティ障害	Schizoid personality disorder
	10002822	反社会性パーソナリティ障害	Antisocial personality disorder
	10033869	妄想性パーソナリティ障害	Paranoid personality disorder
	10040535	共有精神病性障害	Shared psychotic disorder
	10061921	身体疾患による精神病性障害	Psychotic disorder due to a general medical condition
	10061920	精神病性障害	Psychotic disorder
	10006362	短期精神病性障害、産後発症	Brief psychotic disorder, with postpartum onset
	10048549	著明なストレッサーを伴う短期精神病性障害	Brief psychotic disorder with marked stressors
	10056395	著明なストレッサーを伴わない短期精神病性障害	Brief psychotic disorder without marked stressors
	10043431	思考異常	Thinking abnormal

表 2.7.4.7.1-1　　注目すべき有害事象の定義（続き）

関連有害事象	定義		
睡眠障害に関連する夜間の症状	以下の基本語とする。		
	10022035	初期不眠症	Initial insomnia
	10022437	不眠症	Insomnia
	10027590	中期不眠症	Middle insomnia
	10040984	睡眠障害	Sleep disorder
	10061827	睡眠異常	Dyssomnia
	10062519	睡眠の質低下	Poor quality sleep
	10068932	早朝覚醒型不眠症	Terminal insomnia
睡眠障害に関連する日中の症状	以下の基本語とする。		
	10002942	無感情	Apathy
	10003549	無力症	Asthenia
	10016256	疲労	Fatigue
	10020765	過眠症	Hypersomnia
	10024264	嗜眠	Lethargy
	10039897	鎮静	Sedation
	10041349	傾眠	Somnolence
過量投与	以下の基本語とする。		
	10000381	偶発的過量投与	Accidental overdose
	10022523	企図的過量投与	Intentional overdose

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表 2.7.4.7.1-2　　臨床的に重要な臨床検査値の変動の基準：国内試験

低値及び高値の基準がある項目は，低値及び高値で別々に解析する。

項目	判定基準
血液学的検査	
赤血球数	< 3,000,000/ mm^3
ヘマトクリット 女性	≤ 32 %
ヘマトクリット 男性	≤ 37 %
ヘモグロビン 女性	≥ 16.5 g/dL
	≤ 9.5 g/dL
ヘモグロビン 男性	≥ 18.5 g/dL
	≤ 11.5 g/dL
MCV	≥ 1.2 × 基準範囲の上限
	≤ 0.8 × 基準範囲の下限
白血球総数	≥ 16,000/uL
	< 2,800/uL
好中球	≥ 85 %
	≤ 20 %
好酸球	≥ 10 %
好塩基球	≥ 10 %
リンパ球	≥ 75 %
	≤ 10 %
単球	≥ 15 %
血小板数	≥ 700,000/ mm^3
	≤ 75,000/ mm^3
血液生化学検査	
総ビリルビン	≥ 2 × 基準範囲の上限
アルカリホスファターゼ	≥ 3 × 基準範囲の上限
ALT	≥ 3 × 基準範囲の上限
AST	≥ 3 × 基準範囲の上限
γ-GTP	≥ 200 U/L
INR/プロトロンビン時間	≥ 2.0
アルブミン	≤ 2.7 g/dL
コリンエステラーゼ	設定なし
総コレステロール	≥ 302 mg/dL
トリグリセリド	≥ 500 mg/dL
クレアチニン	≥ 1.5 × 基準範囲の上限
	≤ 0.5 × 基準範囲の下限
BUN	> 30 mg/dL
ナトリウム	≥ 155 mEq/L
	≤ 125 mEq/L
カリウム	≥ 6.0 mEq/L
	≤ 3.0 mEq/L
重炭酸塩（HCO3-）	≥ 38 mmol/L
	≤ 12 mmol/L
カルシウム	≥ 12.0 mg/dL
	≤ 7.2 mg/dL
グルコース	≥ 162 mg/dL
	≤ 63 mg/dL
CRP	設定なし

表 2.7.4.7.1-2　　臨床的に重要な臨床検査値の変動の基準：国内試験（続き）

尿検査	
タンパク	ベースラインから 2 段階以上の増加
グルコース	ベースラインから 2 段階以上の増加
潜血	ベースラインから 2 段階以上の増加
ケトン	ベースラインから 2 段階以上の増加
尿沈渣	設定なし
その他	
プロラクチン	≥ 67.5 ug/L

表 2.7.4.7.1-3　　薬物性肝障害に関連する臨床検査値の変動の基準：国内試験

判定基準
AST 又は ALT が基準範囲上限の 3 倍以上
AST 又は ALT が基準範囲上限の 5 倍以上
AST 又は ALT が基準範囲上限の 10 倍以上
AST 又は ALT が基準範囲上限の 20 倍以上
総ビリルビンが基準範囲上限の 2 倍以上
アルカリホスファターゼが基準範囲上限の 1.5 倍以上
AST 又は ALT が基準範囲上限の 3 倍以上，かつ総ビリルビンが基準範囲上限の 2 倍以上
AST 又は ALT が基準範囲上限の 3 倍以上，総ビリルビンが基準範囲上限の 2 倍以上，かつアルカリホスファターゼが基準範囲上限の 1.5 倍以下
AST 又は ALT が基準範囲上限の 3 倍以上, 総ビリルビンが基準範囲上限の 2 倍以上もしくは INR/プロトロンビン時間が基準範囲上限の 1.5 倍以上，かつアルカリホスファターゼが基準範囲上限の 1.5 倍以下

表 2.7.4.7.1-4　　臨床的に重要なバイタルサインの変動の基準：国内試験

項目	判定基準
収縮期血圧	≥ 180 mmHg 及びベースラインからの変化量 ≥ 20 mmHg
	≤ 90 mmHg 及びベースラインからの変化量 ≤ −20 mmHg
拡張期血圧	≥ 105 mmHg 及びベースラインからの変化量 ≥ 15 mmHg
	≤ 50 mmHg 及びベースラインからの変化量 ≤ −15 mmHg
脈拍数	≥ 120 bpm 及びベースラインからの変化量 ≥ 15 bpm
	≤ 50 bpm 及びベースラインからの変化量 ≤ −15 bpm
体重	ベースラインからの変化率 ≥ 7%
	ベースラインからの変化率 ≤ −7%

表 2.7.4.7.1-5　　臨床的に重要な心電図の変動の基準：国内試験

項目	判定基準
心拍数	≥ 120 bpm 及びベースラインからの変化量 ≥ 15 bpm
	≤ 50 bpm 及びベースラインからの変化量 ≤ −15 bpm
RR 間隔	≥ 1200 msec
	< 500 msec
PR 間隔	≥ 260 msec
QRS 間隔	≥ 150 msec
QT 間隔	≥ 500 msec
QTcB	≥ 500 msec 又はベースラインからの変化量 ≥ 60 msec
QTcF	≥ 500 msec 又はベースラインからの変化量 ≥ 60 msec

表 2.7.4.7.1-6

Table 14.1.1.1-4

Disposition of Subjects who Advanced to Run-out Period and Posttreatment observation (339-14-002)

Subjects who Advanced to Run-out Period among Safety Set

Treatment group of run-out period	Placebo	Nalmefene 20 mg	Total
Subjects	N (%)[a]	N (%)[a]	N (%)[a]
Advanced to run-out period	171	172	343
Treated in run-out period	166 (97.1)	165 (95.9)	331 (96.5)
Discontinued in run-out period	0 (0.0)	1 (0.6)	1 (0.3)
Subject requested to be withdrawn from the study	0 (0.0)	0 (0.0)	0 (0.0)
Occurrence of an adverse event making continuation of trial difficult	0 (0.0)	1 (0.6)	1 (0.3)
Psychosocial therapy other than BRENDA is needed	0 (0.0)	0 (0.0)	0 (0.0)
Change in the dose of the investigational medicinal product is needed	0 (0.0)	0 (0.0)	0 (0.0)
Discovery that the subject was enrolled in the trial despite a violation of the inclusion or exclusion criteria	0 (0.0)	0 (0.0)	0 (0.0)
Suspected pregnancy of female subject	0 (0.0)	0 (0.0)	0 (0.0)
Judgment by the investigator or subinvestigator that subject withdrawal is necessary for other reasons	0 (0.0)	0 (0.0)	0 (0.0)

a : Percentages calculated vs number of subjects advanced to run-out period

表 2.7.4.7.1-6

Table 14.1.1.1-4

Disposition of Subjects who Advanced to Run-out Period and Posttreatment observation (339-14-002)

Subjects who Advanced to Run-out Period among Safety Set

Treatment group of run-out period	Placebo	Nalmefene 20 mg	Total
Subjects	N (%)[a]	N (%)[a]	N (%)[a]
Advanced to posttreatment observation	171 (100.0)	171 (99.4)	342 (99.7)
Discontinued in posttreatment observation	1 (0.6)	2 (1.2)	3 (0.9)
Subject requested to be withdrawn from the study	0 (0.0)	1 (0.6)	1 (0.3)
Occurrence of an adverse event making continuation of trial difficult	1 (0.6)	0 (0.0)	1 (0.3)
Psychosocial therapy other than BRENDA is needed	0 (0.0)	0 (0.0)	0 (0.0)
Change in the dose of the investigational medicinal product is needed	0 (0.0)	0 (0.0)	0 (0.0)
Discovery that the subject was enrolled in the trial despite a violation of the inclusion or exclusion criteria	0 (0.0)	0 (0.0)	0 (0.0)
Suspected pregnancy of female subject	0 (0.0)	0 (0.0)	0 (0.0)
Judgment by the investigator or subinvestigator that subject withdrawal is necessary for other reasons	0 (0.0)	1 (0.6)	1 (0.3)
Completed	170 (99.4)	169 (98.3)	339 (98.8)

a : Percentages calculated vs number of subjects advanced to run-out period

＜資料番号5.3.5.2-01 : Table 14.1.1.1-4＞

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Placebo	Overall	244	Mean	158.4	138.6	86.95
			SD	30.6	38.8	18.29
			Min	7	1	7.7
			Median	168.0	156.0	95.82
			Max	182	175	100.0
			P10	161.0	84.0	57.89
			P25	161.0	121.5	80.73
			P75	168.0	165.0	99.41
			P90	175.0	168.0	100.00
	Month 1	244	Mean	27.8	25.5	91.57
			SD	2.1	4.1	13.23
			Min	7	1	7.7
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	20.0	71.43
			P25	28.0	24.5	89.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Placebo	Month 2	238	Mean	27.9	24.7	88.44
			SD	0.8	5.1	18.04
			Min	15	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	17.0	60.71
			P25	28.0	23.0	82.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 3	235	Mean	27.8	24.2	86.46
			SD	2.1	6.1	21.75
			Min	3	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	15.0	53.57
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Placebo	Month 4	231	Mean	27.7	23.9	85.79
			SD	2.4	6.2	22.16
			Min	3	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	14.0	50.00
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	224	Mean	28.0	24.0	85.63
			SD	0.0	6.2	22.30
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	15.0	53.57
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Placebo	Month 6	222	Mean	25.7	22.0	85.45
			SD	3.0	6.6	23.36
			Min	20	0	0.0
			Median	28.0	23.0	96.43
			Max	28	28	100.0
			P10	21.0	13.0	53.57
			P25	22.0	20.0	82.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 20 mg	Overall	248	Mean	136.8	107.4	70.56
			SD	57.5	63.1	31.59
			Min	1	1	1.1
			Median	164.5	139.0	85.29
			Max	176	175	100.0
			P10	14.0	2.0	17.86
			P25	161.0	45.5	43.82
			P75	168.0	161.0	98.78
			P90	174.0	168.0	100.00
	Month 1	248	Mean	25.6	20.7	76.59
			SD	6.5	9.2	29.17
			Min	1	1	3.6
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	14.0	2.0	21.43
			P25	28.0	16.0	62.50
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 20 mg	Month 2	214	Mean	27.5	22.1	79.09
			SD	3.1	8.3	29.02
			Min	2	0	0.0
			Median	28.0	26.5	94.64
			Max	28	28	100.0
			P10	28.0	8.0	28.57
			P25	28.0	18.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 3	208	Mean	27.6	21.4	76.91
			SD	2.8	8.8	30.84
			Min	1	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	5.0	22.73
			P25	28.0	16.0	57.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 20 mg	Month 4	199	Mean	27.7	21.2	75.79
			SD	2.0	8.9	31.58
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	6.0	21.43
			P25	28.0	15.0	53.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	193	Mean	27.8	21.6	77.55
			SD	1.5	8.4	29.84
			Min	14	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	6.0	21.43
			P25	28.0	17.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 20 mg	Month 6	189	Mean	25.5	19.9	78.06
			SD	3.0	7.9	29.29
			Min	21	0	0.0
			Median	28.0	21.0	92.86
			Max	28	28	100.0
			P10	21.0	7.0	25.00
			P25	22.0	16.0	60.71
			P75	28.0	27.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 10 mg	Overall	182	Mean	140.3	113.7	75.06
			SD	54.2	58.6	28.35
			Min	2	1	1.8
			Median	166.0	143.0	88.27
			Max	189	176	100.0
			P10	28.0	10.0	28.57
			P25	161.0	72.0	57.14
			P75	169.0	161.0	98.82
			P90	175.0	168.0	100.00
	Month 1	182	Mean	26.3	22.1	80.72
			SD	5.5	8.1	25.74
			Min	2	1	10.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	27.0	9.0	35.71
			P25	28.0	19.0	71.43
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 10 mg	Month 2	163	Mean	27.5	22.6	81.01
			SD	3.0	7.5	26.31
			Min	3	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	11.0	42.86
			P25	28.0	19.0	70.37
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 3	155	Mean	27.5	22.1	80.14
			SD	3.0	7.9	27.10
			Min	4	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	19.0	71.43
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 10 mg	Month 4	148	Mean	27.8	22.3	79.85
			SD	2.1	7.8	28.05
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	8.0	28.57
			P25	28.0	20.0	71.43
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	144	Mean	27.7	22.2	79.59
			SD	2.5	8.0	28.77
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene 10 mg	Month 6	141	Mean	25.9	20.3	78.83
			SD	3.0	7.8	29.00
			Min	14	0	0.0
			Median	28.0	22.0	95.24
			Max	28	28	100.0
			P10	21.0	10.0	35.71
			P25	24.0	16.0	67.86
			P75	28.0	27.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene total	Overall	430	Mean	138.3	110.1	72.46
			SD	56.1	61.2	30.31
			Min	1	1	1.1
			Median	165.0	140.5	86.40
			Max	189	176	100.0
			P10	14.5	4.0	20.53
			P25	161.0	54.0	52.38
			P75	168.0	161.0	98.80
			P90	175.0	168.0	100.00
	Month 1	430	Mean	25.9	21.3	78.34
			SD	6.1	8.8	27.82
			Min	1	1	3.6
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	14.5	3.5	28.57
			P25	28.0	18.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene total	Month 2	377	Mean	27.5	22.3	79.92
			SD	3.0	8.0	27.86
			Min	2	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	8.0	33.33
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 3	363	Mean	27.5	21.7	78.29
			SD	2.9	8.4	29.31
			Min	1	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	28.57
			P25	28.0	17.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene total	Month 4	347	Mean	27.7	21.7	77.52
			SD	2.0	8.5	30.15
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	25.00
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	337	Mean	27.7	21.9	78.42
			SD	2.0	8.2	29.36
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	8.0	28.57
			P25	28.0	18.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-7
Table 14.1.1.3-2
IMP Intake by Monthly Period (339-14-001)
Safety Set

					IMP	
Treatment group	Monthly period	N	Summary statistics	TLFB days	Days	(%)
Nalmefene total	Month 6	330	Mean	25.7	20.1	78.39
			SD	3.0	7.8	29.13
			Min	14	0	0.0
			Median	28.0	21.5	92.86
			Max	28	28	100.0
			P10	21.0	7.0	27.75
			P25	22.0	16.0	64.29
			P75	28.0	27.0	100.00
			P90	28.0	28.0	100.00

＜資料番号5.3.5.1-01：Table 14.1.1.3-2＞

表 2.7.4.7.1-8

Table 14.1.1.3-3

Overall Time in Study and Exposure in Run-out Period (339-14-002)

Subjects who Advanced to Run-out Period among Safety Set

Treatment group of study 339-14-001	Placebo				Nalmefene											
					20 mg				10 mg				Total			
Treatment group of run-out period	Placebo		Nalmefene 20 mg		Placebo		Nalmefene 20 mg		Placebo		Nalmefene 20 mg		Placebo		Nalmefene 20 mg	
	n	PY	n	PY	n	PY	n	PY	n	PY	n	PY	n	PY	n	PY
Time in study	66	5.1	67	5.1	65	4.9	61	4.7	40	3.1	44	3.3	105	8.0	105	8.0
Exposure	66	3.9	67	3.9	65	3.9	61	3.5	40	2.3	44	2.7	105	6.2	105	6.1

Time in study = Total number of patients days(patients years[PY]) in study.

Exposure = Total number of patients days(PY) with IMP intake. Includes only patients with TLFB records.

＜資料番号5.3.5.2-01：Table 14.1.1.3-3＞

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
Placebo	Overall	172	Mean	330.5	276.0	83.45
			SD	66.6	86.0	18.61
			Min	166	50	13.9
			Median	361.0	306.5	90.47
			Max	391	377	99.7
			P10	195.0	156.0	54.57
			P25	352.0	191.0	75.48
			P75	366.0	353.0	97.81
			P90	372.0	363.0	99.64
	Month 1	172	Mean	28.0	26.0	92.90
			SD	0.0	3.0	10.86
			Min	28	13	46.4
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	22.0	78.57
			P25	28.0	25.0	89.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 2	172	Mean	28.0	25.2	90.05
			SD	0.0	4.4	15.64
			Min	28	8	28.6
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	19.0	67.86
			P25	28.0	24.0	85.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 3	172	Mean	28.0	25.0	89.29
			SD	0.0	5.0	17.72
			Min	28	6	21.4
			Median	28.0	28.0	100.00
			Max	28	28	100.0
			P10	28.0	19.0	67.86
			P25	28.0	24.0	85.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 4	172	Mean	28.0	24.9	88.91
			SD	0.0	5.0	17.92
			Min	28	4	14.3
			Median	28.0	27.5	98.21
			Max	28	28	100.0
			P10	28.0	18.0	64.29
			P25	28.0	24.0	85.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	172	Mean	28.0	24.7	88.33
			SD	0.0	5.5	19.52
			Min	28	2	7.1
			Median	28.0	27.5	98.21
			Max	28	28	100.0
			P10	28.0	17.0	60.71
			P25	28.0	24.0	85.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 6	172	Mean	26.2	22.9	87.40
			SD	2.5	5.5	18.35
			Min	22	0	0.0
			Median	28.0	24.0	95.45
			Max	28	28	100.0
			P10	22.0	16.0	60.71
			P25	23.5	21.0	84.00
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 7	172	Mean	23.2	17.4	73.32
			SD	4.4	7.6	29.23
			Min	3	0	0.0
			Median	22.0	20.0	86.36
			Max	28	28	100.0
			P10	22.0	4.0	22.22
			P25	22.0	13.0	52.87
			P75	27.0	22.0	95.45
			P90	28.0	27.0	100.00
	Month 8	158	Mean	26.6	20.8	75.07
			SD	5.2	9.3	32.79
			Min	1	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	3.0	14.29
			P25	28.0	16.0	57.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 9	145	Mean	27.7	21.5	77.46
			SD	2.5	8.3	29.29
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	32.14
			P25	28.0	16.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 10	141	Mean	27.7	21.7	78.04
			SD	2.3	8.4	29.16
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	8.0	32.14
			P25	28.0	18.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 11	139	Mean	27.7	21.5	77.57
			SD	2.8	8.6	30.21
			Min	4	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	25.00
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 12	136	Mean	27.9	21.9	78.36
			SD	0.8	8.4	29.90
			Min	19	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	9.0	32.14
			P25	28.0	17.5	62.50
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 13	135	Mean	27.3	21.0	77.15
			SD	2.9	8.5	29.81
			Min	1	0	0.0
			Median	28.0	25.0	92.00
			Max	28	28	100.0
			P10	27.0	7.0	25.00
			P25	28.0	16.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 14	95	Mean	8.7	6.5	74.25
			SD	4.9	4.4	35.20
			Min	1	0	0.0
			Median	7.0	7.0	92.86
			Max	28	21	100.0
			P10	3.0	0.0	0.00
			P25	6.0	3.0	57.14
			P75	13.0	9.0	100.00
			P90	14.0	13.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
Nalmefene 20 mg	Overall	137	Mean	356.1	286.9	80.47
			SD	27.5	88.5	23.74
			Min	172	36	9.8
			Median	362.0	327.0	91.51
			Max	374	372	100.0
			P10	351.0	158.0	43.65
			P25	357.0	233.0	69.09
			P75	365.0	357.0	98.90
			P90	370.0	363.0	99.72
	Month 1	137	Mean	28.0	24.7	88.35
			SD	0.0	4.8	17.18
			Min	28	3	10.7
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	18.0	64.29
			P25	28.0	23.0	82.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 2	137	Mean	28.0	24.0	85.77
			SD	0.0	6.1	21.84
			Min	28	3	10.7
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	15.0	53.57
			P25	28.0	21.0	75.00
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 3	137	Mean	28.0	23.5	83.76
			SD	0.0	6.7	24.02
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	13.0	46.43
			P25	28.0	21.0	75.00
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 4	137	Mean	28.0	22.5	80.45
			SD	0.0	7.5	26.86
			Min	28	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	11.0	39.29
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	137	Mean	28.0	22.5	80.24
			SD	0.0	7.3	26.23
			Min	28	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	9.0	32.14
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 6	137	Mean	25.8	20.6	79.71
			SD	2.6	6.6	23.85
			Min	22	2	7.1
			Median	27.0	22.0	90.91
			Max	28	28	100.0
			P10	22.0	11.0	40.91
			P25	23.0	17.0	71.43
			P75	28.0	26.0	96.30
			P90	28.0	28.0	100.00
	Month 7	137	Mean	24.1	19.0	78.26
			SD	3.1	6.8	24.78
			Min	7	1	4.5
			Median	23.0	21.0	89.29
			Max	28	28	100.0
			P10	22.0	10.0	40.91
			P25	22.0	15.0	68.18
			P75	28.0	23.0	96.15
			P90	28.0	28.0	100.00
	Month 8	135	Mean	28.0	22.4	79.97
			SD	0.0	7.1	25.37
			Min	28	1	3.6
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	11.0	39.29
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 9	135	Mean	27.9	22.1	79.20
			SD	1.3	7.4	26.04
			Min	13	0	0.0
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 10	134	Mean	28.0	21.8	78.01
			SD	0.0	7.6	27.14
			Min	28	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 11	134	Mean	27.9	21.8	77.82
			SD	0.9	8.0	28.40
			Min	19	0	0.0
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	18.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 12	132	Mean	27.8	21.6	77.71
			SD	1.6	8.0	28.33
			Min	15	0	0.0
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	28.0	8.0	28.57
			P25	28.0	16.5	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 13	129	Mean	26.7	20.6	76.46
			SD	4.1	8.9	30.77
			Min	2	0	0.0
			Median	28.0	24.0	92.86
			Max	28	28	100.0
			P10	23.0	2.0	25.00
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 14	78	Mean	7.8	6.0	74.20
			SD	3.6	4.0	34.55
			Min	1	0	0.0
			Median	7.0	6.0	87.30
			Max	16	16	100.0
			P10	3.0	0.0	0.00
			P25	6.0	4.0	64.29
			P75	10.0	7.0	100.00
			P90	14.0	12.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
Nalmefene 10 mg	Overall	94	Mean	354.3	283.0	79.67
			SD	34.9	96.1	25.36
			Min	198	5	1.3
			Median	364.0	328.5	90.89
			Max	379	378	99.7
			P10	343.0	112.0	42.43
			P25	358.0	243.0	71.99
			P75	370.0	357.0	98.81
			P90	372.0	364.0	99.46
	Month 1	94	Mean	28.0	24.9	88.91
			SD	0.0	4.9	17.37
			Min	28	3	10.7
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	18.0	64.29
			P25	28.0	23.0	82.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 2	94	Mean	28.0	23.9	85.22
			SD	0.0	6.4	22.95
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	14.0	50.00
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 3	94	Mean	28.0	23.3	83.09
			SD	0.0	7.2	25.80
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	11.0	39.29
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 4	94	Mean	28.0	23.0	81.99
			SD	0.0	7.5	26.84
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	8.0	28.57
			P25	28.0	21.0	75.00
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	94	Mean	28.0	23.1	82.67
			SD	0.0	7.5	26.91
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 6	94	Mean	26.5	21.2	79.98
			SD	2.3	7.2	26.36
			Min	22	0	0.0
			Median	28.0	23.0	92.58
			Max	28	28	100.0
			P10	22.0	10.0	39.29
			P25	25.0	18.0	69.57
			P75	28.0	27.0	100.00
			P90	28.0	28.0	100.00
	Month 7	94	Mean	23.8	18.6	77.47
			SD	2.3	7.2	27.95
			Min	22	0	0.0
			Median	23.0	21.0	90.91
			Max	28	28	100.0
			P10	22.0	7.0	30.77
			P25	22.0	15.0	68.18
			P75	26.0	23.0	95.65
			P90	28.0	27.0	100.00
	Month 8	94	Mean	27.6	21.7	77.47
			SD	2.7	8.8	31.04
			Min	7	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	5.0	17.86
			P25	28.0	18.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 9	92	Mean	27.8	21.7	77.91
			SD	2.2	8.5	29.78
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	6.0	28.57
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 10	91	Mean	27.6	21.4	77.57
			SD	2.8	8.8	30.55
			Min	6	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	28.57
			P25	28.0	16.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 11	89	Mean	27.4	20.6	74.35
			SD	3.6	9.4	33.34
			Min	1	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	3.0	10.71
			P25	28.0	15.0	53.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 12	86	Mean	27.8	20.5	73.17
			SD	1.8	9.6	34.20
			Min	11	0	0.0
			Median	28.0	25.5	91.07
			Max	28	28	100.0
			P10	28.0	4.0	14.29
			P25	28.0	11.0	39.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 13	85	Mean	27.5	20.8	75.19
			SD	2.2	9.3	33.32
			Min	12	0	0.0
			Median	28.0	26.0	96.43
			Max	28	28	100.0
			P10	28.0	3.0	10.71
			P25	28.0	15.0	53.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 14	60	Mean	9.6	7.0	76.12
			SD	5.0	5.0	32.83
			Min	1	0	0.0
			Median	7.0	6.0	93.93
			Max	21	21	100.0
			P10	3.5	1.5	15.34
			P25	6.0	4.0	61.90
			P75	14.0	9.0	100.00
			P90	14.0	14.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
Nalmefene total	Overall	231	Mean	355.3	285.3	80.14
			SD	30.7	91.5	24.36
			Min	172	5	1.3
			Median	363.0	328.0	91.23
			Max	379	378	100.0
			P10	351.0	151.0	42.62
			P25	358.0	234.0	69.09
			P75	366.0	357.0	98.90
			P90	372.0	363.0	99.72
	Month 1	231	Mean	28.0	24.8	88.57
			SD	0.0	4.8	17.22
			Min	28	3	10.7
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	18.0	64.29
			P25	28.0	23.0	82.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 2	231	Mean	28.0	24.0	85.54
			SD	0.0	6.2	22.25
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	15.0	53.57
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 3	231	Mean	28.0	23.4	83.49
			SD	0.0	6.9	24.71
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	12.0	42.86
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 4	231	Mean	28.0	22.7	81.08
			SD	0.0	7.5	26.80
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	10.0	35.71
			P25	28.0	20.0	71.43
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	231	Mean	28.0	22.7	81.23
			SD	0.0	7.4	26.48
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	9.0	32.14
			P25	28.0	20.0	71.43
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 6	231	Mean	26.1	20.9	79.82
			SD	2.5	6.9	24.85
			Min	22	0	0.0
			Median	28.0	22.0	91.30
			Max	28	28	100.0
			P10	22.0	11.0	40.91
			P25	23.0	17.0	69.57
			P75	28.0	27.0	96.43
			P90	28.0	28.0	100.00
	Month 7	231	Mean	24.0	18.8	77.94
			SD	2.8	6.9	26.06
			Min	7	0	0.0
			Median	23.0	21.0	90.91
			Max	28	28	100.0
			P10	22.0	8.0	31.82
			P25	22.0	15.0	68.18
			P75	27.0	23.0	95.83
			P90	28.0	28.0	100.00
	Month 8	229	Mean	27.8	22.1	78.95
			SD	1.7	7.8	27.80
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	9.0	32.14
			P25	28.0	19.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 9	227	Mean	27.8	21.9	78.68
			SD	1.7	7.8	27.56
			Min	7	0	0.0
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	28.0	8.0	32.14
			P25	28.0	18.0	67.86
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 10	225	Mean	27.8	21.6	77.83
			SD	1.8	8.1	28.50
			Min	6	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	9.0	32.14
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 11	223	Mean	27.7	21.3	76.43
			SD	2.4	8.6	30.44
			Min	1	0	0.0
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	28.0	6.0	21.43
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 12	218	Mean	27.8	21.2	75.92
			SD	1.7	8.7	30.78
			Min	11	0	0.0
			Median	28.0	25.0	89.29
			Max	28	28	100.0
			P10	28.0	7.0	25.00
			P25	28.0	16.0	57.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 13	214	Mean	27.0	20.7	75.96
			SD	3.5	9.1	31.74
			Min	2	0	0.0
			Median	28.0	24.0	92.86
			Max	28	28	100.0
			P10	25.0	3.0	17.86
			P25	28.0	16.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 14	138	Mean	8.6	6.4	75.03
			SD	4.3	4.5	33.71
			Min	1	0	0.0
			Median	7.0	6.0	92.86
			Max	21	21	100.0
			P10	3.0	0.0	0.00
			P25	6.0	4.0	64.29
			P75	12.0	8.0	100.00
			P90	14.0	13.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
Total	Overall	403	Mean	344.7	281.4	81.55
			SD	50.7	89.2	22.12
			Min	166	5	1.3
			Median	363.0	319.0	90.76
			Max	391	378	100.0
			P10	259.0	153.0	46.30
			P25	358.0	209.0	71.86
			P75	366.0	356.0	98.56
			P90	372.0	363.0	99.72
	Month 1	403	Mean	28.0	25.3	90.42
			SD	0.0	4.2	14.98
			Min	28	3	10.7
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	19.0	67.86
			P25	28.0	24.0	85.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 2	403	Mean	28.0	24.5	87.47
			SD	0.0	5.5	19.81
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	16.0	57.14
			P25	28.0	23.0	82.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 3	403	Mean	28.0	24.1	85.96
			SD	0.0	6.2	22.16
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	14.0	50.00
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 4	403	Mean	28.0	23.6	84.42
			SD	0.0	6.6	23.72
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	13.0	46.43
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 5	403	Mean	28.0	23.6	84.26
			SD	0.0	6.7	23.99
			Min	28	0	0.0
			Median	28.0	27.0	96.43
			Max	28	28	100.0
			P10	28.0	13.0	46.43
			P25	28.0	22.0	78.57
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 6	403	Mean	26.1	21.7	83.05
			SD	2.5	6.4	22.60
			Min	22	0	0.0
			Median	28.0	23.0	95.45
			Max	28	28	100.0
			P10	22.0	12.0	46.43
			P25	23.0	19.0	78.26
			P75	28.0	27.0	100.00
			P90	28.0	28.0	100.00
	Month 7	403	Mean	23.7	18.2	75.97
			SD	3.6	7.3	27.51
			Min	3	0	0.0
			Median	23.0	21.0	89.29
			Max	28	28	100.0
			P10	22.0	6.0	27.27
			P25	22.0	15.0	62.50
			P75	27.0	22.0	95.45
			P90	28.0	28.0	100.00
	Month 8	387	Mean	27.3	21.6	77.36
			SD	3.6	8.5	29.96
			Min	1	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	25.00
			P25	28.0	18.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 9	372	Mean	27.8	21.8	78.20
			SD	2.1	8.0	28.21
			Min	7	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	8.0	32.14
			P25	28.0	17.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 10	366	Mean	27.8	21.7	77.92
			SD	2.0	8.2	28.72
			Min	6	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	9.0	32.14
			P25	28.0	17.0	64.29
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 11	362	Mean	27.7	21.4	76.87
			SD	2.5	8.6	30.32
			Min	1	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	25.00
			P25	28.0	17.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00

表 2.7.4.7.1-9
Table 3.1-1
治験薬の服薬状況（339-14-001，339-14-002）
Safety Set of Study 339-14-002

Treatment group of study 339-14-001	Monthly period	N	Summary statistics	TLFB days	IMP	
					Days	(%)
	Month 12	354	Mean	27.9	21.5	76.86
			SD	1.4	8.6	30.43
			Min	11	0	0.0
			Median	28.0	26.0	92.86
			Max	28	28	100.0
			P10	28.0	7.0	25.00
			P25	28.0	16.0	57.14
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 13	349	Mean	27.1	20.8	76.42
			SD	3.3	8.8	30.97
			Min	1	0	0.0
			Median	28.0	25.0	92.86
			Max	28	28	100.0
			P10	25.0	5.0	21.43
			P25	28.0	16.0	60.71
			P75	28.0	28.0	100.00
			P90	28.0	28.0	100.00
	Month 14	233	Mean	8.6	6.4	74.71
			SD	4.5	4.4	34.25
			Min	1	0	0.0
			Median	7.0	6.0	92.86
			Max	28	21	100.0
			P10	3.0	0.0	0.00
			P25	6.0	4.0	57.14
			P75	13.0	8.0	100.00
			P90	14.0	13.0	100.00

＜資料番号5.3.5.3-01：Table 3.1-1＞

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Total number of subjects with TEAEs		194 (79.2)	218 (87.9)	156 (84.8)	374 (86.6)
Blood and lymphatic system disorders	血液およびリンパ系障害	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
Leukopenia	白血球減少症	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Lymphadenopathy	リンパ節症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Thrombocytopenia	血小板減少症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	心臓障害	4 (1.6)	16 (6.5)	11 (6.0)	27 (6.3)
Arrhythmia	不整脈	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Palpitations	動悸	2 (0.8)	13 (5.2)	7 (3.8)	20 (4.6)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Tachycardia	頻脈	2 (0.8)	1 (0.4)	2 (1.1)	3 (0.7)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Ear and labyrinth disorders	耳および迷路障害	1 (0.4)	11 (4.4)	4 (2.2)	15 (3.5)
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Tinnitus	耳鳴	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Vertigo	回転性めまい	1 (0.4)	8 (3.2)	2 (1.1)	10 (2.3)
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Ear discomfort	耳不快感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Endocrine disorders	内分泌障害	1 (0.4)	1 (0.4)	2 (1.1)	3 (0.7)
Hyperprolactinaemia	高プロラクチン血症	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Eye disorders	眼障害	7 (2.9)	5 (2.0)	6 (3.3)	11 (2.5)
Abnormal sensation in eye	眼の異常感	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Dry eye	眼乾燥	2 (0.8)	0 (0.0)	2 (1.1)	2 (0.5)
Episcleritis	上強膜炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Eye pain	眼痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Eyelid oedema	眼瞼浮腫	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Eyelid ptosis	眼瞼下垂	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular hyperaemia	眼充血	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Photophobia	羞明	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Visual impairment	視力障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Oscillopsia	動揺視	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	51 (20.8)	128 (51.6)	92 (50.0)	220 (50.9)
Abdominal discomfort	腹部不快感	6 (2.4)	10 (4.0)	7 (3.8)	17 (3.9)
Abdominal distension	腹部膨満	6 (2.4)	9 (3.6)	5 (2.7)	14 (3.2)
Abdominal pain	腹痛	1 (0.4)	7 (2.8)	6 (3.3)	13 (3.0)
Abdominal pain lower	下腹部痛	1 (0.4)	0 (0.0)	2 (1.1)	2 (0.5)
Abdominal pain upper	上腹部痛	4 (1.6)	5 (2.0)	3 (1.6)	8 (1.9)
Chronic gastritis	慢性胃炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	2 (0.8)	13 (5.2)	8 (4.3)	21 (4.9)
Dental caries	齲歯	2 (0.8)	3 (1.2)	3 (1.6)	6 (1.4)
Diarrhoea	下痢	6 (2.4)	12 (4.8)	7 (3.8)	19 (4.4)
Dry mouth	口内乾燥	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Dyspepsia	消化不良	1 (0.4)	2 (0.8)	3 (1.6)	5 (1.2)
Enterocolitis	腸炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Food poisoning	食中毒	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Gastritis	胃炎	2 (0.8)	1 (0.4)	2 (1.1)	3 (0.7)
Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Gingival pain	歯肉痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	15 (6.1)	79 (31.9)	58 (31.5)	137 (31.7)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Gastrointestinal disorders	胃腸障害				
Oral discomfort	口腔内不快感	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Stomatitis	口内炎	3 (1.2)	0 (0.0)	2 (1.1)	2 (0.5)
Swollen tongue	舌腫脹	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Toothache	歯痛	2 (0.8)	3 (1.2)	0 (0.0)	3 (0.7)
Vomiting	嘔吐	5 (2.0)	34 (13.7)	16 (8.7)	50 (11.6)
Oral dysaesthesia	口腔知覚不全	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	痔出血	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia oral	口の感覚鈍麻	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Oral mucosa haematoma	口腔粘膜血腫	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	34 (13.9)	55 (22.2)	24 (13.0)	79 (18.3)
Asthenia	無力症	3 (1.2)	3 (1.2)	0 (0.0)	3 (0.7)
Chest discomfort	胸部不快感	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Chest pain	胸痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	悪寒	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Death	死亡	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Discomfort	不快感	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
Face oedema	顔面浮腫	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	疲労	4 (1.6)	10 (4.0)	5 (2.7)	15 (3.5)
Feeling abnormal	異常感	2 (0.8)	6 (2.4)	5 (2.7)	11 (2.5)
Feeling cold	冷感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Feeling hot	熱感	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Hangover	宿酔	2 (0.8)	2 (0.8)	1 (0.5)	3 (0.7)
Influenza like illness	インフルエンザ様疾患	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	8 (3.3)	24 (9.7)	7 (3.8)	31 (7.2)
Pain	疼痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態				
Pyrexia	発熱	3 (1.2)	3 (1.2)	3 (1.6)	6 (1.4)
Thirst	口渇	3 (1.2)	9 (3.6)	2 (1.1)	11 (2.5)
Peripheral swelling	末梢腫脹	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Injection site swelling	注射部位腫脹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Early satiety	早期満腹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	1 (0.4)	4 (1.6)	2 (1.1)	6 (1.4)
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Chronic hepatitis	慢性肝炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hepatic cirrhosis	肝硬変	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hepatic function abnormal	肝機能異常	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Hepatic steatosis	脂肪肝	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Immune system disorders	免疫系障害	0 (0.0)	4 (1.6)	2 (1.1)	6 (1.4)
Hypersensitivity	過敏症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Seasonal allergy	季節性アレルギー	0 (0.0)	3 (1.2)	2 (1.1)	5 (1.2)

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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Infections and infestations	感染症および寄生虫症	104 (42.4)	74 (29.8)	43 (23.4)	117 (27.1)
Angular cheilitis	口角口唇炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Anisakiasis	アニサキス症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	気管支炎	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Conjunctivitis	結膜炎	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
Cystitis	膀胱炎	2 (0.8)	0 (0.0)	4 (2.2)	4 (0.9)
Furuncle	せつ	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Gastroenteritis	胃腸炎	2 (0.8)	4 (1.6)	2 (1.1)	6 (1.4)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Gingivitis	歯肉炎	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Herpes virus infection	ヘルペスウイルス感染	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Impetigo	膿痂疹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Infection	感染	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Influenza	インフルエンザ	2 (0.8)	3 (1.2)	2 (1.1)	5 (1.2)
Nasopharyngitis	鼻咽頭炎	91 (37.1)	54 (21.8)	40 (21.7)	94 (21.8)
Oesophageal candidiasis	食道カンジダ症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Otitis media	中耳炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	2 (0.8)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症				
Pharyngitis	咽頭炎	1 (0.4)	3 (1.2)	2 (1.1)	5 (1.2)
Rhinitis	鼻炎	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Sinusitis	副鼻腔炎	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Tinea pedis	足部白癬	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Helicobacter infection	ヘリコバクター感染	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Enteritis infectious	感染性腸炎	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Pneumonia bacterial	細菌性肺炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Oral herpes	口腔ヘルペス	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	19 (7.8)	9 (3.6)	8 (4.3)	17 (3.9)
Accidental overdose	偶発的過量投与	2 (0.8)	2 (0.8)	1 (0.5)	3 (0.7)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Fall	転倒	2 (0.8)	2 (0.8)	0 (0.0)	2 (0.5)
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Foot fracture	足骨折	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Fracture	骨折	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Head injury	頭部損傷	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Heat stroke	熱射病	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Ligament sprain	靭帯捻挫	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Rib fracture	肋骨骨折	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Excoriation	擦過傷	2 (0.8)	0 (0.0)	1 (0.5)	1 (0.2)
Contusion	挫傷	4 (1.6)	0 (0.0)	2 (1.1)	2 (0.5)
Wound	創傷	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Thermal burn	熱傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament injury	靭帯損傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Chest injury	胸部損傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0
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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症				
Ear abrasion	耳擦過傷	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Post-traumatic neck syndrome	外傷後頚部症候群	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	26 (10.6)	32 (12.9)	20 (10.9)	52 (12.0)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.4)	2 (0.8)	1 (0.5)	3 (0.7)
Blood bilirubin increased	血中ビリルビン増加	1 (0.4)	1 (0.4)	2 (1.1)	3 (0.7)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Blood creatinine increased	血中クレアチニン増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Blood potassium decreased	血中カリウム減少	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Blood potassium increased	血中カリウム増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Blood pressure increased	血圧上昇	2 (0.8)	3 (1.2)	4 (2.2)	7 (1.6)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Blood prolactin increased	血中プロラクチン増加	2 (0.8)	6 (2.4)	3 (1.6)	9 (2.1)
Blood triglycerides increased	血中トリグリセリド増加	6 (2.4)	3 (1.2)	0 (0.0)	3 (0.7)
Electrocardiogram QT prolonged	心電図QT延長	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.4)	3 (1.2)	0 (0.0)	3 (0.7)
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Glucose urine present	尿中ブドウ糖陽性	4 (1.6)	1 (0.4)	2 (1.1)	3 (0.7)
Blood urine present	尿中血陽性	3 (1.2)	0 (0.0)	2 (1.1)	2 (0.5)
Liver function test abnormal	肝機能検査異常	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)

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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査				
Red blood cell count decreased	赤血球数減少	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Weight decreased	体重減少	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Weight increased	体重増加	0 (0.0)	4 (1.6)	1 (0.5)	5 (1.2)
White blood cell count decreased	白血球数減少	2 (0.8)	2 (0.8)	1 (0.5)	3 (0.7)
White blood cell count increased	白血球数増加	2 (0.8)	1 (0.4)	0 (0.0)	1 (0.2)
Protein urine present	尿中蛋白陽性	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Metabolism and nutrition disorders	代謝および栄養障害	4 (1.6)	17 (6.9)	13 (7.1)	30 (6.9)
Dehydration	脱水	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Diabetes mellitus	糖尿病	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Hyperkalaemia	高カリウム血症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Increased appetite	食欲亢進	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Decreased appetite	食欲減退	3 (1.2)	13 (5.2)	11 (6.0)	24 (5.6)
Hyperlipidaemia	高脂血症	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	22 (9.0)	25 (10.1)	15 (8.2)	40 (9.3)
Arthralgia	関節痛	6 (2.4)	3 (1.2)	1 (0.5)	4 (0.9)
Arthritis	関節炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Back pain	背部痛	11 (4.5)	8 (3.2)	6 (3.3)	14 (3.2)
Muscle spasms	筋痙縮	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Muscular weakness	筋力低下	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Musculoskeletal pain	筋骨格痛	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Myalgia	筋肉痛	1 (0.4)	4 (1.6)	2 (1.1)	6 (1.4)
Neck pain	頚部痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Pain in extremity	四肢痛	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Trigger finger	弾発指	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Musculoskeletal stiffness	筋骨格硬直	2 (0.8)	2 (0.8)	2 (1.1)	4 (0.9)
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Skin papilloma	皮膚乳頭腫	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Nervous system disorders	神経系障害	53 (21.6)	100 (40.3)	63 (34.2)	163 (37.7)
Amnesia	健忘	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Autonomic nervous system imbalance	自律神経失調	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Burning sensation	灼熱感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Disturbance in attention	注意力障害	0 (0.0)	4 (1.6)	1 (0.5)	5 (1.2)
Dizziness	浮動性めまい	10 (4.1)	51 (20.6)	20 (10.9)	71 (16.4)
Dizziness postural	体位性めまい	1 (0.4)	2 (0.8)	1 (0.5)	3 (0.7)
Dysaesthesia	異常感覚	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Dysgeusia	味覚異常	6 (2.4)	5 (2.0)	4 (2.2)	9 (2.1)
Head discomfort	頭部不快感	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Headache	頭痛	20 (8.2)	24 (9.7)	21 (11.4)	45 (10.4)
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Hypoaesthesia	感覚鈍麻	3 (1.2)	5 (2.0)	3 (1.6)	8 (1.9)
Masked facies	仮面状顔貌	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Memory impairment	記憶障害	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Myoclonus	ミオクローヌス	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Neuralgia	神経痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害				
Somnolence	傾眠	17 (6.9)	39 (15.7)	18 (9.8)	57 (13.2)
Syncope	失神	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Tremor	振戦	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Hyposmia	嗅覚減退	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下	5 (2.0)	4 (1.6)	5 (2.7)	9 (2.1)

MedDRA Ver. 19.0
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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	15 (6.1)	46 (18.5)	29 (15.8)	75 (17.4)
Agitation	激越	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Alcoholic hangover	アルコールによる宿酔	2 (0.8)	5 (2.0)	1 (0.5)	6 (1.4)
Alcoholism	アルコール症	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Anticipatory anxiety	予期不安	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Anxiety	不安	1 (0.4)	3 (1.2)	2 (1.1)	5 (1.2)
Apathy	無感情	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Depressed mood	抑うつ気分	0 (0.0)	4 (1.6)	0 (0.0)	4 (0.9)
Depression	うつ病	2 (0.8)	0 (0.0)	1 (0.5)	1 (0.2)
Dysphoria	不快気分	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Initial insomnia	初期不眠症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Insomnia	不眠症	2 (0.8)	20 (8.1)	15 (8.2)	35 (8.1)
Irritability	易刺激性	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Listless	気力低下	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Middle insomnia	中期不眠症	1 (0.4)	8 (3.2)	5 (2.7)	13 (3.0)
Mood swings	気分動揺	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Nightmare	悪夢	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Panic attack	パニック発作	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Restlessness	落ち着きのなさ	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害				
Sleep disorder	睡眠障害	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Stress	ストレス	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Suicidal ideation	自殺念慮	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Abulia	無為	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Alcohol withdrawal syndrome	アルコール離脱症候群	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Depressive symptom	抑うつ症状	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Affect lability	感情不安定	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Terminal insomnia	早朝覚醒型不眠症	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Renal and urinary disorders	腎および尿路障害	2 (0.8)	4 (1.6)	3 (1.6)	7 (1.6)
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Dysuria	排尿困難	2 (0.8)	0 (0.0)	1 (0.5)	1 (0.2)
Nocturia	夜間頻尿	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Pollakiuria	頻尿	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)

MedDRA Ver. 19.0
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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	生殖系および乳房障害	2 (0.8)	7 (2.8)	2 (1.1)	9 (2.1)
Dysmenorrhoea	月経困難症	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Erection increased	勃起増強	0 (0.0)	3 (1.2)	1 (0.5)	4 (0.9)
Metrorrhagia	不正子宮出血	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Premenstrual syndrome	月経前症候群	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Erectile dysfunction	勃起不全	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
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表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	9 (3.7)	10 (4.0)	9 (4.9)	19 (4.4)
Choking sensation	息詰まり感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Cough	咳嗽	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Dyspnoea	呼吸困難	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	1 (0.4)	3 (1.6)	4 (0.9)
Laryngeal pain	喉頭痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Nasal congestion	鼻閉	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Pneumothorax	気胸	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Respiration abnormal	呼吸異常	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Rhinitis allergic	アレルギー性鼻炎	1 (0.4)	0 (0.0)	2 (1.1)	2 (0.5)
Rhinorrhoea	鼻漏	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Wheezing	喘鳴	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Upper respiratory tract inflammation	上気道の炎症	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)
Oropharyngeal discomfort	口腔咽頭不快感	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Oropharyngeal pain	口腔咽頭痛	1 (0.4)	2 (0.8)	1 (0.5)	3 (0.7)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	7 (2.9)	18 (7.3)	10 (5.4)	28 (6.5)
Acne	ざ瘡	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Dermatitis	皮膚炎	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Drug eruption	薬疹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Eczema	湿疹	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Erythema	紅斑	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Erythema multiforme	多形紅斑	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hyperhidrosis	多汗症	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Hyperkeratosis	過角化	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Pruritus	そう痒症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	2 (0.8)	2 (0.8)	0 (0.0)	2 (0.5)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Seborrhoeic dermatitis	脂漏性皮膚炎	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Urticaria	蕁麻疹	1 (0.4)	4 (1.6)	3 (1.6)	7 (1.6)
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-10
Table 14.1.1.3-16
Incidences of Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Vascular disorders	血管障害	7 (2.9)	8 (3.2)	7 (3.8)	15 (3.5)
Hypertension	高血圧	4 (1.6)	4 (1.6)	1 (0.5)	5 (1.2)
Hypotension	低血圧	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Orthostatic hypotension	起立性低血圧	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Peripheral coldness	末梢冷感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hot flush	ほてり	3 (1.2)	3 (1.2)	4 (2.2)	7 (1.6)
Product issues	製品の問題	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Device failure	医療機器不具合	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.
＜資料番号5.3.5.1-01：Table 14.1.1.3-16＞

表 2.7.4.7.1-11

Table 14.1.1.3-17

Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Total number of subjects with drug-related TEAEs		91 (37.1)	176 (71.0)	131 (71.2)	307 (71.1)
Blood and lymphatic system disorders	血液およびリンパ系障害	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
Leukopenia	白血球減少症	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Lymphadenopathy	リンパ節症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Thrombocytopenia	血小板減少症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	心臓障害	3 (1.2)	13 (5.2)	8 (4.3)	21 (4.9)
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Palpitations	動悸	2 (0.8)	12 (4.8)	5 (2.7)	17 (3.9)
Tachycardia	頻脈	2 (0.8)	0 (0.0)	2 (1.1)	2 (0.5)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	8 (3.2)	3 (1.6)	11 (2.5)
Tinnitus	耳鳴	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Vertigo	回転性めまい	0 (0.0)	6 (2.4)	2 (1.1)	8 (1.9)
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Ear discomfort	耳不快感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Endocrine disorders	内分泌障害	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11

Table 14.1.1.3-17

Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Eye disorders	眼障害	2 (0.8)	5 (2.0)	2 (1.1)	7 (1.6)
Abnormal sensation in eye	眼の異常感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Eye irritation	眼刺激	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Eye pain	眼痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Eyelid oedema	眼瞼浮腫	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Photophobia	羞明	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Visual impairment	視力障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Oscillopsia	動揺視	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0

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表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Gastrointestinal disorders	胃腸障害	25 (10.2)	110 (44.4)	75 (40.8)	185 (42.8)
Abdominal discomfort	腹部不快感	4 (1.6)	8 (3.2)	6 (3.3)	14 (3.2)
Abdominal distension	腹部膨満	3 (1.2)	7 (2.8)	4 (2.2)	11 (2.5)
Abdominal pain	腹痛	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)
Abdominal pain lower	下腹部痛	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Abdominal pain upper	上腹部痛	1 (0.4)	4 (1.6)	0 (0.0)	4 (0.9)
Constipation	便秘	2 (0.8)	11 (4.4)	4 (2.2)	15 (3.5)
Diarrhoea	下痢	1 (0.4)	8 (3.2)	3 (1.6)	11 (2.5)
Dry mouth	口内乾燥	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Gastritis	胃炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	10 (4.1)	77 (31.0)	57 (31.0)	134 (31.0)
Oral discomfort	口腔内不快感	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Vomiting	嘔吐	1 (0.4)	27 (10.9)	11 (6.0)	38 (8.8)
Oral dysaesthesia	口腔知覚不全	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia oral	口の感覚鈍麻	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	18 (7.3)	45 (18.1)	21 (11.4)	66 (15.3)
Asthenia	無力症	1 (0.4)	2 (0.8)	0 (0.0)	2 (0.5)
Chest discomfort	胸部不快感	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Chills	悪寒	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Death	死亡	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Discomfort	不快感	2 (0.8)	1 (0.4)	1 (0.5)	2 (0.5)
Face oedema	顔面浮腫	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	疲労	2 (0.8)	6 (2.4)	5 (2.7)	11 (2.5)
Feeling abnormal	異常感	2 (0.8)	5 (2.0)	5 (2.7)	10 (2.3)
Feeling cold	冷感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Feeling hot	熱感	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Hangover	宿酔	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Malaise	倦怠感	5 (2.0)	22 (8.9)	7 (3.8)	29 (6.7)
Pain	疼痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Pyrexia	発熱	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Thirst	口渇	2 (0.8)	9 (3.6)	2 (1.1)	11 (2.5)
Peripheral swelling	末梢腫脹	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態				
Early satiety	早期満腹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	1 (0.4)	3 (1.2)	1 (0.5)	4 (0.9)
Chronic hepatitis	慢性肝炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hepatic cirrhosis	肝硬変	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hepatic function abnormal	肝機能異常	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Immune system disorders	免疫系障害	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Hypersensitivity	過敏症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Infections and infestations	感染症および寄生虫症	3 (1.2)	3 (1.2)	1 (0.5)	4 (0.9)
Angular cheilitis	口角口唇炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Furuncle	せつ	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Gingivitis	歯肉炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Oesophageal candidiasis	食道カンジダ症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Pharyngitis	咽頭炎	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11

Table 14.1.1.3-17

Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Investigations	臨床検査	13 (5.3)	22 (8.9)	11 (6.0)	33 (7.6)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Blood bilirubin increased	血中ビリルビン増加	1 (0.4)	1 (0.4)	1 (0.5)	2 (0.5)
Blood creatinine increased	血中クレアチニン増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Blood potassium decreased	血中カリウム減少	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Blood pressure increased	血圧上昇	1 (0.4)	2 (0.8)	2 (1.1)	4 (0.9)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Blood prolactin increased	血中プロラクチン増加	1 (0.4)	6 (2.4)	3 (1.6)	9 (2.1)
Blood triglycerides increased	血中トリグリセリド増加	2 (0.8)	2 (0.8)	0 (0.0)	2 (0.5)
Electrocardiogram QT prolonged	心電図QT延長	2 (0.8)	0 (0.0)	1 (0.5)	1 (0.2)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	1 (0.4)	3 (1.2)	0 (0.0)	3 (0.7)
Glucose urine present	尿中ブドウ糖陽性	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Blood urine present	尿中血陽性	1 (0.4)	0 (0.0)	2 (1.1)	2 (0.5)
Liver function test abnormal	肝機能検査異常	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Red blood cell count decreased	赤血球数減少	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Weight increased	体重増加	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
White blood cell count decreased	白血球数減少	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
White blood cell count increased	白血球数増加	2 (0.8)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Investigations	臨床検査				
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Metabolism and nutrition disorders	代謝および栄養障害	3 (1.2)	12 (4.8)	10 (5.4)	22 (5.1)
Increased appetite	食欲亢進	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Decreased appetite	食欲減退	3 (1.2)	11 (4.4)	9 (4.9)	20 (4.6)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	0 (0.0)	6 (2.4)	4 (2.2)	10 (2.3)
Arthralgia	関節痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Back pain	背部痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Muscular weakness	筋力低下	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	2 (0.8)	2 (1.1)	4 (0.9)
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Nervous system disorders	神経系障害	43 (17.6)	97 (39.1)	56 (30.4)	153 (35.4)
Amnesia	健忘	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Burning sensation	灼熱感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Disturbance in attention	注意力障害	0 (0.0)	4 (1.6)	1 (0.5)	5 (1.2)
Dizziness	浮動性めまい	9 (3.7)	49 (19.8)	20 (10.9)	69 (16.0)
Dizziness postural	体位性めまい	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Dysaesthesia	異常感覚	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Dysgeusia	味覚異常	6 (2.4)	5 (2.0)	4 (2.2)	9 (2.1)
Head discomfort	頭部不快感	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Headache	頭痛	13 (5.3)	21 (8.5)	18 (9.8)	39 (9.0)
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Hypoaesthesia	感覚鈍麻	1 (0.4)	5 (2.0)	3 (1.6)	8 (1.9)
Masked facies	仮面状顔貌	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Memory impairment	記憶障害	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Myoclonus	ミオクローヌス	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Sedation	鎮静	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Somnolence	傾眠	15 (6.1)	38 (15.3)	17 (9.2)	55 (12.7)
Tremor	振戦	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11

Table 14.1.1.3-17

Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害				
Hyposmia	嗅覚減退	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下	5 (2.0)	4 (1.6)	4 (2.2)	8 (1.9)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Psychiatric disorders	精神障害	4 (1.6)	39 (15.7)	22 (12.0)	61 (14.1)
Agitation	激越	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Alcoholic hangover	アルコールによる宿酔	1 (0.4)	4 (1.6)	0 (0.0)	4 (0.9)
Alcoholism	アルコール症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Anticipatory anxiety	予期不安	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Anxiety	不安	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Apathy	無感情	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Depressed mood	抑うつ気分	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Dysphoria	不快気分	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Initial insomnia	初期不眠症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Insomnia	不眠症	0 (0.0)	17 (6.9)	13 (7.1)	30 (6.9)
Irritability	易刺激性	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Listless	気力低下	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Middle insomnia	中期不眠症	1 (0.4)	7 (2.8)	5 (2.7)	12 (2.8)
Mood swings	気分動揺	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Panic attack	パニック発作	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Restlessness	落ち着きのなさ	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Sleep disorder	睡眠障害	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Abulia	無為	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11

Table 14.1.1.3-17

Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Psychiatric disorders	精神障害				
Depressive symptom	抑うつ症状	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Terminal insomnia	早朝覚醒型不眠症	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Renal and urinary disorders	腎および尿路障害	1 (0.4)	4 (1.6)	2 (1.1)	6 (1.4)
Dysuria	排尿困難	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Nocturia	夜間頻尿	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Pollakiuria	頻尿	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Reproductive system and breast disorders	生殖系および乳房障害	1 (0.4)	5 (2.0)	1 (0.5)	6 (1.4)
Erection increased	勃起増強	0 (0.0)	3 (1.2)	1 (0.5)	4 (0.9)
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Premenstrual syndrome	月経前症候群	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	3 (1.2)	6 (2.4)	5 (2.7)	11 (2.5)
Choking sensation	息詰まり感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Dyspnoea	呼吸困難	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Nasal congestion	鼻閉	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Respiration abnormal	呼吸異常	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Wheezing	喘鳴	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Laryngeal discomfort	喉頭不快感	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Oropharyngeal pain	口腔咽頭痛	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-11
Table 14.1.1.3-17
Incidences of Drug-related Treatment-emergent Adverse Events by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	2 (0.8)	12 (4.8)	5 (2.7)	17 (3.9)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Dermatitis	皮膚炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Eczema	湿疹	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Erythema multiforme	多形紅斑	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hyperhidrosis	多汗症	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Night sweats	寝汗	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Pruritus	そう痒症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Urticaria	蕁麻疹	0 (0.0)	4 (1.6)	0 (0.0)	4 (0.9)
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Vascular disorders	血管障害	5 (2.0)	6 (2.4)	4 (2.2)	10 (2.3)
Hypertension	高血圧	2 (0.8)	2 (0.8)	0 (0.0)	2 (0.5)
Hypotension	低血圧	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Orthostatic hypotension	起立性低血圧	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Peripheral coldness	末梢冷感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hot flush	ほてり	3 (1.2)	3 (1.2)	3 (1.6)	6 (1.4)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.
＜資料番号5.3.5.1-01：Table 14.1.1.3-17＞

表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class / Preferred term	Study	339-14-001 n (%)	339-14-002 n (%)	Total n (%)	339-14-001 n (%)	339-14-002 n (%)	Total n (%)
Total number of subjects with adverse events		135 (78.5)	141 (82.0)	161 (93.6)	117 (85.4)	96 (70.1)	125 (91.2)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Anaemia	貧血	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Cardiac disorders	心臓障害	3 (1.7)	8 (4.7)	10 (5.8)	5 (3.6)	1 (0.7)	6 (4.4)
Arrhythmia	不整脈	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Bradycardia	徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bundle branch block right	右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palpitations	動悸	2 (1.2)	6 (3.5)	7 (4.1)	4 (2.9)	1 (0.7)	5 (3.6)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Tachycardia	頻脈	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	4 (2.3)	4 (2.3)	6 (4.4)	4 (2.9)	9 (6.6)
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Eustachian tube patulous	耳管開放	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperacusis	聴覚過敏	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.5)	2 (1.5)
Vertigo	回転性めまい	0 (0.0)	2 (1.2)	2 (1.2)	5 (3.6)	1 (0.7)	6 (4.4)
Endocrine disorders	内分泌障害	1 (0.6)	2 (1.2)	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.7)
Hyperprolactinaemia	高プロラクチン血症	1 (0.6)	2 (1.2)	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Eye disorders	眼障害	4 (2.3)	1 (0.6)	5 (2.9)	1 (0.7)	6 (4.4)	7 (5.1)
Abnormal sensation in eye	眼の異常感	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Cataract	白内障	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2 (1.5)
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry eye	眼乾燥	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)
Episcleritis	上強膜炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Keratitis	角膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Ocular hyperaemia	眼充血	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Scleritis	強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Corneal disorder	角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	36 (20.9)	67 (39.0)	87 (50.6)	63 (46.0)	42 (30.7)	80 (58.4)
Abdominal discomfort	腹部不快感	4 (2.3)	9 (5.2)	13 (7.6)	6 (4.4)	9 (6.6)	12 (8.8)
Abdominal distension	腹部膨満	4 (2.3)	4 (2.3)	7 (4.1)	8 (5.8)	3 (2.2)	11 (8.0)
Abdominal pain	腹痛	0 (0.0)	2 (1.2)	2 (1.2)	3 (2.2)	1 (0.7)	4 (2.9)
Abdominal pain lower	下腹部痛	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	2 (1.2)	1 (0.6)	3 (1.7)	3 (2.2)	3 (2.2)	5 (3.6)
Chronic gastritis	慢性胃炎	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	2 (1.2)	8 (4.7)	10 (5.8)	8 (5.8)	2 (1.5)	10 (7.3)
Dental caries	齲歯	1 (0.6)	2 (1.2)	3 (1.7)	3 (2.2)	1 (0.7)	4 (2.9)
Diarrhoea	下痢	2 (1.2)	2 (1.2)	4 (2.3)	4 (2.9)	6 (4.4)	7 (5.1)
Dry mouth	口内乾燥	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspepsia	消化不良	1 (0.6)	2 (1.2)	3 (1.7)	2 (1.5)	0 (0.0)	2 (1.5)
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Faeces hard	硬便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Gastric polyps	胃ポリープ	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Gastric ulcer	胃潰瘍	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	2 (1.2)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class / Preferred term	Study	339-14-001 n (%)	339-14-002 n (%)	Total n (%)	339-14-001 n (%)	339-14-002 n (%)	Total n (%)
Gastrointestinal disorders	胃腸障害						
Gingival pain	歯肉痛	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	9 (5.2)	41 (23.8)	46 (26.7)	38 (27.7)	21 (15.3)	50 (36.5)
Oral discomfort	口腔内不快感	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Stomatitis	口内炎	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Toothache	歯痛	2 (1.2)	0 (0.0)	2 (1.2)	3 (2.2)	2 (1.5)	5 (3.6)
Vomiting	嘔吐	3 (1.7)	14 (8.1)	16 (9.3)	12 (8.8)	6 (4.4)	17 (12.4)
Oral dysaesthesia	口腔知覚不全	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Large intestine polyp	大腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Oral mucosa haematoma	口腔粘膜血腫	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Faeces soft	軟便	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	25 (14.5)	33 (19.2)	50 (29.1)	34 (24.8)	12 (8.8)	42 (30.7)
Asthenia	無力症	1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	1 (0.7)	3 (2.2)
Chest discomfort	胸部不快感	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Chest pain	胸痛	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	悪寒	1 (0.6)	2 (1.2)	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.7)
Discomfort	不快感	2 (1.2)	1 (0.6)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Fatigue	疲労	2 (1.2)	3 (1.7)	5 (2.9)	6 (4.4)	0 (0.0)	6 (4.4)
Feeling abnormal	異常感	1 (0.6)	6 (3.5)	7 (4.1)	5 (3.6)	3 (2.2)	7 (5.1)
Feeling hot	熱感	1 (0.6)	2 (1.2)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	2 (1.2)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Influenza like illness	インフルエンザ様疾患	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	7 (4.1)	15 (8.7)	21 (12.2)	15 (10.9)	7 (5.1)	20 (14.6)
Pyrexia	発熱	1 (0.6)	2 (1.2)	3 (1.7)	2 (1.5)	0 (0.0)	2 (1.5)
Thirst	口渇	3 (1.7)	6 (3.5)	7 (4.1)	5 (3.6)	1 (0.7)	6 (4.4)
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Injection site swelling	注射部位腫脹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態						
Early satiety	早期満腹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Vaccination site swelling	ワクチン接種部位腫脹	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	1 (0.6)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Immune system disorders	免疫系障害	0 (0.0)	4 (2.3)	4 (2.3)	2 (1.5)	0 (0.0)	2 (1.5)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Seasonal allergy	季節性アレルギー	0 (0.0)	4 (2.3)	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class / Preferred term	Study	339-14-001 n (%)	339-14-002 n (%)	Total n (%)	339-14-001 n (%)	339-14-002 n (%)	Total n (%)
Infections and infestations	感染症および寄生虫症	70 (40.7)	41 (23.8)	91 (52.9)	42 (30.7)	29 (21.2)	62 (45.3)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Anisakiasis	アニサキス症	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	気管支炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis	結膜炎	2 (1.2)	1 (0.6)	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.7)
Cystitis	膀胱炎	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	2 (1.5)	2 (1.5)
Empyema	蓄膿	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Gastroenteritis	胃腸炎	1 (0.6)	3 (1.7)	4 (2.3)	2 (1.5)	0 (0.0)	2 (1.5)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Gingivitis	歯肉炎	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Herpes virus infection	ヘルペスウイルス感染	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Impetigo	膿痂疹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Influenza	インフルエンザ	1 (0.6)	2 (1.2)	3 (1.7)	2 (1.5)	0 (0.0)	2 (1.5)
Nasopharyngitis	鼻咽頭炎	61 (35.5)	31 (18.0)	76 (44.2)	33 (24.1)	23 (16.8)	51 (37.2)
Oesophageal candidiasis	食道カンジダ症	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症						
Otitis media	中耳炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Pharyngitis	咽頭炎	1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	0 (0.0)	2 (1.5)
Rhinitis	鼻炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Sialoadenitis	唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sinusitis	副鼻腔炎	2 (1.2)	2 (1.2)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Viral diarrhoea	ウイルス性下痢	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Gingival abscess	歯肉膿瘍	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Helicobacter infection	ヘリコバクター感染	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Herpes dermatitis	ヘルペス性皮膚炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	2 (1.5)
Gastroenteritis norovirus	ノロウイルス性胃腸炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	16 (9.3)	8 (4.7)	23 (13.4)	6 (4.4)	10 (7.3)	16 (11.7)
Accidental overdose	偶発的過量投与	2 (1.2)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Alcohol poisoning	アルコール中毒	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2 (1.5)
Chillblains	凍瘡	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Fall	転倒	2 (1.2)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Fibula fracture	腓骨骨折	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Fracture	骨折	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Frostbite	凍傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Hand fracture	手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2 (1.5)
Heat stroke	熱射病	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Joint dislocation	関節脱臼	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament sprain	靭帯捻挫	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	2 (1.5)	3 (2.2)
Rib fracture	肋骨骨折	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Road traffic accident	交通事故	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症						
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Excoriation	擦過傷	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)
Contusion	挫傷	3 (1.7)	2 (1.2)	5 (2.9)	0 (0.0)	2 (1.5)	2 (1.5)
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Thermal burn	熱傷	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament injury	靱帯損傷	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Chest injury	胸部損傷	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Ear abrasion	耳擦過傷	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Tooth fracture	歯牙破折	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Skin abrasion	皮膚擦過傷	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Avulsion fracture	剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2 (1.5)
Post-traumatic neck syndrome	外傷後頚部症候群	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	17 (9.9)	12 (7.0)	24 (14.0)	21 (15.3)	13 (9.5)	28 (20.4)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	1 (0.7)	3 (2.2)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.6)	1 (0.6)	2 (1.5)	1 (0.7)	3 (2.2)
Blood bilirubin increased	血中ビリルビン増加	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Blood potassium increased	血中カリウム増加	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Blood pressure increased	血圧上昇	2 (1.2)	3 (1.7)	4 (2.3)	2 (1.5)	2 (1.5)	4 (2.9)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)
Blood prolactin increased	血中プロラクチン増加	1 (0.6)	0 (0.0)	1 (0.6)	5 (3.6)	2 (1.5)	7 (5.1)
Blood triglycerides increased	血中トリグリセリド増加	4 (2.3)	0 (0.0)	4 (2.3)	2 (1.5)	0 (0.0)	2 (1.5)
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
C-reactive protein increased	C－反応性蛋白増加	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Electrocardiogram QT prolonged	心電図QT延長	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	1 (0.6)	0 (0.0)	1 (0.6)	2 (1.5)	2 (1.5)	4 (2.9)
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine present	尿中ブドウ糖陽性	3 (1.7)	1 (0.6)	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
Blood urine present	尿中血陽性	2 (1.2)	1 (0.6)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Heart rate decreased	心拍数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Liver function test abnormal	肝機能検査異常	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Weight decreased	体重減少	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Weight increased	体重増加	0 (0.0)	2 (1.2)	2 (1.2)	2 (1.5)	1 (0.7)	3 (2.2)
White blood cell count decreased	白血球数減少	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell count increased	白血球数増加	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Urine output increased	尿量増加	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Occult blood positive	便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	2 (1.5)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Metabolism and nutrition disorders	代謝および栄養障害	2 (1.2)	13 (7.6)	14 (8.1)	9 (6.6)	11 (8.0)	18 (13.1)
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Gout	痛風	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.5)	2 (1.5)
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Decreased appetite	食欲減退	2 (1.2)	11 (6.4)	12 (7.0)	6 (4.4)	4 (2.9)	10 (7.3)
Hyperlipidaemia	高脂血症	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	1 (0.7)	2 (1.5)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	15 (8.7)	19 (11.0)	31 (18.0)	16 (11.7)	15 (10.9)	28 (20.4)
Arthralgia	関節痛	5 (2.9)	2 (1.2)	7 (4.1)	2 (1.5)	2 (1.5)	3 (2.2)
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Back pain	背部痛	4 (2.3)	7 (4.1)	11 (6.4)	3 (2.2)	8 (5.8)	11 (8.0)
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal pain	筋骨格痛	1 (0.6)	1 (0.6)	2 (1.2)	1 (0.7)	1 (0.7)	2 (1.5)
Myalgia	筋肉痛	1 (0.6)	0 (0.0)	1 (0.6)	4 (2.9)	1 (0.7)	5 (3.6)
Neck pain	頚部痛	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Osteochondrosis	骨端症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Osteonecrosis	骨壊死	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Osteoporosis	骨粗鬆症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Pain in extremity	四肢痛	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Plantar fasciitis	足底筋膜炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害						
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Muscle tightness	筋緊張	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Intervertebral disc protrusion	椎間板突出	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Musculoskeletal stiffness	筋骨格硬直	2 (1.2)	1 (0.6)	3 (1.7)	2 (1.5)	0 (0.0)	2 (1.5)
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Finger deformity	指変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (1.2)	1 (0.6)	3 (1.7)	0 (0.0)	2 (1.5)	2 (1.5)
Skin papilloma	皮膚乳頭腫	2 (1.2)	1 (0.6)	3 (1.7)	0 (0.0)	1 (0.7)	1 (0.7)
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	36 (20.9)	60 (34.9)	79 (45.9)	45 (32.8)	32 (23.4)	63 (46.0)
Akathisia	アカシジア	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Amnesia	健忘	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Autonomic nervous system imbalance	自律神経失調	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	0 (0.0)	2 (1.2)	2 (1.2)	2 (1.5)	0 (0.0)	2 (1.5)
Dizziness	浮動性めまい	8 (4.7)	27 (15.7)	31 (18.0)	19 (13.9)	8 (5.8)	23 (16.8)
Dizziness postural	体位性めまい	1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	1 (0.7)	3 (2.2)
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Dysgeusia	味覚異常	4 (2.3)	7 (4.1)	10 (5.8)	2 (1.5)	7 (5.1)	8 (5.8)
Dyskinesia	ジスキネジア	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Head discomfort	頭部不快感	1 (0.6)	3 (1.7)	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.7)
Headache	頭痛	12 (7.0)	13 (7.6)	22 (12.8)	4 (2.9)	8 (5.8)	12 (8.8)
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia	感覚鈍麻	2 (1.2)	2 (1.2)	3 (1.7)	3 (2.2)	0 (0.0)	3 (2.2)
Memory impairment	記憶障害	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myoclonus	ミオクローヌス	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害						
Paraesthesia	錯感覚	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Paralysis	麻痺	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Sciatica	坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Somnolence	傾眠	12 (7.0)	12 (7.0)	24 (14.0)	26 (19.0)	9 (6.6)	29 (21.2)
Hyposmia	嗅覚減退	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Cubital tunnel syndrome	肘部管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Poor quality sleep	睡眠の質低下	3 (1.7)	3 (1.7)	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	10 (5.8)	37 (21.5)	46 (26.7)	21 (15.3)	10 (7.3)	28 (20.4)
Abnormal dreams	異常な夢	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	2 (1.2)	3 (1.7)	5 (2.9)	4 (2.9)	1 (0.7)	5 (3.6)
Alcoholism	アルコール症	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)
Depressed mood	抑うつ気分	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Euphoric mood	多幸気分	0 (0.0)	3 (1.7)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Hallucination, auditory	幻聴	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	1 (0.6)	13 (7.6)	14 (8.1)	9 (6.6)	2 (1.5)	11 (8.0)
Irritability	易刺激性	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)
Libido decreased	リビドー減退	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Middle insomnia	中期不眠症	1 (0.6)	5 (2.9)	6 (3.5)	5 (3.6)	2 (1.5)	7 (5.1)
Nightmare	悪夢	1 (0.6)	2 (1.2)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Restlessness	落ち着きのなさ	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Sleep disorder	睡眠障害	0 (0.0)	5 (2.9)	5 (2.9)	1 (0.7)	1 (0.7)	1 (0.7)
Tension	緊張	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Alcohol withdrawal syndrome	アルコール離脱症候群	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Affect lability	感情不安定	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Mental disorder	精神障害	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Terminal insomnia	早朝覚醒型不眠症	1 (0.6)	5 (2.9)	6 (3.5)	1 (0.7)	1 (0.7)	1 (0.7)
Renal and urinary disorders	腎および尿路障害	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.5)	2 (1.5)
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysuria	排尿困難	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2 (1.5)
Ureterolithiasis	尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders	生殖系および乳房障害	1 (0.6)	2 (1.2)	3 (1.7)	6 (4.4)	1 (0.7)	6 (4.4)
Dysmenorrhoea	月経困難症	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	1 (0.7)	1 (0.7)
Erection increased	勃起増強	0 (0.0)	1 (0.6)	1 (0.6)	3 (2.2)	0 (0.0)	3 (2.2)
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Prostatitis	前立腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	8 (4.7)	4 (2.3)	12 (7.0)	7 (5.1)	6 (4.4)	10 (7.3)
Cough	咳嗽	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspnoea	呼吸困難	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Hyperventilation	過換気	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
Nasal inflammation	鼻の炎症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Rhinitis allergic	アレルギー性鼻炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Rhinorrhoea	鼻漏	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Upper respiratory tract inflammation	上気道の炎症	2 (1.2)	1 (0.6)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Oropharyngeal discomfort	口腔咽頭不快感	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	口腔咽頭痛	1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	3 (2.2)	4 (2.9)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	5 (2.9)	14 (8.1)	18 (10.5)	10 (7.3)	5 (3.6)	14 (10.2)
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Angioedema	血管浮腫	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Cold sweat	冷汗	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	2 (1.2)	1 (0.6)	3 (1.7)	0 (0.0)	1 (0.7)	1 (0.7)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
Drug eruption	薬疹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	1 (0.7)	4 (2.9)
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Hyperhidrosis	多汗症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkeratosis	過角化	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	1 (0.7)	2 (1.5)
Pruritus	そう痒症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Psoriasis	乾癬	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	1 (0.6)	3 (1.7)	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.7)
Rash generalised	全身性皮疹	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seborrhoeic dermatitis	脂漏性皮膚炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害						
Urticaria	蕁麻疹	0 (0.0)	2 (1.2)	2 (1.2)	2 (1.5)	0 (0.0)	2 (1.5)
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	血管障害	6 (3.5)	2 (1.2)	7 (4.1)	4 (2.9)	4 (2.9)	6 (4.4)
Hyperaemia	充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Hypertension	高血圧	4 (2.3)	1 (0.6)	4 (2.3)	2 (1.5)	2 (1.5)	3 (2.2)
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Hot flush	ほてり	2 (1.2)	1 (0.6)	3 (1.7)	1 (0.7)	1 (0.7)	1 (0.7)
Product issues	製品の問題	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Device failure	医療機器不具合	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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＜資料番号5.3.5.2-01：Table 14.1.1.3-27＞

