2.7.6.5.7　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（外国人：CPH-101-0299 試験，添付資料番号 5.3.5.1-07）【参考資料】

2.7.6.5.7.1　試験方法の概略

項目	内容
試験の目的	1) 多量飲酒者を対象にナルメフェンの飲酒量低減及び断酒の促進に対する有効性及び用量反応性を検討する。 2) 多量飲酒者を対象にナルメフェンの安全性を評価する。 3) 12 週間の連日投与後にナルメフェンを頓用投与し，多量飲酒の再発予防の効果を探索的に評価する。
試験デザイン	無作為化，二重盲検，多施設共同，並行群間比較，プラセボ対照
対象	多量飲酒者
選択基準	1) 精神疾患の診断・統計マニュアル第 4 版（DSM-IV）でアルコール依存症と診断され，以下の基準に 1 つ以上該当した患者 • 意図したよりも多量又は長時間飲酒することが多い患者 • 飲酒量の低減又は飲酒のコントロールを常に望んでいる患者 2) スクリーニング来院前 6 週間に，HDD が 8 日以上の患者（HDD は男性で 5 ドリンク以上，女性で 4 ドリンク以上のアルコールを消費した日とした） 3) 無作為化前直近の断酒日が連続 3 日の患者 4) 無作為化時にアルコール離脱症状評価尺度（CIWA-Ar）が 8 未満の患者 5) 同意文書に署名した患者 6) 21 歳以上の男性又は女性患者 7) 英語での読解及び記述が可能な患者 8) 定まった住所及び電話番号を有する患者
除外基準	1) 治験治療を妨げるか治験遵守に支障を来す恐れのある精神疾患（精神病，統合失調症，高度のうつ病，摂食障害，双極性感情障害，不安障害など）を有する患者 2) 入院での解毒治療が必要な患者 3) 認知症，てんかん発作，精神遅滞，脳症を有する患者 4) 重篤な合併症のある患者 5) 妊娠又は授乳中の患者 6) 妊娠可能な女性で，適切な避妊法を使用していない患者 7) 薬物検査が繰り返し陽性である患者（スクリーニング時に陽性でその後 3 日以上あけた再テストで陽性の患者） 8) 他の向精神薬（ニコチンを除く）の乱用又は依存のある患者

<table>
<tr><td>項目</td><td>内容</td></tr>
<tr><td></td><td>9) 解毒治療を 3 回以上受けた患者
10) より集中的なアルコール治療プログラムに参加している患者又は参加を予定している患者
11) 現在又は過去 6 ヵ月以内に，ナルトレキソンによる治療を受けている患者
12) 現在，ジスルフィラムの治療を受けている患者
13) 現在，精神疾患の薬物治療（8 週間の安定した抗うつ薬治療は除く）を受けている患者
14) 現在又は過去 1 週間以内に，オピオイドの刺激薬による治療を受けている患者
15) 無作為化前に 14 日を超える断酒日がある患者
16) 組入れ前 6 ヵ月以内に何らかの治験に参加した患者
17) 法的嫌疑で係争中（酒気帯び運転を除く）の患者</td></tr>
<tr><td>使用薬剤,
ロット番号</td><td>被験薬
ナルメフェン塩酸塩錠 5 mg：[redacted]
ナルメフェン塩酸塩錠 20 mg：[redacted]
対照薬
プラセボ錠：[redacted]</td></tr>
<tr><td>用量及び投与方法</td><td>本試験は連日投与期 12 週間とそれに続く継続投与期 40 週間から構成される。被験者はナルメフェン 5 mg 群，20 mg 群，40 mg 群，及びプラセボ群に 1：1：1：1 で無作為割付けされた。連日投与期では，各投与群は以下のとおり，ナルメフェン塩酸塩錠又はプラセボ錠を 1 回 2 錠，1 日 1 回服用した。
<table>
<tr><th>Treatment allocation</th><th>Tablets in one dose</th></tr>
<tr><td>Placebo</td><td>Two placebo tablets</td></tr>
<tr><td>Nalmefene hydrochloride 5 mg</td><td>One 5 mg nalmefene hydrochloride tablet and one placebo tablet</td></tr>
<tr><td>Nalmefene hydrochloride 20 mg</td><td>One 20 mg nalmefene hydrochloride tablet and one placebo tablet</td></tr>
<tr><td>Nalmefene hydrochloride 40 mg</td><td>Two 20 mg nalmefene hydrochloride tablets</td></tr>
</table>
継続投与期では，飲酒の恐れがある場合に，飲酒の約 30～60 分前に連日投与期と同量を頓用した。1 日 1 回までの服用とし，必要であれば，毎日服用可能であった。飲酒の恐れがない日は，治験薬の服用を不要とした。
用量漸増により，初期の有害事象の発現割合が低下する可能性があることから，20 mg 群及び 40 mg 群に無作為化された被験者では，連日投与期の最初の 7 日間は以下のように用量を漸増することとした。</td></tr>
</table>

<table>
<tr><td>項目</td><td>内容</td></tr>
<tr><td></td><td>
<table>
<tr><td>Days of treatment</td><td>1-2</td><td>3-4</td><td>5-6</td><td>7-</td></tr>
<tr><td>Daily dose in the 20 mg group</td><td>5 mg</td><td>10 mg</td><td>20 mg</td><td>20 mg</td></tr>
<tr><td>Daily dose in the 40 mg group</td><td>5 mg</td><td>10 mg</td><td>20 mg</td><td>40 mg</td></tr>
</table>
</td></tr>
<tr><td>投与期間</td><td>連日投与期 12 週間，継続投与期 40 週間</td></tr>
<tr><td>目標被験者数</td><td>272 例（各群 68 例）</td></tr>
<tr><td>目標被験者数の
設定根拠</td><td>被験者内相関を 0.5，平均 6 週，最大 12 週の測定，プラセボ群の多量飲酒率を 60%と仮定すると，検出力 80%，両側有意水準 5%，240 例（各群 60 例）で多量飲酒がなしに対するありの割合の差 20%を検出できる。脱落例を考慮し，約 15%多い 272 例（各群 68 例）を組入れる計画とした。</td></tr>
<tr><td>主な併用薬の規定</td><td>併用禁止薬/療法
• オピオイドの刺激薬
• ナルトレキソン
• ジスルフィラム</td></tr>
<tr><td>評価項目</td><td>有効性
主要評価項目：HDD 数
HDD 数は 1 日のアルコール消費量が男性で 5 ドリンク以上，女性で 4 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した。（1 ドリンクはエタノールとして約 12 g を含む）
アルコール消費量に関する副次的評価項目：
• TAC（Drinks per week）
TAC は 1 週間当たりの平均アルコール消費量（ドリンク/週）と定義した。
• VHDD 数
VHDD 数は 1 日のアルコール消費量が男性で 10 ドリンク以上，女性で 8 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した。
• 飲酒日当たりのアルコール消費量
• 飲酒日数に対する HDD 数の割合
• NDD 数（Abstinence day count）及び NDD の累積日数
NDD は飲酒をしなかった日と定義した。
• 1 日アルコール消費量の最大値
1 日アルコール消費量の最大値は 1 ヵ月間で最も多く飲酒した日のアルコール消費量（ドリンク数）と定義した。
その他の副次的評価項目：
• 血中アルコール濃度</td></tr>
</table>

項目	内容
	• MCV，ALT，γ-GTP，%CDT • ADS • DrInC • OCDS • 近親者による被験者の飲酒パターン及びアルコール中毒の頻度の評価 **安全性** 有害事象，臨床検査値，身体所見，バイタルサイン
解析方法	12 週間の連日投与期と 40 週間の継続投与期はそれぞれ独立して解析した。連日投与期のベースラインはスクリーニング時，継続投与期のベースラインは Month 3 とした。有効性主要評価項目の解析は，連日投与期では，HDD 数のスクリーニング時からの変化量を求め、その群間差を基に行った。継続投与期では，2 ヵ月を 1 期間とした 5 期間の HDD 数の Month 3（Week 8～12）からの変化量を求め，その群間差を基に行った。有効性主要評価項目の解析は，ベースライン後の測定値を 1 つ以上もつ全被験者を含む intent-to-treat 集団で行った。主要評価項目である HDD 数は反復測定のポアソン回帰で解析した（PROC GENMOD）。反復測定の分散分析（PROC MIXED）も行った。
治験依頼者	Biotie Therapies Corp.
治験実施医療機関	米国 13 施設
治験期間	20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日

2.7.6.5.7.2　治験スケジュール

治験スケジュールを表 2.7.6.5.7-1 に示した。

表 2.7.6.5.7-1　　治験スケジュール

	Screen-ing	In-clusion	Week								
			1	3	6	9	12[a]	20	28	36, 44	52[a]
Informed consent	x										
Medical, social and alcohol history	x										
Physical examination	x						x				
SCID	x										
Clinical laboratory	x			x[c]	x		x		x		x
Pregnancy test[b]	x			(x)	(x)	(x)	(x)	(x)	(x)	(x)	(x)
Drug screen	x										
CIWA-Ar		x									
Randomization		x									
Obsessive compulsive drinking scale	x		x	x	x	x	x		x		x
Drinker inventory of consequences	x						x				x
Alcohol dependence scale	x						x				
Motivational enhancement therapy		x	x		x		x				
Electrocardiogram	x										
Breath alcohol	x	x	x	x	x	x	x	x	x	x	x
Blood pressure, heart rate	x	x	x	x	x	x	x		x		x
Study medication check/dispensing		x	x	x	x	x	x	x	x	x	x
Adverse events			x	x	x	x	x	x	x	x	x
Prior/concomitant medication/treatment	x	x	x	x	x	x	x	x	x	x	x
Timeline followback	x	x	x	x	x	x	x	x	x	x	x
Collateral estimate		x					x				x

SCID：DSM-IV の診断をするための構造化面接

Timeline followback で導出される評価項目は，HDD 数，TAC，VHDD 数，飲酒日当たりのアルコール消費量，飲酒日数に対する HDD 数の割合，NDD 数，NDD の累積日数，1 日アルコール消費量の最大値

[a]Week 12/52 assessments were to be completed also upon premature discontinuation.

[b]Human chorionic gonadotropin in urine (women of childbearing potential; repeated when indicated).

[c]Alanine aminotransferase and aspartate aminotransferase only.

＜資料番号 5.3.5.1-07：Text Table 5＞

2.7.6.5.7.3　試験結果

(1)　被験者の内訳

被験者の内訳を図 2.7.6.5.7-1 に，中止例の内訳を表 2.7.6.5.7-2 及び表 2.7.6.5.7-3 に，それぞれ示した。

270 例が無作為に割付けられ，ナルメフェン 5 mg 群 68 例，20 mg 群 66 例，40 mg 群 68 例，プラセボ群 68 例に治験薬が投与された。

270 例のうち，ナルメフェン 5 mg 群 22 例（32.4%），20 mg 群 19 例（28.8%），40 mg 群 25 例（36.8%），プラセボ群 21 例（30.9%）が 12 週間の連日投与期に治験を中止した。全体で最も多かった中止理由は追跡不能であった。有害事象による中止は，ナルメフェン 5 mg 群 4 例（6%），20 mg 群 9 例（14%），40 mg 群 8 例（12%），プラセボ群 2 例（3%）であった。

ナルメフェン 5 mg 群 40 例，20 mg 群 40 例，40 mg 群 37 例，プラセボ群 39 例が 40 週間の継続投与期に移行した。そのうちナルメフェン 5 mg 群 18 例，20 mg 群 15 例，40 mg 群 19 例，プラセボ群 14 例が治験を完了した。最も多かった中止理由は追跡不能で，有害事象による中止は少なかった。

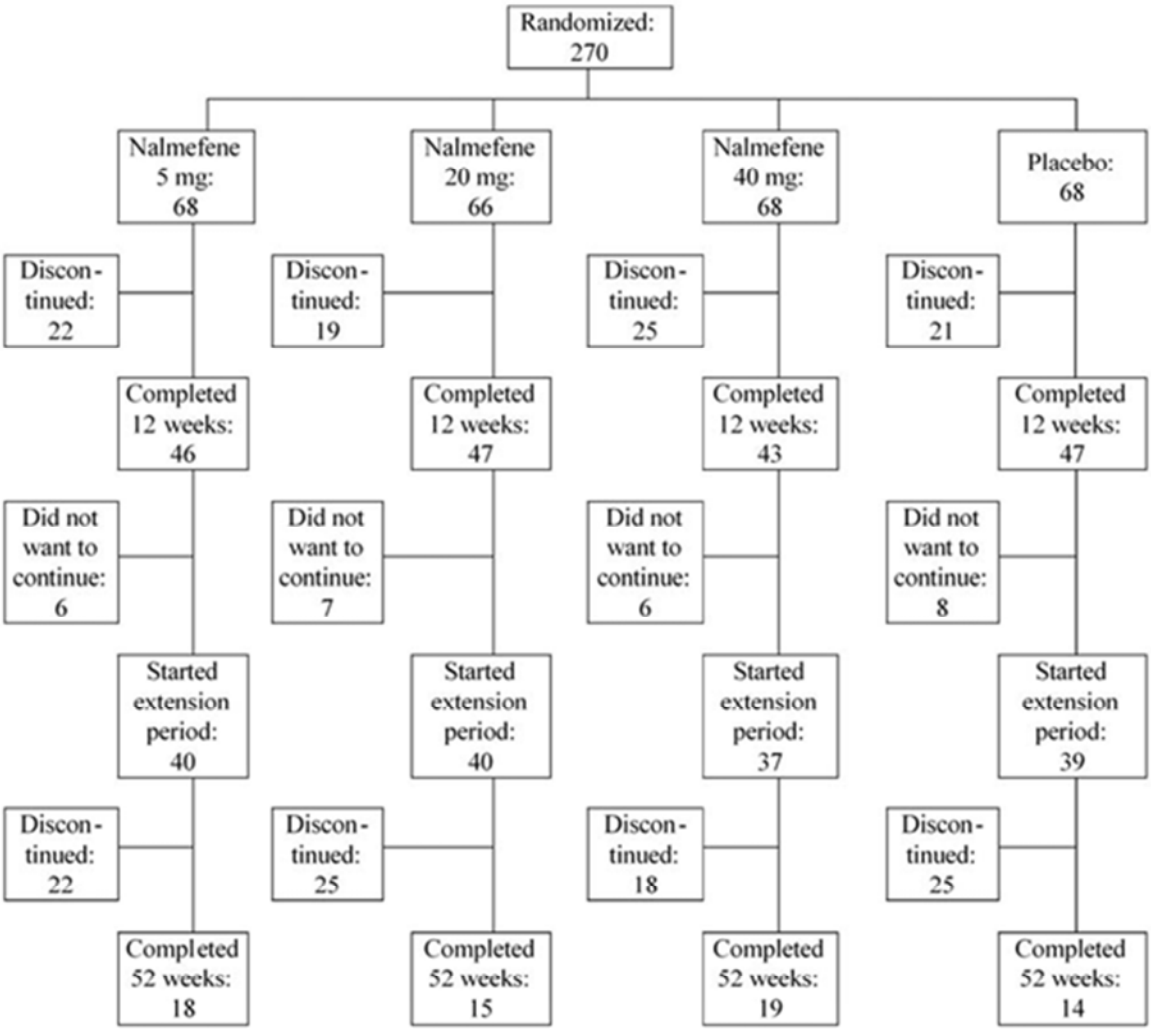


図 2.7.6.5.7-1　　被験者の内訳

＜資料番号 5.3.5.1-07：Text Figure 3＞

表 2.7.6.5.7-2　　中止例の内訳—連日投与期—

Reason	Placebo	5 mg	20 mg	40 mg	Total
Total	21 (30.9)	22 (32.4)	19 (28.8)	25 (36.8)	87 (32.2)
Adverse event	2	4	9	8	23
Lack of efficacy or clear clinical deterioration	2	5	1	2	10
Lost to follow-up	11	11	4	11	37
Subject decision to withdraw from the study[a]	5	1	2	2	10
Other	1[b]	1[c]	3[d]	2[e]	7

Subject count (% of randomized subjects) is shown.
[a]In CRF "Consent withdrawn". [b]Current treatment with opiate. [c]Subject relocated. [d]Non-compliance (2 subjects), subject angry. [e]Job transfer, non-compliance.

＜資料番号 5.3.5.1-07：Text Table 11＞

表 2.7.6.5.7-3　　中止例の内訳—継続投与期—

Reason	Placebo N	5 mg N	20 mg N	40 mg N	Total N
Total	25	22	25	18	90
Adverse event	2	1	1	2	6
Lack of efficacy or clear clinical deterioration	4	3	3	0	10
Lost to follow-up	9	8	14	7	38
Subject decision to withdraw from the study[a]	6	8	5	7	26
Other[b]	4	2	2	2	10

[a]In CRF reason "Consent withdrawn". [b]Medication was removed due to attempted overdose, concomitant surgery, relocation, disulfiram use (placebo); non-compliance with appointments (2 subjects, 5 mg); subject did not feel he needed medication, subject did not like the way the medication made him feel (20 mg); part of subject's medication was lost, history of bipolar disorder and need for treatment (40 mg).

＜資料番号 5.3.5.1-07：Text Table 13＞

(2)　解析したデータセット

ITT 集団は，治験薬を投与され，HDD 数のベースラインからの変化量を評価できる（無作為化後の HDD 数の測定値が 1 つ以上ある）全被験者とした。ITT 集団を有効性解析対象とした。無作為化例を安全性解析対象とした。

有効性解析対象は 237 例（ナルメフェン 5 mg 群：61 例，20 mg 群：59 例，40 mg 群：59 例，プラセボ群：58 例），安全性解析対象は 270 例（ナルメフェン 5 mg 群：68 例，20 mg 群：66 例，40 mg 群：68 例，プラセボ群：68 例）であった（資料番号 5.3.5.1-07：14.2.1，14.3.1.1，14.3.1.2 参照）。

(3)　人口統計学的及び他の基準値の特性

無作為化例の人口統計学的特性を表 2.7.6.5.7-4 に，有効性評価項目のベースライン値（1）を表 2.7.6.5.7-5 に，有効性評価項目のベースライン値（2）を表 2.7.6.5.7-6 に示した。また，継続投与期移行例の人口統計学的特性を表 2.7.6.5.7-7 に，有効性評価項目のベースライン値（1）を表 2.7.6.5.7-8 に，有効性評価項目のベースライン値（2）を表 2.7.6.5.7-9 に示した。

無作為化例の大部分（89.6%）が白人であった（資料番号 5.3.5.1-07：14.1.3 参照）。平均年齢は 45.1 歳（範囲：21～78 歳）で，76 例（28.1%）が女性，194 例（71.9%）が男性であった（資料番号 5.3.5.1-07：14.1.1 参照）。年齢，性別，及び BMI に群間差は認められなかった。

被験者の 27.8%が独居で，35.9%が配偶者又はパートナーと暮らし，22.6%が配偶者又はパートナー及び子供と暮らし，5.9%が独身で子供と暮らしていた（資料番号 5.3.5.1-07：14.1.8 参照）。82.6%が在職又は在学中で 8.5%が退職者であった（資料番号 5.3.5.1-07：14.1.7 参照）。

アルコール関連問題の家族歴を有する被験者は 84.4%であった（資料番号 5.3.5.1-07：14.1.22 参照）。初回飲酒の平均年齢は 15.5 歳（資料番号 5.3.5.1-07：14.1.19 参照），アルコール関連問題の平均初発年齢は 30.7 歳（範囲：13～71 歳）（資料番号 5.3.5.1-07：14.1.20 参照）であり，57.0%にアルコール関連問題の治療歴があった（資料番号 5.3.5.1-07：14.1.11 参照）。初回飲酒の平均年齢，アルコール関連問題の平均初発年齢，及びアルコール関連問題の治療歴に明らかな群間差は認められなかった。

ベースラインの HDD 数，VHDD 数，NDD 数（Abstinence day count），TAC（Drinks per week）に群間差は認められなかった。

継続投与期移行例と無作為化例で人口統計学的特性に明らかな違いは認められなかった。

表 2.7.6.5.7-4　　人口統計学的特性（無作為化例）

	Placebo N=68	5 mg N=68	20 mg N=66	40 mg N=68	Total
Age, years	45.1 (11.1)	45.4 (11.3)	46.5 (10.9)	43.6 (9.1)	45.1 (10.6)
Gender	15 (22.1%) F 53 (77.9%) M	23 (33.8%) F 45 (66.2%) M	18 (27.3%) F 48 (72.7%) M	20 (29.4%) F 48 (70.6%) M	76 (28.1%) F 194 (71.9%) M
BMI, kg/m^2	28.8 (6.4)	27.9 (4.5)	27.1 (4.9)	27.1 (4.7)	27.7 (5.2)

Mean (with SD) is given for age and body mass index (BMI). F = female, M = male.

＜資料番号 5.3.5.1-07：Text Table 15＞

表 2.7.6.5.7-5　　有効性評価項目のベースライン値（1）（無作為化例）

	Placebo N=68			5 mg N=68			20 mg N=66			40 mg N=68		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
HDD count	20.8	6.5	22.0	20.5	6.9	22.5	19.6	7.8	23.0	19.6	7.9	20.0
VHDD count	11.4	10.4	8.0	11.7	9.8	9.0	9.5	9.7	7.0	10.4	10.1	9.0
Abstinence day count	4.1	5.1	2.0	6.0	6.5	3.0	5.3	6.0	4.0	6.1	6.9	3.0
Drinks per week	63.9	41.6	52.0	61.6	37.8	54.4	55.5	34.2	48.5	54.3	31.5	44.7

＜資料番号 5.3.5.1-07：Text Table 19＞

表 2.7.6.5.7-6　　有効性評価項目のベースライン値（2）（無作為化例）

	Placebo N=68			5 mg N=68			20 mg N=66			40 mg N=68		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
OCDS	18.3	4.9	18.0	19.4	4.9	19.0	18.9	5.9	20.0	18.2	5.2	18.0
ADS	16.2	6.2	16.0	16.2	7.5	15.0	17.0	7.5	16.0	16.0	6.2	16.0
DrInC, lifetime	30.2	6.7	30.5	27.7	8.7	29.0	27.2	9.3	29.0	28.8	8.8	29.5
DrInC, recent	43.6	17.0	42.0	43.4	18.5	43.0	44.4	21.7	11.0	41.9	20.2	40.5

Total scores are presented.

＜資料番号 5.3.5.1-07：Text Table 24＞

表 2.7.6.5.7-7　　人口統計学的特性（継続投与期移行例）

	Placebo	5 mg	20 mg	40 mg	Total
Age, years	48.1 (12.1)	46.7 (12.2)	49.9 (10.2)	43.7 (8.5)	47.1 (11.0)
Gender	9 (23.1%) F 30 (79.9%) M	12 (30.0%) F 28 (70.0%) M	14 (35.0%) F 26 (65.0%) M	10 (27.0%) F 27 (73.0%) M	45 (28.8%) F 111 (71.2%) M
BMI, kg/m^2	29.4 (6.7)	28.1 (4.5)	27.1 (5.1)	27.6 (4.8)	28.0 (5.4)

Mean (SD) given for age and body mass index (BMI). F = female, M = male.

＜資料番号 5.3.5.1-07：Text Table 25＞

表 2.7.6.5.7-8　　有効性評価項目のベースライン値（1）（継続投与期移行例）

	Placebo N=39			5 mg N=40			20 mg N=40			40 mg N=37		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
HDD count	21.8	6.4	24.0	21.6	7.2	25.0	18.9	7.9	22.5	17.6	8.0	18.0
VHDD count	12.6	10.6	8.0	12.3	10.1	9.0	9.2	10.0	7.0	8.8	9.2	7.0
Abstinence day count	4.0	5.3	1.0	4.5	6.1	1.5	5.7	6.0	4.0	7.8	7.3	7.0
Drinks per week	69.9	46.3	57.6	67.3	41.2	55.3	52.7	33.7	42.5	46.5	25.1	42.0

＜資料番号 5.3.5.1-07：Text Table 27＞

表 2.7.6.5.7-9　　有効性評価項目のベースライン値（2）（継続投与期移行例）

	Placebo N=39			5 mg N=40			20 mg N=40			40 mg N=37		
	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
OCDS	26.3	6.8	25.0	26.8	6.3	27.0	25.8	8.0	26.0	24.3	6.5	24.0
ADS	17.0	6.3	17.0	15.9	8.3	14.0	17.1	7.4	14.5	16.3	7.1	16.0
DrInC, lifetime	30.1	7.3	31.0	26.1	8.6	26.0	25.9	10.1	27.5	29.4	9.1	31.0
DrInC, recent	44.7	18.5	41.0	40.9	18.3	40.5	42.1	22.3	42.5	41.1	21.9	35.0

Total scores are presented.

＜資料番号 5.3.5.1-07：Text Table 29＞

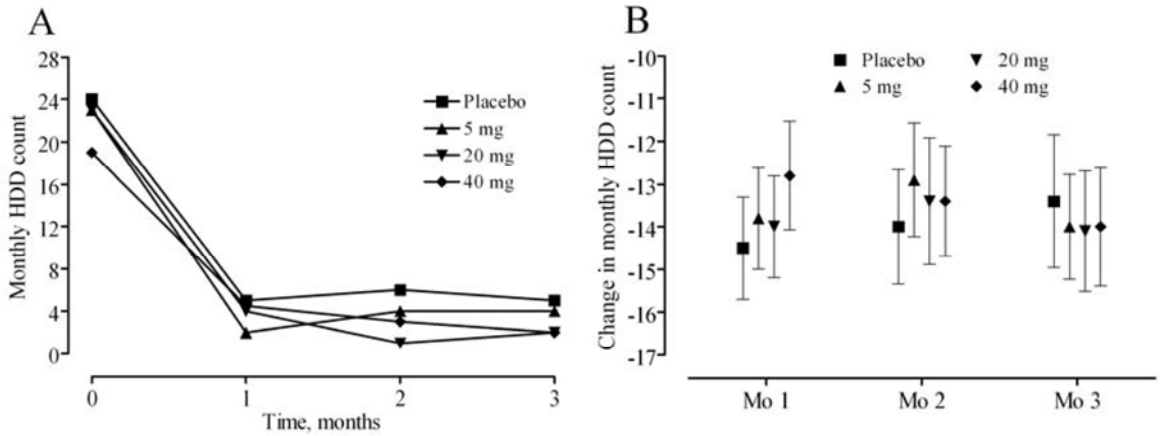
(4)　有効性

(a)　主要評価項目

連日投与期の HDD 数の推移を図 2.7.6.5.7-2 及び表 2.7.6.5.7-10 に示した。また継続投与期の HDD 数の推移を図 2.7.6.5.7-3 及び表 2.7.6.5.7-11 に示した。

ベースラインの HDD 数（平均値）は，全投与群で 19.1～21.2 日であった。連日投与期で，HDD 数（平均値）はベースラインから 13.4～14.1 日減少し，5.0～8.1 日となった。投与群（ナルメフェン 5 mg 群，20 mg 群，40 mg 群，プラセボ群）の間で差は認められなかった（ポアソン回帰 p = 0.4564）（資料番号 5.3.5.1-07：14.2.1 参照）。

継続投与期で，HDD 数は，連日投与期の Month 3 とほぼ同様の値で推移し，投与群（ナルメフェン 5 mg 群，20 mg 群，40 mg 群，プラセボ群）の間で差は認められなかった（ポアソン回帰 p = 0.9579）（資料番号 5.3.5.1-07：15.2.3.1 参照）。



5 mg(n)	61	61	56	53
20 mg(n)	59	59	55	51
40 mg(n)	59	58	54	47
Placebo(n)	58	58	51	48

5 mg(n)	61	56	53
20 mg(n)	59	55	51
40 mg(n)	58	54	47
Placebo(n)	58	51	48

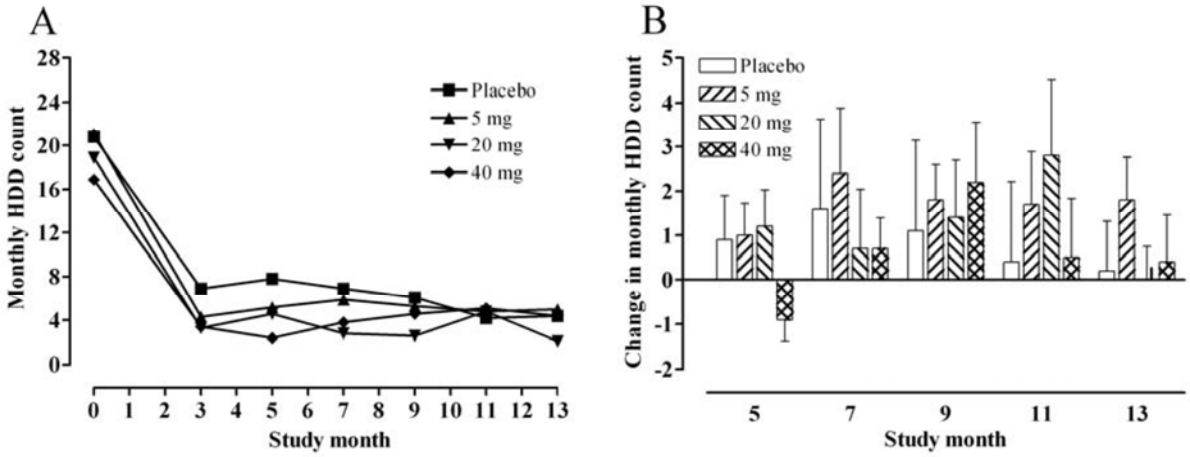
図 2.7.6.5.7-2　　HDD 数の推移－連日投与期－（ITT）

A. Monthly median. B. Mean change from baseline with standard error.
＜資料番号 5.3.5.1-07：Text Figure 4，Text Table 31 より作成＞

表 2.7.6.5.7-10　　HDD 数の推移－連日投与期－（ITT）

Group		Observed				Change from baseline		
		Screening	Mon 1	Mon 2	Mon 3	Mon 1	Mon 2	Mon 3
0	N	58	58	51	48	58	51	48
	Mean	21.2	6.7	7.4	8.1	-14.5	-14.0	-13.4
	SD	6.7	7.0	7.9	9.1	9.1	9.6	10.8
	Q1	16.0	0.0	0.0	0.0	-22.0	-22.0	-22.0
	Median	24.0	5.0	6.0	5.0	-16.5	-16.0	-15.5
	Q3	27.0	9.0	12.0	14.0	-5.0	-6.0	-5.5
5	N	61	61	56	53	61	56	53
	Mean	20.6	6.7	7.8	6.9	-13.8	-12.9	-14.0
	SD	7.1	8.6	9.0	8.4	9.3	10.0	9.0
	Q1	14.0	0.0	0.0	0.0	-23.0	-24.0	-20.0
	Median	23.0	2.0	4.0	4.0	-12.0	-11.5	-13.0
	Q3	27.0	11.0	14.5	11.0	-7.0	-4.0	-7.0
20	N	59	59	55	51	59	55	51
	Mean	19.5	5.6	5.9	5.0	-14.0	-13.4	-14.1
	SD	7.7	6.7	8.4	7.6	9.2	11.0	10.1
	Q1	12.0	0.0	0.0	0.0	-23.0	-23.0	-24.0
	Median	23.0	4.0	1.0	2.0	-14.0	-13.0	-14.0
	Q3	27.0	9.0	9.0	5.0	-7.0	-6.0	-7.0
40	N	59	58	54	47	58	54	47
	Mean	19.1	6.1	5.6	5.0	-12.8	-13.4	-14.0
	SD	8.1	7.1	6.7	7.0	9.7	9.5	9.5
	Q1	11.0	0.0	0.0	0.0	-22.0	-21.0	-22.0
	Median	19.0	4.5	3.0	2.0	-11.5	-13.0	-15.0
	Q3	27.0	10.0	8.0	8.0	-5.0	-5.0	-7.0

＜資料番号 5.3.5.1-07：Text Table 31＞



5 mg(n)	30	30	30	17	16	17	18	5 mg(n)	30	17	16	17	18
20 mg(n)	35	35	35	20	12	12	12	20 mg(n)	35	20	12	12	12
40 mg(n)	33	33	32	23	14	13	16	40 mg(n)	32	23	14	13	16
Placebo(n)	28	28	28	14	11	12	13	Placebo(n)	28	14	11	12	13

図 2.7.6.5.7-3　　HDD 数の推移－継続投与期－（ITT）

A. Monthly mean HDD count in the extension population. B. Changes in the monthly HDD count since month 3. Error bars are standard error of the mean.

＜資料番号 5.3.5.1-07：Text Figure 5，Text Table 32 より作成＞

表 2.7.6.5.7-11　　HDD 数の推移－継続投与期－（ITT）

Group		Screen	Month 3	Month 4-5	Month 6-7	Month 8-9	Month 10-11	Month 12-13
Placebo	Median	23.5	2.0	2.5	2.0	1.0	0.0	0.0
	Mean	20.8	6.9	7.8	6.9	6.1	4.2	4.4
	SD	7.0	9.0	9.7	9.7	9.1	8.4	7.0
	N	28	28	28	14	11	12	13
5 mg	Median	25.0	1.0	0.0	0.0	0.0	0.0	0.5
	Mean	21.1	4.3	5.2	5.9	5.3	4.8	5.0
	SD	7.7	7.0	8.3	8.3	8.4	9.3	8.4
	N	30	30	30	17	16	17	18
20 mg	Median	23.0	1.0	1.0	0.0	0.5	1.0	0.0
	Mean	18.9	3.3	4.6	2.8	2.6	4.8	2.1
	SD	8.0	5.4	7.6	6.5	4.1	7.4	4.0
	N	35	35	35	20	12	12	12
40 mg	Median	18.0	1.0	0.5	2.0	2.0	0.0	2.5
	Mean	16.9	3.4	2.4	3.8	4.6	5.1	4.4
	SD	8.0	5.3	3.9	5.5	5.3	7.4	5.5
	N	33	33	32	23	14	13	16

＜資料番号 5.3.5.1-07：Text Table 32＞

(b)　副次的評価項目

連日投与期の TAC の推移を表 2.7.6.5.7-12 及び図 2.7.6.5.7-4 に，継続投与期の TAC の推移を表 2.7.6.5.7-13 及び図 2.7.6.5.7-5 に示した。

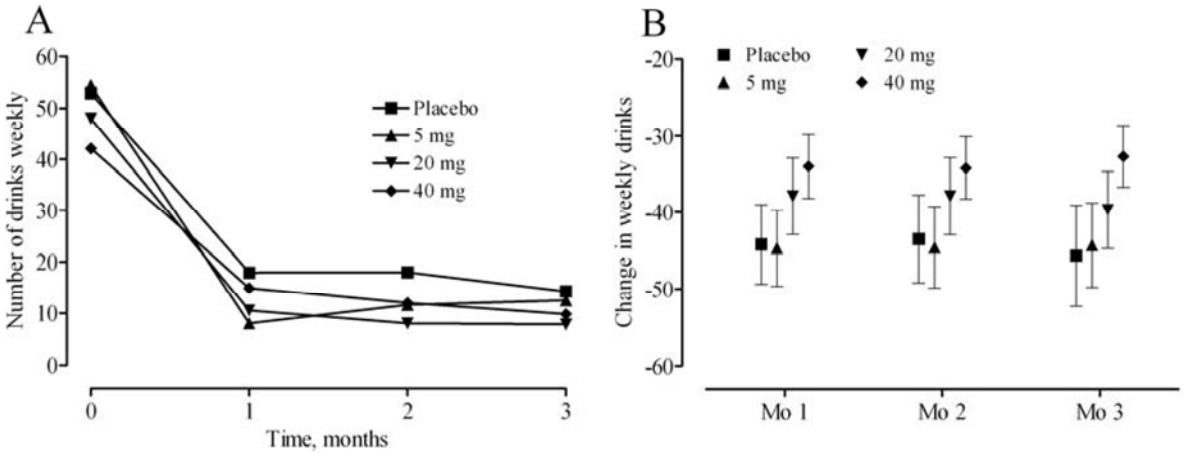
ベースラインの TAC（平均値）は全投与群で 50～67 ドリンク/週であった。連日投与期で，TAC は 33～46 ドリンク/週減少し，14～23 ドリンク/週になった。投与群（ナルメフェン 5 mg 群，

20 mg 群，40 mg 群，プラセボ群）の間で差は認められなかった（資料番号：5.3.5.1-07：14.2.4 参照）。継続投与期では，TAC の変動が認められたが，投与群（ナルメフェン 5 mg 群，20 mg 群，40 mg 群，プラセボ群）の間で差は認められなかった（資料番号：5.3.5.1-07：15.2.3.4 参照）。

表 2.7.6.5.7-12　　TAC の推移－連日投与期－（ITT）

	Placebo						5 mg						20 mg						40 mg					
	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3
Screening	58	67	44	36	53	90	61	62	39	36	54	84	59	56	35	31	48	65	59	50	28	32	42	66
Mo 1	58	22	26	3.0	18	28	61	18	23	1.3	8.0	25	59	18	27	0.8	11	25	58	17	20	1.3	15	26
Mo 2	51	23	27	3.5	18	32	56	19	22	2.0	12	29	55	18	25	0.5	8.0	20	54	16	18	2.0	12	21
Mo 3	48	23	24	3.0	14	32	53	19	22	2.3	13	31	51	14	18	0.8	7.8	16	47	14	17	1.0	9.8	20
Change to Mo 1	58	-44	40	-63	-34	-19	61	-45	39	-58	-35	-18	59	-38	39	-52	-32	-21	58	-34	32	-47	-28	-15
Change to Mo 2	51	-44	41	-53	-34	-15	56	-45	40	-53	-36	-21	55	-38	38	-55	-31	-16	54	-34	30	-52	-23	-18
Change to Mo 3	48	-46	46	-64	-34	-20	53	-44	40	-52	-35	-24	51	-40	36	-56	-31	-17	47	-33	28	-48	-25	-16

＜資料番号 5.3.5.1-07：Text Table 38＞



5 mg(n)	61	61	56	53	5 mg(n)	61	56	53
20 mg(n)	59	59	55	51	20 mg(n)	59	55	51
40 mg(n)	59	58	54	47	40 mg(n)	58	54	47
Placebo(n)	58	58	51	48	Placebo(n)	58	51	48

図 2.7.6.5.7-4　　TAC の推移－連日投与期－（ITT）

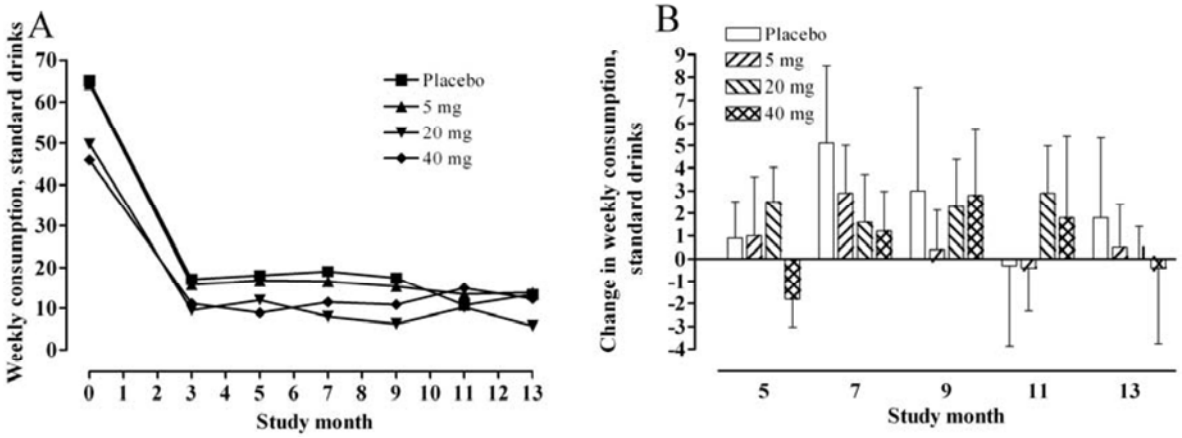
A. Median number of drinks weekly by group. B. Mean change from baseline in number of drinks weekly. Error bars are standard error of the mean.