表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with adverse events		74 (78.7)	67 (71.3)	85 (90.4)	191 (82.7)	163 (70.6)	210 (90.9)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Anaemia	貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Cardiac disorders	心臓障害	3 (3.2)	8 (8.5)	11 (11.7)	8 (3.5)	9 (3.9)	17 (7.4)
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bradycardia	徐脈	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Bundle branch block right	右脚ブロック	0 (0.0)	2 (2.1)	2 (2.1)	0 (0.0)	2 (0.9)	2 (0.9)
Palpitations	動悸	1 (1.1)	4 (4.3)	5 (5.3)	5 (2.2)	5 (2.2)	10 (4.3)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Tachycardia	頻脈	2 (2.1)	1 (1.1)	3 (3.2)	2 (0.9)	1 (0.4)	3 (1.3)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	1 (1.1)	1 (1.1)	6 (2.6)	5 (2.2)	10 (4.3)
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Eustachian tube patulous	耳管開放	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperacusis	聴覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)	2 (0.9)
Vertigo	回転性めまい	0 (0.0)	1 (1.1)	1 (1.1)	5 (2.2)	2 (0.9)	7 (3.0)
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Eye disorders	眼障害	2 (2.1)	2 (2.1)	4 (4.3)	3 (1.3)	8 (3.5)	11 (4.8)
Abnormal sensation in eye	眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cataract	白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Conjunctivitis allergic	アレルギー性結膜炎	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Dry eye	眼乾燥	1 (1.1)	1 (1.1)	2 (2.1)	1 (0.4)	2 (0.9)	3 (1.3)
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Eye swelling	眼部腫脹	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Keratitis	角膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Scleritis	強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Corneal disorder	角膜障害	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	44 (46.8)	39 (41.5)	62 (66.0)	107 (46.3)	81 (35.1)	142 (61.5)
Abdominal discomfort	腹部不快感	4 (4.3)	5 (5.3)	7 (7.4)	10 (4.3)	14 (6.1)	19 (8.2)
Abdominal distension	腹部膨満	2 (2.1)	1 (1.1)	2 (2.1)	10 (4.3)	4 (1.7)	13 (5.6)
Abdominal pain	腹痛	5 (5.3)	1 (1.1)	5 (5.3)	8 (3.5)	2 (0.9)	9 (3.9)
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	0 (0.0)	2 (2.1)	2 (2.1)	3 (1.3)	5 (2.2)	7 (3.0)
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	3 (3.2)	5 (5.3)	6 (6.4)	11 (4.8)	7 (3.0)	16 (6.9)
Dental caries	齲歯	3 (3.2)	0 (0.0)	3 (3.2)	6 (2.6)	1 (0.4)	7 (3.0)
Diarrhoea	下痢	4 (4.3)	1 (1.1)	5 (5.3)	8 (3.5)	7 (3.0)	12 (5.2)
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspepsia	消化不良	1 (1.1)	3 (3.2)	3 (3.2)	3 (1.3)	3 (1.3)	5 (2.2)
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Faeces hard	硬便	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Food poisoning	食中毒	0 (0.0)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Gastric polyps	胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastric ulcer	胃潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	1 (1.1)	1 (1.1)	2 (2.1)	2 (0.9)	1 (0.4)	3 (1.3)
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害						
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	27 (28.7)	17 (18.1)	32 (34.0)	65 (28.1)	38 (16.5)	82 (35.5)
Oral discomfort	口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Stomatitis	口内炎	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Toothache	歯痛	0 (0.0)	2 (2.1)	2 (2.1)	3 (1.3)	4 (1.7)	7 (3.0)
Vomiting	嘔吐	6 (6.4)	5 (5.3)	11 (11.7)	18 (7.8)	11 (4.8)	28 (12.1)
Oral dysaesthesia	口腔知覚不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Large intestine polyp	大腸ポリープ	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Paraesthesia oral	口の錯感覚	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Oral mucosa haematoma	口腔粘膜血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Faeces soft	軟便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	11 (11.7)	12 (12.8)	19 (20.2)	45 (19.5)	24 (10.4)	61 (26.4)
Asthenia	無力症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	1 (0.4)	3 (1.3)
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Chest pain	胸痛	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Discomfort	不快感	1 (1.1)	1 (1.1)	1 (1.1)	2 (0.9)	1 (0.4)	2 (0.9)
Fatigue	疲労	3 (3.2)	3 (3.2)	5 (5.3)	9 (3.9)	3 (1.3)	11 (4.8)
Feeling abnormal	異常感	2 (2.1)	1 (1.1)	3 (3.2)	7 (3.0)	4 (1.7)	10 (4.3)
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	0 (0.0)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	3 (3.2)	4 (4.3)	6 (6.4)	18 (7.8)	11 (4.8)	26 (11.3)
Pyrexia	発熱	2 (2.1)	2 (2.1)	3 (3.2)	4 (1.7)	2 (0.9)	5 (2.2)
Thirst	口渇	2 (2.1)	0 (0.0)	2 (2.1)	7 (3.0)	1 (0.4)	8 (3.5)
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態						
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Vaccination site swelling	ワクチン接種部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Alcoholic liver disease	アルコール性肝疾患	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Immune system disorders	免疫系障害	2 (2.1)	3 (3.2)	5 (5.3)	4 (1.7)	3 (1.3)	7 (3.0)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Seasonal allergy	季節性アレルギー	2 (2.1)	3 (3.2)	5 (5.3)	3 (1.3)	3 (1.3)	6 (2.6)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症	22 (23.4)	21 (22.3)	39 (41.5)	64 (27.7)	50 (21.6)	101 (43.7)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis	結膜炎	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Cystitis	膀胱炎	2 (2.1)	0 (0.0)	2 (2.1)	2 (0.9)	2 (0.9)	4 (1.7)
Empyema	蓄膿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Gastroenteritis	胃腸炎	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	1 (0.4)	4 (1.7)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Influenza	インフルエンザ	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	1 (0.4)	4 (1.7)
Nasopharyngitis	鼻咽頭炎	21 (22.3)	16 (17.0)	34 (36.2)	54 (23.4)	39 (16.9)	85 (36.8)
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症						
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pharyngitis	咽頭炎	1 (1.1)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	3 (1.3)
Rhinitis	鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sialoadenitis	唾液腺炎	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Viral diarrhoea	ウイルス性下痢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingival abscess	歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Enteritis infectious	感染性腸炎	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (0.9)	2 (0.9)
Herpes dermatitis	ヘルペス性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)
Gastroenteritis norovirus	ノロウイルス性胃腸炎	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	2 (2.1)	2 (2.1)	4 (4.3)	8 (3.5)	12 (5.2)	20 (8.7)
Accidental overdose	偶発的過量投与	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Alcohol poisoning	アルコール中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Chillblains	凍瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Fibula fracture	腓骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Fracture	骨折	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Frostbite	凍傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Hand fracture	手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Joint dislocation	関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)	3 (1.3)
Rib fracture	肋骨骨折	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Road traffic accident	交通事故	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症						
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament injury	靱帯損傷	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin abrasion	皮膚擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Avulsion fracture	剥離骨折	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	12 (12.8)	7 (7.4)	18 (19.1)	33 (14.3)	20 (8.7)	46 (19.9)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	1 (0.4)	3 (1.3)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (1.1)	0 (0.0)	1 (1.1)	3 (1.3)	1 (0.4)	4 (1.7)
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Blood pressure increased	血圧上昇	3 (3.2)	0 (0.0)	3 (3.2)	5 (2.2)	2 (0.9)	7 (3.0)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Blood prolactin increased	血中プロラクチン増加	2 (2.1)	1 (1.1)	3 (3.2)	7 (3.0)	3 (1.3)	10 (4.3)
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
C-reactive protein increased	C－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Electrocardiogram QT prolonged	心電図QT延長	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)	4 (1.7)
Glucose urine	尿中ブドウ糖	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Glucose urine present	尿中ブドウ糖陽性	2 (2.1)	1 (1.1)	2 (2.1)	3 (1.3)	1 (0.4)	3 (1.3)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
Blood urine present	尿中血陽性	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Heart rate decreased	心拍数減少	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Weight decreased	体重減少	1 (1.1)	1 (1.1)	2 (2.1)	2 (0.9)	1 (0.4)	3 (1.3)
Weight increased	体重増加	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	2 (0.9)	5 (2.2)
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urine output increased	尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Occult blood positive	便潜血陽性	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Metabolism and nutrition disorders	代謝および栄養障害	2 (2.1)	0 (0.0)	2 (2.1)	11 (4.8)	11 (4.8)	20 (8.7)
Dehydration	脱水	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Gout	痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Decreased appetite	食欲減退	1 (1.1)	0 (0.0)	1 (1.1)	7 (3.0)	4 (1.7)	11 (4.8)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	9 (9.6)	9 (9.6)	18 (19.1)	25 (10.8)	24 (10.4)	46 (19.9)
Arthralgia	関節痛	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	3 (1.3)	5 (2.2)
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Back pain	背部痛	5 (5.3)	4 (4.3)	9 (9.6)	8 (3.5)	12 (5.2)	20 (8.7)
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Muscle spasms	筋痙縮	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Muscle twitching	筋攣縮	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Musculoskeletal pain	筋骨格痛	0 (0.0)	1 (1.1)	1 (1.1)	1 (0.4)	2 (0.9)	3 (1.3)
Myalgia	筋肉痛	0 (0.0)	1 (1.1)	1 (1.1)	4 (1.7)	2 (0.9)	6 (2.6)
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Osteochondrosis	骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Osteonecrosis	骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Osteoporosis	骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Plantar fasciitis	足底筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害						
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Muscle tightness	筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Intervertebral disc protrusion	椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	1 (1.1)	1 (1.1)	2 (0.9)	1 (0.4)	3 (1.3)
Musculoskeletal discomfort	筋骨格不快感	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Finger deformity	指変形	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Ligamentitis	靭帯炎	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	21 (22.3)	19 (20.2)	32 (34.0)	66 (28.6)	51 (22.1)	95 (41.1)
Akathisia	アカシジア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Dizziness	浮動性めまい	6 (6.4)	5 (5.3)	10 (10.6)	25 (10.8)	13 (5.6)	33 (14.3)
Dizziness postural	体位性めまい	0 (0.0)	1 (1.1)	1 (1.1)	2 (0.9)	2 (0.9)	4 (1.7)
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Dysgeusia	味覚異常	2 (2.1)	0 (0.0)	2 (2.1)	4 (1.7)	7 (3.0)	10 (4.3)
Dyskinesia	ジスキネジア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Headache	頭痛	6 (6.4)	8 (8.5)	14 (14.9)	10 (4.3)	16 (6.9)	26 (11.3)
Hyperaesthesia	知覚過敏	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	3 (1.3)
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Monoplegia	単麻痺	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害						
Paraesthesia	錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paralysis	麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sciatica	坐骨神経痛	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (0.9)	2 (0.9)
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Somnolence	傾眠	8 (8.5)	5 (5.3)	11 (11.7)	34 (14.7)	14 (6.1)	40 (17.3)
Hyposmia	嗅覚減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cubital tunnel syndrome	肘部管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Poor quality sleep	睡眠の質低下	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	9 (9.6)	10 (10.6)	15 (16.0)	30 (13.0)	20 (8.7)	43 (18.6)
Abnormal dreams	異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	1 (1.1)	1 (1.1)	2 (2.1)	5 (2.2)	2 (0.9)	7 (3.0)
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (0.9)	2 (0.9)
Depressed mood	抑うつ気分	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Euphoric mood	多幸気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hallucination, auditory	幻聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	6 (6.4)	6 (6.4)	9 (9.6)	15 (6.5)	8 (3.5)	20 (8.7)
Irritability	易刺激性	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (0.9)	2 (0.9)
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Middle insomnia	中期不眠症	1 (1.1)	2 (2.1)	2 (2.1)	6 (2.6)	4 (1.7)	9 (3.9)
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sleep disorder	睡眠障害	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	1 (0.4)	2 (0.9)
Tension	緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	0 (0.0)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental disorder	精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Renal and urinary disorders	腎および尿路障害	2 (2.1)	1 (1.1)	3 (3.2)	2 (0.9)	3 (1.3)	5 (2.2)
Calculus urinary	尿路結石	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)
Ureterolithiasis	尿管結石症	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Reproductive system and breast disorders	生殖系および乳房障害	1 (1.1)	1 (1.1)	2 (2.1)	7 (3.0)	2 (0.9)	8 (3.5)
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Erection increased	勃起増強	1 (1.1)	0 (0.0)	1 (1.1)	4 (1.7)	0 (0.0)	4 (1.7)
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Prostatitis	前立腺炎	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	6 (6.4)	2 (2.1)	8 (8.5)	13 (5.6)	8 (3.5)	18 (7.8)
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Dry throat	咽喉乾燥	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	2 (2.1)	0 (0.0)	2 (2.1)	3 (1.3)	0 (0.0)	3 (1.3)
Hyperventilation	過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Nasal inflammation	鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Rhinitis allergic	アレルギー性鼻炎	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Rhinorrhoea	鼻漏	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (0.9)	2 (0.9)
Wheezing	喘鳴	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	口腔咽頭痛	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	4 (1.7)	6 (2.6)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	6 (6.4)	1 (1.1)	6 (6.4)	16 (6.9)	6 (2.6)	20 (8.7)
Acne	ざ瘡	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Angioedema	血管浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	1 (0.4)	4 (1.7)
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Psoriasis	乾癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Rash generalised	全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害						
Urticaria	蕁麻疹	2 (2.1)	0 (0.0)	2 (2.1)	4 (1.7)	0 (0.0)	4 (1.7)
Pruritus generalised	全身性そう痒症	1 (1.1)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	1 (0.4)
Vascular disorders	血管障害	4 (4.3)	5 (5.3)	7 (7.4)	8 (3.5)	9 (3.9)	13 (5.6)
Hyperaemia	充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Hypertension	高血圧	1 (1.1)	2 (2.1)	3 (3.2)	3 (1.3)	4 (1.7)	6 (2.6)
Hypotension	低血圧	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Hot flush	ほてり	2 (2.1)	3 (3.2)	3 (3.2)	3 (1.3)	4 (1.7)	4 (1.7)
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Total number of subjects with adverse events		326 (80.9)	304 (75.4)	371 (92.1)
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.2)	1 (0.2)	2 (0.5)
Anaemia	貧血	0 (0.0)	1 (0.2)	1 (0.2)
Pancytopenia	汎血球減少症	1 (0.2)	0 (0.0)	1 (0.2)
Cardiac disorders	心臓障害	11 (2.7)	17 (4.2)	27 (6.7)
Arrhythmia	不整脈	1 (0.2)	0 (0.0)	1 (0.2)
Bradycardia	徐脈	0 (0.0)	1 (0.2)	1 (0.2)
Bundle branch block right	右脚ブロック	0 (0.0)	2 (0.5)	2 (0.5)
Palpitations	動悸	7 (1.7)	11 (2.7)	17 (4.2)
Supraventricular extrasystoles	上室性期外収縮	1 (0.2)	0 (0.0)	1 (0.2)
Tachycardia	頻脈	3 (0.7)	2 (0.5)	5 (1.2)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	1 (0.2)	1 (0.2)
Ear and labyrinth disorders	耳および迷路障害	6 (1.5)	9 (2.2)	14 (3.5)
Deafness transitory	一過性難聴	0 (0.0)	1 (0.2)	1 (0.2)
Eustachian tube patulous	耳管開放	0 (0.0)	1 (0.2)	1 (0.2)
Hyperacusis	聴覚過敏	0 (0.0)	1 (0.2)	1 (0.2)
Tinnitus	耳鳴	1 (0.2)	2 (0.5)	2 (0.5)
Vertigo	回転性めまい	5 (1.2)	4 (1.0)	9 (2.2)
Endocrine disorders	内分泌障害	2 (0.5)	2 (0.5)	4 (1.0)
Hyperprolactinaemia	高プロラクチン血症	2 (0.5)	2 (0.5)	4 (1.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Eye disorders	眼障害	7 (1.7)	9 (2.2)	16 (4.0)
Abnormal sensation in eye	眼の異常感	1 (0.2)	0 (0.0)	1 (0.2)
Cataract	白内障	0 (0.0)	1 (0.2)	1 (0.2)
Conjunctival haemorrhage	結膜出血	0 (0.0)	2 (0.5)	2 (0.5)
Conjunctivitis allergic	アレルギー性結膜炎	1 (0.2)	0 (0.0)	1 (0.2)
Dry eye	眼乾燥	2 (0.5)	3 (0.7)	5 (1.2)
Episcleritis	上強膜炎	1 (0.2)	0 (0.0)	1 (0.2)
Eye irritation	眼刺激	1 (0.2)	0 (0.0)	1 (0.2)
Eye swelling	眼部腫脹	1 (0.2)	0 (0.0)	1 (0.2)
Keratitis	角膜炎	0 (0.0)	1 (0.2)	1 (0.2)
Ocular hyperaemia	眼充血	1 (0.2)	0 (0.0)	1 (0.2)
Scleritis	強膜炎	0 (0.0)	1 (0.2)	1 (0.2)
Visual impairment	視力障害	0 (0.0)	1 (0.2)	1 (0.2)
Corneal disorder	角膜障害	0 (0.0)	1 (0.2)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	143 (35.5)	148 (36.7)	229 (56.8)
Abdominal discomfort	腹部不快感	14 (3.5)	23 (5.7)	32 (7.9)
Abdominal distension	腹部膨満	14 (3.5)	8 (2.0)	20 (5.0)
Abdominal pain	腹痛	8 (2.0)	4 (1.0)	11 (2.7)
Abdominal pain lower	下腹部痛	1 (0.2)	0 (0.0)	1 (0.2)
Abdominal pain upper	上腹部痛	5 (1.2)	6 (1.5)	10 (2.5)
Chronic gastritis	慢性胃炎	1 (0.2)	1 (0.2)	2 (0.5)
Constipation	便秘	13 (3.2)	15 (3.7)	26 (6.5)
Dental caries	齲歯	7 (1.7)	3 (0.7)	10 (2.5)
Diarrhoea	下痢	10 (2.5)	9 (2.2)	16 (4.0)
Dry mouth	口内乾燥	1 (0.2)	1 (0.2)	2 (0.5)
Dyspepsia	消化不良	4 (1.0)	5 (1.2)	8 (2.0)
Enterocolitis	腸炎	1 (0.2)	0 (0.0)	1 (0.2)
Faeces hard	硬便	0 (0.0)	1 (0.2)	1 (0.2)
Food poisoning	食中毒	1 (0.2)	1 (0.2)	2 (0.5)
Gastric polyps	胃ポリープ	0 (0.0)	1 (0.2)	1 (0.2)
Gastric ulcer	胃潰瘍	0 (0.0)	1 (0.2)	1 (0.2)
Gastritis	胃炎	4 (1.0)	1 (0.2)	5 (1.2)
Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.2)	1 (0.2)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害			
Gingival pain	歯肉痛	1 (0.2)	0 (0.0)	1 (0.2)
Haemorrhoids	痔核	1 (0.2)	0 (0.0)	1 (0.2)
Nausea	悪心	74 (18.4)	79 (19.6)	128 (31.8)
Oral discomfort	口腔内不快感	1 (0.2)	0 (0.0)	1 (0.2)
Salivary hypersecretion	流涎過多	1 (0.2)	1 (0.2)	2 (0.5)
Stomatitis	口内炎	3 (0.7)	0 (0.0)	3 (0.7)
Toothache	歯痛	5 (1.2)	4 (1.0)	9 (2.2)
Vomiting	嘔吐	21 (5.2)	25 (6.2)	44 (10.9)
Oral dysaesthesia	口腔知覚不全	1 (0.2)	1 (0.2)	1 (0.2)
Large intestine polyp	大腸ポリープ	0 (0.0)	1 (0.2)	1 (0.2)
Paraesthesia oral	口の錯感覚	1 (0.2)	0 (0.0)	1 (0.2)
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	1 (0.2)	1 (0.2)
Oral mucosa haematoma	口腔粘膜血腫	1 (0.2)	0 (0.0)	1 (0.2)
Faeces soft	軟便	0 (0.0)	2 (0.5)	2 (0.5)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	70 (17.4)	57 (14.1)	111 (27.5)
Asthenia	無力症	3 (0.7)	2 (0.5)	5 (1.2)
Chest discomfort	胸部不快感	2 (0.5)	0 (0.0)	2 (0.5)
Chest pain	胸痛	1 (0.2)	1 (0.2)	2 (0.5)
Chills	悪寒	2 (0.5)	2 (0.5)	4 (1.0)
Discomfort	不快感	4 (1.0)	2 (0.5)	4 (1.0)
Fatigue	疲労	11 (2.7)	6 (1.5)	16 (4.0)
Feeling abnormal	異常感	8 (2.0)	10 (2.5)	17 (4.2)
Feeling hot	熱感	1 (0.2)	2 (0.5)	3 (0.7)
Hangover	宿酔	3 (0.7)	1 (0.2)	4 (1.0)
Influenza like illness	インフルエンザ様疾患	1 (0.2)	0 (0.0)	1 (0.2)
Injection site pain	注射部位疼痛	1 (0.2)	0 (0.0)	1 (0.2)
Malaise	倦怠感	25 (6.2)	26 (6.5)	47 (11.7)
Pyrexia	発熱	5 (1.2)	4 (1.0)	8 (2.0)
Thirst	口渇	10 (2.5)	7 (1.7)	15 (3.7)
Peripheral swelling	末梢腫脹	1 (0.2)	0 (0.0)	1 (0.2)
Injection site swelling	注射部位腫脹	1 (0.2)	0 (0.0)	1 (0.2)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態			
Early satiety	早期満腹	1 (0.2)	1 (0.2)	2 (0.5)
Vaccination site swelling	ワクチン接種部位腫脹	0 (0.0)	1 (0.2)	1 (0.2)
Hepatobiliary disorders	肝胆道系障害	3 (0.7)	1 (0.2)	3 (0.7)
Alcoholic liver disease	アルコール性肝疾患	1 (0.2)	0 (0.0)	1 (0.2)
Hepatic function abnormal	肝機能異常	1 (0.2)	1 (0.2)	1 (0.2)
Hepatic steatosis	脂肪肝	1 (0.2)	0 (0.0)	1 (0.2)
Immune system disorders	免疫系障害	4 (1.0)	7 (1.7)	11 (2.7)
Hypersensitivity	過敏症	1 (0.2)	0 (0.0)	1 (0.2)
Seasonal allergy	季節性アレルギー	3 (0.7)	7 (1.7)	10 (2.5)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症	134 (33.3)	91 (22.6)	192 (47.6)
Angular cheilitis	口角口唇炎	1 (0.2)	0 (0.0)	1 (0.2)
Anisakiasis	アニサキス症	1 (0.2)	1 (0.2)	2 (0.5)
Bronchitis	気管支炎	0 (0.0)	1 (0.2)	1 (0.2)
Conjunctivitis	結膜炎	4 (1.0)	1 (0.2)	5 (1.2)
Cystitis	膀胱炎	4 (1.0)	2 (0.5)	6 (1.5)
Empyema	蓄膿	0 (0.0)	1 (0.2)	1 (0.2)
Furuncle	せつ	1 (0.2)	0 (0.0)	1 (0.2)
Gastroenteritis	胃腸炎	4 (1.0)	4 (1.0)	8 (2.0)
Gastroenteritis viral	ウイルス性胃腸炎	1 (0.2)	1 (0.2)	2 (0.5)
Gingivitis	歯肉炎	2 (0.5)	0 (0.0)	2 (0.5)
Herpes virus infection	ヘルペスウイルス感染	1 (0.2)	0 (0.0)	1 (0.2)
Herpes zoster	帯状疱疹	1 (0.2)	1 (0.2)	2 (0.5)
Impetigo	膿痂疹	1 (0.2)	0 (0.0)	1 (0.2)
Infection	感染	1 (0.2)	0 (0.0)	1 (0.2)
Influenza	インフルエンザ	4 (1.0)	3 (0.7)	7 (1.7)
Nasopharyngitis	鼻咽頭炎	115 (28.5)	70 (17.4)	161 (40.0)
Oesophageal candidiasis	食道カンジダ症	1 (0.2)	0 (0.0)	1 (0.2)
Otitis externa	外耳炎	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症			
Otitis media	中耳炎	1 (0.2)	0 (0.0)	1 (0.2)
Periodontitis	歯周炎	2 (0.5)	0 (0.0)	2 (0.5)
Pharyngitis	咽頭炎	4 (1.0)	1 (0.2)	5 (1.2)
Rhinitis	鼻炎	1 (0.2)	0 (0.0)	1 (0.2)
Sialoadenitis	唾液腺炎	0 (0.0)	1 (0.2)	1 (0.2)
Sinusitis	副鼻腔炎	2 (0.5)	2 (0.5)	3 (0.7)
Viral diarrhoea	ウイルス性下痢	0 (0.0)	1 (0.2)	1 (0.2)
Gingival abscess	歯肉膿瘍	0 (0.0)	1 (0.2)	1 (0.2)
Helicobacter infection	ヘリコバクター感染	2 (0.5)	1 (0.2)	3 (0.7)
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	1 (0.2)	1 (0.2)
Enteritis infectious	感染性腸炎	0 (0.0)	2 (0.5)	2 (0.5)
Herpes dermatitis	ヘルペス性皮膚炎	0 (0.0)	1 (0.2)	1 (0.2)
Oral herpes	口腔ヘルペス	1 (0.2)	1 (0.2)	2 (0.5)
Gastroenteritis norovirus	ノロウイルス性胃腸炎	0 (0.0)	2 (0.5)	2 (0.5)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	24 (6.0)	20 (5.0)	43 (10.7)
Accidental overdose	偶発的過量投与	4 (1.0)	0 (0.0)	4 (1.0)
Alcohol poisoning	アルコール中毒	0 (0.0)	1 (0.2)	1 (0.2)
Arthropod sting	節足動物刺傷	0 (0.0)	2 (0.5)	2 (0.5)
Chillblains	凍瘡	0 (0.0)	1 (0.2)	1 (0.2)
Fall	転倒	3 (0.7)	0 (0.0)	3 (0.7)
Fibula fracture	腓骨骨折	0 (0.0)	1 (0.2)	1 (0.2)
Foot fracture	足骨折	1 (0.2)	0 (0.0)	1 (0.2)
Fracture	骨折	2 (0.5)	1 (0.2)	3 (0.7)
Frostbite	凍傷	0 (0.0)	1 (0.2)	1 (0.2)
Hand fracture	手骨折	0 (0.0)	2 (0.5)	2 (0.5)
Heat stroke	熱射病	1 (0.2)	0 (0.0)	1 (0.2)
Injury	損傷	1 (0.2)	0 (0.0)	1 (0.2)
Joint dislocation	関節脱臼	0 (0.0)	1 (0.2)	1 (0.2)
Ligament sprain	靱帯捻挫	2 (0.5)	2 (0.5)	4 (1.0)
Rib fracture	肋骨骨折	2 (0.5)	0 (0.0)	2 (0.5)
Road traffic accident	交通事故	0 (0.0)	1 (0.2)	1 (0.2)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症			
Traumatic haematoma	外傷性血腫	0 (0.0)	1 (0.2)	1 (0.2)
Excoriation	擦過傷	2 (0.5)	1 (0.2)	3 (0.7)
Contusion	挫傷	3 (0.7)	4 (1.0)	7 (1.7)
Wound	創傷	1 (0.2)	0 (0.0)	1 (0.2)
Thermal burn	熱傷	1 (0.2)	1 (0.2)	2 (0.5)
Ligament injury	靭帯損傷	1 (0.2)	1 (0.2)	2 (0.5)
Chest injury	胸部損傷	1 (0.2)	0 (0.0)	1 (0.2)
Ear abrasion	耳擦過傷	1 (0.2)	0 (0.0)	1 (0.2)
Tooth fracture	歯牙破折	0 (0.0)	1 (0.2)	1 (0.2)
Skin abrasion	皮膚擦過傷	0 (0.0)	1 (0.2)	1 (0.2)
Avulsion fracture	剥離骨折	0 (0.0)	1 (0.2)	1 (0.2)
Heat illness	熱中症	0 (0.0)	2 (0.5)	2 (0.5)
Post-traumatic neck syndrome	外傷後頚部症候群	1 (0.2)	0 (0.0)	1 (0.2)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Total (N=403)		
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Investigations	臨床検査	50 (12.4)	32 (7.9)	70 (17.4)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	3 (0.7)	1 (0.2)	3 (0.7)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (0.7)	2 (0.5)	5 (1.2)
Blood bilirubin increased	血中ビリルビン増加	2 (0.5)	0 (0.0)	2 (0.5)
Blood cholesterol increased	血中コレステロール増加	1 (0.2)	0 (0.0)	1 (0.2)
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (0.2)	1 (0.2)
Blood potassium decreased	血中カリウム減少	1 (0.2)	0 (0.0)	1 (0.2)
Blood potassium increased	血中カリウム増加	1 (0.2)	1 (0.2)	2 (0.5)
Blood pressure increased	血圧上昇	7 (1.7)	5 (1.2)	11 (2.7)
Blood prolactin decreased	血中プロラクチン減少	2 (0.5)	0 (0.0)	2 (0.5)
Blood prolactin increased	血中プロラクチン増加	8 (2.0)	3 (0.7)	11 (2.7)
Blood triglycerides increased	血中トリグリセリド増加	6 (1.5)	0 (0.0)	6 (1.5)
Blood uric acid increased	血中尿酸増加	0 (0.0)	1 (0.2)	1 (0.2)
C-reactive protein increased	C－反応性蛋白増加	0 (0.0)	1 (0.2)	1 (0.2)
Electrocardiogram QT prolonged	心電図QT延長	2 (0.5)	1 (0.2)	3 (0.7)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	3 (0.7)	2 (0.5)	5 (1.2)
Glucose urine	尿中ブドウ糖	1 (0.2)	0 (0.0)	1 (0.2)
Glucose urine present	尿中ブドウ糖陽性	6 (1.5)	2 (0.5)	6 (1.5)

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Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Investigations	臨床検査			
Blood urine present	尿中血陽性	3 (0.7)	1 (0.2)	4 (1.0)
Heart rate decreased	心拍数減少	0 (0.0)	1 (0.2)	1 (0.2)
Lipids abnormal	脂質異常	0 (0.0)	1 (0.2)	1 (0.2)
Liver function test abnormal	肝機能検査異常	1 (0.2)	0 (0.0)	1 (0.2)
Neutrophil count decreased	好中球数減少	0 (0.0)	1 (0.2)	1 (0.2)
Red blood cell count decreased	赤血球数減少	1 (0.2)	0 (0.0)	1 (0.2)
Weight decreased	体重減少	2 (0.5)	2 (0.5)	4 (1.0)
Weight increased	体重増加	3 (0.7)	4 (1.0)	7 (1.7)
White blood cell count decreased	白血球数減少	1 (0.2)	0 (0.0)	1 (0.2)
White blood cell count increased	白血球数増加	1 (0.2)	0 (0.0)	1 (0.2)
Protein urine present	尿中蛋白陽性	1 (0.2)	1 (0.2)	2 (0.5)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (0.2)	1 (0.2)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.2)	0 (0.0)	1 (0.2)
Urine output increased	尿量増加	0 (0.0)	1 (0.2)	1 (0.2)
Occult blood positive	便潜血陽性	0 (0.0)	1 (0.2)	1 (0.2)
Liver function test increased	肝機能検査値上昇	1 (0.2)	1 (0.2)	2 (0.5)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Metabolism and nutrition disorders	代謝および栄養障害	13 (3.2)	24 (6.0)	34 (8.4)
Dehydration	脱水	1 (0.2)	1 (0.2)	2 (0.5)
Diabetes mellitus	糖尿病	0 (0.0)	1 (0.2)	1 (0.2)
Gout	痛風	0 (0.0)	3 (0.7)	3 (0.7)
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	1 (0.2)	1 (0.2)
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	1 (0.2)	1 (0.2)
Hyperuricaemia	高尿酸血症	0 (0.0)	1 (0.2)	1 (0.2)
Hypovitaminosis	ビタミン欠乏症	1 (0.2)	0 (0.0)	1 (0.2)
Increased appetite	食欲亢進	1 (0.2)	0 (0.0)	1 (0.2)
Decreased appetite	食欲減退	9 (2.2)	15 (3.7)	23 (5.7)
Hyperlipidaemia	高脂血症	1 (0.2)	2 (0.5)	3 (0.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	40 (9.9)	43 (10.7)	77 (19.1)
Arthralgia	関節痛	8 (2.0)	5 (1.2)	12 (3.0)
Arthritis	関節炎	1 (0.2)	0 (0.0)	1 (0.2)
Back pain	背部痛	12 (3.0)	19 (4.7)	31 (7.7)
Muscle rigidity	筋固縮	0 (0.0)	1 (0.2)	1 (0.2)
Muscle spasms	筋痙縮	2 (0.5)	0 (0.0)	2 (0.5)
Muscle twitching	筋攣縮	1 (0.2)	0 (0.0)	1 (0.2)
Musculoskeletal pain	筋骨格痛	2 (0.5)	3 (0.7)	5 (1.2)
Myalgia	筋肉痛	5 (1.2)	2 (0.5)	7 (1.7)
Neck pain	頚部痛	1 (0.2)	0 (0.0)	1 (0.2)
Osteochondrosis	骨端症	0 (0.0)	1 (0.2)	1 (0.2)
Osteonecrosis	骨壊死	0 (0.0)	1 (0.2)	1 (0.2)
Osteoporosis	骨粗鬆症	0 (0.0)	1 (0.2)	1 (0.2)
Pain in extremity	四肢痛	2 (0.5)	0 (0.0)	2 (0.5)
Plantar fasciitis	足底筋膜炎	0 (0.0)	1 (0.2)	1 (0.2)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	1 (0.2)	1 (0.2)
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	1 (0.2)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001			Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害			
Trigger finger	弾発指	1 (0.2)	0 (0.0)	1 (0.2)
Muscle tightness	筋緊張	0 (0.0)	2 (0.5)	2 (0.5)
Intervertebral disc protrusion	椎間板突出	0 (0.0)	2 (0.5)	2 (0.5)
Musculoskeletal stiffness	筋骨格硬直	4 (1.0)	2 (0.5)	6 (1.5)
Musculoskeletal discomfort	筋骨格不快感	2 (0.5)	2 (0.5)	4 (1.0)
Finger deformity	指変形	0 (0.0)	1 (0.2)	1 (0.2)
Ligamentitis	靭帯炎	1 (0.2)	0 (0.0)	1 (0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	2 (0.5)	3 (0.7)	5 (1.2)
Skin papilloma	皮膚乳頭腫	2 (0.5)	2 (0.5)	4 (1.0)
Prostate cancer	前立腺癌	0 (0.0)	1 (0.2)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	102 (25.3)	111 (27.5)	174 (43.2)
Akathisia	アカシジア	0 (0.0)	1 (0.2)	1 (0.2)
Amnesia	健忘	0 (0.0)	1 (0.2)	1 (0.2)
Autonomic nervous system imbalance	自律神経失調	1 (0.2)	0 (0.0)	1 (0.2)
Disturbance in attention	注意力障害	2 (0.5)	2 (0.5)	4 (1.0)
Dizziness	浮動性めまい	33 (8.2)	40 (9.9)	64 (15.9)
Dizziness postural	体位性めまい	3 (0.7)	3 (0.7)	6 (1.5)
Dysaesthesia	異常感覚	1 (0.2)	0 (0.0)	1 (0.2)
Dysgeusia	味覚異常	8 (2.0)	14 (3.5)	20 (5.0)
Dyskinesia	ジスキネジア	0 (0.0)	1 (0.2)	1 (0.2)
Head discomfort	頭部不快感	2 (0.5)	3 (0.7)	5 (1.2)
Headache	頭痛	22 (5.5)	29 (7.2)	48 (11.9)
Hyperaesthesia	知覚過敏	1 (0.2)	0 (0.0)	1 (0.2)
Hypoaesthesia	感覚鈍麻	5 (1.2)	2 (0.5)	6 (1.5)
Memory impairment	記憶障害	1 (0.2)	0 (0.0)	1 (0.2)
Mental impairment	精神的機能障害	1 (0.2)	0 (0.0)	1 (0.2)
Migraine	片頭痛	0 (0.0)	1 (0.2)	1 (0.2)
Monoplegia	単麻痺	1 (0.2)	0 (0.0)	1 (0.2)
Myoclonus	ミオクローヌス	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Nervous system disorders	神経系障害			
Paraesthesia	錯感覚	0 (0.0)	1 (0.2)	1 (0.2)
Paralysis	麻痺	0 (0.0)	1 (0.2)	1 (0.2)
Sciatica	坐骨神経痛	0 (0.0)	2 (0.5)	2 (0.5)
Sedation	鎮静	1 (0.2)	0 (0.0)	1 (0.2)
Somnolence	傾眠	46 (11.4)	26 (6.5)	64 (15.9)
Hyposmia	嗅覚減退	1 (0.2)	0 (0.0)	1 (0.2)
Cubital tunnel syndrome	肘部管症候群	0 (0.0)	1 (0.2)	1 (0.2)
Poor quality sleep	睡眠の質低下	5 (1.2)	3 (0.7)	7 (1.7)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	40 (9.9)	57 (14.1)	89 (22.1)
Abnormal dreams	異常な夢	0 (0.0)	1 (0.2)	1 (0.2)
Alcoholic hangover	アルコールによる宿酔	7 (1.7)	5 (1.2)	12 (3.0)
Alcoholism	アルコール症	1 (0.2)	0 (0.0)	1 (0.2)
Anxiety	不安	1 (0.2)	3 (0.7)	4 (1.0)
Depressed mood	抑うつ気分	0 (0.0)	3 (0.7)	3 (0.7)
Dysphoria	不快気分	1 (0.2)	0 (0.0)	1 (0.2)
Euphoric mood	多幸気分	0 (0.0)	3 (0.7)	3 (0.7)
Hallucination, auditory	幻聴	0 (0.0)	1 (0.2)	1 (0.2)
Insomnia	不眠症	16 (4.0)	21 (5.2)	34 (8.4)
Irritability	易刺激性	0 (0.0)	4 (1.0)	4 (1.0)
Libido decreased	リビドー減退	0 (0.0)	2 (0.5)	2 (0.5)
Middle insomnia	中期不眠症	7 (1.7)	9 (2.2)	15 (3.7)
Nightmare	悪夢	1 (0.2)	2 (0.5)	3 (0.7)
Restlessness	落ち着きのなさ	0 (0.0)	1 (0.2)	1 (0.2)
Sleep disorder	睡眠障害	2 (0.5)	6 (1.5)	7 (1.7)
Tension	緊張	0 (0.0)	1 (0.2)	1 (0.2)
Abulia	無為	1 (0.2)	1 (0.2)	2 (0.5)
Alcohol withdrawal syndrome	アルコール離脱症候群	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Psychiatric disorders	精神障害			
Depressive symptom	抑うつ症状	1 (0.2)	0 (0.0)	1 (0.2)
Affect lability	感情不安定	1 (0.2)	0 (0.0)	1 (0.2)
Mental disorder	精神障害	0 (0.0)	1 (0.2)	1 (0.2)
Terminal insomnia	早朝覚醒型不眠症	2 (0.5)	6 (1.5)	7 (1.7)
Renal and urinary disorders	腎および尿路障害	3 (0.7)	3 (0.7)	6 (1.5)
Calculus urinary	尿路結石	1 (0.2)	0 (0.0)	1 (0.2)
Dysuria	排尿困難	1 (0.2)	0 (0.0)	1 (0.2)
Nocturia	夜間頻尿	1 (0.2)	0 (0.0)	1 (0.2)
Pollakiuria	頻尿	0 (0.0)	2 (0.5)	2 (0.5)
Ureterolithiasis	尿管結石症	0 (0.0)	1 (0.2)	1 (0.2)
Reproductive system and breast disorders	生殖系および乳房障害	8 (2.0)	4 (1.0)	11 (2.7)
Dysmenorrhoea	月経困難症	2 (0.5)	1 (0.2)	2 (0.5)
Erection increased	勃起増強	4 (1.0)	1 (0.2)	5 (1.2)
Metrorrhagia	不正子宮出血	1 (0.2)	0 (0.0)	1 (0.2)
Prostatitis	前立腺炎	0 (0.0)	1 (0.2)	1 (0.2)
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	1 (0.2)	1 (0.2)
Erectile dysfunction	勃起不全	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	21 (5.2)	12 (3.0)	30 (7.4)
Cough	咳嗽	2 (0.5)	0 (0.0)	2 (0.5)
Dry throat	咽喉乾燥	1 (0.2)	0 (0.0)	1 (0.2)
Dyspnoea	呼吸困難	1 (0.2)	0 (0.0)	1 (0.2)
Epistaxis	鼻出血	3 (0.7)	0 (0.0)	3 (0.7)
Hyperventilation	過換気	0 (0.0)	1 (0.2)	1 (0.2)
Laryngeal pain	喉頭痛	1 (0.2)	0 (0.0)	1 (0.2)
Nasal congestion	鼻閉	1 (0.2)	1 (0.2)	1 (0.2)
Nasal inflammation	鼻の炎症	0 (0.0)	1 (0.2)	1 (0.2)
Pneumothorax	気胸	1 (0.2)	0 (0.0)	1 (0.2)
Rhinitis allergic	アレルギー性鼻炎	2 (0.5)	1 (0.2)	3 (0.7)
Rhinorrhoea	鼻漏	1 (0.2)	2 (0.5)	3 (0.7)
Wheezing	喘鳴	1 (0.2)	0 (0.0)	1 (0.2)
Upper respiratory tract inflammation	上気道の炎症	2 (0.5)	1 (0.2)	3 (0.7)
Laryngeal discomfort	喉頭不快感	2 (0.5)	0 (0.0)	2 (0.5)
Oropharyngeal discomfort	口腔咽頭不快感	1 (0.2)	0 (0.0)	1 (0.2)
Oropharyngeal pain	口腔咽頭痛	4 (1.0)	5 (1.2)	8 (2.0)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	21 (5.2)	20 (5.0)	38 (9.4)
Acne	ざ瘡	1 (0.2)	0 (0.0)	1 (0.2)
Angioedema	血管浮腫	0 (0.0)	1 (0.2)	1 (0.2)
Cold sweat	冷汗	0 (0.0)	1 (0.2)	1 (0.2)
Dermatitis	皮膚炎	2 (0.5)	2 (0.5)	4 (1.0)
Dermatitis atopic	アトピー性皮膚炎	1 (0.2)	1 (0.2)	1 (0.2)
Drug eruption	薬疹	1 (0.2)	0 (0.0)	1 (0.2)
Dry skin	皮膚乾燥	2 (0.5)	0 (0.0)	2 (0.5)
Eczema	湿疹	3 (0.7)	1 (0.2)	4 (1.0)
Erythema	紅斑	1 (0.2)	0 (0.0)	1 (0.2)
Hyperhidrosis	多汗症	0 (0.0)	1 (0.2)	1 (0.2)
Hyperkeratosis	過角化	1 (0.2)	0 (0.0)	1 (0.2)
Night sweats	寝汗	1 (0.2)	3 (0.7)	4 (1.0)
Pruritus	そう痒症	0 (0.0)	1 (0.2)	1 (0.2)
Psoriasis	乾癬	0 (0.0)	1 (0.2)	1 (0.2)
Rash	発疹	2 (0.5)	3 (0.7)	5 (1.2)
Rash generalised	全身性皮疹	0 (0.0)	1 (0.2)	1 (0.2)
Rash papular	丘疹性皮疹	1 (0.2)	0 (0.0)	1 (0.2)
Seborrhoeic dermatitis	脂漏性皮膚炎	1 (0.2)	1 (0.2)	2 (0.5)

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表 2.7.4.7.1-12

Table 14.1.1.3-27

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001			Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害			
Urticaria	蕁麻疹	4 (1.0)	2 (0.5)	6 (1.5)
Pruritus generalised	全身性そう痒症	1 (0.2)	1 (0.2)	1 (0.2)
Vascular disorders	血管障害	14 (3.5)	11 (2.7)	20 (5.0)
Hyperaemia	充血	0 (0.0)	1 (0.2)	1 (0.2)
Hypertension	高血圧	7 (1.7)	5 (1.2)	10 (2.5)
Hypotension	低血圧	1 (0.2)	0 (0.0)	1 (0.2)
Orthostatic hypotension	起立性低血圧	1 (0.2)	0 (0.0)	1 (0.2)
Hot flush	ほてり	5 (1.2)	5 (1.2)	7 (1.7)
Product issues	製品の問題	1 (0.2)	0 (0.0)	1 (0.2)
Device failure	医療機器不具合	1 (0.2)	0 (0.0)	1 (0.2)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with drug-related adverse events		62 (36.0)	109 (63.4)	124 (72.1)	92 (67.2)	59 (43.1)	105 (76.6)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Cardiac disorders	心臓障害	2 (1.2)	7 (4.1)	8 (4.7)	3 (2.2)	1 (0.7)	4 (2.9)
Bundle branch block right	右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palpitations	動悸	2 (1.2)	5 (2.9)	6 (3.5)	3 (2.2)	1 (0.7)	4 (2.9)
Tachycardia	頻脈	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	3 (1.7)	3 (1.7)	4 (2.9)	2 (1.5)	6 (4.4)
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Hyperacusis	聴覚過敏	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Vertigo	回転性めまい	0 (0.0)	2 (1.2)	2 (1.2)	4 (2.9)	0 (0.0)	4 (2.9)
Endocrine disorders	内分泌障害	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Eye disorders	眼障害	1 (0.6)	1 (0.6)	2 (1.2)	1 (0.7)	1 (0.7)	2 (1.5)
Abnormal sensation in eye	眼の異常感	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dry eye	眼乾燥	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	18 (10.5)	59 (34.3)	71 (41.3)	50 (36.5)	35 (25.5)	67 (48.9)
Abdominal discomfort	腹部不快感	3 (1.7)	9 (5.2)	12 (7.0)	5 (3.6)	8 (5.8)	12 (8.8)
Abdominal distension	腹部膨満	2 (1.2)	2 (1.2)	4 (2.3)	7 (5.1)	2 (1.5)	9 (6.6)
Abdominal pain	腹痛	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Abdominal pain lower	下腹部痛	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	1 (0.6)	0 (0.0)	1 (0.6)	3 (2.2)	2 (1.5)	4 (2.9)
Constipation	便秘	2 (1.2)	5 (2.9)	7 (4.1)	6 (4.4)	1 (0.7)	7 (5.1)
Diarrhoea	下痢	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	2 (1.5)	4 (2.9)
Dry mouth	口内乾燥	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspepsia	消化不良	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Faeces hard	硬便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	7 (4.1)	41 (23.8)	45 (26.2)	36 (26.3)	19 (13.9)	47 (34.3)
Oral discomfort	口腔内不快感	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Vomiting	嘔吐	0 (0.0)	12 (7.0)	12 (7.0)	7 (5.1)	4 (2.9)	10 (7.3)
Oral dysaesthesia	口腔知覚不全	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Large intestine polyp	大腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害						
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Faeces soft	軟便	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	13 (7.6)	27 (15.7)	34 (19.8)	26 (19.0)	8 (5.8)	31 (22.6)
Asthenia	無力症	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	1 (0.7)	2 (1.5)
Chest discomfort	胸部不快感	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Chills	悪寒	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Discomfort	不快感	2 (1.2)	1 (0.6)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Fatigue	疲労	1 (0.6)	2 (1.2)	3 (1.7)	4 (2.9)	0 (0.0)	4 (2.9)
Feeling abnormal	異常感	1 (0.6)	4 (2.3)	5 (2.9)	4 (2.9)	3 (2.2)	7 (5.1)
Feeling hot	熱感	1 (0.6)	2 (1.2)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	4 (2.3)	12 (7.0)	15 (8.7)	13 (9.5)	3 (2.2)	14 (10.2)
Pyrexia	発熱	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Thirst	口渇	2 (1.2)	6 (3.5)	6 (3.5)	5 (3.6)	1 (0.7)	6 (4.4)
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Early satiety	早期満腹	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hepatobiliary disorders	肝胆道系障害	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations	感染症および寄生虫症	3 (1.7)	1 (0.6)	4 (2.3)	2 (1.5)	0 (0.0)	2 (1.5)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Gastroenteritis	胃腸炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Gingivitis	歯肉炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Oesophageal candidiasis	食道カンジダ症	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	8 (4.7)	8 (4.7)	14 (8.1)	16 (11.7)	7 (5.1)	21 (15.3)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	1 (0.7)	3 (2.2)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.6)	1 (0.6)	2 (1.5)	1 (0.7)	3 (2.2)
Blood bilirubin increased	血中ビリルビン増加	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Blood pressure increased	血圧上昇	1 (0.6)	3 (1.7)	3 (1.7)	1 (0.7)	2 (1.5)	3 (2.2)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	5 (3.6)	2 (1.5)	7 (5.1)
Blood triglycerides increased	血中トリグリセリド増加	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)
Electrocardiogram QT prolonged	心電図QT延長	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	1 (0.6)	0 (0.0)	1 (0.6)	2 (1.5)	1 (0.7)	3 (2.2)
Glucose urine present	尿中ブドウ糖陽性	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Blood urine present	尿中血陽性	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test abnormal	肝機能検査異常	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Weight decreased	体重減少	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Weight increased	体重増加	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
White blood cell count decreased	白血球数減少	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell count increased	白血球数増加	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Metabolism and nutrition disorders	代謝および栄養障害	2 (1.2)	12 (7.0)	13 (7.6)	6 (4.4)	3 (2.2)	9 (6.6)
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Decreased appetite	食欲減退	2 (1.2)	11 (6.4)	12 (7.0)	5 (3.6)	3 (2.2)	8 (5.8)
Hyperlipidaemia	高脂血症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	0 (0.0)	5 (2.9)	5 (2.9)	5 (3.6)	3 (2.2)	7 (5.1)
Arthralgia	関節痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
Back pain	背部痛	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	1 (0.7)	2 (1.5)
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Muscle tightness	筋緊張	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	28 (16.3)	56 (32.6)	71 (41.3)	44 (32.1)	28 (20.4)	59 (43.1)
Akathisia	アカシジア	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	0 (0.0)	2 (1.2)	2 (1.2)	2 (1.5)	0 (0.0)	2 (1.5)
Dizziness	浮動性めまい	7 (4.1)	25 (14.5)	29 (16.9)	17 (12.4)	7 (5.1)	21 (15.3)
Dizziness postural	体位性めまい	1 (0.6)	1 (0.6)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Dysgeusia	味覚異常	4 (2.3)	7 (4.1)	10 (5.8)	2 (1.5)	7 (5.1)	8 (5.8)
Dyskinesia	ジスキネジア	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Head discomfort	頭部不快感	0 (0.0)	3 (1.7)	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.7)
Headache	頭痛	6 (3.5)	11 (6.4)	16 (9.3)	4 (2.9)	8 (5.8)	12 (8.8)
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia	感覚鈍麻	1 (0.6)	2 (1.2)	2 (1.2)	3 (2.2)	0 (0.0)	3 (2.2)
Memory impairment	記憶障害	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Myoclonus	ミオクローヌス	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia	錯感覚	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Paralysis	麻痺	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害						
Somnolence	傾眠	11 (6.4)	10 (5.8)	21 (12.2)	25 (18.2)	9 (6.6)	28 (20.4)
Hyposmia	嗅覚減退	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下	3 (1.7)	3 (1.7)	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	4 (2.3)	30 (17.4)	34 (19.8)	17 (12.4)	6 (4.4)	21 (15.3)
Abnormal dreams	異常な夢	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	1 (0.6)	3 (1.7)	4 (2.3)	3 (2.2)	0 (0.0)	3 (2.2)
Alcoholism	アルコール症	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Depressed mood	抑うつ気分	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Euphoric mood	多幸気分	0 (0.0)	3 (1.7)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Hallucination, auditory	幻聴	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	0 (0.0)	8 (4.7)	8 (4.7)	7 (5.1)	1 (0.7)	8 (5.8)
Irritability	易刺激性	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)
Libido decreased	リビドー減退	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Middle insomnia	中期不眠症	1 (0.6)	5 (2.9)	6 (3.5)	4 (2.9)	2 (1.5)	6 (4.4)
Nightmare	悪夢	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Restlessness	落ち着きのなさ	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Sleep disorder	睡眠障害	0 (0.0)	5 (2.9)	5 (2.9)	1 (0.7)	1 (0.7)	1 (0.7)
Tension	緊張	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Terminal insomnia	早朝覚醒型不眠症	1 (0.6)	3 (1.7)	4 (2.3)	1 (0.7)	1 (0.7)	1 (0.7)
Renal and urinary disorders	腎および尿路障害	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	1 (0.7)
Dysuria	排尿困難	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)
Reproductive system and breast disorders	生殖系および乳房障害	0 (0.0)	2 (1.2)	2 (1.2)	4 (2.9)	0 (0.0)	4 (2.9)
Erection increased	勃起増強	0 (0.0)	1 (0.6)	1 (0.6)	3 (2.2)	0 (0.0)	3 (2.2)
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	2 (1.2)	1 (0.6)	3 (1.7)	3 (2.2)	1 (0.7)	3 (2.2)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspnoea	呼吸困難	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperventilation	過換気	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	1 (0.7)
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Oropharyngeal pain	口腔咽頭痛	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)			Nalmefene 20 mg (N=137)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	1 (0.6)	8 (4.7)	9 (5.2)	5 (3.6)	2 (1.5)	7 (5.1)
Cold sweat	冷汗	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	2 (1.5)
Hyperhidrosis	多汗症	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	0 (0.0)	2 (1.2)	2 (1.2)	1 (0.7)	1 (0.7)	2 (1.5)
Rash	発疹	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Rash generalised	全身性皮疹	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urticaria	蕁麻疹	0 (0.0)	1 (0.6)	1 (0.6)	2 (1.5)	0 (0.0)	2 (1.5)
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	血管障害	4 (2.3)	2 (1.2)	5 (2.9)	2 (1.5)	1 (0.7)	2 (1.5)
Hypertension	高血圧	2 (1.2)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)
Hot flush	ほてり	2 (1.2)	1 (0.6)	3 (1.7)	1 (0.7)	1 (0.7)	1 (0.7)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-28＞

表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
			(N=94)			(N=231)		
System organ class		Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with drug-related adverse events			59 (62.8)	43 (45.7)	70 (74.5)	151 (65.4)	102 (44.2)	175 (75.8)
Blood and lymphatic system disorders	血液およびリンパ系障害		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Pancytopenia	汎血球減少症		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Cardiac disorders	心臓障害		3 (3.2)	4 (4.3)	7 (7.4)	6 (2.6)	5 (2.2)	11 (4.8)
Bundle branch block right	右脚ブロック		0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Palpitations	動悸		1 (1.1)	2 (2.1)	3 (3.2)	4 (1.7)	3 (1.3)	7 (3.0)
Tachycardia	頻脈		2 (2.1)	1 (1.1)	3 (3.2)	2 (0.9)	1 (0.4)	3 (1.3)
Ventricular extrasystoles	心室性期外収縮		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	耳および迷路障害		0 (0.0)	1 (1.1)	1 (1.1)	4 (1.7)	3 (1.3)	7 (3.0)
Deafness transitory	一過性難聴		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Hyperacusis	聴覚過敏		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinnitus	耳鳴		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Vertigo	回転性めまい		0 (0.0)	1 (1.1)	1 (1.1)	4 (1.7)	1 (0.4)	5 (2.2)
Endocrine disorders	内分泌障害		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Hyperprolactinaemia	高プロラクチン血症		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Eye disorders	眼障害		1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	1 (0.4)	3 (1.3)
Abnormal sensation in eye	眼の異常感		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry eye	眼乾燥		1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Eye irritation	眼刺激		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Visual impairment	視力障害		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	36 (38.3)	26 (27.7)	47 (50.0)	86 (37.2)	61 (26.4)	114 (49.4)
Abdominal discomfort	腹部不快感	3 (3.2)	4 (4.3)	5 (5.3)	8 (3.5)	12 (5.2)	17 (7.4)
Abdominal distension	腹部膨満	1 (1.1)	1 (1.1)	2 (2.1)	8 (3.5)	3 (1.3)	11 (4.8)
Abdominal pain	腹痛	2 (2.1)	0 (0.0)	2 (2.1)	2 (0.9)	1 (0.4)	3 (1.3)
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	0 (0.0)	1 (1.1)	1 (1.1)	3 (1.3)	3 (1.3)	5 (2.2)
Constipation	便秘	2 (2.1)	3 (3.2)	4 (4.3)	8 (3.5)	4 (1.7)	11 (4.8)
Diarrhoea	下痢	1 (1.1)	0 (0.0)	1 (1.1)	4 (1.7)	2 (0.9)	5 (2.2)
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspepsia	消化不良	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Faeces hard	硬便	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Gastritis	胃炎	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Nausea	悪心	27 (28.7)	15 (16.0)	32 (34.0)	63 (27.3)	34 (14.7)	79 (34.2)
Oral discomfort	口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Vomiting	嘔吐	2 (2.1)	2 (2.1)	4 (4.3)	9 (3.9)	6 (2.6)	14 (6.1)
Oral dysaesthesia	口腔知覚不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Large intestine polyp	大腸ポリープ	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Paraesthesia oral	口の錯感覚	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害						
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Faeces soft	軟便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	9 (9.6)	6 (6.4)	13 (13.8)	35 (15.2)	14 (6.1)	44 (19.0)
Asthenia	無力症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Discomfort	不快感	1 (1.1)	1 (1.1)	1 (1.1)	2 (0.9)	1 (0.4)	2 (0.9)
Fatigue	疲労	3 (3.2)	0 (0.0)	3 (3.2)	7 (3.0)	0 (0.0)	7 (3.0)
Feeling abnormal	異常感	2 (2.1)	1 (1.1)	3 (3.2)	6 (2.6)	4 (1.7)	10 (4.3)
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Malaise	倦怠感	3 (3.2)	3 (3.2)	5 (5.3)	16 (6.9)	6 (2.6)	19 (8.2)
Pyrexia	発熱	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thirst	口渇	2 (2.1)	0 (0.0)	2 (2.1)	7 (3.0)	1 (0.4)	8 (3.5)
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	免疫系障害	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Seasonal allergy	季節性アレルギー	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Infections and infestations	感染症および寄生虫症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	7 (7.4)	3 (3.2)	10 (10.6)	23 (10.0)	10 (4.3)	31 (13.4)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	1 (0.4)	3 (1.3)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (1.1)	0 (0.0)	1 (1.1)	3 (1.3)	1 (0.4)	4 (1.7)
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Blood pressure increased	血圧上昇	2 (2.1)	0 (0.0)	2 (2.1)	3 (1.3)	2 (0.9)	5 (2.2)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Blood prolactin increased	血中プロラクチン増加	2 (2.1)	1 (1.1)	3 (3.2)	7 (3.0)	3 (1.3)	10 (4.3)
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Electrocardiogram QT prolonged	心電図QT延長	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	1 (0.4)	3 (1.3)
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood urine present	尿中血陽性	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Weight decreased	体重減少	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Weight increased	体重増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Metabolism and nutrition disorders	代謝および栄養障害	1 (1.1)	0 (0.0)	1 (1.1)	7 (3.0)	3 (1.3)	10 (4.3)
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Decreased appetite	食欲減退	1 (1.1)	0 (0.0)	1 (1.1)	6 (2.6)	3 (1.3)	9 (3.9)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	1 (1.1)	0 (0.0)	1 (1.1)	6 (2.6)	3 (1.3)	8 (3.5)
Arthralgia	関節痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Back pain	背部痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Muscle tightness	筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Musculoskeletal discomfort	筋骨格不快感	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	16 (17.0)	13 (13.8)	22 (23.4)	60 (26.0)	41 (17.7)	81 (35.1)
Akathisia	アカシジア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Dizziness	浮動性めまい	6 (6.4)	4 (4.3)	9 (9.6)	23 (10.0)	11 (4.8)	30 (13.0)
Dizziness postural	体位性めまい	0 (0.0)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Dysgeusia	味覚異常	2 (2.1)	0 (0.0)	2 (2.1)	4 (1.7)	7 (3.0)	10 (4.3)
Dyskinesia	ジスキネジア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Headache	頭痛	3 (3.2)	5 (5.3)	8 (8.5)	7 (3.0)	13 (5.6)	20 (8.7)
Hyperaesthesia	知覚過敏	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	3 (1.3)
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia	錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paralysis	麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害						
Somnolence	傾眠	7 (7.4)	4 (4.3)	9 (9.6)	32 (13.9)	13 (5.6)	37 (16.0)
Hyposmia	嗅覚減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	8 (8.5)	6 (6.4)	11 (11.7)	25 (10.8)	12 (5.2)	32 (13.9)
Abnormal dreams	異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	3 (1.3)
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Euphoric mood	多幸気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hallucination, auditory	幻聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	6 (6.4)	3 (3.2)	7 (7.4)	13 (5.6)	4 (1.7)	15 (6.5)
Irritability	易刺激性	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (0.9)	2 (0.9)
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Middle insomnia	中期不眠症	1 (1.1)	2 (2.1)	2 (2.1)	5 (2.2)	4 (1.7)	8 (3.5)
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sleep disorder	睡眠障害	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	1 (0.4)	2 (0.9)
Tension	緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	0 (0.0)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Renal and urinary disorders	腎および尿路障害	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.4)	2 (0.9)
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Reproductive system and breast disorders	生殖系および乳房障害	1 (1.1)	0 (0.0)	1 (1.1)	5 (2.2)	0 (0.0)	5 (2.2)
Erection increased	勃起増強	1 (1.1)	0 (0.0)	1 (1.1)	4 (1.7)	0 (0.0)	4 (1.7)
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	4 (4.3)	1 (1.1)	5 (5.3)	7 (3.0)	2 (0.9)	8 (3.5)
Dry throat	咽喉乾燥	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Hyperventilation	過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)
Rhinorrhoea	鼻漏	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
Wheezing	喘鳴	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Laryngeal discomfort	喉頭不快感	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10mg			Nalmefene Total		
		(N=94)			(N=231)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	2 (2.1)	1 (1.1)	2 (2.1)	7 (3.0)	3 (1.3)	9 (3.9)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.9)
Rash	発疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash generalised	全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Urticaria	蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Pruritus generalised	全身性そう痒症	1 (1.1)	1 (1.1)	1 (1.1)	1 (0.4)	1 (0.4)	1 (0.4)
Vascular disorders	血管障害	3 (3.2)	5 (5.3)	6 (6.4)	5 (2.2)	6 (2.6)	8 (3.5)
Hypertension	高血圧	0 (0.0)	2 (2.1)	2 (2.1)	0 (0.0)	2 (0.9)	2 (0.9)
Hypotension	低血圧	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	1 (0.4)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Hot flush	ほてり	2 (2.1)	3 (3.2)	3 (3.2)	3 (1.3)	4 (1.7)	4 (1.7)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-28＞

表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Total number of subjects with drug-related adverse events		213 (52.9)	211 (52.4)	299 (74.2)
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.2)	0 (0.0)	1 (0.2)
Pancytopenia	汎血球減少症	1 (0.2)	0 (0.0)	1 (0.2)
Cardiac disorders	心臓障害	8 (2.0)	12 (3.0)	19 (4.7)
Bundle branch block right	右脚ブロック	0 (0.0)	1 (0.2)	1 (0.2)
Palpitations	動悸	6 (1.5)	8 (2.0)	13 (3.2)
Tachycardia	頻脈	3 (0.7)	2 (0.5)	5 (1.2)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	1 (0.2)	1 (0.2)
Ear and labyrinth disorders	耳および迷路障害	4 (1.0)	6 (1.5)	10 (2.5)
Deafness transitory	一過性難聴	0 (0.0)	1 (0.2)	1 (0.2)
Hyperacusis	聴覚過敏	0 (0.0)	1 (0.2)	1 (0.2)
Tinnitus	耳鳴	0 (0.0)	1 (0.2)	1 (0.2)
Vertigo	回転性めまい	4 (1.0)	3 (0.7)	7 (1.7)
Endocrine disorders	内分泌障害	1 (0.2)	2 (0.5)	3 (0.7)
Hyperprolactinaemia	高プロラクチン血症	1 (0.2)	2 (0.5)	3 (0.7)
Eye disorders	眼障害	3 (0.7)	2 (0.5)	5 (1.2)
Abnormal sensation in eye	眼の異常感	1 (0.2)	0 (0.0)	1 (0.2)
Dry eye	眼乾燥	1 (0.2)	1 (0.2)	2 (0.5)
Eye irritation	眼刺激	1 (0.2)	0 (0.0)	1 (0.2)
Visual impairment	視力障害	0 (0.0)	1 (0.2)	1 (0.2)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	104 (25.8)	120 (29.8)	185 (45.9)
Abdominal discomfort	腹部不快感	11 (2.7)	21 (5.2)	29 (7.2)
Abdominal distension	腹部膨満	10 (2.5)	5 (1.2)	15 (3.7)
Abdominal pain	腹痛	2 (0.5)	2 (0.5)	4 (1.0)
Abdominal pain lower	下腹部痛	1 (0.2)	0 (0.0)	1 (0.2)
Abdominal pain upper	上腹部痛	4 (1.0)	3 (0.7)	6 (1.5)
Constipation	便秘	10 (2.5)	9 (2.2)	18 (4.5)
Diarrhoea	下痢	4 (1.0)	2 (0.5)	5 (1.2)
Dry mouth	口内乾燥	1 (0.2)	1 (0.2)	2 (0.5)
Dyspepsia	消化不良	0 (0.0)	3 (0.7)	3 (0.7)
Faeces hard	硬便	0 (0.0)	1 (0.2)	1 (0.2)
Gastritis	胃炎	1 (0.2)	1 (0.2)	2 (0.5)
Nausea	悪心	70 (17.4)	75 (18.6)	124 (30.8)
Oral discomfort	口腔内不快感	1 (0.2)	0 (0.0)	1 (0.2)
Salivary hypersecretion	流涎過多	1 (0.2)	1 (0.2)	2 (0.5)
Vomiting	嘔吐	9 (2.2)	18 (4.5)	26 (6.5)
Oral dysaesthesia	口腔知覚不全	1 (0.2)	1 (0.2)	1 (0.2)
Large intestine polyp	大腸ポリープ	0 (0.0)	1 (0.2)	1 (0.2)
Paraesthesia oral	口の錯感覚	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害			
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	1 (0.2)	1 (0.2)
Faeces soft	軟便	0 (0.0)	2 (0.5)	2 (0.5)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	48 (11.9)	41 (10.2)	78 (19.4)
Asthenia	無力症	1 (0.2)	2 (0.5)	3 (0.7)
Chest discomfort	胸部不快感	2 (0.5)	0 (0.0)	2 (0.5)
Chills	悪寒	1 (0.2)	2 (0.5)	3 (0.7)
Discomfort	不快感	4 (1.0)	2 (0.5)	4 (1.0)
Fatigue	疲労	8 (2.0)	2 (0.5)	10 (2.5)
Feeling abnormal	異常感	7 (1.7)	8 (2.0)	15 (3.7)
Feeling hot	熱感	1 (0.2)	2 (0.5)	3 (0.7)
Hangover	宿酔	1 (0.2)	1 (0.2)	2 (0.5)
Malaise	倦怠感	20 (5.0)	18 (4.5)	34 (8.4)
Pyrexia	発熱	0 (0.0)	1 (0.2)	1 (0.2)
Thirst	口渇	9 (2.2)	7 (1.7)	14 (3.5)
Peripheral swelling	末梢腫脹	1 (0.2)	0 (0.0)	1 (0.2)
Early satiety	早期満腹	1 (0.2)	1 (0.2)	2 (0.5)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Hepatobiliary disorders	肝胆道系障害	1 (0.2)	1 (0.2)	1 (0.2)
Hepatic function abnormal	肝機能異常	1 (0.2)	1 (0.2)	1 (0.2)
Immune system disorders	免疫系障害	2 (0.5)	0 (0.0)	2 (0.5)
Hypersensitivity	過敏症	1 (0.2)	0 (0.0)	1 (0.2)
Seasonal allergy	季節性アレルギー	1 (0.2)	0 (0.0)	1 (0.2)
Infections and infestations	感染症および寄生虫症	5 (1.2)	1 (0.2)	6 (1.5)
Angular cheilitis	口角口唇炎	1 (0.2)	0 (0.0)	1 (0.2)
Furuncle	せつ	1 (0.2)	0 (0.0)	1 (0.2)
Gastroenteritis	胃腸炎	0 (0.0)	1 (0.2)	1 (0.2)
Gingivitis	歯肉炎	1 (0.2)	0 (0.0)	1 (0.2)
Herpes virus infection	ヘルペスウイルス感染	1 (0.2)	0 (0.0)	1 (0.2)
Oesophageal candidiasis	食道カンジダ症	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001		Total (N=403)	
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Investigations	臨床検査	31 (7.7)	18 (4.5)	45 (11.2)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	3 (0.7)	1 (0.2)	3 (0.7)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	3 (0.7)	2 (0.5)	5 (1.2)
Blood bilirubin increased	血中ビリルビン増加	2 (0.5)	0 (0.0)	2 (0.5)
Blood potassium decreased	血中カリウム減少	1 (0.2)	0 (0.0)	1 (0.2)
Blood pressure increased	血圧上昇	4 (1.0)	5 (1.2)	8 (2.0)
Blood prolactin decreased	血中プロラクチン減少	2 (0.5)	0 (0.0)	2 (0.5)
Blood prolactin increased	血中プロラクチン増加	7 (1.7)	3 (0.7)	10 (2.5)
Blood triglycerides increased	血中トリグリセリド増加	2 (0.5)	0 (0.0)	2 (0.5)
Electrocardiogram QT prolonged	心電図QT延長	2 (0.5)	0 (0.0)	2 (0.5)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	3 (0.7)	1 (0.2)	4 (1.0)
Glucose urine present	尿中ブドウ糖陽性	1 (0.2)	0 (0.0)	1 (0.2)
Blood urine present	尿中血陽性	2 (0.5)	1 (0.2)	3 (0.7)
Liver function test abnormal	肝機能検査異常	1 (0.2)	0 (0.0)	1 (0.2)
Neutrophil count decreased	好中球数減少	0 (0.0)	1 (0.2)	1 (0.2)
Red blood cell count decreased	赤血球数減少	1 (0.2)	0 (0.0)	1 (0.2)
Weight decreased	体重減少	0 (0.0)	2 (0.5)	2 (0.5)
Weight increased	体重増加	1 (0.2)	1 (0.2)	2 (0.5)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Investigations	臨床検査			
White blood cell count decreased	白血球数減少	1 (0.2)	0 (0.0)	1 (0.2)
White blood cell count increased	白血球数増加	1 (0.2)	0 (0.0)	1 (0.2)
Protein urine present	尿中蛋白陽性	1 (0.2)	1 (0.2)	2 (0.5)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (0.2)	1 (0.2)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.2)	0 (0.0)	1 (0.2)
Liver function test increased	肝機能検査値上昇	1 (0.2)	0 (0.0)	1 (0.2)
Metabolism and nutrition disorders	代謝および栄養障害	9 (2.2)	15 (3.7)	23 (5.7)
Increased appetite	食欲亢進	1 (0.2)	0 (0.0)	1 (0.2)
Decreased appetite	食欲減退	8 (2.0)	14 (3.5)	21 (5.2)
Hyperlipidaemia	高脂血症	0 (0.0)	1 (0.2)	1 (0.2)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	6 (1.5)	8 (2.0)	13 (3.2)
Arthralgia	関節痛	1 (0.2)	1 (0.2)	1 (0.2)
Back pain	背部痛	1 (0.2)	2 (0.5)	3 (0.7)
Muscle rigidity	筋固縮	0 (0.0)	1 (0.2)	1 (0.2)
Muscle tightness	筋緊張	0 (0.0)	2 (0.5)	2 (0.5)
Musculoskeletal stiffness	筋骨格硬直	2 (0.5)	0 (0.0)	2 (0.5)
Musculoskeletal discomfort	筋骨格不快感	2 (0.5)	2 (0.5)	4 (1.0)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	88 (21.8)	97 (24.1)	152 (37.7)
Akathisia	アカシジア	0 (0.0)	1 (0.2)	1 (0.2)
Disturbance in attention	注意力障害	2 (0.5)	2 (0.5)	4 (1.0)
Dizziness	浮動性めまい	30 (7.4)	36 (8.9)	59 (14.6)
Dizziness postural	体位性めまい	2 (0.5)	2 (0.5)	4 (1.0)
Dysaesthesia	異常感覚	1 (0.2)	0 (0.0)	1 (0.2)
Dysgeusia	味覚異常	8 (2.0)	14 (3.5)	20 (5.0)
Dyskinesia	ジスキネジア	0 (0.0)	1 (0.2)	1 (0.2)
Head discomfort	頭部不快感	1 (0.2)	3 (0.7)	4 (1.0)
Headache	頭痛	13 (3.2)	24 (6.0)	36 (8.9)
Hyperaesthesia	知覚過敏	1 (0.2)	0 (0.0)	1 (0.2)
Hypoaesthesia	感覚鈍麻	4 (1.0)	2 (0.5)	5 (1.2)
Memory impairment	記憶障害	1 (0.2)	0 (0.0)	1 (0.2)
Mental impairment	精神的機能障害	1 (0.2)	0 (0.0)	1 (0.2)
Migraine	片頭痛	0 (0.0)	1 (0.2)	1 (0.2)
Myoclonus	ミオクローヌス	1 (0.2)	0 (0.0)	1 (0.2)
Paraesthesia	錯感覚	0 (0.0)	1 (0.2)	1 (0.2)
Paralysis	麻痺	0 (0.0)	1 (0.2)	1 (0.2)
Sedation	鎮静	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Nervous system disorders	神経系障害			
Somnolence	傾眠	43 (10.7)	23 (5.7)	58 (14.4)
Hyposmia	嗅覚減退	1 (0.2)	0 (0.0)	1 (0.2)
Poor quality sleep	睡眠の質低下	4 (1.0)	3 (0.7)	6 (1.5)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class	Study	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	29 (7.2)	42 (10.4)	66 (16.4)
Abnormal dreams	異常な夢	0 (0.0)	1 (0.2)	1 (0.2)
Alcoholic hangover	アルコールによる宿酔	4 (1.0)	3 (0.7)	7 (1.7)
Alcoholism	アルコール症	1 (0.2)	0 (0.0)	1 (0.2)
Anxiety	不安	0 (0.0)	2 (0.5)	2 (0.5)
Depressed mood	抑うつ気分	0 (0.0)	2 (0.5)	2 (0.5)
Dysphoria	不快気分	1 (0.2)	0 (0.0)	1 (0.2)
Euphoric mood	多幸気分	0 (0.0)	3 (0.7)	3 (0.7)
Hallucination, auditory	幻聴	0 (0.0)	1 (0.2)	1 (0.2)
Insomnia	不眠症	13 (3.2)	12 (3.0)	23 (5.7)
Irritability	易刺激性	0 (0.0)	4 (1.0)	4 (1.0)
Libido decreased	リビドー減退	0 (0.0)	1 (0.2)	1 (0.2)
Middle insomnia	中期不眠症	6 (1.5)	9 (2.2)	14 (3.5)
Nightmare	悪夢	0 (0.0)	1 (0.2)	1 (0.2)
Restlessness	落ち着きのなさ	0 (0.0)	1 (0.2)	1 (0.2)
Sleep disorder	睡眠障害	2 (0.5)	6 (1.5)	7 (1.7)
Tension	緊張	0 (0.0)	1 (0.2)	1 (0.2)
Abulia	無為	1 (0.2)	1 (0.2)	2 (0.5)
Depressive symptom	抑うつ症状	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Psychiatric disorders	精神障害			
Terminal insomnia	早朝覚醒型不眠症	2 (0.5)	4 (1.0)	5 (1.2)
Renal and urinary disorders	腎および尿路障害	2 (0.5)	1 (0.2)	3 (0.7)
Dysuria	排尿困難	1 (0.2)	0 (0.0)	1 (0.2)
Nocturia	夜間頻尿	1 (0.2)	0 (0.0)	1 (0.2)
Pollakiuria	頻尿	0 (0.0)	1 (0.2)	1 (0.2)
Reproductive system and breast disorders	生殖系および乳房障害	5 (1.2)	2 (0.5)	7 (1.7)
Erection increased	勃起増強	4 (1.0)	1 (0.2)	5 (1.2)
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	1 (0.2)	1 (0.2)
Erectile dysfunction	勃起不全	1 (0.2)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	9 (2.2)	3 (0.7)	11 (2.7)
Dry throat	咽喉乾燥	1 (0.2)	0 (0.0)	1 (0.2)
Dyspnoea	呼吸困難	1 (0.2)	0 (0.0)	1 (0.2)
Epistaxis	鼻出血	1 (0.2)	0 (0.0)	1 (0.2)
Hyperventilation	過換気	0 (0.0)	1 (0.2)	1 (0.2)
Nasal congestion	鼻閉	1 (0.2)	1 (0.2)	1 (0.2)
Rhinorrhoea	鼻漏	0 (0.0)	1 (0.2)	1 (0.2)
Wheezing	喘鳴	1 (0.2)	0 (0.0)	1 (0.2)
Laryngeal discomfort	喉頭不快感	2 (0.5)	0 (0.0)	2 (0.5)
Oropharyngeal pain	口腔咽頭痛	2 (0.5)	0 (0.0)	2 (0.5)

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表 2.7.4.7.1-13

Table 14.1.1.3-28

Incidences of Drug-related Adverse Events by MedDRA System Organ Class and Preferred Term in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001		Total (N=403)
System organ class		Study 339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	8 (2.0)	11 (2.7)	18 (4.5)
Cold sweat	冷汗	0 (0.0)	1 (0.2)	1 (0.2)
Dermatitis	皮膚炎	1 (0.2)	0 (0.0)	1 (0.2)
Dry skin	皮膚乾燥	1 (0.2)	0 (0.0)	1 (0.2)
Eczema	湿疹	1 (0.2)	1 (0.2)	2 (0.5)
Hyperhidrosis	多汗症	0 (0.0)	1 (0.2)	1 (0.2)
Night sweats	寝汗	1 (0.2)	3 (0.7)	4 (1.0)
Rash	発疹	0 (0.0)	2 (0.5)	2 (0.5)
Rash generalised	全身性皮疹	0 (0.0)	1 (0.2)	1 (0.2)
Rash papular	丘疹性皮疹	1 (0.2)	0 (0.0)	1 (0.2)
Urticaria	蕁麻疹	2 (0.5)	1 (0.2)	3 (0.7)
Pruritus generalised	全身性そう痒症	1 (0.2)	1 (0.2)	1 (0.2)
Vascular disorders	血管障害	9 (2.2)	8 (2.0)	13 (3.2)
Hypertension	高血圧	2 (0.5)	3 (0.7)	4 (1.0)
Hypotension	低血圧	1 (0.2)	0 (0.0)	1 (0.2)
Orthostatic hypotension	起立性低血圧	1 (0.2)	0 (0.0)	1 (0.2)
Hot flush	ほてり	5 (1.2)	5 (1.2)	7 (1.7)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-28＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N		245	245	242	242	242	239
Total number of subjects with TEAEs		69 (28.2)	16 (6.5)	13 (5.4)	10 (4.1)	23 (9.5)	28 (11.7)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	心臓障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palpitations	動悸	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tachycardia	頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vertigo	回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear discomfort	耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	眼障害	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Abnormal sensation in eye	眼の異常感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye pain	眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid oedema	眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Photophobia	羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visual impairment	視力障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oscillopsia	動揺視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	24 (9.8)	5 (2.0)	3 (1.2)	1 (0.4)	2 (0.8)	2 (0.8)
Abdominal discomfort	腹部不快感	3 (1.2)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal distension	腹部膨満	4 (1.6)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Abdominal pain	腹痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Abdominal pain lower	下腹部痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)
Chronic gastritis	慢性胃炎	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dental caries	齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhoea	下痢	3 (1.2)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry mouth	口内乾燥	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspepsia	消化不良	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	8 (3.3)	2 (0.8)	2 (0.8)	0 (0.0)	1 (0.4)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Placebo (N=245)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感		2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stomatitis	口内炎		1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Swollen tongue	舌腫脹		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Toothache	歯痛		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Vomiting	嘔吐		1 (0.4)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)
Oral dysaesthesia	口腔知覚不全		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	痔出血		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Hypoaesthesia oral	口の感覚鈍麻		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia oral	口の錯感覚		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral mucosa haematoma	口腔粘膜血腫		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

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Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	15 (6.1)	2 (0.8)	4 (1.7)	2 (0.8)	3 (1.2)	4 (1.7)
Asthenia	無力症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0 (0.0)
Chest discomfort	胸部不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	悪寒	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	死亡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discomfort	不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Face oedema	顔面浮腫	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	疲労	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)
Feeling abnormal	異常感	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling hot	熱感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Malaise	倦怠感	4 (1.6)	1 (0.4)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.4)
Pain	疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態						
Pyrexia	発熱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)
Thirst	口渇	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Early satiety	早期満腹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症	8 (3.3)	5 (2.0)	5 (2.1)	10 (4.1)	24 (9.9)	14 (5.9)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis	結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0 (0.0)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingivitis	歯肉炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza	インフルエンザ	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Nasopharyngitis	鼻咽頭炎	6 (2.4)	3 (1.2)	5 (2.1)	11 (4.5)	22 (9.1)	10 (4.2)
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症						
Pharyngitis	咽頭炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinitis	鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Enteritis infectious	感染性腸炎	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.4)	2 (0.8)	1 (0.4)	0 (0.0)	2 (0.8)	2 (0.8)
Accidental overdose	偶発的過量投与	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Heat stroke	熱射病	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Contusion	挫傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症						
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	9 (3.8)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood pressure increased	血圧上昇	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Weight increased	体重増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	代謝および栄養障害	2 (0.8)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Decreased appetite	食欲減退	2 (0.8)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	10 (4.2)
Arthralgia	関節痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Back pain	背部痛	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.5)
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Muscular weakness	筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Myalgia	筋肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)

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Safety Set

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System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	29 (11.8)	7 (2.9)	4 (1.7)	1 (0.4)	4 (1.7)	2 (0.8)
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Burning sensation	灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dizziness	浮動性めまい	7 (2.9)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)
Dizziness postural	体位性めまい	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysgeusia	味覚異常	5 (2.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Head discomfort	頭部不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Headache	頭痛	8 (3.3)	2 (0.8)	2 (0.8)	0 (0.0)	4 (1.7)	0 (0.0)
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Masked facies	仮面状顔貌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Memory impairment	記憶障害	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Placebo (N=245)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害							
Somnolence	傾眠		10 (4.1)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tremor	振戦		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Poor quality sleep	睡眠の質低下		2 (0.8)	2 (0.8)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	2 (0.8)	1 (0.4)	1 (0.4)	3 (1.2)	0 (0.0)	2 (0.8)
Agitation	激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Anticipatory anxiety	予期不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Apathy	無感情	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Initial insomnia	初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Irritability	易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Middle insomnia	中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)
Mood swings	気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nightmare	悪夢	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Sleep disorder	睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stress	ストレス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal ideation	自殺念慮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Terminal insomnia	早朝覚醒型不眠症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders	腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	生殖系および乳房障害	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysmenorrhoea	月経困難症	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erection increased	勃起増強	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	2 (0.8)	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.4)	3 (1.3)
Choking sensation	息詰まり感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspnoea	呼吸困難	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nasal congestion	鼻閉	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Respiration abnormal	呼吸異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Laryngeal discomfort	喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.8)	1 (0.4)
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Rash	発疹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Urticaria	蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害						
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	血管障害	3 (1.2)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Hypertension	高血圧	0 (0.0)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral coldness	末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hot flush	ほてり	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)

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TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		235	227	223	245			
Total number of subjects with TEAEs		14 (6.0)	9 (4.0)	12 (5.4)	194 (79.2)	0	19.5	170
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	17	88.5	160
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	160	160.0	160
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	17	17.0	17
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	160	160.0	160
Cardiac disorders	心臓障害	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	1	58.0	79
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	79	79.0	79
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Palpitations	動悸	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	1	30.5	60
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tachycardia	頻脈	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	56	58.0	60
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear and labyrinth disorders	耳および迷路障害	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	104	104.0	104
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vertigo	回転性めまい	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	104	104.0	104
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear discomfort	耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	168	168.0	168
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	168	168.0	168
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye disorders	眼障害	2 (0.9)	2 (0.9)	0 (0.0)	7 (2.9)	0	105.0	128
Abnormal sensation in eye	眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry eye	眼乾燥	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	49	77.5	106
Episcleritis	上強膜炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	128	128.0	128
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye pain	眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eyelid oedema	眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eyelid ptosis	眼瞼下垂	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	119	119.0	119
Ocular hyperaemia	眼充血	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	105	105.0	105
Photophobia	羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Oscillopsia	動揺視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害	5 (2.1)	4 (1.8)	5 (2.2)	51 (20.8)	0	8.0	169
Abdominal discomfort	腹部不快感	0 (0.0)	2 (0.9)	0 (0.0)	6 (2.4)	0	10.0	124
Abdominal distension	腹部膨満	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.4)	0	2.0	82
Abdominal pain	腹痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	64	64.0	64
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Abdominal pain upper	上腹部痛	0 (0.0)	1 (0.4)	0 (0.0)	4 (1.6)	6	37.0	127
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	10	10.0	10
Constipation	便秘	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	1	85.0	169
Dental caries	齲歯	1 (0.4)	0 (0.0)	1 (0.4)	2 (0.8)	102	128.5	155
Diarrhoea	下痢	1 (0.4)	0 (0.0)	0 (0.0)	6 (2.4)	0	6.5	87
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	12	12.0	12
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastritis	胃炎	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	3	84.0	165
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	126	126.0	126
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	141	141.0	141
Haemorrhoids	痔核	1 (0.4)	1 (0.4)	1 (0.4)	3 (1.2)	106	132.0	168
Nausea	悪心	2 (0.9)	0 (0.0)	0 (0.0)	15 (6.1)	0	6.0	108

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	0.0	0
Salivary hypersecretion	流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Stomatitis	口内炎	1 (0.4)	0 (0.0)	0 (0.0)	3 (1.2)	5	25.0	106
Swollen tongue	舌腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Toothache	歯痛	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	48	100.5	153
Vomiting	嘔吐	1 (0.4)	1 (0.4)	0 (0.0)	5 (2.0)	6	22.0	113
Oral dysaesthesia	口腔知覚不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Haemorrhoidal haemorrhage	痔出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	77	77.0	77
Hypoaesthesia oral	口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oral mucosa haematoma	口腔粘膜血腫	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	159	159.0	159

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	2 (0.9)	1 (0.4)	1 (0.4)	34 (13.9)	0	12.0	153
Asthenia	無力症	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	5	34.0	56
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Chest pain	胸痛	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	153	153.0	153
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	3	3.0	3
Death	死亡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Discomfort	不快感	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.8)	105	106.0	107
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	4	4.0	4
Fatigue	疲労	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	0	41.5	68
Feeling abnormal	異常感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	0.0	0
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Hangover	宿酔	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	1	50.5	100
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	14	14.0	14
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Malaise	倦怠感	0 (0.0)	0 (0.0)	0 (0.0)	8 (3.3)	0	6.5	69
Pain	疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態							
Pyrexia	発熱	0 (0.0)	1 (0.4)	0 (0.0)	3 (1.2)	26	42.0	113
Thirst	口渇	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	10.0	25
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	4	4.0	4
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	81	81.0	81
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	81	81.0	81
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Immune system disorders	免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	15 (6.4)	11 (4.8)	12 (5.4)	104 (42.4)	0	56.5	170
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	72	72.0	72
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis	結膜炎	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.8)	112	124.0	136
Cystitis	膀胱炎	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	56	75.5	95
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	38	45.0	52
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	78	78.0	78
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	30	30.0	30
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	82	82.0	82
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Influenza	インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	7	32.5	58
Nasopharyngitis	鼻咽頭炎	14 (6.0)	8 (3.5)	12 (5.4)	91 (37.1)	0	54.0	170
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	156	156.0	156
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	63	63.0	63
Otitis media	中耳炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	122	122.0	122
Periodontitis	歯周炎	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.8)	121	132.0	143

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症							
Pharyngitis	咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	3	3.0	3
Rhinitis	鼻炎	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	102	102.0	102
Sinusitis	副鼻腔炎	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.8)	116	135.0	154
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	52	104.0	156
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	8	8.0	8
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oral herpes	口腔ヘルペス	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	100	100.0	100
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	2 (0.9)	3 (1.3)	6 (2.7)	19 (7.8)	0	107.0	170
Accidental overdose	偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	6.5	13
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	107	107.0	107
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	82	82.0	82
Fall	転倒	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.8)	37	83.0	129
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fracture	骨折	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.8)	128	138.5	149
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	9	9.0	9
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligament sprain	靭帯捻挫	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	115	115.0	115
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	160	160.0	160
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Excoriation	擦過傷	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	30	91.5	153
Contusion	挫傷	1 (0.4)	1 (0.4)	1 (0.4)	4 (1.6)	16	114.0	163
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Thermal burn	熱傷	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	155	155.0	155

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症							
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	37	37.0	37
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	170	170.0	170
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	68	68.0	68
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	154	154.0	154

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査	4 (1.7)	0 (0.0)	12 (5.4)	26 (10.6)	0	90.0	191
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	171	171.0	171
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	168	168.0	168
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	81	81.0	81
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	161	161.0	161
Blood pressure increased	血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	30.0	60
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood prolactin increased	血中プロラクチン増加	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	83	84.5	86
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	4 (1.8)	6 (2.4)	80	161.0	191
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.8)	163	167.0	171
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	168	168.0	168
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Glucose urine present	尿中ブドウ糖陽性	1 (0.4)	0 (0.0)	2 (0.9)	4 (1.6)	80	127.0	171
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	1 (0.4)	3 (1.2)	80	84.0	164

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査							
Liver function test abnormal	肝機能検査異常	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	85	85.0	85
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Weight increased	体重増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	77	119.0	161
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	83	83.5	84
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	161	161.0	161
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	94	94.0	94
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Metabolism and nutrition disorders	代謝および栄養障害	0 (0.0)	0 (0.0)	1 (0.4)	4 (1.6)	0	7.0	175
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	175	175.0	175
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Decreased appetite	食欲減退	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	6.0	8
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	4 (1.7)	1 (0.4)	5 (2.2)	22 (9.0)	9	83.0	165
Arthralgia	関節痛	0 (0.0)	1 (0.4)	3 (1.3)	6 (2.4)	82	133.0	165
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Back pain	背部痛	3 (1.3)	0 (0.0)	1 (0.4)	11 (4.5)	9	82.0	155
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Muscular weakness	筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	70	70.0	70
Myalgia	筋肉痛	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	104	104.0	104
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	68	68.0	68
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	153	153.0	153
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	31	56.0	81
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	38	90.5	143
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	38	90.5	143

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	2 (0.9)	2 (0.9)	2 (0.9)	53 (21.6)	0	4.0	168
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	141	141.0	141
Burning sensation	灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dizziness	浮動性めまい	1 (0.4)	0 (0.0)	0 (0.0)	10 (4.1)	0	0.0	95
Dizziness postural	体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	2	2.0	2
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysgeusia	味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.4)	0	0.0	15
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Headache	頭痛	0 (0.0)	1 (0.4)	3 (1.3)	20 (8.2)	0	13.5	168
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypoaesthesia	感覚鈍麻	0 (0.0)	1 (0.4)	1 (0.4)	3 (1.2)	58	122.0	154
Masked facies	仮面状顔貌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	7	7.0	7
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	16	16.0	16
Neuralgia	神経痛	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	130	130.0	130
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Placebo (N=245)						
System organ class		First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害								
Somnolence	傾眠		1 (0.4)	0 (0.0)	1 (0.4)	17 (6.9)	0	1.0	145
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tremor	振戦		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	80	80.0	80
Poor quality sleep	睡眠の質低下		0 (0.0)	0 (0.0)	0 (0.0)	5 (2.0)	1	9.0	20

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	1 (0.4)	1 (0.4)	4 (1.8)	15 (6.1)	3	71.0	180
Agitation	激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.8)	21	76.5	132
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	16	95.0	174
Anticipatory anxiety	予期不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anxiety	不安	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	11	11.0	11
Apathy	無感情	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depression	うつ病	1 (0.4)	0 (0.0)	1 (0.4)	2 (0.8)	98	138.0	178
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Initial insomnia	初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Insomnia	不眠症	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	28	104.0	180
Irritability	易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Middle insomnia	中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	23	23.0	23
Mood swings	気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	3	3.0	3
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害							
Sleep disorder	睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Stress	ストレス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Suicidal ideation	自殺念慮	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	165	165.0	165
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	71	71.0	71
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	76	76.0	76
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	3	3.0	3
Renal and urinary disorders	腎および尿路障害	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	66	79.5	93
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysuria	排尿困難	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	66	79.5	93
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Reproductive system and breast disorders	生殖系および乳房障害	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	11	51.5	92
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	11	11.0	11
Erection increased	勃起増強	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Premenstrual syndrome	月経前症候群	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	92	92.0	92
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	0 (0.0)	1 (0.4)	0 (0.0)	9 (3.7)	0	47.0	129
Choking sensation	息詰まり感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	83	83.0	83
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Respiration abnormal	呼吸異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	129	129.0	129
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	66	66.0	66
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	47	63.0	79
Laryngeal discomfort	喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	15	15.0	15
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	7	7.0	7

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	1 (0.4)	1 (0.4)	0 (0.0)	7 (2.9)	4	49.0	127
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis	皮膚炎	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.8)	16	54.5	93
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	49	49.0	49
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	78	78.0	78
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	70	70.0	70
Rash	発疹	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.8)	4	79.0	154
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	49	49.0	49
Urticaria	蕁麻疹	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	127	127.0	127

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Placebo (N=245)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害							
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vascular disorders	血管障害	0 (0.0)	0 (0.0)	1 (0.4)	7 (2.9)	0	8.0	161
Hypertension	高血圧	0 (0.0)	0 (0.0)	1 (0.4)	4 (1.6)	8	30.5	161
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Peripheral coldness	末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hot flush	ほてり	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	0.0	0
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	37	37.0	37
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	37	37.0	37

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N		248	242	224	220	214	208
Total number of subjects with TEAEs		163 (65.7)	12 (5.0)	10 (4.5)	2 (0.9)	5 (2.3)	11 (5.3)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	心臓障害	8 (3.2)	1 (0.4)	2 (0.9)	0 (0.0)	1 (0.5)	3 (1.4)
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Palpitations	動悸	8 (3.2)	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.5)	1 (0.5)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Tachycardia	頻脈	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear and labyrinth disorders	耳および迷路障害	9 (3.6)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinnitus	耳鳴	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vertigo	回転性めまい	6 (2.4)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear discomfort	耳不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	眼障害	3 (1.2)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)
Abnormal sensation in eye	眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Eye pain	眼痛	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid oedema	眼瞼浮腫	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Photophobia	羞明	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oscillopsia	動揺視	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	101 (40.7)	9 (3.7)	5 (2.2)	1 (0.5)	6 (2.8)	2 (1.0)
Abdominal discomfort	腹部不快感	5 (2.0)	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)
Abdominal distension	腹部膨満	8 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Abdominal pain	腹痛	3 (1.2)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	7 (2.8)	3 (1.2)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)
Dental caries	齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Diarrhoea	下痢	9 (3.6)	0 (0.0)	1 (0.4)	1 (0.5)	0 (0.0)	0 (0.0)
Dry mouth	口内乾燥	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Food poisoning	食中毒	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	71 (28.6)	2 (0.8)	2 (0.9)	0 (0.0)	2 (0.9)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene 20 mg (N=248)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stomatitis	口内炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Swollen tongue	舌腫脹		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Toothache	歯痛		2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Vomiting	嘔吐		21 (8.5)	2 (0.8)	5 (2.2)	0 (0.0)	1 (0.5)	5 (2.4)
Oral dysaesthesia	口腔知覚不全		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	痔出血		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia oral	口の感覚鈍麻		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia oral	口の錯感覚		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral mucosa haematoma	口腔粘膜血腫		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	36 (14.5)	4 (1.7)	4 (1.8)	1 (0.5)	3 (1.4)	1 (0.5)
Asthenia	無力症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Chest discomfort	胸部不快感	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	悪寒	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	死亡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discomfort	不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	疲労	3 (1.2)	1 (0.4)	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)
Feeling abnormal	異常感	5 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	17 (6.9)	0 (0.0)	1 (0.4)	0 (0.0)	3 (1.4)	0 (0.0)
Pain	疼痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態						
Pyrexia	発熱	2 (0.8)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thirst	口渇	8 (3.2)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral swelling	末梢腫脹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症	11 (4.4)	7 (2.9)	5 (2.2)	3 (1.4)	6 (2.8)	11 (5.3)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis	結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Gastroenteritis	胃腸炎	1 (0.4)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	1 (0.5)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingivitis	歯肉炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza	インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Nasopharyngitis	鼻咽頭炎	8 (3.2)	7 (2.9)	3 (1.3)	2 (0.9)	5 (2.3)	7 (3.4)
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症						
Pharyngitis	咽頭炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Rhinitis	鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
Accidental overdose	偶発的過量投与	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症						
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	2 (0.8)	1 (0.4)	0 (0.0)	3 (1.4)	0 (0.0)	10 (4.8)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood pressure increased	血圧上昇	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Weight increased	体重増加	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Metabolism and nutrition disorders	代謝および栄養障害	8 (3.2)	5 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Increased appetite	食欲亢進	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Decreased appetite	食欲減退	8 (3.2)	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	6 (2.4)	2 (0.8)	1 (0.4)	0 (0.0)	3 (1.4)	4 (1.9)
Arthralgia	関節痛	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Back pain	背部痛	2 (0.8)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Muscular weakness	筋力低下	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Myalgia	筋肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.0)
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal stiffness	筋骨格硬直	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal discomfort	筋骨格不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Table 14.1.1.3-27

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Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	84 (33.9)	3 (1.2)	2 (0.9)	1 (0.5)	5 (2.3)	4 (1.9)
Amnesia	健忘	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Autonomic nervous system imbalance	自律神経失調	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Burning sensation	灼熱感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.5)
Dizziness	浮動性めまい	46 (18.5)	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.5)	2 (1.0)
Dizziness postural	体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Dysaesthesia	異常感覚	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysgeusia	味覚異常	3 (1.2)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Headache	頭痛	19 (7.7)	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.9)	1 (0.5)
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia	感覚鈍麻	5 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Masked facies	仮面状顔貌	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Memory impairment	記憶障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene 20 mg (N=248)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害							
Somnolence	傾眠		30 (12.1)	3 (1.2)	2 (0.9)	1 (0.5)	1 (0.5)	1 (0.5)
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tremor	振戦		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下		3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	29 (11.7)	3 (1.2)	5 (2.2)	3 (1.4)	1 (0.5)	4 (1.9)
Agitation	激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.5)	0 (0.0)	1 (0.5)
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anticipatory anxiety	予期不安	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Apathy	無感情	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressed mood	抑うつ気分	3 (1.2)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysphoria	不快気分	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Initial insomnia	初期不眠症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	17 (6.9)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	1 (0.5)
Irritability	易刺激性	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Middle insomnia	中期不眠症	3 (1.2)	1 (0.4)	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.5)
Mood swings	気分動揺	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Restlessness	落ち着きのなさ	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Sleep disorder	睡眠障害	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Stress	ストレス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal ideation	自殺念慮	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressive symptom	抑うつ症状	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in sexual arousal	性的興奮障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Renal and urinary disorders	腎および尿路障害	3 (1.2)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pollakiuria	頻尿	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	生殖系および乳房障害	3 (1.2)	2 (0.8)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Erection increased	勃起増強	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	4 (1.6)	2 (0.8)	0 (0.0)	2 (0.9)	1 (0.5)	0 (0.0)
Choking sensation	息詰まり感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Respiration abnormal	呼吸異常	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal discomfort	口腔咽頭不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	4 (1.6)	6 (2.5)	2 (0.9)	2 (0.9)	1 (0.5)	1 (0.5)
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eczema	湿疹	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema	紅斑	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Hyperhidrosis	多汗症	3 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	0 (0.0)	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Urticaria	蕁麻疹	0 (0.0)	1 (0.4)	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害						
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vascular disorders	血管障害	3 (1.2)	1 (0.4)	0 (0.0)	1 (0.5)	2 (0.9)	0 (0.0)
Hypertension	高血圧	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.5)	0 (0.0)	0 (0.0)
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Peripheral coldness	末梢冷感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hot flush	ほてり	2 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		201	194	192	248			
Total number of subjects with TEAEs		6 (3.0)	4 (2.1)	5 (2.6)	218 (87.9)	0	0.0	168
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	91	91.0	91
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pancytopenia	汎血球減少症	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	91	91.0	91
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cardiac disorders	心臓障害	0 (0.0)	1 (0.5)	0 (0.0)	16 (6.5)	0	4.0	133
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	77	77.0	77
Palpitations	動悸	0 (0.0)	1 (0.5)	0 (0.0)	13 (5.2)	0	0.0	133
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	77	77.0	77
Tachycardia	頻脈	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	7	7.0	7
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	0 (0.0)	1 (0.5)	11 (4.4)	0	0.0	154
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	0.0	0
Vertigo	回転性めまい	0 (0.0)	0 (0.0)	1 (0.5)	8 (3.2)	0	0.5	154
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear discomfort	耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye disorders	眼障害	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.0)	0	1.0	84
Abnormal sensation in eye	眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Eye pain	眼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	17	17.0	17
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eyelid oedema	眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Photophobia	羞明	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oscillopsia	動揺視	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害	1 (0.5)	1 (0.5)	2 (1.0)	128 (51.6)	0	0.0	166
Abdominal discomfort	腹部不快感	0 (0.0)	1 (0.5)	1 (0.5)	10 (4.0)	0	7.0	166
Abdominal distension	腹部膨満	0 (0.0)	0 (0.0)	0 (0.0)	9 (3.6)	0	0.0	32
Abdominal pain	腹痛	0 (0.0)	0 (0.0)	0 (0.0)	7 (2.8)	1	7.0	58
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Abdominal pain upper	上腹部痛	0 (0.0)	2 (1.0)	1 (0.5)	5 (2.0)	19	126.0	159
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Constipation	便秘	0 (0.0)	0 (0.0)	1 (0.5)	13 (5.2)	1	4.0	142
Dental caries	齲歯	0 (0.0)	0 (0.0)	2 (1.0)	3 (1.2)	83	166.0	167
Diarrhoea	下痢	1 (0.5)	0 (0.0)	0 (0.0)	12 (4.8)	0	1.0	89
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	2 (1.0)	2 (0.8)	152	158.5	165
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	73	73.0	73
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	10	10.0	10
Gastritis	胃炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	42	42.0	42
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nausea	悪心	1 (0.5)	1 (0.5)	0 (0.0)	79 (31.9)	0	0.0	138

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Salivary hypersecretion	流涎過多	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	108	108.0	108
Stomatitis	口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Swollen tongue	舌腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Toothache	歯痛	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	3	6.0	78
Vomiting	嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	34 (13.7)	0	2.0	73
Oral dysaesthesia	口腔知覚不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Haemorrhoidal haemorrhage	痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypoaesthesia oral	口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oral mucosa haematoma	口腔粘膜血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	2 (1.0)	4 (2.1)	0 (0.0)	55 (22.2)	0	1.0	122
Asthenia	無力症	1 (0.5)	1 (0.5)	0 (0.0)	3 (1.2)	18	93.0	122
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	8	8.0	8
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Death	死亡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Discomfort	不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fatigue	疲労	1 (0.5)	2 (1.0)	0 (0.0)	10 (4.0)	0	14.5	114
Feeling abnormal	異常感	0 (0.0)	0 (0.0)	0 (0.0)	6 (2.4)	0	0.0	49
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	63	63.0	63
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Feeling hot	熱感	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	110	110.0	110
Hangover	宿酔	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	33.0	66
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Malaise	倦怠感	1 (0.5)	2 (1.0)	0 (0.0)	24 (9.7)	0	0.5	125
Pain	疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態							
Pyrexia	発熱	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	2.0	11
Thirst	口渇	0 (0.0)	0 (0.0)	0 (0.0)	9 (3.6)	0	0.0	12
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	3 (1.6)	4 (1.6)	41	168.0	175
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	41	41.0	41
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	168	168.0	168
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	175	175.0	175
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	168	168.0	168
Immune system disorders	免疫系障害	3 (1.5)	0 (0.0)	0 (0.0)	4 (1.6)	58	100.5	109
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	58	58.0	58
Seasonal allergy	季節性アレルギー	3 (1.5)	0 (0.0)	0 (0.0)	3 (1.2)	97	104.0	109

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	11 (5.5)	8 (4.1)	12 (6.3)	74 (29.8)	1	74.5	166
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	145	145.0	145
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bronchitis	気管支炎	1 (0.5)	0 (0.0)	1 (0.5)	2 (0.8)	89	127.0	165
Conjunctivitis	結膜炎	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)	131	131.0	131
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	23	23.0	23
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	5	15.5	62
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)	123	123.0	123
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	65	65.0	65
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Infection	感染	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	161	161.0	161
Influenza	インフルエンザ	1 (0.5)	0 (0.0)	0 (0.0)	3 (1.2)	76	83.0	90
Nasopharyngitis	鼻咽頭炎	7 (3.5)	5 (2.6)	10 (5.2)	54 (21.8)	1	65.5	166
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	151	151.0	151
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Periodontitis	歯周炎	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	85	85.0	85

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Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症							
Pharyngitis	咽頭炎	1 (0.5)	0 (0.0)	0 (0.0)	3 (1.2)	2	84.0	109
Rhinitis	鼻炎	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)	133	133.0	133
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	65	65.0	65
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	30	30.0	30
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Enteritis infectious	感染性腸炎	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)	113	113.0	113
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	48	48.0	48
Oral herpes	口腔ヘルペス	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	99	99.0	99
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	16	16.0	16

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Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	5 (2.5)	0 (0.0)	1 (0.5)	9 (3.6)	11	101.0	154
Accidental overdose	偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	11	20.0	29
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fall	転倒	1 (0.5)	0 (0.0)	0 (0.0)	2 (0.8)	62	86.0	110
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Foot fracture	足骨折	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	101	101.0	101
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injury	損傷	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	103	103.0	103
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	154	154.0	154
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Spinal compression fracture	脊椎圧迫骨折	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	88	88.0	88
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Wound	創傷	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	106	106.0	106
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症							
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

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Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査	6 (3.0)	0 (0.0)	10 (5.2)	32 (12.9)	0	84.5	175
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.5)	0 (0.0)	1 (0.5)	3 (1.2)	84	87.0	172
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.8)	84	128.0	172
Blood bilirubin increased	血中ビリルビン増加	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	87	87.0	87
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	166	166.0	166
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.8)	84	129.5	175
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood pressure increased	血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	4	10.0	28
Blood prolactin decreased	血中プロラクチン減少	1 (0.5)	0 (0.0)	1 (0.5)	2 (0.8)	85	126.5	168
Blood prolactin increased	血中プロラクチン増加	1 (0.5)	0 (0.0)	3 (1.6)	6 (2.4)	84	126.5	168
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	1 (0.5)	3 (1.2)	82	84.0	168
Electrocardiogram QT prolonged	心電図QT延長	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	105	105.0	105
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	1 (0.5)	0 (0.0)	2 (1.0)	3 (1.2)	89	172.0	172
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	168	168.0	168
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査							
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Red blood cell count decreased	赤血球数減少	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	90	90.0	90
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Weight increased	体重増加	0 (0.0)	0 (0.0)	2 (1.0)	4 (1.6)	0	95.5	166
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.8)	77	125.5	174
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	21	21.0	21
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	21	21.0	21
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	77	77.0	77
Metabolism and nutrition disorders	代謝および栄養障害	1 (0.5)	0 (0.0)	1 (0.5)	17 (6.9)	0	7.0	175
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	175	175.0	175
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	13	13.0	13
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	11	11.0	11
Decreased appetite	食欲減退	1 (0.5)	0 (0.0)	0 (0.0)	13 (5.2)	0	3.0	87
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	68	68.0	68

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	0 (0.0)	3 (1.5)	6 (3.1)	25 (10.1)	0	67.0	164
Arthralgia	関節痛	0 (0.0)	0 (0.0)	2 (1.0)	3 (1.2)	8	146.0	153
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	71	71.0	71
Back pain	背部痛	0 (0.0)	2 (1.0)	1 (0.5)	8 (3.2)	4	55.5	147
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	56	56.0	56
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Muscular weakness	筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	67	67.0	67
Myalgia	筋肉痛	0 (0.0)	1 (0.5)	1 (0.5)	4 (1.6)	83	100.5	146
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	161	161.0	161
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.8)	19	80.0	141
Trigger finger	弾発指	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	164	164.0	164
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	1	2.0	3
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	0 (0.0)	0 (0.0)	1 (0.5)	100 (40.3)	0	0.0	163
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Burning sensation	灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	0	23.5	61
Dizziness	浮動性めまい	0 (0.0)	0 (0.0)	0 (0.0)	51 (20.6)	0	0.0	82
Dizziness postural	体位性めまい	1 (0.5)	0 (0.0)	0 (0.0)	2 (0.8)	49	68.5	88
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	8	8.0	8
Dysgeusia	味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.0)	0	0.0	70
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	35	35.0	35
Headache	頭痛	0 (0.0)	0 (0.0)	0 (0.0)	24 (9.7)	0	1.0	79
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.0)	0	0.0	1
Masked facies	仮面状顔貌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Myoclonus	ミオクローヌス	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	108	108.0	108
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

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Safety Set

			Nalmefene 20 mg (N=248)						
System organ class		First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害								
Somnolence	傾眠		0 (0.0)	1 (0.5)	0 (0.0)	39 (15.7)	0	0.0	126
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tremor	振戦		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Poor quality sleep	睡眠の質低下		0 (0.0)	0 (0.0)	1 (0.5)	4 (1.6)	0	0.0	163

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Table 14.1.1.3-27

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Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	0 (0.0)	1 (0.5)	0 (0.0)	46 (18.5)	0	1.0	133
Agitation	激越	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.0)	1	20.0	77
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anticipatory anxiety	予期不安	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	4	4.0	4
Anxiety	不安	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	0.0	3
Apathy	無感情	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	0	1.0	13
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Initial insomnia	初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Insomnia	不眠症	0 (0.0)	0 (0.0)	0 (0.0)	20 (8.1)	0	0.0	77
Irritability	易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	14	14.0	14
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	63	63.0	63
Middle insomnia	中期不眠症	0 (0.0)	1 (0.5)	0 (0.0)	8 (3.2)	0	15.0	133
Mood swings	気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	15	15.0	15
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	51	51.0	51
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害							
Sleep disorder	睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	8.0	16
Stress	ストレス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Suicidal ideation	自殺念慮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	7	7.0	7
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	0	42.0	84
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	4	4.0	4
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	41	41.0	41
Renal and urinary disorders	腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	0	0.0	25
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	0.0	25

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Reproductive system and breast disorders	生殖系および乳房障害	0 (0.0)	0 (0.0)	1 (0.5)	7 (2.8)	0	8.0	143
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	45	45.0	45
Erection increased	勃起増強	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	0.0	1
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.8)	8	75.5	143
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	12	12.0	12

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	1 (0.5)	0 (0.0)	0 (0.0)	10 (4.0)	0	11.0	112
Choking sensation	息詰まり感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	49	49.0	49
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	12	12.0	12
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	24	24.0	24
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	27	27.0	27
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	24	24.0	24
Respiration abnormal	呼吸異常	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal discomfort	喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Oropharyngeal pain	口腔咽頭痛	1 (0.5)	0 (0.0)	0 (0.0)	2 (0.8)	10	61.0	112

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	0 (0.0)	0 (0.0)	2 (1.0)	18 (7.3)	0	12.0	154
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	68	68.0	68
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	12	12.0	12
Eczema	湿疹	0 (0.0)	0 (0.0)	2 (1.0)	3 (1.2)	9	144.0	154
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	11	11.0	11
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	22	22.0	22
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	0.0	0
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash	発疹	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.8)	11	11.5	12
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	37	37.0	37
Urticaria	蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.6)	11	17.5	23

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 20 mg (N=248)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害							
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vascular disorders	血管障害	0 (0.0)	0 (0.0)	1 (0.5)	8 (3.2)	0	15.0	175
Hypertension	高血圧	0 (0.0)	0 (0.0)	1 (0.5)	4 (1.6)	7	18.5	175
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	42	42.0	42
Peripheral coldness	末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Hot flush	ほてり	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.2)	0	1.0	30
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N		184	182	173	166	163	156
Total number of subjects with TEAEs		111 (60.3)	12 (6.6)	4 (2.3)	3 (1.8)	7 (4.3)	4 (2.6)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	心臓障害	4 (2.2)	1 (0.5)	0 (0.0)	1 (0.6)	2 (1.2)	2 (1.3)
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palpitations	動悸	4 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tachycardia	頻脈	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Ear and labyrinth disorders	耳および迷路障害	3 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vertigo	回転性めまい	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoacusis	聴力低下	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear discomfort	耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	眼障害	1 (0.5)	1 (0.5)	1 (0.6)	1 (0.6)	1 (0.6)	1 (0.6)
Abnormal sensation in eye	眼の異常感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Dry eye	眼乾燥	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye pain	眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid oedema	眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Photophobia	羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oscillopsia	動揺視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	65 (35.3)	5 (2.7)	3 (1.7)	1 (0.6)	7 (4.3)	0 (0.0)
Abdominal discomfort	腹部不快感	4 (2.2)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Abdominal distension	腹部膨満	2 (1.1)	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)
Abdominal pain	腹痛	2 (1.1)	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain lower	下腹部痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	3 (1.6)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)
Dental caries	齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Diarrhoea	下痢	2 (1.1)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Dyspepsia	消化不良	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	50 (27.2)	3 (1.6)	3 (1.7)	0 (0.0)	2 (1.2)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene 10 mg (N=184)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stomatitis	口内炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Swollen tongue	舌腫脹		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Toothache	歯痛		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vomiting	嘔吐		9 (4.9)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
Oral dysaesthesia	口腔知覚不全		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	痔出血		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia oral	口の感覚鈍麻		1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia oral	口の錯感覚		1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral mucosa haematoma	口腔粘膜血腫		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	17 (9.2)	1 (0.5)	0 (0.0)	1 (0.6)	2 (1.2)	0 (0.0)
Asthenia	無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	死亡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discomfort	不快感	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	疲労	5 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling abnormal	異常感	3 (1.6)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling drunk	酩酊感	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	5 (2.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain	疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態						
Pyrexia	発熱	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Thirst	口渇	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症	6 (3.3)	2 (1.1)	3 (1.7)	3 (1.8)	6 (3.7)	8 (5.1)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis	結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cystitis	膀胱炎	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza	インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Nasopharyngitis	鼻咽頭炎	5 (2.7)	2 (1.1)	2 (1.2)	3 (1.8)	5 (3.1)	5 (3.2)
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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表 2.7.4.7.1-14

Table 14.1.1.3-27

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Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症						
Pharyngitis	咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)
Rhinitis	鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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Safety Set

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System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	5 (3.2)
Accidental overdose	偶発的過量投与	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症						
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tooth fracture	歯牙破折	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	0 (0.0)	1 (0.5)	1 (0.6)	0 (0.0)	2 (1.2)	5 (3.2)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood pressure increased	血圧上昇	0 (0.0)	1 (0.5)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)

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Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Weight increased	体重増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	代謝および栄養障害	7 (3.8)	3 (1.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Dehydration	脱水	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Decreased appetite	食欲減退	7 (3.8)	2 (1.1)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	4 (2.2)	2 (1.1)	1 (0.6)	1 (0.6)	0 (0.0)	1 (0.6)
Arthralgia	関節痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Back pain	背部痛	0 (0.0)	1 (0.5)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Muscle twitching	筋攣縮	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Muscular weakness	筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myalgia	筋肉痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal stiffness	筋骨格硬直	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal discomfort	筋骨格不快感	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligamentitis	靭帯炎	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

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Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	50 (27.2)	4 (2.2)	0 (0.0)	0 (0.0)	4 (2.5)	3 (1.9)
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Burning sensation	灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dizziness	浮動性めまい	17 (9.2)	2 (1.1)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Dizziness postural	体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysgeusia	味覚異常	4 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head discomfort	頭部不快感	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Headache	頭痛	13 (7.1)	2 (1.1)	1 (0.6)	0 (0.0)	3 (1.8)	2 (1.3)
Hyperaesthesia	知覚過敏	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia	感覚鈍麻	2 (1.1)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Masked facies	仮面状顔貌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene 10 mg (N=184)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害							
Somnolence	傾眠		15 (8.2)	2 (1.1)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Tremor	振戦		1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下		3 (1.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	21 (11.4)	3 (1.6)	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.6)
Agitation	激越	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anticipatory anxiety	予期不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Apathy	無感情	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Initial insomnia	初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	13 (7.1)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Irritability	易刺激性	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Libido decreased	リビドー減退	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Middle insomnia	中期不眠症	4 (2.2)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Mood swings	気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Sleep disorder	睡眠障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stress	ストレス	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal ideation	自殺念慮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Renal and urinary disorders	腎および尿路障害	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Dysuria	排尿困難	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	生殖系および乳房障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erection increased	勃起増強	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	1 (0.5)	1 (0.5)	2 (1.2)	0 (0.0)	0 (0.0)	1 (0.6)
Choking sensation	息詰まり感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Respiration abnormal	呼吸異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Wheezing	喘鳴	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	3 (1.6)	1 (0.5)	1 (0.6)	1 (0.6)	3 (1.8)	0 (0.0)
Acne	ざ瘡	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Cold sweat	冷汗	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urticaria	蕁麻疹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害						
Pruritus generalised	全身性そう痒症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Vascular disorders	血管障害	4 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Hypertension	高血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypotension	低血圧	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral coldness	末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hot flush	ほてり	3 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		152	145	142	184			
Total number of subjects with TEAEs		5 (3.3)	4 (2.8)	6 (4.2)	156 (84.8)	0	0.0	175
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	168	168.0	168
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	168	168.0	168
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cardiac disorders	心臓障害	0 (0.0)	1 (0.7)	0 (0.0)	11 (6.0)	0	28.0	140
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	46	46.0	46
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Palpitations	動悸	0 (0.0)	1 (0.7)	0 (0.0)	7 (3.8)	0	5.0	140
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tachycardia	頻脈	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	7	17.5	28
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	84	84.0	84
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	0	1.5	33
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	33	33.0	33
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vertigo	回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0	0.0	0
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	3	3.0	3
Ear discomfort	耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	2 (1.3)	0 (0.0)	0 (0.0)	2 (1.1)	86	95.0	104
Hyperprolactinaemia	高プロラクチン血症	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	86	86.0	86
Primary hyperaldosteronism	原発性アルドステロン症	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	104	104.0	104
Eye disorders	眼障害	0 (0.0)	0 (0.0)	0 (0.0)	6 (3.3)	0	20.5	80
Abnormal sensation in eye	眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	9	9.0	9
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	80	80.0	80
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	22	22.0	22
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	38	38.0	38
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0	15.5	31
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye pain	眼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	19	19.0	19
Eyelid oedema	眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Photophobia	羞明	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oscillopsia	動揺視	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害	6 (3.9)	2 (1.4)	3 (2.1)	92 (50.0)	0	0.0	165
Abdominal discomfort	腹部不快感	1 (0.7)	0 (0.0)	1 (0.7)	7 (3.8)	0	0.0	143
Abdominal distension	腹部膨満	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.7)	0	8.0	73
Abdominal pain	腹痛	0 (0.0)	1 (0.7)	1 (0.7)	6 (3.3)	0	10.0	161
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	13	93.0	173
Abdominal pain upper	上腹部痛	0 (0.0)	0 (0.0)	1 (0.7)	3 (1.6)	9	47.0	154
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Constipation	便秘	2 (1.3)	0 (0.0)	0 (0.0)	8 (4.3)	1	25.0	110
Dental caries	齲歯	1 (0.7)	1 (0.7)	0 (0.0)	3 (1.6)	56	100.0	136
Diarrhoea	下痢	3 (2.0)	0 (0.0)	0 (0.0)	7 (3.8)	0	32.0	109
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	31	31.0	31
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	1 (0.7)	3 (1.6)	0	81.0	165
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastritis	胃炎	0 (0.0)	1 (0.7)	1 (0.7)	2 (1.1)	119	139.5	160
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	69	69.0	69
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	29	29.0	29
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nausea	悪心	0 (0.0)	0 (0.0)	0 (0.0)	58 (31.5)	0	0.0	55

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Salivary hypersecretion	流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Stomatitis	口内炎	2 (1.3)	0 (0.0)	0 (0.0)	2 (1.1)	101	101.5	102
Swollen tongue	舌腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	23	23.0	23
Toothache	歯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vomiting	嘔吐	2 (1.3)	1 (0.7)	2 (1.4)	16 (8.7)	0	1.0	154
Oral dysaesthesia	口腔知覚不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Haemorrhoidal haemorrhage	痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypoaesthesia oral	口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	6	6.0	6
Oral mucosa haematoma	口腔粘膜血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	0 (0.0)	1 (0.7)	2 (1.4)	24 (13.0)	0	1.0	168
Asthenia	無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Death	死亡	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	168	168.0	168
Discomfort	不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fatigue	疲労	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.7)	0	0.0	1
Feeling abnormal	異常感	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.7)	0	0.0	52
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0	0.0	0
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hangover	宿酔	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	40	40.0	40
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Malaise	倦怠感	0 (0.0)	1 (0.7)	1 (0.7)	7 (3.8)	0	1.0	161
Pain	疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態							
Pyrexia	発熱	0 (0.0)	1 (0.7)	1 (0.7)	3 (1.6)	28	120.0	146
Thirst	口渇	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	1	3.0	5
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatobiliary disorders	肝胆道系障害	1 (0.7)	0 (0.0)	1 (0.7)	2 (1.1)	90	129.0	168
Alcoholic liver disease	アルコール性肝疾患	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	90	90.0	90
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	168	168.0	168
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Immune system disorders	免疫系障害	1 (0.7)	0 (0.0)	1 (0.7)	2 (1.1)	106	136.5	167
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Seasonal allergy	季節性アレルギー	1 (0.7)	0 (0.0)	1 (0.7)	2 (1.1)	106	136.5	167

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	5 (3.3)	8 (5.5)	2 (1.4)	43 (23.4)	0	63.0	165
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis	結膜炎	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	163	163.0	163
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	1 (0.7)	4 (2.2)	0	42.5	152
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	44	60.0	76
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Influenza	インフルエンザ	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	61	117.5	174
Nasopharyngitis	鼻咽頭炎	5 (3.3)	9 (6.2)	4 (2.8)	40 (21.7)	0	76.0	165
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Periodontitis	歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症							
Pharyngitis	咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	27	37.5	48
Rhinitis	鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oral herpes	口腔ヘルペス	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	107	107.0	107
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	0 (0.0)	0 (0.0)	0 (0.0)	8 (4.3)	1	59.0	84
Accidental overdose	偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1	1.0	1
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	60	60.0	60
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	79	79.0	79
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	79	79.0	79
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	54	54.0	54
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	79	79.0	79
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	84	84.0	84
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	58	63.0	68
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症							
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	8	8.0	8
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査	2 (1.3)	0 (0.0)	9 (6.3)	20 (10.9)	13	92.5	175
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	171	171.0	171
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	78	81.0	84
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	168	168.0	168
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood pressure increased	血圧上昇	1 (0.7)	0 (0.0)	0 (0.0)	4 (2.2)	13	38.5	88
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	2 (1.4)	3 (1.6)	39	168.0	175
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	168	168.0	168
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	169	169.0	169
Glucose urine present	尿中ブドウ糖陽性	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.1)	83	90.0	97
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	84	126.0	168

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査							
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	161	161.0	161
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	169	169.0	169
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	56	56.0	56
Weight increased	体重増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	84	84.0	84
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	172	172.0	172
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	166	166.0	166
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Metabolism and nutrition disorders	代謝および栄養障害	1 (0.7)	1 (0.7)	0 (0.0)	13 (7.1)	0	1.0	119
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	8	8.0	8
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperglycaemia	高血糖	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	91	91.0	91
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Decreased appetite	食欲減退	0 (0.0)	1 (0.7)	0 (0.0)	11 (6.0)	0	1.0	119
Hyperlipidaemia	高脂血症	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	91	91.0	91

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	2 (1.3)	0 (0.0)	4 (2.8)	15 (8.2)	0	21.0	164
Arthralgia	関節痛	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.5)	131	131.0	131
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Back pain	背部痛	2 (1.3)	0 (0.0)	1 (0.7)	6 (3.3)	8	77.0	163
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	2 (1.4)	2 (1.1)	163	163.5	164
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	8	8.0	8
Muscular weakness	筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Myalgia	筋肉痛	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	21	83.0	145
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0	1.5	3
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1	1.0	1
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1	1.0	1

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	0 (0.0)	0 (0.0)	2 (1.4)	63 (34.2)	0	0.0	146
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Burning sensation	灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Dizziness	浮動性めまい	0 (0.0)	0 (0.0)	0 (0.0)	20 (10.9)	0	0.0	30
Dizziness postural	体位性めまい	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	146	146.0	146
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysgeusia	味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	0	0.0	5
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Headache	頭痛	0 (0.0)	0 (0.0)	0 (0.0)	21 (11.4)	0	3.0	63
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1	1.0	1
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.6)	0	1.0	11
Masked facies	仮面状顔貌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	141	141.0	141
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	39	39.0	39
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene 10 mg (N=184)						
System organ class		First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害								
Somnolence	傾眠		0 (0.0)	0 (0.0)	0 (0.0)	18 (9.8)	0	0.0	14
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	67	67.0	67
Tremor	振戦		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Poor quality sleep	睡眠の質低下		0 (0.0)	0 (0.0)	1 (0.7)	5 (2.7)	0	0.0	165

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	1 (0.7)	0 (0.0)	1 (0.7)	29 (15.8)	0	1.0	149
Agitation	激越	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1	1.0	1
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	7	7.0	7
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anticipatory anxiety	予期不安	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anxiety	不安	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	78	116.0	154
Apathy	無感情	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	3	3.0	3
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	56	56.0	56
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Initial insomnia	初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Insomnia	不眠症	0 (0.0)	0 (0.0)	1 (0.7)	15 (8.2)	0	0.0	149
Irritability	易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0	0.0	0
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1	1.0	1
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Middle insomnia	中期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	5 (2.7)	0	0.0	27
Mood swings	気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害							
Sleep disorder	睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Stress	ストレス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	11	11.0	11
Suicidal ideation	自殺念慮	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.5)	106	106.0	106
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Renal and urinary disorders	腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.6)	5	11.0	49
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	49	49.0	49
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	11	11.0	11
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	5	5.0	5
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Reproductive system and breast disorders	生殖系および乳房障害	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	0	74.0	148
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erection increased	勃起増強	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	148	148.0	148
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	1 (0.7)	3 (2.1)	0 (0.0)	9 (4.9)	6	77.0	133
Choking sensation	息詰まり感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	18	18.0	18
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Epistaxis	鼻出血	1 (0.7)	1 (0.7)	0 (0.0)	3 (1.6)	16	109.0	114
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Respiration abnormal	呼吸異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.1)	77	100.5	124
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	6	6.0	6
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal discomfort	喉頭不快感	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.1)	7	70.0	133
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.5)	124	124.0	124

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	0 (0.0)	0 (0.0)	1 (0.7)	10 (5.4)	0	22.0	159
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	16	16.0	16
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	28	28.0	28
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	0	0.0	0
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash	発疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	159	159.0	159
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Urticaria	蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.6)	10	29.0	39

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene 10 mg (N=184)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害							
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.1)	0	28.0	56
Vascular disorders	血管障害	0 (0.0)	0 (0.0)	2 (1.4)	7 (3.8)	0	6.0	187
Hypertension	高血圧	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.5)	175	175.0	175
Hypotension	低血圧	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.1)	0	93.5	187
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Peripheral coldness	末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hot flush	ほてり	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.2)	0	3.0	49
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
N		432	424	397	386	377	364
Total number of subjects with TEAEs		274 (63.4)	24 (5.7)	14 (3.5)	5 (1.3)	12 (3.2)	15 (4.1)
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cardiac disorders	心臓障害	12 (2.8)	2 (0.5)	2 (0.5)	1 (0.3)	3 (0.8)	5 (1.4)
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Palpitations	動悸	12 (2.8)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)	2 (0.5)
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Tachycardia	頻脈	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Ear and labyrinth disorders	耳および迷路障害	12 (2.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Tinnitus	耳鳴	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Vertigo	回転性めまい	8 (1.9)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoacusis	聴力低下	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear discomfort	耳不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye disorders	眼障害	4 (0.9)	1 (0.2)	2 (0.5)	1 (0.3)	1 (0.3)	2 (0.5)
Abnormal sensation in eye	眼の異常感	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dry eye	眼乾燥	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Eye pain	眼痛	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid oedema	眼瞼浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Photophobia	羞明	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oscillopsia	動揺視	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害	166 (38.4)	14 (3.3)	8 (2.0)	2 (0.5)	13 (3.4)	2 (0.5)
Abdominal discomfort	腹部不快感	9 (2.1)	1 (0.2)	0 (0.0)	2 (0.5)	1 (0.3)	0 (0.0)
Abdominal distension	腹部膨満	10 (2.3)	1 (0.2)	0 (0.0)	1 (0.3)	1 (0.3)	1 (0.3)
Abdominal pain	腹痛	5 (1.2)	4 (0.9)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
Abdominal pain lower	下腹部痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abdominal pain upper	上腹部痛	0 (0.0)	1 (0.2)	1 (0.3)	0 (0.0)	2 (0.5)	0 (0.0)
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	便秘	10 (2.3)	3 (0.7)	2 (0.5)	0 (0.0)	3 (0.8)	0 (0.0)
Dental caries	齲歯	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
Diarrhoea	下痢	11 (2.5)	0 (0.0)	2 (0.5)	1 (0.3)	1 (0.3)	0 (0.0)
Dry mouth	口内乾燥	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dyspepsia	消化不良	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Food poisoning	食中毒	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gastritis	胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	悪心	121 (28.0)	5 (1.2)	5 (1.3)	0 (0.0)	4 (1.1)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene					
			Total (N=432)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Salivary hypersecretion	流涎過多		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stomatitis	口内炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Swollen tongue	舌腫脹		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Toothache	歯痛		2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Vomiting	嘔吐		30 (6.9)	2 (0.5)	6 (1.5)	0 (0.0)	1 (0.3)	6 (1.6)
Oral dysaesthesia	口腔知覚不全		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Haemorrhoidal haemorrhage	痔出血		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia oral	口の感覚鈍麻		1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Paraesthesia oral	口の錯感覚		1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oral mucosa haematoma	口腔粘膜血腫		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

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Safety Set

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		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	53 (12.3)	5 (1.2)	4 (1.0)	2 (0.5)	5 (1.3)	1 (0.3)
Asthenia	無力症	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Chest discomfort	胸部不快感	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chills	悪寒	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	死亡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discomfort	不快感	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fatigue	疲労	8 (1.9)	1 (0.2)	2 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)
Feeling abnormal	異常感	8 (1.9)	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Feeling drunk	酩酊感	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hangover	宿酔	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Malaise	倦怠感	22 (5.1)	0 (0.0)	1 (0.3)	0 (0.0)	3 (0.8)	0 (0.0)
Pain	疼痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態						
Pyrexia	発熱	2 (0.5)	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Thirst	口渇	10 (2.3)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peripheral swelling	末梢腫脹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Immune system disorders	免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Seasonal allergy	季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total					
		(N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症	17 (3.9)	9 (2.1)	8 (2.0)	6 (1.6)	12 (3.2)	19 (5.2)
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Conjunctivitis	結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cystitis	膀胱炎	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Gastroenteritis	胃腸炎	1 (0.2)	0 (0.0)	2 (0.5)	0 (0.0)	1 (0.3)	2 (0.5)
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gingivitis	歯肉炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Influenza	インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.8)
Nasopharyngitis	鼻咽頭炎	13 (3.0)	9 (2.1)	5 (1.3)	5 (1.3)	10 (2.7)	12 (3.3)
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Periodontitis	歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Infections and infestations	感染症および寄生虫症						
Pharyngitis	咽頭炎	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)	1 (0.3)
Rhinitis	鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)

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Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)	6 (1.6)
Accidental overdose	偶発的過量投与	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Spinal compression fracture	脊椎圧迫骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症						
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Tooth fracture	歯牙破折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	2 (0.5)	2 (0.5)	1 (0.3)	3 (0.8)	2 (0.5)	15 (4.1)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood pressure increased	血圧上昇	1 (0.2)	2 (0.5)	1 (0.3)	1 (0.3)	0 (0.0)	1 (0.3)
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査						
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
Weight increased	体重増加	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.3)
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Metabolism and nutrition disorders	代謝および栄養障害	15 (3.5)	8 (1.9)	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)
Dehydration	脱水	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperglycaemia	高血糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Increased appetite	食欲亢進	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Decreased appetite	食欲減退	15 (3.5)	5 (1.2)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	10 (2.3)	4 (0.9)	2 (0.5)	1 (0.3)	3 (0.8)	5 (1.4)
Arthralgia	関節痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Back pain	背部痛	2 (0.5)	2 (0.5)	1 (0.3)	0 (0.0)	2 (0.5)	1 (0.3)
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Muscle twitching	筋攣縮	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Muscular weakness	筋力低下	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Myalgia	筋肉痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	2 (0.5)
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal stiffness	筋骨格硬直	4 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Musculoskeletal discomfort	筋骨格不快感	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Ligamentitis	靭帯炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	134 (31.0)	7 (1.7)	2 (0.5)	1 (0.3)	9 (2.4)	7 (1.9)
Amnesia	健忘	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Autonomic nervous system imbalance	自律神経失調	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Burning sensation	灼熱感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in attention	注意力障害	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)
Dizziness	浮動性めまい	63 (14.6)	3 (0.7)	1 (0.3)	0 (0.0)	2 (0.5)	2 (0.5)
Dizziness postural	体位性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dysaesthesia	異常感覚	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dysgeusia	味覚異常	7 (1.6)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
Head discomfort	頭部不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Headache	頭痛	32 (7.4)	2 (0.5)	2 (0.5)	1 (0.3)	5 (1.3)	3 (0.8)
Hyperaesthesia	知覚過敏	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypoaesthesia	感覚鈍麻	7 (1.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Masked facies	仮面状顔貌	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Memory impairment	記憶障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mental impairment	精神的機能障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Myoclonus	ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Sedation	鎮静	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene					
			Total (N=432)					
System organ class		First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害							
Somnolence	傾眠		45 (10.4)	5 (1.2)	3 (0.8)	1 (0.3)	1 (0.3)	1 (0.3)
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Tremor	振戦		1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Poor quality sleep	睡眠の質低下		6 (1.4)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	50 (11.6)	6 (1.4)	5 (1.3)	4 (1.0)	2 (0.5)	5 (1.4)
Agitation	激越	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Alcoholic hangover	アルコールによる宿酔	1 (0.2)	2 (0.5)	1 (0.3)	1 (0.3)	0 (0.0)	1 (0.3)
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anticipatory anxiety	予期不安	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Anxiety	不安	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Apathy	無感情	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressed mood	抑うつ気分	3 (0.7)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dysphoria	不快気分	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Initial insomnia	初期不眠症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Insomnia	不眠症	30 (6.9)	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.3)
Irritability	易刺激性	2 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Libido decreased	リビドー減退	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Middle insomnia	中期不眠症	7 (1.6)	1 (0.2)	0 (0.0)	3 (0.8)	0 (0.0)	1 (0.3)
Mood swings	気分動揺	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Restlessness	落ち着きのなさ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

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Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害						
Sleep disorder	睡眠障害	2 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Stress	ストレス	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suicidal ideation	自殺念慮	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abulia	無為	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Depressive symptom	抑うつ症状	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Disturbance in sexual arousal	性的興奮障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Renal and urinary disorders	腎および尿路障害	4 (0.9)	1 (0.2)	0 (0.0)	1 (0.3)	1 (0.3)	0 (0.0)
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dysuria	排尿困難	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nocturia	夜間頻尿	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pollakiuria	頻尿	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	生殖系および乳房障害	4 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Erection increased	勃起増強	4 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erectile dysfunction	勃起不全	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	5 (1.2)	3 (0.7)	2 (0.5)	2 (0.5)	1 (0.3)	1 (0.3)
Choking sensation	息詰まり感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Epistaxis	鼻出血	0 (0.0)	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Respiration abnormal	呼吸異常	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Wheezing	喘鳴	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Laryngeal discomfort	喉頭不快感	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal discomfort	口腔咽頭不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	7 (1.6)	7 (1.7)	3 (0.8)	3 (0.8)	4 (1.1)	1 (0.3)
Acne	ざ瘡	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Cold sweat	冷汗	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dry skin	皮膚乾燥	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Eczema	湿疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema	紅斑	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)
Hyperhidrosis	多汗症	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Night sweats	寝汗	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash	発疹	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Urticaria	蕁麻疹	0 (0.0)	2 (0.5)	2 (0.5)	1 (0.3)	2 (0.5)	0 (0.0)