＜資料番号 5.3.5.1-07：Text Figure 10，Text Table 38 より作成＞

表 2.7.6.5.7-13　　TAC の推移－継続投与期－（ITT）

Group		Screen	Month 3	Month 4-5	Month 6-7	Month 8-9	Month 10-11	Month 12-13
Placebo	Median	42.4	11.0	11.5	9.5	6.0	2.5	4.0
	Mean	65.0	17.1	18.0	19.0	17.4	10.7	13.4
	SD	50.4	18.8	19.0	22.0	19.1	16.6	19.1
	N	28	28	28	14	11	12	13
5 mg	Median	53.5	5.0	3.5	15.0	3.0	3.0	2.0
	Mean	64.3	15.8	16.8	16.6	15.4	13.5	13.9
	SD	38.5	25.1	26.7	18.9	23.7	23.4	22.7
	N	30	30	30	17	16	17	18
20 mg	Median	42.0	6.0	9.0	1.0	5.0	7.0	2.0
	Mean	49.8	9.5	12.0	8.0	6.3	10.2	5.8
	SD	29.9	11.6	14.4	13.4	6.5	11.7	7.7
	N	35	35	35	20	12	12	12
40 mg	Median	39.0	7.0	8.0	7.0	11.0	9.0	8.0
	Mean	45.9	11.1	8.9	11.5	10.9	15.0	12.3
	SD	26.2	14.4	10.0	13.2	9.3	17.2	13.6
	N	33	33	32	23	14	13	16

＜資料番号 5.3.5.1-07：Text Table 39＞



5 mg(n)	30	30	30	17	16	17	18	5 mg(n)	30	17	16	17	18
20 mg(n)	35	35	35	20	12	12	12	20 mg(n)	35	20	12	12	12
40 mg(n)	33	33	32	23	14	13	16	40 mg(n)	32	23	14	13	16
Placebo(n)	28	28	28	14	11	12	13	Placebo(n)	28	14	11	12	13

図 2.7.6.5.7-5　　TAC の推移－継続投与期－（ITT）

A. Weekly mean alcohol consumption in the extension population. B. Change in the consumption since month 3. Error bars are standard error of the mean.

＜資料番号 5.3.5.1-07：Text Figure 11，Text Table 39 より作成＞

連日投与期で，VHDD 数，飲酒日当たりのアルコール消費量，飲酒日数に対する HDD 数の割合，NDD 数，1 日アルコール消費量の最大値は HDD 数の結果と同様であった。

連日投与期の γ-GTP を表 2.7.6.5.7-14 に，ALT を表 2.7.6.5.7-15 に示した。また，継続投与期の臨床検査値を図 2.7.6.5.7-6 に示した。

連日投与期で，MCV 及び ALT は，ほとんど変化しなかった（資料番号：5.3.5.1-07：Text Table 45 参照）。連日投与期で，γ-GTP 及び%CDT は，いずれの投与群でも減少した（資料番号：5.3.5.1-07：Text Table 42 参照）。

表 2.7.6.5.7-14　　γ-GTP－連日投与期－（ITT）

	Placebo						5 mg						20 mg						40 mg					
	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3
Screen	68	73.6	72.7	25	53	85	68	73.5	80.9	26	47.5	87	64	75.7	82.0	29	44	77	68	86.0	135	27	44	85
Week 6	50	64.0	61.1	21.0	40	82	51	46.9	42.2	22	34	62	47	55.2	72.5	21	29	54	52	62.3	56.8	24	39	83
Week 12	50	58.4	64	20.0	37	69	50	56.7	84.8	21	29	63	47	44.4	46.3	22	31	45	49	46.6	43.4	23	33	52

Values are U/L. Reference range: Male: 0-55 (13-64 y); Female: 0-45(13-64 y); 65+y: 0-75.

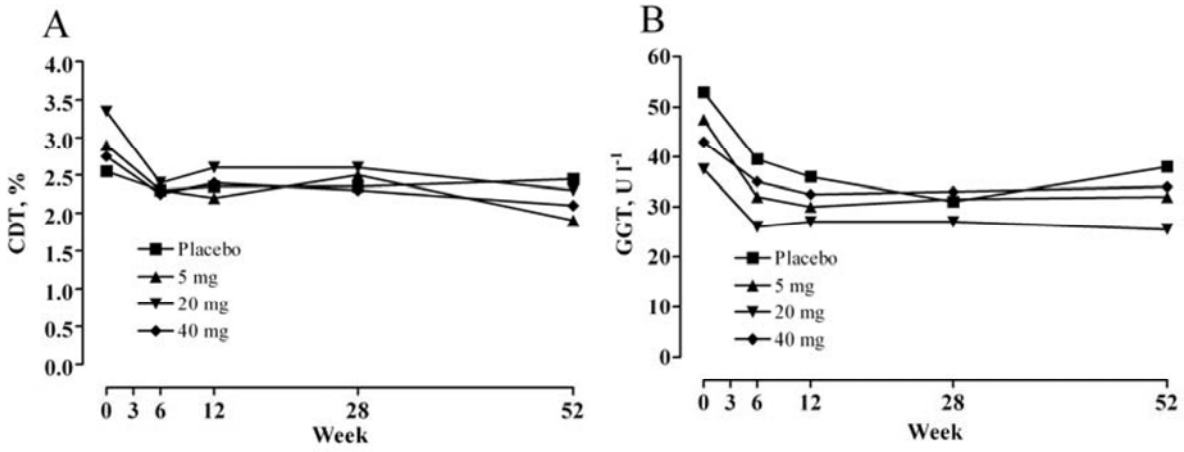
＜資料番号 5.3.5.1-07：Text Table 43＞

表 2.7.6.5.7-15　　ALT－連日投与期－（ITT）

	Placebo						5 mg						20 mg						40 mg					
	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3	N	Mean	SD	Q1	Median	Q3
Screening	68	31.9	19.8	18	26	41	68	31.8	25.1	17	23.5	37	64	30.2	20.2	16	24	36	68	29.9	24.2	16	22	35
Week 3	58	29.2	16.5	17	26	37	54	29.4	24.3	16	22.5	33	50	27.8	20.5	14	21	33	54	27.2	17.3	15	23	33
Week 6	50	28.0	15.9	16	24	36	51	28.1	21.5	16	23	32	47	25.9	22.7	13	19	25	52	24.4	13.5	14	17	33
Week 12	50	27.0	17.2	17	22	33	50	31.6	47.9	15	20	27	47	24.7	22.1	14	17	26	49	36.3	90.9	14	22	28

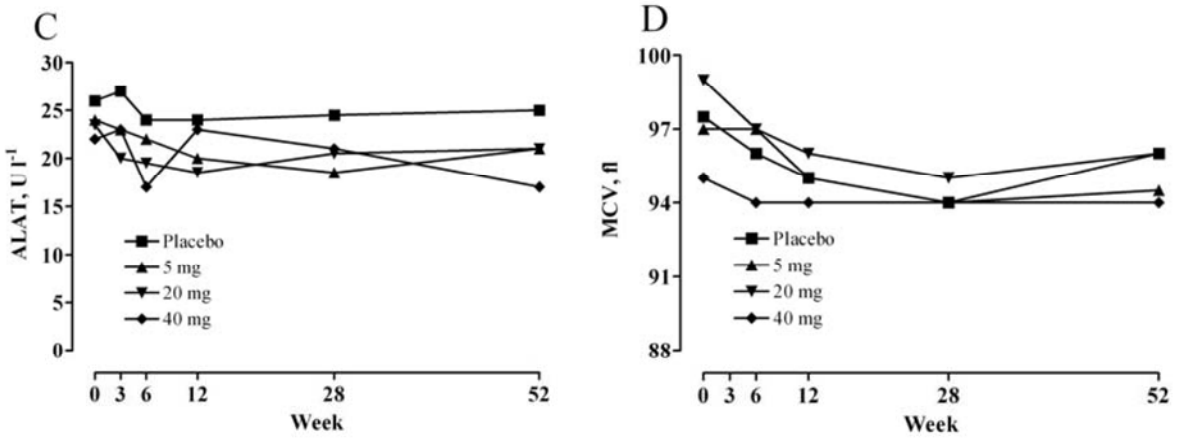
Values are U/L. Reference range: 0-42 (3-64 y), 0-55 (65+y).

＜資料番号 5.3.5.1-07：Text Table 44＞



5 mg(n)	40	38	39	25	19
20 mg(n)	38	36	37	24	13
40 mg(n)	36	34	36	25	19
Placebo(n)	38	37	38	18	16

5 mg(n)	40	38	39	26	21
20 mg(n)	38	36	36	24	16
40 mg(n)	37	35	36	27	23
Placebo(n)	39	38	39	18	21



5 mg(n)	40	37	38	39	26	21
20 mg(n)	38	37	36	36	24	16
40 mg(n)	37	36	35	36	27	23
Placebo(n)	39	39	38	39	18	21

5 mg(n)	39	37	38	25	20
20 mg(n)	39	37	38	23	17
40 mg(n)	37	35	36	27	22
Placebo(n)	38	37	38	18	21

図 2.7.6.5.7-6　　臨床検査値－継続投与期－（ITT）

A. Carbohydrate-deficient transferrin. B. Gamma-glutamyl transferase. C. Alanine aminotransferase (glutamic pyruvic transaminase). D. Mean corpuscular volume. Values are median.

GGT: γ-GTP, ALAT: ALT

＜資料番号 5.3.5.1-07：Text Figure 14＞

連日投与期で，ADS 総スコア，DrlnC，OCDS 総スコア及び近親者による評価のほとんどは，飲酒量の低減及びアルコールへの依存度の低下を示した（資料番号：5.3.5.1-07：Text Table 46，Text Table 47，Text Table 52，Text Table 55，Text Table 56 参照）。

継続投与期では，アルコール消費量に関する副次的評価項目の変化に統計学的及び臨床的に重要な群間差は認められなかった。しかし，断酒していた被験者を除いた飲酒日当たりのアルコール消費量の解析では，他の投与群より 20 mg 群で，飲酒日当たりのアルコール消費量が中量に分類された被験者が多く，超多量に分類された被験者が少ない可能性が示唆された（資料番号：5.3.5.1-07：Text Figure 13B 参照）。OCDS で，プラセボ群での再発の徴候がわずかに認

められ，干渉スケールで最も明らかであった（資料番号 : 5.3.5.1-07 : Text Figure 15 参照）。DrlnC でもプラセボ群での再発の徴候が認められた（資料番号：5.3.5.1-07：Text Figure 16 参照）。

(5) 安全性

(a) 治験薬の曝露状況

連日投与期の曝露期間を表 2.7.6.5.7-16 に，継続投与期の曝露期間を表 2.7.6.5.7-17 に示した。継続投与期では，ナルメフェン群よりプラセボ群で総曝露期間がわずかに短かった。

表 2.7.6.5.7-16　曝露期間（日）－連日投与期－（無作為化例）

	N completing	N terminating prematurely	Mean	SD	Min	Q1	Median	Q3	Max
Placebo	47	21	24.8	19.1	1	8	22	37	64
5 mg	46	22	24.9	22.3	1	8	20	47	72
20 mg	47	19	23.6	19.9	1	4	22	36	62
40 mg	43	25	28.1	21.8	5	7	21	48	65

Number of subjects completing 12 weeks of treatment, and duration of exposure in subjects terminating prematurely.
＜資料番号 5.3.5.1-07：Text Table 57＞

表 2.7.6.5.7-17　曝露期間（日）－継続投与期－（無作為化例）

	N	Mean	SD	Min	Q1	Median	Q3	Max
Placebo	39	239.9	124.9	67	125	243	364	420
5 mg	40	270.4	120.6	83	131.5	352.5	369	424
20 mg	40	264.1	107	81	170	285.5	369	386
40 mg	37	289.4	107	84	189	357	368	415

＜資料番号 5.3.5.1-07：Text Table 58＞

(b) 有害事象

連日投与期に発現割合が高かった有害事象を表 2.7.6.5.7-18 に，継続投与期に発現割合が高かった有害事象を表 2.7.6.5.7-19 に示した。また，連日投与期及び継続投与期に発現した有害事象（器官別大分類）を表 2.7.6.5.7-24 及び表 2.7.6.5.7-25 に，連日投与期及び継続投与期に発現したすべての有害事象を表 2.7.6.5.7-26 及び表 2.7.6.5.7-27 に示した。更に，連日投与期及び継続投与期の重症度別有害事象を表 2.7.6.5.7-28 及び表 2.7.6.5.7-29 に示した。

連日投与期での有害事象の発現割合は，83.3%（225/270 例）であった（資料番号 5.3.5.1-07：14.3.1.1 参照）。発現が多かった有害事象の器官別大分類は，神経系障害，胃腸障害，全身障害および投与局所様態，精神障害，筋骨格，結合組織および骨障害であった。

連日投与期で発現割合が高かった有害事象は，ナルメフェン 40 mg 群で高かった順に頭痛（33.8%），嘔気（25.0%），不眠症 NEC（22.1%）及び浮動性めまい（回転性眩暈を除く）（22.1%）であった（資料番号 5.3.5.1-07：14.3.1.2 参照）。嘔気，不眠症 NEC 及び浮動性めまいはプラセボ群よりもナルメフェン群で発現割合が高く，ナルメフェンのいずれかの用量群に対して差があった（$p < 0.150$）。

継続投与期での有害事象の発現割合は，93%（145/156 例）であった（資料番号 5.3.5.1-07：15.3.1.3.1 参照）。継続投与期で発現割合が高かった有害事象のうちプラセボ群よりナルメフェン群で発現割合が高かった有害事象は，不眠症 NEC，浮動性めまい（回転性眩暈を除く）及び嘔気であった。

表 2.7.6.5.7-18　発現割合が高かった有害事象—連日投与期—（無作為化例）

	Placebo		5 mg			20 mg			40 mg		
Event	Subjects	Events	Subjects	Events	p	Subjects	Events	p	Subjects	Events	p
頭痛NOS	15	21	16	29	1.000	20	32	0.328	23	40	0.181
嘔気	7	8	9	10	0.791	10	12	0.445	17	17	0.041[a]
浮動性めまい（回転性眩暈を除く）	8	10	19	21	0.030[a]	20	22	0.011[a]	15	15	0.169
不眠症NEC	7	7	13	13	0.226	19	20	0.009[a]	15	17	0.102[a]
疲労	9	9	10	10	1.000	4	4	0.243	8	8	1.000
インフルエンザ様疾患	7	8	8	8	1.000	2	2	0.165	7	8	1.000
下痢NOS	4	6	5	6	1.000	3	3	1.000	6	7	0.744
傾眠	1	1	4	4	0.366	5	5	0.113[a]	6	6	0.115[a]
口内乾燥	1	1	5	5	0.208	8	9	0.016[a]	5	5	0.208
消化不良	2	4	3	3	1.000	1	1	1.000	5	8	0.441
錯乱	0	0	1	1	1.000	5	5	0.027[a]	4	4	0.119[a]
皮膚炎NOS	5	7	1	1	0.208	1	2	0.208	4	4	1.000
嘔吐NOS	5	5	3	4	0.718	4	4	1.000	4	5	1.000
上腹部痛	1	2	3	3	0.619	1	1	1.000	3	4	0.619
背部痛	3	3	3	3	1.000	3	4	1.000	3	4	1.000
味覚障害	1	1	0	0	1.000	1	1	1.000	3	3	0.619
振戦NEC	0	0	4	4	0.119[a]	3	4	0.117[a]	3	4	0.244
不安NEC	4	4	1	1	0.366	4	6	1.000	2	2	0.680
食欲減退NOS	1	1	4	4	0.366	0	0	1.000	2	2	1.000
食欲亢進NOS	2	2	1	1	1.000	0	0	0.496	2	2	1.000
血圧上昇	3	3	0	0	0.244	1	1	0.619	2	2	1.000
うつ病NEC	2	4	1	1	1.000	0	0	0.496	2	2	1.000
注意力障害NEC	1	1	1	1	1.000	2	2	0.617	2	2	1.000
易刺激性	0	0	4	4	0.119[a]	0	0		2	2	0.496
関節痛	2	3	2	2	1.000	2	2	1.000	1	1	1.000
異常な夢	1	1	2	2	1.000	1	1	1.000	1	1	1.000
便秘	0	0	3	3	0.244	4	4	0.056[a]	1	1	1.000
咳嗽	0	0	3	3	0.244	2	2	0.241	1	1	1.000
耳の感染症NOS	0	0	2	2	0.496	2	2	0.241	1	1	1.000
嗜眠	0	0	3	3	0.244	1	1	0.493	1	1	1.000
リビドー減退	1	1	2	2	1.000	2	2	0.617	1	1	1.000
四肢痛	0	0	1	1	1.000	4	5	0.056[a]	1	1	1.000
腹部膨満	2	2	2	2	1.000	1	1	1.000	0	0	0.496
筋痛	2	2	3	3	1.000	2	3	1.000	0	0	0.496
そう痒症NOS	1	1	3	4	0.619	2	2	0.617	0	0	1.000
咽喉痛NOS	1	2	4	4	0.366	0	0	1.000	0	0	1.000

MedDRA Version 3.3

[a] $p < 0.150$ for no association between verum and placebo by Fisher's exact test.

＜資料番号 5.3.5.1-07：Text Table 61＞

表 2.7.6.5.7-19　発現割合が高かった有害事象—継続投与期—（無作為化例）

	Placebo		5 mg		20 mg		40 mg	
Event	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
頭痛NOS	11	18	14	34	11	29	17	33
インフルエンザ様疾患	8	8	9	10	4	4	13	19
不眠症NEC	6	6	10	11	15	23	12	19
浮動性めまい（回転性眩暈を除く）	3	4	12	14	14	16	12	12
嘔気	3	4	4	6	8	13	7	11
背部痛	4	5	3	4	4	9	4	5
皮膚炎NOS	5	7	1	1	1	1	4	4
消化不良	3	7	2	2	0	0	4	9
傾眠	1	1	3	3	3	3	4	4
嘔吐NOS	3	3	3	3	3	3	4	5
上腹部痛	1	2	2	3	1	1	3	4
胸痛NEC	1	1	0	0	2	2	3	4
うつ病NEC	3	8	1	1	1	1	3	3
下痢NOS	1	3	4	5	2	3	3	4
口内乾燥	1	1	4	4	5	5	3	3
疲労	5	6	8	9	4	4	3	3
腹痛NOS	0	0	0	0	2	2	2	2
食欲減退NOS	0	0	4	5	0	0	2	2
食欲亢進NOS	1	1	1	1	0	0	2	2
不安NEC	3	3	0	0	2	4	2	2
関節痛	1	2	2	2	3	3	2	2
血圧上昇	3	3	0	0	1	1	2	3
月経困難症	1	1	1	3	0	0	2	2
耳の感染症NOS	0	0	1	1	2	2	2	2
高血圧NOS	1	1	0	0	2	2	2	2
嗜眠	0	0	2	2	1	1	2	6
筋緊張	0	0	0	0	2	4	2	2
筋痛	1	2	2	2	1	1	2	2
副鼻腔炎NOS	0	0	2	2	0	0	2	2
異常な夢	1	1	1	1	1	1	1	1
錯乱	0	0	1	1	2	2	1	1
易刺激性	0	0	3	3	1	1	1	1
四肢痛	0	0	0	0	5	6	1	1
副鼻腔うっ血	2	2	1	1	0	0	1	1
副鼻腔炎に伴う頭痛	2	2	0	0	1	1	1	1
振戦NEC	1	1	3	3	0	0	1	1
気管支炎NOS	1	1	2	2	1	1	0	0
便秘	0	0	2	2	5	6	0	0
咳嗽	0	0	3	3	1	1	0	0
リビドー減退	1	1	1	1	2	2	0	0

MedDRA Version 3.3

＜資料番号 5.3.5.1-07：Text Table 63＞

(c)　治験薬との関連性が否定できない有害事象（副作用）

連日投与期及び継続投与期の重症度別副作用を表 2.7.6.5.7-28 及び表 2.7.6.5.7-29 に示した。

(d)　死亡，その他の重篤な有害事象

i)　死亡

本治験で死亡は報告されなかった。

ii)　その他の重篤な有害事象

連日投与期及び継続投与期の重篤な有害事象を表 2.7.6.5.7-20 及び表 2.7.6.5.7-21 に，連日投与期及び継続投与期の重篤な有害事象一覧表を表 2.7.6.5.7-22 及び表 2.7.6.5.7-23 に示した。

重篤な有害事象は，連日投与期で 4 件，継続投与期で 9 件発現し，いずれもナルメフェン群であった。これらの有害事象は通常一般的に認められるものであり，ナルメフェンの使用によるリスクの増加はないと考えられた。

表 2.7.6.5.7-20　　重篤な有害事象—連日投与期—（無作為化例）

Subject	Event as reported on the SAE report	Corresponding adverse event as coded in the clinical database	Group	Relationship/ Investigator	Relationship/ Sponsor
[redacted]	Acute appendicitis	虫垂炎	40 mg	Unlikely	Unlikely
[redacted]	Psychosis NOS	精神病性障害NOS	40 mg	Unlikely	Unlikely
[redacted]	Pain in neck, radiating down right arm	胸痛NEC	20 mg	Unlikely	Possible
[redacted]	Alcohol intoxication	急性アルコール中毒	5 mg	Unlikely	Unlikely

MedDRA Version 3.3

＜資料番号 5.3.5.1-07：Text Table 65＞

表 2.7.6.5.7-21　重篤な有害事象—継続投与期—（無作為化例）

Subject	Event as reported on the SAE report	Corresponding adverse event as coded in the clinical database	Group	Relationship/ Investigator	Relationship/ Sponsor
[redacted]	Melena	メレナ	20 mg	Unlikely	Possible
[redacted]	Viral meningitis	ウイルス性髄膜炎NEC	20 mg	Unlikely	Unlikely
[redacted]	Ankle fracture Ankle surgery	足関節部骨折 足首手術[a]	20 mg	Unlikely	Unlikely
[redacted]	Tumor removed from bladder	膀胱腫瘍切除	20 mg	Unlikely	Unlikely
[redacted]	Blood pressure of 204/140, chest discomfort, weakness in right arm	胸痛NEC	40 mg	Unlikely	Possible
[redacted]	Appendicitis	虫垂炎	20 mg	Unlikely	Unlikely
[redacted][b]	Chronic chest pain, angioplasty	呼吸困難NOS 四肢痛	40 mg	Unlikely	Unlikely
[redacted][b]	Chest pain, radiating down left arm	呼吸困難NOS 四肢痛	40 mg	Unlikely	Unlikely
[redacted]	Hospitalization for detoxification	急性アルコール中毒	20 mg	Unlikely	Unlikely

MedDRA Version 3.3

[a]Events appear as separate events in adverse event database, but ankle surgery was reported by site as follow-up information on SAE form. [b] Events are erroneously missing from section CSR 15.3.2.2, although classified as SAE in adverse event database.

＜資料番号 5.3.5.1-07：Text Table 66＞

表 2.7.6.5.7-22　重篤な有害事象一覧表—連日投与期－（無作為化例）

Inv #	Pat #	Treat-ment (mg)	Event #	Event	Primary preferred term	System organ class	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel
[redacted]	[redacted]	40	4	APPENDICITIS	虫垂炎	胃腸障害	[redacted] (59)	[redacted] (60)	SEVERE	5	RESOLVED	1
[redacted]	[redacted]	40	2	PSYCHOTIC EPISODE	精神病性障害NOS	精神障害	[redacted] (64)	[redacted] (83)	SEVERE	5	RESOLVED	2
	[redacted]	20	2	CHEST PAIN W/ON HOSPITALIZATION	胸痛NEC	全身障害および投与局所様態	[redacted] (63)	[redacted] (64)	MODERATE	7/5/3	RESOLVED	1
[redacted]	[redacted]	5	4	ALCOHOL INTOXIFICATION	急性アルコール中毒	傷害および中毒	[redacted] (38)	[redacted] (39)	SEVERE	5/6	RESOLVED	2

MedDRA Version 3.3

Actions: 1 = None, 2 = Study drug permanently discontinued, 3 = Study drug temporarily discontinued, 4 = Dose reduced, 5 = Hospitalized, 6 = Supportive, 7 = Medication, 8 = Other

Rel = Relationship: 1 = Unlikely, 2 = Possible, 3 = Probable

＜資料番号 5.3.5.1-07：14.3.2＞

表 2.7.6.5.7-23　重篤な有害事象一覧表—継続投与期—（無作為化例）

Inv #	Pat #	Treat-ment (mg)	Event	Primary preferred term	System organ class	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel
[redacted]		20	MELENA	メレナ	胃腸障害	[redacted] (109)	[redacted] (114)	SEVERE	5	RESOLVED	1
[redacted]		20	MENINGITIS (VIRAL)	ウイルス性髄膜炎NEC	感染症および寄生虫症	[redacted] (338)	[redacted] (354)	SEVERE	5	RESOLVED	1
[redacted]		20	BROKEN ANKLE	足関節部骨折	傷害および中毒	[redacted] (219)	[redacted] (220)	SEVERE	5/7	RESOLVED	1
			ANKLE SURGERY	足首手術	外科および内科処置	[redacted] (251)	[redacted] (252)	SEVERE	5/7	RESOLVED	1
			TUMOR REMOVED FROM BLADDER	膀胱腫瘍切除	外科および内科処置	[redacted] (243)	[redacted] (243)	SEVERE	6/5/7	RESOLVED	1
	[redacted]	40	HYPERTENSION/CHEST DISCOMFORT	胸痛NEC	全身障害および投与局所様態	[redacted] (87)	[redacted] (88)	SEVERE	3/5/7	RESOLVED	2
[redacted]		20	APPENDICITIS	虫垂炎	胃腸障害	[redacted] (136)	[redacted] (148)	SEVERE	5/8/7	RESOLVED	1
[redacted]		20	ALCOHOL INTOXICATION	急性アルコール中毒	傷害および中毒	[redacted] (147)	[redacted] (151)	SEVERE	5/7	RESOLVED	1

MedDRA Version 3.3

Actions: 1 = None, 2 = Study drug permanently discontinued, 3 = Study drug temporarily discontinued, 4 = Dose reduced, 5 = Hospitalized, 6 = Supportive, 7 = Medication, 8 = Other

Rel = Relationship: 1 = Unlikely, 2 = Possible, 3 = Probable

＜資料番号 5.3.5.1-07：15.3.2.2＞

(e)　投与中止に至った有害事象

連日投与期及び継続投与期の有害事象一覧表（投与中止に至った有害事象を含む）を表 2.7.6.5.7-30 及び表 2.7.6.5.7-31 に示した。

連日投与期に投与中止に至った有害事象は 23 例に発現し，その内訳はナルメフェン 5 mg 群で 4 例，20 mg 群で 9 例，40 mg 群で 8 例，プラセボ群で 2 例であった。最もよくみられた投与中止に至った有害事象は嘔気であった。継続投与期に投与中止に至った有害事象は 6 例に発現した（資料番号 5.3.5.1-07：12.3.1.3 参照）。

(f)　臨床検査

i)　治験期間を通しての臨床検査値

全試験を通していずれの臨床検査値も変動はわずかで，群間でも明らかな差は認められなかった。

ii)　個々の臨床的に重要な異常

臨床的に重要な臨床検査値の変動は認められなかった（資料番号 5.3.5.1-07：12.4.2.3 参照）。

(g)　バイタルサイン

バイタルサインはベースラインから明らかな変化は認められず，群間でも差は認められなかった。

(6)　結論

- 有効性の評価では，全投与群で HDD の顕著な減少が認められたが，ナルメフェン群とプラセボ群で統計学的に有意な差は認められなかった。
- ナルメフェンを頓用投与した継続投与期では，飲酒日当たりのアルコール消費量，OCDS 及び DrInC で，プラセボ群よりナルメフェン群で改善の可能性が示唆された。
- 全般的にナルメフェンの忍容性は良好であった。
- これまでの試験結果と同様に，発現割合が高かった有害事象は消化管に関連した事象（嘔気）及び中枢神経系に関連した事象（浮動性めまい及び不眠症 NEC）であった。

2.7.6.5.7.4　付録

(1)　有害事象

表 2.7.6.5.7-24　　有害事象の器官別大分類－連日投与期－（無作為化例）

System organ class	Placebo		5 mg			20 mg			40 mg		
	Subjects	Events	Subjects	Events	p	Subjects	Events	p	Subjects	Events	p
血液およびリンパ系障害	2	2	1	1	1.000	0	0	0.496	0	0	0.496
心臓障害	2	2	2	2	1.000	3	4	0.678	1	1	1.000
耳および迷路障害	1	2	3	3	0.619	1	1	1.000	2	3	1.000
眼障害	1	1	2	2	1.000	2	3	0.617	4	4	0.366
胃腸障害	20	37	25	44	0.466	32	41	0.033[a]	36	56	0.009[a]
全身障害および投与局所様態	20	22	19	26	1.000	15	25	0.434	21	27	1.000
肝・胆道系障害	0	0	0	0		1	1	0.493	1	1	1.000
免疫系障害	3	3	0	0	0.244	2	2	1.000	0	0	0.244
感染症および寄生虫症	2	2	6	7	0.274	7	9	0.094[a]	3	5	1.000
傷害および中毒	6	7	3	3	0.493	1	1	0.115[a]	5	7	1.000
臨床検査	4	4	3	4	1.000	2	3	0.681	7	9	0.531
代謝および栄養障害	3	3	4	5	1.000	5	5	0.489	5	5	0.718
筋骨格、結合組織および骨障害	8	9	12	15	0.468	11	15	0.465	8	11	1.000
良性および悪性新生物（嚢胞およびポリープを含む）	0	0	1	1	1.000	1	1	0.493	0	0	
神経系障害	32	48	36	79	0.607	43	99	0.039[a]	42	99	0.121[a]
精神障害	8	14	15	20	0.169	16	20	0.073[a]	16	24	0.114[a]
腎および尿路障害	3	3	1	1	0.619	2	3	1.000	1	1	0.619
生殖系および乳房障害	1	2	2	3	1.000	2	2	0.617	2	3	1.000
呼吸器、胸郭および縦隔障害	3	3	6	6	0.493	6	7	0.321	4	4	1.000
皮膚および皮下組織障害	7	9	8	11	1.000	7	11	1.000	10	12	0.605
社会環境	1	1	0	0	1.000	0	0	1.000	0	0	1.000
外科および内科処置	1	1	1	1	1.000	0	0	1.000	0	0	1.000
血管障害	0	0	1	1	1.000	4	5	0.056[a]	3	3	0.244

MedDRA Version 3.3

[a] $p < 0.150$ for no association between verum and placebo by Fisher's exact test.

＜資料番号 5.3.5.1-07：Text Table 59＞

表 2.7.6.5.7-25　有害事象の器官別大分類－継続投与期－（無作為化例）

System organ class	Placebo		5 mg		20 mg		40 mg	
	Subjects	Events	Subjects	Events	Subjects	Events	Subjects	Events
血液およびリンパ系障害	2	2	1	1	0	0	0	0
心臓障害	2	2	1	1	1	1	1	1
先天性および家族性／遺伝性障害	0	0	1	1	0	0	0	0
耳および迷路障害	1	2	3	3	6	7	2	3
眼障害	1	1	1	1	3	4	1	1
胃腸障害	15	29	16	30	22	42	18	47
全身障害および投与局所様態	16	20	17	27	12	19	18	36
肝・胆道系障害	0	0	1	1	1	1	1	1
免疫系障害	2	2	0	0	1	1	0	0
感染症および寄生虫症	3	3	8	10	8	11	8	12
傷害および中毒	7	7	4	4	5	5	7	11
臨床検査	7	7	4	5	4	4	6	9
代謝および栄養障害	2	2	5	7	5	6	4	4
筋骨格、結合組織および骨障害	7	10	9	12	9	23	10	17
良性および悪性新生物（嚢胞およびポリープを含む）	0	0	1	1	0	0	0	0
神経系障害	24	38	25	72	30	81	28	86
精神障害	8	18	9	15	10	16	10	17
腎および尿路障害	1	1	2	3	2	3	0	0
生殖系および乳房障害	1	2	1	3	3	3	3	4
呼吸器、胸郭および縦隔障害	4	4	8	8	4	4	1	1
皮膚および皮下組織障害	6	8	6	6	4	4	9	10
社会環境	1	1	0	0	0	0	0	0
外科および内科処置	2	2	2	2	1	2	0	0
血管障害	1	1	1	1	6	6	2	2

MedDRA Version 3.3

＜資料番号 5.3.5.1-07：Text Table 60＞

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
血液およびリンパ系障害															
ANY EVENT	2	2.9%	2	1	1.5%	1	1.000	0	0.0%	0	0.496	0	0.0%	0	0.496
リンパ節症	2	2.9%	2	1	1.5%	1	1.000	0	0.0%	0	0.496	0	0.0%	0	0.496
心臓障害															
ANY EVENT	2	2.9%	2	2	2.9%	2	1.000	3	4.5%	4	0.678	1	1.5%	1	1.000
徐脈NOS	2	2.9%	2	0	0.0%	0	0.496	2	3.0%	2	1.000	0	0.0%	0	0.496
不整脈NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
動悸	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	1	0.493	1	1.5%	1	1.000
頻脈NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
耳および迷路障害															
ANY EVENT	1	1.5%	2	3	4.4%	3	0.619	1	1.5%	1	1.000	2	2.9%	3	1.000
耳痛	1	1.5%	2	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
聴覚過敏	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		1	1.5%	1	1.000
乗物酔い	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
耳鳴	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		2	2.9%	2	0.496
回転性眩暈NEC	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
眼障害															
ANY EVENT	1	1.5%	1	2	2.9%	2	1.000	2	3.0%	2	0.617	4	5.9%	4	0.366
霧視	1	1.5%	1	1	1.5%	1	1.000	1	1.5%	1	1.000	1	1.5%	1	1.000
結膜出血	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
羞明	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		2	2.9%	2	0.496
視覚障害NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
胃腸障害															
ANY EVENT	20	29.4%	37	25	36.8%	44	0.466	32	48.5%	41	0.033[a]	36	52.9%	56	0.009[a]
嘔気	7	10.3%	8	9	13.2%	10	0.791	10	15.2%	12	0.445	17	25.0%	17	0.041[a]
下痢NOS	4	5.9%	6	5	7.4%	6	1.000	3	4.5%	3	1.000	6	8.8%	7	0.744
嘔吐NOS	5	7.4%	5	3	4.4%	4	0.718	4	6.1%	4	1.000	4	5.9%	5	1.000
消化不良	2	2.9%	4	3	4.4%	3	1.000	1	1.5%	1	1.000	5	7.4%	8	0.441

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
胃腸障害															
腹部膨満	2	2.9%	2	2	2.9%	2	1.000	1	1.5%	1	1.000	0	0.0%	0	0.496
上腹部痛	1	1.5%	2	3	4.4%	3	0.619	1	1.5%	1	1.000	3	4.4%	4	0.619
咽喉痛NOS	1	1.5%	2	4	5.9%	4	0.366	0	0.0%	0	1.000	0	0.0%	0	1.000
腹部硬直	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
腸雑音異常	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
口内乾燥	1	1.5%	1	5	7.4%	5	0.208	8	12.1%	9	0.016[a]	5	7.4%	5	0.208
鼓腸	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	2	2.9%	2	1.000
胃食道逆流性疾患	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
消化器不調	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
舌障害NOS	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
歯痛	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
腹痛NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	2	2.9%	2	0.496
虫垂炎	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
口唇のひび割れ	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
便秘	0	0.0%	0	3	4.4%	3	0.244	4	6.1%	4	0.056[a]	1	1.5%	1	1.000
憩室炎NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
白色便	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
吐血	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
裂孔ヘルニア	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
瘢痕ヘルニアNOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
軟便	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
食道逆流	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
口腔内痛	0	0.0%	0	0	0.0%	0		1	1.5%	2	0.493	0	0.0%	0	
悪心	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
咽喉刺激感	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
全身障害および投与局所様態															
ANY EVENT	20	29.4%	23	19	27.9%	26	1.000	15	22.7%	25	0.434	21	30.9%	27	1.000
疲労	9	13.2%	9	10	14.7%	10	1.000	4	6.1%	4	0.243	8	11.8%	8	1.000
インフルエンザ様疾患	7	10.3%	8	8	11.8%	8	1.000	2	3.0%	2	0.165	7	10.3%	8	1.000
アルコールによる宿酔	2	2.9%	2	1	1.5%	4	1.000	0	0.0%	0	0.496	0	0.0%	0	0.496
活力増進	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
上肢浮腫	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
悪寒	1	1.5%	1	0	0.0%	0	1.000	2	3.0%	2	0.617	0	0.0%	0	1.000
脱力	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	2	1.000	0	0.0%	0	1.000
胸痛NEC	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	3	4.4%	4	0.244
胸部絞扼感	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
酩酊感	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
熱感	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
びくびく感	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
嗜眠	0	0.0%	0	3	4.4%	3	0.244	1	1.5%	1	0.493	1	1.5%	1	1.000
倦怠感	0	0.0%	0	0	0.0%	0		1	1.5%	3	0.493	0	0.0%	0	
下肢浮腫	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
疼痛NOS	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	2	0.493	1	1.5%	1	1.000
発熱	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
戦慄	0	0.0%	0	0	0.0%	0		1	1.5%	2	0.493	0	0.0%	0	
不活発	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
口渇	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
肝・胆道系障害															
ANY EVENT	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
肝腫大	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
免疫系障害															
ANY EVENT	3	4.4%	3	0	0.0%	0	0.244	2	3.0%	2	1.000	0	0.0%	0	0.244
虫刺されアレルギー	2	2.9%	2	0	0.0%	0	0.496	0	0.0%	0	0.496	0	0.0%	0	0.496
複合アレルギー	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	1	1.000	0	0.0%	0	1.000
季節性アレルギー	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
感染症および寄生虫症															
ANY EVENT	2	2.9%	2	6	8.8%	7	0.274	7	10.6%	9	0.094[a]	3	4.4%	5	1.000
気管支炎NOS	1	1.5%	1	2	2.9%	2	1.000	1	1.5%	1	1.000	0	0.0%	0	1.000
蜂巣炎	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
耳の感染症NOS	0	0.0%	0	2	2.9%	2	0.496	2	3.0%	2	0.241	1	1.5%	1	1.000
感染性歯肉炎NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
単純ヘルペス	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
インフルエンザ	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
限局性感染	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
ライム病	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
外耳炎（外耳道のせつを除く）NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
咽頭炎NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
レンサ球菌性咽頭炎	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
副鼻腔炎NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
足部白癬	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
歯感染	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
ウイルス感染NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
傷害および中毒															
ANY EVENT	6	8.8%	7	3	4.4%	3	0.493	1	1.5%	1	0.115[a]	5	7.4%	7	1.000
関節捻挫	1	1.5%	2	0	0.0%	0	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
事故NOS	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
熱傷NOS	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
損傷NOS	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
傷害および中毒															
裂傷	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
交通事故	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
急性アルコール中毒	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
節足動物刺傷	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	2	1.000
頭部損傷	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
関節脱臼NEC	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
四肢損傷NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		1	1.5%	1	1.000
筋肉損傷NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
サンバーン	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
手首関節骨折	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
臨床検査															
ANY EVENT	4	5.9%	4	3	4.4%	4	1.000	2	3.0%	3	0.681	7	10.3%	9	0.531
血圧上昇	3	4.4%	3	0	0.0%	0	0.244	1	1.5%	1	0.619	2	2.9%	2	1.000
ロンベルグ徴候陽性	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	1	1.000	1	1.5%	1	1.000
血中ブドウ糖増加	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
血便	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
血中トリグリセリド増加	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
心拍数増加	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	2.9%	2	0.496
肝機能検査NOS異常	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		1	1.5%	1	1.000
血小板数減少	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
子宮頚部スミア異常	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
体重減少	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
体重増加	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
代謝および栄養障害															
ANY EVENT	3	4.4%	3	4	5.9%	5	1.000	5	7.6%	5	0.489	5	7.4%	5	0.718
食欲亢進NOS	2	2.9%	2	1	1.5%	1	1.000	0	0.0%	0	0.496	2	2.9%	2	1.000
食欲減退NOS	1	1.5%	1	4	5.9%	4	0.366	0	0.0%	0	1.000	2	2.9%	2	1.000
食欲不振	0	0.0%	0	0	0.0%	0		3	4.5%	3	0.117[a]	1	1.5%	1	1.000
体液貯留	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
高血糖NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
筋骨格、結合組織および骨障害															
ANY EVENT	8	11.8%	9	12	17.6%	15	0.468	11	16.7%	15	0.465	8	11.8%	11	1.000
関節痛	2	2.9%	3	2	2.9%	2	1.000	2	3.0%	2	1.000	1	1.5%	1	1.000
背部痛	3	4.4%	3	3	4.4%	3	1.000	3	4.5%	4	1.000	3	4.4%	4	1.000
筋痛	2	2.9%	2	3	4.4%	3	1.000	2	3.0%	3	1.000	0	0.0%	0	0.496
脊柱後弯症	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
滑液包炎	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
関節運動範囲減少	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
筋痙攣	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
筋痙縮	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
筋緊張	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	1	0.493	0	0.0%	0	
筋攣縮	0	0.0%	0	2	2.9%	2	0.496	0	0.0%	0		0	0.0%	0	
頚部痛	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		1	1.5%	1	1.000
頚部硬直	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	2.9%	2	0.496
四肢痛	0	0.0%	0	1	1.5%	1	1.000	4	6.1%	5	0.056[a]	1	1.5%	1	1.000
良性および悪性新生物（嚢胞およびポリープを含む）															
ANY EVENT	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	1	0.493	0	0.0%	0	
乳房塊状物NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
嚢胞NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
神経系障害															
ANY EVENT	32	47.1%	48	36	52.9%	79	0.607	43	65.2%	99	0.039[a]	42	61.8%	99	0.121[a]
頭痛NOS	15	22.1%	21	16	23.5%	29	1.000	20	30.3%	32	0.328	23	33.8%	40	0.181
浮動性めまい（回転性眩暈を除く）	8	11.8%	10	19	27.9%	21	0.030[a]	20	30.3%	22	0.011[a]	15	22.1%	15	0.169
不眠症NEC	7	10.3%	7	13	19.1%	13	0.226	19	28.8%	20	0.009[a]	15	22.1%	17	0.102[a]
活動亢進	2	2.9%	2	1	1.5%	1	1.000	0	0.0%	0	0.496	0	0.0%	0	0.496
注意力障害NEC	1	1.5%	1	1	1.5%	1	1.000	2	3.0%	2	0.617	2	2.9%	2	1.000
舌下神経障害NOS	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
中期不眠症	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	1	1.000	2	2.9%	2	1.000
錯感覚NEC	1	1.5%	1	2	2.9%	2	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
橈骨神経麻痺	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
副鼻腔炎に伴う頭痛	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	1	1.000	0	0.0%	0	1.000
傾眠	1	1.5%	1	4	5.9%	4	0.366	5	7.6%	5	0.113[a]	6	8.8%	6	0.115[a]
味覚障害	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	1	1.000	3	4.4%	3	0.619
失調NEC	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
手根管症候群	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
小脳症候群	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
意識レベルの低下	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
構語障害	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	2.9%	2	0.496
知覚過敏	0	0.0%	0	0	0.0%	0		2	3.0%	2	0.241	0	0.0%	0	
反射亢進	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
筋緊張亢進	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
感覚減退	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
反射減弱	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
初期不眠症	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
片頭痛NOS	0	0.0%	0	0	0.0%	0		1	1.5%	2	0.493	1	1.5%	1	1.000

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
神経系障害															
不随意性筋収縮	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
神経圧迫	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
下肢静止不能症候群	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
鎮静	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	2	2.9%	2	0.496
会話障害NEC	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
振戦NEC	0	0.0%	0	4	5.9%	4	0.119[a]	3	4.5%	4	0.117[a]	3	4.4%	4	0.244
精神障害															
ANY EVENT	8	11.8%	14	15	22.1%	20	0.169	16	24.2%	20	0.073[a]	16	23.5%	24	0.114[a]
不安NEC	4	5.9%	4	1	1.5%	1	0.366	4	6.1%	6	1.000	2	2.9%	2	0.680
うつ病NEC	2	2.9%	4	1	1.5%	1	1.000	0	0.0%	0	0.496	2	2.9%	2	1.000
不安増強	1	1.5%	2	0	0.0%	0	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
異常な夢	1	1.5%	1	2	2.9%	2	1.000	1	1.5%	1	1.000	1	1.5%	1	1.000
抑うつ気分を伴う適応障害	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
リビドー減退	1	1.5%	1	2	2.9%	2	1.000	2	3.0%	2	0.617	1	1.5%	1	1.000
妄想症	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
激越	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
アルコール離脱症状	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
怒り	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
錯乱	0	0.0%	0	1	1.5%	1	1.000	5	7.6%	5	0.027[a]	4	5.9%	4	0.119[a]
泣き	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
失見当識	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	1	0.493	1	1.5%	1	1.000
解離	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	1	0.493	1	1.5%	1	1.000
幻覚NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
せっかち	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
易刺激性	0	0.0%	0	4	5.9%	4	0.119[a]	0	0.0%	0		2	2.9%	2	0.496

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
精神障害															
気分変動NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
気分動揺	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
神経過敏	0	0.0%	0	1	1.5%	1	1.000	1	1.5%	1	0.493	1	1.5%	1	1.000
悪夢	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
人格変化	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
早漏	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
精神病性障害NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
落ち着きのなさ	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
睡眠障害NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		1	1.5%	1	1.000
腎および尿路障害															
ANY EVENT	3	4.4%	3	1	1.5%	1	0.619	2	3.0%	3	1.000	1	1.5%	1	0.619
排尿障害	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
頻尿	1	1.5%	1	1	1.5%	1	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
尿変色	1	1.5%	1	0	0.0%	0	1.000	1	1.5%	1	1.000	0	0.0%	0	1.000
腰部痛	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
夜間頻尿	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
生殖系および乳房障害															
ANY EVENT	1	1.5%	2	2	2.9%	3	1.000	2	3.0%	2	0.617	2	2.9%	3	1.000
月経困難症	1	1.5%	1	1	1.5%	2	1.000	0	0.0%	0	1.000	1	1.5%	1	1.000
月経前症候群	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
乳房圧痛	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
射精障害NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
勃起力減退	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
精巣嚢胞	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
腟出血	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
呼吸器、胸郭および縦隔障害															
ANY EVENT	3	4.4%	3	6	8.8%	6	0.493	6	9.1%	7	0.321	4	5.9%	4	1.000
副鼻腔痛	2	2.9%	2	1	1.5%	1	1.000	0	0.0%	0	0.496	0	0.0%	0	0.496
鼻閉	1	1.5%	1	1	1.5%	1	1.000	1	1.5%	1	1.000	0	0.0%	0	1.000
喘息NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
咳嗽	0	0.0%	0	3	4.4%	3	0.244	2	3.0%	2	0.241	1	1.5%	1	1.000
呼吸困難NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
後鼻漏	0	0.0%	0	0	0.0%	0		2	3.0%	2	0.241	0	0.0%	0	
鼻漏	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
副鼻腔うっ血	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		1	1.5%	1	1.000
皮膚および皮下組織障害															
ANY EVENT	7	10.3%	9	8	11.8%	11	1.000	7	10.6%	11	1.000	10	14.7%	12	0.605
皮膚炎NOS	5	7.4%	7	1	1.5%	1	0.208	1	1.5%	2	0.208	4	5.9%	4	1.000
接触性皮膚炎	1	1.5%	1	2	2.9%	3	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
そう痒症NOS	1	1.5%	1	3	4.4%	4	0.619	2	3.0%	2	0.617	0	0.0%	0	1.000
ざ瘡NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
冷湿	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
ざ瘡様皮膚炎	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
紅斑性単純性皮膚炎	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
皮膚描記症	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
寝汗	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	1	1.5%	1	1.000
斑状丘疹状皮疹	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
丘疹	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
皮膚変色	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
皮膚小結節	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
多汗	0	0.0%	0	2	2.9%	2	0.496	2	3.0%	3	0.241	0	0.0%	0	
蕁麻疹NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	2.9%	2	0.496

表 2.7.6.5.7-26　すべての有害事象－連日投与期－（無作為化例）（続き）

	0 mg (N = 68)			5 mg (N = 68)				20 mg (N = 66)				40 mg (N = 68)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
社会環境															
ANY EVENT	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
薬物乱用	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
外科および内科処置															
ANY EVENT	1	1.5%	1	1	1.5%	1	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
口腔手術NOS	1	1.5%	1	0	0.0%	0	1.000	0	0.0%	0	1.000	0	0.0%	0	1.000
抜歯NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	
血管障害															
ANY EVENT	0	0.0%	0	1	1.5%	1	1.000	4	6.1%	5	0.056[a]	3	4.4%	3	0.244
潮紅	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	1.5%	1	1.000
ほてりNOS	0	0.0%	0	0	0.0%	0		2	3.0%	3	0.241	0	0.0%	0	
高血圧NOS	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	2	2.9%	2	0.496
不安定血圧	0	0.0%	0	0	0.0%	0		1	1.5%	1	0.493	0	0.0%	0	
リンパ浮腫NOS	0	0.0%	0	1	1.5%	1	1.000	0	0.0%	0		0	0.0%	0	

MedDRA Version 3.3

p = Ho: No association between active treatment and placebo, fisher's exact test

[a]P-value < 0.150

＜資料番号 5.3.5.1-07：14.3.1.2＞

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
血液およびリンパ系障害															
ANY EVENT	2	5.1%	2	1	2.5%	1	0.615	0	0.0%	0	0.241	0	0.0%	0	0.494
リンパ節症	2	5.1%	2	1	2.5%	1	0.615	0	0.0%	0	0.241	0	0.0%	0	0.494
心臓障害															
ANY EVENT	2	5.1%	2	1	2.5%	1	0.615	1	2.5%	1	0.615	1	2.7%	1	1.000
徐脈NOS	2	5.1%	2	0	0.0%	0	0.241	1	2.5%	1	0.615	0	0.0%	0	0.494
冠動脈疾患NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
頻脈NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
先天性および家族性／遺伝性障害															
ANY EVENT	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
表皮母斑	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
耳および迷路障害															
ANY EVENT	1	2.6%	2	3	7.5%	3	0.615	6	15.0%	7	0.108[a]	2	5.4%	3	0.610
耳痛	1	2.6%	2	0	0.0%	0	0.494	2	5.0%	2	1.000	0	0.0%	0	1.000
耳垢栓塞	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
耳の障害NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
外耳障害NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
聴覚過敏	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
乗物酔い	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
耳鳴	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		1	2.7%	1	0.487
鼓膜障害NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
回転性眩暈NEC	0	0.0%	0	0	0.0%	0		3	7.5%	3	0.241	0	0.0%	0	
眼障害															
ANY EVENT	1	2.6%	1	1	2.5%	1	1.000	3	7.5%	4	0.615	1	2.7%	1	1.000
霧視	1	2.6%	1	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	1.000
結膜出血	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
羞明	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
視覚障害NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
胃腸障害															
ANY EVENT	15	38.5%	29	16	40.0%	30	1.000	22	55.0%	42	0.178	18	48.6%	47	0.488
消化不良	3	7.7%	7	2	5.0%	2	0.675	0	0.0%	0	0.116[a]	4	10.8%	9	0.708
嘔気	3	7.7%	4	4	10.0%	6	1.000	8	20.0%	13	0.193	7	18.9%	11	0.186
嘔吐NOS	3	7.7%	3	3	7.5%	3	1.000	3	7.5%	3	1.000	4	10.8%	5	0.708
腹部膨満	1	2.6%	1	0	0.0%	0	0.494	1	2.5%	1	1.000	0	0.0%	0	1.000
上腹部痛	1	2.6%	2	2	5.0%	3	1.000	1	2.5%	1	1.000	3	8.1%	4	0.352
腹部硬直	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
腸雑音異常	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
下痢NOS	1	2.6%	3	4	10.0%	5	0.359	2	5.0%	3	1.000	3	8.1%	4	0.352
口内乾燥	1	2.6%	1	4	10.0%	4	0.359	5	12.5%	5	0.201	3	8.1%	3	0.352
鼓腸	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	2	5.4%	2	0.610
消化器不調	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
咽喉痛NOS	1	2.6%	2	1	2.5%	1	1.000	0	0.0%	0	0.494	0	0.0%	0	1.000
舌障害NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
歯痛	1	2.6%	1	1	2.5%	1	1.000	0	0.0%	0	0.494	1	2.7%	1	1.000
腹痛NOS	0	0.0%	0	0	0.0%	0		2	5.0%	2	0.494	2	5.4%	2	0.234
虫垂炎	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
口唇のひび割れ	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
口唇炎	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
便秘	0	0.0%	0	2	5.0%	2	0.494	5	12.5%	6	0.055[a]	0	0.0%	0	
白色便	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
出血性胃潰瘍	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
瘢痕ヘルニアNOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
軟便	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
メレナ	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
食道逆流	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
口腔内痛	0	0.0%	0	0	0.0%	0		1	2.5%	2	1.000	0	0.0%	0	

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
胃腸障害															
直腸出血	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
悪心	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
咽喉刺激感	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
全身障害および投与局所様態															
ANY EVENT	16	41.0%	20	17	42.5%	27	1.000	12	30.0%	19	0.352	18	48.6%	36	0.645
インフルエンザ様疾患	8	20.5%	8	9	22.5%	10	1.000	4	10.0%	4	0.225	13	35.1%	19	0.202
疲労	5	12.8%	6	8	20.0%	9	0.546	4	10.0%	4	0.737	3	8.1%	3	0.712
アルコールによる宿酔	2	5.1%	2	1	2.5%	4	0.615	0	0.0%	0	0.241	0	0.0%	0	0.494
胸痛NEC	1	2.6%	1	0	0.0%	0	0.494	2	5.0%	2	1.000	3	8.1%	4	0.352
活力増進	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
悪寒	1	2.6%	1	0	0.0%	0	0.494	1	2.5%	1	1.000	0	0.0%	0	1.000
脱力	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
胸部絞扼感	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
酩酊感	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
びくびく感	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
嗜眠	0	0.0%	0	2	5.0%	2	0.494	1	2.5%	1	1.000	2	5.4%	6	0.234
倦怠感	0	0.0%	0	0	0.0%	0		1	2.5%	3	1.000	0	0.0%	0	
下肢浮腫	0	0.0%	0	0	0.0%	0		2	5.0%	2	0.494	0	0.0%	0	
疼痛NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		1	2.7%	1	0.487
発熱	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
不活発	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
口渇	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
肝・胆道系障害															
ANY EVENT	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	1	2.7%	1	0.487
肝腫大	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	1	2.7%	1	0.487

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
免疫系障害															
ANY EVENT	2	5.1%	2	0	0.0%	0	0.241	1	2.5%	1	0.615	0	0.0%	0	0.494
虫刺されアレルギー	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
複合アレルギー	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
季節性アレルギー	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
感染症および寄生虫症															
ANY EVENT	3	7.7%	3	8	20.0%	10	0.193	8	20.0%	11	0.193	8	21.6%	12	0.109[a]
気管支炎NOS	1	2.6%	1	2	5.0%	2	1.000	1	2.5%	1	1.000	0	0.0%	0	1.000
気道感染NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
ウイルス感染NOS	1	2.6%	1	1	2.5%	1	1.000	0	0.0%	0	0.494	0	0.0%	0	1.000
デング熱	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
耳の感染症NOS	0	0.0%	0	1	2.5%	1	1.000	2	5.0%	2	0.494	2	5.4%	2	0.234
ウイルス性胃腸炎NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	2	5.4%	2	0.234
C型肝炎	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
単純ヘルペス	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
帯状疱疹	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
インフルエンザ	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
限局性感染	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
ウイルス性髄膜炎NEC	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
外耳炎（外耳道のせつを除く）NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
咽頭炎NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
レンサ球菌性咽頭炎	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
副鼻腔炎NOS	0	0.0%	0	2	5.0%	2	0.494	0	0.0%	0		2	5.4%	2	0.234
皮膚感染症NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
歯膿瘍	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
歯感染	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
上気道感染NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	5.4%	2	0.234

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
感染症および寄生虫症															
尿路感染NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
傷害および中毒															
ANY EVENT	7	17.9%	7	4	10.0%	4	0.348	5	12.5%	5	0.546	7	18.9%	11	1.000
事故NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
咬刺傷NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
熱傷NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
損傷NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	1	2.7%	1	1.000
関節脱臼NEC	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
裂傷	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	2	5.4%	2	0.610
交通事故	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
急性アルコール中毒	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	
足関節部骨折	0	0.0%	0	0	0.0%	0		2	5.0%	2	0.494	0	0.0%	0	
節足動物咬傷	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
上顆炎	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
顔面骨骨折	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
頭部損傷	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
関節捻挫	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
四肢損傷NOS	0	0.0%	0	2	5.0%	2	0.494	0	0.0%	0		1	2.7%	1	0.487
筋肉損傷NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
肋骨骨折	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
サンバーン	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
腱損傷	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
腱断裂	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
臨床検査															
ANY EVENT	7	17.9%	7	4	10.0%	5	0.348	4	10.0%	4	0.348	6	16.2%	9	1.000
血圧上昇	3	7.7%	3	0	0.0%	0	0.116[a]	1	2.5%	1	0.359	2	5.4%	3	1.000
血中コレステロール増加	2	5.1%	2	0	0.0%	0	0.241	0	0.0%	0	0.241	0	0.0%	0	0.494
心電図異常NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
ロンベルグ徴候陽性	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	1	2.7%	1	1.000
血中ブドウ糖増加	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
血中トリグリセリド増加	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
心拍数増加	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
心音異常	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	
肝機能検査NOS異常	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	1	2.7%	1	0.487
血小板数減少	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
子宮頚部スミア異常	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
体重減少	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		1	2.7%	1	0.487
体重増加	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
代謝および栄養障害															
ANY EVENT	2	5.1%	2	5	12.5%	7	0.432	5	12.5%	6	0.432	4	10.8%	4	0.425
食欲亢進NOS	1	2.6%	1	1	2.5%	1	1.000	0	0.0%	0	0.494	2	5.4%	2	0.610
ヘモクロマトーシス	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
食欲不振	0	0.0%	0	0	0.0%	0		2	5.0%	2	0.494	0	0.0%	0	
食欲減退NOS	0	0.0%	0	4	10.0%	5	0.116[a]	0	0.0%	0		2	5.4%	2	0.234
糖尿病NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
体液貯留	0	0.0%	0	0	0.0%	0		1	2.5%	2	1.000	0	0.0%	0	
高血糖NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
高脂血症NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
筋骨格、結合組織および骨障害															
ANY EVENT	7	17.9%	10	9	22.5%	12	0.781	9	22.5%	23	0.781	10	27.0%	17	0.414
背部痛	4	10.3%	5	3	7.5%	4	0.712	4	10.0%	9	1.000	4	10.8%	5	1.000
関節痛	1	2.6%	2	2	5.0%	2	1.000	3	7.5%	3	0.615	2	5.4%	2	0.610
脊柱後弯症	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
筋痛	1	2.6%	2	2	5.0%	2	1.000	1	2.5%	1	1.000	2	5.4%	2	0.610
骨棘	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
滑液包炎	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
椎間板ヘルニア	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
関節運動範囲減少	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
関節硬直	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
筋緊張	0	0.0%	0	0	0.0%	0		2	5.0%	4	0.494	2	5.4%	2	0.234
筋攣縮	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
頚部痛	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
頚部硬直	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	5.4%	2	0.234
四肢痛	0	0.0%	0	0	0.0%	0		5	12.5%	6	0.055[a]	1	2.7%	1	0.487
良性および悪性新生物（嚢胞およびポリープを含む）															
ANY EVENT	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
嚢胞NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
神経系障害															
ANY EVENT	24	61.5%	38	25	62.5%	72	1.000	30	75.0%	81	0.232	28	75.7%	86	0.222
頭痛NOS	11	28.2%	18	14	35.0%	34	0.630	11	27.5%	29	1.000	17	45.9%	33	0.154
不眠症NEC	6	15.4%	6	10	25.0%	11	0.402	15	37.5%	23	0.041[a]	12	32.4%	19	0.107[a]
浮動性めまい（回転性眩暈を除く）	3	7.7%	4	12	30.0%	14	0.020[a]	14	35.0%	16	0.005[a]	12	32.4%	12	0.009[a]
副鼻腔炎に伴う頭痛	2	5.1%	2	0	0.0%	0	0.241	1	2.5%	1	0.615	1	2.7%	1	1.000
舌下神経障害NOS	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
中期不眠症	1	2.6%	1	0	0.0%	0	0.494	1	2.5%	1	1.000	1	2.7%	1	1.000

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
神経系障害															
神経圧迫	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	1	2.7%	1	1.000
橈骨神経麻痺	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
傾眠	1	2.6%	1	3	7.5%	3	0.615	3	7.5%	3	0.615	4	10.8%	4	0.194
失神	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
味覚障害	1	2.6%	1	0	0.0%	0	0.494	1	2.5%	1	1.000	0	0.0%	0	1.000
振戦NEC	1	2.6%	1	3	7.5%	3	0.615	0	0.0%	0	0.494	1	2.7%	1	1.000
失調NEC	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
手根管症候群	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
小脳症候群	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
意識レベルの低下	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
注意力障害NEC	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
構語障害	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	5.4%	2	0.234
知覚過敏	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
反射亢進	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
筋緊張亢進	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	3	0.487
感覚減退	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
反射減弱	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	
活動亢進	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
片頭痛NOS	0	0.0%	0	0	0.0%	0		1	2.5%	2	1.000	1	2.7%	1	0.487
不随意性筋収縮	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
錯感覚NEC	0	0.0%	0	2	5.0%	2	0.494	0	0.0%	0		1	2.7%	1	0.487
末梢性ニューロパシーNEC	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
鎮静	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	5.4%	2	0.234
精神障害															
ANY EVENT	8	20.5%	18	9	22.5%	15	1.000	10	25.0%	16	0.790	10	27.0%	17	0.594
不安NEC	3	7.7%	3	0	0.0%	0	0.116[a]	2	5.0%	4	0.675	2	5.4%	2	1.000

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
精神障害															
うつ病NEC	3	7.7%	8	1	2.5%	1	0.359	1	2.5%	1	0.359	3	8.1%	3	1.000
異常な夢	1	2.6%	1	1	2.5%	1	1.000	1	2.5%	1	1.000	1	2.7%	1	1.000
リビドー減退	1	2.6%	1	1	2.5%	1	1.000	2	5.0%	2	1.000	0	0.0%	0	1.000
悪夢	1	2.6%	1	0	0.0%	0	0.494	1	2.5%	1	1.000	0	0.0%	0	1.000
パニック発作	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	1	2.7%	1	1.000
妄想症	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
自殺念慮	1	2.6%	2	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
アルコール離脱症状	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
注意欠陥多動性障害	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
錯乱	0	0.0%	0	1	2.5%	1	1.000	2	5.0%	2	0.494	1	2.7%	1	0.487
泣き	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
抑うつ気分	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	
失見当識	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
解離	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
不安増強	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		1	2.7%	1	0.487
幻覚NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
せっかち	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
易刺激性	0	0.0%	0	3	7.5%	3	0.241	1	2.5%	1	1.000	1	2.7%	1	0.487
気分変動NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
気分障害NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
気分動揺	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
神経過敏	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
人格変化	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
早漏	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
落ち着きのなさ	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
睡眠障害NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
腎および尿路障害															
ANY EVENT	1	2.6%	1	2	5.0%	3	1.000	2	5.0%	3	1.000	0	0.0%	0	1.000
排尿困難	1	2.6%	1	0	0.0%	0	0.494	1	2.5%	1	1.000	0	0.0%	0	1.000
夜間頻尿	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
頻尿	0	0.0%	0	2	5.0%	3	0.494	0	0.0%	0		0	0.0%	0	
尿変色	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
生殖系および乳房障害															
ANY EVENT	1	2.6%	2	1	2.5%	3	1.000	3	7.5%	3	0.615	3	8.1%	4	0.352
月経困難症	1	2.6%	1	1	2.5%	3	1.000	0	0.0%	0	0.494	2	5.4%	2	0.610
月経前症候群	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
良性前立腺肥大症	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
射精障害NOS	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
勃起力減退	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
精巣嚢胞	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
腟分泌物	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
呼吸器、胸郭および縦隔障害															
ANY EVENT	4	10.3%	4	8	20.0%	8	0.348	4	10.0%	4	1.000	1	2.7%	1	0.359
副鼻腔うっ血	2	5.1%	2	1	2.5%	1	0.615	0	0.0%	0	0.241	1	2.7%	1	1.000
鼻閉	1	2.6%	1	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	1.000
副鼻腔痛	1	2.6%	1	1	2.5%	1	1.000	0	0.0%	0	0.494	0	0.0%	0	1.000
咳嗽	0	0.0%	0	3	7.5%	3	0.241	1	2.5%	1	1.000	0	0.0%	0	
後鼻漏	0	0.0%	0	0	0.0%	0		2	5.0%	2	0.494	0	0.0%	0	
鼻炎NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
喘鳴音	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
皮膚および皮下組織障害															
ANY EVENT	6	15.4%	8	6	15.0%	6	1.000	4	10.0%	4	0.518	9	24.3%	10	0.395
皮膚炎NOS	5	12.8%	7	1	2.5%	1	0.108[a]	1	2.5%	1	0.108[a]	4	10.8%	4	1.000
接触性皮膚炎	1	2.6%	1	1	2.5%	1	1.000	0	0.0%	0	0.494	0	0.0%	0	1.000
ざ瘡様皮膚炎	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
紅斑性単純性皮膚炎	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
過角化	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
寝汗	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	1	2.7%	1	0.487
そう痒症NOS	0	0.0%	0	1	2.5%	1	1.000	1	2.5%	1	1.000	0	0.0%	0	
斑状丘疹状皮疹	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
ひび・あかぎれ	0	0.0%	0	0	0.0%	0		0	0.0%	0		1	2.7%	1	0.487
皮膚色素過剰	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
多汗	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
蕁麻疹NOS	0	0.0%	0	0	0.0%	0		0	0.0%	0		2	5.4%	2	0.234
社会環境															
ANY EVENT	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
薬物乱用	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
外科および内科処置															
ANY EVENT	2	5.1%	2	2	5.0%	2	1.000	1	2.5%	2	0.615	0	0.0%	0	0.494
関節注入	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
疣贅切除	1	2.6%	1	0	0.0%	0	0.494	0	0.0%	0	0.494	0	0.0%	0	1.000
足首手術	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
膀胱腫瘍切除	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
整形外科的処置	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	
抜歯NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	

表 2.7.6.5.7-27　すべての有害事象－継続投与期－（無作為化例）（続き）

	0 mg (N = 39)			5 mg (N = 40)				20 mg (N = 40)				40 mg (N = 37)			
	# With event	PCT of PAT	Total events	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =	# With event	PCT of PAT	Total events	p =
血管障害															
ANY EVENT	1	2.6%	1	1	2.5%	1	1.000	6	15.0%	6	0.108[a]	2	5.4%	2	0.610
高血圧NOS	1	2.6%	1	0	0.0%	0	0.494	2	5.0%	2	1.000	2	5.4%	2	0.610
ほてりNOS	0	0.0%	0	0	0.0%	0		3	7.5%	3	0.241	0	0.0%	0	
不安定血圧	0	0.0%	0	0	0.0%	0		1	2.5%	1	1.000	0	0.0%	0	
リンパ浮腫NOS	0	0.0%	0	1	2.5%	1	1.000	0	0.0%	0		0	0.0%	0	