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene					
		Total (N=432)					
System organ class	First occurring day after first dose	0 <= - <= 6	7 <= - <= 13	14 <= - <= 20	21 <= - <= 28	29 <= - <= 56	57 <= - <= 84
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害						
Pruritus generalised	全身性そう痒症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Vascular disorders	血管障害	7 (1.6)	1 (0.2)	0 (0.0)	1 (0.3)	3 (0.8)	0 (0.0)
Hypertension	高血圧	0 (0.0)	1 (0.2)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)
Hypotension	低血圧	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Peripheral coldness	末梢冷感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hot flush	ほてり	5 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		353	339	334	432			
Total number of subjects with TEAEs		11 (3.1)	8 (2.4)	11 (3.3)	374 (86.6)	0	0.0	175
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.3)	0 (0.0)	1 (0.3)	2 (0.5)	91	129.5	168
Leukopenia	白血球減少症	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	168	168.0	168
Lymphadenopathy	リンパ節症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pancytopenia	汎血球減少症	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	91	91.0	91
Thrombocytopenia	血小板減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cardiac disorders	心臓障害	0 (0.0)	2 (0.6)	0 (0.0)	27 (6.3)	0	7.0	140
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Atrial fibrillation	心房細動	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	46	46.0	46
Atrioventricular block first degree	第一度房室ブロック	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	77	77.0	77
Palpitations	動悸	0 (0.0)	2 (0.6)	0 (0.0)	20 (4.6)	0	1.0	140
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	77	77.0	77
Tachycardia	頻脈	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	7	7.0	28
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	84	84.0	84
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	0 (0.0)	1 (0.3)	15 (3.5)	0	0.0	154
Motion sickness	乗物酔い	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	33	33.0	33
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.0	0
Vertigo	回転性めまい	0 (0.0)	0 (0.0)	1 (0.3)	10 (2.3)	0	0.0	154
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3	3.0	3
Ear discomfort	耳不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	2 (0.6)	0 (0.0)	0 (0.0)	3 (0.7)	84	86.0	104
Hyperprolactinaemia	高プロラクチン血症	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	84	85.0	86
Primary hyperaldosteronism	原発性アルドステロン症	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	104	104.0	104
Eye disorders	眼障害	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.5)	0	17.0	84
Abnormal sensation in eye	眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	9	9.0	9
Blepharospasm	眼瞼痙攣	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	80	80.0	80
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	22	22.0	22
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	38	38.0	38
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	15.5	31
Episcleritis	上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	84	84.0	84
Eye pain	眼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	17	17.0	17
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	19	19.0	19
Eyelid oedema	眼瞼浮腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Eyelid ptosis	眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ocular hyperaemia	眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Photophobia	羞明	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Oscillopsia	動揺視	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害	7 (2.0)	3 (0.9)	5 (1.5)	220 (50.9)	0	0.0	166
Abdominal discomfort	腹部不快感	1 (0.3)	1 (0.3)	2 (0.6)	17 (3.9)	0	1.0	166
Abdominal distension	腹部膨満	0 (0.0)	0 (0.0)	0 (0.0)	14 (3.2)	0	1.5	73
Abdominal pain	腹痛	0 (0.0)	1 (0.3)	1 (0.3)	13 (3.0)	0	9.0	161
Abdominal pain lower	下腹部痛	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	13	93.0	173
Abdominal pain upper	上腹部痛	0 (0.0)	2 (0.6)	2 (0.6)	8 (1.9)	9	88.5	159
Chronic gastritis	慢性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Constipation	便秘	2 (0.6)	0 (0.0)	1 (0.3)	21 (4.9)	1	7.0	142
Dental caries	齲歯	1 (0.3)	1 (0.3)	2 (0.6)	6 (1.4)	56	118.0	167
Diarrhoea	下痢	4 (1.1)	0 (0.0)	0 (0.0)	19 (4.4)	0	4.0	109
Dry mouth	口内乾燥	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	15.5	31
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	3 (0.9)	5 (1.2)	0	152.0	165
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	73	73.0	73
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	10	10.0	10
Gastritis	胃炎	0 (0.0)	1 (0.3)	1 (0.3)	3 (0.7)	42	119.0	160
Gastrooesophageal reflux disease	胃食道逆流性疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	69	69.0	69
Gingival bleeding	歯肉出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	29	29.0	29
Gingival pain	歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Haemorrhoids	痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nausea	悪心	1 (0.3)	1 (0.3)	0 (0.0)	137 (31.7)	0	0.0	138

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害							
Oral discomfort	口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Salivary hypersecretion	流涎過多	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	108	108.0	108
Stomatitis	口内炎	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.5)	101	101.5	102
Swollen tongue	舌腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	23	23.0	23
Toothache	歯痛	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	3	6.0	78
Vomiting	嘔吐	2 (0.6)	1 (0.3)	2 (0.6)	50 (11.6)	0	1.5	154
Oral dysaesthesia	口腔知覚不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Haemorrhoidal haemorrhage	痔出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypoaesthesia oral	口の感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	6	6.0	6
Oral mucosa haematoma	口腔粘膜血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	2 (0.6)	5 (1.5)	2 (0.6)	79 (18.3)	0	1.0	168
Asthenia	無力症	1 (0.3)	1 (0.3)	0 (0.0)	3 (0.7)	18	93.0	122
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Death	死亡	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	168	168.0	168
Discomfort	不快感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.0	0
Face oedema	顔面浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fatigue	疲労	1 (0.3)	2 (0.6)	0 (0.0)	15 (3.5)	0	2.0	114
Feeling abnormal	異常感	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.5)	0	0.0	52
Feeling cold	冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	63	63.0	63
Feeling drunk	酩酊感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.0	0
Feeling hot	熱感	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	110	110.0	110
Hangover	宿酔	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	40.0	66
Influenza like illness	インフルエンザ様疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injection site pain	注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Malaise	倦怠感	1 (0.3)	3 (0.9)	1 (0.3)	31 (7.2)	0	1.0	161
Pain	疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態							
Pyrexia	発熱	0 (0.0)	1 (0.3)	1 (0.3)	6 (1.4)	0	19.5	146
Thirst	口渇	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.5)	0	0.0	12
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Injection site swelling	注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatobiliary disorders	肝胆道系障害	1 (0.3)	0 (0.0)	4 (1.2)	6 (1.4)	41	168.0	175
Alcoholic liver disease	アルコール性肝疾患	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	90	90.0	90
Chronic hepatitis	慢性肝炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	41	41.0	41
Hepatic cirrhosis	肝硬変	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	168	168.0	168
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	2 (0.6)	2 (0.5)	168	171.5	175
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	168	168.0	168
Immune system disorders	免疫系障害	4 (1.1)	0 (0.0)	1 (0.3)	6 (1.4)	58	105.0	167
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	58	58.0	58
Seasonal allergy	季節性アレルギー	4 (1.1)	0 (0.0)	1 (0.3)	5 (1.2)	97	106.0	167

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	16 (4.5)	16 (4.7)	14 (4.2)	117 (27.1)	0	65.0	166
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	145	145.0	145
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bronchitis	気管支炎	1 (0.3)	0 (0.0)	1 (0.3)	2 (0.5)	89	127.0	165
Conjunctivitis	結膜炎	0 (0.0)	1 (0.3)	1 (0.3)	2 (0.5)	131	147.0	163
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	1 (0.3)	4 (0.9)	0	42.5	152
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	23	23.0	23
Gastroenteritis	胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.4)	5	30.5	76
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)	123	123.0	123
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Herpes virus infection	ヘルペスウイルス感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	65	65.0	65
Impetigo	膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Infection	感染	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	161	161.0	161
Influenza	インフルエンザ	1 (0.3)	0 (0.0)	1 (0.3)	5 (1.2)	61	83.0	174
Nasopharyngitis	鼻咽頭炎	12 (3.4)	14 (4.1)	14 (4.2)	94 (21.8)	0	70.5	166
Oesophageal candidiasis	食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	151	151.0	151
Otitis media	中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Periodontitis	歯周炎	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	85	85.0	85

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症							
Pharyngitis	咽頭炎	1 (0.3)	0 (0.0)	0 (0.0)	5 (1.2)	2	48.0	109
Rhinitis	鼻炎	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)	133	133.0	133
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinea pedis	足部白癬	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	65	65.0	65
Vulvovaginal candidiasis	外陰部腟カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	30	30.0	30
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Enteritis infectious	感染性腸炎	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)	113	113.0	113
Pneumonia bacterial	細菌性肺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	48	48.0	48
Oral herpes	口腔ヘルペス	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.5)	99	103.0	107
Candida cervicitis	カンジダ性子宮頚管炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	16	16.0	16

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TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	5 (1.4)	0 (0.0)	1 (0.3)	17 (3.9)	1	68.0	154
Accidental overdose	偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	1	11.0	29
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	60	60.0	60
Fall	転倒	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	62	86.0	110
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	79	79.0	79
Foot fracture	足骨折	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	101	101.0	101
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Head injury	頭部損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	79	79.0	79
Heat stroke	熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injury	損傷	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	103	103.0	103
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	154	154.0	154
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	54	54.0	54
Spinal compression fracture	脊椎圧迫骨折	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	79	83.5	88
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	84	84.0	84
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	58	63.0	68
Wound	創傷	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	106	106.0	106
Thermal burn	熱傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症							
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest injury	胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear abrasion	耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Post-traumatic neck syndrome	外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査	8 (2.3)	0 (0.0)	19 (5.7)	52 (12.0)	0	86.0	175
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.3)	0 (0.0)	1 (0.3)	3 (0.7)	84	87.0	172
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	2 (0.6)	3 (0.7)	84	171.0	172
Blood bilirubin increased	血中ビリルビン増加	1 (0.3)	0 (0.0)	0 (0.0)	3 (0.7)	78	84.0	87
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	166	166.0	166
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood glucose increased	血中ブドウ糖増加	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	84	126.0	168
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	84	129.5	175
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood pressure increased	血圧上昇	1 (0.3)	0 (0.0)	0 (0.0)	7 (1.6)	4	14.0	88
Blood prolactin decreased	血中プロラクチン減少	1 (0.3)	0 (0.0)	1 (0.3)	2 (0.5)	85	126.5	168
Blood prolactin increased	血中プロラクチン増加	1 (0.3)	0 (0.0)	5 (1.5)	9 (2.1)	39	166.0	175
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	1 (0.3)	3 (0.7)	82	84.0	168
Electrocardiogram QT prolonged	心電図QT延長	1 (0.3)	0 (0.0)	1 (0.3)	2 (0.5)	105	136.5	168
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	1 (0.3)	0 (0.0)	2 (0.6)	3 (0.7)	89	172.0	172
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	169	169.0	169
Glucose urine present	尿中ブドウ糖陽性	1 (0.3)	0 (0.0)	1 (0.3)	3 (0.7)	83	97.0	168
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	84	126.0	168

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表 2.7.4.7.1-14

Table 14.1.1.3-27

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Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査							
Liver function test abnormal	肝機能検査異常	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	161	161.0	161
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	169	169.0	169
Red blood cell count decreased	赤血球数減少	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	90	90.0	90
Weight decreased	体重減少	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	56	70.0	84
Weight increased	体重増加	0 (0.0)	0 (0.0)	2 (0.6)	5 (1.2)	0	84.0	166
White blood cell count decreased	白血球数減少	0 (0.0)	0 (0.0)	2 (0.6)	3 (0.7)	77	172.0	174
White blood cell count increased	白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	21	21.0	21
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	166	166.0	166
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	21	21.0	21
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	77	77.0	77
Metabolism and nutrition disorders	代謝および栄養障害	2 (0.6)	1 (0.3)	1 (0.3)	30 (6.9)	0	6.0	175
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperglycaemia	高血糖	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	91	91.0	91
Hyperkalaemia	高カリウム血症	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	175	175.0	175
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	13	13.0	13
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	11	11.0	11
Decreased appetite	食欲減退	1 (0.3)	1 (0.3)	0 (0.0)	24 (5.6)	0	1.0	119
Hyperlipidaemia	高脂血症	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	68	79.5	91

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表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	2 (0.6)	3 (0.9)	10 (3.0)	40 (9.3)	0	57.0	164
Arthralgia	関節痛	0 (0.0)	1 (0.3)	2 (0.6)	4 (0.9)	8	138.5	153
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	71	71.0	71
Back pain	背部痛	2 (0.6)	2 (0.6)	2 (0.6)	14 (3.2)	4	57.0	163
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	2 (0.6)	3 (0.7)	56	163.0	164
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Muscular weakness	筋力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Musculoskeletal pain	筋骨格痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	67	67.0	67
Myalgia	筋肉痛	0 (0.0)	1 (0.3)	2 (0.6)	6 (1.4)	21	100.5	146
Neck pain	頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	161	161.0	161
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	19	80.0	141
Trigger finger	弾発指	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	164	164.0	164
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.9)	0	2.0	3
Musculoskeletal discomfort	筋骨格不快感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.5	1
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	0 (0.0)	0 (0.0)	3 (0.9)	163 (37.7)	0	0.0	163
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Autonomic nervous system imbalance	自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Burning sensation	灼熱感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	0	0.0	61
Dizziness	浮動性めまい	0 (0.0)	0 (0.0)	0 (0.0)	71 (16.4)	0	0.0	82
Dizziness postural	体位性めまい	1 (0.3)	0 (0.0)	1 (0.3)	3 (0.7)	49	88.0	146
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Dysgeusia	味覚異常	0 (0.0)	0 (0.0)	0 (0.0)	9 (2.1)	0	0.0	70
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	17.5	35
Headache	頭痛	0 (0.0)	0 (0.0)	0 (0.0)	45 (10.4)	0	1.0	79
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	8 (1.9)	0	0.0	11
Masked facies	仮面状顔貌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Memory impairment	記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	141	141.0	141
Myoclonus	ミオクローヌス	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	39	73.5	108
Neuralgia	神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

			Nalmefene						
						Total (N=432)			
System organ class		First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害								
Somnolence	傾眠		0 (0.0)	1 (0.3)	0 (0.0)	57 (13.2)	0	0.0	126
Syncope	失神		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	67	67.0	67
Tremor	振戦		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Hyposmia	嗅覚減退		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Poor quality sleep	睡眠の質低下		0 (0.0)	0 (0.0)	2 (0.6)	9 (2.1)	0	0.0	165

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	1 (0.3)	1 (0.3)	1 (0.3)	75 (17.4)	0	1.0	149
Agitation	激越	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Alcoholic hangover	アルコールによる宿酔	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.4)	1	15.0	77
Alcoholism	アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anticipatory anxiety	予期不安	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	4	4.0	4
Anxiety	不安	0 (0.0)	0 (0.0)	1 (0.3)	5 (1.2)	0	3.0	154
Apathy	無感情	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3	3.0	3
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.9)	0	1.0	13
Depression	うつ病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	56	56.0	56
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Initial insomnia	初期不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Insomnia	不眠症	0 (0.0)	0 (0.0)	1 (0.3)	35 (8.1)	0	0.0	149
Irritability	易刺激性	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	14
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Listless	気力低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	63	63.0	63
Middle insomnia	中期不眠症	0 (0.0)	1 (0.3)	0 (0.0)	13 (3.0)	0	1.0	133
Mood swings	気分動揺	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	15	15.0	15
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Panic attack	パニック発作	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	51	51.0	51
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害							
Sleep disorder	睡眠障害	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	16
Stress	ストレス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	11	11.0	11
Suicidal ideation	自殺念慮	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	7	56.5	106
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	42.0	84
Alcohol withdrawal syndrome	アルコール離脱症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	4	4.0	4
Affect lability	感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in sexual arousal	性的興奮障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	41	41.0	41
Renal and urinary disorders	腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	7 (1.6)	0	5.0	49
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	49	49.0	49
Dysuria	排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	11	11.0	11
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	2.5	5
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	25

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Reproductive system and breast disorders	生殖系および乳房障害	0 (0.0)	0 (0.0)	2 (0.6)	9 (2.1)	0	8.0	148
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	45	45.0	45
Erection increased	勃起増強	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.9)	0	0.0	1
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	8	75.5	143
Premenstrual syndrome	月経前症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Uterine haemorrhage	子宮出血	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	148	148.0	148
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	12	12.0	12

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	2 (0.6)	3 (0.9)	0 (0.0)	19 (4.4)	0	18.0	133
Choking sensation	息詰まり感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	49	49.0	49
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	18	18.0	18
Dyspnoea	呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Epistaxis	鼻出血	1 (0.3)	1 (0.3)	0 (0.0)	4 (0.9)	12	62.5	114
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	24	24.0	24
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	27	27.0	27
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	24	24.0	24
Respiration abnormal	呼吸異常	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	1 (0.3)	0 (0.0)	2 (0.5)	77	100.5	124
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	6	6.0	6
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal discomfort	喉頭不快感	0 (0.0)	1 (0.3)	0 (0.0)	3 (0.7)	0	7.0	133
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Oropharyngeal pain	口腔咽頭痛	1 (0.3)	1 (0.3)	0 (0.0)	3 (0.7)	10	112.0	124

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	0 (0.0)	0 (0.0)	3 (0.9)	28 (6.5)	0	14.0	159
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	16	16.0	16
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	68	68.0	68
Drug eruption	薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	12	20.0	28
Eczema	湿疹	0 (0.0)	0 (0.0)	2 (0.6)	3 (0.7)	9	144.0	154
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	11	11.0	11
Erythema multiforme	多形紅斑	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	22	22.0	22
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	0
Hyperkeratosis	過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Night sweats	寝汗	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.0	0
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash	発疹	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	11	11.5	12
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.2)	159	159.0	159
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	37	37.0	37
Urticaria	蕁麻疹	0 (0.0)	0 (0.0)	0 (0.0)	7 (1.6)	10	18.0	39

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-14

Table 14.1.1.3-27

Incidences of Treatment-emergent Adverse Events by First Occurring day after First Dose by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

		Nalmefene						
		Total (N=432)						
System organ class	First occurring day after first dose	85 <= - <= 112	113 <= - <= 140	141 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害							
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	28.0	56
Vascular disorders	血管障害	0 (0.0)	0 (0.0)	3 (0.9)	15 (3.5)	0	7.0	187
Hypertension	高血圧	0 (0.0)	0 (0.0)	2 (0.6)	5 (1.2)	7	23.0	175
Hypotension	低血圧	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.5)	0	93.5	187
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	42	42.0	42
Peripheral coldness	末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Hot flush	ほてり	0 (0.0)	0 (0.0)	0 (0.0)	7 (1.6)	0	1.0	49
Product issues	製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Device failure	医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-27＞

表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		172	141	134	1	0	172			
Total number of subjects with adverse events		134 (77.9)	6 (4.3)	1 (0.7)	0 (0.0)	0 (-)	141 (82.0)	0	0.0	172
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	83	83.0	83
Anaemia	貧血	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	83	83.0	83
Pancytopenia	汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Cardiac disorders	心臓障害	7 (4.1)	1 (0.7)	1 (0.7)	0 (0.0)	0 (-)	9 (5.2)	0	1.0	175
Arrhythmia	不整脈	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	168	168.0	168
Bradycardia	徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Bundle branch block left	左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Bundle branch block right	右脚ブロック	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (-)	1 (0.6)	175	175.0	175
Palpitations	動悸	6 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	6 (3.5)	0	1.0	24
Supraventricular extrasystoles	上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Tachycardia	頻脈	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	24	24.0	24
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Ear and labyrinth disorders	耳および迷路障害	4 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	4 (2.3)	0	0.0	70
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Eustachian tube patulous	耳管開放	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	70	70.0	70
Hyperacusis	聴覚過敏	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Tinnitus	耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Vertigo	回転性めまい	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	0.0	0

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	77	83.5	90
Hyperprolactinaemia	高プロラクチン血症	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	77	83.5	90
Eye disorders	眼障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	1	1.0	1
Asthenopia	眼精疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Cataract	白内障	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	129	129.0	129
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Dry eye	眼乾燥	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	1	1.0	1
Eye allergy	眼のアレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Keratitis	角膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Scleritis	強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Corneal disorder	角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害	64 (37.2)	3 (2.1)	1 (0.7)	0 (0.0)	0 (-)	68 (39.5)	0	1.0	181
Abdominal discomfort	腹部不快感	8 (4.7)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	9 (5.2)	0	1.0	126
Abdominal distension	腹部膨満	3 (1.7)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	4 (2.3)	3	21.0	140
Abdominal pain	腹痛	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	58.5	117
Abdominal pain upper	上腹部痛	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	7	7.0	7
Chronic gastritis	慢性胃炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	77	77.0	77
Constipation	便秘	7 (4.1)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	8 (4.7)	0	4.0	129
Dental caries	齲歯	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	33	59.5	86
Diarrhoea	下痢	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (-)	2 (1.2)	31	106.0	181
Dry mouth	口内乾燥	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Dyspepsia	消化不良	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	7	17.5	28
Enterocolitis	腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Faeces hard	硬便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Food poisoning	食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gastric polyps	胃ポリープ	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	154	154.0	154
Gastric ulcer	胃潰瘍	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	154	154.0	154
Gastritis	胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	77	77.0	77

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害									
Nausea	悪心	41 (23.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	41 (23.8)	0	0.0	65
Salivary hypersecretion	流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Stomatitis	口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Toothache	歯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Vomiting	嘔吐	14 (8.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	14 (8.1)	0	1.0	81
Oral dysaesthesia	口腔知覚不全	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Large intestine polyp	大腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Paraesthesia oral	口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Faeces soft	軟便	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	33 (19.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	33 (19.2)	0	0.0	57
Asthenia	無力症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	42	42.0	42
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Chills	悪寒	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	10.5	21
Discomfort	不快感	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	9	9.0	9
Fatigue	疲労	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	0	0.0	7
Feeling abnormal	異常感	6 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	6 (3.5)	0	0.5	15
Feeling hot	熱感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	0.5	1
Hangover	宿酔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Malaise	倦怠感	15 (8.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	15 (8.7)	0	0.0	57
Pyrexia	発熱	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	7.5	15
Thirst	口渇	6 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	6 (3.5)	0	0.0	12
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Hepatobiliary disorders	肝胆道系障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	80	80.0	80
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hepatic function abnormal	肝機能異常	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	80	80.0	80
Hepatic steatosis	脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Immune system disorders	免疫系障害	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	18	66.0	141
Hypersensitivity	過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Seasonal allergy	季節性アレルギー	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	18	66.0	141

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	28 (16.3)	10 (7.1)	2 (1.5)	0 (0.0)	0 (-)	40 (23.3)	0	49.0	182
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Anisakiasis	アニサキス症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	58	58.0	58
Bronchitis	気管支炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	29	29.0	29
Conjunctivitis	結膜炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	67	67.0	67
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Diverticulitis	憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Empyema	蓄膿	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	104	104.0	104
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gastroenteritis	胃腸炎	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	8	36.0	152
Gastroenteritis viral	ウイルス性胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	24	24.0	24
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Influenza	インフルエンザ	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	47	68.5	90
Nasopharyngitis	鼻咽頭炎	17 (9.9)	11 (7.8)	2 (1.5)	0 (0.0)	0 (-)	30 (17.4)	1	75.5	182
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Pharyngitis	咽頭炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo (N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症									
Sialoadenitis	唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Sinusitis	副鼻腔炎	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	19.5	39
Viral diarrhoea	ウイルス性下痢	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	81	81.0	81
Gingival abscess	歯肉膿瘍	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	8	8.0	8
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gastroenteritis norovirus	ノロウイルス性胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	81	81.0	81

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	4 (2.3)	2 (1.4)	1 (0.7)	0 (0.0)	0 (-)	7 (4.1)	8	71.0	172
Accidental overdose	偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Alcohol poisoning	アルコール中毒	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	46	46.0	46
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Fibula fracture	腓骨骨折	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	49	49.0	49
Foot fracture	足骨折	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (-)	1 (0.6)	172	172.0	172
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Frostbite	凍傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hand fracture	手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Joint dislocation	関節脱臼	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	90	90.0	90
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Road traffic accident	交通事故	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	90	90.0	90
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo (N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症									
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Contusion	挫傷	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	71	80.5	90
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Tooth fracture	歯牙破折	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	8	8.0	8
Skin abrasion	皮膚擦過傷	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	116	116.0	116
Avulsion fracture	剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo (N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査	10 (5.8)	2 (1.4)	0 (0.0)	0 (0.0)	0 (-)	12 (7.0)	0	78.5	105
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	80	80.0	80
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood pressure increased	血圧上昇	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	1	2.0	24
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
C-reactive protein increased	Ｃ－反応性蛋白増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	84	84.0	84
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	86	86.0	86

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査									
Blood urine present	尿中血陽性	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	84	84.0	84
Heart rate decreased	心拍数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Weight decreased	体重減少	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	84	84.0	84
Weight increased	体重増加	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	11	58.0	105
Protein urine present	尿中蛋白陽性	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	77	77.0	77
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Urine output increased	尿量増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Occult blood positive	便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Metabolism and nutrition disorders	代謝および栄養障害	10 (5.8)	3 (2.1)	1 (0.7)	0 (0.0)	0 (-)	14 (8.1)	0	0.0	171
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Gout	痛風	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	112	112.0	112
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Dyslipidaemia	脂質異常症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (-)	1 (0.6)	171	171.0	171
Decreased appetite	食欲減退	10 (5.8)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	11 (6.4)	0	0.0	120
Hyperlipidaemia	高脂血症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	88	88.0	88

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	12 (7.0)	6 (4.3)	1 (0.7)	0 (0.0)	0 (-)	19 (11.0)	0	35.0	187
Arthralgia	関節痛	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	42.0	84
Arthritis	関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Back pain	背部痛	4 (2.3)	3 (2.1)	0 (0.0)	0 (0.0)	0 (-)	7 (4.1)	0	76.0	147
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Muscle spasms	筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Musculoskeletal pain	筋骨格痛	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	19	19.0	19
Myalgia	筋肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Osteochondrosis	骨端症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	21	21.0	21
Osteonecrosis	骨壊死	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	134	134.0	134
Osteoporosis	骨粗鬆症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	41	41.0	41
Pain in extremity	四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Periarthritis	関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Plantar fasciitis	足底筋膜炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	113	113.0	113
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害									
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Muscle tightness	筋緊張	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	0.5	1
Intervertebral disc protrusion	椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (-)	2 (1.2)	154	170.5	187
Musculoskeletal discomfort	筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	0.0	0
Finger deformity	指変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	77	77.0	77
Skin papilloma	皮膚乳頭腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	77	77.0	77
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	59 (34.3)	2 (1.4)	1 (0.7)	0 (0.0)	0 (-)	62 (36.0)	0	0.0	171
Akathisia	アカシジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	9	9.0	9
Amnesia	健忘	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	63	63.0	63
Disturbance in attention	注意力障害	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	45.0	90
Dizziness	浮動性めまい	26 (15.1)	2 (1.4)	0 (0.0)	0 (0.0)	0 (-)	28 (16.3)	0	0.0	166
Dizziness postural	体位性めまい	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	30	30.0	30
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Dysgeusia	味覚異常	7 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	7 (4.1)	0	0.0	1
Dyskinesia	ジスキネジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Head discomfort	頭部不快感	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	0	0.0	1
Headache	頭痛	12 (7.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	13 (7.6)	0	1.0	88
Hyperaesthesia	知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hypoaesthesia	感覚鈍麻	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	10.5	21
Mental impairment	精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Monoplegia	単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Paraesthesia	錯感覚	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Paralysis	麻痺	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害									
Sciatica	坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Sedation	鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Somnolence	傾眠	12 (7.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	12 (7.0)	0	0.0	84
Cubital tunnel syndrome	肘部管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Poor quality sleep	睡眠の質低下	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	0	0.0	0
Thrombotic cerebral infarction	血栓性脳梗塞	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (-)	1 (0.6)	171	171.0	171

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	37 (21.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	37 (21.5)	0	0.0	82
Abnormal dreams	異常な夢	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Alcoholic hangover	アルコールによる宿酔	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	0	6.0	61
Anxiety	不安	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	1	1.0	1
Depressed mood	抑うつ気分	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	1	1.0	1
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Euphoric mood	多幸気分	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	0	0.0	1
Hallucination, auditory	幻聴	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Insomnia	不眠症	12 (7.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	13 (7.6)	0	1.0	107
Irritability	易刺激性	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	0.0	0
Libido decreased	リビドー減退	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	21	21.0	21
Middle insomnia	中期不眠症	5 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	5 (2.9)	0	0.0	2
Nightmare	悪夢	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	7.0	14
Restlessness	落ち着きのなさ	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	82	82.0	82
Sleep disorder	睡眠障害	5 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	5 (2.9)	0	0.0	0
Tension	緊張	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	1	1.0	1
Abulia	無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo (N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害									
Mental disorder	精神障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Terminal insomnia	早朝覚醒型不眠症	4 (2.3)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	5 (2.9)	0	9.0	157
Renal and urinary disorders	腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Ureterolithiasis	尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Reproductive system and breast disorders	生殖系および乳房障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	1.0	2
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Erection increased	勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Prostatitis	前立腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Spontaneous penile erection	自発陰茎勃起	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	2	2.0	2
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo			
							(N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	2 (1.2)	2 (1.4)	0 (0.0)	0 (0.0)	0 (-)	4 (2.3)	7	75.5	126
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Epistaxis	鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hyperventilation	過換気	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	7	7.0	7
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Nasal inflammation	鼻の炎症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	126	126.0	126
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Upper respiratory tract inflammation	上気道の炎症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	48	48.0	48
Laryngeal discomfort	喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	103	103.0	103

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Placebo (N=172)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	12 (7.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	12 (7.0)	0	14.0	34
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Angioedema	血管浮腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	15	15.0	15
Cold sweat	冷汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Dry skin	皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Eczema	湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Erythema	紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hyperhidrosis	多汗症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	3	3.0	3
Night sweats	寝汗	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	15.0	30
Pruritus	そう痒症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	10	10.0	10
Rash	発疹	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	3 (1.7)	7	14.0	14
Rash generalised	全身性皮疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	14	14.0	14
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Urticaria	蕁麻疹	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	30	32.0	34
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001								
		Placebo (N=172)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Vascular disorders	血管障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	2 (1.2)	0	7.5	15
Hyperaemia	充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hypertension	高血圧	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	15	15.0	15
Hypotension	低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Orthostatic hypotension	起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	0 (0.0)	-	-	-
Hot flush	ほてり	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (-)	1 (0.6)	0	0.0	0

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-44＞

表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		137	137	137	134	129	137			
Total number of subjects with adverse events		108 (78.8)	10 (7.3)	5 (3.6)	2 (1.5)	0 (0.0)	125 (91.2)	0	0.0	278
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	91	91.0	91
Anaemia	貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pancytopenia	汎血球減少症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	91	91.0	91
Cardiac disorders	心臓障害	4 (2.9)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	6 (4.4)	0	69.0	178
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bradycardia	徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bundle branch block left	左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bundle branch block right	右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Palpitations	動悸	3 (2.2)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	5 (3.6)	0	61.0	178
Supraventricular extrasystoles	上室性期外収縮	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	77	77.0	77
Tachycardia	頻脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ear and labyrinth disorders	耳および迷路障害	5 (3.6)	1 (0.7)	3 (2.2)	0 (0.0)	1 (0.8)	10 (7.3)	0	77.5	364
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	188	188.0	188
Eustachian tube patulous	耳管開放	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperacusis	聴覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinnitus	耳鳴	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.5)	0	87.5	175
Vertigo	回転性めまい	4 (2.9)	1 (0.7)	1 (0.7)	0 (0.0)	1 (0.8)	7 (5.1)	0	1.0	364

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
System organ class / First occurring day after first dose		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	84	84.0	84
Hyperprolactinaemia	高プロラクチン血症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	84	84.0	84
Eye disorders	眼障害	1 (0.7)	0 (0.0)	5 (3.6)	1 (0.7)	2 (1.6)	9 (6.6)	84	197.0	372
Asthenopia	眼精疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.7)	363	363.0	363
Cataract	白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	182	257.5	333
Conjunctivitis allergic	アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry eye	眼乾燥	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	180	180.0	180
Eye allergy	眼のアレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.7)	372	372.0	372
Eye irritation	眼刺激	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	84	84.0	84
Eye swelling	眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Keratitis	角膜炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	217	217.0	217
Scleritis	強膜炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	197	197.0	197
Visual impairment	視力障害	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	188	188.0	188
Corneal disorder	角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			20 mg (N=137)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害		62 (45.3)	4 (2.9)	10 (7.3)	4 (3.0)	0 (0.0)	80 (58.4)	0	1.0	314
Abdominal discomfort	腹部不快感		5 (3.6)	1 (0.7)	6 (4.4)	0 (0.0)	0 (0.0)	12 (8.8)	0	150.5	184
Abdominal distension	腹部膨満		8 (5.8)	0 (0.0)	2 (1.5)	1 (0.7)	0 (0.0)	11 (8.0)	0	2.0	282
Abdominal pain	腹痛		3 (2.2)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.9)	5	53.5	168
Abdominal pain upper	上腹部痛		1 (0.7)	2 (1.5)	2 (1.5)	0 (0.0)	0 (0.0)	5 (3.6)	51	127.0	179
Chronic gastritis	慢性胃炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Constipation	便秘		7 (5.1)	1 (0.7)	2 (1.5)	1 (0.7)	0 (0.0)	11 (8.0)	1	17.0	331
Dental caries	齲歯		1 (0.7)	2 (1.5)	1 (0.7)	0 (0.0)	0 (0.0)	4 (2.9)	83	166.5	206
Diarrhoea	下痢		3 (2.2)	1 (0.7)	2 (1.5)	1 (0.7)	0 (0.0)	7 (5.1)	0	89.0	316
Dry mouth	口内乾燥		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dyspepsia	消化不良		0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	152	158.5	165
Enterocolitis	腸炎		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	73	73.0	73
Faeces hard	硬便		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Food poisoning	食中毒		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	10	10.0	10
Gastric polyps	胃ポリープ		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastric ulcer	胃潰瘍		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastritis	胃炎		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	42	42.0	42
Gastrooesophageal reflux disease	胃食道逆流性疾患		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			20 mg (N=137)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害										
Nausea	悪心		36 (26.3)	3 (2.2)	7 (5.1)	4 (3.0)	0 (0.0)	50 (36.5)	0	0.0	307
Salivary hypersecretion	流涎過多		0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	182	182.0	182
Stomatitis	口内炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Toothache	歯痛		3 (2.2)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	5 (3.6)	3	78.0	193
Vomiting	嘔吐		12 (8.8)	1 (0.7)	1 (0.7)	2 (1.5)	1 (0.8)	17 (12.4)	0	41.0	342
Oral dysaesthesia	口腔知覚不全		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Large intestine polyp	大腸ポリープ		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paraesthesia oral	口の錯感覚		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastrointestinal sounds abnormal	胃腸音異常		0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	174	174.0	174
Faeces soft	軟便		0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	31 (22.6)	3 (2.2)	6 (4.4)	1 (0.7)	1 (0.8)	42 (30.7)	0	3.0	346
Asthenia	無力症	1 (0.7)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	18	93.0	168
Chest discomfort	胸部不快感	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	8	8.0	8
Chest pain	胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chills	悪寒	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Discomfort	不快感	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Fatigue	疲労	5 (3.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	6 (4.4)	0	6.5	114
Feeling abnormal	異常感	5 (3.6)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	7 (5.1)	0	0.0	175
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hangover	宿酔	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	2 (1.5)	66	216.5	367
Malaise	倦怠感	13 (9.5)	2 (1.5)	3 (2.2)	1 (0.7)	1 (0.8)	20 (14.6)	0	5.0	346
Pyrexia	発熱	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2	6.5	11
Thirst	口渇	5 (3.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	6 (4.4)	0	0.0	175
Peripheral swelling	末梢腫脹	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1	1.0	1
Early satiety	早期満腹	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	179	179.0	179

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		20 mg (N=137)								
System organ class / First occurring day after first dose		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic steatosis	脂肪肝	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168
Immune system disorders	免疫系障害	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	58	83.5	109
Hypersensitivity	過敏症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	58	58.0	58
Seasonal allergy	季節性アレルギー	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	109	109.0	109

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
System organ class / Preferred term	First occurring day after first dose	0 <= - <= 84 n (%)	85 <= - <= 168 n (%)	169 <= - <= 252 n (%)	253 <= - <= 336 n (%)	337 <= n (%)	Total n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	22 (16.1)	22 (16.1)	11 (8.0)	7 (5.2)	1 (0.8)	63 (46.0)	1	129.0	364
Angular cheilitis	口角口唇炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	145	145.0	145
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis	結膜炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	131	131.0	131
Cystitis	膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)	259	278.0	297
Diverticulitis	憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Empyema	蓄膿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Furuncle	せつ	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	23	23.0	23
Gastroenteritis	胃腸炎	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	5	33.5	62
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	123	123.0	123
Gingivitis	歯肉炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1	1.0	1
Herpes zoster	帯状疱疹	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168
Infection	感染	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	161	161.0	161
Influenza	インフルエンザ	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	76	83.0	90
Nasopharyngitis	鼻咽頭炎	17 (12.4)	18 (13.1)	10 (7.3)	6 (4.5)	1 (0.8)	52 (38.0)	1	144.5	364
Otitis externa	外耳炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	151	151.0	151
Pharyngitis	咽頭炎	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	2	43.0	84

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症									
Sialoadenitis	唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Viral diarrhoea	ウイルス性下痢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingival abscess	歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	289	289.0	289
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	220	220.0	220
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	186	186.0	186
Oral herpes	口腔ヘルペス	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.5)	99	142.0	185
Gastroenteritis norovirus	ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.7)	5 (3.6)	6 (4.4)	4 (3.0)	0 (0.0)	16 (11.7)	11	195.5	308
Accidental overdose	偶発的過量投与	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	11	11.0	11
Alcohol poisoning	アルコール中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.8)	2 (1.5)	182	260.0	338
Fall	転倒	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	110	110.0	110
Fibula fracture	腓骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Foot fracture	足骨折	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	101	101.0	101
Fracture	骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Frostbite	凍傷	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	212	212.0	212
Hand fracture	手骨折	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	209	212.0	215
Injury	損傷	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	103	103.0	103
Joint dislocation	関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligament sprain	靭帯捻挫	0 (0.0)	1 (0.7)	2 (1.5)	0 (0.0)	0 (0.0)	3 (2.2)	154	170.0	249
Rib fracture	肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Road traffic accident	交通事故	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	219	219.0	219

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
System organ class / First occurring day after first dose		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症									
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	308	308.0	308
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)	253	280.5	308
Wound	創傷	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	106	106.0	106
Ligament injury	靱帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin abrasion	皮膚擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Avulsion fracture	剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)	266	281.0	296

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
System organ class / Preferred term	First occurring day after first dose	0 <= - <= 84 n (%)	85 <= - <= 168 n (%)	169 <= - <= 252 n (%)	253 <= - <= 336 n (%)	337 <= n (%)	Total n (%)	Min	Median	Max
Investigations	臨床検査	10 (7.3)	10 (7.3)	3 (2.2)	5 (3.7)	1 (0.8)	29 (21.2)	10	90.0	356
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.7)	1 (0.7)	1 (0.7)	0 (0.0)	1 (0.8)	4 (2.9)	84	129.5	343
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	3 (2.2)	84	172.0	256
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	87	87.0	87
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.8)	2 (1.5)	166	261.0	356
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	285	285.0	285
Blood potassium decreased	血中カリウム減少	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	84	84.0	84
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	260	260.0	260
Blood pressure increased	血圧上昇	2 (1.5)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.8)	4 (2.9)	10	104.5	342
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	85	126.5	168
Blood prolactin increased	血中プロラクチン増加	2 (1.5)	3 (2.2)	1 (0.7)	1 (0.7)	1 (0.8)	8 (5.8)	84	166.5	346
Blood triglycerides increased	血中トリグリセリド増加	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	82	83.0	84
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	188	188.0	188
C-reactive protein increased	C－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	256	256.0	256
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.7)	1 (0.7)	3 (2.2)	0 (0.0)	5 (3.6)	89	256.0	335
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Glucose urine present	尿中ブドウ糖陽性	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査									
Blood urine present	尿中血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Heart rate decreased	心拍数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	252	252.0	252
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	266	266.0	266
Red blood cell count decreased	赤血球数減少	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	90	90.0	90
Weight decreased	体重減少	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	84	84.0	84
Weight increased	体重増加	0 (0.0)	2 (1.5)	1 (0.7)	0 (0.0)	0 (0.0)	3 (2.2)	164	166.0	217
Protein urine present	尿中蛋白陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Urine output increased	尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Occult blood positive	便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Liver function test increased	肝機能検査値上昇	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.5)	77	199.0	321

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Metabolism and nutrition disorders	代謝および栄養障害	8 (5.8)	2 (1.5)	2 (1.5)	6 (4.5)	0 (0.0)	18 (13.1)	0	127.5	305
Dehydration	脱水	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	321	321.0	321
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	305	305.0	305
Gout	痛風	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	177	238.0	299
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	267	267.0	267
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	266	266.0	266
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	259	259.0	259
Hypovitaminosis	ビタミン欠乏症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	13	13.0	13
Increased appetite	食欲亢進	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	11	11.0	11
Dyslipidaemia	脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Decreased appetite	食欲減退	5 (3.6)	2 (1.5)	1 (0.7)	2 (1.5)	0 (0.0)	10 (7.3)	0	77.5	319
Hyperlipidaemia	高脂血症	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.5)	68	163.0	258

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	10 (7.3)	6 (4.4)	7 (5.1)	5 (3.7)	0 (0.0)	28 (20.4)	0	154.0	317
Arthralgia	関節痛	1 (0.7)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	3 (2.2)	8	146.0	170
Arthritis	関節炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	71	71.0	71
Back pain	背部痛	1 (0.7)	2 (1.5)	3 (2.2)	5 (3.7)	0 (0.0)	11 (8.0)	56	248.0	317
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	170	170.0	170
Muscle spasms	筋痙縮	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	56	56.0	56
Muscle twitching	筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Musculoskeletal pain	筋骨格痛	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.5)	67	149.0	231
Myalgia	筋肉痛	2 (1.5)	2 (1.5)	0 (0.0)	1 (0.7)	0 (0.0)	5 (3.6)	83	117.0	260
Osteochondrosis	骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Osteonecrosis	骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Osteoporosis	骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pain in extremity	四肢痛	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	161	161.0	161
Periarthritis	関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Plantar fasciitis	足底筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害									
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	223	223.0	223
Trigger finger	弾発指	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	164	164.0	164
Muscle tightness	筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Intervertebral disc protrusion	椎間板突出	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	180	180.0	180
Musculoskeletal stiffness	筋骨格硬直	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	3 (2.2)	1	3.0	363
Musculoskeletal discomfort	筋骨格不快感	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Finger deformity	指変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligamentitis	靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	2 (1.5)	309	314.5	320
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	320	320.0	320
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	309	309.0	309

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			20 mg (N=137)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害		45 (32.8)	0 (0.0)	14 (10.2)	3 (2.2)	1 (0.8)	63 (46.0)	0	1.0	342
Akathisia	アカシジア		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Amnesia	健忘		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in attention	注意力障害		2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	47	54.0	61
Dizziness	浮動性めまい		19 (13.9)	0 (0.0)	4 (2.9)	0 (0.0)	0 (0.0)	23 (16.8)	0	0.0	182
Dizziness postural	体位性めまい		1 (0.7)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	3 (2.2)	49	88.0	183
Dysaesthesia	異常感覚		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	8	8.0	8
Dysgeusia	味覚異常		2 (1.5)	0 (0.0)	6 (4.4)	0 (0.0)	0 (0.0)	8 (5.8)	0	178.5	188
Dyskinesia	ジスキネジア		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Head discomfort	頭部不快感		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	35	35.0	35
Headache	頭痛		4 (2.9)	0 (0.0)	6 (4.4)	0 (0.0)	2 (1.6)	12 (8.8)	0	172.0	342
Hyperaesthesia	知覚過敏		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypoaesthesia	感覚鈍麻		3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	0	0.0	1
Mental impairment	精神的機能障害		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Migraine	片頭痛		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	267	267.0	267
Monoplegia	単麻痺		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paraesthesia	錯感覚		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paralysis	麻痺		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			20 mg (N=137)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害										
Sciatica	坐骨神経痛		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	278	278.0	278
Sedation	鎮静		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Somnolence	傾眠		25 (18.2)	2 (1.5)	2 (1.5)	0 (0.0)	0 (0.0)	29 (21.2)	0	0.0	174
Cubital tunnel syndrome	肘部管症候群		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	306	306.0	306
Poor quality sleep	睡眠の質低下		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Thrombotic cerebral infarction	血栓性脳梗塞		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	21 (15.3)	3 (2.2)	2 (1.5)	2 (1.5)	0 (0.0)	28 (20.4)	0	15.0	307
Abnormal dreams	異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcoholic hangover	アルコールによる宿酔	4 (2.9)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	5 (3.6)	1	20.0	194
Anxiety	不安	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	286	286.0	286
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysphoria	不快気分	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Euphoric mood	多幸気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hallucination, auditory	幻聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Insomnia	不眠症	9 (6.6)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	11 (8.0)	0	0.0	307
Irritability	易刺激性	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168
Libido decreased	リビドー減退	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	168	168.0	168
Middle insomnia	中期不眠症	5 (3.6)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	7 (5.1)	0	21.0	252
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sleep disorder	睡眠障害	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	16	16.0	16
Tension	緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Abulia	無為	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	84	84.0	84
Depressive symptom	抑うつ症状	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	4	4.0	4

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害									
Mental disorder	精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Terminal insomnia	早朝覚醒型不眠症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	41	41.0	41
Renal and urinary disorders	腎および尿路障害	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.5)	168	168.5	169
Calculus urinary	尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nocturia	夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pollakiuria	頻尿	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.5)	168	168.5	169
Ureterolithiasis	尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Reproductive system and breast disorders	生殖系および乳房障害	5 (3.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	6 (4.4)	0	6.5	143
Dysmenorrhoea	月経困難症	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	45	45.0	45
Erection increased	勃起増強	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	0	0.0	1
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	143	143.0	143
Prostatitis	前立腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erectile dysfunction	勃起不全	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	12	12.0	12

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	6 (4.4)	1 (0.7)	1 (0.7)	2 (1.5)	0 (0.0)	10 (7.3)	0	38.0	308
Cough	咳嗽	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	49	49.0	49
Dry throat	咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Epistaxis	鼻出血	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	12	12.0	12
Hyperventilation	過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal pain	喉頭痛	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	24	24.0	24
Nasal congestion	鼻閉	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	27	27.0	27
Nasal inflammation	鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pneumothorax	気胸	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	24	24.0	24
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	262	262.0	262
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	214	214.0	214
Wheezing	喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal discomfort	喉頭不快感	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0	0.0	0
Oropharyngeal pain	口腔咽頭痛	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	0 (0.0)	4 (2.9)	10	188.5	308

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	8 (5.8)	2 (1.5)	1 (0.7)	3 (2.2)	0 (0.0)	14 (10.2)	0	43.0	329
Acne	ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Angioedema	血管浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	329	329.0	329
Dermatitis atopic	アトピー性皮膚炎	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	68	68.0	68
Dry skin	皮膚乾燥	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	12	12.0	12
Eczema	湿疹	1 (0.7)	2 (1.5)	0 (0.0)	1 (0.7)	0 (0.0)	4 (2.9)	9	149.0	315
Erythema	紅斑	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	11	11.0	11
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Night sweats	寝汗	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	2 (1.5)	0	91.5	183
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash	発疹	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	12	12.0	12
Rash generalised	全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash papular	丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	256	256.0	256
Urticaria	蕁麻疹	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	11	14.5	18
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			20 mg (N=137)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Vascular disorders	血管障害		3 (2.2)	0 (0.0)	2 (1.5)	1 (0.7)	0 (0.0)	6 (4.4)	23	108.5	256
Hyperaemia	充血		0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	176	176.0	176
Hypertension	高血圧		1 (0.7)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	3 (2.2)	23	175.0	256
Hypotension	低血圧		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Orthostatic hypotension	起立性低血圧		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	42	42.0	42
Hot flush	ほてり		1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	30	30.0	30

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-44＞

表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class / Preferred term		Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N			94	94	94	91	85	94			
Total number of subjects with adverse events			63 (67.0)	11 (11.7)	9 (9.6)	2 (2.2)	0 (0.0)	85 (90.4)	0	1.0	287
Blood and lymphatic system disorders	血液およびリンパ系障害		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anaemia	貧血		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pancytopenia	汎血球減少症		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cardiac disorders	心臓障害		3 (3.2)	1 (1.1)	6 (6.4)	2 (2.2)	1 (1.2)	13 (13.8)	5	196.0	350
Arrhythmia	不整脈		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bradycardia	徐脈		0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	182	182.0	182
Bundle branch block left	左脚ブロック		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.1)	350	350.0	350
Bundle branch block right	右脚ブロック		0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (2.1)	252	267.5	283
Palpitations	動悸		1 (1.1)	1 (1.1)	3 (3.2)	0 (0.0)	0 (0.0)	5 (5.3)	5	193.0	208
Supraventricular extrasystoles	上室性期外収縮		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tachycardia	頻脈		2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	3 (3.2)	7	28.0	221
Ventricular extrasystoles	心室性期外収縮		0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	336	336.0	336
Ear and labyrinth disorders	耳および迷路障害		0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	281	281.0	281
Deafness transitory	一過性難聴		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eustachian tube patulous	耳管開放		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperacusis	聴覚過敏		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinnitus	耳鳴		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Vertigo	回転性めまい		0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	281	281.0	281

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperprolactinaemia	高プロラクチン血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye disorders	眼障害	2 (2.1)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	4 (4.3)	0	123.5	256
Asthenopia	眼精疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cataract	白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis allergic	アレルギー性結膜炎	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	38	38.0	38
Dry eye	眼乾燥	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	2 (2.1)	0	128.0	256
Eye allergy	眼のアレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye irritation	眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Eye swelling	眼部腫脹	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	19	19.0	19
Keratitis	角膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Scleritis	強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Visual impairment	視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Corneal disorder	角膜障害	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	228	228.0	228

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			10 mg (N=94)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害		37 (39.4)	8 (8.5)	13 (13.8)	4 (4.4)	0 (0.0)	62 (66.0)	0	12.5	332
Abdominal discomfort	腹部不快感		3 (3.2)	1 (1.1)	2 (2.1)	1 (1.1)	0 (0.0)	7 (7.4)	0	143.0	286
Abdominal distension	腹部膨満		2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	21	47.0	73
Abdominal pain	腹痛		3 (3.2)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	5 (5.3)	0	11.0	161
Abdominal pain upper	上腹部痛		0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (2.1)	243	287.5	332
Chronic gastritis	慢性胃炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Constipation	便秘		2 (2.1)	1 (1.1)	3 (3.2)	0 (0.0)	0 (0.0)	6 (6.4)	3	139.5	222
Dental caries	齲歯		1 (1.1)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.2)	56	100.0	136
Diarrhoea	下痢		2 (2.1)	2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	5 (5.3)	1	101.0	285
Dry mouth	口内乾燥		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dyspepsia	消化不良		1 (1.1)	0 (0.0)	0 (0.0)	2 (2.2)	0 (0.0)	3 (3.2)	81	298.0	304
Enterocolitis	腸炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Faeces hard	硬便		0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	173	173.0	173
Food poisoning	食中毒		0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	276	276.0	276
Gastric polyps	胃ポリープ		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastric ulcer	胃潰瘍		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastritis	胃炎		0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	160	172.5	185
Gastrooesophageal reflux disease	胃食道逆流性疾患		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			10 mg (N=94)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害										
Nausea	悪心		27 (28.7)	1 (1.1)	4 (4.3)	0 (0.0)	0 (0.0)	32 (34.0)	0	0.0	182
Salivary hypersecretion	流涎過多		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Stomatitis	口内炎		0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	102	102.0	102
Toothache	歯痛		0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (2.1)	170	213.5	257
Vomiting	嘔吐		2 (2.1)	4 (4.3)	3 (3.2)	2 (2.2)	0 (0.0)	11 (11.7)	0	143.0	320
Oral dysaesthesia	口腔知覚不全		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Large intestine polyp	大腸ポリープ		0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	191	191.0	191
Paraesthesia oral	口の錯感覚		1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	6	6.0	6
Gastrointestinal sounds abnormal	胃腸音異常		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Faeces soft	軟便		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	9 (9.6)	2 (2.1)	7 (7.4)	1 (1.1)	1 (1.2)	20 (21.3)	0	133.0	371
Asthenia	無力症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest discomfort	胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Chest pain	胸痛	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.2)	2 (2.1)	180	275.5	371
Chills	悪寒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Discomfort	不快感	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0	0.0	0
Fatigue	疲労	3 (3.2)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	5 (5.3)	0	1.0	243
Feeling abnormal	異常感	2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	3 (3.2)	0	52.0	182
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hangover	宿酔	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	184	184.0	184
Malaise	倦怠感	2 (2.1)	1 (1.1)	3 (3.2)	0 (0.0)	0 (0.0)	6 (6.4)	0	171.5	198
Pyrexia	発熱	0 (0.0)	2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	3 (3.2)	120	146.0	285
Thirst	口渇	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	1	3.0	5
Peripheral swelling	末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Early satiety	早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene							
			10 mg (N=94)							
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Hepatobiliary disorders	肝胆道系障害		0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	90	90.0	90
Alcoholic liver disease	アルコール性肝疾患		0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	90	90.0	90
Hepatic function abnormal	肝機能異常		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic steatosis	脂肪肝		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Immune system disorders	免疫系障害		0 (0.0)	2 (2.1)	1 (1.1)	2 (2.2)	0 (0.0)	5 (5.3)	106	176.0	319
Hypersensitivity	過敏症		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Seasonal allergy	季節性アレルギー		0 (0.0)	2 (2.1)	1 (1.1)	2 (2.2)	0 (0.0)	5 (5.3)	106	176.0	319

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
System organ class / Preferred term	First occurring day after first dose	0 <= - <= 84 n (%)	85 <= - <= 168 n (%)	169 <= - <= 252 n (%)	253 <= - <= 336 n (%)	337 <= n (%)	Total n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	14 (14.9)	8 (8.5)	12 (12.8)	5 (5.5)	1 (1.2)	40 (42.6)	0	132.0	364
Angular cheilitis	口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis	結膜炎	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	163	163.0	163
Cystitis	膀胱炎	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0	76.0	152
Diverticulitis	憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.1)	353	353.0	353
Empyema	蓄膿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Furuncle	せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastroenteritis	胃腸炎	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	76	146.5	217
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingivitis	歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Herpes zoster	帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Infection	感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Influenza	インフルエンザ	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	2 (2.1)	174	230.5	287
Nasopharyngitis	鼻咽頭炎	12 (12.8)	9 (9.6)	10 (10.6)	3 (3.3)	1 (1.2)	35 (37.2)	0	127.0	364
Otitis externa	外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pharyngitis	咽頭炎	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	48	48.0	48

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症									
Sialoadenitis	唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	296	296.0	296
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Viral diarrhoea	ウイルス性下痢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingival abscess	歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	221	221.0	221
Oral herpes	口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastroenteritis norovirus	ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	207	207.0	207

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	2 (2.1)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	4 (4.3)	1	126.5	318
Accidental overdose	偶発的過量投与	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1	1.0	1
Alcohol poisoning	アルコール中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fall	転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fibula fracture	腓骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Foot fracture	足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Fracture	骨折	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	199	199.0	199
Frostbite	凍傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hand fracture	手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Injury	損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Joint dislocation	関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligament sprain	靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rib fracture	肋骨骨折	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	54	54.0	54
Road traffic accident	交通事故	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症									
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Wound	創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligament injury	靱帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	318	318.0	318
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin abrasion	皮膚擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Avulsion fracture	剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	318	318.0	318
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
System organ class / Preferred term	First occurring day after first dose	0 <= - <= 84 n (%)	85 <= - <= 168 n (%)	169 <= - <= 252 n (%)	253 <= - <= 336 n (%)	337 <= n (%)	Total n (%)	Min	Median	Max
Investigations	臨床検査	5 (5.3)	4 (4.3)	7 (7.4)	2 (2.2)	1 (1.2)	19 (20.2)	13	169.0	343
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	171	171.0	171
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood potassium decreased	血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood pressure increased	血圧上昇	3 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.2)	13	14.0	63
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Blood prolactin increased	血中プロラクチン増加	0 (0.0)	1 (1.1)	2 (2.1)	0 (0.0)	0 (0.0)	3 (3.2)	168	175.0	252
Blood triglycerides increased	血中トリグリセリド増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.1)	341	341.0	341
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
C-reactive protein increased	Ｃ－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.2)	2 (2.1)	168	255.5	343
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	169	169.0	169
Glucose urine present	尿中ブドウ糖陽性	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	83	90.0	97

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査									
Blood urine present	尿中血陽性	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	168	168.0	168
Heart rate decreased	心拍数減少	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	235	235.0	235
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Red blood cell count decreased	赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Weight decreased	体重減少	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	56	129.5	203
Weight increased	体重増加	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	84	156.0	228
Protein urine present	尿中蛋白陽性	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	166	166.0	166
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	259	259.0	259
Urine output increased	尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Occult blood positive	便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	303	303.0	303
Liver function test increased	肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Metabolism and nutrition disorders	代謝および栄養障害	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0	4.0	8
Dehydration	脱水	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	8	8.0	8
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gout	痛風	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypovitaminosis	ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Increased appetite	食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dyslipidaemia	脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Decreased appetite	食欲減退	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0	0.0	0
Hyperlipidaemia	高脂血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			10 mg (N=94)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害		5 (5.3)	4 (4.3)	4 (4.3)	4 (4.4)	2 (2.4)	19 (20.2)	1	171.0	382
Arthralgia	関節痛		0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	131	151.0	171
Arthritis	関節炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Back pain	背部痛		2 (2.1)	3 (3.2)	1 (1.1)	3 (3.3)	0 (0.0)	9 (9.6)	18	163.0	330
Muscle rigidity	筋固縮		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Muscle spasms	筋痙縮		0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	163	163.0	163
Muscle twitching	筋攣縮		1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	8	8.0	8
Musculoskeletal pain	筋骨格痛		0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	252	252.0	252
Myalgia	筋肉痛		0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	305	305.0	305
Osteochondrosis	骨端症		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Osteonecrosis	骨壊死		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Osteoporosis	骨粗鬆症		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pain in extremity	四肢痛		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Periarthritis	関節周囲炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.1)	382	382.0	382
Plantar fasciitis	足底筋膜炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Spinal osteoarthritis	変形性脊椎症		0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	190	190.0	190

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害									
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Trigger finger	弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Muscle tightness	筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Intervertebral disc protrusion	椎間板突出	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.1)	342	342.0	342
Musculoskeletal discomfort	筋骨格不快感	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1	1.0	1
Finger deformity	指変形	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	276	276.0	276
Ligamentitis	靭帯炎	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1	1.0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
System organ class / First occurring day after first dose		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	20 (21.3)	3 (3.2)	5 (5.3)	4 (4.4)	0 (0.0)	32 (34.0)	0	5.5	320
Akathisia	アカシジア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Amnesia	健忘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in attention	注意力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dizziness	浮動性めまい	6 (6.4)	1 (1.1)	3 (3.2)	0 (0.0)	0 (0.0)	10 (10.6)	0	1.0	206
Dizziness postural	体位性めまい	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	173	173.0	173
Dysaesthesia	異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dysgeusia	味覚異常	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0	2.5	5
Dyskinesia	ジスキネジア	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Headache	頭痛	6 (6.4)	2 (2.1)	4 (4.3)	2 (2.2)	0 (0.0)	14 (14.9)	0	168.0	320
Hyperaesthesia	知覚過敏	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	1	1.0	1
Hypoaesthesia	感覚鈍麻	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Mental impairment	精神的機能障害	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0	0.0	0
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Monoplegia	単麻痺	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	141	141.0	141
Paraesthesia	錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paralysis	麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			10 mg (N=94)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害										
Sciatica	坐骨神経痛		0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	288	288.0	288
Sedation	鎮静		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Somnolence	傾眠		8 (8.5)	0 (0.0)	2 (2.1)	1 (1.1)	0 (0.0)	11 (11.7)	0	1.0	281
Cubital tunnel syndrome	肘部管症候群		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Poor quality sleep	睡眠の質低下		0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	165	165.0	165
Thrombotic cerebral infarction	血栓性脳梗塞		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
System organ class / First occurring day after first dose		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	9 (9.6)	0 (0.0)	5 (5.3)	1 (1.1)	0 (0.0)	15 (16.0)	0	4.0	288
Abnormal dreams	異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcoholic hangover	アルコールによる宿酔	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	7	129.0	251
Anxiety	不安	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	170	170.0	170
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	266	266.0	266
Dysphoria	不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Euphoric mood	多幸気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hallucination, auditory	幻聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Insomnia	不眠症	6 (6.4)	0 (0.0)	2 (2.1)	1 (1.1)	0 (0.0)	9 (9.6)	0	3.0	288
Irritability	易刺激性	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	172	172.0	172
Libido decreased	リビドー減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Middle insomnia	中期不眠症	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	1	88.0	175
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sleep disorder	睡眠障害	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0	0.0	0
Tension	緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Abulia	無為	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	172	172.0	172
Depressive symptom	抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害									
Mental disorder	精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Renal and urinary disorders	腎および尿路障害	2 (2.1)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	3 (3.2)	5	49.0	314
Calculus urinary	尿路結石	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	49	49.0	49
Nocturia	夜間頻尿	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	5	5.0	5
Pollakiuria	頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ureterolithiasis	尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	314	314.0	314
Reproductive system and breast disorders	生殖系および乳房障害	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	0	111.5	223
Dysmenorrhoea	月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erection increased	勃起増強	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0	0.0	0
Metrorrhagia	不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Prostatitis	前立腺炎	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	223	223.0	223
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erectile dysfunction	勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	2 (2.1)	4 (4.3)	2 (2.1)	0 (0.0)	0 (0.0)	8 (8.5)	6	119.0	203
Cough	咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry throat	咽喉乾燥	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	18	18.0	18
Epistaxis	鼻出血	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	109	111.5	114
Hyperventilation	過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal pain	喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nasal congestion	鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Nasal inflammation	鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pneumothorax	気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	124	124.0	124
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	178	178.0	178
Wheezing	喘鳴	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	6	6.0	6
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal discomfort	喉頭不快感	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	133	133.0	133
Oropharyngeal pain	口腔咽頭痛	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)	0 (0.0)	2 (2.1)	124	163.5	203

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			10 mg (N=94)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害		5 (5.3)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	6 (6.4)	10	28.5	159
Acne	ざ瘡		1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	16	16.0	16
Angioedema	血管浮腫		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cold sweat	冷汗		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis	皮膚炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis atopic	アトピー性皮膚炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dry skin	皮膚乾燥		1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	28	28.0	28
Eczema	湿疹		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erythema	紅斑		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperhidrosis	多汗症		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Night sweats	寝汗		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pruritus	そう痒症		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash	発疹		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash generalised	全身性皮疹		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash papular	丘疹性皮疹		0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	159	159.0	159
Seborrhoeic dermatitis	脂漏性皮膚炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Urticaria	蕁麻疹		2 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	10	19.5	29
Pruritus generalised	全身性そう痒症		1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	56	56.0	56

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			10 mg (N=94)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Vascular disorders	血管障害		3 (3.2)	1 (1.1)	3 (3.2)	0 (0.0)	0 (0.0)	7 (7.4)	0	165.0	182
Hyperaemia	充血		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hypertension	高血圧		0 (0.0)	1 (1.1)	2 (2.1)	0 (0.0)	0 (0.0)	3 (3.2)	165	175.0	182
Hypotension	低血圧		1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0	0.0	0
Orthostatic hypotension	起立性低血圧		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hot flush	ほてり		2 (2.1)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	3 (3.2)	0	6.0	178

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-44＞

表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		231	231	231	225	214	231			
Total number of subjects with adverse events		171 (74.0)	21 (9.1)	14 (6.1)	4 (1.8)	0 (0.0)	210 (90.9)	0	1.0	287
Blood and lymphatic system disorders	血液およびリンパ系障害	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	91	91.0	91
Anaemia	貧血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pancytopenia	汎血球減少症	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	91	91.0	91
Cardiac disorders	心臓障害	7 (3.0)	2 (0.9)	7 (3.0)	2 (0.9)	1 (0.5)	19 (8.2)	0	178.0	350
Arrhythmia	不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bradycardia	徐脈	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	182	182.0	182
Bundle branch block left	左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	350	350.0	350
Bundle branch block right	右脚ブロック	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	252	267.5	283
Palpitations	動悸	4 (1.7)	2 (0.9)	4 (1.7)	0 (0.0)	0 (0.0)	10 (4.3)	0	150.5	208
Supraventricular extrasystoles	上室性期外収縮	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	77	77.0	77
Tachycardia	頻脈	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	3 (1.3)	7	28.0	221
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	336	336.0	336
Ear and labyrinth disorders	耳および迷路障害	5 (2.2)	1 (0.4)	3 (1.3)	1 (0.4)	1 (0.5)	11 (4.8)	0	154.0	364
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	188	188.0	188
Eustachian tube patulous	耳管開放	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hyperacusis	聴覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Tinnitus	耳鳴	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	0	87.5	175
Vertigo	回転性めまい	4 (1.7)	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.5)	8 (3.5)	0	77.5	364

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Hyperprolactinaemia	高プロラクチン血症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Eye disorders	眼障害	3 (1.3)	0 (0.0)	6 (2.6)	2 (0.9)	2 (0.9)	13 (5.6)	0	197.0	372
Asthenopia	眼精疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	363	363.0	363
Cataract	白内障	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	182	257.5	333
Conjunctivitis allergic	アレルギー性結膜炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	38	38.0	38
Dry eye	眼乾燥	1 (0.4)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	3 (1.3)	0	180.0	256
Eye allergy	眼のアレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	372	372.0	372
Eye irritation	眼刺激	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Eye swelling	眼部腫脹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	19	19.0	19
Keratitis	角膜炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	217	217.0	217
Scleritis	強膜炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	197	197.0	197
Visual impairment	視力障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	188	188.0	188
Corneal disorder	角膜障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	228	228.0	228

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			Total (N=231)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害		99 (42.9)	12 (5.2)	23 (10.0)	8 (3.6)	0 (0.0)	142 (61.5)	0	3.0	332
Abdominal discomfort	腹部不快感		8 (3.5)	2 (0.9)	8 (3.5)	1 (0.4)	0 (0.0)	19 (8.2)	0	143.0	286
Abdominal distension	腹部膨満		10 (4.3)	0 (0.0)	2 (0.9)	1 (0.4)	0 (0.0)	13 (5.6)	0	3.0	282
Abdominal pain	腹痛		6 (2.6)	3 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	9 (3.9)	0	49.0	168
Abdominal pain upper	上腹部痛		1 (0.4)	2 (0.9)	3 (1.3)	1 (0.4)	0 (0.0)	7 (3.0)	51	169.0	332
Chronic gastritis	慢性胃炎		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Constipation	便秘		9 (3.9)	2 (0.9)	5 (2.2)	1 (0.4)	0 (0.0)	17 (7.4)	1	36.0	331
Dental caries	齲歯		2 (0.9)	4 (1.7)	1 (0.4)	0 (0.0)	0 (0.0)	7 (3.0)	56	136.0	206
Diarrhoea	下痢		5 (2.2)	3 (1.3)	2 (0.9)	2 (0.9)	0 (0.0)	12 (5.2)	0	95.0	316
Dry mouth	口内乾燥		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dyspepsia	消化不良		1 (0.4)	2 (0.9)	0 (0.0)	2 (0.9)	0 (0.0)	5 (2.2)	81	165.0	304
Enterocolitis	腸炎		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	73	73.0	73
Faeces hard	硬便		0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	173	173.0	173
Food poisoning	食中毒		1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.9)	10	143.0	276
Gastric polyps	胃ポリープ		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastric ulcer	胃潰瘍		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gastritis	胃炎		1 (0.4)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	3 (1.3)	42	160.0	185
Gastrooesophageal reflux disease	胃食道逆流性疾患		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			Total (N=231)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害										
Nausea	悪心		63 (27.3)	4 (1.7)	11 (4.8)	4 (1.8)	0 (0.0)	82 (35.5)	0	0.0	307
Salivary hypersecretion	流涎過多		0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	182	182.0	182
Stomatitis	口内炎		0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	102	102.0	102
Toothache	歯痛		3 (1.3)	1 (0.4)	2 (0.9)	1 (0.4)	0 (0.0)	7 (3.0)	3	163.0	257
Vomiting	嘔吐		14 (6.1)	5 (2.2)	4 (1.7)	4 (1.8)	1 (0.5)	28 (12.1)	0	82.0	342
Oral dysaesthesia	口腔知覚不全		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Large intestine polyp	大腸ポリープ		0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	191	191.0	191
Paraesthesia oral	口の錯感覚		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	6	6.0	6
Gastrointestinal sounds abnormal	胃腸音異常		0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	174	174.0	174
Faeces soft	軟便		0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	168	168.0	168

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	40 (17.3)	5 (2.2)	13 (5.6)	2 (0.9)	2 (0.9)	62 (26.8)	0	7.0	371
Asthenia	無力症	1 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	18	93.0	168
Chest discomfort	胸部不快感	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	8	8.0	8
Chest pain	胸痛	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	2 (0.9)	180	275.5	371
Chills	悪寒	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Discomfort	不快感	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0	0.0	0
Fatigue	疲労	8 (3.5)	1 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	11 (4.8)	0	2.0	243
Feeling abnormal	異常感	7 (3.0)	0 (0.0)	3 (1.3)	0 (0.0)	0 (0.0)	10 (4.3)	0	24.5	182
Feeling hot	熱感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hangover	宿酔	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	3 (1.3)	66	184.0	367
Malaise	倦怠感	15 (6.5)	3 (1.3)	6 (2.6)	1 (0.4)	1 (0.5)	26 (11.3)	0	10.5	346
Pyrexia	発熱	2 (0.9)	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)	5 (2.2)	2	120.0	285
Thirst	口渇	7 (3.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	8 (3.5)	0	0.5	175
Peripheral swelling	末梢腫脹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Early satiety	早期満腹	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	179	179.0	179

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	90	129.0	168
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	90	90.0	90
Hepatic function abnormal	肝機能異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hepatic steatosis	脂肪肝	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	168	168.0	168
Immune system disorders	免疫系障害	1 (0.4)	3 (1.3)	1 (0.4)	2 (0.9)	0 (0.0)	7 (3.0)	58	167.0	319
Hypersensitivity	過敏症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	58	58.0	58
Seasonal allergy	季節性アレルギー	0 (0.0)	3 (1.3)	1 (0.4)	2 (0.9)	0 (0.0)	6 (2.6)	106	171.5	319

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
							Total (N=231)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	36 (15.6)	30 (13.0)	23 (10.0)	12 (5.3)	2 (0.9)	103 (44.6)	0	129.0	364
Angular cheilitis	口角口唇炎	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	145	145.0	145
Anisakiasis	アニサキス症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Bronchitis	気管支炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Conjunctivitis	結膜炎	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	131	147.0	163
Cystitis	膀胱炎	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	0 (0.0)	4 (1.7)	0	205.5	297
Diverticulitis	憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	353	353.0	353
Empyema	蓄膿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Furuncle	せつ	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	23	23.0	23
Gastroenteritis	胃腸炎	3 (1.3)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	4 (1.7)	5	69.0	217
Gastroenteritis viral	ウイルス性胃腸炎	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	123	123.0	123
Gingivitis	歯肉炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Herpes zoster	帯状疱疹	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	168	168.0	168
Infection	感染	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	161	161.0	161
Influenza	インフルエンザ	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)	0 (0.0)	4 (1.7)	76	132.0	287
Nasopharyngitis	鼻咽頭炎	29 (12.6)	27 (11.7)	20 (8.7)	9 (4.0)	2 (0.9)	87 (37.7)	0	137.0	364
Otitis externa	外耳炎	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	151	151.0	151
Pharyngitis	咽頭炎	3 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	2	48.0	84

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症									
Sialoadenitis	唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	296	296.0	296
Sinusitis	副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Viral diarrhoea	ウイルス性下痢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Gingival abscess	歯肉膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	289	289.0	289
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	220	220.0	220
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	186	203.5	221
Oral herpes	口腔ヘルペス	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	99	142.0	185
Gastroenteritis norovirus	ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	207	207.0	207

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
							Total (N=231)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	3 (1.3)	5 (2.2)	7 (3.0)	5 (2.2)	0 (0.0)	20 (8.7)	1	190.5	318
Accidental overdose	偶発的過量投与	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	1	6.0	11
Alcohol poisoning	アルコール中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	2 (0.9)	182	260.0	338
Fall	転倒	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	110	110.0	110
Fibula fracture	腓骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Foot fracture	足骨折	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	101	101.0	101
Fracture	骨折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	199	199.0	199
Frostbite	凍傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	212	212.0	212
Hand fracture	手骨折	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	209	212.0	215
Injury	損傷	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	103	103.0	103
Joint dislocation	関節脱臼	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Ligament sprain	靭帯捻挫	0 (0.0)	1 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	3 (1.3)	154	170.0	249
Rib fracture	肋骨骨折	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	54	54.0	54
Road traffic accident	交通事故	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	219	219.0	219

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
							Total (N=231)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症									
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	308	308.0	308
Contusion	挫傷	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)	253	280.5	308
Wound	創傷	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	106	106.0	106
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	318	318.0	318
Tooth fracture	歯牙破折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Skin abrasion	皮膚擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Avulsion fracture	剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	318	318.0	318
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)	266	281.0	296

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
							Total (N=231)			
System organ class / Preferred term	First occurring day after first dose	0 <= - <= 84 n (%)	85 <= - <= 168 n (%)	169 <= - <= 252 n (%)	253 <= - <= 336 n (%)	337 <= n (%)	Total n (%)	Min	Median	Max
Investigations	臨床検査	15 (6.5)	14 (6.1)	10 (4.3)	7 (3.1)	2 (0.9)	48 (20.8)	10	166.5	356
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.4)	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.5)	4 (1.7)	84	129.5	343
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.4)	0 (0.0)	2 (0.9)	1 (0.4)	0 (0.0)	4 (1.7)	84	171.5	256
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	87	87.0	87
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.9)	166	261.0	356
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	285	285.0	285
Blood potassium decreased	血中カリウム減少	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	84	84.0	84
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	260	260.0	260
Blood pressure increased	血圧上昇	5 (2.2)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.5)	7 (3.0)	10	28.0	342
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	85	126.5	168
Blood prolactin increased	血中プロラクチン増加	2 (0.9)	4 (1.7)	3 (1.3)	1 (0.4)	1 (0.5)	11 (4.8)	84	168.0	346
Blood triglycerides increased	血中トリグリセリド増加	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	3 (1.3)	82	84.0	341
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	188	188.0	188
C-reactive protein increased	Ｃ－反応性蛋白増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	1 (0.5)	3 (1.3)	168	256.0	343
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.4)	1 (0.4)	3 (1.3)	0 (0.0)	5 (2.2)	89	256.0	335
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	169	169.0	169
Glucose urine present	尿中ブドウ糖陽性	1 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	83	97.0	168