MedDRA Version 3.3

p = Ho: No association between active treatment and placebo, fisher's exact test

[a]P-value < 0.150

＜資料番号 5.3.5.1-07：15.3.1.3.2＞

(2) 重症度別有害事象及び副作用

表 2.7.6.5.7-28 重症度別有害事象及び副作用－連日投与期－（無作為化例）

		Patients		Total	Severity of events			Relationship to study med			Outcome		
	Patients at risk	reporting event at least once		number of events	Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
血液およびリンパ系障害													
ANY EVENT													
0 mg	68	2	2.9%	2									
5 mg	68	1	1.5%	1									
20 mg	66	0	0.0%	0									
40 mg	68	0	0.0%	0									
リンパ節症 (Blood)													
0 mg	68	2	2.9%	2	1	1	0	1	1	0	1	1	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
心臓障害													
ANY EVENT													
0 mg	68	2	2.9%	2									
5 mg	68	2	2.9%	2									
20 mg	66	3	4.5%	4									
40 mg	68	1	1.5%	1									
徐脈NOS (Card)													
0 mg	68	2	2.9%	2	2	0	0	0	2	0	2	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	2	3.0%	2	1	1	0	1	1	0	1	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
不整脈NOS (Card)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
動悸 (Card)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	1	1.5%	1	0	0	1	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	1	0	0	0	1	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
心臓障害													
頻脈NOS (Card)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳および迷路障害													
ANY EVENT													
0 mg	68	1	1.5%	2									
5 mg	68	3	4.4%	3									
20 mg	66	1	1.5%	1									
40 mg	68	2	2.9%	3									
耳痛 (Ear)													
0 mg	68	1	1.5%	2	2	0	0	2	0	0	1	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
聴覚過敏 (Ear)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
乗物酔い (Ear)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳鳴 (Ear)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	0	1	1	1	1	0	1	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
耳および迷路障害													
回転性眩暈NEC (Ear)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
眼障害													
ANY EVENT													
0 mg	68	1	1.5%	1									
5 mg	68	2	2.9%	2									
20 mg	66	2	3.0%	2									
40 mg	68	4	5.9%	4									
霧視 (Eye)													
0 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	0	1	0	0	1	0	1	0
結膜出血 (Eye)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
羞明 (Eye)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	1	1	0	2	0	0	1	1	0
視覚障害NOS (Eye)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
ANY EVENT													
0 mg	68	20	29.4%	37									
5 mg	68	25	36.8%	44									
20 mg	66	32	48.5%	41									
40 mg	68	36	52.9%	56									
嘔気 (Gastr)													
0 mg	68	7	10.3%	8	3	5	0	1	5	2	2	6	0
5 mg	68	9	13.2%	10	4	5	1	1	5	4	0	10	0
20 mg	66	10	15.2%	12	4	6	2	0	6	6	1	11	0
40 mg	68	17	25.0%	17	5	11	1	0	8	9	4	13	0
下痢NOS (Gastr)													
0 mg	68	4	5.9%	6	3	2	1	1	5	0	0	5	1
5 mg	68	5	7.4%	6	2	4	0	2	4	0	0	6	0
20 mg	66	3	4.5%	3	2	1	0	1	2	0	0	3	0
40 mg	68	6	8.8%	7	2	5	0	2	5	0	1	6	0
嘔吐NOS (Gastr)													
0 mg	68	5	7.4%	5	2	3	0	3	2	0	0	5	0
5 mg	68	3	4.4%	4	0	0	4	1	3	0	0	4	0
20 mg	66	4	6.1%	4	0	3	1	1	2	1	0	4	0
40 mg	68	4	5.9%	5	0	2	3	1	3	1	0	5	0
消化不良 (Gastr)													
0 mg	68	2	2.9%	4	4	0	0	1	3	0	0	4	0
5 mg	68	3	4.4%	3	1	2	0	1	1	1	0	3	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	5	7.4%	8	4	4	0	3	5	0	0	8	0
腹部膨満 (Gastr)													
0 mg	68	2	2.9%	2	2	0	0	0	1	1	1	1	0
5 mg	68	2	2.9%	2	1	1	0	2	0	0	1	1	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
上腹部痛 (Gastr)													
0 mg	68	1	1.5%	2	0	2	0	2	0	0	1	1	0
5 mg	68	3	4.4%	3	0	3	0	1	1	1	0	3	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	3	4.4%	4	2	1	1	2	2	0	1	2	1
咽喉痛NOS (Gastr)													
0 mg	68	1	1.5%	2	1	1	0	2	0	0	1	1	0
5 mg	68	4	5.9%	4	2	2	0	3	1	0	0	4	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
腹部硬直 (Gastr)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
腸雑音異常 (Gastr)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
口内乾燥 (Gastr)													
0 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
5 mg	68	5	7.4%	5	2	1	2	1	1	3	0	5	0
20 mg	66	8	12.1%	9	4	5	0	1	6	2	3	6	0
40 mg	68	5	7.4%	5	1	3	1	1	3	1	0	5	0
鼓腸 (Gastr)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	2	0	0	1	1	0	0	2	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
胃食道逆流性疾患 (Gastr)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
消化器不調 (Gastr)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
舌障害NOS (Gastr)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
歯痛 (Gastr)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
腹痛NOS (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	0	1	0	0	1	0	1	0
40 mg	68	2	2.9%	2	1	1	0	1	0	1	0	2	0
虫垂炎 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
口唇のひび割れ (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
便秘 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	3	4.4%	3	0	3	0	1	2	0	1	2	0
20 mg	66	4	6.1%	4	2	2	0	1	2	1	0	4	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
憩室炎NOS (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
白色便 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
吐血 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
裂孔ヘルニア (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
瘢痕ヘルニアNOS (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
軟便 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
食道逆流 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
口腔内痛 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	2	2	0	0	2	0	0	0	2	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
悪心 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
咽喉刺激感 (Gastr)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
ANY EVENT													
0 mg	68	20	29.4%	23									
5 mg	68	19	27.9%	26									
20 mg	66	15	22.7%	25									
40 mg	68	21	30.9%	27									
疲労 (Genrl)													
0 mg	68	9	13.2%	9	2	6	1	2	6	1	2	7	0
5 mg	68	10	14.7%	10	5	4	1	0	8	2	3	7	0
20 mg	66	4	6.1%	4	1	1	2	1	3	0	1	3	0
40 mg	68	8	11.8%	8	4	2	2	1	5	2	1	7	0
インフルエンザ様疾患 (Genrl)													
0 mg	68	7	10.3%	8	5	2	1	6	2	0	2	6	0
5 mg	68	8	11.8%	8	2	4	2	7	1	0	1	7	0
20 mg	66	2	3.0%	2	1	1	0	2	0	0	0	2	0
40 mg	68	7	10.3%	8	5	2	1	7	1	0	0	8	0
アルコールによる宿酔 (Genrl)													
0 mg	68	2	2.9%	2	1	0	1	2	0	0	0	2	0
5 mg	68	1	1.5%	4	0	2	2	2	2	0	0	4	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
活力増進 (Genrl)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
上肢浮腫 (Genrl)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
悪寒 (Genrl)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	2	3.0%	2	0	1	1	1	0	1	0	2	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
脱力 (Genrl)													
0 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	2	0	0	2	0	2	0	0	2	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
胸痛NEC (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	3	4.4%	4	1	1	2	2	2	0	0	2	2
胸部絞扼感 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	1	1.5%	1	0	1	0	0	0	1	0	1	0
酩酊感 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	0	1	0	1	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
熱感 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
びくびく感 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
嗜眠 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	3	4.4%	3	2	1	0	1	1	1	1	2	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	1	0	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
倦怠感 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	3	1	0	2	0	3	0	0	3	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
下肢浮腫 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
疼痛NOS (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	1	1.5%	2	1	0	1	0	2	0	0	2	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
発熱 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	0	1	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
戦慄 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	2	0	1	1	0	2	0	0	2	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
不活発 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	0	1	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
口渇 (Genrl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
肝・胆道系障害													
ANY EVENT													
0 mg	68	0	0.0%	0									
5 mg	68	0	0.0%	0									
20 mg	66	1	1.5%	1									
40 mg	68	1	1.5%	1									
肝腫大 (Hepat)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
免疫系障害													
ANY EVENT													
0 mg	68	3	4.4%	3									
5 mg	68	0	0.0%	0									
20 mg	66	2	3.0%	2									
40 mg	68	0	0.0%	0									
虫刺されアレルギー (Immun)													
0 mg	68	2	2.9%	2	0	1	1	2	0	0	0	2	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
複合アレルギー (Immun)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
季節性アレルギー (Immun)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
感染症および寄生虫症													
ANY EVENT													
0 mg	68	2	2.9%	2									
5 mg	68	6	8.8%	7									
20 mg	66	7	10.6%	9									
40 mg	68	3	4.4%	5									
気管支炎NOS (Infec)													
0 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
5 mg	68	2	2.9%	2	0	1	1	2	0	0	0	2	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
蜂巣炎 (Infec)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳の感染症NOS (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	2	2.9%	2	0	2	0	2	0	0	1	1	0
20 mg	66	2	3.0%	2	2	0	0	2	0	0	0	2	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
感染性歯肉炎NOS (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
単純ヘルペス (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
インフルエンザ (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
限局性感染 (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
ライム病 (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
外耳炎（外耳道のせつを除く）NOS													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
咽頭炎NOS (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
レンサ球菌性咽頭炎 (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
副鼻腔炎NOS (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
足部白癬 (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
歯感染 (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
ウイルス感染NOS (Infec)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
傷害および中毒													
ANY EVENT													
0 mg	68	6	8.8%	7									
5 mg	68	3	4.4%	3									
20 mg	66	1	1.5%	1									
40 mg	68	5	7.4%	7									
関節捻挫 (Inj&P)													
0 mg	68	1	1.5%	2	0	2	0	2	0	0	2	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
事故NOS (Inj&P)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
熱傷NOS (Inj&P)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
傷害および中毒													
損傷NOS (Inj&P)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
裂傷 (Inj&P)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
交通事故 (Inj&P)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
急性アルコール中毒 (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	0	1	1	0	0	0	0	1
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
節足動物刺傷 (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	2	2	0	0	2	0	0	0	2	0
頭部損傷 (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
傷害および中毒													
関節脱臼NEC (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
四肢損傷NOS (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
筋肉損傷NOS (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
サンバーン (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
手首関節骨折 (Inj&P)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
臨床検査													
ANY EVENT													
0 mg	68	4	5.9%	4									
5 mg	68	3	4.4%	4									
20 mg	66	2	3.0%	3									
40 mg	68	7	10.3%	9									

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
臨床検査													
血圧上昇 (Inv)													
0 mg	68	3	4.4%	3	1	2	0	1	2	0	2	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	2	2.9%	2	2	0	0	1	1	0	1	1	0
ロンベルグ徴候陽性 (Inv)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	1	0	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
血中ブドウ糖増加 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
血便 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
血中トリグリセリド増加 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	1	0	0
心拍数増加 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	1	1	0	0	1	1	1	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
臨床検査													
肝機能検査NOS異常 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
血小板数減少 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
子宮頚部スミア異常 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
体重減少 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
体重増加 (Inv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
代謝および栄養障害													
ANY EVENT													
0 mg	68	3	4.4%	3									
5 mg	68	4	5.9%	5									
20 mg	66	5	7.6%	5									
40 mg	68	5	7.4%	5									
食欲亢進NOS (Metab)													
0 mg	68	2	2.9%	2	1	1	0	1	1	0	1	1	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	1	1	0	0	2	0	0	2	0
食欲減退NOS (Metab)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
5 mg	68	4	5.9%	4	1	2	1	0	4	0	0	4	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	2	0	0	0	2	0	0	2	0
食欲不振 (Metab)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	3	4.5%	3	1	1	1	1	0	2	0	3	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
体液貯留 (Metab)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
高血糖NOS (Metab)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
筋骨格、結合組織および骨障害													
ANY EVENT													
0 mg	68	8	11.8%	9									
5 mg	68	12	17.6%	15									
20 mg	66	11	16.7%	15									
40 mg	68	8	11.8%	11									
関節痛 (Musc)													
0 mg	68	2	2.9%	3	2	1	0	3	0	0	1	2	0
5 mg	68	2	2.9%	2	1	1	0	2	0	0	1	1	0
20 mg	66	2	3.0%	2	1	1	0	1	1	0	1	1	0
40 mg	68	1	1.5%	1	1	0	0	0	0	1	0	1	0
背部痛 (Musc)													
0 mg	68	3	4.4%	3	1	2	0	3	0	0	1	2	0
5 mg	68	3	4.4%	3	0	1	2	2	1	0	1	2	0
20 mg	66	3	4.5%	4	2	1	1	4	0	0	0	4	0
40 mg	68	3	4.4%	4	1	3	0	4	0	0	1	3	0
筋痛 (Musc)													
0 mg	68	2	2.9%	2	1	1	0	1	1	0	0	2	0
5 mg	68	3	4.4%	3	2	1	0	3	0	0	1	2	0
20 mg	66	2	3.0%	3	2	1	0	3	0	0	0	1	2
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
脊柱後弯症 (Musc)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
滑液包炎 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
筋骨格、結合組織および骨障害													
関節運動範囲減少 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
筋痙攣 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	0	0	1	0	0	1	0
筋痙縮 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
筋緊張 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
筋攣縮 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	2	2.9%	2	1	1	0	1	1	0	0	2	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
頚部痛 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
筋骨格、結合組織および骨障害													
頚部硬直 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	1	1	0	2	0	0	1	1	0
四肢痛 (Musc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
20 mg	66	4	6.1%	5	1	4	0	5	0	0	3	2	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
良性および悪性新生物（嚢胞およびポリープを含む）													
ANY EVENT													
0 mg	68	0	0.0%	0									
5 mg	68	1	1.5%	1									
20 mg	66	1	1.5%	1									
40 mg	68	0	0.0%	0									
乳房塊状物NOS (Neopl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
嚢胞NOS (Neopl)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
ANY EVENT													
0 mg	68	32	47.1%	48									
5 mg	68	36	52.9%	79									
20 mg	66	43	65.2%	99									
40 mg	68	42	61.8%	99									
頭痛NOS (Nerv)													
0 mg	68	15	22.1%	21	15	4	2	7	14	0	2	19	0
5 mg	68	16	23.5%	29	11	16	2	9	19	1	0	29	0
20 mg	66	20	30.3%	32	15	12	5	10	21	1	1	30	1
40 mg	68	23	33.8%	40	24	14	2	15	20	5	3	37	0
浮動性めまい（回転性眩暈を除く） (Nerv)													
0 mg	68	8	11.8%	10	6	4	0	0	5	5	2	8	0
5 mg	68	19	27.9%	21	11	6	4	0	9	12	3	18	0
20 mg	66	20	30.3%	22	10	5	7	2	12	8	2	20	0
40 mg	68	15	22.1%	15	6	7	2	0	10	5	0	15	0
不眠症NEC (Nerv)													
0 mg	68	7	10.3%	7	5	2	0	1	6	0	2	5	0
5 mg	68	13	19.1%	13	6	6	1	5	6	2	1	12	0
20 mg	66	19	28.8%	20	5	10	5	6	8	6	3	17	0
40 mg	68	15	22.1%	17	6	7	4	2	14	1	3	14	0
活動亢進 (Nerv)													
0 mg	68	2	2.9%	2	1	1	0	1	1	0	0	2	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
注意力障害NEC (Nerv)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	1	1.5%	1	0	0	1	0	0	1	1	0	0
20 mg	66	2	3.0%	2	1	1	0	0	1	1	0	2	0
40 mg	68	2	2.9%	2	1	1	0	0	2	0	0	2	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
舌下神経障害NOS (Nerv)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
中期不眠症 (Nerv)													
0 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	2	2.9%	2	1	1	0	0	0	2	0	2	0
錯感覚NEC (Nerv)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	2	2.9%	2	2	0	0	1	1	0	1	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
橈骨神経麻痺 (Nerv)													
0 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
副鼻腔炎に伴う頭痛 (Nerv)													
0 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	0	1	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
傾眠 (Nerv)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
5 mg	68	4	5.9%	4	2	0	2	0	3	1	1	3	0
20 mg	66	5	7.6%	5	3	2	0	1	2	2	2	3	0
40 mg	68	6	8.8%	6	3	3	0	0	3	3	0	6	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
味覚障害 (Nerv)													
0 mg	68	1	1.5%	1	1	0	0	0	0	1	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	3	4.4%	3	2	1	0	0	1	2	2	1	0
失調NEC (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
手根管症候群 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
小脳症候群 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
意識レベルの低下 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
構語障害 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	1	1	0	0	2	0	0	2	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
知覚過敏 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	2	3.0%	2	2	0	0	1	1	0	2	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
反射亢進 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
筋緊張亢進 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
感覚減退 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
反射減弱 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
初期不眠症 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
片頭痛NOS (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	2	0	0	2	1	1	0	0	2	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
不随意性筋収縮 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
神経圧迫 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	1	0	0	0	0	1
下肢静止不能症候群 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
鎮静 (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	0	1	0	1	0
40 mg	68	2	2.9%	2	0	1	1	0	2	0	0	2	0
会話障害NEC (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
振戦NEC (Nerv)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	4	5.9%	4	3	1	0	0	4	0	0	4	0
20 mg	66	3	4.5%	4	0	3	1	0	4	0	1	3	0
40 mg	68	3	4.4%	4	4	0	0	1	3	0	1	3	0
精神障害													
ANY EVENT													
0 mg	68	8	11.8%	14									
5 mg	68	15	22.1%	20									
20 mg	66	16	24.2%	20									
40 mg	68	16	23.5%	24									
不安NEC (Psych)													
0 mg	68	4	5.9%	4	2	2	0	3	1	0	1	3	0
5 mg	68	1	1.5%	1	0	0	1	0	0	1	1	0	0
20 mg	66	4	6.1%	6	2	0	4	0	6	0	2	4	0
40 mg	68	2	2.9%	2	1	1	0	1	1	0	0	2	0
うつ病NEC (Psych)													
0 mg	68	2	2.9%	4	0	1	3	0	4	0	1	3	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	1	1	0	0	2	0	1	1	0
不安増強 (Psych)													
0 mg	68	1	1.5%	2	0	2	0	1	1	0	1	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
異常な夢 (Psych)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	2	2.9%	2	1	1	0	0	2	0	0	2	0
20 mg	66	1	1.5%	1	0	0	1	0	1	0	0	1	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
抑うつ気分を伴う適応障害 (Psych)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
リビドー減退 (Psych)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	2	2.9%	2	0	1	1	0	2	0	2	0	0
20 mg	66	2	3.0%	2	1	1	0	0	2	0	1	1	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
妄想症 (Psych)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
激越 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
アルコール離脱症状 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
怒り (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
錯乱 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	5	7.6%	5	0	5	0	0	1	4	1	4	0
40 mg	68	4	5.9%	4	2	1	1	0	2	2	1	3	0
泣き (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
失見当識 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
20 mg	66	1	1.5%	1	0	1	0	0	0	1	0	1	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
解離 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	0	1	0	1	0
20 mg	66	1	1.5%	1	0	0	1	0	0	1	0	1	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
幻覚NOS (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
せっかち (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
易刺激性 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	4	5.9%	4	2	1	1	1	3	0	1	3	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	0	1	1	1	1	0	1	1	0
気分変動NOS (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
気分動揺 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
神経過敏 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	1	1.5%	1	1	0	0	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
悪夢 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
人格変化 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
早漏 (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
精神病性障害NOS (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0
落ち着きのなさ (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
睡眠障害NOS (Psych)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
腎および尿路障害													
ANY EVENT													
0 mg	68	3	4.4%	3									
5 mg	68	1	1.5%	1									
20 mg	66	2	3.0%	3									
40 mg	68	1	1.5%	1									

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
腎および尿路障害													
排尿障害 (Renal)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
頻尿 (Renal)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
尿変色 (Renal)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	0	1	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
腰部痛 (Renal)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
夜間頻尿 (Renal)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
生殖系および乳房障害													
ANY EVENT													
0 mg	68	1	1.5%	2									
5 mg	68	2	2.9%	3									
20 mg	66	2	3.0%	2									
40 mg	68	2	2.9%	3									

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
生殖系および乳房障害													
月経困難症 (Repro)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	1	1.5%	2	0	2	0	2	0	0	0	2	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
月経前症候群 (Repro)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
乳房圧痛 (Repro)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
射精障害NOS (Repro)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
勃起力減退 (Repro)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	1	0	0	1	0
精巣嚢胞 (Repro)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
生殖系および乳房障害													
膣出血 (Repro)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害													
ANY EVENT													
0 mg	68	3	4.4%	3									
5 mg	68	6	8.8%	6									
20 mg	66	6	9.1%	7									
40 mg	68	4	5.9%	4									
副鼻腔痛 (Resp)													
0 mg	68	2	2.9%	2	1	1	0	0	2	0	1	1	0
5 mg	68	1	1.5%	1	0	1	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
鼻閉 (Resp)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
喘息NOS (Resp)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
呼吸器、胸郭および縦隔障害													
咳嗽 (Resp)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	3	4.4%	3	1	2	0	3	0	0	1	2	0
20 mg	66	2	3.0%	2	1	1	0	2	0	0	1	1	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
呼吸困難NOS (Resp)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	0	1	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	0	1	0	0	1	0	1	0
後鼻漏 (Resp)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	2	3.0%	2	2	0	0	2	0	0	1	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
鼻漏 (Resp)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
副鼻腔うっ血 (Resp)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
皮膚および皮下組織障害													
ANY EVENT													
0 mg	68	7	10.3%	9									
5 mg	68	8	11.8%	11									
20 mg	66	7	10.6%	11									
40 mg	68	10	14.7%	12									

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
皮膚および皮下組織障害													
皮膚炎NOS (Skin)													
0 mg	68	5	7.4%	7	4	2	1	3	4	0	2	5	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
20 mg	66	1	1.5%	2	1	1	0	0	2	0	2	0	0
40 mg	68	4	5.9%	4	0	4	0	4	0	0	0	4	0
接触性皮膚炎 (Skin)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	2	2.9%	3	1	2	0	3	0	0	0	3	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
そう痒症NOS (Skin)													
0 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
5 mg	68	3	4.4%	4	0	2	2	1	1	2	1	3	0
20 mg	66	2	3.0%	2	0	1	1	0	2	0	0	1	1
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
ざ瘡NOS (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
冷湿 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
ざ瘡様皮膚炎 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	1	0	0	0	1	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
皮膚および皮下組織障害													
紅斑性単純性皮膚炎 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	1	0	0
皮膚描記症 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	0	1	0	0	1	0
寝汗 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	0	1	0
40 mg	68	1	1.5%	1	0	0	1	1	0	0	0	1	0
斑状丘疹状皮疹 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
丘疹 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	0	1	0	0	1	0	1	0
皮膚変色 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
皮膚および皮下組織障害													
皮膚小結節 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	1	0	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
多汗 (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	2	2.9%	2	1	0	1	1	0	1	0	2	0
20 mg	66	2	3.0%	3	0	2	1	0	2	1	0	3	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
蕁麻疹NOS (Skin)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	2	2.9%	2	0	1	1	0	2	0	0	2	0
社会環境													
ANY EVENT													
0 mg	68	1	1.5%	1									
5 mg	68	0	0.0%	0									
20 mg	66	0	0.0%	0									
40 mg	68	0	0.0%	0									
薬物乱用 (SocCi)													
0 mg	68	1	1.5%	1	1	0	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
外科および内科処置													
ANY EVENT													
0 mg	68	1	1.5%	1									
5 mg	68	1	1.5%	1									
20 mg	66	0	0.0%	0									
40 mg	68	0	0.0%	0									
口腔手術NOS (Surg)													
0 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
抜歯NOS (Surg)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	0	1	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
血管障害													
ANY EVENT													
0 mg	68	0	0.0%	0									
5 mg	68	1	1.5%	1									
20 mg	66	4	6.1%	5									
40 mg	68	3	4.4%	3									
潮紅 (Vasc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	1	1.5%	1	0	1	0	0	1	0	0	1	0
ほてりNOS (Vasc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	2	3.0%	3	0	2	1	0	3	0	1	2	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-28　重症度別有害事象及び副作用－連日投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Probably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
血管障害													
高血圧NOS (Vasc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	1	0	0	1	0	0	1	0	0
40 mg	68	2	2.9%	2	0	0	2	0	2	0	2	0	0
不安定血圧 (Vasc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	66	1	1.5%	1	0	1	0	0	1	0	1	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
リンパ浮腫NOS (Vasc)													
0 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	68	1	1.5%	1	0	1	0	1	0	0	1	0	0
20 mg	66	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	68	0	0.0%	0	0	0	0	0	0	0	0	0	0

MedDRA Version 3.3

＜資料番号 5.3.5.1-07：14.3.1.4＞

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
血液およびリンパ系障害													
ANY EVENT													
0 mg	39	2	5.1%	2									
5 mg	40	1	2.5%	1									
20 mg	40	0	0.0%	0									
40 mg	37	0	0.0%	0									
リンパ節症 (Blood)													
0 mg	39	2	5.1%	2	1	1	0	1	1	0	1	1	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
心臓障害													
ANY EVENT													
0 mg	39	2	5.1%	2									
5 mg	40	1	2.5%	1									
20 mg	40	1	2.5%	1									
40 mg	37	1	2.7%	1									
徐脈NOS (Card)													
0 mg	39	2	5.1%	2	2	0	0	0	2	0	2	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
冠動脈疾患NOS (Card)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
頻脈NOS (Card)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	1	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
先天性および家族性／遺伝性障害													
ANY EVENT													
0 mg	39	0	0.0%	0									
5 mg	40	1	2.5%	1									
20 mg	40	0	0.0%	0									
40 mg	37	0	0.0%	0									
表皮母斑 (Cong)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳および迷路障害													
ANY EVENT													
0 mg	39	1	2.6%	2									
5 mg	40	3	7.5%	3									
20 mg	40	6	15.0%	7									
40 mg	37	2	5.4%	3									
耳痛 (Ear)													
0 mg	39	1	2.6%	2	2	0	0	2	0	0	1	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	1	1	0	2	0	0	0	2	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳垢栓塞 (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳の障害NOS (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
耳および迷路障害													
外耳障害NOS (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
聴覚過敏 (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
乗物酔い (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳鳴 (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0
鼓膜障害NOS (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0
回転性眩暈NEC (Ear)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	3	7.5%	3	2	1	0	3	0	0	1	2	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
眼障害													
ANY EVENT													
0 mg	39	1	2.6%	1									
5 mg	40	1	2.5%	1									
20 mg	40	3	7.5%	4									
40 mg	37	1	2.7%	1									
霧視 (Eye)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	0	1	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
結膜出血 (Eye)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
羞明 (Eye)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
視覚障害NOS (Eye)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
胃腸障害													
ANY EVENT													
0 mg	39	15	38.5%	29									
5 mg	40	16	40.0%	30									
20 mg	40	22	55.0%	42									
40 mg	37	18	48.6%	47									

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
消化不良 (Gastr)													
0 mg	39	3	7.7%	7	5	1	1	2	5	0	0	7	0
5 mg	40	2	5.0%	2	1	1	0	1	1	0	0	2	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	4	10.8%	9	6	3	0	5	4	0	0	9	0
嘔気 (Gastr)													
0 mg	39	3	7.7%	4	2	2	0	2	2	0	0	4	0
5 mg	40	4	10.0%	6	2	4	0	2	2	2	0	6	0
20 mg	40	8	20.0%	13	2	10	1	1	7	5	0	13	0
40 mg	37	7	18.9%	11	3	7	1	0	4	7	0	11	0
嘔吐NOS (Gastr)													
0 mg	39	3	7.7%	3	1	2	0	2	1	0	0	3	0
5 mg	40	3	7.5%	3	0	1	2	2	1	0	0	3	0
20 mg	40	3	7.5%	3	1	2	0	2	0	1	0	3	0
40 mg	37	4	10.8%	5	1	1	3	1	3	1	0	5	0
腹部膨満 (Gastr)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
上腹部痛 (Gastr)													
0 mg	39	1	2.6%	2	0	2	0	2	0	0	1	1	0
5 mg	40	2	5.0%	3	0	3	0	2	0	1	0	3	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
40 mg	37	3	8.1%	4	2	1	1	2	2	0	1	2	1
腹部硬直 (Gastr)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
腸雑音異常 (Gastr)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
下痢NOS (Gastr)													
0 mg	39	1	2.6%	3	3	0	0	0	3	0	0	2	1
5 mg	40	4	10.0%	5	1	3	1	3	2	0	1	4	0
20 mg	40	2	5.0%	3	1	2	0	1	1	1	0	3	0
40 mg	37	3	8.1%	4	1	3	0	1	3	0	0	4	0
口内乾燥 (Gastr)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	1	0	0
5 mg	40	4	10.0%	4	2	1	1	1	1	2	0	4	0
20 mg	40	5	12.5%	5	2	3	0	0	3	2	1	4	0
40 mg	37	3	8.1%	3	0	2	1	0	2	1	0	3	0
鼓腸 (Gastr)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	2	0	0	1	1	0	0	2	0
消化器不調 (Gastr)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
咽喉痛NOS (Gastr)													
0 mg	39	1	2.6%	2	1	1	0	2	0	0	1	1	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
舌障害NOS (Gastr)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
歯痛 (Gastr)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
腹痛NOS (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	0	1	1	1	0	1	0	2	0
40 mg	37	2	5.4%	2	1	1	0	1	0	1	0	2	0
虫垂炎 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0
口唇のひび割れ (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
口唇炎 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	0	1	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
便秘 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	2	5.0%	2	0	2	0	1	1	0	1	1	0
20 mg	40	5	12.5%	6	4	2	0	3	2	1	0	6	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
白色便 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
出血性胃潰瘍 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
瘢痕ヘルニアNOS (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
軟便 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	1	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
メレナ (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
胃腸障害													
食道逆流 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0
口腔内痛 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	2	2	0	0	2	0	0	0	2	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
直腸出血 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
悪心 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
咽喉刺激感 (Gastr)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0
全身障害および投与局所様態													
ANY EVENT													
0 mg	39	16	41.0%	20									
5 mg	40	17	42.5%	27									
20 mg	40	12	30.0%	19									
40 mg	37	18	48.6%	36									

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
インフルエンザ様疾患 (Genrl)													
0 mg	39	8	20.5%	8	4	3	1	7	1	0	1	7	0
5 mg	40	9	22.5%	10	3	6	1	10	0	0	0	10	0
20 mg	40	4	10.0%	4	3	1	0	4	0	0	0	4	0
40 mg	37	13	35.1%	19	6	10	3	18	1	0	1	18	0
疲労 (Genrl)													
0 mg	39	5	12.8%	6	2	4	0	1	4	1	1	5	0
5 mg	40	8	20.0%	9	3	4	2	1	5	3	3	6	0
20 mg	40	4	10.0%	4	2	0	2	1	2	1	0	4	0
40 mg	37	3	8.1%	3	1	1	1	0	2	1	0	3	0
アルコールによる宿酔 (Genrl)													
0 mg	39	2	5.1%	2	1	0	1	2	0	0	0	2	0
5 mg	40	1	2.5%	4	0	2	2	2	2	0	0	4	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
胸痛NEC (Genrl)													
0 mg	39	1	2.6%	1	0	1	0	0	0	1	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	1	1	0	2	0	0	0	2	0
40 mg	37	3	8.1%	4	0	1	3	2	2	0	0	2	2
活力増進 (Genrl)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
悪寒 (Genrl)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
脱力 (Genrl)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
胸部絞扼感 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
酩酊感 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
びくびく感 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
嗜眠 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	2	5.0%	2	1	1	0	1	1	0	1	1	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	1	0	0
40 mg	37	2	5.4%	6	2	4	0	1	1	4	0	6	0
倦怠感 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	3	0	3	0	0	3	0	0	3	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
全身障害および投与局所様態													
下肢浮腫 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	0	2	0	2	0	0	2	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
疼痛NOS (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
発熱 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
不活発 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	0	1	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
口渇 (Genrl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
肝・胆道系障害													
ANY EVENT													
0 mg	39	0	0.0%	0									
5 mg	40	1	2.5%	1									
20 mg	40	1	2.5%	1									
40 mg	37	1	2.7%	1									