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査									
Blood urine present	尿中血陽性	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	168	168.0	168
Heart rate decreased	心拍数減少	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	235	235.0	235
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	252	252.0	252
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	266	266.0	266
Red blood cell count decreased	赤血球数減少	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	90	90.0	90
Weight decreased	体重減少	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	3 (1.3)	56	84.0	203
Weight increased	体重増加	1 (0.4)	2 (0.9)	2 (0.9)	0 (0.0)	0 (0.0)	5 (2.2)	84	166.0	228
Protein urine present	尿中蛋白陽性	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	166	166.0	166
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	259	259.0	259
Urine output increased	尿量増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Occult blood positive	便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	303	303.0	303
Liver function test increased	肝機能検査値上昇	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.9)	77	199.0	321

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Metabolism and nutrition disorders	代謝および栄養障害	10 (4.3)	2 (0.9)	2 (0.9)	6 (2.7)	0 (0.0)	20 (8.7)	0	77.5	305
Dehydration	脱水	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.9)	8	164.5	321
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	305	305.0	305
Gout	痛風	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	177	238.0	299
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	267	267.0	267
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	266	266.0	266
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	259	259.0	259
Hypovitaminosis	ビタミン欠乏症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	13	13.0	13
Increased appetite	食欲亢進	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	11	11.0	11
Dyslipidaemia	脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Decreased appetite	食欲減退	6 (2.6)	2 (0.9)	1 (0.4)	2 (0.9)	0 (0.0)	11 (4.8)	0	68.0	319
Hyperlipidaemia	高脂血症	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.9)	68	163.0	258

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
							Total (N=231)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	15 (6.5)	10 (4.3)	11 (4.8)	9 (4.0)	2 (0.9)	47 (20.3)	0	163.0	382
Arthralgia	関節痛	1 (0.4)	2 (0.9)	2 (0.9)	0 (0.0)	0 (0.0)	5 (2.2)	8	146.0	171
Arthritis	関節炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	71	71.0	71
Back pain	背部痛	3 (1.3)	5 (2.2)	4 (1.7)	8 (3.6)	0 (0.0)	20 (8.7)	18	240.0	330
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	170	170.0	170
Muscle spasms	筋痙縮	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	56	109.5	163
Muscle twitching	筋攣縮	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	8	8.0	8
Musculoskeletal pain	筋骨格痛	1 (0.4)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	3 (1.3)	67	231.0	252
Myalgia	筋肉痛	2 (0.9)	2 (0.9)	0 (0.0)	2 (0.9)	0 (0.0)	6 (2.6)	83	131.5	305
Osteochondrosis	骨端症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Osteonecrosis	骨壊死	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Osteoporosis	骨粗鬆症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pain in extremity	四肢痛	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	161	161.0	161
Periarthritis	関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.4)	382	382.0	382
Plantar fasciitis	足底筋膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	190	190.0	190

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害									
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	223	223.0	223
Trigger finger	弾発指	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	164	164.0	164
Muscle tightness	筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Intervertebral disc protrusion	椎間板突出	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	180	180.0	180
Musculoskeletal stiffness	筋骨格硬直	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.7)	1	172.5	363
Musculoskeletal discomfort	筋骨格不快感	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0	0.5	1
Finger deformity	指変形	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	276	276.0	276
Ligamentitis	靱帯炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)	309	314.5	320
Skin papilloma	皮膚乳頭腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	320	320.0	320
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	309	309.0	309

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			Total (N=231)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害		65 (28.1)	3 (1.3)	19 (8.2)	7 (3.1)	1 (0.5)	95 (41.1)	0	2.0	342
Akathisia	アカシジア		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Amnesia	健忘		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Disturbance in attention	注意力障害		2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	47	54.0	61
Dizziness	浮動性めまい		25 (10.8)	1 (0.4)	7 (3.0)	0 (0.0)	0 (0.0)	33 (14.3)	0	0.0	206
Dizziness postural	体位性めまい		1 (0.4)	1 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	4 (1.7)	49	130.5	183
Dysaesthesia	異常感覚		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	8	8.0	8
Dysgeusia	味覚異常		4 (1.7)	0 (0.0)	6 (2.6)	0 (0.0)	0 (0.0)	10 (4.3)	0	176.0	188
Dyskinesia	ジスキネジア		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Head discomfort	頭部不快感		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	35	35.0	35
Headache	頭痛		10 (4.3)	2 (0.9)	10 (4.3)	2 (0.9)	2 (0.9)	26 (11.3)	0	170.5	342
Hyperaesthesia	知覚過敏		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1	1.0	1
Hypoaesthesia	感覚鈍麻		3 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0	0.0	1
Mental impairment	精神的機能障害		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Migraine	片頭痛		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	267	267.0	267
Monoplegia	単麻痺		0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	141	141.0	141
Paraesthesia	錯感覚		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Paralysis	麻痺		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害									
Sciatica	坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)	278	283.0	288
Sedation	鎮静	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Somnolence	傾眠	33 (14.3)	2 (0.9)	4 (1.7)	1 (0.4)	0 (0.0)	40 (17.3)	0	0.5	281
Cubital tunnel syndrome	肘部管症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	306	306.0	306
Poor quality sleep	睡眠の質低下	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0	82.5	165
Thrombotic cerebral infarction	血栓性脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		Total (N=231)								
System organ class / Preferred term	First occurring day after first dose	0 <= - <= 84 n (%)	85 <= - <= 168 n (%)	169 <= - <= 252 n (%)	253 <= - <= 336 n (%)	337 <= n (%)	Total n (%)	Min	Median	Max
Psychiatric disorders	精神障害	30 (13.0)	3 (1.3)	7 (3.0)	3 (1.3)	0 (0.0)	43 (18.6)	0	9.0	307
Abnormal dreams	異常な夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Alcoholic hangover	アルコールによる宿酔	5 (2.2)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	7 (3.0)	1	20.0	251
Anxiety	不安	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	170	228.0	286
Depressed mood	抑うつ気分	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	266	266.0	266
Dysphoria	不快気分	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Euphoric mood	多幸気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Hallucination, auditory	幻聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Insomnia	不眠症	15 (6.5)	1 (0.4)	2 (0.9)	2 (0.9)	0 (0.0)	20 (8.7)	0	0.5	307
Irritability	易刺激性	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	168	170.0	172
Libido decreased	リビドー減退	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	168	168.0	168
Middle insomnia	中期不眠症	6 (2.6)	0 (0.0)	3 (1.3)	0 (0.0)	0 (0.0)	9 (3.9)	0	21.0	252
Nightmare	悪夢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Restlessness	落ち着きのなさ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Sleep disorder	睡眠障害	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0	8.0	16
Tension	緊張	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Abulia	無為	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	84	128.0	172
Depressive symptom	抑うつ症状	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	4	4.0	4

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害									
Mental disorder	精神障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Terminal insomnia	早朝覚醒型不眠症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	41	41.0	41
Renal and urinary disorders	腎および尿路障害	2 (0.9)	1 (0.4)	1 (0.4)	1 (0.4)	0 (0.0)	5 (2.2)	5	168.0	314
Calculus urinary	尿路結石	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	49	49.0	49
Nocturia	夜間頻尿	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	5	5.0	5
Pollakiuria	頻尿	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	168	168.5	169
Ureterolithiasis	尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	314	314.0	314
Reproductive system and breast disorders	生殖系および乳房障害	6 (2.6)	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	8 (3.5)	0	6.5	223
Dysmenorrhoea	月経困難症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	45	45.0	45
Erection increased	勃起増強	4 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.7)	0	0.0	1
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	143	143.0	143
Prostatitis	前立腺炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	223	223.0	223
Spontaneous penile erection	自発陰茎勃起	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Erectile dysfunction	勃起不全	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	12	12.0	12

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

	Treatment group of study 339-14-001	Nalmefene								
		Total (N=231)								
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	8 (3.5)	5 (2.2)	3 (1.3)	2 (0.9)	0 (0.0)	18 (7.8)	0	110.5	308
Cough	咳嗽	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	49	49.0	49
Dry throat	咽喉乾燥	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	18	18.0	18
Epistaxis	鼻出血	1 (0.4)	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	12	109.0	114
Hyperventilation	過換気	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal pain	喉頭痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	24	24.0	24
Nasal congestion	鼻閉	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	27	27.0	27
Nasal inflammation	鼻の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Pneumothorax	気胸	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	24	24.0	24
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.9)	124	193.0	262
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	178	196.0	214
Wheezing	喘鳴	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	6	6.0	6
Upper respiratory tract inflammation	上気道の炎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Laryngeal discomfort	喉頭不快感	1 (0.4)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0	66.5	133
Oropharyngeal pain	口腔咽頭痛	1 (0.4)	2 (0.9)	1 (0.4)	2 (0.9)	0 (0.0)	6 (2.6)	10	163.5	308

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

Treatment group of study 339-14-001		Nalmefene								
							Total (N=231)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	13 (5.6)	3 (1.3)	1 (0.4)	3 (1.3)	0 (0.0)	20 (8.7)	0	28.5	329
Acne	ざ瘡	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	16	16.0	16
Angioedema	血管浮腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Cold sweat	冷汗	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	329	329.0	329
Dermatitis atopic	アトピー性皮膚炎	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	68	68.0	68
Dry skin	皮膚乾燥	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	12	20.0	28
Eczema	湿疹	1 (0.4)	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)	4 (1.7)	9	149.0	315
Erythema	紅斑	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	11	11.0	11
Hyperhidrosis	多汗症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Night sweats	寝汗	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	2 (0.9)	0	91.5	183
Pruritus	そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash	発疹	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	12	12.0	12
Rash generalised	全身性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
Rash papular	丘疹性皮疹	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	159	159.0	159
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	256	256.0	256
Urticaria	蕁麻疹	4 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.7)	10	14.5	29
Pruritus generalised	全身性そう痒症	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	56	56.0	56

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001	Nalmefene								
			Total (N=231)								
System organ class		First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Vascular disorders	血管障害		6 (2.6)	1 (0.4)	5 (2.2)	1 (0.4)	0 (0.0)	13 (5.6)	0	165.0	256
Hyperaemia	充血		0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	176	176.0	176
Hypertension	高血圧		1 (0.4)	1 (0.4)	3 (1.3)	1 (0.4)	0 (0.0)	6 (2.6)	23	175.0	256
Hypotension	低血圧		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0	0.0	0
Orthostatic hypotension	起立性低血圧		1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	42	42.0	42
Hot flush	ほてり		3 (1.3)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	4 (1.7)	0	18.0	178

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-44＞

表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class		Treatment group of study 339-14-001					Total			
							(N=403)			
	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
N		403	372	365	226	214	403			
Total number of subjects with adverse events		305 (75.7)	27 (7.3)	15 (4.1)	4 (1.8)	0 (0.0)	351 (87.1)	0	1.0	287
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	83	87.0	91
Anaemia	貧血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	83	83.0	83
Pancytopenia	汎血球減少症	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	91	91.0	91
Cardiac disorders	心臓障害	14 (3.5)	3 (0.8)	8 (2.2)	2 (0.9)	1 (0.5)	28 (6.9)	0	105.0	350
Arrhythmia	不整脈	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	168	168.0	168
Bradycardia	徐脈	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	182	182.0	182
Bundle branch block left	左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	350	350.0	350
Bundle branch block right	右脚ブロック	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.4)	0 (0.0)	3 (0.7)	175	252.0	283
Palpitations	動悸	10 (2.5)	2 (0.5)	4 (1.1)	0 (0.0)	0 (0.0)	16 (4.0)	0	14.5	208
Supraventricular extrasystoles	上室性期外収縮	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	77	77.0	77
Tachycardia	頻脈	3 (0.7)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	4 (1.0)	7	26.0	221
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	336	336.0	336
Ear and labyrinth disorders	耳および迷路障害	9 (2.2)	1 (0.3)	3 (0.8)	1 (0.4)	1 (0.5)	15 (3.7)	0	1.0	364
Deafness transitory	一過性難聴	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	188	188.0	188
Eustachian tube patulous	耳管開放	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	70	70.0	70
Hyperacusis	聴覚過敏	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Tinnitus	耳鳴	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	0	87.5	175
Vertigo	回転性めまい	6 (1.5)	1 (0.3)	1 (0.3)	1 (0.4)	1 (0.5)	10 (2.5)	0	0.5	364

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class		Treatment group of study 339-14-001					Total (N=403)			
	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Endocrine disorders	内分泌障害	2 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	77	84.0	90
Hyperprolactinaemia	高プロラクチン血症	2 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	77	84.0	90
Eye disorders	眼障害	4 (1.0)	0 (0.0)	6 (1.6)	2 (0.9)	2 (0.9)	14 (3.5)	0	192.5	372
Asthenopia	眼精疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	363	363.0	363
Cataract	白内障	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	129	129.0	129
Conjunctival haemorrhage	結膜出血	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.4)	0 (0.0)	2 (0.5)	182	257.5	333
Conjunctivitis allergic	アレルギー性結膜炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	38	38.0	38
Dry eye	眼乾燥	2 (0.5)	0 (0.0)	1 (0.3)	1 (0.4)	0 (0.0)	4 (1.0)	0	90.5	256
Eye allergy	眼のアレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	372	372.0	372
Eye irritation	眼刺激	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	84	84.0	84
Eye swelling	眼部腫脹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	19	19.0	19
Keratitis	角膜炎	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	217	217.0	217
Scleritis	強膜炎	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	197	197.0	197
Visual impairment	視力障害	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	188	188.0	188
Corneal disorder	角膜障害	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	228	228.0	228

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害	163 (40.4)	15 (4.0)	24 (6.6)	8 (3.5)	0 (0.0)	210 (52.1)	0	1.0	332
Abdominal discomfort	腹部不快感	16 (4.0)	3 (0.8)	8 (2.2)	1 (0.4)	0 (0.0)	28 (6.9)	0	34.5	286
Abdominal distension	腹部膨満	13 (3.2)	1 (0.3)	2 (0.5)	1 (0.4)	0 (0.0)	17 (4.2)	0	7.0	282
Abdominal pain	腹痛	7 (1.7)	4 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	11 (2.7)	0	49.0	168
Abdominal pain upper	上腹部痛	2 (0.5)	2 (0.5)	3 (0.8)	1 (0.4)	0 (0.0)	8 (2.0)	7	148.0	332
Chronic gastritis	慢性胃炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	77	77.0	77
Constipation	便秘	16 (4.0)	3 (0.8)	5 (1.4)	1 (0.4)	0 (0.0)	25 (6.2)	0	8.0	331
Dental caries	齲歯	3 (0.7)	5 (1.3)	1 (0.3)	0 (0.0)	0 (0.0)	9 (2.2)	33	100.0	206
Diarrhoea	下痢	6 (1.5)	3 (0.8)	3 (0.8)	2 (0.9)	0 (0.0)	14 (3.5)	0	95.0	316
Dry mouth	口内乾燥	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Dyspepsia	消化不良	3 (0.7)	2 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)	7 (1.7)	7	152.0	304
Enterocolitis	腸炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	73	73.0	73
Faeces hard	硬便	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	173	173.0	173
Food poisoning	食中毒	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.5)	10	143.0	276
Gastric polyps	胃ポリープ	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	154	154.0	154
Gastric ulcer	胃潰瘍	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	154	154.0	154
Gastritis	胃炎	1 (0.2)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	3 (0.7)	42	160.0	185
Gastrooesophageal reflux disease	胃食道逆流性疾患	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	77	77.0	77

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class		Treatment group of study 339-14-001					Total (N=403)			
	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Gastrointestinal disorders	胃腸障害									
Nausea	悪心	104 (25.8)	4 (1.1)	11 (3.0)	4 (1.8)	0 (0.0)	123 (30.5)	0	0.0	307
Salivary hypersecretion	流涎過多	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	182	182.0	182
Stomatitis	口内炎	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	102	102.0	102
Toothache	歯痛	3 (0.7)	1 (0.3)	2 (0.5)	1 (0.4)	0 (0.0)	7 (1.7)	3	163.0	257
Vomiting	嘔吐	28 (6.9)	5 (1.3)	4 (1.1)	4 (1.8)	1 (0.5)	42 (10.4)	0	17.5	342
Oral dysaesthesia	口腔知覚不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Large intestine polyp	大腸ポリープ	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	191	191.0	191
Paraesthesia oral	口の錯感覚	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	6	6.0	6
Gastrointestinal sounds abnormal	胃腸音異常	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	174	174.0	174
Faeces soft	軟便	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	84.0	168

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
General disorders and administration site conditions	一般・全身障害および投与部位の状態	73 (18.1)	5 (1.3)	13 (3.6)	2 (0.9)	2 (0.9)	95 (23.6)	0	1.0	371
Asthenia	無力症	2 (0.5)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	18	67.5	168
Chest discomfort	胸部不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Chest pain	胸痛	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.5)	2 (0.5)	180	275.5	371
Chills	悪寒	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	21
Discomfort	不快感	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	9
Fatigue	疲労	11 (2.7)	1 (0.3)	2 (0.5)	0 (0.0)	0 (0.0)	14 (3.5)	0	1.5	243
Feeling abnormal	異常感	13 (3.2)	0 (0.0)	3 (0.8)	0 (0.0)	0 (0.0)	16 (4.0)	0	0.5	182
Feeling hot	熱感	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.5	1
Hangover	宿酔	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.5)	3 (0.7)	66	184.0	367
Malaise	倦怠感	30 (7.4)	3 (0.8)	6 (1.6)	1 (0.4)	1 (0.5)	41 (10.2)	0	1.0	346
Pyrexia	発熱	4 (1.0)	2 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)	7 (1.7)	0	15.0	285
Thirst	口渇	13 (3.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	14 (3.5)	0	0.0	175
Peripheral swelling	末梢腫脹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Early satiety	早期満腹	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	179	179.0	179

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Hepatobiliary disorders	肝胆道系障害	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	80	90.0	168
Alcoholic liver disease	アルコール性肝疾患	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	90	90.0	90
Hepatic function abnormal	肝機能異常	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	80	80.0	80
Hepatic steatosis	脂肪肝	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	168	168.0	168
Immune system disorders	免疫系障害	3 (0.7)	4 (1.1)	1 (0.3)	2 (0.9)	0 (0.0)	10 (2.5)	18	125.0	319
Hypersensitivity	過敏症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	58	58.0	58
Seasonal allergy	季節性アレルギー	2 (0.5)	4 (1.1)	1 (0.3)	2 (0.9)	0 (0.0)	9 (2.2)	18	141.0	319

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症	64 (15.9)	40 (10.8)	25 (6.8)	12 (5.3)	2 (0.9)	143 (35.5)	0	105.0	364
Angular cheilitis	口角口唇炎	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	145	145.0	145
Anisakiasis	アニサキス症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	58	58.0	58
Bronchitis	気管支炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	29	29.0	29
Conjunctivitis	結膜炎	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	67	131.0	163
Cystitis	膀胱炎	1 (0.2)	1 (0.3)	0 (0.0)	2 (0.9)	0 (0.0)	4 (1.0)	0	205.5	297
Diverticulitis	憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	353	353.0	353
Empyema	蓄膿	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	104	104.0	104
Furuncle	せつ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	23	23.0	23
Gastroenteritis	胃腸炎	5 (1.2)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	7 (1.7)	5	62.0	217
Gastroenteritis viral	ウイルス性胃腸炎	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	24	73.5	123
Gingivitis	歯肉炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Herpes zoster	帯状疱疹	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	168	168.0	168
Infection	感染	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	161	161.0	161
Influenza	インフルエンザ	2 (0.5)	2 (0.5)	1 (0.3)	1 (0.4)	0 (0.0)	6 (1.5)	47	90.0	287
Nasopharyngitis	鼻咽頭炎	46 (11.4)	38 (10.2)	22 (6.0)	9 (4.0)	2 (0.9)	117 (29.0)	0	117.0	364
Otitis externa	外耳炎	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	151	151.0	151
Pharyngitis	咽頭炎	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	2	48.0	84

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total (N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Infections and infestations	感染症および寄生虫症									
Sialoadenitis	唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	296	296.0	296
Sinusitis	副鼻腔炎	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	19.5	39
Viral diarrhoea	ウイルス性下痢	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	81	81.0	81
Gingival abscess	歯肉膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Helicobacter infection	ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	289	289.0	289
Helicobacter gastritis	ヘリコバクター性胃炎	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	220	220.0	220
Enteritis infectious	感染性腸炎	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)	186	203.5	221
Oral herpes	口腔ヘルペス	0 (0.0)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	99	142.0	185
Gastroenteritis norovirus	ノロウイルス性胃腸炎	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	81	144.0	207

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	7 (1.7)	7 (1.9)	8 (2.2)	5 (2.2)	0 (0.0)	27 (6.7)	1	154.0	318
Accidental overdose	偶発的過量投与	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	1	6.0	11
Alcohol poisoning	アルコール中毒	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	46	46.0	46
Arthropod sting	節足動物刺傷	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.5)	2 (0.5)	182	260.0	338
Fall	転倒	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	110	110.0	110
Fibula fracture	腓骨骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	49	49.0	49
Foot fracture	足骨折	0 (0.0)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	101	136.5	172
Fracture	骨折	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	199	199.0	199
Frostbite	凍傷	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	212	212.0	212
Hand fracture	手骨折	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)	209	212.0	215
Injury	損傷	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	103	103.0	103
Joint dislocation	関節脱臼	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	90	90.0	90
Ligament sprain	靭帯捻挫	0 (0.0)	1 (0.3)	2 (0.5)	0 (0.0)	0 (0.0)	3 (0.7)	154	170.0	249
Rib fracture	肋骨骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	54	54.0	54
Road traffic accident	交通事故	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	90	90.0	90
Traumatic haematoma	外傷性血腫	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	219	219.0	219

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total (N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Injury, poisoning and procedural complications	傷害、中毒および処置合併症									
Excoriation	擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	308	308.0	308
Contusion	挫傷	1 (0.2)	1 (0.3)	0 (0.0)	2 (0.9)	0 (0.0)	4 (1.0)	71	171.5	308
Wound	創傷	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	106	106.0	106
Ligament injury	靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	318	318.0	318
Tooth fracture	歯牙破折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Skin abrasion	皮膚擦過傷	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	116	116.0	116
Avulsion fracture	剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	318	318.0	318
Heat illness	熱中症	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.5)	266	281.0	296

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査	25 (6.2)	16 (4.3)	10 (2.7)	7 (3.1)	2 (0.9)	60 (14.9)	0	89.5	356
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.2)	1 (0.3)	1 (0.3)	0 (0.0)	1 (0.5)	4 (1.0)	84	129.5	343
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	2 (0.5)	0 (0.0)	2 (0.5)	1 (0.4)	0 (0.0)	5 (1.2)	80	171.0	256
Blood bilirubin increased	血中ビリルビン増加	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	87	87.0	87
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.5)	2 (0.5)	166	261.0	356
Blood creatine phosphokinase increased	血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	285	285.0	285
Blood potassium decreased	血中カリウム減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	84	84.0	84
Blood potassium increased	血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	260	260.0	260
Blood pressure increased	血圧上昇	8 (2.0)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.5)	10 (2.5)	1	19.0	342
Blood prolactin decreased	血中プロラクチン減少	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	85	126.5	168
Blood prolactin increased	血中プロラクチン増加	2 (0.5)	4 (1.1)	3 (0.8)	1 (0.4)	1 (0.5)	11 (2.7)	84	168.0	346
Blood triglycerides increased	血中トリグリセリド増加	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	3 (0.7)	82	84.0	341
Blood uric acid increased	血中尿酸増加	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	188	188.0	188
C-reactive protein increased	Ｃ－反応性蛋白増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	84	84.0	84
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.4)	1 (0.5)	3 (0.7)	168	256.0	343
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.3)	1 (0.3)	3 (1.3)	0 (0.0)	5 (1.2)	89	256.0	335
Glucose urine	尿中ブドウ糖	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	169	169.0	169
Glucose urine present	尿中ブドウ糖陽性	1 (0.2)	3 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	83	91.5	168

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Investigations	臨床検査									
Blood urine present	尿中血陽性	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	84	126.0	168
Heart rate decreased	心拍数減少	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	235	235.0	235
Lipids abnormal	脂質異常	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	252	252.0	252
Neutrophil count decreased	好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	266	266.0	266
Red blood cell count decreased	赤血球数減少	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	90	90.0	90
Weight decreased	体重減少	3 (0.7)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	4 (1.0)	56	84.0	203
Weight increased	体重増加	2 (0.5)	3 (0.8)	2 (0.5)	0 (0.0)	0 (0.0)	7 (1.7)	11	164.0	228
Protein urine present	尿中蛋白陽性	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	77	121.5	166
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	259	259.0	259
Urine output increased	尿量増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Occult blood positive	便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	303	303.0	303
Liver function test increased	肝機能検査値上昇	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.5)	77	199.0	321

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class		Treatment group of study 339-14-001					Total (N=403)			
	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Metabolism and nutrition disorders	代謝および栄養障害	20 (5.0)	5 (1.3)	3 (0.8)	6 (2.7)	0 (0.0)	34 (8.4)	0	12.5	305
Dehydration	脱水	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.5)	8	164.5	321
Diabetes mellitus	糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	305	305.0	305
Gout	痛風	0 (0.0)	1 (0.3)	1 (0.3)	1 (0.4)	0 (0.0)	3 (0.7)	112	177.0	299
Hypercholesterolaemia	高コレステロール血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	267	267.0	267
Hypertriglyceridaemia	高トリグリセリド血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	266	266.0	266
Hyperuricaemia	高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	259	259.0	259
Hypovitaminosis	ビタミン欠乏症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	13	13.0	13
Increased appetite	食欲亢進	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	11	11.0	11
Dyslipidaemia	脂質異常症	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	171	171.0	171
Decreased appetite	食欲減退	16 (4.0)	3 (0.8)	1 (0.3)	2 (0.9)	0 (0.0)	22 (5.5)	0	1.0	319
Hyperlipidaemia	高脂血症	1 (0.2)	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)	3 (0.7)	68	88.0	258

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class	First occurring day after first dose	Treatment group of study 339-14-001					Total (N=403)			
		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	27 (6.7)	16 (4.3)	12 (3.3)	9 (4.0)	2 (0.9)	66 (16.4)	0	131.0	382
Arthralgia	関節痛	3 (0.7)	2 (0.5)	2 (0.5)	0 (0.0)	0 (0.0)	7 (1.7)	0	131.0	171
Arthritis	関節炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	71	71.0	71
Back pain	背部痛	7 (1.7)	8 (2.2)	4 (1.1)	8 (3.5)	0 (0.0)	27 (6.7)	0	147.0	330
Muscle rigidity	筋固縮	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	170	170.0	170
Muscle spasms	筋痙縮	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	56	109.5	163
Muscle twitching	筋攣縮	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Musculoskeletal pain	筋骨格痛	2 (0.5)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	4 (1.0)	19	149.0	252
Myalgia	筋肉痛	2 (0.5)	2 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)	6 (1.5)	83	131.5	305
Osteochondrosis	骨端症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	21	21.0	21
Osteonecrosis	骨壊死	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	134	134.0	134
Osteoporosis	骨粗鬆症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	41	41.0	41
Pain in extremity	四肢痛	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	161	161.0	161
Periarthritis	関節周囲炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)	382	382.0	382
Plantar fasciitis	足底筋膜炎	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	113	113.0	113
Spinal osteoarthritis	変形性脊椎症	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	190	190.0	190

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total (N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害									
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	223	223.0	223
Trigger finger	弾発指	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	164	164.0	164
Muscle tightness	筋緊張	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	0.5	1
Intervertebral disc protrusion	椎間板突出	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	180	180.0	180
Musculoskeletal stiffness	筋骨格硬直	2 (0.5)	1 (0.3)	1 (0.3)	0 (0.0)	2 (0.9)	6 (1.5)	1	170.5	363
Musculoskeletal discomfort	筋骨格不快感	4 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	0	0.0	1
Finger deformity	指変形	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	276	276.0	276
Ligamentitis	靭帯炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.2)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	3 (0.7)	77	309.0	320
Skin papilloma	皮膚乳頭腫	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.5)	77	198.5	320
Prostate cancer	前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	309	309.0	309

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害	124 (30.8)	5 (1.3)	20 (5.5)	7 (3.1)	1 (0.5)	157 (39.0)	0	1.0	342
Akathisia	アカシジア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	9	9.0	9
Amnesia	健忘	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	63	63.0	63
Disturbance in attention	注意力障害	3 (0.7)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	0	54.0	90
Dizziness	浮動性めまい	51 (12.7)	3 (0.8)	7 (1.9)	0 (0.0)	0 (0.0)	61 (15.1)	0	0.0	206
Dizziness postural	体位性めまい	2 (0.5)	1 (0.3)	2 (0.5)	0 (0.0)	0 (0.0)	5 (1.2)	30	88.0	183
Dysaesthesia	異常感覚	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	8	8.0	8
Dysgeusia	味覚異常	11 (2.7)	0 (0.0)	6 (1.6)	0 (0.0)	0 (0.0)	17 (4.2)	0	1.0	188
Dyskinesia	ジスキネジア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Head discomfort	頭部不快感	4 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	0	0.5	35
Headache	頭痛	22 (5.5)	3 (0.8)	10 (2.7)	2 (0.9)	2 (0.9)	39 (9.7)	0	36.0	342
Hyperaesthesia	知覚過敏	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Hypoaesthesia	感覚鈍麻	5 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	0	0.0	21
Mental impairment	精神的機能障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Migraine	片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	267	267.0	267
Monoplegia	単麻痺	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	141	141.0	141
Paraesthesia	錯感覚	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Paralysis	麻痺	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Nervous system disorders	神経系障害									
Sciatica	坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.5)	278	283.0	288
Sedation	鎮静	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Somnolence	傾眠	45 (11.2)	2 (0.5)	4 (1.1)	1 (0.4)	0 (0.0)	52 (12.9)	0	0.0	281
Cubital tunnel syndrome	肘部管症候群	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	306	306.0	306
Poor quality sleep	睡眠の質低下	4 (1.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	0	0.0	165
Thrombotic cerebral infarction	血栓性脳梗塞	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	171	171.0	171

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害	67 (16.6)	3 (0.8)	7 (1.9)	3 (1.3)	0 (0.0)	80 (19.9)	0	1.0	307
Abnormal dreams	異常な夢	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Alcoholic hangover	アルコールによる宿酔	8 (2.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	10 (2.5)	0	15.0	251
Anxiety	不安	1 (0.2)	0 (0.0)	1 (0.3)	1 (0.4)	0 (0.0)	3 (0.7)	1	170.0	286
Depressed mood	抑うつ気分	2 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	3 (0.7)	1	1.0	266
Dysphoria	不快気分	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Euphoric mood	多幸気分	3 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0	0.0	1
Hallucination, auditory	幻聴	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Insomnia	不眠症	27 (6.7)	2 (0.5)	2 (0.5)	2 (0.9)	0 (0.0)	33 (8.2)	0	1.0	307
Irritability	易刺激性	2 (0.5)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	4 (1.0)	0	84.0	172
Libido decreased	リビドー減退	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	21	94.5	168
Middle insomnia	中期不眠症	11 (2.7)	0 (0.0)	3 (0.8)	0 (0.0)	0 (0.0)	14 (3.5)	0	1.5	252
Nightmare	悪夢	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	7.0	14
Restlessness	落ち着きのなさ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	82	82.0	82
Sleep disorder	睡眠障害	7 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (1.7)	0	0.0	16
Tension	緊張	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1	1.0	1
Abulia	無為	1 (0.2)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	84	128.0	172
Depressive symptom	抑うつ症状	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	4	4.0	4

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Psychiatric disorders	精神障害									
Mental disorder	精神障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Terminal insomnia	早朝覚醒型不眠症	5 (1.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.5)	0	25.0	157
Renal and urinary disorders	腎および尿路障害	2 (0.5)	1 (0.3)	1 (0.3)	1 (0.4)	0 (0.0)	5 (1.2)	5	168.0	314
Calculus urinary	尿路結石	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	49	49.0	49
Nocturia	夜間頻尿	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	5	5.0	5
Pollakiuria	頻尿	0 (0.0)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.5)	168	168.5	169
Ureterolithiasis	尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	314	314.0	314
Reproductive system and breast disorders	生殖系および乳房障害	8 (2.0)	1 (0.3)	1 (0.3)	0 (0.0)	0 (0.0)	10 (2.5)	0	1.5	223
Dysmenorrhoea	月経困難症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	45	45.0	45
Erection increased	勃起増強	5 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.2)	0	0.0	1
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	143	143.0	143
Prostatitis	前立腺炎	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	223	223.0	223
Spontaneous penile erection	自発陰茎勃起	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	2	2.0	2
Erectile dysfunction	勃起不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	12	12.0	12

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class	First occurring day after first dose	Treatment group of study 339-14-001					Total (N=403)			
		0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	10 (2.5)	7 (1.9)	3 (0.8)	2 (0.9)	0 (0.0)	22 (5.5)	0	106.0	308
Cough	咳嗽	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	49	49.0	49
Dry throat	咽喉乾燥	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	18	18.0	18
Epistaxis	鼻出血	1 (0.2)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	12	109.0	114
Hyperventilation	過換気	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	7	7.0	7
Laryngeal pain	喉頭痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	24	24.0	24
Nasal congestion	鼻閉	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	27	27.0	27
Nasal inflammation	鼻の炎症	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	126	126.0	126
Pneumothorax	気胸	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	24	24.0	24
Rhinitis allergic	アレルギー性鼻炎	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.5)	124	193.0	262
Rhinorrhoea	鼻漏	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)	178	196.0	214
Wheezing	喘鳴	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	6	6.0	6
Upper respiratory tract inflammation	上気道の炎症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	48	48.0	48
Laryngeal discomfort	喉頭不快感	1 (0.2)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0	66.5	133
Oropharyngeal pain	口腔咽頭痛	1 (0.2)	3 (0.8)	1 (0.3)	2 (0.9)	0 (0.0)	7 (1.7)	10	124.0	308

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

System organ class		Treatment group of study 339-14-001					Total			
							(N=403)			
	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	25 (6.2)	3 (0.8)	1 (0.3)	3 (1.3)	0 (0.0)	32 (7.9)	0	15.5	329
Acne	ざ瘡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	16	16.0	16
Angioedema	血管浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	15	15.0	15
Cold sweat	冷汗	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Dermatitis	皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	329	329.0	329
Dermatitis atopic	アトピー性皮膚炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	68	68.0	68
Dry skin	皮膚乾燥	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	12	20.0	28
Eczema	湿疹	1 (0.2)	2 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)	4 (1.0)	9	149.0	315
Erythema	紅斑	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	11	11.0	11
Hyperhidrosis	多汗症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	3	3.0	3
Night sweats	寝汗	3 (0.7)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	4 (1.0)	0	15.0	183
Pruritus	そう痒症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	10	10.0	10
Rash	発疹	4 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)	7	13.0	14
Rash generalised	全身性皮疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	14	14.0	14
Rash papular	丘疹性皮疹	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	159	159.0	159
Seborrhoeic dermatitis	脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	256	256.0	256
Urticaria	蕁麻疹	6 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.5)	10	23.5	34
Pruritus generalised	全身性そう痒症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	56	56.0	56

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表 2.7.4.7.1-15

Table 14.1.1.3-44

Incidences of Adverse Events Categorized by the First Occurring Day After First Dose Among Subjects Treated with Nalmefene in Either Study 339-14-001 or 339-14-002

Safety Set

		Treatment group of study 339-14-001					Total			
							(N=403)			
System organ class	First occurring day after first dose	0 <= - <= 84	85 <= - <= 168	169 <= - <= 252	253 <= - <= 336	337 <=	Total			
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	Min	Median	Max
Vascular disorders	血管障害	8 (2.0)	1 (0.3)	5 (1.4)	1 (0.4)	0 (0.0)	15 (3.7)	0	42.0	256
Hyperaemia	充血	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.2)	176	176.0	176
Hypertension	高血圧	2 (0.5)	1 (0.3)	3 (0.8)	1 (0.4)	0 (0.0)	7 (1.7)	15	175.0	256
Hypotension	低血圧	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0	0.0	0
Orthostatic hypotension	起立性低血圧	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	42	42.0	42
Hot flush	ほてり	4 (1.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	5 (1.2)	0	6.0	178

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-44＞

表 2.7.4.7.1-16
Table 14.1.1.3-81
Listing of Serious Adverse Events Other Than Death in Japanese (339-14-001)
Safety Set

Treatment group	Subject ID	Sex Age (years)	Preferred term	Days since first IMP[a] (days) Days since last IMP[b] (days) Outcome Duration[c] (days)	Causality Severity	Seriousness Action regarding IMP
Placebo	[redacted]	[redacted]	アルコール症	16 1 RECOVERING/RESOLVING 76	NOT RELATED MODERATE	Y NOT APPLICABLE
	[redacted]	[redacted]	出血性吻合部潰瘍	107 0 RECOVERED/RESOLVED 16	RELATED MODERATE	Y DRUG WITHDRAWN
Nalmefene 20 mg	[redacted]	[redacted]	動悸	14 0 RECOVERED/RESOLVED 15	RELATED MILD	N DOSE NOT CHANGED
			易刺激性	14 0 RECOVERED/RESOLVED 15	RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0
IMP = investigational medicinal product.
a : Date of onset - date of first IMP administration
b : Date of onset - date of last IMP administration
c : Date of outcome - Date of onset + 1

表 2.7.4.7.1-16
Table 14.1.1.3-81
Listing of Serious Adverse Events Other Than Death in Japanese (339-14-001)
Safety Set

Treatment group	Subject ID	Sex Age (years)	Preferred term	Days since first IMP[a] (days) Days since last IMP[b] (days) Outcome Duration[c] (days)	Causality Severity	Seriousness Action regarding IMP
Nalmefene 20 mg	[redacted]		慢性肝炎	41 1 RECOVERED/RESOLVED 14	RELATED MODERATE	Y DRUG WITHDRAWN
	[redacted]	[redacted]	悪心	1 1 RECOVERED/RESOLVED 169	RELATED MILD	N DOSE NOT CHANGED
			鼻咽頭炎	1 1 RECOVERED/RESOLVED 10	NOT RELATED MILD	N DOSE NOT CHANGED
			背部痛	11 2 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0
IMP = investigational medicinal product.
a : Date of onset - date of first IMP administration
b : Date of onset - date of last IMP administration
c : Date of outcome - Date of onset + 1

表 2.7.4.7.1-16
Table 14.1.1.3-81
Listing of Serious Adverse Events Other Than Death in Japanese (339-14-001)
Safety Set

Treatment group	Subject ID	Sex Age (years)	Preferred term	Days since first IMP[a] (days) Days since last IMP[b] (days) Outcome Duration[c] (days)	Causality Severity	Seriousness Action regarding IMP
Nalmefene 20 mg	[redacted]		胃腸炎	17 1 RECOVERED/RESOLVED 40	NOT RELATED MODERATE	Y DOSE NOT CHANGED
Nalmefene 10 mg	[redacted]	[redacted]	大腿骨骨折	79 1 NOT RECOVERED/NOT RESOLVED 5	NOT RELATED SEVERE	Y DRUG WITHDRAWN
			頭部損傷	79 1 NOT RECOVERED/NOT RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
			脊椎圧迫骨折	79 1 NOT RECOVERED/NOT RESOLVED 5	NOT RELATED MODERATE	Y DOSE NOT CHANGED

MedDRA Ver. 19.0
IMP = investigational medicinal product.
a : Date of onset - date of first IMP administration
b : Date of onset - date of last IMP administration
c : Date of outcome - Date of onset + 1
＜資料番号5.3.5.1-01 : Table 14.1.1.3-81＞

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
P-N20-N20	[redacted]	[redacted] [redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 366, 190	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted]	鼻咽頭炎	TREATMENT (339-14-001) 116, - 1 RECOVERED/RESOLVED 12	NOT RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-002) 181, 5 0 RECOVERED/RESOLVED 16	NOT RELATED MILD	N DOSE NOT CHANGED
					脂質異常症	RUN-OUT 347, 171 0 NOT RECOVERED/NOT RESOLVED 54	NOT RELATED MILD	N DOSE NOT CHANGED

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IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
P-N20-N20	[redacted]				血栓性脳梗塞	RUN-OUT 347, 171 0 RECOVERED/RESOLVED WITH SEQUELAE 54	NOT RELATED MODERATE	Y DOSE NOT CHANGED
					下痢	RUN-OUT 357, 181 0 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
N20-N20-P	[redacted]	[redacted] [redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 373, 197	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted]	器質化肺炎	RUN-OUT 356, 180 0 RECOVERING/RESOLVING 66	RELATED SEVERE	Y NOT APPLICABLE

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IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20-P	[redacted]				骨粗鬆症	FOLLOW-UP 396, 220 24 NOT RECOVERED/NOT RESOLVED 26	NOT RELATED MODERATE	N NOT APPLICABLE
					血中ブドウ糖増加	FOLLOW-UP 411, 235 39 NOT RECOVERED/NOT RESOLVED 11	NOT RELATED MODERATE	N NOT APPLICABLE
N20-N20	[redacted]	[redacted] [redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 317, 149	20[redacted]-[redacted]-[redacted]	筋肉痛	TREATMENT (339-14-001) 84, - 1 NOT RECOVERED/NOT RESOLVED 78	NOT RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20	[redacted]				悪心	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					下痢	TREATMENT (339-14-002) 171, 3 0 RECOVERED/RESOLVED 5	RELATED MILD	N DOSE NOT CHANGED
					節足動物刺傷	TREATMENT (339-14-002) 182, 14 0 RECOVERED/RESOLVED 43	NOT RELATED MILD	N DOSE NOT CHANGED

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IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20	[redacted]				体位性めまい	TREATMENT (339-14-002) 183, 15 0 RECOVERED/RESOLVED 14	NOT RELATED MILD	N DOSE NOT CHANGED
					前立腺癌	TREATMENT (339-14-002) 309, 141 0 NOT RECOVERED/NOT RESOLVED 15	NOT RELATED MILD	Y DRUG WITHDRAWN
	[redacted]	[redacted] [redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 321, 146	20[redacted]-[redacted]-[redacted]	悪心	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 28	RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20	[redacted]				嘔吐	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					倦怠感	TREATMENT (339-14-001) 6, - 0 RECOVERED/RESOLVED 22	RELATED MILD	N DOSE NOT CHANGED
					ビタミン欠乏症	TREATMENT (339-14-001) 13, - 0 RECOVERED/RESOLVED 43	NOT RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20	[redacted]				下痢	TREATMENT (339-14-001) 22, - 0 RECOVERED/RESOLVED 5	RELATED MILD	N DOSE NOT CHANGED
					下痢	TREATMENT (339-14-001) 48, - 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-001) 83, - 2 NOT RECOVERED/NOT RESOLVED 86	RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20	[redacted]				悪心	TREATMENT (339-14-002) 176, 1 0 RECOVERED/RESOLVED 13	RELATED MILD	N DOSE NOT CHANGED
					擦過傷	TREATMENT (339-14-002) 308, 133 0 RECOVERED/RESOLVED 17	NOT RELATED MILD	N DOSE NOT CHANGED
					挫傷	TREATMENT (339-14-002) 308, 133 0 RECOVERED/RESOLVED 17	NOT RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N20-N20	[redacted]				食欲減退	TREATMENT (339-14-002) 319, 144 0 RECOVERED/RESOLVED 6	NOT RELATED MILD	N DOSE NOT CHANGED
					肝機能検査値上昇	TREATMENT (339-14-002) 321, 146 1 NOT RECOVERED/NOT RESOLVED 4	NOT RELATED MILD	N NOT APPLICABLE
					脱水	TREATMENT (339-14-002) 321, 146 1 NOT RECOVERED/NOT RESOLVED 4	NOT RELATED MODERATE	Y DRUG WITHDRAWN

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IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N10-N20-N20	[redacted]	[redacted] [redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 364, 197	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted]	腹痛	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					腹痛	TREATMENT (339-14-001) 143, - 1 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-001) 143, - 1 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

表 2.7.4.7.1-17

Table 14.1.1.3-189

Listing of Serious Adverse Events Other Than Death in Japanese (339-14-002)

Safety Set

Treatment group	Subject ID	Sex Age (years)	Administration Start date (339-14-001 x) Start date (339-14-002 y) End date (339-14-002 z) Duration[a] (x to z) (days), Duration[a] (y to z) (days)	Start date of the period in study 339-14-002 Treatment Run-out Posttreatment	Preferred term	Period of onset Days since first IMP[b] (days) Days since last IMP[c] (days) Outcome Duration[d] (days)	Causality Severity	Seriousness Action regarding IMP
N10-N20-N20	[redacted]				胃腸炎	TREATMENT (339-14-002) 217, 50 2 RECOVERED/RESOLVED 4	NOT RELATED MODERATE	Y DOSE NOT CHANGED
					血中プロラクチン増加	TREATMENT (339-14-002) 252, 85 0 RECOVERED/RESOLVED 85	RELATED MILD	N DOSE NOT CHANGED
					血中プロラクチン増加	FOLLOW-UP 364, 197 1 RECOVERED/RESOLVED 29	RELATED MILD	N NOT APPLICABLE

MedDRA Ver. 19.0

IMP = investigational medicinal product.

a : End date of administration - Start date of administration + 1. b : Date of onset - Start date of administration in study 339-14-001, Date of onset - Start date of administration in study 339-14-002

c : Date of onset - date of last IMP administration. d : Date of outcome - Date of onset + 1

N10 : Nalmefene 10mg , N20 : Nalmefene 20mg, P : Placebo.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-189＞

表 2.7.4.7.1-18

Table 14.1.1.3-35

Incidences of Treatment-emergent Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term (339-14-001)

Safety Set

System organ class Preferred term		Placebo (N=245) n (%)	Nalmefene 20 mg (N=248) n (%)	 10 mg (N=184) n (%)	 Total (N=432) n (%)
Total number of subjects with TEAEs leading to discontinuation		11 (4.5)	45 (18.1)	33 (17.9)	78 (18.1)
Cardiac disorders	心臓障害	0 (0.0)	5 (2.0)	2 (1.1)	7 (1.6)
Palpitations	動悸	0 (0.0)	5 (2.0)	1 (0.5)	6 (1.4)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Tinnitus	耳鳴	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Vertigo	回転性めまい	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hypoacusis	聴力低下	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Endocrine disorders	内分泌障害	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Primary hyperaldosteronism	原発性アルドステロン症	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Eye disorders	眼障害	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Photophobia	羞明	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Visual impairment	視力障害	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Gastrointestinal disorders	胃腸障害	0 (0.0)	29 (11.7)	16 (8.7)	45 (10.4)
Abdominal discomfort	腹部不快感	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Constipation	便秘	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Diarrhoea	下痢	0 (0.0)	3 (1.2)	1 (0.5)	4 (0.9)
Dyspepsia	消化不良	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Nausea	悪心	0 (0.0)	21 (8.5)	12 (6.5)	33 (7.6)
Vomiting	嘔吐	0 (0.0)	10 (4.0)	5 (2.7)	15 (3.5)

MedDRA Ver. 19.0

TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-18
Table 14.1.1.3-35
Incidences of Treatment-emergent Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	1 (0.4)	8 (3.2)	4 (2.2)	12 (2.8)
Fatigue	疲労	0 (0.0)	1 (0.4)	2 (1.1)	3 (0.7)
Feeling abnormal	異常感	1 (0.4)	1 (0.4)	0 (0.0)	1 (0.2)
Feeling cold	冷感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hangover	宿酔	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Malaise	倦怠感	0 (0.0)	3 (1.2)	2 (1.1)	5 (1.2)
Thirst	口渇	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Chronic hepatitis	慢性肝炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Infections and infestations	感染症および寄生虫症	7 (2.9)	2 (0.8)	1 (0.5)	3 (0.7)
Herpes zoster	帯状疱疹	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Nasopharyngitis	鼻咽頭炎	7 (2.9)	0 (0.0)	1 (0.5)	1 (0.2)
Pneumonia bacterial	細菌性肺炎	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Anastomotic ulcer haemorrhage	出血性吻合部潰瘍	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Femur fracture	大腿骨骨折	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-18
Table 14.1.1.3-35
Incidences of Treatment-emergent Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Prostatic specific antigen increased	前立腺特異性抗原増加	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
White blood cell count increased	白血球数増加	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Urine ketone body present	尿中ケトン体陽性	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Metabolism and nutrition disorders	代謝および栄養障害	0 (0.0)	1 (0.4)	4 (2.2)	5 (1.2)
Decreased appetite	食欲減退	0 (0.0)	1 (0.4)	4 (2.2)	5 (1.2)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Muscular weakness	筋力低下	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Nervous system disorders	神経系障害	2 (0.8)	25 (10.1)	16 (8.7)	41 (9.5)
Amnesia	健忘	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Disturbance in attention	注意力障害	0 (0.0)	1 (0.4)	1 (0.5)	2 (0.5)
Dizziness	浮動性めまい	1 (0.4)	16 (6.5)	9 (4.9)	25 (5.8)
Dysgeusia	味覚異常	0 (0.0)	3 (1.2)	2 (1.1)	5 (1.2)
Head discomfort	頭部不快感	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Headache	頭痛	1 (0.4)	9 (3.6)	7 (3.8)	16 (3.7)
Hypoaesthesia	感覚鈍麻	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Neuralgia	神経痛	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Somnolence	傾眠	0 (0.0)	4 (1.6)	1 (0.5)	5 (1.2)
Poor quality sleep	睡眠の質低下	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-18
Table 14.1.1.3-35
Incidences of Treatment-emergent Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Psychiatric disorders	精神障害	1 (0.4)	12 (4.8)	9 (4.9)	21 (4.9)
Agitation	激越	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Anticipatory anxiety	予期不安	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Anxiety	不安	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Apathy	無感情	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Depressed mood	抑うつ気分	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Depression	うつ病	1 (0.4)	0 (0.0)	1 (0.5)	1 (0.2)
Initial insomnia	初期不眠症	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Insomnia	不眠症	0 (0.0)	5 (2.0)	5 (2.7)	10 (2.3)
Irritability	易刺激性	0 (0.0)	0 (0.0)	2 (1.1)	2 (0.5)
Listless	気力低下	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Middle insomnia	中期不眠症	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Mood swings	気分動揺	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Panic attack	パニック発作	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Sleep disorder	睡眠障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Abulia	無為	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Renal and urinary disorders	腎および尿路障害	0 (0.0)	2 (0.8)	1 (0.5)	3 (0.7)
Dysuria	排尿困難	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Pollakiuria	頻尿	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.

表 2.7.4.7.1-18
Table 14.1.1.3-35
Incidences of Treatment-emergent Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term (339-14-001)
Safety Set

		Placebo	Nalmefene		
			20 mg	10 mg	Total
System organ class		(N=245)	(N=248)	(N=184)	(N=432)
Preferred term		n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	生殖系および乳房障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Metrorrhagia	不正子宮出血	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.5)
Choking sensation	息詰まり感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Oropharyngeal discomfort	口腔咽頭不快感	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	0 (0.0)	4 (1.6)	2 (1.1)	6 (1.4)
Cold sweat	冷汗	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Erythema multiforme	多形紅斑	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hyperhidrosis	多汗症	0 (0.0)	3 (1.2)	0 (0.0)	3 (0.7)
Pruritus generalised	全身性そう痒症	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Vascular disorders	血管障害	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)
Hot flush	ほてり	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)

MedDRA Ver. 19.0
TEAE = treatment-emergent adverse event.
＜資料番号5.3.5.1-01 : Table 14.1.1.3-35＞

表 2.7.4.7.1-19

Table 14.1.1.3-59

Incidences of Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term in Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo	Nalmefene			Total
			20 mg	10 mg	Total	
System organ class		(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with adverse events leading to discontinuation		32 (18.6)	8 (5.8)	2 (2.1)	10 (4.3)	42 (10.4)
Cardiac disorders	心臓障害	3 (1.7)	0 (0.0)	1 (1.1)	1 (0.4)	4 (1.0)
Palpitations	動悸	3 (1.7)	0 (0.0)	1 (1.1)	1 (0.4)	4 (1.0)
Gastrointestinal disorders	胃腸障害	15 (8.7)	2 (1.5)	2 (2.1)	4 (1.7)	19 (4.7)
Abdominal discomfort	腹部不快感	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
Nausea	悪心	13 (7.6)	1 (0.7)	1 (1.1)	2 (0.9)	15 (3.7)
Vomiting	嘔吐	4 (2.3)	0 (0.0)	1 (1.1)	1 (0.4)	5 (1.2)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	8 (4.7)	1 (0.7)	1 (1.1)	2 (0.9)	10 (2.5)
Asthenia	無力症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Chills	悪寒	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Fatigue	疲労	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Feeling abnormal	異常感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Feeling hot	熱感	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Malaise	倦怠感	3 (1.7)	1 (0.7)	1 (1.1)	2 (0.9)	5 (1.2)
Thirst	口渇	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Road traffic accident	交通事故	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-19

Table 14.1.1.3-59

Incidences of Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term in Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo	Nalmefene			Total
			20 mg	10 mg	Total	
System organ class		(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)
Investigations	臨床検査	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.4)	3 (0.7)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
Blood pressure increased	血圧上昇	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
Metabolism and nutrition disorders	代謝および栄養障害	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.4)	5 (1.2)
Dehydration	脱水	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
Decreased appetite	食欲減退	4 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.4)	4 (1.0)
Osteochondrosis	骨端症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Osteoporosis	骨粗鬆症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Systemic lupus erythematosus	全身性エリテマトーデス	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
Musculoskeletal discomfort	筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
Prostate cancer	前立腺癌	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)

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表 2.7.4.7.1-19

Table 14.1.1.3-59

Incidences of Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term in Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo	Nalmefene			Total
			20 mg	10 mg	Total	
System organ class		(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders	神経系障害	18 (10.5)	1 (0.7)	0 (0.0)	1 (0.4)	19 (4.7)
Akathisia	アカシジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Disturbance in attention	注意力障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Dizziness	浮動性めまい	10 (5.8)	1 (0.7)	0 (0.0)	1 (0.4)	11 (2.7)
Dizziness postural	体位性めまい	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Headache	頭痛	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.4)	6 (1.5)
Paralysis	麻痺	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Somnolence	傾眠	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Psychiatric disorders	精神障害	8 (4.7)	1 (0.7)	0 (0.0)	1 (0.4)	9 (2.2)
Alcoholic hangover	アルコールによる宿酔	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Euphoric mood	多幸気分	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Insomnia	不眠症	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.4)	4 (1.0)
Sleep disorder	睡眠障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Mental disorder	精神障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Terminal insomnia	早朝覚醒型不眠症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Reproductive system and breast disorders	生殖系および乳房障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Erection increased	勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

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表 2.7.4.7.1-19

Table 14.1.1.3-59

Incidences of Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term in Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo	Nalmefene			Total
			20 mg	10 mg	Total	
System organ class		(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	4 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)
Cold sweat	冷汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Night sweats	寝汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Rash generalised	全身性皮疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Urticaria	蕁麻疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Vascular disorders	血管障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
Hot flush	ほてり	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-59＞

表 2.7.4.7.1-20

Table 14.1.1.3-64

Incidences of Adverse Events Leading to Discontinuation by MedDRA System Organ Class and Preferred Term in Run-out Period (339-14-002)

Subjects who Advanced to Run-out Period among Safety Set

Treatment group of run-out period		Placebo	Nalmefene 20 mg
System organ class		(N=171)	(N=172)
Preferred term		n (%)	n (%)
Total number of subjects with adverse events leading to discontinuation		0 (0.0)	1 (0.6)
Investigations	臨床検査	0 (0.0)	1 (0.6)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	0 (0.0)	1 (0.6)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-64＞

表 2.7.4.7.1-21
Table 14.1.1.3-62
Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests (339-14-001)
Safety Set

Parameters (Unit)	Criteria	Placebo (N=245)			Nalmefene 20 mg (N=248)			Nalmefene 10 mg (N=184)			Nalmefene Total (N=432)		
		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology													
Red blood cell count (/mm^3)	< 3,000,000 /mm^3	239	0	(0.0)	245	1	(0.4)	180	0	(0.0)	425	1	(0.2)
Hematocrit (%)													
Female	<= 32 %	90	2	(2.2)	74	3	(4.1)	47	1	(2.1)	121	4	(3.3)
Male	<= 37 %	149	0	(0.0)	171	5	(2.9)	133	4	(3.0)	304	9	(3.0)
Hemoglobin (g/dL)													
Female	>= 16.5 g/dL	90	0	(0.0)	74	0	(0.0)	47	0	(0.0)	121	0	(0.0)
	<= 9.5 g/dL	90	1	(1.1)	74	1	(1.4)	47	0	(0.0)	121	1	(0.8)
Male	>= 18.5 g/dL	149	0	(0.0)	171	0	(0.0)	133	0	(0.0)	304	0	(0.0)
	<= 11.5 g/dL	149	0	(0.0)	171	2	(1.2)	133	1	(0.8)	304	3	(1.0)
MCV	>= 1.2 x ULN	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 0.8 x LLN	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Total white blood cell count (/uL)	>= 16,000 /uL	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	< 2,800 / uL	239	2	(0.8)	245	0	(0.0)	180	3	(1.7)	425	3	(0.7)
Neutrophils (%)	>= 85 %	239	1	(0.4)	245	2	(0.8)	180	0	(0.0)	425	2	(0.5)
	<= 20 %	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-21
Table 14.1.1.3-62
Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests (339-14-001)
Safety Set

		Placebo			Nalmefene								
					20 mg			10 mg			Total		
		(N=245)			(N=248)			(N=184)			(N=432)		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology													
Eosinophils (%)	>= 10 %	239	9	(3.8)	245	4	(1.6)	180	2	(1.1)	425	6	(1.4)
Basophils (%)	>= 10 %	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Lymphocytes (%)	>= 75 %	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 10 %	239	1	(0.4)	245	2	(0.8)	180	0	(0.0)	425	2	(0.5)
Monocytes (%)	>= 15 %	239	0	(0.0)	245	1	(0.4)	180	1	(0.6)	425	2	(0.5)
Platelet count (/mm^3)	>= 700,000 /mm^3	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 75,000 /mm^3	239	0	(0.0)	245	1	(0.4)	180	0	(0.0)	425	1	(0.2)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-21
Table 14.1.1.3-62
Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests (339-14-001)
Safety Set

		Placebo			Nalmefene								
			(N=245)		20 mg (N=248)			10 mg (N=184)			Total (N=432)		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry													
Total bilirubin	>= 2 x ULN	239	3	(1.3)	245	2	(0.8)	180	1	(0.6)	425	3	(0.7)
Alkaline phosphatase	>= 3 x ULN	238	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
ALT	>= 3 x ULN	239	0	(0.0)	245	1	(0.4)	180	2	(1.1)	425	3	(0.7)
AST	>= 3 x ULN	239	4	(1.7)	245	4	(1.6)	180	3	(1.7)	425	7	(1.6)
Gamma-GTP (U/L)	>= 200 U/L	239	19	(7.9)	245	18	(7.3)	180	9	(5.0)	425	27	(6.4)
INR/prothrombin time	>= 2.0	239	0	(0.0)	245	2	(0.8)	180	0	(0.0)	425	2	(0.5)
Albumin (g/dL)	<= 2.7 g/dL	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Total cholesterol (mg/dL)	>= 302 mg/dL	239	2	(0.8)	245	4	(1.6)	180	1	(0.6)	425	5	(1.2)
Triglycerides (mg/dL)	>= 500 mg/dL	239	13	(5.4)	245	5	(2.0)	180	5	(2.8)	425	10	(2.4)
Creatinine	>= 1.5 x ULN	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 0.5 x LLN	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
BUN (mg/dL)	> 30 mg/dL	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Sodium (mEq/L)	>= 155 mEq/L	239	1	(0.4)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 125 mEq/L	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Potassium (mEq/L)	>= 6.0 mEq/L	239	1	(0.4)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 3.0 mEq/L	239	2	(0.8)	245	3	(1.2)	180	0	(0.0)	425	3	(0.7)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-21

Table 14.1.1.3-62

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests (339-14-001)

Safety Set

		Placebo			Nalmefene								
			(N=245)		20 mg (N=248)			10 mg (N=184)			Total (N=432)		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry													
Bicarbonate (mmol/L)	>= 38 mmol/L	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 12 mmol/L	239	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Calcium (mg/dL)	>= 12.0 mg/dL	238	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
	<= 7.2 mg/dL	238	0	(0.0)	245	0	(0.0)	180	0	(0.0)	425	0	(0.0)
Glucose (mg/dL)	>= 162 mg/dL	239	10	(4.2)	245	9	(3.7)	180	6	(3.3)	425	15	(3.5)
	<= 63 mg/dL	239	3	(1.3)	245	0	(0.0)	180	1	(0.6)	425	1	(0.2)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-21

Table 14.1.1.3-62

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests (339-14-001)

Safety Set

		Placebo			Nalmefene								
					20 mg			10 mg			Total		
		(N=245)			(N=248)			(N=184)			(N=432)		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Urine													
Protein	Increase equal to or greater than 2 grade from baseline	238	3	(1.3)	245	7	(2.9)	179	6	(3.4)	424	13	(3.1)
Glucose	Increase equal to or greater than 2 grade from baseline	238	10	(4.2)	245	13	(5.3)	179	7	(3.9)	424	20	(4.7)
Occult blood	Increase equal to or greater than 2 grade from baseline	238	19	(8.0)	245	18	(7.3)	179	12	(6.7)	424	30	(7.1)
Ketones	Increase equal to or greater than 2 grade from baseline	238	9	(3.8)	245	11	(4.5)	179	7	(3.9)	424	18	(4.2)
Other													
Prolactin (ug/L)	>= 67.5 ug/L	239	0	(0.0)	245	0	(0.0)	180	1	(0.6)	425	1	(0.2)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

＜資料番号5.3.5.1-01 : Table 14.1.1.3-62＞

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Red blood cell count (/mm^3)	< 3,000,000 /mm^3	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Hematocrit (%)										
Female	<= 32 %	64	0	(0.0)	64	0	(0.0)	64	0	(0.0)
Male	<= 37 %	108	0	(0.0)	106	3	(2.8)	108	3	(2.8)
Hemoglobin (g/dL)										
Female	>= 16.5 g/dL	64	0	(0.0)	64	0	(0.0)	64	0	(0.0)
	<= 9.5 g/dL	64	0	(0.0)	64	0	(0.0)	64	0	(0.0)
Male	>= 18.5 g/dL	108	0	(0.0)	106	1	(0.9)	108	1	(0.9)
	<= 11.5 g/dL	108	0	(0.0)	106	1	(0.9)	108	1	(0.9)
MCV	>= 1.2 x ULN	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 0.8 x LLN	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Total white blood cell count (/uL)	>= 16,000 /uL	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	< 2,800 / uL	172	0	(0.0)	170	1	(0.6)	172	1	(0.6)
Neutrophils (%)	>= 85 %	172	1	(0.6)	170	1	(0.6)	172	2	(1.2)
	<= 20 %	172	0	(0.0)	170	1	(0.6)	172	1	(0.6)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Eosinophils (%)	>= 10 %	172	8	(4.7)	170	5	(2.9)	172	10	(5.8)
Basophils (%)	>= 10 %	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Lymphocytes (%)	>= 75 %	172	0	(0.0)	170	1	(0.6)	172	1	(0.6)
	<= 10 %	172	1	(0.6)	170	2	(1.2)	172	3	(1.7)
Monocytes (%)	>= 15 %	172	0	(0.0)	170	1	(0.6)	172	1	(0.6)
Platelet count (/mm^3)	>= 700,000 /mm^3	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 75,000 /mm^3	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Total bilirubin	>= 2 x ULN	172	2	(1.2)	170	2	(1.2)	172	4	(2.3)
Alkaline phosphatase	>= 3 x ULN	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
ALT	>= 3 x ULN	172	0	(0.0)	170	1	(0.6)	172	1	(0.6)
AST	>= 3 x ULN	172	1	(0.6)	170	2	(1.2)	172	3	(1.7)
Gamma-GTP (U/L)	>= 200 U/L	172	15	(8.7)	170	5	(2.9)	172	17	(9.9)
INR/prothrombin time	>= 2.0	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Albumin (g/dL)	<= 2.7 g/dL	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Total cholesterol (mg/dL)	>= 302 mg/dL	172	1	(0.6)	170	1	(0.6)	172	2	(1.2)
Triglycerides (mg/dL)	>= 500 mg/dL	172	7	(4.1)	170	4	(2.4)	172	8	(4.7)
Creatinine	>= 1.5 x ULN	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 0.5 x LLN	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
BUN (mg/dL)	> 30 mg/dL	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Sodium (mEq/L)	>= 155 mEq/L	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 125 mEq/L	172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Potassium (mEq/L)	>= 6.0 mEq/L	172	1	(0.6)	170	0	(0.0)	172	1	(0.6)
	<= 3.0 mEq/L	172	1	(0.6)	170	1	(0.6)	172	1	(0.6)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001			Placebo (N=172)					
		Study	339-14-001			339-14-002			Total	
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry											
Bicarbonate (mmol/L)	>= 38 mmol/L		172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 12 mmol/L		172	0	(0.0)	170	1	(0.6)	172	1	(0.6)
Calcium (mg/dL)	>= 12.0 mg/dL		172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 7.2 mg/dL		172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
Glucose (mg/dL)	>= 162 mg/dL		172	5	(2.9)	170	5	(2.9)	172	10	(5.8)
	<= 63 mg/dL		172	2	(1.2)	170	0	(0.0)	172	2	(1.2)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Urine										
Protein	Increase equal to or greater than 2 grade from baseline	172	0	(0.0)	170	4	(2.4)	172	4	(2.3)
Glucose	Increase equal to or greater than 2 grade from baseline	172	5	(2.9)	170	8	(4.7)	172	10	(5.8)
Occult blood	Increase equal to or greater than 2 grade from baseline	172	18	(10.5)	170	13	(7.6)	172	24	(14.0)
Ketones	Increase equal to or greater than 2 grade from baseline	172	4	(2.3)	170	8	(4.7)	172	10	(5.8)
Other										
Prolactin (ug/L)	>= 67.5 ug/L	172	0	(0.0)	170	1	(0.6)	172	1	(0.6)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

＜資料番号5.3.5.2-01 : Table 14.1.1.3-113＞

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Red blood cell count (/mm^3)	< 3,000,000 /mm^3	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Hematocrit (%)										
Female	<= 32 %	33	1	(3.0)	33	0	(0.0)	33	1	(3.0)
Male	<= 37 %	104	3	(2.9)	104	4	(3.8)	104	5	(4.8)
Hemoglobin (g/dL)										
Female	>= 16.5 g/dL	33	0	(0.0)	33	0	(0.0)	33	0	(0.0)
	<= 9.5 g/dL	33	0	(0.0)	33	0	(0.0)	33	0	(0.0)
Male	>= 18.5 g/dL	104	0	(0.0)	104	0	(0.0)	104	0	(0.0)
	<= 11.5 g/dL	104	1	(1.0)	104	1	(1.0)	104	2	(1.9)
MCV	>= 1.2 x ULN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 0.8 x LLN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Total white blood cell count (/uL)	>= 16,000 /uL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	< 2,800 / uL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Neutrophils (%)	>= 85 %	137	2	(1.5)	137	0	(0.0)	137	2	(1.5)
	<= 20 %	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Eosinophils (%)	>= 10 %	137	2	(1.5)	137	3	(2.2)	137	4	(2.9)
Basophils (%)	>= 10 %	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Lymphocytes (%)	>= 75 %	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 10 %	137	2	(1.5)	137	0	(0.0)	137	2	(1.5)
Monocytes (%)	>= 15 %	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Platelet count (/mm^3)	>= 700,000 /mm^3	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 75,000 /mm^3	137	0	(0.0)	137	1	(0.7)	137	1	(0.7)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Total bilirubin	>= 2 x ULN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Alkaline phosphatase	>= 3 x ULN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
ALT	>= 3 x ULN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
AST	>= 3 x ULN	137	0	(0.0)	137	2	(1.5)	137	2	(1.5)
Gamma-GTP (U/L)	>= 200 U/L	137	8	(5.8)	137	10	(7.3)	137	12	(8.8)
INR/prothrombin time	>= 2.0	137	1	(0.7)	137	0	(0.0)	137	1	(0.7)
Albumin (g/dL)	<= 2.7 g/dL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Total cholesterol (mg/dL)	>= 302 mg/dL	137	3	(2.2)	137	2	(1.5)	137	3	(2.2)
Triglycerides (mg/dL)	>= 500 mg/dL	137	1	(0.7)	137	2	(1.5)	137	3	(2.2)
Creatinine	>= 1.5 x ULN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 0.5 x LLN	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
BUN (mg/dL)	> 30 mg/dL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Sodium (mEq/L)	>= 155 mEq/L	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 125 mEq/L	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Potassium (mEq/L)	>= 6.0 mEq/L	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 3.0 mEq/L	137	2	(1.5)	137	0	(0.0)	137	2	(1.5)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Bicarbonate (mmol/L)	>= 38 mmol/L	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 12 mmol/L	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Calcium (mg/dL)	>= 12.0 mg/dL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 7.2 mg/dL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
Glucose (mg/dL)	>= 162 mg/dL	137	5	(3.6)	137	8	(5.8)	137	12	(8.8)
	<= 63 mg/dL	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Urine										
Protein	Increase equal to or greater than 2 grade from baseline	137	4	(2.9)	137	5	(3.6)	137	8	(5.8)
Glucose	Increase equal to or greater than 2 grade from baseline	137	9	(6.6)	137	7	(5.1)	137	14	(10.2)
Occult blood	Increase equal to or greater than 2 grade from baseline	137	11	(8.0)	137	6	(4.4)	137	14	(10.2)
Ketones	Increase equal to or greater than 2 grade from baseline	137	4	(2.9)	137	5	(3.6)	137	9	(6.6)
Other										
Prolactin (ug/L)	>= 67.5 ug/L	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

＜資料番号5.3.5.2-01 : Table 14.1.1.3-113＞

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Red blood cell count (/mm^3)	< 3,000,000 /mm^3	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Hematocrit (%)										
Female	<= 32 %	19	1	(5.3)	19	1	(5.3)	19	1	(5.3)
Male	<= 37 %	75	3	(4.0)	75	3	(4.0)	75	4	(5.3)
Hemoglobin (g/dL)										
Female	>= 16.5 g/dL	19	0	(0.0)	19	0	(0.0)	19	0	(0.0)
	<= 9.5 g/dL	19	0	(0.0)	19	0	(0.0)	19	0	(0.0)
Male	>= 18.5 g/dL	75	0	(0.0)	75	0	(0.0)	75	0	(0.0)
	<= 11.5 g/dL	75	1	(1.3)	75	0	(0.0)	75	1	(1.3)
MCV	>= 1.2 x ULN	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 0.8 x LLN	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Total white blood cell count (/uL)	>= 16,000 /uL	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	< 2,800 / uL	94	1	(1.1)	94	1	(1.1)	94	1	(1.1)
Neutrophils (%)	>= 85 %	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 20 %	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Eosinophils (%)	>= 10 %	94	1	(1.1)	94	1	(1.1)	94	1	(1.1)
Basophils (%)	>= 10 %	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Lymphocytes (%)	>= 75 %	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 10 %	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Monocytes (%)	>= 15 %	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Platelet count (/mm^3)	>= 700,000 /mm^3	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 75,000 /mm^3	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Total bilirubin	>= 2 x ULN	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Alkaline phosphatase	>= 3 x ULN	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
ALT	>= 3 x ULN	94	1	(1.1)	94	0	(0.0)	94	1	(1.1)
AST	>= 3 x ULN	94	1	(1.1)	94	0	(0.0)	94	1	(1.1)
Gamma-GTP (U/L)	>= 200 U/L	94	0	(0.0)	94	2	(2.1)	94	2	(2.1)
INR/prothrombin time	>= 2.0	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Albumin (g/dL)	<= 2.7 g/dL	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Total cholesterol (mg/dL)	>= 302 mg/dL	94	1	(1.1)	94	0	(0.0)	94	1	(1.1)
Triglycerides (mg/dL)	>= 500 mg/dL	94	0	(0.0)	94	1	(1.1)	94	1	(1.1)
Creatinine	>= 1.5 x ULN	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 0.5 x LLN	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
BUN (mg/dL)	> 30 mg/dL	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Sodium (mEq/L)	>= 155 mEq/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 125 mEq/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Potassium (mEq/L)	>= 6.0 mEq/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 3.0 mEq/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Bicarbonate (mmol/L)	>= 38 mmol/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 12 mmol/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Calcium (mg/dL)	>= 12.0 mg/dL	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 7.2 mg/dL	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
Glucose (mg/dL)	>= 162 mg/dL	94	1	(1.1)	94	1	(1.1)	94	1	(1.1)
	<= 63 mg/dL	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Urine										
Protein	Increase equal to or greater than 2 grade from baseline	94	4	(4.3)	94	5	(5.3)	94	8	(8.5)
Glucose	Increase equal to or greater than 2 grade from baseline	94	5	(5.3)	94	3	(3.2)	94	8	(8.5)
Occult blood	Increase equal to or greater than 2 grade from baseline	94	6	(6.4)	94	3	(3.2)	94	9	(9.6)
Ketones	Increase equal to or greater than 2 grade from baseline	94	3	(3.2)	94	3	(3.2)	94	5	(5.3)
Other										
Prolactin (ug/L)	>= 67.5 ug/L	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

＜資料番号5.3.5.2-01 : Table 14.1.1.3-113＞

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene total (N=231)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology										
Red blood cell count (/mm^3)	< 3,000,000 /mm^3	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Hematocrit (%)										
Female	<= 32 %	52	2	(3.8)	52	1	(1.9)	52	2	(3.8)
Male	<= 37 %	179	6	(3.4)	179	7	(3.9)	179	9	(5.0)
Hemoglobin (g/dL)										
Female	>= 16.5 g/dL	52	0	(0.0)	52	0	(0.0)	52	0	(0.0)
	<= 9.5 g/dL	52	0	(0.0)	52	0	(0.0)	52	0	(0.0)
Male	>= 18.5 g/dL	179	0	(0.0)	179	0	(0.0)	179	0	(0.0)
	<= 11.5 g/dL	179	2	(1.1)	179	1	(0.6)	179	3	(1.7)
MCV	>= 1.2 x ULN	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 0.8 x LLN	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Total white blood cell count (/uL)	>= 16,000 /uL	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	< 2,800 / uL	231	1	(0.4)	231	1	(0.4)	231	1	(0.4)
Neutrophils (%)	>= 85 %	231	2	(0.9)	231	0	(0.0)	231	2	(0.9)
	<= 20 %	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001				Nalmefene total (N=231)					
		Study	339-14-001			339-14-002			Total	
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology											
Eosinophils (%)	>= 10 %		231	3	(1.3)	231	4	(1.7)	231	5	(2.2)
Basophils (%)	>= 10 %		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Lymphocytes (%)	>= 75 %		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 10 %		231	2	(0.9)	231	0	(0.0)	231	2	(0.9)
Monocytes (%)	>= 15 %		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Platelet count (/mm^3)	>= 700,000 /mm^3		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 75,000 /mm^3		231	0	(0.0)	231	1	(0.4)	231	1	(0.4)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene total (N=231)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Total bilirubin	>= 2 x ULN	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Alkaline phosphatase	>= 3 x ULN	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
ALT	>= 3 x ULN	231	1	(0.4)	231	0	(0.0)	231	1	(0.4)
AST	>= 3 x ULN	231	1	(0.4)	231	2	(0.9)	231	3	(1.3)
Gamma-GTP (U/L)	>= 200 U/L	231	8	(3.5)	231	12	(5.2)	231	14	(6.1)
INR/prothrombin time	>= 2.0	231	1	(0.4)	231	0	(0.0)	231	1	(0.4)
Albumin (g/dL)	<= 2.7 g/dL	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Total cholesterol (mg/dL)	>= 302 mg/dL	231	4	(1.7)	231	2	(0.9)	231	4	(1.7)
Triglycerides (mg/dL)	>= 500 mg/dL	231	1	(0.4)	231	3	(1.3)	231	4	(1.7)
Creatinine	>= 1.5 x ULN	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 0.5 x LLN	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
BUN (mg/dL)	> 30 mg/dL	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Sodium (mEq/L)	>= 155 mEq/L	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 125 mEq/L	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Potassium (mEq/L)	>= 6.0 mEq/L	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 3.0 mEq/L	231	2	(0.9)	231	0	(0.0)	231	2	(0.9)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene total (N=231)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry										
Bicarbonate (mmol/L)	>= 38 mmol/L	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 12 mmol/L	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Calcium (mg/dL)	>= 12.0 mg/dL	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 7.2 mg/dL	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
Glucose (mg/dL)	>= 162 mg/dL	231	6	(2.6)	231	9	(3.9)	231	13	(5.6)
	<= 63 mg/dL	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene total (N=231)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Urine										
Protein	Increase equal to or greater than 2 grade from baseline	231	8	(3.5)	231	10	(4.3)	231	16	(6.9)
Glucose	Increase equal to or greater than 2 grade from baseline	231	14	(6.1)	231	10	(4.3)	231	22	(9.5)
Occult blood	Increase equal to or greater than 2 grade from baseline	231	17	(7.4)	231	9	(3.9)	231	23	(10.0)
Ketones	Increase equal to or greater than 2 grade from baseline	231	7	(3.0)	231	8	(3.5)	231	14	(6.1)
Other										
Prolactin (ug/L)	>= 67.5 ug/L	231	0	(0.0)	231	0	(0.0)	231	0	(0.0)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

＜資料番号5.3.5.2-01 : Table 14.1.1.3-113＞

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001									
							Total (N=403)			
		Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology											
Red blood cell count (/mm^3)	< 3,000,000 /mm^3		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Hematocrit (%)											
Female	<= 32 %		116	2	(1.7)	116	1	(0.9)	116	2	(1.7)
Male	<= 37 %		287	6	(2.1)	285	10	(3.5)	287	12	(4.2)
Hemoglobin (g/dL)											
Female	>= 16.5 g/dL		116	0	(0.0)	116	0	(0.0)	116	0	(0.0)
	<= 9.5 g/dL		116	0	(0.0)	116	0	(0.0)	116	0	(0.0)
Male	>= 18.5 g/dL		287	0	(0.0)	285	1	(0.4)	287	1	(0.3)
	<= 11.5 g/dL		287	2	(0.7)	285	2	(0.7)	287	4	(1.4)
MCV	>= 1.2 x ULN		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 0.8 x LLN		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Total white blood cell count (/uL)	>= 16,000 /uL		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	< 2,800 / uL		403	1	(0.2)	401	2	(0.5)	403	2	(0.5)
Neutrophils (%)	>= 85 %		403	3	(0.7)	401	1	(0.2)	403	4	(1.0)
	<= 20 %		403	0	(0.0)	401	1	(0.2)	403	1	(0.2)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001									
							Total (N=403)			
		Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Hematology											
Eosinophils (%)	>= 10 %		403	11	(2.7)	401	9	(2.2)	403	15	(3.7)
Basophils (%)	>= 10 %		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Lymphocytes (%)	>= 75 %		403	0	(0.0)	401	1	(0.2)	403	1	(0.2)
	<= 10 %		403	3	(0.7)	401	2	(0.5)	403	5	(1.2)
Monocytes (%)	>= 15 %		403	0	(0.0)	401	1	(0.2)	403	1	(0.2)
Platelet count (/mm^3)	>= 700,000 /mm^3		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 75,000 /mm^3		403	0	(0.0)	401	1	(0.2)	403	1	(0.2)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.
b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.
ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001									
							Total (N=403)			
		Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry											
Total bilirubin	>= 2 x ULN		403	2	(0.5)	401	2	(0.5)	403	4	(1.0)
Alkaline phosphatase	>= 3 x ULN		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
ALT	>= 3 x ULN		403	1	(0.2)	401	1	(0.2)	403	2	(0.5)
AST	>= 3 x ULN		403	2	(0.5)	401	4	(1.0)	403	6	(1.5)
Gamma-GTP (U/L)	>= 200 U/L		403	23	(5.7)	401	17	(4.2)	403	31	(7.7)
INR/prothrombin time	>= 2.0		403	1	(0.2)	401	0	(0.0)	403	1	(0.2)
Albumin (g/dL)	<= 2.7 g/dL		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Total cholesterol (mg/dL)	>= 302 mg/dL		403	5	(1.2)	401	3	(0.7)	403	6	(1.5)
Triglycerides (mg/dL)	>= 500 mg/dL		403	8	(2.0)	401	7	(1.7)	403	12	(3.0)
Creatinine	>= 1.5 x ULN		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 0.5 x LLN		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
BUN (mg/dL)	> 30 mg/dL		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Sodium (mEq/L)	>= 155 mEq/L		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 125 mEq/L		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Potassium (mEq/L)	>= 6.0 mEq/L		403	1	(0.2)	401	0	(0.0)	403	1	(0.2)
	<= 3.0 mEq/L		403	3	(0.7)	401	1	(0.2)	403	3	(0.7)

a : N= number of subjects in safety set with
at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline
potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001									
							Total (N=403)			
		Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Blood chemistry											
Bicarbonate (mmol/L)	>= 38 mmol/L		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 12 mmol/L		403	0	(0.0)	401	1	(0.2)	403	1	(0.2)
Calcium (mg/dL)	>= 12.0 mg/dL		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 7.2 mg/dL		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
Glucose (mg/dL)	>= 162 mg/dL		403	11	(2.7)	401	14	(3.5)	403	23	(5.7)
	<= 63 mg/dL		403	2	(0.5)	401	0	(0.0)	403	2	(0.5)

a : N= number of subjects in safety set with

at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

表 2.7.4.7.1-22

Table 14.1.1.3-113

Incidences of Potentially Clinically Significant Abnormalities in Laboratory Tests in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Total (N=403)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Urine										
Protein	Increase equal to or greater than 2 grade from baseline	403	8	(2.0)	401	14	(3.5)	403	20	(5.0)
Glucose	Increase equal to or greater than 2 grade from baseline	403	19	(4.7)	401	18	(4.5)	403	32	(7.9)
Occult blood	Increase equal to or greater than 2 grade from baseline	403	35	(8.7)	401	22	(5.5)	403	47	(11.7)
Ketones	Increase equal to or greater than 2 grade from baseline	403	11	(2.7)	401	16	(4.0)	403	24	(6.0)
Other										
Prolactin (ug/L)	>= 67.5 ug/L	403	0	(0.0)	401	1	(0.2)	403	1	(0.2)

a : N= number of subjects in safety set with at least one post-baseline laboratory value for the laboratory test.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the laboratory test.

ULN : upper limit of normal, LLN : lower limit of normal

＜資料番号5.3.5.2-01 : Table 14.1.1.3-113＞

表 2.7.4.7.1-23
Table 14.1.1.3-65
Incidences of Potentially Clinically Significant Abnormalities in Vital Signs and Body Weight (339-14-001)
Safety Set

		Placebo			Nalmefene								
					20 mg			10 mg			Total		
		(N=245)			(N=248)			(N=184)			(N=432)		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Systolic blood pressure (mmHg)	>= 180 mmHg and increase >= 20 mmHg from baseline	245	2	(0.8)	248	2	(0.8)	183	1	(0.5)	431	3	(0.7)
	<= 90 mmHg and decrease <= -20 mmHg from baseline	245	2	(0.8)	248	3	(1.2)	183	3	(1.6)	431	6	(1.4)
Diastolic blood pressure (mmHg)	>= 105 mmHg and increase >= 15 mmHg from baseline	245	6	(2.4)	248	8	(3.2)	183	4	(2.2)	431	12	(2.8)
	<= 50 mmHg and decrease <= -15 mmHg from baseline	245	2	(0.8)	248	1	(0.4)	183	4	(2.2)	431	5	(1.2)
Pulse rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	245	0	(0.0)	248	0	(0.0)	183	1	(0.5)	431	1	(0.2)
	<= 50 bpm and decrease <= -15 bpm from baseline	245	1	(0.4)	248	1	(0.4)	183	1	(0.5)	431	2	(0.5)
Body weight	Increase >= 7% from baseline	245	7	(2.9)	248	11	(4.4)	183	2	(1.1)	431	13	(3.0)
	Decrease <= -7% from baseline	245	6	(2.4)	248	4	(1.6)	183	10	(5.5)	431	14	(3.2)

a : N= number of subjects in safety set with at least one post-baseline vital signs value for the vital signs.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the vital signs.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-65＞

表 2.7.4.7.1-24

Table 14.1.1.3-131

Incidences of Potentially Clinically Significant Abnormalities in Vital Signs and Body Weight in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Placebo (N=172)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Systolic blood pressure (mmHg)	>= 180 mmHg and increase >= 20 mmHg from baseline	172	1	(0.6)	172	1	(0.6)	172	1	(0.6)
	<= 90 mmHg and decrease <= -20 mmHg from baseline	172	1	(0.6)	172	2	(1.2)	172	2	(1.2)
Diastolic blood pressure (mmHg)	>= 105 mmHg and increase >= 15 mmHg from baseline	172	4	(2.3)	172	4	(2.3)	172	6	(3.5)
	<= 50 mmHg and decrease <= -15 mmHg from baseline	172	1	(0.6)	172	3	(1.7)	172	4	(2.3)
Pulse rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	172	0	(0.0)	172	1	(0.6)	172	1	(0.6)
	<= 50 bpm and decrease <= -15 bpm from baseline	172	1	(0.6)	172	0	(0.0)	172	1	(0.6)
Body weight	Increase >= 7% from baseline	172	7	(4.1)	172	11	(6.4)	172	14	(8.1)
	Decrease <= -7% from baseline	172	2	(1.2)	172	11	(6.4)	172	13	(7.6)

a : N= number of subjects in safety set with at least one post-baseline vital signs value for the vital signs.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the vital signs.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-131＞

表 2.7.4.7.1-24

Table 14.1.1.3-131

Incidences of Potentially Clinically Significant Abnormalities in Vital Signs and Body Weight in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 20 mg (N=137)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Systolic blood pressure (mmHg)	>= 180 mmHg and increase >= 20 mmHg from baseline	137	0	(0.0)	137	1	(0.7)	137	1	(0.7)
	<= 90 mmHg and decrease <= -20 mmHg from baseline	137	1	(0.7)	137	3	(2.2)	137	3	(2.2)
Diastolic blood pressure (mmHg)	>= 105 mmHg and increase >= 15 mmHg from baseline	137	4	(2.9)	137	4	(2.9)	137	6	(4.4)
	<= 50 mmHg and decrease <= -15 mmHg from baseline	137	1	(0.7)	137	0	(0.0)	137	1	(0.7)
Pulse rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	137	0	(0.0)	137	1	(0.7)	137	1	(0.7)
	<= 50 bpm and decrease <= -15 bpm from baseline	137	1	(0.7)	137	2	(1.5)	137	3	(2.2)
Body weight	Increase >= 7% from baseline	137	9	(6.6)	137	11	(8.0)	137	13	(9.5)
	Decrease <= -7% from baseline	137	4	(2.9)	137	10	(7.3)	137	11	(8.0)

a : N= number of subjects in safety set with at least one post-baseline vital signs value for the vital signs.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the vital signs.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-131＞

表 2.7.4.7.1-24

Table 14.1.1.3-131

Incidences of Potentially Clinically Significant Abnormalities in Vital Signs and Body Weight in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene 10 mg (N=94)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Systolic blood pressure (mmHg)	>= 180 mmHg and increase >= 20 mmHg from baseline	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 90 mmHg and decrease <= -20 mmHg from baseline	94	2	(2.1)	94	1	(1.1)	94	2	(2.1)
Diastolic blood pressure (mmHg)	>= 105 mmHg and increase >= 15 mmHg from baseline	94	2	(2.1)	94	3	(3.2)	94	4	(4.3)
	<= 50 mmHg and decrease <= -15 mmHg from baseline	94	2	(2.1)	94	4	(4.3)	94	4	(4.3)
Pulse rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	94	1	(1.1)	94	2	(2.1)	94	3	(3.2)
	<= 50 bpm and decrease <= -15 bpm from baseline	94	1	(1.1)	94	4	(4.3)	94	4	(4.3)
Body weight	Increase >= 7% from baseline	94	2	(2.1)	94	6	(6.4)	94	6	(6.4)
	Decrease <= -7% from baseline	94	7	(7.4)	94	13	(13.8)	94	13	(13.8)

a : N= number of subjects in safety set with at least one post-baseline vital signs value for the vital signs.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the vital signs.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-131＞

表 2.7.4.7.1-24

Table 14.1.1.3-131

Incidences of Potentially Clinically Significant Abnormalities in Vital Signs and Body Weight in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

	Treatment group of study 339-14-001	Nalmefene total (N=231)								
	Study	339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Systolic blood pressure (mmHg)	>= 180 mmHg and increase >= 20 mmHg from baseline	231	0	(0.0)	231	1	(0.4)	231	1	(0.4)
	<= 90 mmHg and decrease <= -20 mmHg from baseline	231	3	(1.3)	231	4	(1.7)	231	5	(2.2)
Diastolic blood pressure (mmHg)	>= 105 mmHg and increase >= 15 mmHg from baseline	231	6	(2.6)	231	7	(3.0)	231	10	(4.3)
	<= 50 mmHg and decrease <= -15 mmHg from baseline	231	3	(1.3)	231	4	(1.7)	231	5	(2.2)
Pulse rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	231	1	(0.4)	231	3	(1.3)	231	4	(1.7)
	<= 50 bpm and decrease <= -15 bpm from baseline	231	2	(0.9)	231	6	(2.6)	231	7	(3.0)
Body weight	Increase >= 7% from baseline	231	11	(4.8)	231	17	(7.4)	231	19	(8.2)
	Decrease <= -7% from baseline	231	11	(4.8)	231	23	(10.0)	231	24	(10.4)

a : N= number of subjects in safety set with at least one post-baseline vital signs value for the vital signs.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the vital signs.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-131＞

表 2.7.4.7.1-24

Table 14.1.1.3-131

Incidences of Potentially Clinically Significant Abnormalities in Vital Signs and Body Weight in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001						Total (N=403)		
		Study	339-14-001			339-14-002		Total		
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Systolic blood pressure (mmHg)	>= 180 mmHg and increase >= 20 mmHg from baseline		403	1	(0.2)	403	2	(0.5)	403	2	(0.5)
	<= 90 mmHg and decrease <= -20 mmHg from baseline		403	4	(1.0)	403	6	(1.5)	403	7	(1.7)
Diastolic blood pressure (mmHg)	>= 105 mmHg and increase >= 15 mmHg from baseline		403	10	(2.5)	403	11	(2.7)	403	16	(4.0)
	<= 50 mmHg and decrease <= -15 mmHg from baseline		403	4	(1.0)	403	7	(1.7)	403	9	(2.2)
Pulse rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline		403	1	(0.2)	403	4	(1.0)	403	5	(1.2)
	<= 50 bpm and decrease <= -15 bpm from baseline		403	3	(0.7)	403	6	(1.5)	403	8	(2.0)
Body weight	Increase >= 7% from baseline		403	18	(4.5)	403	28	(6.9)	403	33	(8.2)
	Decrease <= -7% from baseline		403	13	(3.2)	403	34	(8.4)	403	37	(9.2)

a : N= number of subjects in safety set with at least one post-baseline vital signs value for the vital signs.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the vital signs.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-131＞

表 2.7.4.7.1-25
Table 14.1.1.3-69
Incidences of Potentially Clinically Significant Abnormalities in 12-Lead ECG Parameters (339-14-001)
Safety Set

		Placebo			Nalmefene								
					20 mg			10 mg			Total		
		(N=245)			(N=248)			(N=184)			(N=432)		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Heart rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	238	0	(0.0)	245	0	(0.0)	179	0	(0.0)	424	0	(0.0)
	<= 50 bpm and decrease <= -15 bpm from baseline	238	0	(0.0)	245	2	(0.8)	179	2	(1.1)	424	4	(0.9)
RR interval (msec)	>= 1200 msec	238	5	(2.1)	245	14	(5.7)	179	7	(3.9)	424	21	(5.0)
	< 500 msec	238	0	(0.0)	245	0	(0.0)	179	0	(0.0)	424	0	(0.0)
PR interval (msec)	>= 260 msec	238	1	(0.4)	244	1	(0.4)	179	0	(0.0)	423	1	(0.2)
QRS interval (msec)	>= 150 msec	238	0	(0.0)	245	5	(2.0)	179	2	(1.1)	424	7	(1.7)
QT interval (msec)	>= 500 msec	238	1	(0.4)	245	2	(0.8)	179	0	(0.0)	424	2	(0.5)
QTcB (msec)	>= 500 msec or increase >= 60 msec from baseline	238	1	(0.4)	245	2	(0.8)	179	0	(0.0)	424	2	(0.5)
QTcF (msec)	>= 500 msec or increase >= 60 msec from baseline	238	0	(0.0)	245	1	(0.4)	179	1	(0.6)	424	2	(0.5)

a : N= number of subjects in safety set with at least one post-baseline ECG value for the 12-Lead ECG parameters.

b : n= number of subjects with post-baseline potentially clinically significant abnormality for the 12-Lead ECG parameters.

＜資料番号5.3.5.1-01 : Table 14.1.1.3-69＞

表 2.7.4.7.1-26
Table 14.1.1.3-70
Categorical Analysis of 12-Lead ECG Parameters (339-14-001)
Safety Set

			QTcB interval (ms)									
			Measured value						Change from baseline			
Treatment			> 450		> 480		> 500		> 30		> 60	
group	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Placebo	Screening	245	20	(8.2)	3	(1.2)	0	(0.0)				
(N=245)	Baseline	245	20	(8.2)	3	(1.2)	0	(0.0)				
	Week 12	230	17	(7.4)	0	(0.0)	0	(0.0)	12	(5.2)	1	(0.4)
	Week 24	219	21	(9.6)	0	(0.0)	0	(0.0)	11	(5.0)	0	(0.0)
	Last[c]	238	24	(10.1)	0	(0.0)	0	(0.0)	13	(5.5)	0	(0.0)
	Worst value in post baseline	238	32	(13.4)	0	(0.0)	0	(0.0)	20	(8.4)	1	(0.4)
Nalmefene 20 mg	Screening	248	19	(7.7)	2	(0.8)	0	(0.0)				
(N=248)	Baseline	248	19	(7.7)	2	(0.8)	0	(0.0)				
	Week 12	195	11	(5.6)	1	(0.5)	1	(0.5)	6	(3.1)	0	(0.0)
	Week 24	189	19	(10.1)	1	(0.5)	0	(0.0)	10	(5.3)	0	(0.0)
	Last[c]	245	22	(9.0)	3	(1.2)	1	(0.4)	12	(4.9)	0	(0.0)
	Worst value in post baseline	245	27	(11.0)	4	(1.6)	2	(0.8)	18	(7.3)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation

表 2.7.4.7.1-26
Table 14.1.1.3-70
Categorical Analysis of 12-Lead ECG Parameters (339-14-001)
Safety Set

			QTcB interval (ms)									
			Measured value						Change from baseline			
Treatment			> 450		> 480		> 500		> 30		> 60	
group	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Nalmefene 10 mg	Screening	184	15	(8.2)	0	(0.0)	0	(0.0)				
(N=184)	Baseline	184	15	(8.2)	0	(0.0)	0	(0.0)				
	Week 12	149	10	(6.7)	1	(0.7)	0	(0.0)	8	(5.4)	0	(0.0)
	Week 24	139	12	(8.6)	2	(1.4)	0	(0.0)	5	(3.6)	0	(0.0)
	Last[c]	179	17	(9.5)	3	(1.7)	0	(0.0)	8	(4.5)	0	(0.0)
	Worst value in post baseline	179	21	(11.7)	3	(1.7)	0	(0.0)	14	(7.8)	0	(0.0)
Nalmefene total	Screening	432	34	(7.9)	2	(0.5)	0	(0.0)				
(N=432)	Baseline	432	34	(7.9)	2	(0.5)	0	(0.0)				
	Week 12	344	21	(6.1)	2	(0.6)	1	(0.3)	14	(4.1)	0	(0.0)
	Week 24	328	31	(9.5)	3	(0.9)	0	(0.0)	15	(4.6)	0	(0.0)
	Last[c]	424	39	(9.2)	6	(1.4)	1	(0.2)	20	(4.7)	0	(0.0)
	Worst value in post baseline	424	48	(11.3)	7	(1.7)	2	(0.5)	32	(7.5)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation

＜資料番号5.3.5.1-01 : Table 14.1.1.3-70＞

表 2.7.4.7.1-26
Table 14.1.1.3-70
Categorical Analysis of 12-Lead ECG Parameters (339-14-001)
Safety Set

			QTcF interval (ms)									
			Measured value						Change from baseline			
Treatment			> 450		> 480		> 500		> 30		> 60	
group	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Placebo	Screening	245	10	(4.1)	1	(0.4)	1	(0.4)				
(N=245)	Baseline	245	10	(4.1)	1	(0.4)	1	(0.4)				
	Week 12	230	6	(2.6)	1	(0.4)	0	(0.0)	4	(1.7)	0	(0.0)
	Week 24	219	4	(1.8)	0	(0.0)	0	(0.0)	2	(0.9)	0	(0.0)
	Last[c]	238	5	(2.1)	0	(0.0)	0	(0.0)	2	(0.8)	0	(0.0)
	Worst value in post baseline	238	9	(3.8)	1	(0.4)	0	(0.0)	4	(1.7)	0	(0.0)
Nalmefene 20 mg	Screening	248	8	(3.2)	2	(0.8)	1	(0.4)				
(N=248)	Baseline	248	8	(3.2)	2	(0.8)	1	(0.4)				
	Week 12	195	4	(2.1)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)
	Week 24	189	8	(4.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Last[c]	245	10	(4.1)	1	(0.4)	1	(0.4)	0	(0.0)	0	(0.0)
	Worst value in post baseline	245	12	(4.9)	1	(0.4)	1	(0.4)	1	(0.4)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation

表 2.7.4.7.1-26
Table 14.1.1.3-70
Categorical Analysis of 12-Lead ECG Parameters (339-14-001)
Safety Set

			QTcF interval (ms)									
			Measured value						Change from baseline			
Treatment			> 450		> 480		> 500		> 30		> 60	
group	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Nalmefene 10 mg	Screening	184	6	(3.3)	0	(0.0)	0	(0.0)				
(N=184)	Baseline	184	6	(3.3)	0	(0.0)	0	(0.0)				
	Week 12	149	2	(1.3)	0	(0.0)	0	(0.0)	2	(1.3)	1	(0.7)
	Week 24	139	8	(5.8)	1	(0.7)	0	(0.0)	3	(2.2)	0	(0.0)
	Last[c]	179	10	(5.6)	1	(0.6)	0	(0.0)	4	(2.2)	0	(0.0)
	Worst value in post baseline	179	10	(5.6)	1	(0.6)	0	(0.0)	5	(2.8)	1	(0.6)
Nalmefene total	Screening	432	14	(3.2)	2	(0.5)	1	(0.2)				
(N=432)	Baseline	432	14	(3.2)	2	(0.5)	1	(0.2)				
	Week 12	344	6	(1.7)	0	(0.0)	0	(0.0)	3	(0.9)	1	(0.3)
	Week 24	328	16	(4.9)	1	(0.3)	0	(0.0)	3	(0.9)	0	(0.0)
	Last[c]	424	20	(4.7)	2	(0.5)	1	(0.2)	4	(0.9)	0	(0.0)
	Worst value in post baseline	424	22	(5.2)	2	(0.5)	1	(0.2)	6	(1.4)	1	(0.2)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation

＜資料番号5.3.5.1-01 : Table 14.1.1.3-70＞

表 2.7.4.7.1-27

Table 14.1.1.3-144

Incidences of Potentially Clinically Significant Abnormalities in 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001			Placebo (N=172)					
		Study	339-14-001			339-14-002			Total	
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Heart rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline		172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
	<= 50 bpm and decrease <= -15 bpm from baseline		172	0	(0.0)	170	2	(1.2)	172	2	(1.2)
RR interval (msec)	>= 1200 msec		172	5	(2.9)	170	9	(5.3)	172	11	(6.4)
	< 500 msec		172	0	(0.0)	170	0	(0.0)	172	0	(0.0)
PR interval (msec)	>= 260 msec		172	1	(0.6)	170	0	(0.0)	172	1	(0.6)
QRS interval (msec)	>= 150 msec		172	0	(0.0)	170	2	(1.2)	172	2	(1.2)
QT interval (msec)	>= 500 msec		172	1	(0.6)	170	0	(0.0)	172	1	(0.6)
QTcB (msec)	>= 500 msec or increase >= 60 msec from baseline		172	1	(0.6)	170	1	(0.6)	172	1	(0.6)
QTcF (msec)	>= 500 msec or increase >= 60 msec from baseline		172	0	(0.0)	170	0	(0.0)	172	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline ECG value for the 12-Lead ECG parameters.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the 12-Lead ECG parameters.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-144＞

表 2.7.4.7.1-27

Table 14.1.1.3-144

Incidences of Potentially Clinically Significant Abnormalities in 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 20 mg (N=137)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Heart rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
	<= 50 bpm and decrease <= -15 bpm from baseline	137	2	(1.5)	137	3	(2.2)	137	4	(2.9)
RR interval (msec)	>= 1200 msec	137	11	(8.0)	137	12	(8.8)	137	16	(11.7)
	< 500 msec	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)
PR interval (msec)	>= 260 msec	137	1	(0.7)	137	1	(0.7)	137	1	(0.7)
QRS interval (msec)	>= 150 msec	137	3	(2.2)	137	2	(1.5)	137	3	(2.2)
QT interval (msec)	>= 500 msec	137	1	(0.7)	137	1	(0.7)	137	1	(0.7)
QTcB (msec)	>= 500 msec or increase >= 60 msec from baseline	137	1	(0.7)	137	0	(0.0)	137	1	(0.7)
QTcF (msec)	>= 500 msec or increase >= 60 msec from baseline	137	0	(0.0)	137	0	(0.0)	137	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline ECG value for the 12-Lead ECG parameters.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the 12-Lead ECG parameters.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-144＞

表 2.7.4.7.1-27

Table 14.1.1.3-144

Incidences of Potentially Clinically Significant Abnormalities in 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

Treatment group of study 339-14-001		Nalmefene 10 mg (N=94)								
Study		339-14-001			339-14-002			Total		
Parameters (Unit)	Criteria	N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Heart rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
	<= 50 bpm and decrease <= -15 bpm from baseline	94	2	(2.1)	94	2	(2.1)	94	3	(3.2)
RR interval (msec)	>= 1200 msec	94	5	(5.3)	94	7	(7.4)	94	11	(11.7)
	< 500 msec	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
PR interval (msec)	>= 260 msec	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
QRS interval (msec)	>= 150 msec	94	2	(2.1)	94	3	(3.2)	94	3	(3.2)
QT interval (msec)	>= 500 msec	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
QTcB (msec)	>= 500 msec or increase >= 60 msec from baseline	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)
QTcF (msec)	>= 500 msec or increase >= 60 msec from baseline	94	0	(0.0)	94	0	(0.0)	94	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline ECG value for the 12-Lead ECG parameters.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the 12-Lead ECG parameters.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-144＞

表 2.7.4.7.1-27

Table 14.1.1.3-144

Incidences of Potentially Clinically Significant Abnormalities in 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001			Nalmefene total (N=231)					
		Study	339-14-001			339-14-002			Total	
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Heart rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
	<= 50 bpm and decrease <= -15 bpm from baseline		231	4	(1.7)	231	5	(2.2)	231	7	(3.0)
RR interval (msec)	>= 1200 msec		231	16	(6.9)	231	19	(8.2)	231	27	(11.7)
	< 500 msec		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)
PR interval (msec)	>= 260 msec		231	1	(0.4)	231	1	(0.4)	231	1	(0.4)
QRS interval (msec)	>= 150 msec		231	5	(2.2)	231	5	(2.2)	231	6	(2.6)
QT interval (msec)	>= 500 msec		231	1	(0.4)	231	1	(0.4)	231	1	(0.4)
QTcB (msec)	>= 500 msec or increase >= 60 msec from baseline		231	1	(0.4)	231	0	(0.0)	231	1	(0.4)
QTcF (msec)	>= 500 msec or increase >= 60 msec from baseline		231	0	(0.0)	231	0	(0.0)	231	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline ECG value for the 12-Lead ECG parameters.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the 12-Lead ECG parameters.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-144＞

表 2.7.4.7.1-27

Table 14.1.1.3-144

Incidences of Potentially Clinically Significant Abnormalities in 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

		Treatment group of study 339-14-001						Total (N=403)		
		Study	339-14-001			339-14-002		Total		
Parameters (Unit)	Criteria		N[a]	n[b]	(%)	N[a]	n[b]	(%)	N[a]	n[b]	(%)
Heart rate (bpm)	>= 120 bpm and increase >= 15 bpm from baseline		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
	<= 50 bpm and decrease <= -15 bpm from baseline		403	4	(1.0)	401	7	(1.7)	403	9	(2.2)
RR interval (msec)	>= 1200 msec		403	21	(5.2)	401	28	(7.0)	403	38	(9.4)
	< 500 msec		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)
PR interval (msec)	>= 260 msec		403	2	(0.5)	401	1	(0.2)	403	2	(0.5)
QRS interval (msec)	>= 150 msec		403	5	(1.2)	401	7	(1.7)	403	8	(2.0)
QT interval (msec)	>= 500 msec		403	2	(0.5)	401	1	(0.2)	403	2	(0.5)
QTcB (msec)	>= 500 msec or increase >= 60 msec from baseline		403	2	(0.5)	401	1	(0.2)	403	2	(0.5)
QTcF (msec)	>= 500 msec or increase >= 60 msec from baseline		403	0	(0.0)	401	0	(0.0)	403	0	(0.0)

a : N= number of subjects in safety set with

at least one post-baseline ECG value for the 12-Lead ECG parameters.

b : n= number of subjects with post-baseline

potentially clinically significant abnormality for the 12-Lead ECG parameters.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-144＞

表 2.7.4.7.1-28

Table 14.1.1.3-153

Categorical Analysis of 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

				QTcB interval (ms)									
				Measured value						Change from baseline			
				> 450		> 480		> 500		> 30		> 60	
Treatment group of study 339-14-001	Study	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Placebo (N=172)	339-14-001	Baseline	172	12	(7.0)	1	(0.6)	0	(0.0)				
		Week 12	172	9	(5.2)	0	(0.0)	0	(0.0)	9	(5.2)	1	(0.6)
		Week 24	172	14	(8.1)	0	(0.0)	0	(0.0)	6	(3.5)	0	(0.0)
		Worst value in study 339-14-001	172	20	(11.6)	0	(0.0)	0	(0.0)	12	(7.0)	1	(0.6)
	339-14-002	Week 12 (Week 36)	138	8	(5.8)	0	(0.0)	0	(0.0)	10	(7.2)	0	(0.0)
		Week 24 (Week 48)	133	10	(7.5)	0	(0.0)	0	(0.0)	8	(6.0)	1	(0.8)
		Worst value in study 339-14-002	170	16	(9.4)	0	(0.0)	0	(0.0)	15	(8.8)	1	(0.6)
		Last 2[c]	172	13	(7.6)	0	(0.0)	0	(0.0)	9	(5.2)	1	(0.6)
		Worst value in post baseline in treatment period	172	26	(15.1)	0	(0.0)	0	(0.0)	21	(12.2)	1	(0.6)
Nalmefene 20 mg (N=137)	339-14-001	Baseline	137	11	(8.0)	1	(0.7)	0	(0.0)				
		Week 12	137	5	(3.6)	1	(0.7)	1	(0.7)	3	(2.2)	0	(0.0)
		Week 24	137	12	(8.8)	0	(0.0)	0	(0.0)	4	(2.9)	0	(0.0)
		Worst value in study 339-14-001	137	14	(10.2)	1	(0.7)	1	(0.7)	6	(4.4)	0	(0.0)
	339-14-002	Week 12 (Week 36)	134	9	(6.7)	2	(1.5)	0	(0.0)	5	(3.7)	0	(0.0)
		Week 24 (Week 48)	126	9	(7.1)	0	(0.0)	0	(0.0)	8	(6.3)	0	(0.0)
		Worst value in study 339-14-002	137	15	(10.9)	2	(1.5)	0	(0.0)	14	(10.2)	0	(0.0)
		Last 2[c]	137	10	(7.3)	0	(0.0)	0	(0.0)	10	(7.3)	0	(0.0)
		Worst value in post baseline in treatment period	137	20	(14.6)	2	(1.5)	1	(0.7)	20	(14.6)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation in treatment period

(Week x) : Total period from baseline in study 339-14-001

excluding screening period in study 339-14-002.

表 2.7.4.7.1-28

Table 14.1.1.3-153

Categorical Analysis of 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

				QTcB interval (ms)									
				Measured value						Change from baseline			
				> 450		> 480		> 500		> 30		> 60	
Treatment group of study 339-14-001	Study	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Nalmefene 10 mg (N=94)	339-14-001	Baseline	94	7	(7.4)	0	(0.0)	0	(0.0)				
		Week 12	94	5	(5.3)	0	(0.0)	0	(0.0)	5	(5.3)	0	(0.0)
		Week 24	94	8	(8.5)	1	(1.1)	0	(0.0)	4	(4.3)	0	(0.0)
		Worst value in study 339-14-001	94	11	(11.7)	1	(1.1)	0	(0.0)	8	(8.5)	0	(0.0)
	339-14-002	Week 12 (Week 36)	88	5	(5.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
		Week 24 (Week 48)	84	8	(9.5)	0	(0.0)	0	(0.0)	3	(3.6)	0	(0.0)
		Worst value in study 339-14-002	94	10	(10.6)	0	(0.0)	0	(0.0)	3	(3.2)	0	(0.0)
		Last 2[c]	94	8	(8.5)	0	(0.0)	0	(0.0)	3	(3.2)	0	(0.0)
		Worst value in post baseline in treatment period	94	15	(16.0)	1	(1.1)	0	(0.0)	10	(10.6)	0	(0.0)
Nalmefene total (N=231)	339-14-001	Baseline	231	18	(7.8)	1	(0.4)	0	(0.0)				
		Week 12	231	10	(4.3)	1	(0.4)	1	(0.4)	8	(3.5)	0	(0.0)
		Week 24	231	20	(8.7)	1	(0.4)	0	(0.0)	8	(3.5)	0	(0.0)
		Worst value in study 339-14-001	231	25	(10.8)	2	(0.9)	1	(0.4)	14	(6.1)	0	(0.0)
	339-14-002	Week 12 (Week 36)	222	14	(6.3)	2	(0.9)	0	(0.0)	5	(2.3)	0	(0.0)
		Week 24 (Week 48)	210	17	(8.1)	0	(0.0)	0	(0.0)	11	(5.2)	0	(0.0)
		Worst value in study 339-14-002	231	25	(10.8)	2	(0.9)	0	(0.0)	17	(7.4)	0	(0.0)
		Last 2[c]	231	18	(7.8)	0	(0.0)	0	(0.0)	13	(5.6)	0	(0.0)
		Worst value in post baseline in treatment period	231	35	(15.2)	3	(1.3)	1	(0.4)	30	(13.0)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation in treatment period

(Week x) : Total period from baseline in study 339-14-001

excluding screening period in study 339-14-002.

表 2.7.4.7.1-28

Table 14.1.1.3-153

Categorical Analysis of 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

				QTcB interval (ms)									
				Measured value						Change from baseline			
Treatment group of				> 450		> 480		> 500		> 30		> 60	
study 339-14-001	Study	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Total	339-14-001	Baseline	403	30	(7.4)	2	(0.5)	0	(0.0)				
(N=403)		Week 12	403	19	(4.7)	1	(0.2)	1	(0.2)	17	(4.2)	1	(0.2)
		Week 24	403	34	(8.4)	1	(0.2)	0	(0.0)	14	(3.5)	0	(0.0)
		Worst value in study 339-14-001	403	45	(11.2)	2	(0.5)	1	(0.2)	26	(6.5)	1	(0.2)
	339-14-002	Week 12 (Week 36)	360	22	(6.1)	2	(0.6)	0	(0.0)	15	(4.2)	0	(0.0)
		Week 24 (Week 48)	343	27	(7.9)	0	(0.0)	0	(0.0)	19	(5.5)	1	(0.3)
		Worst value in study 339-14-002	401	41	(10.2)	2	(0.5)	0	(0.0)	32	(8.0)	1	(0.2)
		Last 2[c]	403	31	(7.7)	0	(0.0)	0	(0.0)	22	(5.5)	1	(0.2)
		Worst value in post baseline in treatment period	403	61	(15.1)	3	(0.7)	1	(0.2)	51	(12.7)	1	(0.2)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation in treatment period

(Week x) : Total period from baseline in study 339-14-001

excluding screening period in study 339-14-002.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-153＞

表 2.7.4.7.1-28

Table 14.1.1.3-153

Categorical Analysis of 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

				QTcF interval (ms)									
				Measured value						Change from baseline			
				> 450		> 480		> 500		> 30		> 60	
Treatment group of study 339-14-001	Study	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Placebo (N=172)	339-14-001	Baseline	172	6	(3.5)	1	(0.6)	1	(0.6)				
		Week 12	172	4	(2.3)	1	(0.6)	0	(0.0)	2	(1.2)	0	(0.0)
		Week 24	172	3	(1.7)	0	(0.0)	0	(0.0)	1	(0.6)	0	(0.0)
		Worst value in study 339-14-001	172	6	(3.5)	1	(0.6)	0	(0.0)	2	(1.2)	0	(0.0)
	339-14-002	Week 12 (Week 36)	138	1	(0.7)	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)
		Week 24 (Week 48)	133	3	(2.3)	0	(0.0)	0	(0.0)	3	(2.3)	0	(0.0)
		Worst value in study 339-14-002	170	5	(2.9)	1	(0.6)	0	(0.0)	4	(2.4)	0	(0.0)
		Last 2[c]	172	4	(2.3)	1	(0.6)	0	(0.0)	3	(1.7)	0	(0.0)
		Worst value in post baseline in treatment period	172	7	(4.1)	1	(0.6)	0	(0.0)	5	(2.9)	0	(0.0)
Nalmefene 20 mg (N=137)	339-14-001	Baseline	137	5	(3.6)	1	(0.7)	0	(0.0)				
		Week 12	137	4	(2.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
		Week 24	137	7	(5.1)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
		Worst value in study 339-14-001	137	9	(6.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	339-14-002	Week 12 (Week 36)	134	4	(3.0)	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)
		Week 24 (Week 48)	126	4	(3.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
		Worst value in study 339-14-002	137	5	(3.6)	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)
		Last 2[c]	137	4	(2.9)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
		Worst value in post baseline in treatment period	137	11	(8.0)	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation in treatment period

(Week x) : Total period from baseline in study 339-14-001

excluding screening period in study 339-14-002.

表 2.7.4.7.1-28

Table 14.1.1.3-153

Categorical Analysis of 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

				QTcF interval (ms)									
				Measured value						Change from baseline			
				> 450		> 480		> 500		> 30		> 60	
Treatment group of study 339-14-001	Study	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Nalmefene 10 mg (N=94)	339-14-001	Baseline	94	2	(2.1)	0	(0.0)	0	(0.0)				
		Week 12	94	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
		Week 24	94	5	(5.3)	1	(1.1)	0	(0.0)	1	(1.1)	0	(0.0)
		Worst value in study 339-14-001	94	5	(5.3)	1	(1.1)	0	(0.0)	2	(2.1)	0	(0.0)
	339-14-002	Week 12 (Week 36)	88	2	(2.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
		Week 24 (Week 48)	84	3	(3.6)	0	(0.0)	0	(0.0)	3	(3.6)	0	(0.0)
		Worst value in study 339-14-002	94	4	(4.3)	0	(0.0)	0	(0.0)	3	(3.2)	0	(0.0)
		Last 2[c]	94	3	(3.2)	0	(0.0)	0	(0.0)	3	(3.2)	0	(0.0)
		Worst value in post baseline in treatment period	94	6	(6.4)	1	(1.1)	0	(0.0)	4	(4.3)	0	(0.0)
Nalmefene total (N=231)	339-14-001	Baseline	231	7	(3.0)	1	(0.4)	0	(0.0)				
		Week 12	231	4	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)	0	(0.0)
		Week 24	231	12	(5.2)	1	(0.4)	0	(0.0)	1	(0.4)	0	(0.0)
		Worst value in study 339-14-001	231	14	(6.1)	1	(0.4)	0	(0.0)	2	(0.9)	0	(0.0)
	339-14-002	Week 12 (Week 36)	222	6	(2.7)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)
		Week 24 (Week 48)	210	7	(3.3)	0	(0.0)	0	(0.0)	3	(1.4)	0	(0.0)
		Worst value in study 339-14-002	231	9	(3.9)	0	(0.0)	0	(0.0)	4	(1.7)	0	(0.0)
		Last 2[c]	231	7	(3.0)	0	(0.0)	0	(0.0)	3	(1.3)	0	(0.0)
		Worst value in post baseline in treatment period	231	17	(7.4)	1	(0.4)	0	(0.0)	5	(2.2)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation in treatment period

(Week x) : Total period from baseline in study 339-14-001

excluding screening period in study 339-14-002.

表 2.7.4.7.1-28

Table 14.1.1.3-153

Categorical Analysis of 12-Lead ECG Parameters in Study 339-14-001 and Study 339-14-002 Treatment Period

Safety Set

				QTcF interval (ms)									
				Measured value						Change from baseline			
				> 450		> 480		> 500		> 30		> 60	
Treatment group of study 339-14-001	Study	Timepoint	N[a]	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)	n[b]	(%)
Total (N=403)	339-14-001	Baseline	403	13	(3.2)	2	(0.5)	1	(0.2)				
		Week 12	403	8	(2.0)	1	(0.2)	0	(0.0)	3	(0.7)	0	(0.0)
		Week 24	403	15	(3.7)	1	(0.2)	0	(0.0)	2	(0.5)	0	(0.0)
		Worst value in study 339-14-001	403	20	(5.0)	2	(0.5)	0	(0.0)	4	(1.0)	0	(0.0)
	339-14-002	Week 12 (Week 36)	360	7	(1.9)	0	(0.0)	0	(0.0)	2	(0.6)	0	(0.0)
		Week 24 (Week 48)	343	10	(2.9)	0	(0.0)	0	(0.0)	6	(1.7)	0	(0.0)
		Worst value in study 339-14-002	401	14	(3.5)	1	(0.2)	0	(0.0)	8	(2.0)	0	(0.0)
		Last 2[c]	403	11	(2.7)	1	(0.2)	0	(0.0)	6	(1.5)	0	(0.0)
		Worst value in post baseline in treatment period	403	24	(6.0)	2	(0.5)	0	(0.0)	10	(2.5)	0	(0.0)

a : N= number of subjects who underwent 12-lead ECG.

b : n= number of subjects with abnormal finding.

c : Last post baseline observation in treatment period

(Week x) : Total period from baseline in study 339-14-001 excluding screening period in study 339-14-002.

＜資料番号5.3.5.2-01 : Table 14.1.1.3-153＞

表 2.7.4.7.1-29
Table 14.1.1.3-34
Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Run-out Period (339-14-002)
Subjects who Advanced to Run-out Period among Safety Set

Treatment group of run-out period		Placebo	Nalmefene 20 mg
System organ class Preferred term		(N=171) n (%)	(N=172) n (%)
Total number of subjects with adverse events		20 (11.7)	30 (17.4)
Cardiac disorders	心臓障害	0 (0.0)	4 (2.3)
Arrhythmia	不整脈	0 (0.0)	1 (0.6)
Bundle branch block left	左脚ブロック	0 (0.0)	1 (0.6)
Bundle branch block right	右脚ブロック	0 (0.0)	1 (0.6)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	1 (0.6)
Ear and labyrinth disorders	耳および迷路障害	0 (0.0)	1 (0.6)
Vertigo	回転性めまい	0 (0.0)	1 (0.6)
Eye disorders	眼障害	1 (0.6)	2 (1.2)
Asthenopia	眼精疲労	0 (0.0)	1 (0.6)
Eye allergy	眼のアレルギー	0 (0.0)	1 (0.6)
Visual acuity reduced	視力低下	1 (0.6)	0 (0.0)
Gastrointestinal disorders	胃腸障害	2 (1.2)	2 (1.2)
Constipation	便秘	0 (0.0)	1 (0.6)
Diarrhoea	下痢	0 (0.0)	1 (0.6)
Dyspepsia	消化不良	1 (0.6)	0 (0.0)
Nausea	悪心	1 (0.6)	0 (0.0)

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表 2.7.4.7.1-29
Table 14.1.1.3-34
Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Run-out Period (339-14-002)
Subjects who Advanced to Run-out Period among Safety Set

	Treatment group of run-out period	Placebo	Nalmefene 20 mg
System organ class		(N=171)	(N=172)
Preferred term		n (%)	n (%)
General disorders and administration site conditions	一般・全身障害および投与部位の状態	1 (0.6)	2 (1.2)
Chest pain	胸痛	0 (0.0)	1 (0.6)
Feeling abnormal	異常感	1 (0.6)	0 (0.0)
Hangover	宿酔	0 (0.0)	1 (0.6)
Immune system disorders	免疫系障害	1 (0.6)	0 (0.0)
Seasonal allergy	季節性アレルギー	1 (0.6)	0 (0.0)
Infections and infestations	感染症および寄生虫症	2 (1.2)	8 (4.7)
Conjunctivitis	結膜炎	1 (0.6)	0 (0.0)
Diverticulitis	憩室炎	0 (0.0)	1 (0.6)
Nasopharyngitis	鼻咽頭炎	1 (0.6)	7 (4.1)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	2 (1.2)	1 (0.6)
Arthropod sting	節足動物刺傷	1 (0.6)	0 (0.0)
Foot fracture	足骨折	0 (0.0)	1 (0.6)
Excoriation	擦過傷	1 (0.6)	0 (0.0)

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表 2.7.4.7.1-29
Table 14.1.1.3-34
Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Run-out Period (339-14-002)
Subjects who Advanced to Run-out Period among Safety Set

	Treatment group of run-out period	Placebo	Nalmefene 20 mg
System organ class		(N=171)	(N=172)
Preferred term		n (%)	n (%)
Investigations	臨床検査	9 (5.3)	9 (5.2)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	2 (1.2)	1 (0.6)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	0 (0.0)
Blood bicarbonate decreased	血中重炭酸塩減少	1 (0.6)	0 (0.0)
Blood cholesterol increased	血中コレステロール増加	0 (0.0)	1 (0.6)
Blood glucose increased	血中ブドウ糖増加	1 (0.6)	0 (0.0)
Blood pressure increased	血圧上昇	0 (0.0)	1 (0.6)
Blood prolactin increased	血中プロラクチン増加	2 (1.2)	1 (0.6)
Blood triglycerides increased	血中トリグリセリド増加	2 (1.2)	2 (1.2)
Electrocardiogram QT prolonged	心電図QT延長	0 (0.0)	2 (1.2)
Gamma-glutamyltransferase increased	γーグルタミルトランスフェラーゼ増加	3 (1.8)	1 (0.6)
Weight increased	体重増加	1 (0.6)	0 (0.0)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)
Metabolism and nutrition disorders	代謝および栄養障害	0 (0.0)	1 (0.6)
Dyslipidaemia	脂質異常症	0 (0.0)	1 (0.6)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	1 (0.6)	4 (2.3)
Back pain	背部痛	0 (0.0)	1 (0.6)
Periarthritis	関節周囲炎	1 (0.6)	1 (0.6)
Musculoskeletal stiffness	筋骨格硬直	0 (0.0)	2 (1.2)

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表 2.7.4.7.1-29

Table 14.1.1.3-34

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Run-out Period (339-14-002)

Subjects who Advanced to Run-out Period among Safety Set

	Treatment group of run-out period	Placebo	Nalmefene 20 mg
System organ class		(N=171)	(N=172)
Preferred term		n (%)	n (%)
Nervous system disorders	神経系障害	0 (0.0)	2 (1.2)
Dizziness	浮動性めまい	0 (0.0)	1 (0.6)
Thrombotic cerebral infarction	血栓性脳梗塞	0 (0.0)	1 (0.6)
Respiratory, thoracic and mediastinal disorders	呼吸器、胸郭および縦隔障害	1 (0.6)	0 (0.0)
Organising pneumonia	器質化肺炎	1 (0.6)	0 (0.0)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	0 (0.0)	1 (0.6)
Dermatitis atopic	アトピー性皮膚炎	0 (0.0)	1 (0.6)
Vascular disorders	血管障害	0 (0.0)	1 (0.6)
Hypertension	高血圧	0 (0.0)	1 (0.6)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-34＞

表 2.7.4.7.1-30

Table 14.1.1.3-40

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Posttreatment observation (339-14-002)

Subjects who Advanced to Posttreatment observation among Safety Set

Treatment group of run-out period		Placebo	Nalmefene 20 mg	Total
System organ class		(N=171)	(N=171)	(N=342)
Preferred term		n (%)	n (%)	n (%)
Total number of subjects with adverse events		22 (12.9)	32 (18.7)	54 (15.8)
Blood and lymphatic system disorders	血液およびリンパ系障害	1 (0.6)	1 (0.6)	2 (0.6)
Anaemia	貧血	1 (0.6)	1 (0.6)	2 (0.6)
Cardiac disorders	心臓障害	0 (0.0)	1 (0.6)	1 (0.3)
Ventricular extrasystoles	心室性期外収縮	0 (0.0)	1 (0.6)	1 (0.3)
Gastrointestinal disorders	胃腸障害	2 (1.2)	1 (0.6)	3 (0.9)
Abdominal pain upper	上腹部痛	1 (0.6)	0 (0.0)	1 (0.3)
Diarrhoea	下痢	1 (0.6)	0 (0.0)	1 (0.3)
Gastritis	胃炎	0 (0.0)	1 (0.6)	1 (0.3)
Hepatobiliary disorders	肝胆道系障害	0 (0.0)	1 (0.6)	1 (0.3)
Hepatitis alcoholic	アルコール性肝炎	0 (0.0)	1 (0.6)	1 (0.3)
Infections and infestations	感染症および寄生虫症	6 (3.5)	4 (2.3)	10 (2.9)
Acute sinusitis	急性副鼻腔炎	1 (0.6)	0 (0.0)	1 (0.3)
Herpes zoster	帯状疱疹	0 (0.0)	1 (0.6)	1 (0.3)
Nasopharyngitis	鼻咽頭炎	5 (2.9)	2 (1.2)	7 (2.0)
Pneumonia	肺炎	0 (0.0)	1 (0.6)	1 (0.3)

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表 2.7.4.7.1-30

Table 14.1.1.3-40

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Posttreatment observation (339-14-002)

Subjects who Advanced to Posttreatment observation among Safety Set

Treatment group of run-out period		Placebo	Nalmefene 20 mg	Total
System organ class		(N=171)	(N=171)	(N=342)
Preferred term		n (%)	n (%)	n (%)
Injury, poisoning and procedural complications	傷害、中毒および処置合併症	2 (1.2)	3 (1.8)	5 (1.5)
Hand fracture	手骨折	0 (0.0)	1 (0.6)	1 (0.3)
Ligament sprain	靭帯捻挫	1 (0.6)	1 (0.6)	2 (0.6)
Mouth injury	口腔内損傷	0 (0.0)	1 (0.6)	1 (0.3)
Excoriation	擦過傷	0 (0.0)	1 (0.6)	1 (0.3)
Contusion	挫傷	0 (0.0)	2 (1.2)	2 (0.6)
Avulsion fracture	剥離骨折	1 (0.6)	0 (0.0)	1 (0.3)

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表 2.7.4.7.1-30
Table 14.1.1.3-40
Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Posttreatment observation (339-14-002)
Subjects who Advanced to Posttreatment observation among Safety Set

Treatment group of run-out period System organ class Preferred term		Placebo (N=171) n (%)	Nalmefene 20 mg (N=171) n (%)	Total (N=342) n (%)
Investigations	臨床検査	10 (5.8)	21 (12.3)	31 (9.1)
Alanine aminotransferase increased	アラニンアミノトランスフェラーゼ増加	1 (0.6)	1 (0.6)	2 (0.6)
Aspartate aminotransferase increased	アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.6)	1 (0.3)
Blood creatinine increased	血中クレアチニン増加	0 (0.0)	1 (0.6)	1 (0.3)
Blood glucose increased	血中ブドウ糖増加	1 (0.6)	0 (0.0)	1 (0.3)
Blood potassium increased	血中カリウム増加	1 (0.6)	1 (0.6)	2 (0.6)
Blood prolactin increased	血中プロラクチン増加	1 (0.6)	4 (2.3)	5 (1.5)
Blood triglycerides increased	血中トリグリセリド増加	2 (1.2)	2 (1.2)	4 (1.2)
C-reactive protein increased	Ｃ－反応性蛋白増加	1 (0.6)	1 (0.6)	2 (0.6)
Electrocardiogram QT prolonged	心電図QT延長	1 (0.6)	2 (1.2)	3 (0.9)
Gamma-glutamyltransferase increased	γ－グルタミルトランスフェラーゼ増加	0 (0.0)	1 (0.6)	1 (0.3)
Glucose urine present	尿中ブドウ糖陽性	1 (0.6)	2 (1.2)	3 (0.9)
Blood urine present	尿中血陽性	0 (0.0)	2 (1.2)	2 (0.6)
Weight increased	体重増加	0 (0.0)	1 (0.6)	1 (0.3)
Platelet count increased	血小板数増加	0 (0.0)	1 (0.6)	1 (0.3)
Protein urine present	尿中蛋白陽性	1 (0.6)	1 (0.6)	2 (0.6)
Blood alkaline phosphatase increased	血中アルカリホスファターゼ増加	0 (0.0)	1 (0.6)	1 (0.3)
Human chorionic gonadotropin increased	ヒト絨毛性ゴナドトロピン増加	0 (0.0)	1 (0.6)	1 (0.3)
Metabolism and nutrition disorders	代謝および栄養障害	0 (0.0)	2 (1.2)	2 (0.6)
Hypoalbuminaemia	低アルブミン血症	0 (0.0)	1 (0.6)	1 (0.3)
Increased appetite	食欲亢進	0 (0.0)	1 (0.6)	1 (0.3)

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表 2.7.4.7.1-30

Table 14.1.1.3-40

Incidences of Adverse Events by MedDRA System Organ Class and Preferred Term in Posttreatment observation (339-14-002)

Subjects who Advanced to Posttreatment observation among Safety Set

System organ class Preferred term	Treatment group of run-out period	Placebo (N=171) n (%)	Nalmefene 20 mg (N=171) n (%)	Total (N=342) n (%)
Musculoskeletal and connective tissue disorders	筋骨格系および結合組織障害	2 (1.2)	0 (0.0)	2 (0.6)
Back pain	背部痛	1 (0.6)	0 (0.0)	1 (0.3)
Osteoporosis	骨粗鬆症	1 (0.6)	0 (0.0)	1 (0.3)
Nervous system disorders	神経系障害	1 (0.6)	0 (0.0)	1 (0.3)
Cervicogenic headache	頚原性頭痛	1 (0.6)	0 (0.0)	1 (0.3)
Psychiatric disorders	精神障害	0 (0.0)	1 (0.6)	1 (0.3)
Middle insomnia	中期不眠症	0 (0.0)	1 (0.6)	1 (0.3)
Terminal insomnia	早朝覚醒型不眠症	0 (0.0)	1 (0.6)	1 (0.3)
Skin and subcutaneous tissue disorders	皮膚および皮下組織障害	0 (0.0)	1 (0.6)	1 (0.3)
Pruritus	そう痒症	0 (0.0)	1 (0.6)	1 (0.3)
Vascular disorders	血管障害	1 (0.6)	1 (0.6)	2 (0.6)
Hypertension	高血圧	1 (0.6)	1 (0.6)	2 (0.6)

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＜資料番号5.3.5.2-01 : Table 14.1.1.3-40＞

2.7.4.7.2　海外試験の図表

表 2.7.4.7.2-1　アルコール使用障害の海外試験一覧表

試験略名（試験番号）， 資料番号 （実施国） ［資料の取扱い］	試験デザイン	ナルメフェン塩酸塩 投与量及び投与方法 （いずれも経口投与）	投与期間	安全性解析対象
可変用量でのプラセボ対照二重盲検試験（CPH-101-0801）， 5.3.5.1-05 （フィンランド） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	治療期：可変用量 10，20（目標用量），40 mg，又はプラセボ 退薬期：可変用量 10，20（目標用量），40 mg，又はプラセボ 頓用，1 日 1 回まで	治療期 28 週間 退薬期 24 週間	計 403 例 ナルメフェン群：242 例 プラセボ群：161 例
可変用量でのプラセボ対照二重盲検試験（CPH-101-0701）， 5.3.5.1-06 （英国） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	可変用量 10，20（目標用量），40 mg，又はプラセボ 頓用，1 日 1 回まで	28 週間	計 167 例 ナルメフェン群：85 例 プラセボ群：82 例
プラセボ対照二重盲検試験（CPH-101-0299），5.3.5.1-07 （米国） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	固定用量 5，20，40 mg 又はプラセボ 連日投与期（1～12 週）：連日投与，1 日 1 回 継続投与期（13～52 週）：頓用，1 日 1 回まで	52 週間 （連日投与 12 週間 ＋ 頓用 40 週間）	計 270 例 5 mg 群：68 例 20 mg 群：66 例 40 mg 群：68 例 プラセボ群：68 例
プラセボ対照二重盲検試験（CPH-101-0399），5.3.5.1-08 （フィンランド） ［参考］	多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較	固定用量 10，40 mg，又はプラセボ 連日投与，1 日 1 回	16 週間	計 150 例 10 mg 群：50 例 40 mg 群：50 例 プラセボ群：50 例
可変用量での長期試験（CPH-101-0400），5.3.5.2-02 （フィンランド） ［参考］	多施設共同，非盲検，非対照	可変用量 10，20（目標用量）又は 40 mg 頓用，1 日 1 回まで	52 週間	60 例

表 2.7.4.7.2-2

Table 12 Withdrawals by Primary Reason (APTS) - High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo n (%)	Nalmefene n (%)	Total n (%)
Patients Treated	369	475	844
Completed	236 (64.0)	251 (52.8)	487 (57.7)
Withdrawn	133 (36.0)	224 (47.2)	357 (42.3)
Primary Reason			
Adverse Event (s)	19 (5.1)	65 (13.7)	84 (10.0)
Lack of Efficacy	25 (6.8)	18 (3.8)	43 (5.1)
Non-compliance	3 (0.8)	13 (2.7)	16 (1.9)
Protocol Violation	20 (5.4)	28 (5.9)	48 (5.7)
Withdrawal of Consent	47 (12.7)	71 (14.9)	118 (14.0)
Lost to Follow-up	10 (2.7)	11 (2.3)	21 (2.5)
Other	9 (2.4)	18 (3.8)	27 (3.2)

＜資料番号5.3.5.3-03 : Table 12＞

表 2.7.4.7.2-3

Table 13 Run-out Period: Withdrawals by Primary Reason (APTS) - High or Very High DRL at Baseline and Randomisation - Studies 12014A and 12023A Pooled

	Placebo-Placebo n (%)	Nalmefene-Placebo n (%)	Nalmefene-Nalmefene n (%)	Total n (%)
Patients Treated	208	83	91	382
Completed	202 (97.1)	79 (95.2)	87 (95.6)	368 (96.3)
Withdrawn	6 (2.9)	4 (4.8)	4 (4.4)	14 (3.7)
Primary Reason				
Protocol Violation	1 (0.5)	2 (2.4)	0 (0.0)	3 (0.8)
Withdrawal of Consent	2 (1.0)	1 (1.2)	1 (1.1)	4 (1.0)
Lost to Follow-up	1 (0.5)	0 (0.0)	1 (1.1)	2 (0.5)
Other	2 (1.0)	1 (1.2)	2 (2.2)	5 (1.3)

Only patients with a completed visit 10 are included

＜資料番号5.3.5.3-03 : Table 13＞

表 2.7.4.7.2-4
Panel 7 Patient Disposition (APRS) – Alcohol-use Disorders Pool

	Placebo	Nalmefene 5 mg	Nalmefene 10 mg	Nalmefene 20 mg[a]	Nalmefene 40 mg
	n (%)	n (%)	n (%)	n (%)	n (%)
Patients randomised (APRS)	361	68	50	453	118
Patients completed[b,c]	226 (62.6)	46 (67.6)	39 (78.0)	241 (53.2)	83 (70.3)
Patients withdrawn[b] reason	135 (37.4)	22 (32.4)	11 (22.0)	212 (46.8)	35 (29.7)
Adverse event (s)	11 (3.0)	4 (5.9)	6 (12.0)	77 (17.0)	14 (11.9)
Lack of efficacy	24 (6.6)	5 (7.4)	1 (2.0)	7 (1.6)	3 (2.5)
Withdrawal of consent	45 (12.5)	1 (1.5)	2 (4.0)	68 (15.0)	4 (3.4)
Lost to follow-up	47 (13.0)	11 (16.2)	2 (4.0)	49 (10.8)	12 (10.2)
Other	6 (1.7)	1 (1.5)		7 (1.5)	2 (1.7)
Unknown	2 (0.6)			4 (0.9)	
Patients re-randomised in Study CPH-101-0801[d]	27			30	
Patients completed	23 (85.2)			26 (86.7)	
Patients withdrawn reason	4 (14.8)			4 (13.3)	
Adverse event (s)				1 (3.3)	
Other	4 (14.8)			3 (10.0)	
Patients in optional extension in Study CPH-101-0299[e]	39	40		40	37
Patients completed	14 (35.9)	18 (45.0)		15 (37.5)	19 (51.4)
Patients withdrawn reason	25 (64.1)	22 (55.0)		25 (62.5)	18 (48.6)
Adverse event (s)	2 (5.1)	1 (2.5)		1 (2.5)	2 (5.4)
Other	23 (59.0)	21 (52.5)		24 (60.0)	16 (43.2)

[a] Patients in the nalmefene groups in the flexible-dose studies CPH-101-0801, CPH-101-0701, and CPH-101-0400 are included in the nalmefene 20 mg group, although their actual dose may differ.

[b] Excluding the optional 24-week run-out period in study CPH-101-0801 and the optional 40-week treatment period in study CPH-101-0299

[c] Excluding the 12-week safety follow-up period in study CPH-101-0701

[d] Only patients in the nalmefene group were eligible for optional re-randomisation to continue nalmefene treatment or switch to placebo treatment. The number of patients re-randomised to the run-out period served as the denominator in calculating the proportion (%).

[e] The number of patients included in the optional 40-week treatment period served as the denominator in calculating the proportion (%).

＜資料番号5.3.5.3-03：Panel 7＞

表 2.7.4.7.2-5

Table 51 IMP Intake by Month (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

Treatment group	Month	Patients N	Summary statistics	TLFB days	IMP	
					Days	%
Placebo	1	365	Mean	27	21	77.0
			Min	5	1	3.6
			Max	28	28	100.0
			Median	28	23	82.1
			p10	28	11	42.9
			p25	28	16	60.7
			p75	28	27	96.4
			p90	28	28	100.0
	2	337	Mean	27	20	73.7
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	23	85.7
			p10	28	7	32.1
			p25	28	14	53.6
			p75	28	28	100.0
			p90	28	28	100.0
	3	310	Mean	27	20	72.1
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	22	78.6
			p10	28	6	26.8
			p25	28	13	53.6
			p75	28	27	100.0
			p90	28	28	100.0
	4	292	Mean	27	19	68.2
			Min	2	0	0.0
			Max	28	28	100.0
			Median	28	21	76.8
			p10	28	5	21.4
			p25	28	12	46.4
			p75	28	27	96.4
			p90	28	28	100.0
	5	275	Mean	27	19	69.9
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	22	78.6
			p10	28	5	21.4
			p25	28	13	50.0
			p75	28	28	100.0
			p90	28	28	100.0
	6	261	Mean	27	19	69.7
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	21	78.6
			p10	25	5	21.4
			p25	28	12	50.0
			p75	28	27	100.0
			p90	28	28	100.0

表 2.7.4.7.2-5

Table 51 IMP Intake by Month (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

Treatment group	Month	Patients N	Summary statistics	TLFB days	IMP Days	IMP %
Placebo	7	153	Mean	13	8	66.7
			Min	1	0	0.0
			Max	28	28	100.0
			Median	7	6	81.3
			p10	2	0	0.0
			p25	5	2	39.3
			p75	28	11	100.0
			p90	28	23	100.0
	8	39	Mean	28	16	55.9
			Min	23	0	0.0
			Max	28	28	100.0
			Median	28	17	60.7
			p10	28	1	3.6
			p25	28	6	21.4
			p75	28	25	89.3
			p90	28	28	100.0
	9	35	Mean	26	15	52.6
			Min	7	0	0.0
			Max	28	28	100.0
			Median	28	15	53.6
			p10	21	0	0.0
			p25	28	3	10.7
			p75	28	27	96.4
			p90	28	28	100.0
	10	31	Mean	28	17	60.4
			Min	28	0	0.0
			Max	28	28	100.0
			Median	28	19	67.9
			p10	28	2	7.1
			p25	28	7	25.0
			p75	28	28	100.0
			p90	28	28	100.0
	11	31	Mean	28	15	54.0
			Min	28	0	0.0
			Max	28	28	100.0
			Median	28	14	50.0
			p10	28	1	3.6
			p25	28	5	17.9
			p75	28	28	100.0
			p90	28	28	100.0
	12	31	Mean	28	14	48.6
			Min	14	0	0.0
			Max	28	28	100.0
			Median	28	13	46.4
			p10	28	0	0.0
			p25	28	1	3.6
			p75	28	27	96.4
			p90	28	28	100.0

表 2.7.4.7.2-5

Table 51 IMP Intake by Month (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

Treatment group	Month	Patients N	Summary statistics	TLFB days	IMP	
					Days	%
Placebo	13	29	Mean	27	15	56.4
			Min	22	0	0.0
			Max	28	28	100.0
			Median	28	20	71.4
			p10	26	0	0.0
			p25	28	2	7.4
			p75	28	25	92.9
			p90	28	28	100.0
Nalmefene	1	470	Mean	26	18	65.7
			Min	1	1	3.6
			Max	28	28	100.0
			Median	28	20	71.4
			p10	27	3	18.0
			p25	28	11	42.9
			p75	28	26	92.9
			p90	28	28	100.0
	2	416	Mean	27	17	61.4
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	18	67.9
			p10	28	2	7.1
			p25	28	9	32.1
			p75	28	26	92.9
			p90	28	28	100.0
	3	369	Mean	27	16	60.0
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	18	67.9
			p10	28	1	3.6
			p25	28	8	28.6
			p75	28	26	92.9
			p90	28	28	100.0
	4	340	Mean	27	16	57.0
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	16	58.9
			p10	28	0	0.0
			p25	28	6	25.0
			p75	28	26	92.9
			p90	28	28	100.0
	5	311	Mean	27	15	56.2
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	16	60.7
			p10	28	0	0.0
			p25	28	7	25.0
			p75	28	26	92.9
			p90	28	28	100.0

表 2.7.4.7.2-5

Table 51 IMP Intake by Month (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

Treatment group	Month	Patients N	Summary statistics	TLFB days	IMP	
					Days	%
Nalmefene	6	292	Mean	27	15	56.5
			Min	5	0	0.0
			Max	28	28	100.0
			Median	28	15	57.1
			p10	26	0	0.0
			p25	28	7	25.0
			p75	28	26	92.9
			p90	28	28	100.0
	7	201	Mean	18	9	52.1
			Min	1	0	0.0
			Max	28	28	100.0
			Median	22	6	50.0
			p10	3	0	0.0
			p25	7	1	10.7
			p75	28	14	100.0
			p90	28	28	100.0
	8	97	Mean	27	12	44.5
			Min	2	0	0.0
			Max	28	28	100.0
			Median	28	11	39.3
			p10	28	0	0.0
			p25	28	2	10.7
			p75	28	22	78.6
			p90	28	28	100.0
	9	88	Mean	27	13	46.5
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	12	42.9
			p10	28	0	0.0
			p25	28	5	17.9
			p75	28	22	78.6
			p90	28	28	100.0
	10	85	Mean	28	14	48.5
			Min	19	0	0.0
			Max	28	28	100.0
			Median	28	11	39.3
			p10	28	0	0.0
			p25	28	5	17.9
			p75	28	24	85.7
			p90	28	28	100.0
	11	83	Mean	28	13	46.9
			Min	7	0	0.0
			Max	28	28	100.0
			Median	28	10	35.7
			p10	28	0	0.0
			p25	28	5	17.9
			p75	28	24	85.7
			p90	28	28	100.0

表 2.7.4.7.2-5

Table 51 IMP Intake by Month (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

Treatment group	Month	Patients N	Summary statistics	TLFB days	IMP	
					Days	%
Nalmefene	12	82	Mean	27	13	44.9
			Min	1	0	0.0
			Max	28	28	100.0
			Median	28	9	32.1
			p10	28	0	0.0
			p25	28	3	10.7
			p75	28	25	89.3
			p90	28	28	100.0
	13	80	Mean	26	12	46.1
			Min	4	0	0.0
			Max	28	28	100.0
			Median	28	9	42.9
			p10	22	0	0.0
			p25	27	3	10.7
			p75	28	22	85.2
			p90	28	28	100.0

TLFB days with IMP and % days with IMP are summary statistics based on individual patient.