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
肝・胆道系障害													
肝腫大 (Hepat)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0
免疫系障害													
ANY EVENT													
0 mg	39	2	5.1%	2									
5 mg	40	0	0.0%	0									
20 mg	40	1	2.5%	1									
40 mg	37	0	0.0%	0									
虫刺されアレルギー (Immun)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
複合アレルギー (Immun)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
季節性アレルギー (Immun)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
ANY EVENT													
0 mg	39	3	7.7%	3									
5 mg	40	8	20.0%	10									
20 mg	40	8	20.0%	11									
40 mg	37	8	21.6%	12									
気管支炎NOS (Infec)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	0	1	0
5 mg	40	2	5.0%	2	0	1	1	2	0	0	0	2	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
気道感染NOS (Infec)													
0 mg	39	1	2.6%	1	0	0	1	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
ウイルス感染NOS (Infec)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
デング熱 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
耳の感染症NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	2	5.0%	2	1	1	0	2	0	0	0	2	0
40 mg	37	2	5.4%	2	0	2	0	2	0	0	0	2	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
ウイルス性胃腸炎NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	2	5.4%	2	1	1	0	2	0	0	0	2	0
C型肝炎 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
単純ヘルペス (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
帯状疱疹 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
インフルエンザ (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
限局性感染 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
ウイルス性髄膜炎NEC (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
外耳炎（外耳道のせつを除く）NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
咽頭炎NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
レンサ球菌性咽頭炎 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
副鼻腔炎NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	2	5.0%	2	2	0	0	2	0	0	0	2	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	0	0	2	1	1	0	0	2	0
皮膚感染症NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
感染症および寄生虫症													
歯膿瘍 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0
歯感染 (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
上気道感染NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	1	0	1	2	0	0	1	1	0
尿路感染NOS (Infec)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
傷害および中毒													
ANY EVENT													
0 mg	39	7	17.9%	7									
5 mg	40	4	10.0%	4									
20 mg	40	5	12.5%	5									
40 mg	37	7	18.9%	11									
事故NOS (Inj&P)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
傷害および中毒													
咬刺傷NOS (Inj&P)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
熱傷NOS (Inj&P)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
損傷NOS (Inj&P)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0
関節脱臼NEC (Inj&P)													
0 mg	39	1	2.6%	1	0	0	1	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
裂傷 (Inj&P)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	1	1	0	2	0	0	1	1	0
交通事故 (Inj&P)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
傷害および中毒													
急性アルコール中毒 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	0	1	1	0	0	0	0	1
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
足関節部骨折 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	0	0	2	2	0	0	0	2	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
節足動物咬傷 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
上顎炎 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
顔面骨骨折 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
頭部損傷 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
傷害および中毒													
関節捻挫 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
四肢損傷NOS (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	2	5.0%	2	1	1	0	2	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0
筋肉損傷NOS (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
肋骨骨折 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
サンバーン (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
腱損傷 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
傷害および中毒													
腱断裂 (Inj&P)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	1	0	0
臨床検査													
ANY EVENT													
0 mg	39	7	17.9%	7									
5 mg	40	4	10.0%	5									
20 mg	40	4	10.0%	4									
40 mg	37	6	16.2%	9									
血圧上昇 (Inv)													
0 mg	39	3	7.7%	3	1	2	0	1	2	0	2	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	2	5.4%	3	2	1	0	2	1	0	2	1	0
血中コレステロール増加 (Inv)													
0 mg	39	2	5.1%	2	1	1	0	2	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
心電図異常NOS (Inv)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
ロンベルグ徴候陽性 (Inv)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
臨床検査													
血中ブドウ糖増加 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
血中トリグリセリド増加 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	1	0	0
心拍数増加 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	1	0	0
心音異常 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
肝機能検査NOS異常 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
血小板数減少 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
臨床検査													
子宮頚部スミア異常 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
体重減少 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
体重増加 (Inv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
代謝および栄養障害													
ANY EVENT													
0 mg	39	2	5.1%	2									
5 mg	40	5	12.5%	7									
20 mg	40	5	12.5%	6									
40 mg	37	4	10.8%	4									
食欲亢進NOS (Metab)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	1	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	1	1	0	0	2	0	0	2	0
ヘモクロマトーシス (Metab)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
代謝および栄養障害													
食欲不振 (Metab)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	1	1	0	1	0	1	0	2	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
食欲減退NOS (Metab)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	4	10.0%	5	1	2	2	2	3	0	2	3	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	2	0	0	0	2	0	0	2	0
糖尿病NOS (Metab)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
体液貯留 (Metab)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	2	1	1	0	2	0	0	1	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
高血糖NOS (Metab)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
高脂血症NOS (Metab)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
筋骨格、結合組織および骨障害													
ANY EVENT													
0 mg	39	7	17.9%	10									
5 mg	40	9	22.5%	12									
20 mg	40	9	22.5%	23									
40 mg	37	10	27.0%	17									
背部痛 (Musc)													
0 mg	39	4	10.3%	5	1	3	1	5	0	0	1	4	0
5 mg	40	3	7.5%	4	0	2	1	4	0	0	0	4	0
20 mg	40	4	10.0%	9	2	5	2	9	0	0	1	8	0
40 mg	37	4	10.8%	5	1	4	0	5	0	0	1	4	0
関節痛 (Musc)													
0 mg	39	1	2.6%	2	2	0	0	2	0	0	0	2	0
5 mg	40	2	5.0%	2	0	2	0	2	0	0	1	1	0
20 mg	40	3	7.5%	3	1	1	1	2	1	0	1	2	0
40 mg	37	2	5.4%	2	0	2	0	2	0	0	2	0	0
脊柱後弯症 (Musc)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
筋痛 (Musc)													
0 mg	39	1	2.6%	2	1	1	0	0	1	1	0	2	0
5 mg	40	2	5.0%	2	1	1	0	2	0	0	1	1	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	2	5.4%	2	1	1	0	2	0	0	0	2	0
骨棘 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
筋骨格、結合組織および骨障害													
滑液包炎 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
椎間板ヘルニア (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	0	1	0	0	1	0	0
関節運動範囲減少 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	1	0	0
関節硬直 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
筋緊張 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	4	1	3	0	0	4	0	0	4	0
40 mg	37	2	5.4%	2	0	2	0	1	1	0	0	2	0
筋攣縮 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
筋骨格、結合組織および骨障害													
頚部痛 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
頚部硬直 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	1	1	0	2	0	0	1	1	0
四肢痛 (Musc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	5	12.5%	6	1	5	0	6	0	0	3	3	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
良性および悪性新生物（嚢胞およびポリープを含む）													
ANY EVENT													
0 mg	39	0	0.0%	0									
5 mg	40	1	2.5%	1									
20 mg	40	0	0.0%	0									
40 mg	37	0	0.0%	0									
嚢胞NOS (Neopl)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
ANY EVENT													
0 mg	39	24	61.5%	38									
5 mg	40	25	62.5%	72									
20 mg	40	30	75.0%	81									
40 mg	37	28	75.7%	86									
頭痛NOS (Nerv)													
0 mg	39	11	28.2%	18	14	4	0	8	10	0	2	16	0
5 mg	40	14	35.0%	34	12	17	4	14	17	3	2	32	0
20 mg	40	11	27.5%	29	12	16	1	18	11	0	2	27	0
40 mg	37	17	45.9%	33	21	10	2	16	17	0	0	33	0
不眠症NEC (Nerv)													
0 mg	39	6	15.4%	6	6	0	0	3	3	0	1	5	0
5 mg	40	10	25.0%	11	6	4	1	5	3	3	1	10	0
20 mg	40	15	37.5%	23	5	12	6	5	13	5	1	21	1
40 mg	37	12	32.4%	19	10	4	4	4	9	6	1	18	0
浮動性めまい（回転性眩暈を除く）(Nerv)													
0 mg	39	3	7.7%	4	2	2	0	1	2	1	0	4	0
5 mg	40	12	30.0%	14	8	4	2	0	8	6	1	13	0
20 mg	40	14	35.0%	16	11	3	2	5	7	4	3	13	0
40 mg	37	12	32.4%	12	6	6	0	0	7	5	0	12	0
副鼻腔炎に伴う頭痛 (Nerv)													
0 mg	39	2	5.1%	2	1	0	1	2	0	0	0	2	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	1	2.7%	1	0	0	0	0	1	0	1	0	0
舌下神経障害NOS (Nerv)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
中期不眠症 (Nerv)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
40 mg	37	1	2.7%	1	0	1	0	0	0	1	0	1	0
神経圧迫 (Nerv)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	0	1
橈骨神経麻痺 (Nerv)													
0 mg	39	1	2.6%	1	0	0	1	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
傾眠 (Nerv)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	1	0	0
5 mg	40	3	7.5%	3	1	1	1	0	2	1	1	2	0
20 mg	40	3	7.5%	3	2	1	0	1	1	1	2	1	0
40 mg	37	4	10.8%	4	2	2	0	0	2	2	0	4	0
失神 (Nerv)													
0 mg	39	1	2.6%	1	0	0	1	0	1	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
味覚障害 (Nerv)													
0 mg	39	1	2.6%	1	1	0	0	0	0	1	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
振戦NEC (Nerv)													
0 mg	39	1	2.6%	1	0	0	1	0	1	0	1	0	0
5 mg	40	3	7.5%	3	2	1	0	1	2	0	1	2	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
失調NEC (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
手根管症候群 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
小脳症候群 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0
意識レベルの低下 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
注意力障害NEC (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	0	1	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
構語障害 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	1	1	0	0	2	0	0	2	0
知覚過敏 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
反射亢進 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
筋緊張亢進 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	1	2.7%	3	0	3	0	0	0	3	0	3	0
感覚減退 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	0	1	0
反射減弱 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
神経系障害													
活動亢進 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
片頭痛NOS (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	2	0	0	2	1	1	0	0	2	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
不随意性筋収縮 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
錯感覚NEC (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	2	5.0%	2	2	0	0	2	0	0	0	2	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	0	1	0
末梢性ニューロパシーNEC (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	0	1	0	1	0	0
鎮静 (Nerv)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	0	1	1	0	2	0	0	2	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
ANY EVENT													
0 mg	39	8	20.5%	18									
5 mg	40	9	22.5%	15									
20 mg	40	10	25.0%	16									
40 mg	37	10	27.0%	17									
不安NEC (Psych)													
0 mg	39	3	7.7%	3	2	1	0	2	1	0	1	2	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	4	2	0	2	0	4	0	1	3	0
40 mg	37	2	5.4%	2	1	1	0	2	0	0	1	1	0
うつ病NEC (Psych)													
0 mg	39	3	7.7%	8	1	2	5	5	3	0	2	6	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
40 mg	37	3	8.1%	3	1	2	0	1	2	0	1	2	0
異常な夢 (Psych)													
0 mg	39	1	2.6%	1	1	0	0	0	1	0	0	1	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
20 mg	40	1	2.5%	1	0	0	1	0	1	0	0	1	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	1	0	0
リビドー減退 (Psych)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
20 mg	40	2	5.0%	2	1	1	0	0	2	0	1	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
悪夢 (Psych)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
パニック発作 (Psych)													
0 mg	39	1	2.6%	1	0	0	1	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
妄想症 (Psych)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
自殺念慮 (Psych)													
0 mg	39	1	2.6%	2	1	0	1	2	0	0	0	2	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
アルコール離脱症状 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
注意欠陥多動性障害 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	0	1	0	0	1	0	0
錯乱 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
20 mg	40	2	5.0%	2	0	2	0	0	0	2	0	2	0
40 mg	37	1	2.7%	1	1	0	0	0	1	0	0	1	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
泣き (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
抑うつ気分 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	0	1	1	0	0	1	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
失見当識 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
解離 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	0	0	1	0	1	0
40 mg	37	1	2.7%	1	1	0	0	0	0	1	1	0	0
不安増強 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
幻覚NOS (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
せっかち (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
易刺激性 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	3	7.5%	3	2	1	0	1	2	0	0	3	0
20 mg	40	1	2.5%	1	1	0	0	0	0	1	0	1	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
気分変動NOS (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
気分障害NOS (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
気分動揺 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
神経過敏 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
精神障害													
人格変化 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
早漏 (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
落ち着きのなさ (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
睡眠障害NOS (Psych)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
腎および尿路障害													
ANY EVENT													
0 mg	39	1	2.6%	1									
5 mg	40	2	5.0%	3									
20 mg	40	2	5.0%	3									
40 mg	37	0	0.0%	0									
排尿困難 (Renal)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
腎および尿路障害													
夜間頻尿 (Renal)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
頻尿 (Renal)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	2	5.0%	3	1	1	1	2	1	0	0	3	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
尿変色 (Renal)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
生殖系および乳房障害													
ANY EVENT													
0 mg	39	1	2.6%	2									
5 mg	40	1	2.5%	3									
20 mg	40	3	7.5%	3									
40 mg	37	3	8.1%	4									
月経困難症 (Repro)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	1	2.5%	3	0	3	0	3	0	0	0	3	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	2	0	0	2	0	0	0	2	0
月経前症候群 (Repro)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
生殖系および乳房障害													
良性前立腺肥大症 (Repro)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
射精障害NOS (Repro)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
勃起力減退 (Repro)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	0	1	0	1	0	0	1	0
精巣嚢胞 (Repro)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
腟分泌物 (Repro)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害													
ANY EVENT													
0 mg	39	4	10.3%	4									
5 mg	40	8	20.0%	8									
20 mg	40	4	10.0%	4									
40 mg	37	1	2.7%	1									

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
呼吸器、胸郭および縦隔障害													
副鼻腔うっ血 (Resp)													
0 mg	39	2	5.1%	2	2	0	0	2	0	0	0	2	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	0	1	0	1	0	0	0	1	0
鼻閉 (Resp)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
副鼻腔痛 (Resp)													
0 mg	39	1	2.6%	1	0	1	0	0	1	0	1	0	0
5 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
咳嗽 (Resp)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	3	7.5%	3	1	2	0	3	0	0	0	3	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
後鼻漏 (Resp)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	2	0	0	2	0	0	1	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
鼻炎NOS (Resp)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
呼吸器、胸郭および縦隔障害													
喘鳴音 (Resp)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
皮膚および皮下組織障害													
ANY EVENT													
0 mg	39	6	15.4%	8									
5 mg	40	6	15.0%	6									
20 mg	40	4	10.0%	4									
40 mg	37	9	24.3%	10									
皮膚炎NOS (Skin)													
0 mg	39	5	12.8%	7	4	2	1	4	3	0	3	4	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	0	1	0
20 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
40 mg	37	4	10.8%	4	0	4	0	3	1	0	1	3	0
接触性皮膚炎 (Skin)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
ざ瘡様皮膚炎 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	0	1	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
紅斑性単純性皮膚炎 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
皮膚および皮下組織障害													
過角化 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
寝汗 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
40 mg	37	1	2.7%	1	0	0	1	1	0	0	0	1	0
そう痒症NOS (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
斑状丘疹状皮疹 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	0	1	0
ひび・あかぎれ (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	1	2.7%	1	1	0	0	1	0	0	1	0	0
皮膚色素過剰 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	1	0	0	1	0	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
皮膚および皮下組織障害													
多汗 (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
蕁麻疹NOS (Skin)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	2	5.4%	2	1	1	0	1	1	0	0	2	0
社会環境													
ANY EVENT													
0 mg	39	1	2.6%	1									
5 mg	40	0	0.0%	0									
20 mg	40	0	0.0%	0									
40 mg	37	0	0.0%	0									
薬物乱用 (SocCi)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
外科および内科処置													
ANY EVENT													
0 mg	39	2	5.1%	2									
5 mg	40	2	5.0%	2									
20 mg	40	1	2.5%	2									
40 mg	37	0	0.0%	0									

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
外科および内科処置													
関節注入 (Surg)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
疣贅切除 (Surg)													
0 mg	39	1	2.6%	1	0	1	0	1	0	0	0	1	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
足首手術 (Surg)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
膀胱腫瘍切除 (Surg)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	0	1	1	0	0	0	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
整形外科的処置 (Surg)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	1	0	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
抜歯NOS (Surg)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	0	1	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

表 2.7.6.5.7-29　重症度別有害事象及び副作用－継続投与期－（無作為化例）（続き）

	Patients at risk	Patients reporting event at least once		Total number of events	Severity of events			Relationship to study med			Outcome		
					Mild	Moderate	Severe	Pprobably	Possibly	Not related	Resolved	Unresolved	Resolved w/sequelae
血管障害													
ANY EVENT													
0 mg	39	1	2.6%	1									
5 mg	40	1	2.5%	1									
20 mg	40	6	15.0%	6									
40 mg	37	2	5.4%	2									
高血圧NOS (Vasc)													
0 mg	39	1	2.6%	1	1	0	0	1	0	0	1	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	2	5.0%	2	2	0	0	2	0	0	2	0	0
40 mg	37	2	5.4%	2	0	0	2	0	2	0	2	0	0
ほてりNOS (Vasc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	3	7.5%	3	1	2	0	1	2	0	2	1	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
不安定血圧 (Vasc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
20 mg	40	1	2.5%	1	0	1	0	0	1	0	1	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0
リンパ浮腫NOS (Vasc)													
0 mg	39	0	0.0%	0	0	0	0	0	0	0	0	0	0
5 mg	40	1	2.5%	1	0	1	0	1	0	0	1	0	0
20 mg	40	0	0.0%	0	0	0	0	0	0	0	0	0	0
40 mg	37	0	0.0%	0	0	0	0	0	0	0	0	0	0