＜資料番号5.3.5.3-03 : Table 51＞

表 2.7.4.7.2-6

Table 66 Run-out Period: IMP Intake (APTS): High or Very High DRL at Baseline and Randomisation - Studies 12014A and 12023A

Treatment group	Patients N	Summary statistics	TLFB days	IMP	
				Days	%
Placebo - Placebo	205	Mean	27	19	70.4
		Min	1	0	0.0
		Max	55	42	100.0
		Median	28	21	81.4
		p10	21	5	18.5
		p25	24	13	50.0
		p75	30	26	100.0
		p90	35	29	100.0
Nalmefene - Placebo	81	Mean	29	16	56.5
		Min	14	0	0.0
		Max	74	42	100.0
		Median	28	16	55.2
		p10	21	0	0.0
		p25	23	7	21.7
		p75	33	26	92.9
		p90	40	31	100.0
Nalmefene - Nalmefene	87	Mean	29	17	59.3
		Min	10	0	0.0
		Max	52	42	100.0
		Median	28	18	66.7
		p10	21	0	0.0
		p25	27	8	28.6
		p75	33	25	93.1
		p90	37	31	100.0

TLFB days with IMP and % days with IMP are summary statistics based on individual patient.
Only patients with a completed visit 10 are included
＜資料番号5.3.5.3-03：Table 66＞

表 2.7.4.7.2-7

Panel 25 Exposure to Nalmefene by Mean Daily Dose (APRS) - Alcohol-use Disorders Pool

	Mean daily dose						
	> 0 and ≤ 5 mg	> 5 and ≤ 10 mg	> 10 and ≤ 20 mg	> 20 and ≤ 30 mg	> 30 mg	Any dose	Percent[a]
Duration	Number of patients						
(Weeks)	n	n	n	n	n	n	
> 0 and ≤ 1	8	3	26		7	44	6.5
> 1 and ≤ 2	9	5	12		3	29	4.3
> 2 and ≤ 4	12	9	20	5	7	53	7.9
> 4 and ≤ 12	44	26	39	3	19	131	19.4
> 12 and ≤ 24	45	53	30	5	58	191	28.3
> 24 and ≤ 48	38	41	46	13	14	152	22.6
> 48 and ≤ 96	25	20	16	5	8	74	11.0
Any	181	157	189	31	116	674	100.0
Percent[a]	26.9	23.3	28.0	4.6	17.2	100.0	

[a] Percent of total population with TFLB records

＜資料番号5.3.5.3-03 : Panel 25＞

表 2.7.4.7.2-8
Panel 12 Patient Demographics (APRS) - Alcohol-use Disorders Pool

	Placebo		Nalmefene	
Number of patients	361		689	
Age (years)				
Mean (SD)	47.1 (9.7)		47.9 (9.5)	
Range [min;max]	[21;77]		[21;78]	
Age Groups (years) n %				
< 65	347	96.1	661	95.9
≥ 65	14	3.9	28	4.1
Sex n %				
Woman	86	23.8	172	25.0
Man	275	76.2	517	75.0
Race n %				
Caucasian	352	97.5	670	97.2
Black	4	1.1	9	1.3
Hispanic	4	1.1	9	1.3
Other	1	0.3	1	0.1

SD = standard deviation
＜資料番号5.3.5.3-03 : Panel 12＞

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs	246	(66.7)	368	(77.5)
血液およびリンパ系障害	0	(0.0)	1	(0.2)
貧血	0	(0.0)	1	(0.2)
心臓障害	8	(2.2)	35	(7.4)
狭心症	1	(0.3)	1	(0.2)
不整脈	1	(0.3)	3	(0.6)
心房細動	0	(0.0)	1	(0.2)
心房粗動	0	(0.0)	1	(0.2)
徐脈	1	(0.3)	0	(0.0)
左脚ブロック	0	(0.0)	1	(0.2)
心筋梗塞	0	(0.0)	1	(0.2)
心筋虚血	0	(0.0)	1	(0.2)
動悸	1	(0.3)	5	(1.1)
洞性頻脈	0	(0.0)	3	(0.6)
頻脈	4	(1.1)	20	(4.2)
心室性期外収縮	0	(0.0)	1	(0.2)
耳および迷路障害	5	(1.4)	7	(1.5)
聴覚障害	0	(0.0)	1	(0.2)
耳痛	1	(0.3)	0	(0.0)
耳鳴	2	(0.5)	3	(0.6)
回転性めまい	1	(0.3)	3	(0.6)
聴力低下	1	(0.3)	0	(0.0)
眼障害	7	(1.9)	9	(1.9)
複視	0	(0.0)	1	(0.2)
眼乾燥	0	(0.0)	1	(0.2)
眼刺激	1	(0.3)	1	(0.2)
眼痛	1	(0.3)	0	(0.0)
流涙増加	0	(0.0)	1	(0.2)
眼窩周囲浮腫	1	(0.3)	0	(0.0)
網膜障害	1	(0.3)	0	(0.0)
霧視	3	(0.8)	2	(0.4)
視力低下	1	(0.3)	1	(0.2)
視力障害	0	(0.0)	1	(0.2)
変視症	0	(0.0)	1	(0.2)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
胃腸障害	80	(21.7)	169	(35.6)
腹部不快感	0	(0.0)	2	(0.4)
腹部膨満	1	(0.3)	0	(0.0)
腹痛	4	(1.1)	7	(1.5)
下腹部痛	0	(0.0)	1	(0.2)
上腹部痛	7	(1.9)	10	(2.1)
呼気臭	0	(0.0)	1	(0.2)
大腸炎	0	(0.0)	1	(0.2)
潰瘍性大腸炎	0	(0.0)	1	(0.2)
便秘	3	(0.8)	5	(1.1)
下痢	22	(6.0)	19	(4.0)
口内乾燥	5	(1.4)	16	(3.4)
消化不良	8	(2.2)	5	(1.1)
鼓腸	3	(0.8)	3	(0.6)
食中毒	1	(0.3)	0	(0.0)
排便回数増加	1	(0.3)	1	(0.2)
穿孔性胃潰瘍	0	(0.0)	1	(0.2)
胃炎	0	(0.0)	1	(0.2)
アルコール性胃炎	0	(0.0)	1	(0.2)
びらん性胃炎	0	(0.0)	1	(0.2)
胃食道逆流性疾患	2	(0.5)	0	(0.0)
痔核	1	(0.3)	0	(0.0)
胃酸過多	1	(0.3)	0	(0.0)
鼠径ヘルニア	1	(0.3)	0	(0.0)
悪心	24	(6.5)	115	(24.2)
膵嚢胞	1	(0.3)	0	(0.0)
急性膵炎	1	(0.3)	1	(0.2)
慢性膵炎	1	(0.3)	0	(0.0)
消化性潰瘍	0	(0.0)	1	(0.2)
レッチング	1	(0.3)	0	(0.0)
歯の障害	1	(0.3)	1	(0.2)
歯痛	2	(0.5)	3	(0.6)
嘔吐	13	(3.5)	40	(8.4)
潰瘍性食道炎	0	(0.0)	1	(0.2)
肛門出血	0	(0.0)	1	(0.2)
大腸ポリープ	1	(0.3)	0	(0.0)
排便痛	1	(0.3)	0	(0.0)
口の感覚鈍麻	2	(0.5)	1	(0.2)
食道障害	1	(0.3)	0	(0.0)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
一般・全身障害および投与部位の状態	31	(8.4)	81	(17.1)
無力症	1	(0.3)	8	(1.7)
胸部不快感	1	(0.3)	0	(0.0)
悪寒	0	(0.0)	3	(0.6)
疲労	22	(6.0)	43	(9.1)
異常感	0	(0.0)	6	(1.3)
冷感	1	(0.3)	2	(0.4)
酩酊感	0	(0.0)	2	(0.4)
熱感	1	(0.3)	1	(0.2)
歩行障害	0	(0.0)	1	(0.2)
宿酔	1	(0.3)	3	(0.6)
インフルエンザ様疾患	1	(0.3)	3	(0.6)
倦怠感	0	(0.0)	5	(1.1)
粘膜過形成	0	(0.0)	1	(0.2)
疼痛	0	(0.0)	1	(0.2)
発熱	2	(0.5)	6	(1.3)
予想外の治療反応	0	(0.0)	1	(0.2)
口渇	2	(0.5)	2	(0.4)
末梢腫脹	1	(0.3)	0	(0.0)
限局性浮腫	0	(0.0)	1	(0.2)
体温変動感	1	(0.3)	1	(0.2)
非心臓性胸痛	0	(0.0)	4	(0.8)
肝胆道系障害	7	(1.9)	4	(0.8)
急性胆嚢炎	1	(0.3)	0	(0.0)
胆石症	2	(0.5)	0	(0.0)
肝臓痛	0	(0.0)	1	(0.2)
脂肪肝	1	(0.3)	0	(0.0)
アルコール性肝炎	1	(0.3)	1	(0.2)
胆汁うっ滞性黄疸	1	(0.3)	0	(0.0)
肝障害	1	(0.3)	0	(0.0)
胆道ジスキネジア	0	(0.0)	1	(0.2)
肝損傷	0	(0.0)	1	(0.2)
免疫系障害	0	(0.0)	3	(0.6)
食物アレルギー	0	(0.0)	1	(0.2)
季節性アレルギー	0	(0.0)	1	(0.2)
節足動物咬傷アレルギー	0	(0.0)	1	(0.2)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
感染症および寄生虫症	89	(24.1)	85	(17.9)
細菌尿	0	(0.0)	1	(0.2)
気管支炎	4	(1.1)	8	(1.7)
蜂巣炎	1	(0.3)	0	(0.0)
結膜炎	3	(0.8)	1	(0.2)
膀胱炎	1	(0.3)	0	(0.0)
耳感染	1	(0.3)	0	(0.0)
感染性湿疹	0	(0.0)	1	(0.2)
精巣上体炎 {ss}	1	(0.4)	0	(0.0)
毛包炎	1	(0.3)	0	(0.0)
胃腸炎	7	(1.9)	2	(0.4)
ウイルス性胃腸炎	0	(0.0)	2	(0.4)
消化管感染	1	(0.3)	0	(0.0)
歯肉炎	1	(0.3)	0	(0.0)
単純ヘルペス	1	(0.3)	0	(0.0)
帯状疱疹	1	(0.3)	0	(0.0)
麦粒腫	1	(0.3)	0	(0.0)
膿痂疹	0	(0.0)	1	(0.2)
感染	1	(0.3)	0	(0.0)
インフルエンザ	10	(2.7)	10	(2.1)
喉頭炎	0	(0.0)	1	(0.2)
限局性感染	0	(0.0)	1	(0.2)
下気道感染	3	(0.8)	0	(0.0)
鼻咽頭炎	39	(10.6)	38	(8.0)
歯周炎	0	(0.0)	1	(0.2)
咽頭炎	0	(0.0)	4	(0.8)
肺炎	1	(0.3)	3	(0.6)
鼻炎	7	(1.9)	5	(1.1)
敗血症	0	(0.0)	1	(0.2)
副鼻腔炎	2	(0.5)	5	(1.1)
足部白癬	1	(0.3)	0	(0.0)
扁桃炎	1	(0.3)	1	(0.2)
歯膿瘍	0	(0.0)	1	(0.2)
上気道感染	4	(1.1)	4	(0.8)
尿路感染	6	(1.6)	2	(0.4)
ウイルス性上気道感染	2	(0.5)	1	(0.2)
創傷感染	0	(0.0)	1	(0.2)
歯感染	0	(0.0)	1	(0.2)
ウイルス性気管支炎	1	(0.3)	0	(0.0)
細菌性尿路感染	2	(0.5)	0	(0.0)
ヘリコバクター感染	0	(0.0)	1	(0.2)
細菌感染	1	(0.3)	0	(0.0)
口腔真菌感染	0	(0.0)	1	(0.2)
細菌性気管支炎	1	(0.3)	0	(0.0)
ウイルス性気道感染	1	(0.3)	0	(0.0)
気道感染	0	(0.0)	1	(0.2)
細菌性下気道感染	0	(0.0)	1	(0.2)
ロタウイルス感染	0	(0.0)	1	(0.2)
感染性胸水	1	(0.3)	0	(0.0)
咬傷感染	0	(0.0)	1	(0.2)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
傷害、中毒および処置合併症	49	(13.3)	34	(7.2)
労働災害	0	(0.0)	1	(0.2)
偶発的過量投与	22	(6.0)	13	(2.7)
アルコール中毒	1	(0.3)	2	(0.4)
動物咬傷	1	(0.3)	0	(0.0)
足関節部骨折	1	(0.3)	1	(0.2)
節足動物咬傷	1	(0.3)	0	(0.0)
脳振盪	1	(0.3)	0	(0.0)
転倒	8	(2.2)	9	(1.9)
大腿骨頚部骨折	0	(0.0)	1	(0.2)
腓骨骨折	2	(0.5)	1	(0.2)
足骨折	1	(0.3)	0	(0.0)
手骨折	1	(0.3)	1	(0.2)
頭部損傷	0	(0.0)	1	(0.2)
損傷	0	(0.0)	1	(0.2)
企図的過量投与	4	(1.1)	1	(0.2)
裂傷	0	(0.0)	1	(0.2)
靭帯捻挫	3	(0.8)	3	(0.6)
橈骨骨折	0	(0.0)	1	(0.2)
肋骨骨折	2	(0.5)	3	(0.6)
交通事故	0	(0.0)	1	(0.2)
硬膜下出血	0	(0.0)	1	(0.2)
腱断裂	0	(0.0)	1	(0.2)
脛骨骨折	1	(0.3)	0	(0.0)
尺骨骨折	0	(0.0)	1	(0.2)
肉離れ	2	(0.5)	0	(0.0)
挫傷	3	(0.8)	3	(0.6)
創傷	1	(0.3)	0	(0.0)
熱傷	2	(0.5)	0	(0.0)
四肢損傷	2	(0.5)	1	(0.2)
歯牙破折	0	(0.0)	1	(0.2)
四肢圧挫損傷	0	(0.0)	1	(0.2)
処置による疼痛	0	(0.0)	2	(0.4)
骨挫傷	2	(0.5)	0	(0.0)
体内異物	1	(0.3)	0	(0.0)
各種物質毒性	1	(0.3)	0	(0.0)
半月板損傷	1	(0.3)	0	(0.0)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
臨床検査	14	(3.8)	27	(5.7)
アラニンアミノトランスフェラーゼ増加	0	(0.0)	3	(0.6)
アスパラギン酸アミノトランスフェラーゼ増加	1	(0.3)	1	(0.2)
血中重炭酸塩減少	0	(0.0)	1	(0.2)
血中コレステロール増加	0	(0.0)	1	(0.2)
血中クレアチニン増加	2	(0.5)	0	(0.0)
血中ブドウ糖増加	0	(0.0)	1	(0.2)
血圧上昇	2	(0.5)	6	(1.3)
収縮期血圧上昇	0	(0.0)	1	(0.2)
血中プロラクチン増加	0	(0.0)	1	(0.2)
血中トリグリセリド増加	1	(0.3)	1	(0.2)
血中尿素増加	2	(0.5)	0	(0.0)
Ｃ－反応性蛋白増加	0	(0.0)	1	(0.2)
心電図異常	0	(0.0)	1	(0.2)
γ－グルタミルトランスフェラーゼ増加	3	(0.8)	3	(0.6)
脂質増加	1	(0.3)	0	(0.0)
単球数減少	0	(0.0)	1	(0.2)
血小板数減少	0	(0.0)	1	(0.2)
プロトロンビン時間短縮	0	(0.0)	1	(0.2)
トランスフェリン増加	0	(0.0)	1	(0.2)
体重減少	0	(0.0)	4	(0.8)
体重増加	4	(1.1)	3	(0.6)
心電図2相性T波	0	(0.0)	1	(0.2)
QRS軸異常	0	(0.0)	1	(0.2)
胃内pH低下	1	(0.3)	1	(0.2)
肝酵素上昇	2	(0.5)	0	(0.0)
代謝および栄養障害	18	(4.9)	38	(8.0)
アルコール不耐性	1	(0.3)	4	(0.8)
糖尿病	1	(0.3)	1	(0.2)
高コレステロール血症	4	(1.1)	1	(0.2)
高血糖	0	(0.0)	1	(0.2)
高ナトリウム血症	1	(0.3)	0	(0.0)
過食	1	(0.3)	0	(0.0)
低アルブミン血症	0	(0.0)	1	(0.2)
低カリウム血症	1	(0.3)	0	(0.0)
食欲亢進	2	(0.5)	3	(0.6)
食物渇望	0	(0.0)	1	(0.2)
食欲障害	1	(0.3)	0	(0.0)
脂質代謝障害	1	(0.3)	0	(0.0)
食欲減退	4	(1.1)	27	(5.7)
高脂血症	1	(0.3)	0	(0.0)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
筋骨格系および結合組織障害	36	(9.8)	58	(12.2)
関節痛	2	(0.5)	5	(1.1)
関節炎	1	(0.3)	3	(0.6)
背部痛	11	(3.0)	18	(3.8)
滑液包炎	1	(0.3)	1	(0.2)
外骨腫	1	(0.3)	0	(0.0)
関節腫脹	1	(0.3)	0	(0.0)
筋痙縮	0	(0.0)	11	(2.3)
筋攣縮	0	(0.0)	1	(0.2)
筋骨格痛	2	(0.5)	1	(0.2)
筋肉痛	7	(1.9)	4	(0.8)
頚部痛	4	(1.1)	1	(0.2)
変形性関節症	4	(1.1)	4	(0.8)
四肢痛	2	(0.5)	5	(1.1)
足底筋膜炎	0	(0.0)	1	(0.2)
変形性脊椎症	0	(0.0)	1	(0.2)
腱炎	1	(0.3)	2	(0.4)
筋肉疲労	0	(0.0)	1	(0.2)
筋緊張	0	(0.0)	1	(0.2)
椎間板突出	0	(0.0)	2	(0.4)
筋骨格系胸痛	2	(0.5)	3	(0.6)
筋骨格硬直	0	(0.0)	3	(0.6)
靭帯骨棘	0	(0.0)	1	(0.2)
四肢不快感	0	(0.0)	1	(0.2)
筋拘縮	0	(0.0)	2	(0.4)
筋硬化症	0	(0.0)	1	(0.2)
脊椎痛	0	(0.0)	1	(0.2)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1	(0.3)	1	(0.2)
喉頭癌	1	(0.3)	0	(0.0)
前立腺癌 {ss}	0	(0.0)	1	(0.3)
神経系障害	77	(20.9)	208	(43.8)
味覚消失	0	(0.0)	3	(0.6)
アカシジア	0	(0.0)	1	(0.2)
健忘	0	(0.0)	1	(0.2)
失語症	0	(0.0)	1	(0.2)
反射消失	1	(0.3)	0	(0.0)
頚腕症候群	0	(0.0)	1	(0.2)
意識レベルの低下	0	(0.0)	7	(1.5)
注意力障害	2	(0.5)	11	(2.3)
浮動性めまい	22	(6.0)	104	(21.9)
味覚異常	5	(1.4)	17	(3.6)
てんかん	1	(0.3)	0	(0.0)
頭部不快感	0	(0.0)	2	(0.4)
頭痛	35	(9.5)	60	(12.6)
知覚過敏	0	(0.0)	2	(0.4)
過眠症	1	(0.3)	4	(0.8)
感覚鈍麻	1	(0.3)	10	(2.1)
嗜眠	0	(0.0)	3	(0.6)
記憶障害	0	(0.0)	1	(0.2)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
神経系障害	77	(20.9)	208	(43.8)
錯感覚	0	(0.0)	10	(2.1)
嗅覚錯誤	0	(0.0)	1	(0.2)
精神運動亢進	1	(0.3)	0	(0.0)
神経根障害	0	(0.0)	1	(0.2)
坐骨神経痛	1	(0.3)	2	(0.4)
鎮静	1	(0.3)	4	(0.8)
痙攣発作	0	(0.0)	3	(0.6)
感覚障害	0	(0.0)	1	(0.2)
傾眠	9	(2.4)	20	(4.2)
昏迷	0	(0.0)	5	(1.1)
くも膜下出血	0	(0.0)	1	(0.2)
失神	0	(0.0)	1	(0.2)
振戦	9	(2.4)	17	(3.6)
平衡障害	0	(0.0)	3	(0.6)
腰髄神経根障害	1	(0.3)	0	(0.0)
アルコール性痙攣	0	(0.0)	1	(0.2)
下肢静止不能症候群	0	(0.0)	1	(0.2)
睡眠の質低下	0	(0.0)	3	(0.6)
精神障害	55	(14.9)	163	(34.3)
異常な夢	1	(0.3)	3	(0.6)
抑うつ気分を伴う適応障害	1	(0.3)	0	(0.0)
感情障害	0	(0.0)	1	(0.2)
攻撃性	0	(0.0)	2	(0.4)
激越	0	(0.0)	7	(1.5)
アルコール乱用	0	(0.0)	1	(0.2)
アルコールによる宿酔	0	(0.0)	1	(0.2)
アルコール症	3	(0.8)	5	(1.1)
快感消失	0	(0.0)	1	(0.2)
神経性無食欲症	0	(0.0)	1	(0.2)
無オルガズム症	1	(0.3)	0	(0.0)
不安	11	(3.0)	12	(2.5)
無感情	0	(0.0)	5	(1.1)
自殺既遂	1	(0.3)	0	(0.0)
錯乱状態	0	(0.0)	5	(1.1)
興味の減少	0	(0.0)	2	(0.4)
抑うつ気分	2	(0.5)	7	(1.5)
うつ病	3	(0.8)	5	(1.1)
現実感消失	0	(0.0)	2	(0.4)
失見当識	1	(0.3)	4	(0.8)
解離	0	(0.0)	1	(0.2)
薬物乱用	0	(0.0)	1	(0.2)
不快気分	1	(0.3)	1	(0.2)
多幸気分	1	(0.3)	4	(0.8)
自己否定気分	0	(0.0)	1	(0.2)
感情の平板化	0	(0.0)	2	(0.4)
全般性不安障害	1	(0.3)	0	(0.0)
幻覚	0	(0.0)	2	(0.4)
触覚性幻覚	0	(0.0)	1	(0.2)
幻視	0	(0.0)	1	(0.2)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
精神障害	55	(14.9)	163	(34.3)
軽躁	0	(0.0)	1	(0.2)
錯覚	0	(0.0)	1	(0.2)
初期不眠症	0	(0.0)	2	(0.4)
不眠症	16	(4.3)	69	(14.5)
易刺激性	2	(0.5)	4	(0.8)
リビドー減退	1	(0.3)	7	(1.5)
気力低下	0	(0.0)	3	(0.6)
リビドー消失	0	(0.0)	2	(0.4)
中期不眠症	0	(0.0)	3	(0.6)
神経過敏	1	(0.3)	3	(0.6)
悪夢	2	(0.5)	2	(0.4)
パニック発作	1	(0.3)	1	(0.2)
落ち着きのなさ	2	(0.5)	7	(1.5)
睡眠障害	4	(1.1)	32	(6.7)
思考異常	0	(0.0)	2	(0.4)
精神緩慢	0	(0.0)	1	(0.2)
身体醜形障害	0	(0.0)	1	(0.2)
アルコール離脱症候群	4	(1.1)	8	(1.7)
抑うつ症状	0	(0.0)	1	(0.2)
白日夢	1	(0.3)	0	(0.0)
双極性障害	0	(0.0)	1	(0.2)
大うつ病	3	(0.8)	0	(0.0)
精神障害	0	(0.0)	1	(0.2)
適応障害	2	(0.5)	0	(0.0)
腎および尿路障害	3	(0.8)	8	(1.7)
膀胱不快感	1	(0.3)	0	(0.0)
糖尿	0	(0.0)	1	(0.2)
頻尿	0	(0.0)	1	(0.2)
多尿	1	(0.3)	1	(0.2)
蛋白尿	0	(0.0)	1	(0.2)
有痛性排尿困難	0	(0.0)	2	(0.4)
尿失禁	0	(0.0)	1	(0.2)
尿閉	0	(0.0)	1	(0.2)
白血球尿	1	(0.3)	0	(0.0)
尿臭異常	0	(0.0)	1	(0.2)
生殖系および乳房障害	5	(1.4)	6	(1.3)
良性前立腺肥大症 {ss}	1	(0.4)	2	(0.6)
頻発月経 {ss}	1	(0.8)	0	(0.0)
精巣痛 {ss}	1	(0.4)	0	(0.0)
子宮ポリープ {ss}	1	(0.8)	1	(0.7)
自発陰茎勃起 {ss}	0	(0.0)	1	(0.3)
勃起不全 {ss}	1	(0.4)	2	(0.6)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
呼吸器、胸郭および縦隔障害	12	(3.3)	14	(2.9)
喘息	2	(0.5)	3	(0.6)
咳嗽	2	(0.5)	3	(0.6)
発声障害	1	(0.3)	0	(0.0)
呼吸困難	0	(0.0)	4	(0.8)
喉頭浮腫	0	(0.0)	1	(0.2)
気胸	2	(0.5)	0	(0.0)
アレルギー性鼻炎	2	(0.5)	0	(0.0)
鼻漏	0	(0.0)	2	(0.4)
くしゃみ	1	(0.3)	0	(0.0)
喉頭蓋嚢胞	0	(0.0)	1	(0.2)
横隔膜障害	1	(0.3)	0	(0.0)
口腔咽頭プラーク	1	(0.3)	0	(0.0)
口腔咽頭痛	2	(0.5)	2	(0.4)
皮膚および皮下組織障害	24	(6.5)	48	(10.1)
脱毛症	1	(0.3)	1	(0.2)
水疱	1	(0.3)	0	(0.0)
アレルギー性皮膚炎	0	(0.0)	1	(0.2)
接触性皮膚炎	0	(0.0)	1	(0.2)
皮膚乾燥	1	(0.3)	0	(0.0)
湿疹	5	(1.4)	3	(0.6)
紅斑	2	(0.5)	0	(0.0)
結節性紅斑	0	(0.0)	1	(0.2)
多汗症	3	(0.8)	28	(5.9)
神経皮膚炎	1	(0.3)	0	(0.0)
寝汗	0	(0.0)	4	(0.8)
痒疹	1	(0.3)	0	(0.0)
そう痒症	3	(0.8)	2	(0.4)
乾癬	1	(0.3)	0	(0.0)
発疹	3	(0.8)	1	(0.2)
紅斑性皮疹	0	(0.0)	1	(0.2)
全身性皮疹	1	(0.3)	1	(0.2)
斑状皮疹	0	(0.0)	1	(0.2)
丘疹性皮疹	0	(0.0)	1	(0.2)
そう痒性皮疹	0	(0.0)	1	(0.2)
酒さ	1	(0.3)	0	(0.0)
皮膚剥脱	1	(0.3)	0	(0.0)
皮膚潰瘍	1	(0.3)	0	(0.0)
毛細血管拡張症	1	(0.3)	0	(0.0)
蕁麻疹	0	(0.0)	1	(0.2)
爪破損	1	(0.3)	0	(0.0)
白斑症	0	(0.0)	1	(0.2)
社会環境	1	(0.3)	2	(0.4)
閉経 {ss}	0	(0.0)	1	(0.7)
職場でのストレス	1	(0.3)	0	(0.0)
アルコール摂取	0	(0.0)	1	(0.2)

表 2.7.4.7.2-9
Table 109 TEAEs by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation
- Alcohol Dependence Pool

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
外科および内科処置	2	(0.5)	1	(0.2)
足関節手術	1	(0.3)	0	(0.0)
アルコールの解毒	0	(0.0)	1	(0.2)
手首手術	1	(0.3)	0	(0.0)
血管障害	13	(3.5)	23	(4.8)
動脈炎	1	(0.3)	0	(0.0)
潮紅	1	(0.3)	0	(0.0)
血腫	1	(0.3)	1	(0.2)
高血圧	9	(2.4)	15	(3.2)
低血圧	1	(0.3)	0	(0.0)
不安定血圧	0	(0.0)	1	(0.2)
末梢冷感	0	(0.0)	1	(0.2)
ほてり	0	(0.0)	6	(1.3)

Patients are only counted once for each System Organ Class/Preferred Term
{ss} Sex specific
Dictionary: MedDRA 19.0
＜資料番号5.3.5.3-03 : Table 109＞

表 2.7.4.7.2-10
Table 86 TEAEs Leading to Withdrawal by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	369		475	
Men	245	(66.4)	334	(70.3)
Women	124	(33.6)	141	(29.7)
Patients with TEAEs Leading to Withdrawal	26	(7.0)	78	(16.4)
心臓障害	1	(0.3)	2	(0.4)
不整脈	0	(0.0)	1	(0.2)
徐脈	1	(0.3)	0	(0.0)
心筋梗塞	0	(0.0)	1	(0.2)
耳および迷路障害	0	(0.0)	2	(0.4)
聴覚障害	0	(0.0)	1	(0.2)
耳鳴	0	(0.0)	1	(0.2)
眼障害	0	(0.0)	2	(0.4)
複視	0	(0.0)	1	(0.2)
変視症	0	(0.0)	1	(0.2)
胃腸障害	2	(0.5)	24	(5.1)
腹痛	0	(0.0)	2	(0.4)
上腹部痛	1	(0.3)	1	(0.2)
下痢	0	(0.0)	1	(0.2)
口内乾燥	0	(0.0)	1	(0.2)
悪心	0	(0.0)	18	(3.8)
嘔吐	1	(0.3)	4	(0.8)
一般・全身障害および投与部位の状態	0	(0.0)	14	(2.9)
無力症	0	(0.0)	1	(0.2)
悪寒	0	(0.0)	1	(0.2)
疲労	0	(0.0)	7	(1.5)
異常感	0	(0.0)	3	(0.6)
冷感	0	(0.0)	1	(0.2)
倦怠感	0	(0.0)	1	(0.2)
発熱	0	(0.0)	1	(0.2)
非心臓性胸痛	0	(0.0)	1	(0.2)
肝胆道系障害	3	(0.8)	1	(0.2)
急性胆嚢炎	1	(0.3)	0	(0.0)
アルコール性肝炎	1	(0.3)	0	(0.0)
肝障害	1	(0.3)	0	(0.0)
肝損傷	0	(0.0)	1	(0.2)
感染症および寄生虫症	3	(0.8)	0	(0.0)
精巣上体炎 {ss}	1	(0.4)	0	(0.0)
尿路感染	1	(0.3)	0	(0.0)
感染性胸水	1	(0.3)	0	(0.0)

表 2.7.4.7.2-10
Table 86 TEAEs Leading to Withdrawal by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

System Organ Class Preferred Term	Placebo n	Placebo (%)	Nalmefene n	Nalmefene (%)
傷害、中毒および処置合併症	3	(0.8)	2	(0.4)
アルコール中毒	1	(0.3)	2	(0.4)
転倒	1	(0.3)	0	(0.0)
腓骨骨折	1	(0.3)	0	(0.0)
肋骨骨折	1	(0.3)	0	(0.0)
脛骨骨折	1	(0.3)	0	(0.0)
各種物質毒性	1	(0.3)	0	(0.0)
臨床検査	1	(0.3)	0	(0.0)
血中尿素増加	1	(0.3)	0	(0.0)
代謝および栄養障害	0	(0.0)	4	(0.8)
糖尿病	0	(0.0)	1	(0.2)
食欲亢進	0	(0.0)	1	(0.2)
食欲減退	0	(0.0)	2	(0.4)
筋骨格系および結合組織障害	1	(0.3)	2	(0.4)
関節痛	1	(0.3)	0	(0.0)
筋痙縮	0	(0.0)	1	(0.2)
椎間板突出	0	(0.0)	1	(0.2)
神経系障害	0	(0.0)	37	(7.8)
味覚消失	0	(0.0)	1	(0.2)
意識レベルの低下	0	(0.0)	2	(0.4)
注意力障害	0	(0.0)	3	(0.6)
浮動性めまい	0	(0.0)	25	(5.3)
味覚異常	0	(0.0)	2	(0.4)
頭痛	0	(0.0)	9	(1.9)
嗅覚錯誤	0	(0.0)	1	(0.2)
痙攣発作	0	(0.0)	1	(0.2)
傾眠	0	(0.0)	2	(0.4)
振戦	0	(0.0)	2	(0.4)
平衡障害	0	(0.0)	1	(0.2)
精神障害	12	(3.3)	27	(5.7)
抑うつ気分を伴う適応障害	1	(0.3)	0	(0.0)
激越	0	(0.0)	1	(0.2)
アルコール症	1	(0.3)	1	(0.2)
不安	2	(0.5)	0	(0.0)
無感情	0	(0.0)	1	(0.2)
自殺既遂	1	(0.3)	0	(0.0)
興味の減少	0	(0.0)	2	(0.4)
うつ病	2	(0.5)	1	(0.2)
失見当識	0	(0.0)	4	(0.8)
幻覚	0	(0.0)	1	(0.2)
軽躁	0	(0.0)	1	(0.2)
錯覚	0	(0.0)	1	(0.2)
不眠症	1	(0.3)	7	(1.5)
易刺激性	0	(0.0)	1	(0.2)
神経過敏	0	(0.0)	1	(0.2)
悪夢	0	(0.0)	1	(0.2)
睡眠障害	0	(0.0)	5	(1.1)

表 2.7.4.7.2-10

Table 86 TEAEs Leading to Withdrawal by SOC and Preferred Term (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
精神障害				
アルコール離脱症候群	1	(0.3)	3	(0.6)
抑うつ症状	0	(0.0)	1	(0.2)
双極性障害	0	(0.0)	1	(0.2)
大うつ病	3	(0.8)	0	(0.0)
適応障害	1	(0.3)	0	(0.0)
生殖系および乳房障害	0	(0.0)	1	(0.2)
勃起不全 {ss}	0	(0.0)	1	(0.3)
呼吸器、胸郭および縦隔障害	1	(0.3)	2	(0.4)
喉頭浮腫	0	(0.0)	1	(0.2)
気胸	1	(0.3)	0	(0.0)
喉頭蓋嚢胞	0	(0.0)	1	(0.2)
皮膚および皮下組織障害	2	(0.5)	6	(1.3)
多汗症	0	(0.0)	6	(1.3)
発疹	1	(0.3)	0	(0.0)
全身性皮疹	1	(0.3)	0	(0.0)

Patients are only counted once for each System Organ Class/Preferred Term

{ss} Sex specific

Dictionary: MedDRA 19.0

＜資料番号5.3.5.3-03：Table 86＞

表 2.7.4.7.2-11
Panel 27 Deaths (Safety Populations) - All Studies

Study (Indication)	Treatment & dose	Patient/Sex/ Age (years)	Adverse event(s)	Time from first/ last dose to adverse event onset (Days)	Causality
12014A (alcohol dependence)	Placebo as-needed	[redacted]	自殺既遂	33/5[a]	NR
	Placebo as-needed	[redacted]	自殺既遂	30/5[a]	POS
12023A (alcohol dependence)	Nalmefene 20 mg as-needed	[redacted]	突然死	46/3	NR
12013A (alcohol dependence)	Nalmefene 20 mg as-needed	[redacted]	外傷性脳損傷	128/15	NR
CPH-101-0701 (alcohol-use disorders)	Placebo	[redacted]	播種性癌	226/40	UNL
IX-317-003 (interstitial cystitis)	unknown	[redacted]	Metastatic prostatic carcinoma	473/150	NR
IX-302-003 (pruritus)	Nalmefene 1 mg/day	[redacted]	Complications due to long-standing post-stroke status and renal failure	32/21	NR
IX-319-003 (rheumatoid arthritis)	Nalmefene 20 mg b.i.d	[redacted]	Acute myocardial infarction	4 weeks/0	NR

MedDRA Version 13.0 : 12014A, 12023A, 12013A
MedDRA Version 5.1 : CPH-101-0701
M = man; IMP = investigational medicinal product; NR = not related; POS = possibly related; UNL = unlikely;
b.i.d. = bis in die (twice daily)
[a] No information is available on IMP intake for the 5 days prior to the event.
＜資料番号5.3.5.3-03：Panel 27＞

表 2.7.4.7.2-12

Panel 52 TEAEs with an Incidence of 5% or More in Patients Treated with Nalmefene (Safety Population) - Alcohol-use Disorders Pool

	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene total	
Preferred term	n	%	n	%	n	%	n	%	n	%	n	%
Patients treated	361		68		50		453		118		689	
Patients with TEAEs												
悪心	39	10.8	10	14.7	11	22.0	142	31.3	26	22.0	189	27.4
不眠症	48	13.3	15	22.1	11	22.0	128	28.3	35	29.7	189	27.4
浮動性めまい	32	8.9	20	29.4	16	32.0	114	25.2	30	25.4	180	26.1
頭痛	74	20.5	17	25.0	10	20.0	96	21.2	32	27.1	155	22.5
疲労	40	11.1	11	16.2	5	10.0	89	19.6	15	12.7	120	17.4
インフルエンザ様疾患	47	13.0	11	16.2	9	18.0	67	14.8	31	26.3	118	17.1
嘔吐NOS	17	4.7	4	5.9	4	8.0	61	13.5	8	6.8	77	11.2
倦怠感	4	1.1			6	12.0	49	10.8	1	0.8	56	8.1
下痢NOS	35	9.7	6	8.8	4	8.0	27	6.0	18	15.3	55	8.0
多汗	10	2.8	2	2.9	2	4.0	43	9.5	3	2.5	50	7.3
アルコールによる宿酔	14	3.9	1	1.5	5	10.0	37	8.2	2	1.7	45	6.5
口内乾燥	7	1.9	5	7.4	3	6.0	27	6.0	9	7.6	44	6.4
背部痛	26	7.2	4	5.9	1	2.0	31	6.8	5	4.2	41	6.0
食欲減退NOS	3	0.8	5	7.4	5	10.0	24	5.3	3	2.5	37	5.4

MedDRA Version 5.1

NOS = not otherwise specified

[a] Patients in the nalmefene groups in the flexible-dose studies CPH-101-0801, CPH-101-0701, and CPH-101-0400 are included in the nalmefene 20 mg group, although their actual dose may differ.

＜資料番号5.3.5.3-03：Panel 52＞

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Patients treated	361		68		50		453		118		689	
感染症および寄生虫症												
気管支炎NOS	7	1.9	2	2.9	1	2.0	8	1.8			11	1.6
耳の感染症NOS	1	0.3	2	2.9			4	0.9	2	1.7	8	1.2
胃腸炎NOS	2	0.6			1	2.0	7	1.5			8	1.2
ウイルス性胃腸炎NOS							6	1.3	2	1.7	8	1.2
咽頭炎	4	1.1					7	1.5	1	0.8	8	1.2
副鼻腔炎NOS	4	1.1	2	2.9			4	0.9	2	1.7	8	1.2
歯感染	2	0.6	1	1.5	1	2.0	4	0.9	1	0.8	7	1.0
上気道感染NOS							5	1.1	2	1.7	7	1.0
インフルエンザ	3	0.8	1	1.5			5	1.1			6	0.9
気道感染NOS	2	0.6					6	1.3			6	0.9
外耳炎NOS							5	1.1			5	0.7
限局性感染	1	0.3			1	2.0	3	0.7			4	0.6
肺炎NOS							4	0.9			4	0.6
急性気管支炎NOS	2	0.6			1	2.0	2	0.4			3	0.4
単純ヘルペス							2	0.4	1	0.8	3	0.4
下気道感染NOS	6	1.7					3	0.7			3	0.4
扁桃炎					1	2.0	1	0.2	1	0.8	3	0.4
歯膿瘍	1	0.3					2	0.4	1	0.8	3	0.4
尿路感染NOS	1	0.3					3	0.7			3	0.4
ウイルス感染NOS	2	0.6	1	1.5			2	0.4			3	0.4
齲歯[b]							2	0.4			2	0.3
膿瘍NOS							1	0.2			1	0.1
感染性関節炎NOS							1	0.2			1	0.1
デング熱							1	0.2			1	0.1
外耳感染NOS					1	2.0					1	0.1
眼瞼感染NOS							1	0.2			1	0.1
真菌感染NOS					1	2.0					1	0.1
感染性歯肉炎NOS[c]							1	0.2			1	0.1
ハンタウイルス感染NOS							1	0.2			1	0.1
C型肝炎							1	0.2			1	0.1
帯状疱疹			1	1.5							1	0.1

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
感染症および寄生虫症												
感染NOS	1	0.3					1	0.2			1	0.1
虹彩炎					1	2.0					1	0.1
ライム病							1	0.2			1	0.1
ウイルス性髄膜炎NEC[d]							1	0.2			1	0.1
爪真菌感染NOS							1	0.2			1	0.1
中耳炎NOS							1	0.2			1	0.1
急性中耳炎NOS							1	0.2			1	0.1
レンサ球菌性咽頭炎									1	0.8	1	0.1
術後創感染[c]							1	0.2			1	0.1
歯髄炎							1	0.2			1	0.1
皮膚真菌感染NOS							1	0.2			1	0.1
皮膚感染症	1	0.3	1	1.5							1	0.1
足部白癬	1	0.3					1	0.2			1	0.1
腟カンジダ症	1	0.3					1	0.2			1	0.1
腟感染NOS					1	2.0					1	0.1
蜂巣炎	1	0.3										
眼感染症NOS	3	0.8										
膿痂疹NOS	1	0.3										
腎盂腎炎NOS	1	0.3										
疥癬寄生	1	0.3										
急性扁桃炎NOS	1	0.3										
創傷感染	2	0.6										
良性および悪性新生物(嚢胞およびポリープを含む)[d]												
乳房腫瘤NOS							1	0.2			1	0.1
嚢胞NOS			1	1.5							1	0.1
脂肪腫NOS							1	0.2			1	0.1
皮膚の新生物NOS							1	0.2			1	0.1
皮膚乳頭腫							1	0.2			1	0.1
乳房脂肪腫	1	0.3										
舌の良性新生物	1	0.3										

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
血液およびリンパ系障害												
血小板減少症							3	0.7			3	0.4
貧血NOS	2	0.6					1	0.2			1	0.1
リンパ節症	2	0.6	1	1.5							1	0.1
白血球増加症NOS[d]	1	0.3										
白血球減少症NOS	1	0.3										
大赤血球症	1	0.3										
免疫系障害												
過敏症NOS	3	0.8					2	0.4	3	2.5	5	0.7
季節性アレルギー	1	0.3					5	1.1			5	0.7
アレルギー増悪							1	0.2			1	0.1
複合アレルギー	1	0.3					1	0.2			1	0.1
虫刺されアレルギー[c]	2	0.6										
内分泌障害												
後天性甲状腺機能低下症	1	0.3										
代謝および栄養障害												
食欲減退NOS	3	0.8	5	7.4	5	10.0	24	5.3	3	2.5	37	5.4
食欲不振							12	2.6	1	0.8	13	1.9
高トリグリセリド血症	1	0.3					8	1.8			8	1.2
食欲亢進NOS	4	1.1	1	1.5	2	4.0	2	0.4	2	1.7	7	1.0
痛風	3	0.8					5	1.1	1	0.8	6	0.9
痛風増悪	1	0.3					2	0.4			2	0.3
高血糖NOS							2	0.4			2	0.3
高カリウム血症							2	0.4			2	0.3
食欲障害NOS									1	0.8	1	0.1
糖尿病NOS							1	0.2			1	0.1
体液貯留							1	0.2			1	0.1
食物欲求	1	0.3					1	0.2			1	0.1
飢餓							1	0.2			1	0.1
高コレステロール血症	2	0.6					1	0.2			1	0.1
高脂血症NOS	2	0.6	1	1.5							1	0.1
低カリウム血症							1	0.2			1	0.1
多飲症							1	0.2			1	0.1

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
代謝および栄養障害												
異脂肪血症	1	0.3										
ヘモクロマトーシス	1	0.3										
精神障害												
不眠症	48	13.3	15	22.1	11	22.0	128	28.3	35	29.7	189	27.4
アルコールによる宿酔	14	3.9	1	1.5	5	10.0	37	8.2	2	1.7	45	6.5
うつ病	19	5.3	2	2.9	3	6.0	23	5.1	4	3.4	32	4.6
不安	9	2.5	2	2.9	3	6.0	16	3.5	5	4.2	26	3.8
易刺激性	5	1.4	4	5.9	2	4.0	13	2.9	5	4.2	24	3.5
リビドー減退	1	0.3	2	2.9	2	4.0	10	2.2	4	3.4	18	2.6
解離	1	0.3	1	1.5			11	2.4	2	1.7	14	2.0
悪夢	3	0.8					13	2.9	1	0.8	14	2.0
睡眠障害NOS	1	0.3	1	1.5			12	2.6	1	0.8	14	2.0
無感情							10	2.2			10	1.5
錯乱[c]			1	1.5			5	1.1	4	3.4	10	1.5
異常な夢	2	0.6	2	2.9			6	1.3	1	0.8	9	1.3
幻覚NOS	1	0.3					8	1.8	1	0.8	9	1.3
神経過敏	2	0.6	1	1.5	1	2.0	5	1.1	2	1.7	9	1.3
激越			1	1.5			7	1.5			8	1.2
攻撃性	1	0.3					7	1.5			7	1.0
錯乱状態							7	1.5			7	1.0
失見当識			1	1.5			4	0.9	1	0.8	6	0.9
パニック発作	1	0.3					5	1.1	1	0.8	6	0.9
落ち着きのなさ	2	0.6	1	1.5			4	0.9	1	0.8	6	0.9
多幸気分							4	0.9			4	0.6
リビドー亢進							4	0.9			4	0.6
中期不眠症	1	0.3					2	0.4	2	1.7	4	0.6
気分動揺							3	0.7	1	0.8	4	0.6
早朝覚醒							3	0.7			3	0.4
幻視							3	0.7			3	0.4
アルコール離脱症状[d]					1	2.0			1	0.8	2	0.3
抑うつ気分	2	0.6	1	1.5			1	0.2			2	0.3
現実感消失							2	0.4			2	0.3

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
精神障害												
対象への恐怖							2	0.4			2	0.3
幻聴							2	0.4			2	0.3
過覚醒					1	2.0	1	0.2			2	0.3
錯覚					1	2.0	1	0.2			2	0.3
人格変化			1	1.5			1	0.2			2	0.3
恐怖症							2	0.4			2	0.3
アルコール症							1	0.2			1	0.1
怒り	1	0.3							1	0.8	1	0.1
快感消失							1	0.2			1	0.1
注意欠陥多動性障害									1	0.8	1	0.1
泣き			1	1.5							1	0.1
譫妄							1	0.2			1	0.1
振戦譫妄							1	0.2			1	0.1
妄想NOS							1	0.2			1	0.1
社会的行為障害NOS							1	0.2			1	0.1
高揚状態							1	0.2			1	0.1
せっかち									1	0.8	1	0.1
言葉もれ							1	0.2			1	0.1
精神障害NEC[d]					1	2.0					1	0.1
気分変動NOS	1	0.3					1	0.2			1	0.1
気分障害NOS			1	1.5							1	0.1
パニック障害NOS							1	0.2			1	0.1
妄想症	1	0.3					1	0.2			1	0.1
早漏			1	1.5							1	0.1
精神病性障害NOS									1	0.8	1	0.1
ストレス症状							1	0.2			1	0.1
涙ぐむ	1	0.3					1	0.2			1	0.1
思考異常NEC[d]					1	2.0					1	0.1
抑うつ気分を伴う適応障害	1	0.3										
感情不安定	1	0.3										
アルコール離脱症候群	2	0.6										
死別反応	1	0.3										

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
精神障害												
転換性障害	1	0.3										
感情的苦悩	1	0.3										
他の精神疾患に関連する不眠	1	0.3										
自殺念慮	2	0.6										
神経系障害												
浮動性めまい	32	8.9	20	29.4	16	32.0	114	25.2	30	25.4	180	26.1
頭痛	74	20.5	17	25.0	10	20.0	96	21.2	32	27.1	155	22.5
傾眠	2	0.6	5	7.4	3	6.0	12	2.6	6	5.1	26	3.8
振戦	3	0.8	5	7.4			13	2.9	4	3.4	22	3.2
味覚異常	3	0.8					18	4.0			18	2.6
注意力障害	1	0.3	1	1.5	2	4.0	9	2.0	2	1.7	14	2.0
錯感覚	2	0.6	3	4.4	1	2.0	5	1.1	1	0.8	10	1.5
下肢静止不能症候群							10	2.2			10	1.5
感覚減退	1	0.3					8	1.8	1	0.8	9	1.3
味覚障害[d]	2	0.6					1	0.2	6	5.1	7	1.0
片頭痛NOS	2	0.6					5	1.1	1	0.8	6	0.9
記憶障害	2	0.6					2	0.4	2	1.7	4	0.6
平衡障害NOS							3	0.7			3	0.4
反射減弱			1	1.5	1	2.0	1	0.2			3	0.4
鎮静	1	0.3					1	0.2	2	1.7	3	0.4
会話障害							3	0.7			3	0.4
手根管症候群			1	1.5			1	0.2			2	0.3
小脳症候群							1	0.2	1	0.8	2	0.3
意識レベルの低下							1	0.2	1	0.8	2	0.3
構語障害									2	1.7	2	0.3
知覚過敏							2	0.4			2	0.3
筋緊張亢進							1	0.2	1	0.8	2	0.3
活動亢進[c]	2	0.6	1	1.5	1	2.0					2	0.3
嗅覚錯誤	1	0.3					2	0.4			2	0.3
坐骨神経痛	3	0.8					2	0.4			2	0.3
感覚障害NOS	1	0.3					2	0.4			2	0.3
副鼻腔炎に伴う頭痛	2	0.6					1	0.2	1	0.8	2	0.3

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
神経系障害												
睡眠時無呼吸症候群							2	0.4			2	0.3
失神	1	0.3					2	0.4			2	0.3
味覚消失							1	0.2			1	0.1
アルコール性痙攣							1	0.2			1	0.1
失調NEC[d]			1	1.5							1	0.1
前兆NOS							1	0.2			1	0.1
灼熱感NOS	1	0.3			1	2.0					1	0.1
小脳性運動失調					1	2.0					1	0.1
協調運動異常							1	0.2			1	0.1
痙攣NOS	1	0.3					1	0.2			1	0.1
異常感覚							1	0.2			1	0.1
ジスキネジーNEC[d]									1	0.8	1	0.1
錐体外路疾患							1	0.2			1	0.1
顔面不全麻痺							1	0.2			1	0.1
頭部不快感							1	0.2			1	0.1
反射亢進							1	0.2			1	0.1
初期不眠症							1	0.2			1	0.1
意識消失	2	0.6					1	0.2			1	0.1
不随意性筋収縮			1	1.5							1	0.1
筋固縮	1	0.3							1	0.8	1	0.1
筋痙直増悪									1	0.8	1	0.1
神経圧迫	1	0.3							1	0.8	1	0.1
末梢性ニューロパシーNEC[d]									1	0.8	1	0.1
舌下神経障害NOS	1	0.3										
橈骨神経麻痺	1	0.3										
眼障害												
羞明			1	1.5			1	0.2	3	2.5	5	0.7
霧視	2	0.6	1	1.5			3	0.7	1	0.8	5	0.7
視覚障害NOS	2	0.6					4	0.9	1	0.8	5	0.7
結膜炎	4	1.1			1	2.0	3	0.7			4	0.6
眼部不快感							3	0.7			3	0.4
眼精疲労							2	0.4			2	0.3

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
眼障害												
アレルギー性結膜炎							2	0.4			2	0.3
眼刺激							2	0.4			2	0.3
眼痛							2	0.4			2	0.3
結膜出血	1	0.3					1	0.2			1	0.1
結膜充血							1	0.2			1	0.1
眼乾燥NOS	1	0.3					1	0.2			1	0.1
眼の炎症NOS							1	0.2			1	0.1
眼瞼浮腫	1	0.3					1	0.2			1	0.1
流涙増加							1	0.2			1	0.1
視覚異常NEC[d]									1	0.8	1	0.1
白内障	1	0.3										
角膜出血	1	0.3										
近視	1	0.3										
耳および迷路障害												
耳鳴	1	0.3	1	1.5	3	6.0	3	0.7	7	5.9	14	2.0
回転性眩暈	5	1.4					8	1.8	1	0.8	9	1.3
耳痛[d]	1	0.3					2	0.4			2	0.3
聴覚過敏			1	1.5					1	0.8	2	0.3
耳垢栓塞	1	0.3					1	0.2			1	0.1
耳の障害NOS			1	1.5							1	0.1
耳痛							1	0.2			1	0.1
外耳障害NOS							1	0.2			1	0.1
聴力低下							1	0.2			1	0.1
迷路炎NOS							1	0.2			1	0.1
乗物酔い			1	1.5							1	0.1
鼓膜障害NOS									1	0.8	1	0.1
心臓障害												
動悸	3	0.8	1	1.5	3	6.0	15	3.3	2	1.7	21	3.0
不整脈NOS	1	0.3					9	2.0			9	1.3
頻脈NOS	3	0.8	1	1.5	2	4.0	5	1.1	1	0.8	9	1.3
狭心症	1	0.3					3	0.7	1	0.8	4	0.6
徐脈NOS	2	0.6					3	0.7			3	0.4

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
心臓障害												
心房細動	1	0.3					2	0.4			2	0.3
不安定狭心症							1	0.2			1	0.1
心房粗動							1	0.2			1	0.1
第一度房室ブロック							1	0.2			1	0.1
冠動脈疾患NOS			1	1.5							1	0.1
心筋虚血							1	0.2			1	0.1
頻脈性不整脈							1	0.2			1	0.1
心室性期外収縮	1	0.3					1	0.2			1	0.1
心室肥大	1	0.3					1	0.2			1	0.1
左脚ブロック	1	0.3										
右脚ブロック	1	0.3										
上室性期外収縮	1	0.3										
血管障害												
高血圧NOS	13	3.6			1	2.0	12	2.6	2	1.7	15	2.2
ほてりNOS	3	0.8					7	1.5			7	1.0
潮紅	2	0.6					5	1.1	1	0.8	6	0.9
熱射病							1	0.2			1	0.1
不安定血圧							1	0.2			1	0.1
リンパ浮腫NOS			1	1.5							1	0.1
血栓症NOS[c]							1	0.2			1	0.1
血腫NOS	1	0.3										
呼吸器、胸郭および縦隔障害												
咳嗽	7	1.9	4	5.9			12	2.6	1	0.8	17	2.5
呼吸困難NOS	5	1.4					7	1.5	2	1.7	9	1.3
鼻咽頭炎	4	1.1					8	1.8			8	1.2
喘息NOS	2	0.6					5	1.1			5	0.7
鼻閉	2	0.6	1	1.5			2	0.4			3	0.4
咽喉頭疼痛							3	0.7			3	0.4
鼻炎NOS	3	0.8	1	1.5	1	2.0	1	0.2			3	0.4
副鼻腔うっ血	2	0.6	2	2.9					1	0.8	3	0.4
副鼻腔痛	3	0.8	1	1.5	1	2.0			1	0.8	3	0.4
上顎洞炎							2	0.4			2	0.3

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
呼吸器、胸郭および縦隔障害												
後鼻漏							2	0.4			2	0.3
アレルギー性鼻炎NOS	1	0.3					2	0.4			2	0.3
鼻漏	1	0.3							2	1.7	2	0.3
喘鳴音	1	0.3	1	1.5			1	0.2			2	0.3
カタル	2	0.6					1	0.2			1	0.1
咽喉乾燥							1	0.2			1	0.1
鼻出血	3	0.8					1	0.2			1	0.1
過換気							1	0.2			1	0.1
鼻茸							1	0.2			1	0.1
あくび							1	0.2			1	0.1
喀血	1	0.3										
喉頭炎NOS	1	0.3										
湿性咳嗽	1	0.3										
季節性鼻炎	1	0.3										
くしゃみ	1	0.3										
変色痰	1	0.3										
咽喉絞扼感	1	0.3										
胃腸障害												
悪心	39	10.8	10	14.7	11	22.0	142	31.3	26	22.0	189	27.4
嘔吐NOS	17	4.7	4	5.9	4	8.0	61	13.5	8	6.8	77	11.2
下痢NOS	35	9.7	6	8.8	4	8.0	27	6.0	18	15.3	55	8.0
口内乾燥	7	1.9	5	7.4	3	6.0	27	6.0	9	7.6	44	6.4
腹痛NOS	11	3.0			5	10.0	20	4.4	2	1.7	27	3.9
便秘	5	1.4	3	4.4	1	2.0	12	2.6	6	5.1	22	3.2
消化不良	14	3.9	3	4.4	1	2.0	10	2.2	8	6.8	22	3.2
上腹部痛	8	2.2	3	4.4	1	2.0	4	0.9	5	4.2	13	1.9
腹部膨満	3	0.8	2	2.9			5	1.1			7	1.0
歯痛	4	1.1	1	1.5			5	1.1	1	0.8	7	1.0
咽喉痛NOS[d]	2	0.6	4	5.9	1	2.0					5	0.7
鼓腸	2	0.6					1	0.2	3	2.5	4	0.6
胃炎NOS	2	0.6			1	2.0	2	0.4			3	0.4
吐血	1	0.3					3	0.7			3	0.4

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
胃腸障害												
軟便	1	0.3					2	0.4	1	0.8	3	0.4
口腔内潰瘍形成							3	0.7			3	0.4
レッチング							2	0.4	1	0.8	3	0.4
腹部不快感	1	0.3					2	0.4			2	0.3
下腹部痛							2	0.4			2	0.3
虫垂炎							1	0.2	1	0.8	2	0.3
消化器不調	1	0.3					2	0.4			2	0.3
胃食道逆流性疾患	1	0.3					2	0.4			2	0.3
痔核							1	0.2	1	0.8	2	0.3
口の感覚鈍麻							2	0.4			2	0.3
メレナ							2	0.4			2	0.3
食道逆流[d]							1	0.2	1	0.8	2	0.3
膵炎NOS	1	0.3					2	0.4			2	0.3
直腸出血	1	0.3					1	0.2	1	0.8	2	0.3
唾液欠乏							1	0.2			1	0.1
口唇のひび割れ			1	1.5							1	0.1
口唇炎			1	1.5							1	0.1
憩室炎NOS			1	1.5							1	0.1
嚥下障害	2	0.6					1	0.2			1	0.1
心窩部不快感							1	0.2			1	0.1
便失禁							1	0.2			1	0.1
白色便							1	0.2			1	0.1
出血性胃潰瘍	1	0.3					1	0.2			1	0.1
歯肉痛							1	0.2			1	0.1
歯肉炎	1	0.3			1	2.0					1	0.1
舌痛							1	0.2			1	0.1
裂孔ヘルニア			1	1.5							1	0.1
口唇感覚鈍麻[c]							1	0.2			1	0.1
イレウス[d]					1	2.0					1	0.1
瘢痕ヘルニアNOS			1	1.5							1	0.1
食道炎NOS							1	0.2			1	0.1
口腔内痛							1	0.2			1	0.1

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
胃腸障害												
急性膵炎							1	0.2			1	0.1
流涎過多							1	0.2			1	0.1
胃不快感							1	0.2			1	0.1
咽喉刺激感									1	0.8	1	0.1
舌障害NOS	1	0.3					1	0.2			1	0.1
舌浮腫							1	0.2			1	0.1
腹部ヘルニアNOS	1	0.3										
腹部硬直	1	0.3										
腸雑音異常	1	0.3										
セリアック病	1	0.3										
排便回数増加	1	0.3										
胃食道逆流性疾患[c]	1	0.3										
消化器痛NOS	1	0.3										
胃腸潰瘍NOS	1	0.3										
痔出血	1	0.3										
口唇乾燥	1	0.3										
食物の逆流	1	0.3										
舌苔	1	0.3										
肝・胆道系障害[d]												
肝腫大	1	0.3	1	1.5			1	0.2	1	0.8	3	0.4
肝障害NOS	1	0.3										
肝炎NOS	1	0.3										
高ビリルビン血症	2	0.6										
皮膚および皮下組織障害												
多汗	10	2.8	2	2.9	2	4.0	43	9.5	3	2.5	50	7.3
そう痒症	5	1.4	3	4.4			14	3.1	1	0.8	18	2.6
皮膚炎NOS	10	2.8	1	1.5	1	2.0	3	0.7	7	5.9	12	1.7
発疹NOS	7	1.9					10	2.2			10	1.5
蕁麻疹NOS					1	2.0	1	0.2	4	3.4	6	0.9
寝汗	2	0.6					4	0.9	1	0.8	5	0.7
紅斑	3	0.8					3	0.7			3	0.4
ざ瘡増悪					1	2.0	1	0.2			2	0.3

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
皮膚および皮下組織障害												
冷湿[d]					1	2.0	1	0.2			2	0.3
挫傷	4	1.1					2	0.4			2	0.3
接触性皮膚炎	2	0.6	2	2.9							2	0.3
湿疹	1	0.3					2	0.4			2	0.3
皮膚疼痛	1	0.3					2	0.4			2	0.3
皮膚圧痛							2	0.4			2	0.3
ざ瘡NOS									1	0.8	1	0.1
脱毛症							1	0.2			1	0.1
ざ瘡様皮膚炎			1	1.5							1	0.1
紅斑性単純性皮膚炎[c]									1	0.8	1	0.1
皮膚描記症[c]									1	0.8	1	0.1
斑状出血	2	0.6			1	2.0					1	0.1
過角化			1	1.5							1	0.1
爪囲炎							1	0.2			1	0.1
全身性そう痒症							1	0.2			1	0.1
乾癬増悪	2	0.6					1	0.2			1	0.1
全身性皮疹							1	0.2			1	0.1
斑状皮疹							1	0.2			1	0.1
斑状丘疹状皮疹									1	0.8	1	0.1
丘疹									1	0.8	1	0.1
そう痒性皮疹	1	0.3					1	0.2			1	0.1
酒さ					1	2.0					1	0.1
ひび・あかぎれ									1	0.8	1	0.1
皮膚変色							1	0.2			1	0.1
皮膚亀裂							1	0.2			1	0.1
皮膚色素過剰							1	0.2			1	0.1
皮膚小結節							1	0.2			1	0.1
顔面腫脹	1	0.3					1	0.2			1	0.1
皮膚乾燥	1	0.3										
表皮嚢胞	1	0.3										
顔面浮腫	1	0.3										
せつ	1	0.3										

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
皮膚および皮下組織障害												
挫傷発生の増加傾向	1	0.3										
爪の障害NOS	1	0.3										
立毛	1	0.3										
皮膚病変NOS	1	0.3										
皮膚異常臭	2	0.6										
日光蕁麻疹	1	0.3										
筋骨格、結合組織および骨障害[d]												
背部痛	26	7.2	4	5.9	1	2.0	31	6.8	5	4.2	41	6.0
関節痛	20	5.5	3	4.4			27	6.0	4	3.4	34	4.9
筋緊張	6	1.7	1	1.5			23	5.1	2	1.7	26	3.8
四肢痛[b]	4	1.1	1	1.5	2	4.0	16	3.5	3	2.5	22	3.2
筋痛	8	2.2	3	4.4			10	2.2	3	2.5	16	2.3
筋骨格硬直	2	0.6			2	4.0	7	1.5	3	2.5	12	1.7
筋痙縮	5	1.4	1	1.5			9	2.0	1	0.8	11	1.6
頚部痛	5	1.4	1	1.5			3	0.7	1	0.8	5	0.7
滑液包炎	1	0.3	2	2.9			2	0.4			4	0.6
筋攣縮			2	2.9			2	0.4			4	0.6
腫脹NOS	3	0.8					4	0.9			4	0.6
筋肉疲労							2	0.4			2	0.3
腱炎							2	0.4			2	0.3
関節炎NOS							1	0.2			1	0.1
関節症NOS					1	2.0					1	0.1
関節症NOS[c]							1	0.2			1	0.1
骨棘	1	0.3	1	1.5							1	0.1
バニオン							1	0.2			1	0.1
線維筋痛							1	0.2			1	0.1
痛風性関節炎							1	0.2			1	0.1
尺骨部痛							1	0.2			1	0.1
椎間板変性症NOS							1	0.2			1	0.1
椎間板ヘルニア									1	0.8	1	0.1
関節運動範囲減少									1	0.8	1	0.1
関節硬直									1	0.8	1	0.1

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
筋骨格、結合組織および骨障害[d]												
局所腫脹							1	0.2			1	0.1
筋脱力NOS							1	0.2			1	0.1
筋骨格痛							1	0.2			1	0.1
末梢腫脹							1	0.2			1	0.1
慢性関節リウマチ							1	0.2			1	0.1
重感							1	0.2			1	0.1
ガングリオン	1	0.3										
脊柱後弯症	1	0.3										
中足骨痛	1	0.3										
筋骨格系胸痛	1	0.3										
肩回旋筋腱板症候群	1	0.3										
腱鞘炎	1	0.3										
腎および尿路障害												
頻尿	2	0.6	2	2.9			5	1.1	3	2.5	10	1.5
多尿							3	0.7			3	0.4
夜間頻尿	1	0.3					2	0.4			2	0.3
着色尿							1	0.2			1	0.1
排尿困難[c]	1	0.3					1	0.2			1	0.1
排尿困難	1	0.3					1	0.2			1	0.1
腰部痛[c]							1	0.2			1	0.1
尿意切迫							1	0.2			1	0.1
蛋白尿	1	0.3					1	0.2			1	0.1
尿変色[c]	1	0.3					1	0.2			1	0.1
血尿	1	0.3										
排尿異常NOS[d]	1	0.3										
妊娠、産褥および周産期の状態												
自然流産NOS	1	0.3										
子宮外妊娠	1	0.3										

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
生殖系および乳房障害												
勃起機能不全NOS	2	0.6					5	1.1	1	0.8	6	0.9
月経困難症	1	0.3	1	1.5					2	1.7	3	0.4
前立腺炎							2	0.4			2	0.3
良性前立腺肥大症							1	0.2			1	0.1
乳房圧痛			1	1.5							1	0.1
射精障害NOS							1	0.2			1	0.1
勃起増強							1	0.2			1	0.1
インポテンス[d]									1	0.8	1	0.1
閉経期症状							1	0.2			1	0.1
月経障害NOS							1	0.2			1	0.1
月経前症候群	1	0.3					1	0.2			1	0.1
持続勃起症							1	0.2			1	0.1
自発陰茎勃起							1	0.2			1	0.1
精巣嚢胞									1	0.8	1	0.1
腟分泌物							1	0.2			1	0.1
腟出血	1	0.3					1	0.2			1	0.1
卵巣嚢胞	1	0.3										
性交後出血	1	0.3										
先天性および家族性／遺伝性障害[d]												
表皮母斑			1	1.5							1	0.1
過度驚愕	1	0.3										
全身障害および投与局所様態												
寝汗							1	0.2			1	0.1
疲労	40	11.1	11	16.2	5	10.0	89	19.6	15	12.7	120	17.4
インフルエンザ様疾患	47	13.0	11	16.2	9	18.0	67	14.8	31	26.3	118	17.1
倦怠感	4	1.1			6	12.0	49	10.8	1	0.8	56	8.1
胸痛	8	2.2			2	4.0	10	2.2	5	4.2	17	2.5
嗜眠	2	0.6	3	4.4			9	2.0	3	2.5	15	2.2
悪寒	1	0.3					10	2.2	1	0.8	11	1.6
無力症	1	0.3					9	2.0			9	1.3
異常感	3	0.8			2	4.0	7	1.5			9	1.3

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
全身障害および投与局所様態												
発熱	3	0.8					7	1.5	1	0.8	8	1.2
転倒	3	0.8					6	1.3			6	0.9
疼痛NOS	1	0.3	1	1.5			3	0.7	2	1.7	6	0.9
胸部不快感			1	1.5			3	0.7	1	0.8	5	0.7
状態悪化	1	0.3			2	4.0			3	2.5	5	0.7
酩酊感					1	2.0	2	0.4	2	1.7	5	0.7
冷感							4	0.9			4	0.6
熱感	1	0.3					4	0.9			4	0.6
圧迫感NOS							4	0.9			4	0.6
口渇	4	1.1					3	0.7	1	0.8	4	0.6
脱力[c]	1	0.3			1	2.0	2	0.4			3	0.4
末梢性浮腫	3	0.8					2	0.4			2	0.3
不快気分							1	0.2			1	0.1
活力増進	1	0.3							1	0.8	1	0.1
熱感および冷感							1	0.2			1	0.1
びくびく感									1	0.8	1	0.1
歩行異常							1	0.2			1	0.1
意味不明な障害NOS							1	0.2			1	0.1
局所の炎症							1	0.2			1	0.1
粘膜乾燥NOS							1	0.2			1	0.1
戦慄[d]							1	0.2			1	0.1
不活発							1	0.2			1	0.1
圧痛NOS							1	0.2			1	0.1
鎮痛効果	1	0.3										
運動耐性低下	1	0.3										
宿酔	1	0.3										
臨床検査												
血圧上昇	9	2.5					6	1.3	3	2.5	9	1.3
肝機能検査NOS異常	5	1.4	1	1.5			4	0.9	3	2.5	8	1.2
血中トリグリセリド増加	10	2.8			2	4.0	4	0.9	1	0.8	7	1.0
トランスフェリン増加	5	1.4					5	1.1			5	0.7
血中コレステロール増加	4	1.1					3	0.7	1	0.8	4	0.6

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
臨床検査												
γ－グルタミルトランスフェラーゼ増加	6	1.7					4	0.9			4	0.6
心拍数増加							2	0.4	2	1.7	4	0.6
体重増加			2	2.9			2	0.4			4	0.6
血中ビリルビン増加	2	0.6					2	0.4	1	0.8	3	0.4
血中ブドウ糖増加	7	1.9					2	0.4	1	0.8	3	0.4
血便			1	1.5	1	2.0	1	0.2			3	0.4
アラニン・アミノトランスフェラーゼ増加	3	0.8					2	0.4			2	0.3
心音異常			1	1.5			1	0.2			2	0.3
ロンベルグ徴候陽性	1	0.3					1	0.2	1	0.8	2	0.3
体重減少	1	0.3	1	1.5					1	0.8	2	0.3
関節鏡検査					1	2.0					1	0.1
アスパラギン酸アミノトランスフェラーゼ増加	2	0.6					1	0.2			1	0.1
血中カリウム減少							1	0.2			1	0.1
血中尿酸増加	3	0.8					1	0.2			1	0.1
心拍数不整	1	0.3					1	0.2			1	0.1
臨床検査異常NOS							1	0.2			1	0.1
平均赤血球容積増加							1	0.2			1	0.1
血小板数減少			1	1.5							1	0.1
子宮頚部スミア異常									1	0.8	1	0.1
トランスアミナーゼ上昇							1	0.2			1	0.1
血中カリウム増加	1	0.3										
血中尿素増加	1	0.3										
心雑音NOS	1	0.3										
心電図T波振幅増加	1	0.3										
心電図異常NOS	1	0.3										
糖尿陽性[d]	1	0.3										
傷害および中毒[d]												
四肢損傷NOS	2	0.6	2	2.9	1	2.0	7	1.5	2	1.7	12	1.7
アルコール中毒	1	0.3					4	0.9			4	0.6
損傷NOS	3	0.8					2	0.4	2	1.7	4	0.6
筋肉損傷NOS	1	0.3	1	1.5			2	0.4	1	0.8	4	0.6
足関節部骨折	1	0.3					3	0.7			3	0.4

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
傷害および中毒[d]												
頭部損傷	2	0.6					2	0.4	1	0.8	3	0.4
関節捻挫	7	1.9					2	0.4	1	0.8	3	0.4
開放創	3	0.8					3	0.7			3	0.4
肋骨骨折							2	0.4	1	0.8	3	0.4
創傷NOS							3	0.7			3	0.4
急性アルコール中毒[d]			1	1.5			1	0.2			2	0.3
関節脱臼	1	0.3					1	0.2	1	0.8	2	0.3
関節靭帯断裂							2	0.4			2	0.3
裂傷	1	0.3							2	1.7	2	0.3
筋挫傷	1	0.3					2	0.4			2	0.3
頚部損傷NOS							2	0.4			2	0.3
皮膚裂傷	2	0.6					2	0.4			2	0.3
サンバーン							2	0.4			2	0.3
腱断裂							1	0.2	1	0.8	2	0.3
外傷性胸部損傷NOS							2	0.4			2	0.3
節足動物咬傷							1	0.2			1	0.1
節足動物刺傷									1	0.8	1	0.1
背部損傷NOS	1	0.3					1	0.2			1	0.1
化学物質中毒							1	0.2			1	0.1
鎖骨骨折							1	0.2			1	0.1
脳振盪	1	0.3					1	0.2			1	0.1
上顎炎	2	0.6							1	0.8	1	0.1
顔面骨骨折									1	0.8	1	0.1
眼内異物	2	0.6					1	0.2			1	0.1
靭帯損傷NOS							1	0.2			1	0.1
靭帯捻挫							1	0.2			1	0.1
筋断裂							1	0.2			1	0.1
非偶発的過量投与							1	0.2			1	0.1
眼窩周囲血腫							1	0.2			1	0.1
外傷性気胸							1	0.2			1	0.1
交通事故	1	0.3					1	0.2			1	0.1
腱損傷									1	0.8	1	0.1

表 2.7.4.7.2-13
Table 149 TEAEs by SOC and Preferred Term (Safety Population) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene Total	
	n	%	n	%	n	%	n	%	n	%	n	%
傷害および中毒[d]												
熱傷							1	0.2			1	0.1
歯牙損傷	1	0.3			1	2.0					1	0.1
手首関節骨折			1	1.5							1	0.1
事故NOS	1	0.3										
咬刺傷NOS	1	0.3										
熱傷NOS[c]	1	0.3										
足骨折	1	0.3										
手骨折	2	0.6										
外科および内科処置												
抜歯NOS			1	1.5			1	0.2			2	0.3
アルコールの解毒	1	0.3					1	0.2			1	0.1
足首手術							1	0.2			1	0.1
膀胱腫瘍切除							1	0.2			1	0.1
白内障による水晶体摘出							1	0.2			1	0.1
解毒NOS							1	0.2			1	0.1
鼡径部ヘルニア修復					1	2.0					1	0.1
針穿刺[c]					1	2.0					1	0.1
整形外科的処置			1	1.5							1	0.1
関節注入	1	0.3										
手術NOS	1	0.3										
口腔手術NOS	1	0.3										
疣贅切除	1	0.3										
社会環境												
薬物乱用[d]	1	0.3										
作業能力障害者	1	0.3										

MedDRA Version 5.1
NOS = not otherwise specified; NEC = not elsewhere classified

[a] Patients in the nalmefene groups in the flexible-dose studies CPH-101-0801, CPH-101-0701, and CPH-101-0400 are included in the nalmefene 20 mg group, although their actual dose may differ.