MedDRA Version 3.3

＜資料番号 5.3.5.1-07：15.3.1.3.4＞

(3) 有害事象一覧表

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
血液およびリンパ系障害	リンパ節症	0	[redacted]		4	MILD ENLARGEMENT OF POSTAURICULAR LYMPHNODES	[redacted] (85)	[redacted] (148)	MILD	1	RESOLVED	1	NO
			[redacted]		6	ENLARGED MAXILLARY NODES	[redacted] (84)		MODERATE	1	PERSISTS	2	NO
		5	[redacted]		12	LYMPH NODE SWELLING	[redacted] (83)	[redacted] (110)	MODERATE	1	RESOLVED	1	NO
心臓障害	不整脈NOS	20	[redacted]		17	DYSRHYTHMIA	[redacted] (3)	[redacted] (4)	MODERATE	3/4	RESOLVED	2	NO
	徐脈NOS	0	[redacted]	[redacted]	11	BRADYCARDIA	[redacted] (98)		MILD	1	PERSISTS	2	NO
				[redacted]	7	BRADYCARDIA	[redacted] (84)		MILD	1	PERSISTS	2	NO
		20	[redacted]		8	BRADYCARDIA	[redacted] (90)		MILD	1	PERSISTS	2	NO
			[redacted]		4	BRADYCARDIA	[redacted] (12)	[redacted] (12)	MODERATE	1	RESOLVED	1	NO
	動悸	5	[redacted]		4	PALPITATIONS	[redacted] (1)	[redacted] (2)	MODERATE	2	RESOLVED	2	NO
		20	[redacted]		9	PALPITATIONS	[redacted] (3)	[redacted] (4)	SEVERE	3/4	RESOLVED	2	NO
		40	[redacted]		16	POUNDING (HEART)	[redacted] (18)	[redacted] (18)	MODERATE	3/7	RESOLVED	3	NO
	頻脈NOS	5	[redacted]		2	TACHYCARDIA	[redacted] (71)	[redacted] (71)	MILD	1	RESOLVED	1	NO
耳および迷路障害	耳痛	0	[redacted]		2	RT EARACHE	[redacted] (9)	[redacted] (16)	MILD	4	RESOLVED	1	NO
					3	RT EAR ACHE	[redacted] (42)		MILD	1	PERSISTS	1	NO
	聴覚過敏	5	[redacted]		6	INCREASED SENSITIVITY TO SOUND	[redacted] (0)	[redacted] (5)	MODERATE	2	RESOLVED	2	NO
		40	[redacted]		3	INCREASED SENSITIVITY TO NOISE	[redacted] (0)	[redacted] (0)	SEVERE	1	RESOLVED	2	NO
	乗物酔い	5	[redacted]		3	MOTION SICKNESS	[redacted] (1)	[redacted] (1)	MILD	7	RESOLVED	1	NO
	耳鳴	5	[redacted]		3	RINGING IN EARS	[redacted] (2)		MODERATE	1	PERSISTS	2	NO
		40	[redacted]	[redacted]	22	EARS RINGING	[redacted] (74)	[redacted] (74)	SEVERE	1	RESOLVED	1	NO
			[redacted]		2	RINGING IN EARS	[redacted] (1)		MODERATE	1	PERSISTS	2	NO
	回転性眩暈NEC	20	[redacted]		2	VERTIGO	[redacted] (43)	[redacted] (61)	MODERATE	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
眼障害	結膜出血	20	[redacted]		4	PETECHIAE OF EYE	[redacted] (6)	[redacted] (14)	MODERATE	1	RESOLVED	1	NO
	羞明	5	[redacted]		3	INCREASED SENSITIVITY TO LIGHT	[redacted] (0)	[redacted] (5)	MODERATE	2	RESOLVED	2	NO
		40	[redacted]		4	SENSITIVITY TO LIGHT	[redacted] (0)	[redacted] (6)	MODERATE	1	RESOLVED	1	NO
			[redacted]		5	INCREASE SENSITIVITY TO LIGHT	[redacted] (1)		MILD	8	PERSISTS	1	NO
	霧視	0	[redacted]		1	BLURRED VISION	[redacted] (77)	[redacted] (78)	MODERATE	1	RESOLVED	2	NO
		5	[redacted]		2	BLURRED VISION (FUZZY)	[redacted] (4)	[redacted] (249)	MILD	8	RESOLVED	2	NO
		20	[redacted]		3	BLURRED VISION	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
		40	[redacted]		2	BLURRED VISION	[redacted] (14)	[redacted] (17)	SEVERE	3	RESOLVED	3	NO
	視覚障害NOS	40	[redacted]		5	VISUAL DISTURBANCE	[redacted] (1)	[redacted] (8)	MILD	1	RESOLVED	1	NO
胃腸障害	腹部膨満	0	[redacted]		4	BLOATED ABDOMEN	[redacted] (0)	[redacted] (7)	MILD	4	RESOLVED	3	NO
			[redacted]		5	BLOATING	[redacted] (29)		MILD	1	PERSISTS	2	NO
		5	[redacted]		11	BLOATING	[redacted] (81)	[redacted] (87)	MODERATE	7	RESOLVED	1	NO
			[redacted]		9	SWELLING IN DUODENALARA	[redacted] (56)		MILD	8	PERSISTS	1	NO
		20	[redacted]		5	ABDOMINAL DISTENSION	[redacted] (105)		MODERATE	1	PERSISTS	2	NO
	腹痛NOS	20	[redacted]		2	ABDOMINAL CRAMPS	[redacted] (17)	[redacted] (64)	SEVERE	4	RESOLVED	3	NO
		40	[redacted]		3	INTERMITTENT ABDOMINAL CRAMPING	[redacted] (3)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
			[redacted]		2	ABDOMINAL PAIN	[redacted] (2)	[redacted] (2)	MILD	1	RESOLVED	1	NO
	上腹部痛	0	[redacted]		9	RUQ PAIN	[redacted] (77)	[redacted] (79)	MODERATE	1	RESOLVED	1	NO
					10	RUQ PAIN	[redacted] (84)		MODERATE	1	PERSISTS	1	NO
		5	[redacted]		3	STOMACH CRAMPS	[redacted] (25)	[redacted] (25)	MODERATE	1	RESOLVED	2	NO
			[redacted]		1	STOMACH PAIN	[redacted] (1)	[redacted] (4)	MODERATE	8	RESOLVED	3	NO
			[redacted]		7	STOMACH CRAMPING	[redacted] (63)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		3	STOMACH CRAMPS	[redacted] (31)	[redacted] (48)	MILD	1	RESOLVED	2	NO
		40	[redacted]		7	STOMACH PAINS	[redacted] (35)	[redacted] (38)	MILD	1	RESOLVED	2	NO
					11	STOMACH CRAMPS	[redacted] (80)	[redacted] (81)	SEVERE	7	RESOLVED	2	NO
			[redacted]		11	SLIGHT TENDERNESS RUQ	[redacted] (84)		MILD	6	PERSISTS	1	NO
			[redacted]		9	STOMACH CRAMPS	[redacted] (38)	[redacted] (39)	MODERATE	1	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	腹部硬直	0	[redacted]		5	ACHE/GUARDING ABDOMINAL	[redacted] (91)		MILD	1	PERSISTS	1	NO
	虫垂炎	40	[redacted]		4	APPENDICITIS	[redacted] (59)	[redacted] (60)	SEVERE	5	RESOLVED	1	YES
	腸雑音異常	0	[redacted]		1	STOMACH GURGLING	[redacted] (1)	[redacted] (3)	MILD	7	RESOLVED	2	NO
	口唇のひび割れ	5	[redacted]		2	CHAPPED LIPS	[redacted] (1)		MODERATE	6	PERSISTS	1	NO
	便秘	5	[redacted]		2	CONSTIPATION	[redacted] (2)		MODERATE	1	PERSISTS	2	NO
			[redacted]		3	CONSTIPATION	[redacted] (15)	[redacted] (21)	MODERATE	1	RESOLVED	2	NO
			[redacted]		1	CONSTIPATION	[redacted] (3)	[redacted] (15)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		1	CONSTIPATION	[redacted] (13)	[redacted] (96)	MODERATE	4	RESOLVED	3	NO
			[redacted]		3	CONSTIPATION	[redacted] (4)		MODERATE	8	RESOLVED	2	NO
			[redacted]		3	CONSTIPATION	[redacted] (8)	[redacted] (109)	MILD	6	RESOLVED	2	NO
			[redacted]		2	CONSTIPATION	[redacted] (3)	[redacted] (4)	MILD	7	RESOLVED	1	NO
		40	[redacted]		2	CONSTIPATION	[redacted] (1)	[redacted] (2)	MILD	1	RESOLVED	2	NO
	下痢NOS	0	[redacted]		2	DIARRHEA	[redacted] (2)	[redacted] (2)	MILD	1	RESOLVED	2	NO
					3	DIARRHEA	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	2	NO
					4	DIARRHEA	[redacted] (12)	[redacted] (12)	MILD	1	RESOLVED	2	NO
			[redacted]		1	DIARRHEA	[redacted] (1)	[redacted] (2)	MODERATE	6	RESOLVED	2	NO
			[redacted]		1	DIARRHEA	[redacted] (3)	[redacted] (5)	SEVERE	7	RESOLVED	2	NO
			[redacted]		2	DIARRHEA	[redacted] (4)	[redacted] (81)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]		5	DIARRHEA	[redacted] (25)	[redacted] (25)	MODERATE	1	RESOLVED	2	NO
					8	DIARRHEA	[redacted] (60)	[redacted] (60)	MILD	4	RESOLVED	2	NO
			[redacted]		1	DIARRHEA	[redacted] (2)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		6	DIARRHEA	[redacted] (63)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
			[redacted]		4	DIARRHEA	[redacted] (1)	[redacted] (6)	MODERATE	1	RESOLVED	2	NO
			[redacted]		4	DIARRHEA	[redacted] (35)	[redacted] (36)	MODERATE	1	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	下痢NOS	20	[redacted]		1	DIARRHEA	[redacted] (5)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		2	DIARRHEA	[redacted] (3)	[redacted] (7)	MILD	1	RESOLVED	2	NO
			[redacted]		1	DIARRHEA	[redacted] (21)	[redacted] (22)	MODERATE	1	RESOLVED	1	NO
		40	[redacted]		3	DIARRHEA	[redacted] (65)	[redacted] (96)	MILD	1	RESOLVED	1	NO
			[redacted]		1	DIARRHEA	[redacted] (11)	[redacted] (13)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	DIARRHEA	[redacted] (30)	[redacted] (32)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	DIARRHEA	[redacted] (58)	[redacted] (58)	MILD	1	RESOLVED	1	NO
			[redacted]		1	DIARRHEA	[redacted] (3)		MODERATE	1	PERSISTS	2	NO
			[redacted]		2	DIARRHEA	[redacted] (17)	[redacted] (17)	MODERATE	1	RESOLVED	2	NO
					3	DIARRHEA	[redacted] (24)	[redacted] (24)	MODERATE	1	RESOLVED	2	NO
	憩室炎NOS	5	[redacted]		10	DIVERTICULITIS	[redacted] (56)		MILD	7	PERSISTS	1	NO
	口内乾燥	0	[redacted]		1	DRY MOUTH	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
		5	[redacted]		1	DRY MOUTH	[redacted] (2)	[redacted] (18)	MILD	1	RESOLVED	2	NO
			[redacted]		2	DRY MOUTH	[redacted] (0)	[redacted] (3)	SEVERE	1	RESOLVED	3	NO
			[redacted]		2	DRY MOUTH	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
			[redacted]		2	DRY MOUTH	[redacted] (9)	[redacted] (88)	SEVERE	1	RESOLVED	3	NO
			[redacted]		5	DRY MOUTH	[redacted] (63)	[redacted] (74)	MILD	1	RESOLVED	1	NO
		20	[redacted]		2	DRY MOUTH	[redacted] (0)	[redacted] (13)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	DRY MOUTH	[redacted] (0)		MILD	1	PERSISTS	2	NO
			[redacted]		3	DRY MOUTH	[redacted] (9)	[redacted] (9)	MODERATE	1	RESOLVED	2	NO
			[redacted]		1	DRY MOUTH	[redacted] (1)	[redacted] (36)	MODERATE	1	RESOLVED	3	NO
			[redacted]		4	DRY MOUTH	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
			[redacted]		4	DRY MOUTH	[redacted] (0)		MILD	1	PERSISTS	2	NO
			[redacted]		1	DRY MOUTH	[redacted] (1)	[redacted] (8)	MILD	1	RESOLVED	1	NO
					5	DRY MOUTH	[redacted] (39)		MODERATE	1	PERSISTS	2	NO
			[redacted]		2	DRY MOUTH	[redacted] (0)	[redacted] (134)	MODERATE	6	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	口内乾燥	40	[redacted]		2	DRY MOUTH	[redacted] (0)	[redacted] (1)	SEVERE	8	RESOLVED	3	NO
			[redacted]		2	DRY MOUTH	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	1	NO
			[redacted]		3	DRY MOUTH	[redacted] (3)	[redacted] (58)	MODERATE	1	RESOLVED	2	NO
			[redacted]		9	DRY MOUTH	[redacted] (0)	[redacted] (0)	MODERATE	6	RESOLVED	2	NO
			[redacted]		6	DRY MOUTH	[redacted] (0)	[redacted] (3)	MODERATE	3/4	RESOLVED	2	NO
	消化不良	0	[redacted]		4	STOMACH UPSET	[redacted] (0)	[redacted] (0)	MILD	7	RESOLVED	1	NO
			[redacted]		4	STOMACH UPSET	[redacted] (14)	[redacted] (15)	MILD	7	RESOLVED	2	NO
					5	STOMACH UPSET	[redacted] (21)	[redacted] (21)	MILD	7	RESOLVED	2	NO
					6	STOMACH UPSET	[redacted] (41)	[redacted] (114)	MILD	4	RESOLVED	2	NO
		5	[redacted]		1	STOMACH UPSET	[redacted] (1)	[redacted] (9)	MODERATE	8	RESOLVED	3	NO
			[redacted]		6	HEARTBURN	[redacted] (55)	[redacted] (55)	MILD	7	RESOLVED	2	NO
			[redacted]		2	UPSET STOMACH	[redacted] (26)	[redacted] (30)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		2	UPSET STOMACH	[redacted] (4)	[redacted] (4)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		10	HEARTBURN	[redacted] (61)	[redacted] (61)	MODERATE	7	RESOLVED	1	NO
					11	HEARTBURN	[redacted] (72)	[redacted] (72)	MODERATE	7	RESOLVED	1	NO
				[redacted]	27	HEARTBURN	[redacted] (1)	[redacted] (1)	MODERATE	7	RESOLVED	2	NO
				[redacted]	1	UPSET STOMACH	[redacted] (1)	[redacted] (8)	MODERATE	8	RESOLVED	2	NO
				[redacted]	1	STOMACH UPSET	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
					5	STOMACH UPSET	[redacted] (21)	[redacted] (21)	MILD	1	RESOLVED	1	NO
					8	STOMACH UPSET	[redacted] (48)	[redacted] (57)	MILD	1	RESOLVED	2	NO
				[redacted]	1	STOMACH UPSET	[redacted] (1)	[redacted] (18)	MILD	1	RESOLVED	2	NO
	白色便	20	[redacted]		7	LIGHT COLORED STOOL	[redacted] (11)	[redacted] (11)	MODERATE	1	RESOLVED	2	NO
	鼓腸	0	[redacted]		2	FLATULANCE	[redacted] (1)	[redacted] (3)	MILD	1	RESOLVED	2	NO
		40	[redacted]		2	EXCESSIVE GAS	[redacted] (21)	[redacted] (21)	MILD	7	RESOLVED	2	NO
			[redacted]		2	GAS PAINS & CONSTIPATION	[redacted] (61)	[redacted] (65)	MILD	7	RESOLVED	1	NO
	胃食道逆流性疾患	0	[redacted]		1	GASTRIC REFLUX	[redacted] (2)		MILD	7	PERSISTS	1	NO
	消化器不調	0	[redacted]		2	GASTROINTESTINAL UPSET	[redacted] (0)		MILD	8/7	PERSISTS	2	NO
	吐血	20	[redacted]		1	VOMITING BLOOD	[redacted] (12)	[redacted] (12)	MODERATE	6	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	裂孔ヘルニア	5	[redacted]		8	HIATAL HERNIA	[redacted] (56)		MILD	8	PERSISTS	1	NO
	瘢痕ヘルニアNOS	5	[redacted]		6	VENTRAL HERNIA	[redacted] (81)		MODERATE	6	PERSISTS	1	NO
	軟便	20	[redacted]		8	LOOSE STOOLS	[redacted] (35)		MILD	1	PERSISTS	2	NO
	嘔気	0	[redacted]		1	NAUSEA	[redacted] (4)	[redacted] (4)	MODERATE	1	RESOLVED	2	NO
			[redacted]		2	NAUSEA (FLU-LIKE)	[redacted] (7)	[redacted] (15)	MODERATE	1	RESOLVED	2	NO
			[redacted]		2	NAUSEA	[redacted] (82)	[redacted] (82)	MILD	1	RESOLVED	1	NO
			[redacted]		1	NAUSEA	[redacted] (12)		MILD	1	PERSISTS	3	NO
			[redacted]		2	NAUSEA	[redacted] (4)	[redacted] (5)	MILD	1	RESOLVED	2	NO
					4	NAUSEA	[redacted] (19)	[redacted] (20)	MODERATE	7	RESOLVED	2	NO
			[redacted]		3	NAUSEA	[redacted] (0)		MODERATE	2/4	PERSISTS	3	NO
			[redacted]		1	NAUSEA	[redacted] (4)	[redacted] (13)	MODERATE	8	RESOLVED	2	NO
		5	[redacted]		7	NAUSEA	[redacted] (39)	[redacted] (40)	MILD	4	RESOLVED	2	NO
			[redacted]		1	NAUSEA	[redacted] (1)	[redacted] (1)	MODERATE	8	RESOLVED	2	NO
			[redacted]		2	NAUSEA	[redacted] (1)	[redacted] (3)	MODERATE	1	RESOLVED	2	NO
			[redacted]		8	NAUSEA	[redacted] (53)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
			[redacted]		1	NAUSEA	[redacted] (0)	[redacted] (4)	SEVERE	3	RESOLVED	3	NO
					3	NAUSEA	[redacted] (10)	[redacted] (11)	MODERATE	2	RESOLVED	3	NO
			[redacted]		3	NAUSEA	[redacted] (0)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		2	NAUSEA	[redacted] (2)	[redacted] (2)	MILD	2	RESOLVED	3	NO
			[redacted]		1	NAUSEA	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
			[redacted]		1	NAUSEA	[redacted] (1)	[redacted] (21)	MILD	3/4/2	RESOLVED	3	NO
		20	[redacted]		2	NAUSEA	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
			[redacted]		2	NAUSEA	[redacted] (1)	[redacted] (42)	MODERATE	1	RESOLVED	3	NO
					4	NAUSEA	[redacted] (43)	[redacted] (219)	MILD	1	RESOLVED	3	NO
			[redacted]		1	NAUSEA	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
			[redacted]		2	NAUSEA	[redacted] (0)	[redacted] (4)	MILD	4	RESOLVED	2	NO
					3	NAUSEA	[redacted] (34)	[redacted] (35)	MODERATE	2	RESOLVED	3	NO
			[redacted]		9	NAUSEA	[redacted] (29)	[redacted] (32)	SEVERE	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	嘔気	20	[redacted]		3	NAUSEA	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	2	NO
					1	NAUSEA	[redacted] (0)	[redacted] (7)	MODERATE	1	RESOLVED	2	NO
					2	NAUSEA	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
					1	NAUSEA	[redacted] (0)	[redacted] (11)	MODERATE	1	RESOLVED	3	NO
					2	NAUSEA	[redacted] (0)		MILD	6/2	PERSISTS	3	NO
		40			2	NAUSEA	[redacted] (0)	[redacted] (4)	MODERATE	4	RESOLVED	3	NO
					1	NAUSEA	[redacted] (1)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
					1	NAUSEA	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	3	NO
					1	"BUTTERFLIES IN STOMACH"	[redacted] (0)		MILD	1	PERSISTS	2	NO
					3	NAUSEA	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
					1	NAUSEA	[redacted] (0)	[redacted] (3)	MODERATE	7/2	RESOLVED	2	NO
					13	NAUSEA	[redacted] (18)	[redacted] (18)	MODERATE	3/7	RESOLVED	3	NO
					21	NAUSEA	[redacted] (0)	[redacted] (1)	MODERATE	3	RESOLVED	2	NO
					7	NAUSEA	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
					1	NAUSEOUSNESS	[redacted] (22)	[redacted] (92)	MODERATE	8	RESOLVED	3	NO
					2	NAUSEA	[redacted] (0)	[redacted] (19)	MILD	1	RESOLVED	3	NO
					3	NAUSEA	[redacted] (1)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
					3	NAUSEA	[redacted] (0)	[redacted] (3)	MODERATE	3/4	RESOLVED	2	NO
					1	NAUSEA	[redacted] (1)		MILD	8	PERSISTS	2	NO
					1	NAUSEA	[redacted] (0)	[redacted] (3)	MODERATE	1	RESOLVED	3	NO
					1	NAUSEA	[redacted] (0)	[redacted] (18)	MODERATE	1	RESOLVED	2	NO
					3	NAUSEA	[redacted] (0)		MILD	6	PERSISTS	3	NO
	食道逆流	40			10	ACID REFLUX	[redacted] (4)	[redacted] (4)	MILD	7	PERSISTS	1	NO
	口腔内痛	20			3	ORAL PAIN ASSOCIATED W/ROOT CANAL	[redacted] (37)	[redacted] (41)	MILD	7	RESOLVED	1	NO
					4	ORAL PAIN ASSOCIATED W/PERIODONTAL SURGERY	[redacted] (64)	[redacted] (71)	MILD	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	悪心	40	[redacted]		19	DRY HEAVES	[redacted] (74)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
	咽喉痛NOS	0	[redacted]		1	SORE-THROAT	[redacted] (0)	[redacted] (3)	MODERATE	4	RESOLVED	1	NO
					4	SORE THROAT	[redacted] (42)		MILD	1	PERSISTS	1	NO
		5	[redacted]		3	SORE THROAT	[redacted] (79)	[redacted] (83)	MILD	7	RESOLVED	1	NO
			[redacted]		9	SORE THROAT	[redacted] (6)	[redacted] (15)	MODERATE	7	RESOLVED	1	NO
			[redacted]		11	SORE THROAT	[redacted] (66)	[redacted] (72)	MILD	7	RESOLVED	2	NO
			[redacted]		6	SORE THROAT	[redacted] (5)	[redacted] (7)	MODERATE	7	RESOLVED	1	NO
	咽喉刺激感	40	[redacted]		21	THROAT BURNING	[redacted] (74)	[redacted] (75)	SEVERE	1	RESOLVED	1	NO
	舌障害NOS	0	[redacted]		5	1/2 INCH SQUARED AREA OF REDNESS ON TONGUE	[redacted] (78)	[redacted] (148)	MILD	1	RESOLVED	1	NO
	歯痛	0	[redacted]		11	TOOTH PAIN	[redacted] (81)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		1	INTERMITTENT TOOTHACHE	[redacted] (2)	[redacted] (10)	MILD	7	RESOLVED	1	NO
	嘔吐NOS	0	[redacted]		1	VOMITING	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
			[redacted]		5	VOMITING	[redacted] (20)	[redacted] (20)	MILD	3/7	RESOLVED	2	NO
			[redacted]		5	NAUSEA VOMITING	[redacted] (48)	[redacted] (50)	MODERATE	3	RESOLVED	1	NO
			[redacted]		1	NAUSEA, VOMITING	[redacted] (19)	[redacted] (20)	MODERATE	1	RESOLVED	1	NO
			[redacted]		3	VOMITING	[redacted] (4)	[redacted] (5)	MODERATE	8	RESOLVED	1	NO
		5	[redacted]		4	VOMITING	[redacted] (25)	[redacted] (25)	SEVERE	7	RESOLVED	2	NO
					6	VOMITING	[redacted] (60)	[redacted] (60)	SEVERE	4	RESOLVED	2	NO
			[redacted]		1	NAUSEA & VOMITING	[redacted] (1)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
			[redacted]		8	NAUSEA & VOMITING	[redacted] (18)	[redacted] (18)	SEVERE	3/6	RESOLVED	1	NO
		20	[redacted]		6	VOMITING	[redacted] (2)	[redacted] (3)	SEVERE	1	RESOLVED	2	NO
			[redacted]		7	VOMITING	[redacted] (34)	[redacted] (35)	MODERATE	2	RESOLVED	3	NO
			[redacted]		3	NAUSEA & VOMITING	[redacted] (4)	[redacted] (6)	MODERATE	8/3	RESOLVED	2	NO
			[redacted]		2	VOMITING	[redacted] (21)	[redacted] (22)	MODERATE	1	RESOLVED	1	NO
		40	[redacted]		2	VOMITING	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	3	NO
			[redacted]		11	VOMITING	[redacted] (4)	[redacted] (4)	SEVERE	1	RESOLVED	2	NO
			[redacted]		2	VOMITING	[redacted] (37)	[redacted] (37)	SEVERE	1	RESOLVED	1	NO
			[redacted]		1	EMESIS	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
					2	EMESIS	[redacted] (1)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	アルコールによる宿酔	0	[redacted]		5	HANGOVER	[redacted] (46)	[redacted] (47)	SEVERE	7	RESOLVED	1	NO
			[redacted]		2	HANGOVER	[redacted] (58)	[redacted] (58)	MILD	1	RESOLVED	1	NO
		5	[redacted]		5	HANGOVERS WORSE	[redacted] (1)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
					7	HANGOVERS WORSE	[redacted] (4)	[redacted] (7)	MODERATE	1	RESOLVED	2	NO
					12	HEADACHE/HANGOVER	[redacted] (46)	[redacted] (46)	SEVERE	7	RESOLVED	1	NO
					13	HEADACHE/HANGOVER	[redacted] (58)	[redacted] (58)	SEVERE	7	RESOLVED	1	NO
	胸痛NEC	20	[redacted]		2	CHEST PAIN W/ON HOSPITALIZATION	[redacted] (63)	[redacted] (64)	MODERATE	7/5/3	RESOLVED	1	YES
		40	[redacted]		3	CHEST PAIN	[redacted] (0)	[redacted] (0)	MILD	4	RESOLVED	2	NO
			[redacted]		23	CHEST PAIN	[redacted] (62)	[redacted] (62)	SEVERE	6	RESOLVED	2	NO
			[redacted]		3	CHEST PAIN	[redacted] (65)	[redacted] (65)	SEVERE	7	RESOLVED	1	NO
					4	CHEST PAIN	[redacted] (74)	[redacted] (74)	MODERATE	7	RESOLVED	1	NO
	胸部絞扼感	20	[redacted]		6	CHEST TIGHTNESS	[redacted] (2)	[redacted] (4)	MILD	3	RESOLVED	1	NO
		40	[redacted]		4	CHEST TIGHTNESS	[redacted] (18)	[redacted] (18)	MODERATE	3/7	RESOLVED	3	NO
	活力増進	0	[redacted]		3	INCREASED ENERGY	[redacted] (82)		MILD	1	PERSISTS	1	NO
		40	[redacted]		2	INCREASE ENERGY	[redacted] (0)	[redacted] (3)	MODERATE	1	RESOLVED	2	NO
	疲労	0	[redacted]		4	FATIGUE	[redacted] (69)	[redacted] (74)	SEVERE	1	RESOLVED	1	NO
			[redacted]		1	TIREDNESS	[redacted] (1)	[redacted] (54)	MODERATE	3/4	RESOLVED	2	NO
			[redacted]		2	FATIGUE	[redacted] (1)	[redacted] (26)	MODERATE	1	RESOLVED	2	NO
			[redacted]		2	FATIGUE	[redacted] (12)		MODERATE	1	PERSISTS	3	NO
			[redacted]		1	FATIGUE	[redacted] (0)	[redacted] (82)	MODERATE	1	RESOLVED	2	NO
			[redacted]		1	FATIGUE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	2	NO
				[redacted]	7	FATIGUE	[redacted] (49)	[redacted] (114)	MODERATE	4	RESOLVED	2	NO
				[redacted]	2	FATIGUE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	1	NO
			[redacted]		1	FATIGUE	[redacted] (1)		MODERATE	8	PERSISTS	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	疲労	5	[redacted]		3	FATIGUE	[redacted] (0)	[redacted] (3)	SEVERE	1	RESOLVED	3	NO
					8	TIREDNESS	[redacted] (21)	[redacted] (161)	MILD	1	RESOLVED	2	NO
					1	TIREDNESS	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
					15	FATIGUED	[redacted] (66)		MILD	1	PERSISTS	2	NO
					1	FATIGUE	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
					2	TIREDNESS	[redacted] (1)	[redacted] (4)	MILD	1	RESOLVED	3	NO
					12	FATIGUE	[redacted] (2)		MODERATE	3	RESOLVED	2	NO
					2	FATIGUE	[redacted] (64)		MODERATE	1	PERSISTS	2	NO
					3	TIREDNESS	[redacted] (1)	[redacted] (21)	MILD	3/4	RESOLVED	2	NO
					3	FATIGUE	[redacted] (1)	[redacted] (76)	MILD	1	RESOLVED	2	NO
		20			1	FATIGUE	[redacted] (0)	[redacted] (4)	MODERATE	8	RESOLVED	1	NO
					1	FATIGUE	[redacted] (0)	[redacted] (8)	SEVERE	1	RESOLVED	2	NO
					1	FATIGUE	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	2	NO
					4	FATIGUE	[redacted] (2)		MILD	1	PERSISTS	2	NO
		40			3	FATIGUE	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	3	NO
					1	FATIGUE	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
					1	FATIGUE	[redacted] (5)	[redacted] (12)	MILD	1	RESOLVED	2	NO
					1	TIREDNESS	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
					2	FATIGUE	[redacted] (0)	[redacted] (7)	SEVERE	2	RESOLVED	3	NO
					2	TIREDNESS	[redacted] (4)	[redacted] (52)	MILD	3	RESOLVED	2	NO
					3	FATIGUE	[redacted] (1)		MILD	8	PERSISTS	2	NO
					1	EXHAUSTED FEELING	[redacted] (0)	[redacted] (1)	MILD	1	RESOLVED	1	NO
	酩酊感	20			1	ALCOHOL-LIKE EFFECTS	[redacted] (1)	[redacted] (37)	MODERATE	2	RESOLVED	3	NO
		40			1	ALCOHOL-LIKE EFFECTS	[redacted] (0)	[redacted] (19)	MODERATE	1	RESOLVED	2	NO
	熱感	20			1	SWEATY, HOT FEELING, STOMACH "GROWLED"	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	びくびく感	40	[redacted]		1	FEELING JITTERY	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
	インフルエンザ様疾患	0	[redacted]		2	VIRAL RESPIRATORY INFECTION	[redacted] (6)	[redacted] (24)	SEVERE	7	RESOLVED	1	NO
			[redacted]		1	FLU	[redacted] (91)		MILD	7	PERSISTS	1	NO
			[redacted]		2	COUGH, COLD, CONGESTION	[redacted] (4)	[redacted] (6)	MODERATE	7	RESOLVED	2	NO
			[redacted]		2	COLD SYMPTOMS	[redacted] (48)	[redacted] (67)	MILD	1	PERSISTS	2	NO
					6	COLD/COUGH	[redacted] (48)	[redacted] (74)	MILD	1/7	RESOLVED	1	NO
			[redacted]		1	HEAD COLD	[redacted] (64)	[redacted] (66)	MILD	1	RESOLVED	1	NO
			[redacted]		4	UPPER RESPIRATORY INFECTION	[redacted] (95)	[redacted] (107)	MILD	1	RESOLVED	1	NO
			[redacted]		4	FLU - NV	[redacted] (74)	[redacted] (78)	MODERATE	1	RESOLVED	1	NO
		5	[redacted]		2	UPPER RESPIRATORY INFECTION	[redacted] (60)	[redacted] (67)	MODERATE	1	RESOLVED	1	NO
			[redacted]		2	FLU SYMPTOMS	[redacted] (78)	[redacted] (98)	MODERATE	7	RESOLVED	1	NO
			[redacted]		5	COLD	[redacted] (35)	[redacted] (43)	MODERATE	3/7	RESOLVED	1	NO
			[redacted]		4	CONGESTION	[redacted] (1)		SEVERE	7	PERSISTS	1	NO
			[redacted]		12	COLD	[redacted] (66)	[redacted] (72)	MILD	7	RESOLVED	2	NO
			[redacted]		1	COLD / CONGESTION	[redacted] (87)	[redacted] (104)	MILD	7	RESOLVED	1	NO
			[redacted]		4	COLD SXS	[redacted] (47)	[redacted] (50)	SEVERE	7	RESOLVED	1	NO
			[redacted]		2	FLU	[redacted] (24)	[redacted] (28)	MODERATE	7	RESOLVED	1	NO
		20	[redacted]		2	UPPER RESPIRATORY INFECTION	[redacted] (38)	[redacted] (44)	MILD	1	RESOLVED	1	NO
			[redacted]		7	URI - VIRAL	[redacted] (50)	[redacted] (66)	MODERATE	1	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	インフルエンザ様疾患	40	[redacted]		2	CHEST COLD	[redacted] (9)	[redacted] (12)	MILD	1	RESOLVED	1	NO
			[redacted]		1	CHEST COLD	[redacted] (90)	[redacted] (92)	MILD	7	RESOLVED	1	NO
					3	SINUS COLD	[redacted] (45)	[redacted] (48)	MILD	7	RESOLVED	1	NO
			[redacted]		7	FLU-LIKE SYMPTOMS	[redacted] (14)	[redacted] (19)	SEVERE	3	RESOLVED	2	NO
			[redacted]		3	CHEST COLD	[redacted] (92)	[redacted] (99)	MILD	1	RESOLVED	1	NO
			[redacted]		3	CONGESTION	[redacted] (3)	[redacted] (3)	MODERATE	7	RESOLVED	1	NO
			[redacted]		8	URI	[redacted] (56)	[redacted] (62)	MODERATE	7	RESOLVED	1	NO
			[redacted]		3	"FLU LIKE SYMPTOMS"	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	1	NO
	嗜眠	5	[redacted]		1	FEELS HUNG OVER IN MORNING (QUEASY, LOW ENERGY)	[redacted] (96)		MODERATE	1	PERSISTS	1	NO
			[redacted]		5	"DRAINED" FEELING	[redacted] (0)	[redacted] (87)	MILD	1	RESOLVED	2	NO
			[redacted]		2	LETHARGIC	[redacted] (1)	[redacted] (4)	MILD	1	RESOLVED	3	NO
		20	[redacted]		4	DECREASED ENERGY	[redacted] (7)		MILD	1	PERSISTS	2	NO
		40	[redacted]		2	LACK OF ENERGY	[redacted] (1)	[redacted] (27)	MILD	1	RESOLVED	2	NO
	倦怠感	20	[redacted]		2	MALAISE	[redacted] (1)	[redacted] (2)	MILD	1	RESOLVED	2	NO
					8	MALAISE	[redacted] (2)	[redacted] (3)	SEVERE	1	RESOLVED	2	NO
					13	MALAISE	[redacted] (13)	[redacted] (15)	SEVERE	2	RESOLVED	2	NO
	下肢浮腫	20	[redacted]		5	SWELLING OF (RT) POSTERIOR HEEL	[redacted] (58)		MODERATE	7	PERSISTS	1	NO
		0	[redacted]		3	EDEMA DORSUM RIGHT HAND WITH BRUISING INTO THIRD & FOURTH DIGITS	[redacted] (90)		MODERATE	1	PERSISTS	1	NO
	疼痛NOS	5	[redacted]		1	PAIN IN (LEFT) SIDE	[redacted] (41)	[redacted] (43)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		3	BODYACHES	[redacted] (1)	[redacted] (2)	MILD	1	RESOLVED	2	NO
					14	BODYACHES	[redacted] (13)	[redacted] (15)	SEVERE	2	RESOLVED	2	NO
		40	[redacted]		12	BODYACHE	[redacted] (103)	[redacted] (103)	MODERATE	7	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	発熱	20	[redacted]		2	FEVER	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	1	NO
	悪寒	0	[redacted]		7	CHILLS	[redacted] (32)	[redacted] (32)	MILD	1	RESOLVED	1	NO
		20	[redacted]		4	CHILLS	[redacted] (34)	[redacted] (35)	MODERATE	2	RESOLVED	3	NO
			[redacted]		4	CHILLS	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	1	NO
	戦慄	20	[redacted]		7	SHIVERS	[redacted] (29)	[redacted] (32)	SEVERE	1	RESOLVED	2	NO
					10	SHIVERS	[redacted] (37)	[redacted] (38)	MODERATE	1	RESOLVED	2	NO
	不活発	20	[redacted]		2	SLUGGISHNESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
	口渇	40	[redacted]		13	SEVERE THIRST	[redacted] (19)	[redacted] (19)	SEVERE	6	RESOLVED	2	NO
	脱力	0	[redacted]		2	PHYSICALLY WEAK	[redacted] (4)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
		20	[redacted]		4	WEAKNESS	[redacted] (2)	[redacted] (3)	SEVERE	1	RESOLVED	2	NO
					15	WEAKNESS	[redacted] (13)	[redacted] (15)	SEVERE	2	RESOLVED	2	NO
肝・胆道系障害	肝腫大	20	[redacted]		4	1" LIVER ENLARGEMENT	[redacted] (105)		MODERATE	1	PERSISTS	2	NO
		40	[redacted]		4	HEPATAMEGALY	[redacted] (84)		MILD	1	PERSISTS	1	NO
免疫系障害	虫刺されアレルギー	0	[redacted]		2	WASP STING - SWELLING & REDNESS	[redacted] (33)	[redacted] (35)	MODERATE	1	RESOLVED	1	NO
			[redacted]		3	BEE STING (ALLERGIC REACTION)	[redacted] (69)	[redacted] (79)	SEVERE	7	RESOLVED	1	NO
	複合アレルギー	0	[redacted]		4	ALLERGIES	[redacted] (41)		MILD	7	PERSISTS	1	NO
		20	[redacted]		1	ALLERGIES	[redacted] (1)	[redacted] (1)	MILD	7	RESOLVED	1	NO
	季節性アレルギー	20	[redacted]		3	SEASONAL ALLERGIES	[redacted] (46)	[redacted] (137)	MODERATE	7	RESOLVED	1	NO
感染症および寄生虫症	気管支炎NOS	0	[redacted]		8	BRONCHITIS	[redacted] (36)	[redacted] (38)	MODERATE	7	RESOLVED	2	NO
		5	[redacted]		6	BRONCHITIS	[redacted] (31)	[redacted] (39)	MODERATE	7	RESOLVED	1	NO
			[redacted]		5	BRONCHITIS	[redacted] (58)	[redacted] (67)	SEVERE	6	RESOLVED	1	NO
		20	[redacted]		2	BRONCHITIS	[redacted] (13)	[redacted] (74)	MILD	7	RESOLVED	1	NO
	蜂巣炎	0	[redacted]		6	CELLULITIS - RT CALF	[redacted] (1)	[redacted] (8)	MODERATE	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
感染症および寄生虫症	耳の感染症NOS	5	[redacted]		10	(LEFT) EAR INFECTION (INNER AND OUTER)	[redacted] (51)	[redacted] (110)	MODERATE	7	RESOLVED	1	NO
			[redacted]		1	EAR INFECTION	[redacted] (62)		MODERATE	7	PERSISTS	1	NO
		20	[redacted]		3	EAR INFECTION	[redacted] (13)	[redacted] (74)	MILD	7	RESOLVED	1	NO
			[redacted]		6	EAR INFECTION	[redacted] (1)	[redacted] (8)	MILD	7	RESOLVED	1	NO
		40	[redacted]		19	EAR INFECTION	[redacted] (11)	[redacted] (17)	MODERATE	7	RESOLVED	1	NO
	感染性歯肉炎NOS	20	[redacted]		2	GUM INFECTION (S/P DENTAL IMPLANTS)	[redacted] (74)	[redacted] (77)	MILD	7	RESOLVED	1	NO
	単純ヘルペス	20	[redacted]		9	HERPES SIMPLEX	[redacted] (3)	[redacted] (7)	MILD	7	RESOLVED	1	NO
		40	[redacted]		4	COLD SORE - TONGUE	[redacted] (47)	[redacted] (63)	MILD	1	RESOLVED	1	NO
	インフルエンザ	5	[redacted]		3	INFLUENZA	[redacted] (13)	[redacted] (14)	MODERATE	7	RESOLVED	1	NO
	限局性感染	20	[redacted]		3	FOOT INFECTION	[redacted] (54)	[redacted] (64)	MILD	7	RESOLVED	1	NO
	ライム病	20	[redacted]		1	LYME DISEASE	[redacted] (28)	[redacted] (68)	MODERATE	7/2	RESOLVED	1	NO
	外耳炎（外耳道のせつを除く）NOS	20	[redacted]		1	ERYTHEMA RIGHT EXTERNAL CANAL	[redacted] (83)	[redacted] (95)	MILD	1	RESOLVED	1	NO
	咽頭炎NOS	40	[redacted]		13	SCRATCHY THROAT	[redacted] (103)	[redacted] (103)	MODERATE	1	RESOLVED	2	NO
	レンサ球菌性咽頭炎	40	[redacted]		20	STREP THROAT	[redacted] (11)	[redacted] (17)	MODERATE	7	RESOLVED	1	NO
	副鼻腔炎NOS	40	[redacted]		16	SINUS INFECTION	[redacted] (18)	[redacted] (27)	SEVERE	7	RESOLVED	2	NO
	足部白癬	20	[redacted]		6	FUNGUS INFECTION - TOE	[redacted] (73)		MODERATE	7	PERSISTS	1	NO
	歯感染	5	[redacted]		2	TOOTH INFECTION	[redacted] (23)	[redacted] (36)	MODERATE	7	RESOLVED	1	NO
	ウイルス感染NOS	5	[redacted]		1	VIRAL INFECTION	[redacted] (2)	[redacted] (19)	MODERATE	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
傷害および中毒	事故NOS	0	[redacted]		2	SLIGHT TENDERNESS LEFT LOWER ANTERIOR CHEST (RIB) SECONDARY TO FALL	[redacted] (81)		MILD	1	PERSISTS	1	NO
	急性アルコール中毒	5	[redacted]		4	ALCOHOL INTOXIFICATION	[redacted] (38)	[redacted] (39)	SEVERE	5/6	RESOLVED	1	YES
	節足動物刺傷	40	[redacted]		2	INSECT (BEE) STING	[redacted] (14)	[redacted] (20)	MILD	7	RESOLVED	1	NO
					3	INSECT (BEE) STING	[redacted] (32)	[redacted] (34)	MILD	7	RESOLVED	1	NO
	熱傷NOS	0	[redacted]		5	BURN ON (RIGHT) NECK	[redacted] (7)	[redacted] (8)	MODERATE	7	RESOLVED	1	NO
	頭部損傷	40	[redacted]		24	INJURED HEAD & CHIN	[redacted] (73)	[redacted] (74)	MILD	1	RESOLVED	1	NO
	損傷NOS	0	[redacted]		5	CUT ON (RIGHT) EAR LOBE	[redacted] (98)	[redacted] (113)	MILD	1	RESOLVED	1	NO
	関節脱臼NEC	40	[redacted]		2	DISLOCATED SHOULDER	[redacted] (58)	[redacted] (64)	MODERATE	8/7	RESOLVED	1	NO
	関節捻挫	0	[redacted]		1	SPRAINED ANKLE	[redacted] (42)		MODERATE	1	PERSISTS	1	NO
					2	STRAINED SHOULDER	[redacted] (43)		MODERATE	1	PERSISTS	1	NO
		40	[redacted]		1	TWISTED KNEE	[redacted] (4)	[redacted] (13)	MODERATE	7	RESOLVED	1	NO
	裂傷	0	[redacted]		1	(RIGHT) ELBOW LACERATION	[redacted] (10)	[redacted] (13)	MODERATE	7	RESOLVED	1	NO
	四肢損傷NOS	5	[redacted]		5	JAMMED FINGER	[redacted] (87)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		23	INJURED KNEE	[redacted] (73)		MILD	1	PERSISTS	1	NO
	筋肉損傷NOS	40	[redacted]		2	GLUTEOUS STRAIN	[redacted] (38)	[redacted] (39)	MILD	1	RESOLVED	1	NO
	交通事故	0	[redacted]		5	CAR ACCIDENT	[redacted] (64)	[redacted] (64)	MILD	1	RESOLVED	1	NO
	サンバーン	20	[redacted]		3	SUNBURN	[redacted] (84)	[redacted] (145)	MILD	1	RESOLVED	1	NO
	手首関節骨折	5	[redacted]		1	BROKEN (LEFT) WRIST	[redacted] (62)		MILD	6/7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
臨床検査	血中ブドウ糖増加	20	[redacted]		3	INCREASE IN BLOOD SUGAR	[redacted] (42)		MODERATE	1	PERSISTS	2	NO
	血便	5	[redacted]		6	SMALL BLOOD TRACE IN STOOL	[redacted] (26)	[redacted] (26)	MODERATE	8	RESOLVED	1	NO
	血圧上昇	0	[redacted]		2	ELEVATED BLOOD PRESSURE	[redacted] (44)	[redacted] (83)	MILD	1	RESOLVED	2	NO
			[redacted]		3	ELEVATED BLOOD PRESSURE	[redacted] (7)		MODERATE	1	PERSISTS	1	NO
			[redacted]		5	INCREASE IN BLOOD PRESSURE	[redacted] (61)		MODERATE	6/7	PERSISTS	2	NO
		20	[redacted]		11	INCREASED BLOOD PRESSURE	[redacted] (47)		MODERATE	8	PERSISTS	2	NO
		40	[redacted]		7	INCREASED BLOOD PRESSURE	[redacted] (42)		MILD	1	PERSISTS	2	NO
			[redacted]		1	INCREASED BLOOD PRESSURE	[redacted] (12)	[redacted] (28)	MILD	1	RESOLVED	1	NO
	血中トリグリセリド増加	40	[redacted]		6	ELEVATED TRIGLYCERIDES	[redacted] (86)		SEVERE	6	PERSISTS	2	NO
	心拍数増加	40	[redacted]		6	INCREASED HEART RATE	[redacted] (7)		MILD	1	PERSISTS	2	NO
			[redacted]		3	ELEVATED HEART RATE	[redacted] (18)	[redacted] (18)	MODERATE	3/7	RESOLVED	3	NO
	肝機能検査NOS異常	5	[redacted]		3	ELEVATED LFTS	[redacted] (88)		MODERATE	2	PERSISTS	2	NO
		40	[redacted]		3	ELEVATED LFT'S	[redacted] (90)	[redacted] (98)	SEVERE	3	RESOLVED	2	NO
	血小板数減少	5	[redacted]		4	DECREASED PLATELETS	[redacted] (88)	[redacted] (98)	MODERATE	2	RESOLVED	2	NO
	ロンベルグ徴候陽性	0	[redacted]		12	SWAY ON ROMBERG	[redacted] (98)		MILD	1	PERSISTS	2	NO
		20	[redacted]		9	SLIGHT SWAY ON ROMBERG	[redacted] (90)		MILD	1	PERSISTS	2	NO
		40	[redacted]		7	SWAY ON ROMBERG	[redacted] (88)	[redacted] (368)	MODERATE	1	RESOLVED	2	NO
	子宮頚部スミア異常	40	[redacted]		4	ABNORMAL PAP SMEAR	[redacted] (46)		MODERATE	7/8	RESOLVED	1	NO
	体重減少	40	[redacted]		6	WEIGHT LOSS	[redacted] (82)	[redacted] (217)	MILD	1	RESOLVED	1	NO
	体重増加	5	[redacted]		12	WEIGHT GAIN	[redacted] (59)		MODERATE	6	PERSISTS	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
代謝および栄養障害	食欲不振	20	[redacted]		3	LOSS OF APPETITE	[redacted] (1)	[redacted] (61)	MODERATE	1	RESOLVED	3	NO
			[redacted]		2	LOSS OF APPETITE	[redacted] (0)	[redacted] (2)	SEVERE	1	RESOLVED	3	NO
			[redacted]		10	LOSS OF APPETITE	[redacted] (23)	[redacted] (42)	MILD	1	RESOLVED	1	NO
		40	[redacted]		1	LOSS OF APPETITE	[redacted] (3)	[redacted] (4)	MILD	1	RESOLVED	2	NO
	食欲減退NOS	0	[redacted]		2	DECREASE IN CONSUMPTION OF FOOD	[redacted] (7)		MILD	1	PERSISTS	2	NO
		5	[redacted]		2	APPETITE SUPPRESSED	[redacted] (0)	[redacted] (2)	MILD	8	RESOLVED	2	NO
			[redacted]		2	APPETITE DECREASE	[redacted] (1)	[redacted] (66)	MODERATE	1	RESOLVED	2	NO
			[redacted]		2	DECREASED APPETITE	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
			[redacted]		11	DECREASED APPETITE	[redacted] (2)	[redacted] (9)	SEVERE	3	RESOLVED	2	NO
		40	[redacted]		2	DECREASED APPETITE	[redacted] (10)	[redacted] (321)	MILD	1	RESOLVED	2	NO
			[redacted]		3	DECREASED APPETITE	[redacted] (34)	[redacted] (126)	MILD	1	RESOLVED	2	NO
	食欲亢進NOS	0	[redacted]		3	INCREASED APPETITE	[redacted] (12)	[redacted] (23)	MILD	1	RESOLVED	1	NO
			[redacted]		1	INCREASED CRAVING FOR SNACKS AND SWEETS	[redacted] (52)		MODERATE	1	PERSISTS	2	NO
		5	[redacted]		9	APPETITE INCREASE	[redacted] (12)	[redacted] (12)	MILD	1	RESOLVED	2	NO
		40	[redacted]		2	INCREASED APPETITE FOR SUGAR	[redacted] (28)	[redacted] (349)	MODERATE	1	RESOLVED	2	NO
				[redacted]	6	INCREASED APPETITE	[redacted] (20)	[redacted] (104)	MILD	4	RESOLVED	2	NO
	体液貯留	20	[redacted]		5	WATER RETENTION "BLOATING"	[redacted] (28)	[redacted] (28)	MILD	7	RESOLVED	1	NO
	高血糖NOS	20	[redacted]		4	ELEVATED GLUCOSE	[redacted] (41)	[redacted] (195)	MILD	8	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
筋骨格、結合組織および骨障害	関節痛	0	[redacted]		4	HIP PAIN	[redacted] (9)		MODERATE	8	PERSISTS	1	NO
			[redacted]		2	JOINT PAIN	[redacted] (18)	[redacted] (18)	MILD	7	RESOLVED	1	NO
					3	ARTHRITIC PAIN	[redacted] (19)	[redacted] (19)	MILD	7	RESOLVED	1	NO
		5	[redacted]		8	SHOULDER PAIN - RIGHT	[redacted] (78)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
			[redacted]		2	KNEE PAIN	[redacted] (89)		MILD	1	PERSISTS	1	NO
		20	[redacted]		2	HIP PAIN	[redacted] (55)	[redacted] (56)	MODERATE	7	RESOLVED	1	NO
			[redacted]		5	JOINT PAIN	[redacted] (85)		MILD	7	PERSISTS	2	NO
		40	[redacted]		1	JOINT ACHYNESS	[redacted] (0)	[redacted] (2)	MILD	4/2	RESOLVED	3	NO
	背部痛	0	[redacted]		1	BACK PAIN	[redacted] (7)	[redacted] (84)	MODERATE	7	RESOLVED	1	NO
			[redacted]		5	LEFT BACK PAIN	[redacted] (70)		MODERATE	1	PERSISTS	1	NO
			[redacted]		1	LOW BACK PAIN	[redacted] (5)	[redacted] (9)	MILD	7	RESOLVED	1	NO
		5	[redacted]		10	SHARP PAINS IN BACK	[redacted] (15)	[redacted] (15)	MODERATE	1	RESOLVED	1	NO
			[redacted]		5	LOWER BACK PAIN	[redacted] (73)		SEVERE	7	PERSISTS	2	NO
			[redacted]		5	BACK PAIN	[redacted] (4)	[redacted] (17)	SEVERE	6/7	RESOLVED	1	NO
		20	[redacted]		2	BACK PAIN	[redacted] (45)	[redacted] (46)	SEVERE	7	RESOLVED	1	NO
			[redacted]		7	BACK PAIN	[redacted] (46)	[redacted] (46)	MILD	7	RESOLVED	1	NO
					10	BACK PAIN	[redacted] (70)	[redacted] (70)	MODERATE	7	RESOLVED	1	NO
			[redacted]		19	BACK PAIN	[redacted] (34)	[redacted] (41)	MILD	7	RESOLVED	1	NO
		40	[redacted]		2	BACK PAIN	[redacted] (55)	[redacted] (57)	MODERATE	7	RESOLVED	1	NO
					3	BACK PAIN	[redacted] (76)	[redacted] (91)	MODERATE	7	RESOLVED	1	NO
			[redacted]		2	SORE BACK	[redacted] (7)		MODERATE	1	PERSISTS	1	NO
			[redacted]		3	BACK PAIN	[redacted] (60)	[redacted] (60)	MILD	7	RESOLVED	1	NO
	滑液包炎	5	[redacted]		13	BURSITIS	[redacted] (21)		MODERATE	7	PERSISTS	2	NO
	関節運動範囲減少	40	[redacted]		18	LIMITED RANGE OF MOTION IN SHOULDER	[redacted] (104)		MILD	1	PERSISTS	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
筋骨格、結合組織および骨障害	脊柱後弯症	0	[redacted]		4	KYPHOSIS	[redacted] (89)		MILD	1	PERSISTS	1	NO
	筋痙攣	40	[redacted]		5	CRAMPS	[redacted] (0)	[redacted] (0)		7	RESOLVED	2	NO
	筋痙縮	5	[redacted]		2	MUSCLE SPASMS	[redacted] (25)	[redacted] (25)	MILD	1	RESOLVED	2	NO
	筋緊張	5	[redacted]		1	MUSCLE TIGHTNESS	[redacted] (1)	[redacted] (10)	MILD	1	RESOLVED	2	NO
		20	[redacted]		4	TIGHTNESS OF MUSCLES IN LEGS	[redacted] (2)	[redacted] (33)	MILD	1	RESOLVED	2	NO
	筋攣縮	5	[redacted]		5	TWITCHING (RIGHT) EYE	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	1	NO
			[redacted]		7	FACIAL TWITCH	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
	筋痛	0	[redacted]		1	SORE MUSCLES	[redacted] (12)	[redacted] (17)	MILD	7	RESOLVED	1	NO
			[redacted]		8	MUSCLE ACHES	[redacted] (49)	[redacted] (114)	MODERATE	4	RESOLVED	2	NO
		5	[redacted]		5	MUSCLE ACHES	[redacted] (9)	[redacted] (19)	MODERATE	7	RESOLVED	1	NO
			[redacted]		2	MUSCLE SORENESS	[redacted] (18)	[redacted] (18)	MILD	7	RESOLVED	1	NO
			[redacted]		7	MUSCLE ACHES/TENSION	[redacted] (19)		MILD	7	PERSISTS	1	NO
		20	[redacted]		2	MUSCLE PAIN - LEFT SHOULDER	[redacted] (8)	[redacted] (8)	MODERATE	7	RESOLVED	1	NO
			[redacted]		7	MUSCLE ACHES	[redacted] (7)	[redacted] (7)	MILD	7	RESOLVED	1	NO
					8	MUSCLE ACHES	[redacted] (41)	[redacted] (41)	MILD	7	RESOLVED	1	NO
	頚部痛	5	[redacted]		3	NECK PAIN / SHOULDER PAIN	[redacted] (60)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		8	NECK ACHE	[redacted] (22)	[redacted] (22)	MILD	7	RESOLVED	1	NO
	頚部硬直	40	[redacted]		16	STIFF NECK/BACK/ARM	[redacted] (36)		MILD	7	PERSISTS	1	NO
			[redacted]		1	STIFF NECK	[redacted] (59)	[redacted] (62)	MODERATE	7	RESOLVED	1	NO
	四肢痛	5	[redacted]		2	LEFT ARM ACHE	[redacted] (3)		MILD	1	PERSISTS	1	NO
		20	[redacted]		7	PAIN IN UPPER LEFT LEG	[redacted] (63)	[redacted] (143)	MODERATE	7	RESOLVED	1	NO
			[redacted]		4	PAIN OF POSTERIOR HEEL (RIGHT)	[redacted] (54)		MODERATE	7	PERSISTS	1	NO
					6	(LEFT) BICEP TENDON PAIN	[redacted] (58)		MODERATE	1	PERSISTS	1	NO
			[redacted]		11	SORE THUMB	[redacted] (21)	[redacted] (43)	MILD	7	RESOLVED	1	NO
			[redacted]		18	(RIGHT) HEEL PAIN	[redacted] (21)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		24	SORENESS IN ARM	[redacted] (62)	[redacted] (76)	MODERATE	6	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
良性および悪性新生物（嚢胞およびポリープを含む）	乳房塊状物NOS	20	[redacted]		11	LEFT BREAST MASS	[redacted] (84)		MODERATE	1	PERSISTS	1	NO
	嚢胞NOS	5	[redacted]		14	CYST (RIGHT) LOWER LEG	[redacted] (70)	[redacted] (70)	MODERATE	3/8	RESOLVED	1	NO
神経系障害	失調NEC	5	[redacted]		5	ATAXIA - HEEL-TOE WALK	[redacted] (83)		MILD	1	PERSISTS	2	NO
	手根管症候群	5	[redacted]		9	WORSENING OF CARPAL TUNNEL SYNDROME	[redacted] (98)	[redacted] (196)	MODERATE	1	RESOLVED	1	NO
	小脳症候群	40	[redacted]		5	DYSMETRIA	[redacted] (84)		MILD	1	PERSISTS	1	NO
	意識レベルの低下	40	[redacted]		4	SLOWED REACTIONS	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
	注意力障害NEC	0	[redacted]		2	INABILITY TO FOCUS ON TASKS	[redacted] (30)	[redacted] (38)	MILD	2	RESOLVED	2	NO
		5	[redacted]		2	CAN NOT CONCENTRATE	[redacted] (0)		SEVERE	1	PERSISTS	3	NO
		20	[redacted]		3	DECREASED CONCENTRATION	[redacted] (1)	[redacted] (37)	MODERATE	2	RESOLVED	3	NO
			[redacted]		3	DIFFICULTY FOCUSING	[redacted] (0)	[redacted] (28)	MILD	1	RESOLVED	2	NO
		40	[redacted]		3	DECREASED CONCENTRATION	[redacted] (0)	[redacted] (3)	MODERATE	2	RESOLVED	2	NO
			[redacted]		1	DECREASED CONCENTRATION	[redacted] (0)	[redacted] (11)	MILD	1	RESOLVED	2	NO
	浮動性めまい（回転性眩暈を除く）	0	[redacted]		2	DIZZINESS	[redacted] (2)	[redacted] (33)	MILD	1	RESOLVED	2	NO
			[redacted]		2	DIZZINESS	[redacted] (10)	[redacted] (11)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	LIGHTHEADED	[redacted] (0)	[redacted] (3)	MILD	1	RESOLVED	3	NO
			[redacted]		1	DIZZINESS	[redacted] (1)	[redacted] (26)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
					3	LIGHTHEADEDNESS	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	2	NO
			[redacted]		3	DIZZINESS	[redacted] (4)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		1	LIGHTHEADED	[redacted] (30)	[redacted] (38)	MILD	2	RESOLVED	2	NO
			[redacted]		1	DIZZINESS	[redacted] (0)		MODERATE	2/7/4	PERSISTS	3	NO
					2	LIGHTHEADEDNESS	[redacted] (0)		MODERATE	2/4	PERSISTS	3	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	浮動性めまい（回転性眩暈を除く）	5	[redacted]	[redacted]	2	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (5)	SEVERE	2	RESOLVED	2	NO
				[redacted]	1	DIZZINESS	[redacted] (0)		MILD	1	PERSISTS	2	NO
				[redacted]	1	DIZZINESS	[redacted] (0)	[redacted] (3)	SEVERE	1	RESOLVED	3	NO
				[redacted]	3	DIZZINESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
				[redacted]	1	DIZZINESS	[redacted] (0)		MILD	1	PERSISTS	2	NO
				[redacted]	1	DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	3	NO
					8	DIZZINESS	[redacted] (11)	[redacted] (11)	MODERATE	1	RESOLVED	3	NO
				[redacted]	6	LIGHTHEADED	[redacted] (2)	[redacted] (2)	MODERATE	6	RESOLVED	3	NO
				[redacted]	1	DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	3	NO
				[redacted]	1	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (21)	MILD	1	RESOLVED	2	NO
				[redacted]	1	DIZZINESS, LIGHTHEADED	[redacted] (0)	[redacted] (11)	SEVERE	8	RESOLVED	3	NO
				[redacted]	1	DIZZINESS	[redacted] (0)		SEVERE	1	PERSISTS	3	NO
				[redacted]	2	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (5)	MILD	1	RESOLVED	3	NO
				[redacted]	4	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
					6	GIDDY	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
				[redacted]	4	DIZZINESS	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	3	NO
				[redacted]	1	DIZZINESS	[redacted] (0)	[redacted] (1)	MILD	1	RESOLVED	2	NO
				[redacted]	1	DIZZINESS	[redacted] (0)	[redacted] (5)	MILD	1	RESOLVED	2	NO
				[redacted]	3	DIZZINESS	[redacted] (0)	[redacted] (2)	MODERATE	2	RESOLVED	3	NO
				[redacted]	2	DIZZINESS	[redacted] (1)	[redacted] (21)	MILD	3/4	RESOLVED	3	NO
				[redacted]	1	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	浮動性めまい（回転性眩暈を除く）	20	[redacted]	[redacted]	3	LIGHTHEADEDNESS	[redacted] (10)	[redacted] (25)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	5	DIZZINESS	[redacted] (2)	[redacted] (3)	SEVERE	1	RESOLVED	2	NO
			[redacted]	[redacted]	16	DIZZINESS	[redacted] (13)	[redacted] (15)	SEVERE	2	RESOLVED	2	NO
			[redacted]	[redacted]	2	LIGHTHEADED	[redacted] (0)		MILD	1	PERSISTS	2	NO
			[redacted]	[redacted]	1	VERY MILD DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	1	LIGHTHEADED	[redacted] (0)	[redacted] (0)	SEVERE	6	RESOLVED	3	NO
			[redacted]	[redacted]	2	LIGHTHEADED	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	2	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (11)	MILD	1	RESOLVED	3	NO
			[redacted]	[redacted]	1	LIGHTHEADED, DISCONNECTED	[redacted] (0)	[redacted] (6)	SEVERE	1	RESOLVED	3	NO
			[redacted]	[redacted]	4	DIZZINESS	[redacted] (29)	[redacted] (32)	SEVERE	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	DIZZINESS	[redacted] (0)	[redacted] (2)	SEVERE	1	RESOLVED	3	NO
			[redacted]	[redacted]	1	LIGHTHEADEDNESS	[redacted] (35)	[redacted] (36)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	5	DIZZINESS	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	1	NO
			[redacted]	[redacted]	2	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	4	DIZZINESS	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	3	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	4	DIZZINESS	[redacted] (2)	[redacted] (8)	MODERATE	2/4	RESOLVED	3	NO
			[redacted]	[redacted]	2	DIZZINESS	[redacted] (0)	[redacted] (11)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	LIGHTHEADED	[redacted] (0)		MODERATE	8/2	PERSISTS	3	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	浮動性めまい（回転性眩暈を除く）	40	[redacted]		3	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (7)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	DIZZINESS	[redacted] (0)	[redacted] (1)	MILD	8	RESOLVED	3	NO
			[redacted]		1	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (4)	MILD	1	RESOLVED	2	NO
			[redacted]		1	DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]		2	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (3)	SEVERE	2	RESOLVED	2	NO
			[redacted]		1	LIGHTHEADED	[redacted] (4)	[redacted] (6)	MILD	1	RESOLVED	2	NO
			[redacted]		5	DIZZINESS	[redacted] (18)	[redacted] (18)	SEVERE	3/7	RESOLVED	3	NO
			[redacted]		2	DIZZINESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
			[redacted]		22	DIZZINESS	[redacted] (0)	[redacted] (1)	MODERATE	3	RESOLVED	2	NO
			[redacted]		12	DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	3	NO
			[redacted]		1	DIZZY, SPACEY	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	LIGHTHEADEDNESS	[redacted] (2)	[redacted] (63)	MILD	7	RESOLVED	2	NO
			[redacted]		2	DIZZINESS	[redacted] (1)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
			[redacted]		2	DIZZINESS	[redacted] (1)	[redacted] (6)	MODERATE	1	RESOLVED	2	NO
	構語障害	40	[redacted]		4	SLURRED SPEECH	[redacted] (0)	[redacted] (1)	MILD	3	RESOLVED	2	NO
			[redacted]		10	SLURRED SPEECH	[redacted] (2)	[redacted] (3)	MODERATE	1	RESOLVED	2	NO
	頭痛NOS	0	[redacted]		1	HEADACHE	[redacted] (3)	[redacted] (24)	MILD	7	RESOLVED	2	NO
					3	HEADACHE	[redacted] (51)	[redacted] (51)	MILD	7	RESOLVED	1	NO
			[redacted]		7	HA	[redacted] (52)	[redacted] (52)	MILD	7	RESOLVED	1	NO
			[redacted]		1	HEADACHE	[redacted] (6)	[redacted] (6)	MILD	1	RESOLVED	1	NO
			[redacted]		1	HEADACHES	[redacted] (3)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		1	HEADACHE	[redacted] (7)	[redacted] (9)	MILD	1	RESOLVED	2	NO
			[redacted]		2	HEADACHE	[redacted] (25)	[redacted] (26)	SEVERE	3	RESOLVED	2	NO
					4	HEADACHE	[redacted] (38)		MILD	4	PERSISTS	2	NO
			[redacted]		2	HEADACHE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	2	NO
					4	HEADACHE	[redacted] (12)	[redacted] (13)	MILD	1	RESOLVED	2	NO
			[redacted]		1	HEADACHE	[redacted] (19)		MILD	7	PERSISTS	2	NO
			[redacted]		2	HEADACHE	[redacted] (1)	[redacted] (2)	SEVERE	6/7	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	0	[redacted]	[redacted]	5	HEADACHE	[redacted] (0)	[redacted] (84)	MODERATE	7	RESOLVED	2	NO
			[redacted]	[redacted]	1	H/A	[redacted] (2)	[redacted] (3)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	2	HEADACHE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	1	HEADACHES	[redacted] (0)	[redacted] (2)	MILD	1	RESOLVED	2	NO
					2	HEADACHES - INTERMITTENT	[redacted] (33)	[redacted] (83)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	HEADACHES	[redacted] (2)	[redacted] (16)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	2	HEADACHE	[redacted] (0)	[redacted] (0)	MODERATE	7	RESOLVED	2	NO
					4	HEADACHE	[redacted] (20)	[redacted] (20)	MODERATE	7	RESOLVED	2	NO
					6	HEADACHE	[redacted] (51)	[redacted] (51)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]	[redacted]	4	HEADACHE	[redacted] (4)	[redacted] (5)	SEVERE	7	RESOLVED	3	NO
			[redacted]	[redacted]	1	HEADACHE	[redacted] (3)	[redacted] (3)	MODERATE	7	RESOLVED	2	NO
			[redacted]	[redacted]	5	HEADACHE	[redacted] (21)	[redacted] (21)	MODERATE	7	RESOLVED	2	NO
					6	HEADACHE	[redacted] (39)	[redacted] (39)	MODERATE	7	RESOLVED	2	NO
					7	HEADACHE	[redacted] (25)	[redacted] (26)	MILD	7	RESOLVED	2	NO
					9	HEADACHE	[redacted] (44)	[redacted] (44)	MODERATE	7	RESOLVED	2	NO
					10	HEADACHE	[redacted] (74)	[redacted] (74)	MODERATE	7	RESOLVED	2	NO
					11	HEADACHE	[redacted] (78)	[redacted] (78)	MODERATE	7	RESOLVED	2	NO
					12	HEADACHE	[redacted] (80)	[redacted] (80)	MODERATE	7	RESOLVED	2	NO
			[redacted]	[redacted]	5	HEADACHES	[redacted] (0)	[redacted] (1)	MODERATE	7	RESOLVED	2	NO
					6	HEADACHES	[redacted] (5)	[redacted] (5)	MODERATE	7	RESOLVED	2	NO
			[redacted]	[redacted]	4	HEADACHE	[redacted] (50)	[redacted] (50)	MODERATE	7	RESOLVED	1	NO
					5	HEADACHE	[redacted] (60)	[redacted] (60)	MODERATE	7	RESOLVED	1	NO
			[redacted]	[redacted]	4	PAINS IN HEAD	[redacted] (2)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
					6	SHARP PAINS IN HEAD	[redacted] (5)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	9	HEADACHE	[redacted] (60)	[redacted] (60)	MILD	4	RESOLVED	2	NO
			[redacted]	[redacted]	1	HEADACHE	[redacted] (1)	[redacted] (5)	MILD	7	RESOLVED	2	NO
					4	HEADACHE	[redacted] (28)	[redacted] (28)	MILD	7	RESOLVED	2	NO
					5	HEADACHE	[redacted] (55)	[redacted] (55)	MILD	7	RESOLVED	2	NO
			[redacted]	[redacted]	7	HEADACHE	[redacted] (18)	[redacted] (18)	SEVERE	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	5	[redacted]		1	HEADACHE	[redacted] (20)	[redacted] (20)	MILD	7	RESOLVED	1	NO
					3	HEADACHE	[redacted] (28)	[redacted] (28)	MILD	7	RESOLVED	1	NO
					5	H/A	[redacted] (67)	[redacted] (67)	MILD	7	RESOLVED	1	NO
					3	INTERMITTENT H/A	[redacted] (50)	[redacted] (235)	MODERATE	7	RESOLVED	1	NO
					2	H/A	[redacted] (3)	[redacted] (6)	MILD	1	RESOLVED	2	NO
					5	HEADACHE	[redacted] (56)	[redacted] (56)	MODERATE	7	RESOLVED	1	NO
					1	HEADACHE	[redacted] (0)	[redacted] (0)	MILD	7	RESOLVED	1	NO
					5	HEADACHE	[redacted] (1)	[redacted] (21)	MODERATE	1	RESOLVED	2	NO
					2	HEADACHE	[redacted] (0)	[redacted] (8)	MILD	7	RESOLVED	2	NO
		20			5	HEADACHE	[redacted] (20)	[redacted] (21)	MODERATE	7	RESOLVED	2	NO
					7	HEADACHE	[redacted] (2)	[redacted] (3)	SEVERE	1	RESOLVED	2	NO
					2	HEADACHE	[redacted] (19)	[redacted] (19)	MILD	1	RESOLVED	1	NO
					1	HEADACHES	[redacted] (0)		MILD	4	PERSISTS	2	NO
					2	HEADACHE	[redacted] (4)	[redacted] (4)	MILD	7	RESOLVED	2	NO
					3	HEADACHE	[redacted] (6)	[redacted] (6)	MILD	7	RESOLVED	2	NO
					4	HEADACHE	[redacted] (10)	[redacted] (10)	MODERATE	7	RESOLVED	2	NO
					17	HEADACHE	[redacted] (68)	[redacted] (68)	MODERATE	7	RESOLVED	2	NO
					5	HEADACHE	[redacted] (2)	[redacted] (2)	MODERATE	6/7	RESOLVED	2	NO
					5	HEADACHE	[redacted] (60)	[redacted] (60)	MODERATE	7	RESOLVED	2	NO
					6	HEADACHE	[redacted] (83)	[redacted] (83)	MODERATE	7	RESOLVED	2	NO
					7	HEADACHE	[redacted] (89)	[redacted] (95)	MODERATE	7/8	RESOLVED	2	NO
					1	HEADACHE	[redacted] (5)	[redacted] (5)	MILD	7	RESOLVED	2	NO
					3	HEADACHE	[redacted] (12)	[redacted] (12)	MILD	7	RESOLVED	2	NO
					4	HEADACHE	[redacted] (21)	[redacted] (21)	MODERATE	7	RESOLVED	2	NO
					1	HEADACHE	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
					6	HEADACHE	[redacted] (29)	[redacted] (32)	SEVERE	1	RESOLVED	2	NO
					3	HEADACHE	[redacted] (14)	[redacted] (20)	SEVERE	7	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	20	[redacted]		4	HEADACHES	[redacted] (4)	[redacted] (4)	SEVERE	7	RESOLVED	2	NO
					5	HEADACHES	[redacted] (19)	[redacted] (22)	MILD	1	RESOLVED	2	NO
					12	HEADACHES	[redacted] (66)	[redacted] (81)	MILD	7	RESOLVED	2	NO
			[redacted]		9	HA	[redacted] (81)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
			[redacted]		2	HEADACHE	[redacted] (25)	[redacted] (25)	MILD	7	RESOLVED	1	NO
					6	HEADACHE	[redacted] (42)	[redacted] (42)	MILD	7	RESOLVED	1	NO
					8	HEADACHE	[redacted] (53)	[redacted] (53)	MILD	7	RESOLVED	1	NO
					9	HEADACHE	[redacted] (57)	[redacted] (57)	MILD	7	RESOLVED	1	NO
				[redacted]	1	HEADACHE	[redacted] (8)	[redacted] (8)	MODERATE	7	RESOLVED	1	NO
					5	HEADACHE	[redacted] (21)	[redacted] (21)	MODERATE	7	RESOLVED	1	NO
			[redacted]		5	HEADACHE	[redacted] (0)	[redacted] (8)	SEVERE	2/3	RESOLVED	3	NO
				[redacted]	6	HEADACHE	[redacted] (2)	[redacted] (3)	MILD	7	RESOLVED	1	NO
				[redacted]	2	HEADACHE	[redacted] (1)	[redacted] (8)	MODERATE	7	RESOLVED	2	NO
			[redacted]		1	HEADACHE	[redacted] (2)	[redacted] (2)	MILD	1	RESOLVED	1	NO
		40	[redacted]		4	HEADACHE	[redacted] (6)	[redacted] (6)	MODERATE	2	PERSISTS	3	NO
					5	HEADACHE	[redacted] (29)	[redacted] (29)	MODERATE	2	PERSISTS	3	NO
			[redacted]		4	HEADACHE	[redacted] (0)	[redacted] (0)	MODERATE	7	RESOLVED	2	NO
				[redacted]	5	HEADACHE	[redacted] (1)	[redacted] (6)	MODERATE	7	RESOLVED	2	NO
				[redacted]	4	HEADACHE	[redacted] (0)	[redacted] (3)	MILD	1	RESOLVED	2	NO
			[redacted]		3	HEADACHES	[redacted] (14)	[redacted] (38)	MILD	7	RESOLVED	2	NO
				[redacted]	5	HEADACHE	[redacted] (37)	[redacted] (37)	MILD	7	RESOLVED	2	NO
					6	HEADACHE	[redacted] (84)	[redacted] (85)	MODERATE	7	RESOLVED	2	NO
				[redacted]	3	HEADACHE	[redacted] (41)	[redacted] (41)	MODERATE	7	RESOLVED	2	NO
				[redacted]	7	MILD HEADACHES	[redacted] (21)	[redacted] (60)	MILD	1	RESOLVED	2	NO
					27	HEADACHE	[redacted] (87)	[redacted] (87)	MILD	7	RESOLVED	2	NO
				[redacted]	2	HEADACHE	[redacted] (16)	[redacted] (17)	MODERATE	1	RESOLVED	2	NO
					3	HEADACHE	[redacted] (22)	[redacted] (26)	SEVERE	7	RESOLVED	2	NO
				[redacted]	8	HEADACHE	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
					18	HEADACHE	[redacted] (52)	[redacted] (52)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	40	[redacted]		1	HEADACHE	[redacted] (7)	[redacted] (9)	SEVERE	3/4	RESOLVED	3	NO
					2	HEADACHE	[redacted] (13)	[redacted] (32)	MILD	3/4	RESOLVED	2	NO
					4	HEADACHE	[redacted] (36)	[redacted] (67)	MODERATE	3/2	RESOLVED	3	NO
			[redacted]		1	HEADACHE	[redacted] (34)	[redacted] (34)	MILD	7	RESOLVED	1	NO
			[redacted]		5	HEADACHE	[redacted] (5)	[redacted] (7)	MODERATE	7	RESOLVED	2	NO
			[redacted]		5	HEADACHE	[redacted] (7)	[redacted] (8)	MILD	7	RESOLVED	1	NO
					6	HEADACHE	[redacted] (15)	[redacted] (15)	MILD	1	RESOLVED	1	NO
					7	HEADACHE	[redacted] (19)	[redacted] (19)	MILD	1	RESOLVED	1	NO
					8	HEADACHE	[redacted] (21)	[redacted] (21)	MILD	7	RESOLVED	1	NO
				[redacted]	2	H/A	[redacted] (42)	[redacted] (84)	MILD	7	RESOLVED	1	NO
				[redacted]	1	HEADACHE (RIGHT TEMPORAL)	[redacted] (18)	[redacted] (54)	MODERATE	7	RESOLVED	2	NO
				[redacted]	4	HEADACHE	[redacted] (0)	[redacted] (3)	MILD	3/4	RESOLVED	1	NO
					8	HEADACHE	[redacted] (6)	[redacted] (9)	MILD	2	RESOLVED	1	NO
				[redacted]	2	HEADACHE (FRONTAL)	[redacted] (22)	[redacted] (22)	MODERATE	7	RESOLVED	1	NO
					3	HEADACHE	[redacted] (40)	[redacted] (40)	MILD	7	RESOLVED	1	NO
					4	HEADACHE	[redacted] (73)	[redacted] (73)	MILD	7	RESOLVED	1	NO
			[redacted]		1	HEADACHE	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
			[redacted]		4	HEADACHE	[redacted] (6)	[redacted] (6)	MILD	7	RESOLVED	1	NO
					6	HEADACHE	[redacted] (22)	[redacted] (22)	MODERATE	7	RESOLVED	1	NO
					9	HEADACHE	[redacted] (48)	[redacted] (77)	MILD	7	RESOLVED	2	NO
				[redacted]	4	HEADACHE	[redacted] (14)	[redacted] (17)	MILD	1	RESOLVED	1	NO
			[redacted]		1	HEADACHE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	2	NO
					2	HEADACHE	[redacted] (7)	[redacted] (7)	MILD	1	RESOLVED	2	NO
					3	"SHARP PAIN RT SIDE OF HEAD" LASTED X 2 SEC.	[redacted] (19)	[redacted] (19)	MODERATE	1	RESOLVED	1	NO
				[redacted]	2	HEADACHE	[redacted] (0)		MILD	6	PERSISTS	3	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	知覚過敏	20	[redacted]		4	SENSITIVITY TO BUMPS UNDER ARM	[redacted] (4)		MILD	1	PERSISTS	2	NO
			[redacted]		5	DECREASED PAIN THRESHOLD	[redacted] (19)		MILD	1	PERSISTS	1	NO
	反射亢進	20	[redacted]		4	HYPERREFLEXIC PATELLAR REFLEX	[redacted] (86)		MILD	1	PERSISTS	1	NO
	筋緊張亢進	20	[redacted]		6	JAW TENSION/CLENCHING RT SIDE ONLY	[redacted] (70)	[redacted] (72)	MILD	1	RESOLVED	1	NO
	感覚減退	20	[redacted]		2	DECREASED SENSITIVITY TO TOUCH	[redacted] (1)	[redacted] (1)	MILD	2	RESOLVED	2	NO
		40	[redacted]		1	NUMBNESS IN FACE	[redacted] (0)	[redacted] (1)	MODERATE	3	RESOLVED	2	NO
	舌下神経障害NOS	0	[redacted]		6	TONGUE DEVIATES TO LEFT	[redacted] (89)		MILD	1	PERSISTS	1	NO
	反射減弱	5	[redacted]		4	HYPOACTIVE DTR'S	[redacted] (83)		MODERATE	1	PERSISTS	2	NO
	活動亢進	0	[redacted]		4	FEELING "HYPER" AFTERNOONS	[redacted] (6)	[redacted] (45)	MILD	1	RESOLVED	2	NO
			[redacted]		5	FIDGETY	[redacted] (69)	[redacted] (72)	MODERATE	1	RESOLVED	1	NO
		5	[redacted]		4	"HYPER" FEELING	[redacted] (0)	[redacted] (87)	MILD	1	RESOLVED	2	NO
	初期不眠症	20	[redacted]		3	EARLY INSOMNIA	[redacted] (1)		MODERATE	1	PERSISTS	2	NO
	不眠症NEC	0	[redacted]		2	SLEEP PROBLEMS	[redacted] (79)	[redacted] (153)	MILD	7	RESOLVED	2	NO
			[redacted]		1	DIFFICULTY FALLING ASLEEP	[redacted] (40)	[redacted] (47)	MILD	1	RESOLVED	1	NO
			[redacted]		5	DIFFICULTY SLEEPING	[redacted] (19)		MILD		PERSISTS	2	NO
			[redacted]		6	NOT SLEEPING WELL	[redacted] (0)	[redacted] (85)	MILD	1	RESOLVED	2	NO
			[redacted]		3	INSOMNIA	[redacted] (1)	[redacted] (26)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	INSOMNIA	[redacted] (2)	[redacted] (256)	MILD	7	RESOLVED	2	NO
			[redacted]		8	INSOMNIA	[redacted] (34)		MODERATE	7	PERSISTS	2	NO
		5	[redacted]		1	INSOMNIA	[redacted] (0)	[redacted] (5)	SEVERE	2	RESOLVED	2	NO
			[redacted]		4	INSOMNIA	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]		1	INSOMNIA	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	INSOMNIA	[redacted] (15)		MILD	7	PERSISTS	2	NO
			[redacted]		3	INSOMNIA	[redacted] (1)	[redacted] (12)	MODERATE	7/8	RESOLVED	3	NO
			[redacted]		3	INSOMNIA	[redacted] (1)	[redacted] (5)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	不眠症NEC	5	[redacted]		15	TROUBLE SLEEPING	[redacted] (4)	[redacted] (4)	MILD	7	RESOLVED	1	NO
					2	INSOMNIA	[redacted] (3)	[redacted] (3)	MILD	7	RESOLVED	1	NO
					3	INSOMNIA	[redacted] (3)	[redacted] (6)	MILD	1	RESOLVED	1	NO
					3	INSOMNIA	[redacted] (1)	[redacted] (21)	MODERATE	1	RESOLVED	1	NO
					6	INSOMNIA	[redacted] (3)	[redacted] (21)	MODERATE	3/4	RESOLVED	2	NO
					3	INSOMNIA	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
					3	INSOMNIA	[redacted] (33)	[redacted] (33)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		6	NOT SLEEPING WELL	[redacted] (34)	[redacted] (46)	SEVERE	7	RESOLVED	2	NO
					1	INSOMNIA	[redacted] (0)	[redacted] (219)	SEVERE	7	RESOLVED	3	NO
					11	SLEEPLESSNESS	[redacted] (3)	[redacted] (4)	SEVERE	3/4	RESOLVED	2	NO
					5	INSOMNIA	[redacted] (34)	[redacted] (35)	MODERATE	2	RESOLVED	3	NO
					2	INSOMNIA	[redacted] (0)	[redacted] (5)	MODERATE	7	RESOLVED	2	NO
					3	SLEEPLESSNESS	[redacted] (11)	[redacted] (26)	MILD	1	RESOLVED	2	NO
					3	INSOMNIA	[redacted] (2)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
					3	RESTLESS SLEEP	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
					1	INSOMNIA	[redacted] (22)	[redacted] (22)	MILD	7	RESOLVED	1	NO
					1	INSOMNIA, SLEEPLESSNESS	[redacted] (0)	[redacted] (1)	SEVERE	3/7	RESOLVED	3	NO
					1	INSOMNIA	[redacted] (2)	[redacted] (16)	MILD	1	RESOLVED	2	NO
					3	INSOMNIA	[redacted] (7)		MODERATE	7	PERSISTS	1	NO
					3	INSOMNIA	[redacted] (30)	[redacted] (30)	MODERATE	7	RESOLVED	1	NO
					4	INSOMNIA	[redacted] (38)	[redacted] (38)	MODERATE	7	RESOLVED	1	NO
					2	INSOMNIA	[redacted] (0)		MODERATE	1	PERSISTS	1	NO
					3	INSOMNIA	[redacted] (0)	[redacted] (8)	SEVERE	2/4/7	RESOLVED	3	NO
					3	INSOMNIA	[redacted] (10)	[redacted] (42)	MILD	7	RESOLVED	2	NO
					3	INSOMNIA	[redacted] (0)		MILD	6/2	PERSISTS	2	NO
					1	INSOMNIA	[redacted] (0)	[redacted] (3)	MODERATE	1	RESOLVED	3	NO
					2	DECREASED SLEEP	[redacted] (65)	[redacted] (65)	MODERATE	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	不眠症NEC	40	[redacted]	[redacted]	2	DECREASED SLEEP	[redacted] (0)	[redacted] (63)	MODERATE	8	RESOLVED	2	NO
			[redacted]	[redacted]	5	DIFFICULTY SLEEPING	[redacted] (1)	[redacted] (6)	MODERATE	4	RESOLVED	2	NO
			[redacted]	[redacted]	3	INSOMNIA, INTERMITTENT	[redacted] (0)		MODERATE	2	PERSISTS	3	NO
			[redacted]	[redacted]	2	INSOMNIA	[redacted] (2)	[redacted] (3)	MODERATE	7	RESOLVED	1	NO
			[redacted]	[redacted]	2	SLEEPLESSNESS	[redacted] (0)	[redacted] (2)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	LOSS OF SLEEP	[redacted] (0)	[redacted] (6)	SEVERE	1	RESOLVED	2	NO
			[redacted]	[redacted]	4	INSOMNIA	[redacted] (43)	[redacted] (349)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	5	SLEEPLESSNESS	[redacted] (20)	[redacted] (104)	MODERATE	4/3	RESOLVED	2	NO
			[redacted]	[redacted]	2	INSOMNIA	[redacted] (1)	[redacted] (5)	SEVERE	1	RESOLVED	2	NO
			[redacted]	[redacted]	14	INSOMNIA	[redacted] (19)	[redacted] (19)	SEVERE	1	RESOLVED	2	NO
			[redacted]	[redacted]	3	INSOMNIA	[redacted] (58)	[redacted] (64)	SEVERE	2	RESOLVED	2	NO
			[redacted]	[redacted]	1	INSOMNIA	[redacted] (3)	[redacted] (6)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	4	INSOMNIA	[redacted] (59)		MILD	7	PERSISTS	1	NO
			[redacted]	[redacted]	1	INSOMNIA	[redacted] (1)	[redacted] (3)	MODERATE	7	RESOLVED	2	NO
			[redacted]	[redacted]	2	INSOMNIA	[redacted] (6)	[redacted] (6)	MILD	7	RESOLVED	2	NO
			[redacted]	[redacted]	2	RESTLESS SLEEP	[redacted] (6)	[redacted] (34)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	1	INSOMNIA (LIGHT SLEEP FREQUENT AWAKENINGS)	[redacted] (0)		MILD	7	PERSISTS	2	NO
	中期不眠症	0	[redacted]	[redacted]	1	AWAKENING DURING SLEEP	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
		20	[redacted]	[redacted]	1	MIDDLE INSOMNIA	[redacted] (0)	[redacted] (91)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]	[redacted]	2	MIDDLE INSOMNIA	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	3	"BROKEN SLEEP"	[redacted] (5)	[redacted] (14)	MILD	6	RESOLVED	3	NO
	片頭痛NOS	20	[redacted]	[redacted]	1	MIGRAINE	[redacted] (2)	[redacted] (2)	SEVERE	1	RESOLVED	2	NO
					2	MIGRAINE	[redacted] (104)	[redacted] (107)	SEVERE	1	RESOLVED	1	NO
		40	[redacted]	[redacted]	5	MIGRAINE HEADACHE	[redacted] (81)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
	不随意性筋収縮	5	[redacted]	[redacted]	7	MUSCLE CONTRACTIONS IN CHEST	[redacted] (75)	[redacted] (80)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	神経圧迫	40	[redacted]		8	"PINCHED NERVE" RT ELBOW	[redacted] (45)	[redacted] (130)	SEVERE	3/7	RESOLVED	1	NO
	錯感覚NEC	0	[redacted]		2	TINGLING IN FINGERS / NUMBNESS	[redacted] (13)	[redacted] (15)	MILD	1	RESOLVED	2	NO
		5	[redacted]		1	TINGLING IN HANDS BILATERALLY X APPROX 2 HOURS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	1	NO
			[redacted]		1	"WARMTH AND TINGLING" IN FACE	[redacted] (7)		MILD	6	PERSISTS	2	NO
		40	[redacted]		1	FACE TINGLING ARM TINGLING	[redacted] (2)	[redacted] (3)	MILD	1	RESOLVED	2	NO
	橈骨神経麻痺	0	[redacted]		3	LEFT HAND PALSY	[redacted] (93)	[redacted] (195)	SEVERE	1	RESOLVED	1	NO
	下肢静止不能症候群	20	[redacted]		3	INCREASED NEED TO STRETCH	[redacted] (0)	[redacted] (11)	MILD	1	RESOLVED	2	NO
	鎮静	20	[redacted]		2	SEDATION	[redacted] (1)	[redacted] (37)	MODERATE	2	RESOLVED	3	NO
		40	[redacted]		2	SEDATION	[redacted] (1)	[redacted] (18)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	SEDATED	[redacted] (0)	[redacted] (1)	SEVERE	3	RESOLVED	2	NO
	副鼻腔炎に伴う頭痛	0	[redacted]		1	SINUS HEADACHE	[redacted] (7)	[redacted] (7)	SEVERE	7	RESOLVED	1	NO
		20	[redacted]		5	SINUS HEADACHE	[redacted] (35)	[redacted] (40)	SEVERE	7	RESOLVED	1	NO
	傾眠	0	[redacted]		9	DROWSINESS	[redacted] (0)		MILD	1	PERSISTS	2	NO
		5	[redacted]		1	SLEEPINESS	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
			[redacted]		1	DROWSINESS	[redacted] (0)		SEVERE	1	PERSISTS	3	NO
			[redacted]		2	DROWSINESS	[redacted] (0)	[redacted] (41)	MILD	1	RESOLVED	2	NO
			[redacted]		2	DROWSINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
		20	[redacted]		1	DROWSINESS	[redacted] (1)		MODERATE	1	PERSISTS	1	NO
			[redacted]		3	SLEEPINESS	[redacted] (107)		MILD	1	PERSISTS	2	NO
			[redacted]		1	DROWSINESS	[redacted] (0)	[redacted] (0)	MODERATE	2	RESOLVED	3	NO
			[redacted]		1	DROWSINESS	[redacted] (8)	[redacted] (84)	MILD	1	RESOLVED	3	NO
			[redacted]		1	GROGGY	[redacted] (1)	[redacted] (1)	MILD	2	RESOLVED	2	NO
		40	[redacted]		4	SLEEPINESS	[redacted] (0)	[redacted] (0)	MILD	4	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	傾眠	40	[redacted]	[redacted]	1	DROWSINESS	[redacted] (0)	[redacted] (1)	MODERATE	8	RESOLVED	3	NO
			[redacted]	[redacted]	6	DROWSINESS	[redacted] (2)	[redacted] (4)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	1	DROWSINESS	[redacted] (1)	[redacted] (12)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	1	DROWSINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	15	DROWSINESS	[redacted] (15)	[redacted] (15)	MILD	1	RESOLVED	2	NO
	会話障害NEC	20	[redacted]	[redacted]	10	IMPAIRED SPEECH	[redacted] (89)	[redacted] (95)	MODERATE	8	RESOLVED	2	NO
	味覚障害	0	[redacted]	[redacted]	1	ODD TASTE IN MOUTH	[redacted] (3)		MILD	1	RESOLVED	3	NO
		20	[redacted]	[redacted]	5	"DULL" TASTE IN MOUTH	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
		40	[redacted]	[redacted]	6	METALLIC TASTE	[redacted] (1)	[redacted] (7)	MODERATE	4	RESOLVED	2	NO
			[redacted]	[redacted]	2	METALLIC TASTE	[redacted] (0)		MILD	1	PERSISTS	3	NO
			[redacted]	[redacted]	1	METALLIC TASTE	[redacted] (1)		MILD	1	PERSISTS	3	NO
	振戦NEC	5	[redacted]	[redacted]	1	TREMORS (HANDS)	[redacted] (7)	[redacted] (7)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	10	SHAKES	[redacted] (60)	[redacted] (60)	MILD	4	RESOLVED	2	NO
			[redacted]	[redacted]	13	SHAKINESS / TREMORS	[redacted] (7)	[redacted] (8)	MODERATE	3	RESOLVED	2	NO
			[redacted]	[redacted]	4	TREMOR	[redacted] (42)	[redacted] (56)	MILD	1	RESOLVED	2	NO
		20	[redacted]	[redacted]	1	SHAKES	[redacted] (4)	[redacted] (4)	MODERATE	8/3	RESOLVED	2	NO
			[redacted]	[redacted]	12	NIGHTTIME SHAKES	[redacted] (2)	[redacted] (2)	SEVERE	1	RESOLVED	2	NO
			[redacted]	[redacted]	13	NIGHTTIME SHAKES	[redacted] (6)	[redacted] (6)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	5	TREMOR	[redacted] (0)		MODERATE	6/2	PERSISTS	2	NO
		40	[redacted]	[redacted]	20	SHAKING	[redacted] (74)	[redacted] (74)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	7	TREMORS	[redacted] (6)	[redacted] (9)	MILD	2	RESOLVED	2	NO
			[redacted]	[redacted]	4	HAND BUZZING	[redacted] (1)	[redacted] (6)	MILD	8	RESOLVED	2	NO
			[redacted]	[redacted]	7	TREMOR	[redacted] (0)		MILD	1	PERSISTS	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
精神障害	異常な夢	0	[redacted]		2	STRANGE DREAMS	[redacted] (24)	[redacted] (85)	MILD	1	RESOLVED	2	NO
		5	[redacted]		5	INCREASED DREAMING	[redacted] (3)	[redacted] (21)	MILD	3/4	RESOLVED	2	NO
			[redacted]		1	VIVID DREAMS	[redacted] (0)	[redacted] (58)	MODERATE	1	RESOLVED	2	NO
		20	[redacted]		7	BAD DREAMS	[redacted] (32)	[redacted] (41)	SEVERE	1	RESOLVED	2	NO
		40	[redacted]		4	DREAMING	[redacted] (7)		MILD	1	PERSISTS	2	NO
	抑うつ気分を伴う適応障害	0	[redacted]		5	SITUATIONAL DEPRESSION	[redacted] (38)		MILD	8/7	PERSISTS	1	NO
	激越	5	[redacted]		1	AGITATED	[redacted] (1)	[redacted] (3)	MODERATE	1	RESOLVED	2	NO
	アルコール離脱症状	40	[redacted]		5	ALCOHOL WITHDRAWAL	[redacted] (63)	[redacted] (65)	MILD	1	RESOLVED	1	NO
	怒り	40	[redacted]		3	ANGER, IRRITABLE	[redacted] (1)	[redacted] (1)	MODERATE	1	RESOLVED	1	NO
	不安NEC	0	[redacted]		3	EDGY, ANXIOUS	[redacted] (0)	[redacted] (85)	MILD	1	RESOLVED	2	NO
			[redacted]		1	ANXIETY	[redacted] (56)	[redacted] (60)	MODERATE	3	RESOLVED	1	NO
			[redacted]		9	ANXIETY	[redacted] (26)		MODERATE	7	PERSISTS	1	NO
			[redacted]		8	ANXIETY	[redacted] (32)	[redacted] (32)	MILD	1	RESOLVED	1	NO
		5	[redacted]		1	ANXIETY	[redacted] (0)		SEVERE	2	PERSISTS	3	NO
		20	[redacted]		1	ANXIETY	[redacted] (10)	[redacted] (12)	SEVERE	3/4/7	RESOLVED	2	NO
					4	ANXIETY	[redacted] (25)	[redacted] (26)	MILD	1	RESOLVED	2	NO
			[redacted]		1	ANXIOUS	[redacted] (1)		SEVERE	1	PERSISTS	2	NO
			[redacted]		10	ANXIETY	[redacted] (3)	[redacted] (4)	SEVERE	3/4	RESOLVED	2	NO
			[redacted]		8	ANXIETY	[redacted] (10)	[redacted] (12)	SEVERE	1	RESOLVED	2	NO
					11	ANXIETY	[redacted] (30)		MILD	7	PERSISTS	2	NO
		40	[redacted]		2	ANXIETY	[redacted] (0)	[redacted] (3)	MODERATE	3/4	RESOLVED	2	NO
			[redacted]		6	ANXIETY	[redacted] (18)	[redacted] (19)	MILD	7	RESOLVED	1	NO
	錯乱	5	[redacted]		2	FOGGY HEAD	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
		20	[redacted]		1	SPACEY	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	SPACY	[redacted] (0)	[redacted] (13)	MODERATE	1	RESOLVED	3	NO
			[redacted]		1	LACK OF MENTAL CLARITY	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
			[redacted]		2	"FOGGY"	[redacted] (0)		MODERATE	4	PERSISTS	3	NO
			[redacted]		5	SPACEY FEELING	[redacted] (0)	[redacted] (11)	MODERATE	1	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
精神障害	錯乱	40	[redacted]		1	LOSS OF MENTAL CLARITY	[redacted] (0)	[redacted] (7)	SEVERE	2	RESOLVED	3	NO
			[redacted]		1	"SPACEY & UNFOCUSED"	[redacted] (1)	[redacted] (1)	MODERATE	8	RESOLVED	3	NO
			[redacted]		2	"FOGGY"	[redacted] (1)		MILD	8	PERSISTS	2	NO
			[redacted]		1	"CLOUDY HEAD"	[redacted] (2)	[redacted] (5)	MILD	1	RESOLVED	2	NO
	泣き	5	[redacted]		4	CRYING	[redacted] (2)	[redacted] (7)	MODERATE	1	RESOLVED	1	NO
	うつ病NEC	0	[redacted]		4	DEPRESSION	[redacted] (44)	[redacted] (44)	SEVERE	6	RESOLVED	2	NO
					5	DEPRESSION	[redacted] (54)	[redacted] (54)	SEVERE	6	RESOLVED	2	NO
					6	DEPRESSION	[redacted] (56)	[redacted] (57)	SEVERE	6	RESOLVED	2	NO
			[redacted]		6	DEPRESSION	[redacted] (61)		MODERATE	6/7	PERSISTS	2	NO
		5	[redacted]		4	DEPRESSION	[redacted] (63)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		2	DEPRESSION	[redacted] (12)	[redacted] (16)	MODERATE	1	RESOLVED	2	NO
			[redacted]		1	DEPRESSED	[redacted] (1)		MILD	6	PERSISTS	2	NO
	失見当識	5	[redacted]		5	DISORIENTATION	[redacted] (0)	[redacted] (5)	SEVERE	2	RESOLVED	2	NO
		20	[redacted]		4	DISORIENTATION	[redacted] (1)	[redacted] (37)	MODERATE	2	RESOLVED	3	NO
		40	[redacted]		2	UNAWARE - DISORIENTED	[redacted] (0)	[redacted] (1)	SEVERE	3	RESOLVED	2	NO
	解離	5	[redacted]		4	"DETACHED" FEELING	[redacted] (1)	[redacted] (21)	MILD	3/4/2	RESOLVED	3	NO
		20	[redacted]		2	UNFOCUSED DETACHED FEELING	[redacted] (0)	[redacted] (1)	SEVERE	3	RESOLVED	3	NO
		40	[redacted]		9	DISSOCIATIVE FEELINGS	[redacted] (6)	[redacted] (9)	MODERATE	2	RESOLVED	1	NO
	不安増強	0	[redacted]		1	INCREASED ANXIETY	[redacted] (4)	[redacted] (4)	MODERATE	1	RESOLVED	2	NO
					4	INCREASED ANXIETY	[redacted] (45)		MODERATE	1	PERSISTS	1	NO
		40	[redacted]		1	INCREASED ANXIETY	[redacted] (6)	[redacted] (59)	MODERATE	1	RESOLVED	1	NO
	幻覚NOS	40	[redacted]		5	HALLUCINATIONS	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
	せっかち	40	[redacted]		28	IMPATIENT	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
	易刺激性	5	[redacted]		1	IRRITABILITY	[redacted] (3)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		4	IRRITABILITY	[redacted] (0)		SEVERE	1	PERSISTS	2	NO
			[redacted]		1	IRRITABLE	[redacted] (59)	[redacted] (81)	MODERATE	1	RESOLVED	1	NO
			[redacted]		2	IRRITABILITY	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
		40	[redacted]		29	IRRITABLE	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
			[redacted]		3	IRRITABLE	[redacted] (4)		MODERATE	1	PERSISTS	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
精神障害	リビドー減退	0	[redacted]		4	DECREASED LIBIDO	[redacted] (68)	[redacted] (82)	MODERATE	1	RESOLVED	1	NO
		5	[redacted]		5	LOW SEX DRIVE	[redacted] (0)		SEVERE	1	PERSISTS	2	NO
			[redacted]		10	DECREASED LIBIDO	[redacted] (5)		MODERATE	1	PERSISTS	2	NO
		20	[redacted]		4	DECREASED LIBIDO	[redacted] (1)	[redacted] (39)	MODERATE	1	RESOLVED	2	NO
			[redacted]		3	DECREASED LIBIDO	[redacted] (19)		MILD	1	PERSISTS	2	NO
		40	[redacted]		4	DECREASED SEX DRIVE	[redacted] (1)		MILD	8	PERSISTS	2	NO
	気分変動NOS	20	[redacted]		1	SLIGHT ALTERATION OF MOOD	[redacted] (4)	[redacted] (38)	MILD	1	RESOLVED	1	NO
	気分動揺	20	[redacted]		4	MOOD SWINGS	[redacted] (0)		MODERATE	6/3	PERSISTS	2	NO
		40	[redacted]		6	MOOD CHANGES	[redacted] (0)	[redacted] (0)	SEVERE	1	RESOLVED	2	NO
	神経過敏	5	[redacted]		8	SHAKY	[redacted] (3)	[redacted] (3)	MODERATE	6	RESOLVED	1	NO
		20	[redacted]		3	TREMULOUSNESS	[redacted] (6)	[redacted] (9)	MILD	1	RESOLVED	2	NO
		40	[redacted]		1	TREMULOUSNESS	[redacted] (0)	[redacted] (3)	MODERATE	3/4	RESOLVED	2	NO
	悪夢	20	[redacted]		3	INTENSE NIGHTMARES	[redacted] (6)	[redacted] (19)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		1	NIGHTMARES	[redacted] (58)	[redacted] (64)	SEVERE	2	RESOLVED	2	NO
	妄想症	0	[redacted]		1	PARANOIA	[redacted] (12)	[redacted] (13)	MODERATE	1	RESOLVED	1	NO
	人格変化	5	[redacted]		3	PERSONALITY CHANGE	[redacted] (1)		MILD	1	PERSISTS	2	NO
	早漏	5	[redacted]		5	PREMATURE EJACULATION	[redacted] (45)	[redacted] (52)	MODERATE	1	RESOLVED	1	NO
	精神病性障害NOS	40	[redacted]		2	PSYCHOTIC EPISODE	[redacted] (64)	[redacted] (83)	SEVERE	5	RESOLVED	1	YES
	落ち着きのなさ	5	[redacted]		2	RESTLESSNESS	[redacted] (1)	[redacted] (31)	MILD	1	RESOLVED	2	NO
	睡眠障害NOS	5	[redacted]		11	CHANGE IN SLEEP PATTERN	[redacted] (15)	[redacted] (19)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		4	SLEEP DISTURBANCE	[redacted] (0)	[redacted] (8)	MODERATE	7/2	RESOLVED	2	NO
腎および尿路障害	排尿障害	0	[redacted]		2	BURNING SENSATION WITH URINATION	[redacted] (5)	[redacted] (5)	MILD	1	RESOLVED	2	NO
	腰部痛	20	[redacted]		10	RT FLANK PAIN	[redacted] (84)		MILD	1	PERSISTS	1	NO
	夜間頻尿	20	[redacted]		4	NOCTURIA	[redacted] (0)		MODERATE	6/8/2	PERSISTS	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
腎および尿路障害	頻尿	0	[redacted]		3	URINARY FREQUENCY	[redacted] (4)	[redacted] (11)	MILD	1	RESOLVED	1	NO
		5	[redacted]		4	URINARY FREQUENCY (INCREASED)	[redacted] (5)	[redacted] (31)	MILD	1	RESOLVED	1	NO
		40	[redacted]		7	INCREASED URINARY FREQUENCY	[redacted] (5)	[redacted] (7)	MODERATE	1	RESOLVED	1	NO
	尿変色	0	[redacted]		5	DARKER COLORED URINE	[redacted] (0)		MILD	4	PERSISTS	2	NO
		20	[redacted]		6	"GOLDEN" URINE	[redacted] (10)	[redacted] (13)	SEVERE	1	RESOLVED	2	NO
生殖系および乳房障害	乳房圧痛	5	[redacted]		6	BREAST TENDERNESS	[redacted] (1)		MODERATE	1	PERSISTS	1	NO
	月経困難症	0	[redacted]		3	MENSTRUAL CRAMPS	[redacted] (48)	[redacted] (49)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]		4	MENSTRUAL CRAMPS	[redacted] (6)	[redacted] (6)	MODERATE	7	RESOLVED	1	NO
					6	MENSTRUAL CRAMPS	[redacted] (66)	[redacted] (66)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		2	MENSTRUAL CRAMPS	[redacted] (31)	[redacted] (35)	MILD	7	RESOLVED	1	NO
	射精障害NOS	20	[redacted]		3	DIFFICULTY WITH EJACULATION	[redacted] (1)		MODERATE	1	RESOLVED	2	NO
	勃起力減退	40	[redacted]		3	ERECTILE DYSFUNCTION	[redacted] (25)	[redacted] (85)	SEVERE	6/7	RESOLVED	2	NO
	月経前症候群	0	[redacted]		2	PMS	[redacted] (43)		MODERATE	7	PERSISTS	1	NO
	精巣嚢胞	40	[redacted]		4	TESTICULAR CYST	[redacted] (42)	[redacted] (58)	MILD	6	RESOLVED	1	NO
	腟出血	20	[redacted]		6	VAGINAL BLEEDING OR BLEEDING FROM URETHRA	[redacted] (12)	[redacted] (58)	MODERATE	6/8	RESOLVED	1	NO
呼吸器、胸郭および縦隔障害	喘息NOS	20	[redacted]		9	BRONCHIAL ASTHMA	[redacted] (58)	[redacted] (64)	MODERATE	7	RESOLVED	1	NO
	咳嗽	5	[redacted]		4	COUGH	[redacted] (79)	[redacted] (83)	MILD	7	RESOLVED	1	NO
			[redacted]		10	COUGHING	[redacted] (6)		MODERATE	7	PERSISTS	1	NO
			[redacted]		5	COUGH	[redacted] (6)	[redacted] (15)	MODERATE	6/8/7	RESOLVED	1	NO
		20	[redacted]		12	COUGH	[redacted] (49)		MODERATE	7	PERSISTS	1	NO
			[redacted]		1	COUGH	[redacted] (42)	[redacted] (43)	MILD	7	RESOLVED	1	NO
		40	[redacted]		6	COUGH	[redacted] (34)	[redacted] (40)	MILD	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
呼吸器、胸郭および縦隔障害	呼吸困難NOS	20	[redacted]		12	SHORTNESS OF BREATH	[redacted] (3)	[redacted] (4)	SEVERE	3/4	RESOLVED	2	NO
		40	[redacted]		12	SOB	[redacted] (18)	[redacted] (18)	SEVERE	3/7	RESOLVED	3	NO
	鼻閉	0	[redacted]		4	NASAL CONGESTION	[redacted] (26)	[redacted] (26)	MILD	1	RESOLVED	1	NO
		5	[redacted]		9	SEVERE NASAL CONGESTION	[redacted] (51)	[redacted] (74)	SEVERE	7	RESOLVED	1	NO
		20	[redacted]		6	STUFFY NOSE	[redacted] (35)	[redacted] (42)	MILD	1	RESOLVED	1	NO
	後鼻漏	20	[redacted]		1	POST NASAL DRIP	[redacted] (84)		MILD	1	PERSISTS	1	NO
			[redacted]		5	POST NASAL DRIP	[redacted] (82)	[redacted] (92)	MILD	1	RESOLVED	1	NO
	鼻漏	40	[redacted]		4	RHINORRHEA	[redacted] (14)		MILD	1	PERSISTS	1	NO
	副鼻腔うっ血	5	[redacted]		3	SINUS CONGESTION	[redacted] (23)	[redacted] (26)	MILD	7	RESOLVED	1	NO
		40	[redacted]		7	SINUS CONGESTION	[redacted] (27)	[redacted] (27)	MODERATE	7	RESOLVED	1	NO
	副鼻腔痛	0	[redacted]		2	SINUS PROBLEM	[redacted] (0)		MODERATE	7	PERSISTS	2	NO
			[redacted]		4	SINUS PROBLEMS	[redacted] (2)	[redacted] (2)	MILD	7	RESOLVED	2	NO
		5	[redacted]		4	SINUS PROBLEMS	[redacted] (1)		MODERATE	7	PERSISTS	2	NO
皮膚および皮下組織障害	ざ瘡NOS	40	[redacted]		10	ACNE	[redacted] (31)		MILD	1	PERSISTS	2	NO
	冷湿	20	[redacted]		2	COLD SWEATS	[redacted] (4)	[redacted] (91)	MODERATE	8/3	RESOLVED	2	NO
	ざ瘡様皮膚炎	5	[redacted]		3	ACNE / RASH	[redacted] (17)		MILD	1	PERSISTS	2	NO
	接触性皮膚炎	0	[redacted]		3	POISON IVY	[redacted] (74)	[redacted] (86)	MILD	1	RESOLVED	1	NO
		5	[redacted]		1	ALLERGIC DERMATITIS "POISON IVY"	[redacted] (11)	[redacted] (18)	MODERATE	1	RESOLVED	1	NO
					2	ALLERGIC DERMATITIS "POISON IVY"	[redacted] (39)	[redacted] (40)	MODERATE	1	RESOLVED	1	NO
				[redacted]	2	ALLERGIC DERMATITIS "POISON IVY"	[redacted] (2)	[redacted] (14)	MILD	7	RESOLVED	1	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
皮膚および皮下組織障害	皮膚炎NOS	0	[redacted]		6	RASH	[redacted] (56)		MILD	7	PERSISTS	2	NO
					8	RASH	[redacted] (77)	[redacted] (84)	SEVERE	8	RESOLVED	2	NO
					10	RASH	[redacted] (98)		MODERATE	1	PERSISTS	1	NO
				[redacted]	1	RASH	[redacted] (31)		MILD	7	RESOLVED	2	NO
				[redacted]	1	RASH	[redacted] (86)	[redacted] (93)	MILD	1	RESOLVED	1	NO
				[redacted]	4	SKIN RASH	[redacted] (6)	[redacted] (26)	MILD	1	RESOLVED	2	NO
				[redacted]	1	WORSENING OF SKIN RASH - UPPER AND LOWER EXTREMITIES	[redacted] (50)		MODERATE	7	RESOLVED	1	NO
		5	[redacted]		1	SKIN RASH ON FACE	[redacted] (1)	[redacted] (13)	MILD	6	RESOLVED	2	NO
		20	[redacted]		5	RASH ON HANDS	[redacted] (8)		MILD	2/7	PERSISTS	2	NO
					6	RASH	[redacted] (38)		MODERATE	1	PERSISTS	2	NO
		40	[redacted]		3	FACIAL RASH	[redacted] (1)	[redacted] (34)	MODERATE	1	RESOLVED	1	NO
			[redacted]		3	RASH ON BUTTOCKS	[redacted] (35)	[redacted] (86)	MODERATE	7	RESOLVED	1	NO
			[redacted]		4	RASH	[redacted] (13)	[redacted] (14)	MODERATE	1	RESOLVED	1	NO
			[redacted]		6	RASH (RED BUMPS OVER BODY)	[redacted] (11)	[redacted] (14)	MODERATE	3	RESOLVED	1	NO
	紅斑性単純性皮膚炎	40	[redacted]		4	ERYTHEMATOUS ECZEMA	[redacted] (92)		MILD	1	PERSISTS	1	NO
	皮膚描記症	40	[redacted]		1	WHITE SPOTS ON BODY	[redacted] (11)	[redacted] (12)	MILD	2	RESOLVED	2	NO
	寝汗	20	[redacted]		4	NIGHT SWEATS	[redacted] (3)	[redacted] (20)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		8	NIGHT SWEATS	[redacted] (27)	[redacted] (104)	SEVERE	4	RESOLVED	1	NO
	そう痒症NOS	0	[redacted]		3	ITCHY HANDS	[redacted] (1)	[redacted] (28)	MILD	1	RESOLVED	2	NO
		5	[redacted]		3	ITCHY WHEN SWEATING	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
			[redacted]		3	ITCHING	[redacted] (1)	[redacted] (3)	MODERATE	1	RESOLVED	1	NO
			[redacted]		2	FOOT ITCHING	[redacted] (0)	[redacted] (4)	SEVERE	3	RESOLVED	3	NO
					4	FOOT ITCHING	[redacted] (10)	[redacted] (11)	SEVERE	2	RESOLVED	3	NO
		20	[redacted]		7	ITCHY SOLES OF FEET	[redacted] (2)	[redacted] (359)	MODERATE	7	RESOLVED	2	NO
			[redacted]		1	ITCHING	[redacted] (0)	[redacted] (2)	SEVERE	3/4/7	RESOLVED	2	NO