[b] MedDRA Version 5.1のLLTで読み替えた

[c] MedDRA Version 4.0で読み替えた

[d] MedDRA Version 3.3で読み替えた
＜資料番号5.3.5.3-03：Table 149＞

表 2.7.4.7.2-14
Table 229 TEAEs with an Onset 6 Months after Randomisation or Later by SOC and Preferred Term (APTS): Patients with DRL High or Very High at Baseline and Randomisation - Study 12013A

System Organ Class Preferred Term	Placebo n	 (%)	Nalmefene n	 (%)
Number of Patients	33		105	
Men	24	(72.7)	80	(76.2)
Women	9	(27.3)	25	(23.8)
Patients with TEAEs After 6 Months	14	(42.4)	40	(38.1)
血液およびリンパ系障害	0	(0.0)	1	(1.0)
貧血	0	(0.0)	1	(1.0)
心臓障害	0	(0.0)	4	(3.8)
心房細動	0	(0.0)	1	(1.0)
心房粗動	0	(0.0)	1	(1.0)
頻脈	0	(0.0)	3	(2.9)
耳および迷路障害	1	(3.0)	0	(0.0)
聴力低下	1	(3.0)	0	(0.0)
眼障害	0	(0.0)	1	(1.0)
霧視	0	(0.0)	1	(1.0)
胃腸障害	4	(12.1)	7	(6.7)
上腹部痛	0	(0.0)	1	(1.0)
下痢	0	(0.0)	1	(1.0)
消化不良	1	(3.0)	0	(0.0)
びらん性胃炎	0	(0.0)	1	(1.0)
胃食道逆流性疾患	1	(3.0)	0	(0.0)
悪心	0	(0.0)	1	(1.0)
歯痛	1	(3.0)	1	(1.0)
嘔吐	1	(3.0)	4	(3.8)
潰瘍性食道炎	0	(0.0)	1	(1.0)
一般・全身障害および投与部位の状態	0	(0.0)	4	(3.8)
無力症	0	(0.0)	1	(1.0)
異常感	0	(0.0)	1	(1.0)
疼痛	0	(0.0)	1	(1.0)
非心臓性胸痛	0	(0.0)	1	(1.0)
免疫系障害	0	(0.0)	1	(1.0)
節足動物咬傷アレルギー	0	(0.0)	1	(1.0)
感染症および寄生虫症	6	(18.2)	9	(8.6)
結膜炎	0	(0.0)	1	(1.0)
膿痂疹	0	(0.0)	1	(1.0)
インフルエンザ	1	(3.0)	1	(1.0)
下気道感染	2	(6.1)	0	(0.0)
鼻咽頭炎	2	(6.1)	3	(2.9)
肺炎	0	(0.0)	1	(1.0)
鼻炎	0	(0.0)	1	(1.0)
敗血症	0	(0.0)	1	(1.0)
副鼻腔炎	0	(0.0)	1	(1.0)
扁桃炎	0	(0.0)	1	(1.0)
口腔真菌感染	0	(0.0)	1	(1.0)
ウイルス性気道感染	1	(3.0)	0	(0.0)

表 2.7.4.7.2-14
Table 229 TEAEs with an Onset 6 Months after Randomisation or Later by SOC and Preferred Term (APTS): Patients with DRL High or Very High at Baseline and Randomisation - Study 12013A

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
傷害、中毒および処置合併症	5	(15.2)	3	(2.9)
偶発的過量投与	2	(6.1)	2	(1.9)
転倒	1	(3.0)	0	(0.0)
橈骨骨折	0	(0.0)	1	(1.0)
挫傷	1	(3.0)	0	(0.0)
熱傷	1	(3.0)	0	(0.0)
四肢損傷	1	(3.0)	0	(0.0)
臨床検査	1	(3.0)	5	(4.8)
アラニンアミノトランスフェラーゼ増加	0	(0.0)	1	(1.0)
アスパラギン酸アミノトランスフェラーゼ増加	1	(3.0)	1	(1.0)
血中重炭酸塩減少	0	(0.0)	1	(1.0)
血中プロラクチン増加	0	(0.0)	1	(1.0)
体重減少	0	(0.0)	1	(1.0)
心電図2相性T波	0	(0.0)	1	(1.0)
代謝および栄養障害	1	(3.0)	2	(1.9)
高コレステロール血症	1	(3.0)	0	(0.0)
高血糖	0	(0.0)	1	(1.0)
低アルブミン血症	0	(0.0)	1	(1.0)
食欲減退	0	(0.0)	1	(1.0)
筋骨格系および結合組織障害	2	(6.1)	4	(3.8)
関節痛	0	(0.0)	1	(1.0)
背部痛	1	(3.0)	2	(1.9)
筋骨格痛	1	(3.0)	0	(0.0)
変形性関節症	1	(3.0)	1	(1.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	(0.0)	1	(1.0)
前立腺癌 {ss}	0	(0.0)	1	(1.3)
神経系障害	1	(3.0)	7	(6.7)
頭痛	0	(0.0)	4	(3.8)
感覚鈍麻	0	(0.0)	1	(1.0)
傾眠	1	(3.0)	0	(0.0)
振戦	0	(0.0)	2	(1.9)
精神障害	1	(3.0)	10	(9.5)
アルコール乱用	0	(0.0)	1	(1.0)
アルコールによる宿酔	0	(0.0)	1	(1.0)
神経性無食欲症	0	(0.0)	1	(1.0)
不安	1	(3.0)	0	(0.0)
抑うつ気分	0	(0.0)	1	(1.0)
うつ病	0	(0.0)	2	(1.9)
不眠症	1	(3.0)	5	(4.8)
中期不眠症	0	(0.0)	1	(1.0)
アルコール離脱症候群	0	(0.0)	1	(1.0)
生殖系および乳房障害	0	(0.0)	1	(1.0)
良性前立腺肥大症 {ss}	0	(0.0)	1	(1.3)
呼吸器、胸郭および縦隔障害	0	(0.0)	4	(3.8)
咳嗽	0	(0.0)	2	(1.9)
呼吸困難	0	(0.0)	1	(1.0)
口腔咽頭痛	0	(0.0)	1	(1.0)

表 2.7.4.7.2-14

Table 229 TEAEs with an Onset 6 Months after Randomisation or Later by SOC and Preferred Term (APTS): Patients with DRL High or Very High at Baseline and Randomisation - Study 12013A

	Placebo		Nalmefene	
System Organ Class Preferred Term	n	(%)	n	(%)
皮膚および皮下組織障害	1	(3.0)	1	(1.0)
湿疹	1	(3.0)	0	(0.0)
多汗症	0	(0.0)	1	(1.0)
血管障害	0	(0.0)	1	(1.0)
血腫	0	(0.0)	1	(1.0)

Patients are only counted once for each System Organ Class/Preferred Term

{ss} Sex specific

Dictionary: MedDRA 19.0

＜資料番号5.3.5.3-03：Table 229＞

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12013A	Nalmefene	[redacted]	365	神経性無食欲症	Atypical anorexia nervosa	[redacted]20[redacted]	288	0		C	1	NR	Moderate	Y	2
		[redacted]	364	アルコール離脱症候群	Alcohol withdrawal syndrome symptoms with: tremor, anxiety, agitation, insomnia	[redacted]20[redacted]	167	0	11 days	I	1	POS	Moderate	Y	1
			364	心室性期外収縮	Ventricular premature complexes	[redacted]20[redacted]	168	1		C	0	PRO	Mild	Y	1
		[redacted]	72	頭痛	Headache	[redacted]20[redacted]	28	1	5 days	I	0	NR	Severe	Y	1
			384	失神	Syncope	[redacted]20[redacted]	306	0	1 day	I	0	NR	Mild	Y	1
			335	不安	Anxiety	[redacted]20[redacted]	77	0	3 days	C	1	POS	Moderate	Y	1
			36	アルコール症	Hospitalization on the detox ward for patients request. medical reason - alcoholic dependence.	[redacted]20[redacted]	36	1	9 days	C	0	NR	Moderate	Y	1
		[redacted]	324	アルコール離脱症候群	Alcohol withdrawal syndrom after continuously alkohol use	[redacted]20[redacted]	354	31	9 days	C	1	NR	Severe	Y	1
		[redacted]	340	動脈炎	Endarteritis of left femoral arteria	[redacted]20[redacted]	35	0	102 days	C	0	NR	Moderate	Y	1
		[redacted]	110	食道癌	Carcinoma oesophagi	[redacted]20[redacted]	123	14		I	3	NR	Severe	Y	4
		[redacted]	282	靭帯断裂	Shoulder surgery due to the shoulder ligament rupture	[redacted]20[redacted]	343	62	2 hours	C	0	NR	Severe	Y	1

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12013A	Nalmefene	[redacted]	366	潰瘍性食道炎	Oesophagitis ulcerosa	[redacted]20[redacted]	306	1	42 days	C	1	NR	Moderate	Y	1
			366	肺炎	Pneumonia of the right lung	[redacted]20[redacted]	369	4	39 days	C	1	NR	Moderate	Y	1
		[redacted]	230	肺結核	newly diagnosed focal tuberculosis of the upper lobe of right lung, mycobacterium tuberculosis (+)	[redacted]20[redacted]	358	129		C	1	NR	Moderate	Y	4
		[redacted]	355	心房細動	Atrial fibrillation with rapid ventricular response	[redacted]20[redacted]	273	9	91 days	C	1	NR	Moderate	Y	1
		[redacted]	349	アルコール離脱症候群	Alcohol withdrawal syndrome with delirium	[redacted]20[redacted]	68	0	6 days	C	1	NR	Moderate	Y	1
		[redacted]	323	大腸腺腫性ポリポーシス	Polyposis of colon	[redacted]20[redacted]	66	14	4 days	C	0	NR	Moderate	Y	1
		[redacted]	354	アルコール離脱症候群	Alcohol withdrawal syndrome and hospitalisation	[redacted]20[redacted]	342	1	10 days	C	3	NR	Severe	Y	1
		[redacted]	233	アルコール離脱症候群	Sings of alcohol withdrawal: nervous, anxious, sweaty	[redacted]20[redacted]	5	0	6 days	C	0	NR	Moderate	Y	1
			233	アルコール乱用	Compulsive drinking episode	[redacted]20[redacted]	30	3	6 days	I	1	NR	Moderate	Y	1
			233	てんかん	Epileptic seizure	[redacted]20[redacted]	256	24	15 minutes	I	1, 3	NR	Severe	Y	1
		[redacted]	333	気管支肺炎	Bronchopneumonia	[redacted]20[redacted]	170	0	24 days	C	1	NR	Moderate	Y	1
		[redacted]	114	外傷性脳損傷	Open craniocerebral trauma	[redacted]20[redacted]	128	15	1 hour	C	3	NR	Severe	Y	5

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12013A	Nalmefene	[redacted]	11	悪夢	Nightmare	[redacted]20[redacted]	2	0	20 days	C	3	POS	Severe	Y	1
			11	失見当識	Disorientation	[redacted]20[redacted]	3	0	19 days	C	3	POS	Moderate	Y	1
			11	食欲減退	Loss of apettite	[redacted]20[redacted]	3	0	19 days	C	3	POS	Moderate	Y	1
		[redacted]	321	前立腺癌	Carcinoma of prostate	[redacted]20[redacted]	298	89		C	0	NR	Mild	Y	4
		[redacted]	2	複視	Double vision	[redacted]20[redacted]	0	0	3 days	C	3	PRO	Severe	Y	1
			2	不眠症	Insomnia	[redacted]20[redacted]	0	0	3 days	C	3	PRO	Severe	Y	1
			2	平衡障害	Loss of balance	[redacted]20[redacted]	0	0	3 days	C	3	PRO	Moderate	Y	1
		[redacted]	367	転倒	Fall	[redacted]20[redacted]	299	1	15 minutes	C	1	NR	Severe	Y	1
			367	上肢骨折	Fracture right arm	[redacted]20[redacted]	299	1		C	1	NR	Moderate	Y	4
		[redacted]	45	アルコール離脱症候群	Alkohol withdrawal syndrome	[redacted]20[redacted]	64	20	19 hours 35 minutes	C	1, 3	NR	Moderate	Y	1
		[redacted]	316	転倒	Fall from stairs	[redacted]20[redacted]	97	2	5 days	I	0	NR	Moderate	Y	1
			316	尺骨骨折	Fracture of right olecranon	[redacted]20[redacted]	97	2	5 days	I	0	NR	Moderate	Y	1
		[redacted]	366	大腸穿孔	Sigmoideus diverticulum, complecated with perforation and diffusive serous-fibrinous peritonitis.	[redacted]20[redacted]	277	0		C	1	NR	Severe	Y	2
		[redacted]	200	心房細動	Atrial fibrillation	[redacted]20[redacted]	200	1	19 hours 19 minutes	C	3	NR	Moderate	Y	1
			200	アルコール離脱症候群	Admission to psychiatric ward due to withdrawal alcohol syndrome	[redacted]20[redacted]	201	2	9 days 2 hours 40 minutes	I	3	NR	Moderate	Y	1
		[redacted]	96	自殺行為	Suicidal behavior reported by the patient's wife, denied by the patient	[redacted]20[redacted]	93	3	1 hour	C	3	NR	Severe	Y	1

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12013A	Nalmefene	[redacted]	371	アルコール中毒	Pathological intoxication (alcohol induced psyhotic disorder, with hallucinations, with onset during intoxication (dsm-iv-tr :291.3)	[redacted]20[redacted]	325	0	2 days	I	1	POS	Moderate	Y	1
		[redacted]	209	うつ病	Depression episodes	[redacted]20[redacted]	204	0	30 days	C	3	NR	Moderate	Y	1
		[redacted]	195	非心臓性胸痛	Chest pain unspecified non cardial	[redacted]20[redacted]	258	64	3 days	I	1	NR	Severe	Y	1
		[redacted]	1	アルコールによる宿酔	Alcohol hangover	[redacted]20[redacted]	5	5	11 days	C	1	NR	Moderate	Y	1
		[redacted]	145	失見当識	Disorientation	[redacted]20[redacted]	0	0	3 days	C	0	PRO	Severe	Y	1
		[redacted]	117	アルコール離脱症候群	Alcohol withdrawal syndrome	[redacted]20[redacted]	167	51	23 hours 58 minutes	C	1, 3	NR	Mild	Y	1
	Placebo	[redacted]	353	脛骨骨折	Helical fracture of right tibia	[redacted]20[redacted]	229	0	106 days	C	1	NR	Severe	Y	1
			353	腓骨骨折	Dislocation fracture of right fibula	[redacted]20[redacted]	229	0	106 days	C	1	NR	Severe	Y	1
		[redacted]	349	アルコール離脱症候群	Abstinent syndroms: nausea, sweating, tremor, anxiety and consience problems. no psychotic symptoms.	[redacted]20[redacted]	9	8	14 days	C	0	NR	Severe	Y	1

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12013A	Placebo	[redacted]	111	肺炎	Pneumonia septic	[redacted]20[redacted]	147	37	121 days	C	1	NR	Severe	Y	1
			111	四肢膿瘍	Right leg abscess	[redacted]20[redacted]	147	37	9 days	C	0	NR	Severe	Y	1
			111	膿胸	empyema of the right pleura	[redacted]20[redacted]	173	63	4 days	C	1	NR	Severe	Y	1
		[redacted]	363	アルコール乱用	Drinking bout	[redacted]20[redacted]	157	0	10 days	C	1	POS	Severe	Y	1
			363	アルコール乱用	Drinking bout	[redacted]20[redacted]	281	0	23 days	C	1	POS	Severe	Y	1
		[redacted]	362	腎盂腎炎	Pyelonephritis	[redacted]20[redacted]	227	2	14 days	C	1	NR	Moderate	Y	1
		[redacted]	341	肋骨骨折	3 fractured ribs	[redacted]20[redacted]	138	0	79 days	C	1	NR	Severe	Y	1
			341	気胸	Pneumothorax	[redacted]20[redacted]	138	0	1 day	C	0	NR	Severe	Y	1
		[redacted]	365	腸憩室	Enteric diverticulum	[redacted]20[redacted]	87	23		C	0	NR	Moderate	Y	4
			365	クローン病	Crohn`s disease	[redacted]20[redacted]	99	0		C	1	NR	Mild	Y	4
			365	肝障害	Hepatosis	[redacted]20[redacted]	99	0		C	1	NR	Mild	Y	2
		[redacted]	377	高血圧	Aggravated hypertension	[redacted]20[redacted]	56	3	6 days	I	1	NR	Moderate	Y	1
12014A	Nalmefene	[redacted]	93	アルコール症	Excessive drinking relapse	[redacted]20[redacted]	119	27	11 days	C	3	NR	Severe	Y	1
		[redacted]	30	非心臓性胸痛	Non cardiac chest pain.	[redacted]20[redacted]	14	1	3 days	C	1	POS	Mild	Y	1
		[redacted]	76	アルコール症	Alcohol relapse	[redacted]20[redacted]	72	0	38 days	C	1, 3	NR	Moderate	Y	1
			8	浮動性めまい	Dizziness	[redacted]20[redacted]	0	0	3 days	C	0	PRO	Severe	Y	1
			203	手骨折	Subcapital fracture of the metacarpus v left side	[redacted]20[redacted]	26	0	118 days	C	1	NR	Moderate	Y	1
		[redacted]	44	喉頭蓋嚢胞	Epiglottic cyste	[redacted]20[redacted]	45	2		C	1, 3	NR	Moderate	Y	4
			60	多発性関節炎	Polyarthritis	[redacted]20[redacted]	26	0		C	1	POS	Severe	Y	2
			84	背部痛	Worsening of recurrent lumbago	[redacted]20[redacted]	60	1		C	1	NR	Severe	Y	2
		[redacted]	111	四肢痛	Leg pain	[redacted]20[redacted]	63	1	7 days	I	0	NR	Severe	Y	1
			82	うつ病	Depression	[redacted]20[redacted]	83	2		C	1	NR	Moderate	Y	2
			260	足関節部骨折	Fracture of the right ankle joint	[redacted]20[redacted]	94	2	118 days	C	0	NR	Moderate	Y	1

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12014A	Nalmefene	[redacted]	212	穿孔性胃潰瘍	Burst gastric ulcer	[redacted]20[redacted]	6	0	4 days	C	0	NR	Severe	Y	1
			212	腓骨骨折	Broken fibula	[redacted]20[redacted]	143	0		C	0	NR	Severe	Y	4
		[redacted]	82	腱炎	Paratendinitis hamstring left side	[redacted]20[redacted]	91	10	50 days	C	1	NR	Severe	Y	1
		[redacted]	112	アルコール中毒	The patient went to a hospitaltreatment since today for a withdrawal cure. hospitalisation because of signs of alcohol intoxication.	[redacted]20[redacted]	112	1	14 days	I	1, 3	NR	Severe	Y	3
		[redacted]	60	鼻出血	Epistaxis	[redacted]20[redacted]	19	1	6 days	I	0	POS	Severe	Y	1
		[redacted]		大腿骨頚部骨折	Fracture right neck of the femur	[redacted]20[redacted]	1	1		C	1	NR	Moderate	Y	2
		[redacted]	112	椎間板突出	Worsening of prolapse of an intervertebral disk	[redacted]20[redacted]	167	56		C	3	NR	Moderate	Y	4
	Placebo	[redacted]	193	アルコール中毒	Alcohol intoxication	[redacted]20[redacted]	3	3	16 hours 40 minutes	I	0	NR	Moderate	Y	1
		[redacted]	2	術後創感染	Wound infection after excission of a fibroma simplex on the right leg	[redacted]20[redacted]	153	152	19 days	C	1	NR	Moderate	Y	1
		[redacted]	184	痔核	Worsening of hemorrhoids	[redacted]20[redacted]	102	10	6 days	C	0	NR	Moderate	Y	1
		[redacted]	78	急性胆嚢炎	Acute cholecystitis	[redacted]20[redacted]	78	1	53 days	C	3	NR	Moderate	Y	3

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12014A	Placebo	[redacted]	195	喉頭癌	Larynx carcinoma	[redacted]20[redacted]	91	0	15 days	C	0	NR	Moderate	Y	1
			29	自殺既遂	Suicide	[redacted]20[redacted]	33	5	1 day	C	3	NR	Severe	Y	5
			202	アルコール症	Worsening of alkohol dependence	[redacted]20[redacted]	8	2	9 days	C	0	POS	Severe	Y	1
		[redacted]	87	胆道仙痛	Biliary colic	[redacted]20[redacted]	10	1	1 day	C	1	NR	Severe	Y	1
			26	自殺既遂	Suicide	[redacted]20[redacted]	30	5	1 day	C	1, 3	POS	Severe	Y	5
			90	高血圧	Worsening of arterial hypertension	[redacted]20[redacted]	34	3	3 days	C	1	NR	Severe	Y	1
		[redacted]	193	痙攣	Seizure	[redacted]20[redacted]	21	1	5 minutes	I	0	NR	Severe	Y	1
			59	硬膜下血腫	Chronic subdural hematoma	[redacted]20[redacted]	14	0	295 days	C	1, 3	NR	Severe	Y	1
		[redacted]	155	アルコール乱用	Heavy drinking	[redacted]20[redacted]	152	2	7 days	I	3	NR	Severe	Y	1
			155	心停止	Asystole	[redacted]20[redacted]	161	7	1 day	I	1, 3	NR	Severe	Y	1
			155	痙攣	Convulsions	[redacted]20[redacted]	161	7	1 day	I	1, 3	NR	Severe	Y	1
			155	腎不全	Renal insufficiency	[redacted]20[redacted]	161	7	10 days	I	1, 3	NR	Severe	Y	1
			155	血中カリウム増加	High potassium	[redacted]20[redacted]	161	7	10 days	I	3	NR	Severe	Y	1
			155	血中乳酸増加	High serum lactate	[redacted]20[redacted]	161	7	10 days	I	3	NR	Severe	Y	1
			155	血中ナトリウム減少	Low sodium vallue	[redacted]20[redacted]	161	7	10 days	I	3	NR	Severe	Y	1
		[redacted]	123	悪性黒色腫	Melanoma cutis	[redacted]20[redacted]	104	0		C	3	NR	Severe	Y	4
			76	肋骨骨折	He suffered several costal fractures	[redacted]20[redacted]	75	0	29 days	C	1, 3	POS	Severe	Y	1
			76	転倒	Patient fell down the stairs under the influence of alcohol.	[redacted]20[redacted]	75	0	1 day	C	1, 3	POS	Severe	Y	3
			76	気胸	Patient suffered a pneumothorax making hospitalisation necessary	[redacted]20[redacted]	75	0	29 days	C	1, 3	POS	Severe	Y	1

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12014A	Placebo	[redacted]	142	アルコール症	Hospitalization due to alcohol dependency	[redacted]20[redacted]	70	0	4 days	C	1	NR	Mild	Y	1
12023A	Nalmefene	[redacted]	126	アルコール症	Heavy relapse of severe alcoholism	[redacted]20[redacted]	118	19	139 days	C	1, 3	NR	Severe	Y	1
		[redacted]	181	頭部損傷	Injury of skull after beating	[redacted]20[redacted]	118	16	30 days	C	1	NR	Severe	Y	1
		[redacted]	68	心筋梗塞	Myocardial infarction	[redacted]20[redacted]	33	0	1 day	C	1, 3	NR	Severe	Y	1
		[redacted]	91	転倒	Fall to the ground	[redacted]20[redacted]	91	1	5 minutes	C	0	NR	Severe	Y	1
			91	くも膜下出血	Subarachnoidal heamorrhages	[redacted]20[redacted]	91	1	37 days	C	0	NR	Severe	Y	1
		[redacted]	203	腱断裂	Left shoulder tendon rupture	[redacted]20[redacted]	91	0		C	1	NR	Severe	Y	2
		[redacted]	44	突然死	Sudden death	[redacted]20[redacted]	46	3	1 day	C	3	NR	Severe	Y	5
	Placebo	[redacted]	194	浮動性めまい	Dizzy turn	[redacted]20[redacted]	130	1	11 hours	C	0	NR	Moderate	Y	1
		[redacted]	65	腓骨骨折	Left perone broke	[redacted]20[redacted]	32	0	171 days	C	1, 3	NR	Severe	Y	1
			65	脛骨骨折	Left tibia broke	[redacted]20[redacted]	32	0	171 days	C	1, 3	NR	Severe	Y	1
		[redacted]	169	皮下組織膿瘍	Abscess on the buttock	[redacted]20[redacted]	147	1	1 day	C	1, 3	NR	Severe	Y	3
		[redacted]	205	てんかん	Epileptic seizure	[redacted]20[redacted]	50	0	1 day	C	0	POS	Severe	Y	1
		[redacted]	84	企図的過量投与	intentionaloverdose of investigational product (purpose was to try increase of therapeutical effect)	[redacted]20[redacted]	77	0		C	0	NR	Moderate	Y	1

表 2.7.4.7.2-15
Listing 12 SAEs (APTS) - Alcohol Dependence Pool

Study protocol	Treatment group	Patient/Sex/Age/Race /Weight at baseline	Days on IMP	Preferred term	Verbatim	AE start date	Days since first IMP	Days since last-IMP	Dura-tion	Pattern of adverse event	Action taken	Caus-ality	Inten-sity	SAE	Out-come
12023A	Placebo	[redacted]	183	企図的過量投与	Intentional overdose of ixprim without suicidal intention	[redacted]20[redacted]	156	1	1 day	I	0	NR	Severe	Y	1
		[redacted]	196	動脈炎	Arteritis ofinfrarenal abdominal aorta and left common iliac artery	[redacted]20[redacted]	152	0	25 days	C	1	NR	Severe	Y	1
		[redacted]	1	アルコール中毒	Alcohol intoxication	[redacted]20[redacted]	4	4	24 days	I	1, 3	NR	Severe	Y	1
			1	薬物毒性	Zopiclone intoxication	[redacted]20[redacted]	4	4	24 days	I	1, 3	NR	Severe	Y	1
		[redacted]	91	膿胸	Right pleural cavity empyema icd-10: j86.9	[redacted]20[redacted]	97	7	47 days	C	1, 3	POS	Severe	Y	1
		[redacted]	164	急性膵炎	Acute panchreatitis	[redacted]20[redacted]	109	1	39 days	C	0	NR	Severe	Y	1
		[redacted]	150	偶発的過量投与	`accidental overdosage on paracetamol`	[redacted]20[redacted]	148	0	2 days	I	1	NR	Severe	Y	1
			150	肺炎	Pneumonia	[redacted]20[redacted]	148	0	39 days	C	1, 3	NR	Moderate	Y	1

MedDRA Version 13.0
[redacted]
Action taken: 0 = No action taken, 1 = Change in concomitant medication, 2 = Change in IMP, 3 = Patient withdrawal
Causality: NR = Not related, POS = Possible, PRO = Probable
Outcome: 1 = Recovered, 2 = Recovering, 3 = Recovered with sequelae, 4 = Not recovered, 5 = Death
Days on IMP: Duration from the first dose to the last dose
Pattern of adverse event: C = Continuosly, I = Intermittently
Dictionary: MedDRA 13.0
＜資料番号5.3.5.3-03：Listing 12＞

表 2.7.4.7.2-16
Table 78 SAEs by Preferred Term (APTS) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene total	
	n	%	n	%	n	%	n	%	n	%	n	%
Patients treated	361		68		50		453		118		689	
Patients with SAEs												
うつ病							3	0.7			3	0.4
膵炎NOS	1	0.3					3	0.7			3	0.4
足関節部骨折							2	0.4			2	0.3
メレナ							2	0.4			2	0.3
急性アルコール中毒[b]			1	1.5			1	0.2			2	0.3
虫垂炎							1	0.2	1	0.8	2	0.3
胸痛	1	0.3					1	0.2	1	0.8	2	0.3
アルコール中毒							1	0.2			1	0.1
アルコール性痙攣							1	0.2			1	0.1
不安定狭心症							1	0.2			1	0.1
足首手術							1	0.2			1	0.1
膀胱腫瘍切除							1	0.2			1	0.1
滑液包炎							1	0.2			1	0.1
譫妄							1	0.2			1	0.1
振戦譫妄							1	0.2			1	0.1
吐血							1	0.2			1	0.1
ハンタウイルス感染NOS							1	0.2			1	0.1
頭部損傷	1	0.3					1	0.2			1	0.1
聴力低下							1	0.2			1	0.1
ウイルス性髄膜炎NOS							1	0.2			1	0.1
非偶発的過量投与							1	0.2			1	0.1
外傷性気胸							1	0.2			1	0.1
術後創感染[c]							1	0.2			1	0.1
気道感染NOS							1	0.2			1	0.1
肋骨骨折							1	0.2			1	0.1
坐骨神経痛							1	0.2			1	0.1
外傷性胸部損傷NOS							1	0.2			1	0.1
アルコールによる宿酔					1	2.0					1	2.0

表 2.7.4.7.2-16
Table 78 SAEs by Preferred Term (APTS) - Alcohol-use Disorders Pool

Preferred term	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene total	
	n	%	n	%	n	%	n	%	n	%	n	%
関節鏡検査					1	2.0					1	0.1
状態悪化	1	0.3			1	2.0					1	0.1
呼吸困難NOS	1	0.3							1	0.8	1	0.1
イレウス[d]					1	2.0					1	0.1
鼠径部ヘルニア修復					1	2.0					1	0.1
四肢痛									1	0.8	1	0.1
精神病性障害NOS									1	0.8	1	0.1
腹部ヘルニアNOS	1	0.3									0	0.0
アルコールの解毒	1	0.3									0	0.0
血管形成	1	0.3									0	0.0
下痢NOS	1	0.3									0	0.0
浮動性めまい	1	0.3									0	0.0
子宮外妊娠	1	0.3									0	0.0
脳炎NOS	1	0.3									0	0.0
胃炎NOS	1	0.3									0	0.0
胃腸潰瘍NOS	1	0.3									0	0.0
下気道感染NOS	1	0.3									0	0.0
手術NOS	1	0.3									0	0.0
自殺企図	1	0.3									0	0.0

MedDRA Version 5.1

[a] Patients in the nalmefene groups in the flexible-dose studies CPH-101-0801, CPH-101-0701, and CPH-101-0400 are included in the nalmefene 20 mg group, although their actual dose may differ.

[b] MedDRA Version 3.3で読み替えた

[c] MedDRA Version 4.0で読み替えた

[d] MedDRA Version 5.1のLLTで読み替えた

＜資料番号5.3.5.3-03 : Table 78＞

表 2.7.4.7.2-17
Listing 15 SAEs - Alcohol-use Disorders Pool

Study	Patient	SAE no.	Preferred term	SAE term	Treatment	Related?
CPH-101-0299		CPH-1014-00	虫垂炎	Acute appendicitis, surgery	Nalmefene 40 mg/day	No
		CPH-1017-00	メレナ	Melaena	Nalmefene 20 mg/day	No
		CPH-1027-01	ウイルス性髄膜炎NEC	Viral meningitis	Nalmefene 20 mg/day	No
		CPH-1022-01	足関節部骨折, 足首手術	Ankle fracture Repeat ankle surgery	Nalmefene 20 mg/day	No
		CPH-1024-01	膀胱腫瘍切除	Bladder tumour	Nalmefene 20 mg/day	No
		CPH-1019-00	胸痛NEC	Hypertension	Nalmefene 40 mg/day	No
		CPH-1020-00	精神病性障害NOS	Psychosis NOS; auditory hallucination	Nalmefene 40 mg/day	No
		CPH-1021-00	胸痛NEC	Pain in neck and right arm	Nalmefene 20 mg/day	No
		CPH-1012-00	急性アルコール中毒	Hospitalisation for alcohol intoxication	Nalmefene 5 mg/day	No
		CPH-1018-00	虫垂炎	Acute appendicitis, surgery	Nalmefene 20 mg/day	No
		CPH-1025-01	呼吸困難NOS;四肢痛	Angioplasty due to chest pain	Nalmefene 40 mg/day	No
		CPH-1026-01	呼吸困難NOS;四肢痛	Hospitalisation for chest pain	Nalmefene 40 mg/day	No
		CPH-1023-01	急性アルコール中毒	Inpatient detoxification	Nalmefene 20 mg/day	No
CPH-101-0399		CPH-1009-00	手術NOS	Tendon rupture shoulder, hospitalised	Placebo	No
		CPH-1011-00	血管形成	Angioplasty	Placebo	No
		CPH-1001-00	頭部損傷	Alcohol intoxication, fall; wound; inpatient observation	Placebo	No
		CPH-1002-00	状態悪化	Inpatient detoxification	Placebo	No
		CPH-1003-00	状態悪化	Inpatient detoxification	Placebo	No
		CPH-1005-00	イレウス	Acute ileus	Nalmefene 10 mg/day	No
		CPH-1007-00	胃炎NOS	Gastritis	Placebo	No
		CPH-1004-00	腹部ヘルニアNOS	Incarcerated umbilical hernia	Placebo	No
		CPH-1008-00	アルコールの解毒[b]	Inpatient detoxification	Placebo	No
		CPH-1010-00	アルコールの解毒[b]	Inpatient detoxification	Placebo	No
		CPH-1015-00	鼠径部ヘルニア修復	Surgery for inguinal hernia	Nalmefene 10 mg/day	No
		CPH-1006-00	状態悪化; アルコールによる宿酔	Inpatient detoxification	Nalmefene 10 mg/day	No
		CPH-1016-00	関節鏡検査	Arthroscopy for knee trauma	Nalmefene 10 mg/day	No

表 2.7.4.7.2-17
Listing 15 SAEs - Alcohol-use Disorders Pool

Study	Patient	SAE no.	Preferred term	SAE term	Treatment	Related?
CPH-101-0400	[redacted]	CPH-1028-02	非偶発的過量投与	Clonazepam and alcohol overdose	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1035-02	非偶発的過量投与	Clonazepam and alcohol overdose	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1030-02	足関節部骨折	Traumatic ankle fracture	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1032-02	術後創感染	Wound infection	Nalmefene 10, 20, or 40 mg as-needed	No
CPH-101-0701		CPH-1049-02	下気道感染NOS[a]	Chest infection, death due to carcinomatosis	Placebo	No
		CPH-1036-02	膵炎NOS	Digestive pain, pancreatitis	Placebo	No
		CPH-1057-03	自殺企図	Paracetamol overdose, suicide attempt	Placebo	No
		CPH-1059-03	自殺企図	Paracetamol overdose, suicide attempt	Placebo	No
		CPH-1060-03	自殺企図	Paracetamol overdose, suicide attempt	Placebo	No
		CPH-1061-03	自殺企図	Overdose, suicide attempt	Placebo	No
		CPH-1043-02	下痢NOS	Diarrhoea due to Clostridium difficile	Placebo	No
		CPH-1039-02	膵炎NOS	Hospital admission, details unknown, suspected pancreatitis	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1040-02	膵炎NOS	Abdominal pain	Nalmefene 10, 20, or 40 mg as-needed	No
CPH-101-0801		CPH-1048-02	肋骨骨折;外傷性気胸	Assault and battery victim	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1029-02	膵炎NOS	Alcoholic pancreatitis	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1034-02	膵炎NOS	Alcoholic pancreatitis	Nalmefene 10, 20, or 40 mg as-needed	Yes
		CPH-1045-02	子宮外妊娠	Extrauterine pregnancy	Placebo	No
		CPH-1044-02	うつ病;頭部損傷;外傷性胸部損傷NOS	Suicide attempt	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1047-02	胃腸潰瘍NOS	Oesophageal ulcer, Helicobacter - positive	Placebo	No
		CPH-1042-02	坐骨神経痛	Sciatic syndrome	Nalmefene 10, 20, or 40 mg as-needed	No

表 2.7.4.7.2-17
Listing 15 SAEs - Alcohol-use Disorders Pool

Study	Patient	SAE no.	Preferred term	SAE term	Treatment	Related?
CPH-101-0801	[redacted]	CPH-1031-02	アルコール中毒	Unconsciousness	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1037-02	アルコール中毒;メレナ;吐血	Unconsciousness, haematemesis, melaena	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1046-02	うつ病	Depression with suicidal thoughts	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1041-02	胸痛	Hospitalisation for coronary angiography	Placebo	No
		CPH-1051-02	ハンタウイルス感染NOS	Epidemic nephropathy	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1055-02	聴力低下	Unilateral loss of hearing	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1052-02	浮動性めまい;呼吸困難NOS	Dizziness, dyspnoea	Placebo	No
		CPH-1050-02	気道感染NOS	Infection in the respiratory tract	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1063-03	脳炎NOS	Encephalitis	Placebo	No
		CPH-1053-02	アルコール性痙攣;振戦譫妄	Convulsions, psychotic symptoms	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1058-03	譫妄	Unconscious due to alcohol use	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1062-03	不安定狭心症	Chest pain	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1064-03	滑液包炎	Bursitis of left knee	Nalmefene 10, 20, or 40 mg as-needed	No
		CPH-1054-02	うつ病	Heavy drinking, depression	Nalmefene 10, 20, or 40 mg as-needed	No

MedDRA Version 3.3 : CPH-101-0299
MedDRA Version 3.1 : CPH-101-0399
MedDRA Version 4.0 : CPH-101-0400
MedDRA Version 5.1 : CPH-101-0701, CPH-101-0801
NOS = not otherwise specified
[a] patient died of disseminated carcinoma
[b] MedDRA Version 3.3
＜資料番号5.3.5.3-03：Listing 15＞

表 2.7.4.7.2-18
Listing 16 SAEs - Studies in Other Addiction Indications

Study	Patient	SAE no.	Preferred term	SAE term	Treatment	Related?
CPH-101-0600	[redacted]	CPH-1033-02	顎痛;胸痛; 賦形剤に対する反応;四肢痛	Reaction to dye used in stress test	Nalmefene 100 mg/day	No
		CPH-1056-02	腎感染NOS	Kidney infection	Placebo	No
SP-N0406		-	深部静脈血栓症	Right lower extremity deep venous thrombosis	Nalmefene 20 mg/day	U
		-	故意の自傷行為	Suicidal gesture	Nalmefene 40 mg/day	No
		-	虫垂炎	Appendicitis	Placebo	No
		-	自殺念慮	Suicidal ideation	Nalmefene 20 mg/day	No
		-	胸痛	Chest pain	Nalmefene 20 mg/day	P
SP-N0408		-	起立性低血圧	Postural hypotensive event	Nalmefene 80 mg/day	No
		-	肝酵素上昇	Elevated liver enzymes	Nalmefene 80 mg/day	Yes

MedDRA Version 5.0 : CPH-101-0600
MedDRA Version 13.0 : SP-N0406, SP-N0408
NOS = not otherwise specified; U = unlikely; P = possible
＜資料番号5.3.5.3-03 : Listing 16＞

表 2.7.4.7.2-19
Table 90 Adverse Events Leading to Withdrawal - Alcohol Use Disorders Pool

	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene total	
Preferred term	n	%	n	%	n	%	n	%	n	%	n	%
Patients treated	361		68		50		453		118		689	
Patients with TEAEs leading to withdrawal	13	3.6	5	7.4	6	12.0	78	17.2	16	13.6	105	15.2
悪心	4	1.1	3	4.4	2	4.0	22	4.9	5	4.2	32	4.6
浮動性めまい	2	0.6	2	2.9	2	4.0	13	2.9	3	2.5	20	2.9
不眠症	2	0.6	1	1.5	1	2.0	9	2.0	1	0.8	12	1.7
頭痛	1	0.3					7	1.5	3	2.5	10	1.5
解離			1	1.5			4	0.9	1	0.8	6	0.9
嘔吐NOS	1	0.3					5	1.1			5	0.7
悪夢	1	0.3					4	0.9	1	0.8	5	0.7
注意力障害NEC[b]	1	0.3					3	0.7	1	0.8	4	0.6
疲労							3	0.7	1	0.8	4	0.6
動悸			1	1.5			3	0.7			4	0.6
睡眠障害NOS							3	0.7	1	0.8	4	0.6
多汗			1	1.5			3	0.7			4	0.6
不安			1	1.5			2	0.4	1	0.8	4	0.6
激越							3	0.7			3	0.4
失見当識			1	1.5			2	0.4			3	0.4
倦怠感					1	2.0	2	0.4			3	0.4
傾眠							2	0.4	1	0.8	3	0.4
皮膚炎NOS							1	0.2	2	1.7	3	0.4
腹痛NOS							2	0.4			2	0.3
異常な夢							2	0.4			2	0.3
攻撃性							2	0.4			2	0.3
眼精疲労							2	0.4			2	0.3
錯乱状態							2	0.4			2	0.3
消化不良							2	0.4			2	0.3
呼吸困難NOS							2	0.4			2	0.3
幻覚NOS							2	0.4			2	0.3
筋硬直							2	0.4			2	0.3

表 2.7.4.7.2-19
Table 90 Adverse Events Leading to Withdrawal - Alcohol Use Disorders Pool

	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene total	
Preferred term	n	%	n	%	n	%	n	%	n	%	n	%
視覚障害NOS							2	0.4			2	0.3
過敏症NOS	1	0.3							2	1.7	2	0.3
肝機能検査NOS異常			1	1.5					1	0.8	2	0.3
上腹部痛							1	0.2			1	0.1
アルコール離脱症候群							1	0.2			1	0.1
貧血NOS							1	0.2			1	0.1
不整脈NOS							1	0.2			1	0.1
便秘							1	0.2			1	0.1
うつ病							1	0.2			1	0.1
便失禁							1	0.2			1	0.1
酩酊感							1	0.2			1	0.1
気分不良[c]							1	0.2			1	0.1
出血性胃潰瘍							1	0.2			1	0.1
幻聴							1	0.2			1	0.1
幻視							1	0.2			1	0.1
頭部不快感							1	0.2			1	0.1
感覚減退							1	0.2			1	0.1
臨床検査異常NOS							1	0.2			1	0.1
嗜眠							1	0.2			1	0.1
リビドー減退							1	0.2			1	0.1
ライム病							1	0.2			1	0.1
筋痛	1	0.3					1	0.2			1	0.1
Pain in right knee joint							1	0.2			1	0.1
膵炎NOS							1	0.2			1	0.1
パニック発作							1	0.2			1	0.1
妄想症							1	0.2			1	0.1
咽喉頭疼痛							1	0.2			1	0.1
持続勃起症							1	0.2			1	0.1
全身性そう痒症							1	0.2			1	0.1
Psychotic fear							1	0.2			1	0.1

表 2.7.4.7.2-19
Table 90 Adverse Events Leading to Withdrawal - Alcohol Use Disorders Pool

	Placebo		Nalmefene 5 mg		Nalmefene 10 mg		Nalmefene 20 mg[a]		Nalmefene 40 mg		Nalmefene total	
Preferred term	n	%	n	%	n	%	n	%	n	%	n	%
悪寒							1	0.2			1	0.1
鎮静							1	0.2			1	0.1
圧迫感NOS							1	0.2			1	0.1
Several adverse events							1	0.2			1	0.1
Side effects							1	0.2			1	0.1
蕁麻疹NOS							1	0.2			1	0.1
脱力[d]							1	0.2			1	0.1
関節痛									1	0.8	1	0.1
錯乱[d]									1	0.8	1	0.1
下痢NOS									1	0.8	1	0.1
聴覚過敏			1	1.5							1	0.1
インフルエンザ様疾患			1	1.5							1	0.1
神経過敏									1	0.8	1	0.1
夜間頻尿									1	0.8	1	0.1
血小板数減少			1	1.5							1	0.1
そう痒症NOS[d]			1	1.5							1	0.1
精神病性障害NOS									1	0.8	1	0.1
振戦NEC[b]	1	0.3							1	0.8	1	0.1
胸痛NEC[b]	1	0.3										
頻尿	1	0.3										
胃内ガス貯留[c]	1	0.3										
肝炎NOS	1	0.3										
作業能力障害者	1	0.3										

MedDRA Version 5.1
NEC: not elsewhere classified; NOS = not otherwise specified
[a] Patients in the nalmefene groups in the flexible-dose studies CPH-101-0801, CPH-101-0701, and CPH-101-0400 are included in the nalmefene 20 m although their actual dose may differ.
[b] MedDRA Version 3.3で読み替えた
[c] MedDRA Version 5.1のLLTで読み替えた
[d] MedDRA Version 4.0で読み替えた
＜資料番号5.3.5.3-03：Table 90＞

表 2.7.4.7.2-20
Table 195 Summary of Post-baseline PCS Laboratory Values (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo			Nalmefene		
Parameter (Unit)	n	PCS	(%)	n	PCS	(%)
Number of patients	365			467		
SUB CATEGORY: ELECTROLYTES						
S-Bicarbonate (mmol/L)						
High	326	0	(0.0)	418	0	(0.0)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: <= 12 mmol/L HIGH: >= 38 mmol/L LOW: <= 12 mmol/L HIGH: >= 38 mmol/L LOW: <= 12 mmol/L HIGH: >= 38 mmol/L						
S-Calcium (mmol/L)						
High	326	1	(0.3)	418	0	(0.0)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: <= 1.8 mmol/L HIGH: >= 3 mmol/L LOW: <= 1.8 mmol/L HIGH: >= 3 mmol/L LOW: <= 1.8 mmol/L HIGH: >= 3 mmol/L						
S-Potassium (mmol/L)						
High	326	1	(0.3)	419	0	(0.0)
Low	326	1	(0.3)	419	1	(0.2)
PCS Criteria: [NALMEFENE] LOW: <= 3 mmol/L HIGH: >= 6 mmol/L LOW: <= 3 mmol/L HIGH: >= 6 mmol/L LOW: <= 3 mmol/L HIGH: >= 6 mmol/L						
S-Sodium (mmol/L)						
High	326	2	(0.6)	419	4	(1.0)
Low	326	0	(0.0)	419	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: <= 125 mmol/L HIGH: >= 155 mmol/L LOW: <= 125 mmol/L HIGH: >= 155 mmol/L LOW: <= 125 mmol/L HIGH: >= 155 mmol/L						
SUB CATEGORY: ENDOCRINE, METABOLIC						
S-Albumin (g/L)						
High	326	0	(0.0)	418	0	(0.0)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: <= 27 g/L HIGH: N/A LOW: <= 27 g/L HIGH: N/A LOW: <= 27 g/L HIGH: N/A						
S-Glucose (mmol/L)						
High	326	13	(4.0)	418	26	(6.2)
Low	326	3	(0.9)	418	6	(1.4)
PCS Criteria: [NALMEFENE] LOW: <= 3.5 mmol/L HIGH: >= 9 mmol/L LOW: <= 3.5 mmol/L HIGH: >= 8.1 mmol/L LOW: <= 3.5 mmol/L HIGH: >= 9 mmol/L LOW: <= 3.5 mmol/L HIGH: >= 8.1 mmol/L LOW: <= 3.5 mmol/L HIGH: >= 9 mmol/L LOW: <= 3.5 mmol/L HIGH: >= 8.1 mmol/L						

表 2.7.4.7.2-20
Table 195 Summary of Post-baseline PCS Laboratory Values (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo			Nalmefene		
Parameter (Unit)	n	PCS	(%)	n	PCS	(%)
S-Prolactin (mIU/L)						
High	325	1	(0.3)	416	2	(0.5)
Low	325	0	(0.0)	416	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 1350 mIU/L LOW: N/A HIGH: >= 1350 mIU/L LOW: N/A HIGH: >= 1350 mIU/L						
SUB CATEGORY: HAEMATOLOGY						
B-Basophils/Leukocytes (%)						
High	324	0	(0.0)	415	0	(0.0)
Low	324	0	(0.0)	415	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 10 % LOW: N/A HIGH: >= 10 % LOW: N/A HIGH: >= 10 %						
B-Hemoglobin (g/dL)						
High	325	2	(0.6)	419	2	(0.5)
Low	325	3	(0.9)	419	2	(0.5)
PCS Criteria: [NALMEFENE] LOW:Women <= 9.5 g/dL - Men <= 11.5 g/dL HIGH:Women >= 16.5 g/dL - Men >= 18.5 g/dL LOW:Women <= 9.5 g/dL - Men <= 11.5 g/dL HIGH:Women >= 16.5 g/dL - Men >= 18.5 g/dL LOW:Women <= 9.5 g/dL - Men <= 11.5 g/dL HIGH:Women >= 16.5 g/dL - Men >= 18.5 g/dL						
B-Leukocytes (10E9/L)						
High	325	2	(0.6)	419	3	(0.7)
Low	325	1	(0.3)	419	2	(0.5)
PCS Criteria: [NALMEFENE] LOW: <= 2.8 10E9/L HIGH: >= 16 10E9/L LOW: <= 2.8 10E9/L HIGH: >= 16 10E9/L LOW: <= 2.8 10E9/L HIGH: >= 16 10E9/L						
B-Lymphocytes/Leukocytes (%)						
High	324	0	(0.0)	415	0	(0.0)
Low	324	2	(0.6)	415	6	(1.4)
PCS Criteria: [NALMEFENE] LOW: <= 10 % HIGH: >= 75 % LOW: <= 10 % HIGH: >= 75 % LOW: <= 10 % HIGH: >= 75 %						
B-Mean Corpuscular Volume (fL)						
High	325	2	(0.6)	413	3	(0.7)
Low	325	0	(0.0)	413	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: <= 0.8 fL HIGH: >= 1.2 fL LOW: <= 0.8 fL HIGH: >= 1.2 fL LOW: <= 0.8 fL HIGH: >= 1.2 fL						

表 2.7.4.7.2-20

Table 195 Summary of Post-baseline PCS Laboratory Values (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo			Nalmefene		
Parameter (Unit)	n	PCS	(%)	n	PCS	(%)
B-Monocytes/Leukocytes (%)						
High	324	4	(1.2)	415	11	(2.7)
Low	324	0	(0.0)	415	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 15 % LOW: N/A HIGH: >= 15 % LOW: N/A HIGH: >= 15 %						
B-Neutrophils/Leukocytes (%)						
High	324	3	(0.9)	415	2	(0.5)
Low	324	0	(0.0)	415	1	(0.2)
PCS Criteria: [NALMEFENE] LOW: <= 20 % HIGH: >= 85 % LOW: <= 20 % HIGH: >= 85 % LOW: <= 20 % HIGH: >= 85 %						
B-Platelet (10E9/L)						
High	323	3	(0.9)	415	0	(0.0)
Low	323	2	(0.6)	415	3	(0.7)
PCS Criteria: [NALMEFENE] LOW: <= 75 10E9/L HIGH: >= 600 10E9/L LOW: <= 75 10E9/L HIGH: >= 600 10E9/L LOW: <= 75 10E9/L HIGH: >= 600 10E9/L						
Eosinophils/Leukocytes (%)						
High	324	5	(1.5)	415	3	(0.7)
Low	324	0	(0.0)	415	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 10 % LOW: N/A HIGH: >= 10 % LOW: N/A HIGH: >= 10 %						
S-Prothrombin Intl. Normalized Ratio						
High	322	0	(0.0)	409	0	(0.0)
Low	322	0	(0.0)	409	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 2 % LOW: N/A HIGH: >= 2 % LOW: N/A HIGH: >= 2 %						
SUB CATEGORY: INFECTION						
S-C-Reactive Protein (mg/L)						
High	326	7	(2.1)	419	10	(2.4)
Low	326	0	(0.0)	419	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 25 mg/L LOW: N/A HIGH: >= 25 mg/L LOW: N/A HIGH: >= 25mg/L						

表 2.7.4.7.2-20
Table 195 Summary of Post-baseline PCS Laboratory Values (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo			Nalmefene		
Parameter (Unit)	n	PCS	(%)	n	PCS	(%)
SUB CATEGORY: KIDNEY						
S-Creatinine (µmol/L)						
High	326	1	(0.3)	418	1	(0.2)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: <= 0.5 µmol/L HIGH: >= 1.5 µmol/L LOW: <= 0.5 µmol/L HIGH: >= 1.5 µmol/L LOW: <= 0.5 µmol/L HIGH: >= 1.5 µmol/L						
S-Urea (mmol/L)						
High	326	3	(0.9)	418	2	(0.5)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 11 mmol/L LOW: N/A HIGH: >= 11 mmol/L LOW: N/A HIGH: >= 11 mmol/L						
SUB CATEGORY: LIPIDS						
S-Cholesterol (mmol/L)						
High	326	88	(27.0)	418	96	(23.0)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 6.2 mmol/L LOW: N/A HIGH: >= 7.8 mmol/L LOW: N/A HIGH: >= 6.2 mmol/L LOW: N/A HIGH: >= 7.8 mmol/L LOW: N/A HIGH: >= 6.2 mmol/L LOW: N/A HIGH: >= 7.8 mmol/L						
S-Triglycerides (mmol/L)						
High	326	24	(7.4)	418	19	(4.5)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 5.65 mmol/L LOW: N/A HIGH: >= 4.2 mmol/L LOW: N/A HIGH: >= 5.65 mmol/L LOW: N/A HIGH: >= 4.2 mmol/L LOW: N/A HIGH: >= 5.65 mmol/L LOW: N/A HIGH: >= 4.2 mmol/L						
SUB CATEGORY: LIVER						
S-Alanine Aminotransferase (IU/L)						
High	326	9	(2.8)	418	15	(3.6)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 3 IU/L LOW: N/A HIGH: >= 3 IU/L LOW: N/A HIGH: >= 3 IU/L						
S-Alkaline Phosphatase (IU/L)						
High	326	1	(0.3)	418	0	(0.0)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 3 IU/L LOW: N/A HIGH: >= 3 IU/L LOW: N/A HIGH: >= 3 IU/L						

表 2.7.4.7.2-20
Table 195 Summary of Post-baseline PCS Laboratory Values (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo			Nalmefene		
Parameter (Unit)	n	PCS	(%)	n	PCS	(%)
S-Aspartate Aminotransferase (IU/L)						
High	326	10	(3.1)	418	14	(3.3)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 3 IU/L LOW: N/A HIGH: >= 3 IU/L LOW: N/A HIGH: >= 3 IU/L						
S-Bilirubin (µmol/L)						
High	326	2	(0.6)	418	1	(0.2)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 2 µmol/L LOW: N/A HIGH: >= 2 µmol/L LOW: N/A HIGH: >= 2 µmol/L						
S-Bilirubin, Direct (µmol/L)						
High	324	2	(0.6)	408	1	(0.2)
Low	324	0	(0.0)	408	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 12 µmol/L LOW: N/A HIGH: >= 12 µmol/L LOW: N/A HIGH: >= 12 µmol/L						
S-Gamma Glutamyl Transferase (IU/L)						
High	326	52	(16.0)	418	36	(8.6)
Low	326	0	(0.0)	418	0	(0.0)
PCS Criteria: [NALMEFENE] LOW: N/A HIGH: >= 200 IU/L LOW: N/A HIGH: >= 200 IU/L LOW: N/A HIGH: >= 200 IU/L						

＜資料番号5.3.5.3-03：Table 195＞

表 2.7.4.7.2-21

Panel 72 Post-baseline PCS Glucose and Lipid Parameter Values (APTS) - Patients with a High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

Laboratory test	Placebo			Nalmefene		
	N	n	(%)	N	n	(%)
PCS high glucose						
Fasting and non-fasting	326	13	(4.0)	418	26	(6.2)
Fasting	182	5	(2.7)	230	15	(6.5)
PCS low glucose						
Fasting and non-fasting	326	3	(0.9)	418	6	(1.4)
Fasting	182	1	(0.5)	230	4	(1.7)
PCS high total cholesterol						
Fasting and non-fasting	326	88	(27.0)	418	96	(23.0)
Fasting	182	75	(41.2)	229	88	(38.4)
PCS high triglycerides						
Fasting and non-fasting	326	24	(7.4)	418	19	(4.5)
Fasting	182	17	(9.3)	229	12	(5.2)

N = number of patients with assessments; n = number of patients with PCS high/low values

＜資料番号5.3.5.3-03：Panel 72＞

表 2.7.4.7.2-22

Table 225 Summary of Post-baseline PCS ECG Parameters (APTS): High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Placebo			Nalmefene		
Parameter (Unit)	n	PCS	(%)	n	PCS	(%)
Number of patients	325			419		
PR Duration Mean (msec)						
High	323	0	(0.0)	417	0	(0.0)
Low	323	0	(0.0)	417	0	(0.0)
QRS Duration (msec)						
High	323	2	(0.6)	417	2	(0.5)
Low	323	0	(0.0)	417	0	(0.0)
QT Duration Mean (msec)						
High	320	0	(0.0)	413	0	(0.0)
Low	320	0	(0.0)	413	0	(0.0)
QTcB (msec)						
High	320	3	(0.9)	413	3	(0.7)
Low	320	0	(0.0)	413	0	(0.0)
QTcF (msec)						
High	320	1	(0.3)	413	1	(0.2)
Low	320	0	(0.0)	413	0	(0.0)
RR Duration Mean (msec)						
High	323	15	(4.6)	417	17	(4.1)
Low	323	1	(0.3)	417	0	(0.0)
Ventricular Rate Mean (bpm)						
High	323	1	(0.3)	417	0	(0.0)
Low	323	7	(2.2)	417	4	(1.0)

＜資料番号5.3.5.3-03 : Table 225＞

表 2.7.4.7.2-23
Table 107 Run-out Period: TEAEs by SOC and Preferred Term (APTS) - Alcohol Dependence Pool

System Organ Class Preferred Term	Placebo-Placebo n	 (%)	Nalmefene-Placebo n	 (%)	Nalmefene-Nalmefene n	 (%)
Number of Patients	415		172		171	
Men	294	(70.8)	128	(74.4)	114	(66.7)
Women	121	(29.2)	44	(25.6)	57	(33.3)
Patients with TEAEs	52	(12.5)	28	(16.3)	20	(11.7)
血液およびリンパ系障害	2	(0.5)	0	(0.0)	0	(0.0)
貧血	1	(0.2)	0	(0.0)	0	(0.0)
血小板減少症	1	(0.2)	0	(0.0)	0	(0.0)
心臓障害	0	(0.0)	1	(0.6)	2	(1.2)
心房細動	0	(0.0)	0	(0.0)	1	(0.6)
洞性頻脈	0	(0.0)	0	(0.0)	1	(0.6)
頻脈	0	(0.0)	1	(0.6)	0	(0.0)
耳および迷路障害	0	(0.0)	0	(0.0)	1	(0.6)
回転性めまい	0	(0.0)	0	(0.0)	1	(0.6)
胃腸障害	5	(1.2)	5	(2.9)	3	(1.8)
腹部膨満	1	(0.2)	0	(0.0)	0	(0.0)
腹痛	2	(0.5)	2	(1.2)	0	(0.0)
齲歯	0	(0.0)	1	(0.6)	0	(0.0)
下痢	1	(0.2)	0	(0.0)	0	(0.0)
食中毒	0	(0.0)	1	(0.6)	0	(0.0)
胃腸障害	1	(0.2)	0	(0.0)	0	(0.0)
消化器痛	1	(0.2)	0	(0.0)	0	(0.0)
悪心	0	(0.0)	0	(0.0)	3	(1.8)
嘔吐	0	(0.0)	1	(0.6)	0	(0.0)

表 2.7.4.7.2-23
Table 107 Run-out Period: TEAEs by SOC and Preferred Term (APTS) - Alcohol Dependence Pool

System Organ Class	Placebo-Placebo		Nalmefene-Placebo		Nalmefene-Nalmefene	
Preferred Term	n	(%)	n	(%)	n	(%)
一般・全身障害および投与部位の状態	4	(1.0)	1	(0.6)	2	(1.2)
無力症	1	(0.2)	0	(0.0)	1	(0.6)
疲労	1	(0.2)	1	(0.6)	0	(0.0)
末梢性浮腫	0	(0.0)	0	(0.0)	1	(0.6)
末梢腫脹	1	(0.2)	0	(0.0)	0	(0.0)
非心臓性胸痛	1	(0.2)	0	(0.0)	0	(0.0)
肝胆道系障害	0	(0.0)	1	(0.6)	1	(0.6)
アルコール性肝炎	0	(0.0)	1	(0.6)	1	(0.6)
感染症および寄生虫症	18	(4.3)	10	(5.8)	10	(5.8)
気管支炎	2	(0.5)	0	(0.0)	0	(0.0)
膀胱炎	0	(0.0)	1	(0.6)	0	(0.0)
胃腸炎	1	(0.2)	2	(1.2)	2	(1.2)
インフルエンザ	2	(0.5)	1	(0.6)	2	(1.2)
鼻咽頭炎	6	(1.4)	2	(1.2)	3	(1.8)
咽頭炎	0	(0.0)	1	(0.6)	1	(0.6)
鼻炎	3	(0.7)	1	(0.6)	0	(0.0)
扁桃炎	1	(0.2)	0	(0.0)	0	(0.0)
上気道感染	1	(0.2)	0	(0.0)	0	(0.0)
尿路感染	1	(0.2)	0	(0.0)	0	(0.0)
ウイルス性上気道感染	1	(0.2)	0	(0.0)	0	(0.0)
歯感染	0	(0.0)	0	(0.0)	1	(0.6)
細菌性上気道感染	0	(0.0)	1	(0.6)	0	(0.0)
細菌性結膜炎	0	(0.0)	0	(0.0)	1	(0.6)
処置後感染	0	(0.0)	1	(0.6)	0	(0.0)

表 2.7.4.7.2-23
Table 107 Run-out Period: TEAEs by SOC and Preferred Term (APTS) - Alcohol Dependence Pool

System Organ Class	Placebo-Placebo		Nalmefene-Placebo		Nalmefene-Nalmefene	
Preferred Term	n	(%)	n	(%)	n	(%)
傷害、中毒および処置合併症	8	(1.9)	5	(2.9)	1	(0.6)
偶発的過量投与	1	(0.2)	0	(0.0)	0	(0.0)
足関節部骨折	1	(0.2)	0	(0.0)	0	(0.0)
転倒	2	(0.5)	1	(0.6)	0	(0.0)
企図的過量投与	2	(0.5)	2	(1.2)	0	(0.0)
靭帯捻挫	1	(0.2)	0	(0.0)	0	(0.0)
多発性外傷	1	(0.2)	0	(0.0)	0	(0.0)
交通事故	1	(0.2)	0	(0.0)	0	(0.0)
挫傷	0	(0.0)	0	(0.0)	1	(0.6)
創傷	1	(0.2)	0	(0.0)	0	(0.0)
熱傷	0	(0.0)	1	(0.6)	0	(0.0)
処置後合併症	1	(0.2)	0	(0.0)	0	(0.0)
眼挫傷	0	(0.0)	1	(0.6)	0	(0.0)
臨床検査	8	(1.9)	1	(0.6)	2	(1.2)
アラニンアミノトランスフェラーゼ増加	2	(0.5)	0	(0.0)	1	(0.6)
アスパラギン酸アミノトランスフェラーゼ増加	2	(0.5)	0	(0.0)	1	(0.6)
血中ブドウ糖増加	1	(0.2)	0	(0.0)	0	(0.0)
Ｃ－反応性蛋白増加	1	(0.2)	0	(0.0)	0	(0.0)
心電図Ｔ波振幅減少	0	(0.0)	0	(0.0)	1	(0.6)
γ－グルタミルトランスフェラーゼ増加	2	(0.5)	0	(0.0)	1	(0.6)
ヘモグロビン減少	1	(0.2)	0	(0.0)	0	(0.0)
国際標準比増加	1	(0.2)	0	(0.0)	0	(0.0)
プロトロンビン時間延長	1	(0.2)	0	(0.0)	0	(0.0)
トランスフェリン増加	1	(0.2)	0	(0.0)	0	(0.0)
白血球数増加	0	(0.0)	1	(0.6)	0	(0.0)
肝酵素上昇	1	(0.2)	0	(0.0)	0	(0.0)
ホルモン値異常	1	(0.2)	0	(0.0)	0	(0.0)

表 2.7.4.7.2-23
Table 107 Run-out Period: TEAEs by SOC and Preferred Term (APTS) - Alcohol Dependence Pool

System Organ Class	Placebo-Placebo		Nalmefene-Placebo		Nalmefene-Nalmefene	
Preferred Term	n	(%)	n	(%)	n	(%)
代謝および栄養障害	0	(0.0)	0	(0.0)	1	(0.6)
食欲減退	0	(0.0)	0	(0.0)	1	(0.6)
筋骨格系および結合組織障害	1	(0.2)	2	(1.2)	1	(0.6)
背部痛	0	(0.0)	1	(0.6)	1	(0.6)
側腹部痛	0	(0.0)	1	(0.6)	0	(0.0)
変形性関節症	1	(0.2)	0	(0.0)	0	(0.0)
神経系障害	2	(0.5)	2	(1.2)	2	(1.2)
健忘	0	(0.0)	1	(0.6)	0	(0.0)
小脳症候群	0	(0.0)	1	(0.6)	0	(0.0)
浮動性めまい	1	(0.2)	0	(0.0)	2	(1.2)
頭痛	1	(0.2)	0	(0.0)	1	(0.6)
精神障害	6	(1.4)	4	(2.3)	1	(0.6)
攻撃性	0	(0.0)	1	(0.6)	0	(0.0)
アルコール症	1	(0.2)	2	(1.2)	0	(0.0)
不安	3	(0.7)	0	(0.0)	0	(0.0)
うつ病	1	(0.2)	0	(0.0)	0	(0.0)
幻覚	1	(0.2)	0	(0.0)	0	(0.0)
不眠症	1	(0.2)	0	(0.0)	1	(0.6)
アルコール離脱症候群	1	(0.2)	0	(0.0)	0	(0.0)
大うつ病	0	(0.0)	1	(0.6)	0	(0.0)
自殺行為	1	(0.2)	0	(0.0)	0	(0.0)
腎および尿路障害	1	(0.2)	0	(0.0)	0	(0.0)
腎臓痛	1	(0.2)	0	(0.0)	0	(0.0)
生殖系および乳房障害	0	(0.0)	1	(0.6)	0	(0.0)
勃起不全 {ss}	0	(0.0)	1	(0.8)	0	(0.0)
呼吸器、胸郭および縦隔障害	1	(0.2)	1	(0.6)	0	(0.0)
咳嗽	1	(0.2)	1	(0.6)	0	(0.0)

表 2.7.4.7.2-23
Table 107 Run-out Period: TEAEs by SOC and Preferred Term (APTS) - Alcohol Dependence Pool

System Organ Class	Placebo-Placebo		Nalmefene-Placebo		Nalmefene-Nalmefene	
Preferred Term	n	(%)	n	(%)	n	(%)
皮膚および皮下組織障害	0	(0.0)	0	(0.0)	3	(1.8)
紅斑	0	(0.0)	0	(0.0)	1	(0.6)
発疹	0	(0.0)	0	(0.0)	1	(0.6)
斑状皮疹	0	(0.0)	0	(0.0)	1	(0.6)
社会環境	0	(0.0)	1	(0.6)	0	(0.0)
閉経 {ss}	0	(0.0)	1	(2.3)	0	(0.0)
外科および内科処置	1	(0.2)	0	(0.0)	0	(0.0)
智歯抜歯	1	(0.2)	0	(0.0)	0	(0.0)

Patients are only counted once for each SOC/Preferred Term
Only patients with a Completed Visit 10 are included
{ss} Sex specific
Dictionary: MedDRA 19.0
＜資料番号5.3.5.3-03 : Table 107＞

表 2.7.4.7.2-24

Table 129 Duration and Time to Onset of Frequent Adverse Events (APTS) - High or Very High DRL at Baseline and Randomisation - Alcohol Dependence Pool

	Incidence								
	Placebo			Nalmefene			Duration (median, days)		Time to First Onset (median, days)	
Patients Preferred Term	e	n	%	e	n	%	Placebo	Nalmefene	Placebo	Nalmefene
APTS		369			475					
悪心	26	24	(6.5)	184	115	(24.2)	5.0	4.0	8.0	0.0
浮動性めまい	28	22	(6.0)	150	104	(21.9)	2.0	3.0	0.5	0.0
不眠症	23	16	(4.3)	97	69	(14.5)	3.5	7.0	45.5	1.0
頭痛	41	35	(9.5)	83	60	(12.6)	3.0	3.0	10.0	1.0
疲労	26	22	(6.0)	65	43	(9.1)	22.5	6.0	17.0	0.0
嘔吐	16	13	(3.5)	47	40	(8.4)	2.0	2.0	75.0	9.0
鼻咽頭炎	44	39	(10.6)	44	38	(8.0)	11.0	8.0	65.0	78.5
睡眠障害	4	4	(1.1)	36	32	(6.7)	82.5	3.0	7.0	0.0
多汗症	3	3	(0.8)	42	28	(5.9)	18.0	4.0	7.0	0.0
食欲減退	4	4	(1.1)	41	27	(5.7)	88.0	9.0	48.0	1.0
下痢	24	22	(6.0)	23	19	(4.0)	3.0	3.0	7.5	12.0
偶発的過量投与	29	22	(6.0)	18	13	(2.7)	1.0	1.0	43.0	50.0

e=number of events; n=number of patients; %=frequency relative to the APTS

Medians, among patients with the event, are estimated using the Kaplan-Meier method

Longest duration and time to first onset for each patient within a preferred term

＜資料番号5.3.5.3-03 : Table 129＞

2.7.4.8 文献

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セリンクロ錠　10mg

第 2 部（モジュール 2）：CTD の概要（サマリー）

2.7.5 参考文献

大塚製薬株式会社

2.7.5 参考文献

2.7.5.1 2.7.1 章の参考文献

なし

2.7.5.2 2.7.2 章の参考文献

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2.7.5.4 2.7.4 章の参考文献

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