表 2.7.6.5.7-30　有害事象一覧表－連日投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
皮膚および皮下組織障害	斑状丘疹状皮疹	40	[redacted]		5	MACULAR, PAPULAR RASH	[redacted] (83)	[redacted] (85)	MILD	1	RESOLVED	1	NO
	丘疹	40	[redacted]		1	RASH, SCALY & PAPULAR - ABD, LEGS, ARMS	[redacted] (14)	[redacted] (23)	SEVERE	3/2	RESOLVED	3	NO
	皮膚変色	20	[redacted]		7	DISCOLORATION UNDER ARM	[redacted] (38)		MODERATE	1	PERSISTS	2	NO
	皮膚小結節	20	[redacted]		8	CONEFORM LESIONS UNDER ARM	[redacted] (38)		MODERATE	1	PERSISTS	1	NO
	多汗	5	[redacted]		5	PERSPIRATION	[redacted] (10)	[redacted] (11)	SEVERE	2	RESOLVED	3	NO
			[redacted]		1	SWEATING	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	1	NO
		20	[redacted]		6	DIAPHORESIS	[redacted] (34)	[redacted] (35)	MODERATE	2	RESOLVED	3	NO
			[redacted]		5	SWEATS	[redacted] (37)	[redacted] (38)	MODERATE	1	RESOLVED	2	NO
					8	SWEATS	[redacted] (29)	[redacted] (32)	SEVERE	1	RESOLVED	2	NO
	蕁麻疹NOS	40	[redacted]		2	RASH/HIVES	[redacted] (11)	[redacted] (15)	SEVERE	7/2	RESOLVED	2	NO
			[redacted]		17	HIVES	[redacted] (22)	[redacted] (23)	MODERATE	7	RESOLVED	2	NO
社会環境	薬物乱用	0	[redacted]		7	INCREASED USE OF COCAINE	[redacted] (42)	[redacted] (42)	MILD	1	RESOLVED	1	NO
外科および内科処置	口腔手術NOS	0	[redacted]		7	ORAL SURGERY	[redacted] (34)	[redacted] (37)	MODERATE	7	RESOLVED	1	NO
	抜歯NOS	5	[redacted]		1	DENTAL EXTRACTIONS	[redacted] (68)	[redacted] (69)	MODERATE	1	RESOLVED	1	NO
血管障害	潮紅	40	[redacted]		5	FLUSHING OF FACE	[redacted] (0)	[redacted] (3)	MODERATE	3/4	RESOLVED	2	NO
	ほてりNOS	20	[redacted]		1	INCREASED HOT FLASHES	[redacted] (2)		MODERATE	1	PERSISTS	2	NO
			[redacted]		2	NIGHTTIME SWEATS	[redacted] (2)	[redacted] (2)	SEVERE	1	RESOLVED	2	NO
					3	NIGHTTIME SWEATS	[redacted] (6)	[redacted] (6)	MODERATE	1	RESOLVED	2	NO
	高血圧NOS	20	[redacted]		10	HIGH BLOOD PRESSURE	[redacted] (35)		MILD	7	PERSISTS	1	NO
		40	[redacted]		4	HYPERTENSION	[redacted] (64)		SEVERE	8	PERSISTS	2	NO
				[redacted]	4	HYPERTENSION	[redacted] (0)		SEVERE	4/7	PERSISTS	2	NO
	不安定血圧	20	[redacted]		2	LABILE BLOOD PRESSURE	[redacted] (10)		MODERATE	3/4/7	PERSISTS	2	NO
	リンパ浮腫NOS	5	[redacted]		2	FIRM, IMMOBILE LYMPHNODE	[redacted] (99)		MODERATE	1	PERSISTS	1	NO

MedDRA Version 3.3

Action: 1 = None, 2 = Study drug permanently discontinued, 3 = Study drug temporarily discontinued, 4 = Dose reduced, 5 = Hospitalized, 6 = Supportive, 7 = Medication, 8 = Other

Rel = Relationship: 1 = Unlikely, 2 = Possible, 3 = Probable

SAE = Serious adverse event

＜資料番号 5.3.5.1-07：Table 14.3.1.7＞

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
血液およびリンパ系障害	リンパ節症	0	[redacted]		MILD ENLARGEMENT OF POSTAURICULAR LYMPHNODES	[redacted] (85)	[redacted] (148)	MILD	1	RESOLVED	1	NO
			[redacted]		ENLARGED MAXILLARY NODES	[redacted] (84)		MODERATE	1	PERSISTS	2	NO
		5	[redacted]		LYMPH NODE SWELLING	[redacted] (83)	[redacted] (110)	MODERATE	1	RESOLVED	1	NO
心臓障害	徐脈NOS	0	[redacted]		BRADYCARDIA	[redacted] (98)		MILD	1	PERSISTS	2	NO
			[redacted]		BRADYCARDIA	[redacted] (84)		MILD	1	PERSISTS	2	NO
		20	[redacted]		BRADYCARDIA	[redacted] (12)	[redacted] (12)	MODERATE	1	RESOLVED	1	NO
	冠動脈疾患NOS	5	[redacted]		CORONARY ARTERY DISEASE	[redacted] (295)		MODERATE	7	PERSISTS	1	NO
	頻脈NOS	40	[redacted]		TACHYCARDIA	[redacted] (368)		MILD	1	PERSISTS	2	NO
先天性および家族性／遺伝性障害	表皮母斑	5	[redacted]		MOLES REMOVED	[redacted] (137)	[redacted] (137)	MILD	1	RESOLVED	1	NO
耳および迷路障害	耳垢栓塞	20	[redacted]		(R) EAR CERUMEN	[redacted] (364)		MODERATE	1	PERSISTS	1	NO
	耳の障害NOS	5	[redacted]		(L) INNER EAR ITCHING	[redacted] (263)		MODERATE	1	PERSISTS	1	NO
	耳痛	0	[redacted]		RT EARACHE	[redacted] (9)	[redacted] (16)	MILD	4	RESOLVED	1	NO
					RT EAR ACHE	[redacted] (42)		MILD	1	PERSISTS	1	NO
		20	[redacted]		(R) EAR PAIN, (R) SCALP PAIN	[redacted] (239)	[redacted] (246)	MODERATE	7	RESOLVED	1	NO
			[redacted]		EAR ACHE - BILAT.	[redacted] (306)	[redacted] (311)	MILD	1	RESOLVED	1	NO
	外耳障害NOS	20	[redacted]		TM'S NOT VISUALIZED SECONDARY TO CERUMEN, NASAL MUCOSA ERYTHEMATOUS, BLEEDING VESSEL (L) NARE	[redacted] (382)		MILD	1	PERSISTS	1	NO
	聴覚過敏	40	[redacted]		INCREASED SENSITIVITY TO NOISE	[redacted] (0)	[redacted] (0)	SEVERE	1	RESOLVED	2	NO
	乗物酔い	5	[redacted]		MOTION SICKNESS	[redacted] (1)	[redacted] (1)	MILD	7	RESOLVED	1	NO
	耳鳴	5	[redacted]		RINGING IN EARS	[redacted] (2)		MODERATE	1	PERSISTS	2	NO
		40	[redacted]		EARS RINGING	[redacted] (74)	[redacted] (74)	SEVERE	1	RESOLVED	1	NO
	鼓膜障害NOS	40	[redacted]		ERYTHEMATOUS TYMPANIC MEMBRANES	[redacted] (363)		MILD	1	PERSISTS	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
耳および迷路障害	回転性眩暈NEC	20	[redacted]		VERTIGO	[redacted] (43)	[redacted] (61)	MODERATE	7	RESOLVED	1	NO
			[redacted]		VERTIGO	[redacted] (107)	[redacted] (132)	MILD	8	RESOLVED	1	NO
				[redacted]	VERTIGO	[redacted] (336)		MILD	7	PERSISTS	1	NO
眼障害	結膜出血	20	[redacted]		PETECHIAE OF EYE	[redacted] (6)	[redacted] (14)	MODERATE	1	RESOLVED	1	NO
	羞明	20	[redacted]		PHOTOPHOBIA	[redacted] (350)		MILD	7	PERSISTS	1	NO
		40	[redacted]		SENSITIVITY TO LIGHT	[redacted] (0)	[redacted] (6)	MODERATE	1	RESOLVED	1	NO
	霧視	0	[redacted]		BLURRED VISION	[redacted] (77)	[redacted] (78)	MODERATE	1	RESOLVED	2	NO
		5	[redacted]		BLURRED VISION (FUZZY)	[redacted] (4)	[redacted] (249)	MILD	8	RESOLVED	2	NO
		20	[redacted]		BLURRED VISION	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
	視覚障害NOS	20	[redacted]		SEEING SPOTS	[redacted] (341)		MILD	1	PERSISTS	1	NO
胃腸障害	腹部膨満	0	[redacted]		BLOATING	[redacted] (29)		MILD	1	PERSISTS	2	NO
		20	[redacted]		ABDOMINAL DISTENSION	[redacted] (105)		MODERATE	1	PERSISTS	2	NO
	腹痛NOS	20	[redacted]		ABDOMINAL CRAMPS	[redacted] (17)	[redacted] (64)	SEVERE	4	RESOLVED	3	NO
			[redacted]		PAIN IN ABDOMEN	[redacted] (243)	[redacted] (244)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		INTERMITTENT ABDOMINAL CRAMPING	[redacted] (3)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
				[redacted]	ABDOMINAL PAIN	[redacted] (2)	[redacted] (2)	MILD	1	RESOLVED	1	NO
	上腹部痛	0	[redacted]		RUQ PAIN	[redacted] (77)	[redacted] (79)	MODERATE	1	RESOLVED	1	NO
					RUQ PAIN	[redacted] (84)		MODERATE	1	PERSISTS	1	NO
		5	[redacted]		STOMACH PAIN	[redacted] (1)	[redacted] (4)	MODERATE	8	RESOLVED	3	NO
			[redacted]		STOMACH CRAMPING	[redacted] (63)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
					STOMACH PAIN	[redacted] (316)	[redacted] (353)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		STOMACH CRAMPS	[redacted] (31)	[redacted] (48)	MILD	1	RESOLVED	2	NO
		40	[redacted]		STOMACH PAINS	[redacted] (35)	[redacted] (38)	MILD	1	RESOLVED	2	NO
					STOMACH CRAMPS	[redacted] (80)	[redacted] (81)	SEVERE	7	RESOLVED	2	NO
			[redacted]		SLIGHT TENDERNESS RUQ	[redacted] (84)		MILD	6	PERSISTS	1	NO
			[redacted]		STOMACH CRAMPS	[redacted] (38)	[redacted] (39)	MODERATE	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	腹部硬直	0	[redacted]		ACHE/GUARDING ABDOMINAL	[redacted] (91)		MILD	1	PERSISTS	1	NO
	虫垂炎	20	[redacted]		APPENDICITIS	[redacted] (136)	[redacted] (148)	SEVERE	5/8/7	RESOLVED	1	YES
		40	[redacted]		APPENDICITIS	[redacted] (59)	[redacted] (60)	SEVERE	5	RESOLVED	1	YES
	腸雑音異常	0	[redacted]		STOMACH GURGLING	[redacted] (1)	[redacted] (3)	MILD	7	RESOLVED	2	NO
	口唇のひび割れ	5	[redacted]		CHAPPED LIPS	[redacted] (1)		MODERATE	6	PERSISTS	1	NO
	口唇炎	5	[redacted]		BUMPS AROUND MOUTH	[redacted] (269)		SEVERE	1	PERSISTS	1	NO
	便秘	5	[redacted]		CONSTIPATION	[redacted] (2)		MODERATE	1	PERSISTS	2	NO
			[redacted]		CONSTIPATION	[redacted] (3)	[redacted] (15)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		CONSTIPATION	[redacted] (13)	[redacted] (96)	MODERATE	4	RESOLVED	3	NO
			[redacted]		CONSTIPATION	[redacted] (4)		MODERATE	8	RESOLVED	2	NO
			[redacted]		CONSTIPATION	[redacted] (8)	[redacted] (109)	MILD	6	RESOLVED	2	NO
			[redacted]		CONSTIPATION	[redacted] (199)	[redacted] (199)	MILD	7	RESOLVED	1	NO
					CONSTIPATION	[redacted] (290)	[redacted] (290)	MILD	7	RESOLVED	1	NO
			[redacted]		CONSTIPATION	[redacted] (3)	[redacted] (4)	MILD	7	RESOLVED	1	NO
	下痢NOS	0	[redacted]		DIARRHEA	[redacted] (2)	[redacted] (2)	MILD	1	RESOLVED	2	NO
					DIARRHEA	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	2	NO
					DIARRHEA	[redacted] (12)	[redacted] (12)	MILD	1	RESOLVED	2	NO
		5	[redacted]		DIARRHEA	[redacted] (157)		SEVERE	7	PERSISTS	1	NO
			[redacted]		DIARRHEA	[redacted] (2)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		DIARRHEA	[redacted] (63)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
					DIARRHEA	[redacted] (356)	[redacted] (360)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DIARRHEA	[redacted] (35)	[redacted] (36)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		DIARRHEA	[redacted] (3)	[redacted] (7)	MILD	1	RESOLVED	2	NO
					DIARRHEA	[redacted] (198)	[redacted] (200)	MODERATE	1	RESOLVED	3	NO
			[redacted]		DIARRHEA	[redacted] (21)	[redacted] (22)	MODERATE	1	RESOLVED	1	NO
		40	[redacted]		DIARRHEA	[redacted] (65)	[redacted] (96)	MILD	1	RESOLVED	1	NO
			[redacted]		DIARRHEA	[redacted] (11)	[redacted] (13)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DIARRHEA	[redacted] (17)	[redacted] (17)	MODERATE	1	RESOLVED	2	NO
					DIARRHEA	[redacted] (24)	[redacted] (24)	MODERATE	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	口内乾燥	0	[redacted]		DRY MOUTH	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
		5	[redacted]		DRY MOUTH	[redacted] (2)	[redacted] (18)	MILD	1	RESOLVED	2	NO
			[redacted]		DRY MOUTH	[redacted] (0)	[redacted] (3)	SEVERE	1	RESOLVED	3	NO
			[redacted]		DRY MOUTH	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
			[redacted]		DRY MOUTH	[redacted] (63)	[redacted] (74)	MILD	1	RESOLVED	1	NO
		20	[redacted]		DRY MOUTH	[redacted] (0)		MILD	1	PERSISTS	2	NO
			[redacted]		DRY MOUTH	[redacted] (9)	[redacted] (9)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DRY MOUTH	[redacted] (1)	[redacted] (36)	MODERATE	1	RESOLVED	3	NO
			[redacted]		DRY MOUTH	[redacted] (198)	[redacted] (200)	MILD	1	RESOLVED	3	NO
			[redacted]		DRY MOUTH	[redacted] (0)	[redacted] (134)	MODERATE	6	RESOLVED	2	NO
		40	[redacted]		DRY MOUTH	[redacted] (0)	[redacted] (1)	SEVERE	8	RESOLVED	3	NO
			[redacted]		DRY MOUTH	[redacted] (3)	[redacted] (58)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DRY MOUTH	[redacted] (0)	[redacted] (0)	MODERATE	6	RESOLVED	2	NO
	消化不良	0	[redacted]		UPSET STOMACH	[redacted] (131)	[redacted] (150)	MODERATE	6	RESOLVED	1	NO
			[redacted]		STOMACH UPSET	[redacted] (0)	[redacted] (0)	MILD	7	RESOLVED	1	NO
			[redacted]		STOMACH UPSET	[redacted] (14)	[redacted] (15)	MILD	7	RESOLVED	2	NO
					STOMACH UPSET	[redacted] (21)	[redacted] (21)	MILD	7	RESOLVED	2	NO
					STOMACH UPSET	[redacted] (41)	[redacted] (114)	MILD	4	RESOLVED	2	NO
					STOMACH UPSET	[redacted] (227)	[redacted] (240)	SEVERE	7	RESOLVED	2	NO
					STOMACH UPSET	[redacted] (244)	[redacted] (277)	MILD	7	RESOLVED	2	NO
		5	[redacted]		HEARTBURN	[redacted] (55)	[redacted] (55)	MILD	7	RESOLVED	2	NO
			[redacted]		UPSET STOMACH	[redacted] (26)	[redacted] (30)	MODERATE	1	RESOLVED	1	NO
		40	[redacted]		HEARTBURN	[redacted] (61)	[redacted] (61)	MODERATE	7	RESOLVED	1	NO
					HEARTBURN	[redacted] (72)	[redacted] (72)	MODERATE	7	RESOLVED	1	NO
				[redacted]	HEARTBURN	[redacted] (1)	[redacted] (1)	MODERATE	7	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	消化不良	40	[redacted]		STOMACH UPSET	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
					STOMACH UPSET	[redacted] (21)	[redacted] (21)	MILD	1	RESOLVED	1	NO
					STOMACH UPSET	[redacted] (48)	[redacted] (57)	MILD	1	RESOLVED	2	NO
					STOMACH UPSET	[redacted] (360)	[redacted] (360)	MILD	7	RESOLVED	1	NO
					STOMACH UPSET	[redacted] (364)	[redacted] (364)	MILD	7	RESOLVED	1	NO
			[redacted]		STOMACH UPSET	[redacted] (1)	[redacted] (18)	MILD	1	RESOLVED	2	NO
	白色便	20	[redacted]		LIGHT COLORED STOOL	[redacted] (11)	[redacted] (11)	MODERATE	1	RESOLVED	2	NO
	鼓腸	0	[redacted]		FLATULANCE	[redacted] (1)	[redacted] (3)	MILD	1	RESOLVED	2	NO
		40	[redacted]		EXCESSIVE GAS	[redacted] (21)	[redacted] (21)	MILD	7	RESOLVED	2	NO
			[redacted]		GAS PAINS & CONSTIPATION	[redacted] (61)	[redacted] (65)	MILD	7	RESOLVED	1	NO
	出血性胃潰瘍	20	[redacted]		BLEEDING ULCER	[redacted] (109)		SEVERE	2	PERSISTS	1	NO
	消化器不調	0	[redacted]		GASTROINTESTINAL UPSET	[redacted] (0)		MILD	8/7	PERSISTS	2	NO
	瘢痕ヘルニアNOS	5	[redacted]		VENTRAL HERNIA	[redacted] (81)		MODERATE	6	PERSISTS	1	NO
	軟便	20	[redacted]		LOOSE STOOLS	[redacted] (35)		MILD	1	PERSISTS	2	NO
		40	[redacted]		LOOSE STOOLS	[redacted] (198)	[redacted] (332)	MODERATE	1	RESOLVED	1	NO
	メレナ	20	[redacted]		MELENA	[redacted] (109)	[redacted] (114)	SEVERE	5	RESOLVED	1	YES
	嘔気	0	[redacted]		NAUSEA	[redacted] (4)	[redacted] (4)	MODERATE	1	RESOLVED	2	NO
			[redacted]		NAUSEA (FLU-LIKE)	[redacted] (7)	[redacted] (15)	MODERATE	1	RESOLVED	2	NO
					NAUSEA	[redacted] (130)	[redacted] (141)	MILD	1	RESOLVED	1	NO
			[redacted]		NAUSEA	[redacted] (82)	[redacted] (82)	MILD	1	RESOLVED	1	NO
		5	[redacted]		NAUSEA	[redacted] (236)	[redacted] (239)	MILD	1	RESOLVED	3	NO
					NAUSEA	[redacted] (257)	[redacted] (263)	MODERATE	1	RESOLVED	3	NO
			[redacted]		NAUSEA	[redacted] (1)	[redacted] (3)	MODERATE	1	RESOLVED	2	NO
			[redacted]		NAUSEA	[redacted] (53)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
					NAUSEA	[redacted] (316)	[redacted] (353)	MODERATE	1	RESOLVED	1	NO
			[redacted]		NAUSEA	[redacted] (0)	[redacted] (5)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	嘔気	20	[redacted]	[redacted]	NAUSEA	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
					INTERMITTENT NAUSEA	[redacted] (102)	[redacted] (109)	MODERATE	2	RESOLVED	3	NO
				[redacted]	NAUSEA	[redacted] (1)	[redacted] (42)	MODERATE	1	RESOLVED	3	NO
					NAUSEA	[redacted] (43)	[redacted] (219)	MILD	1	RESOLVED	3	NO
			[redacted]		NAUSEA	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
			[redacted]		NAUSEA	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	2	NO
			[redacted]		NAUSEA	[redacted] (0)	[redacted] (7)	MODERATE	1	RESOLVED	2	NO
					NAUSEA	[redacted] (271)	[redacted] (274)	MODERATE	1	RESOLVED	1	NO
				[redacted]	NAUSEA	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
			[redacted]		NAUSEA	[redacted] (198)	[redacted] (200)	MODERATE	1	RESOLVED	3	NO
			[redacted]		NAUSEA	[redacted] (97)	[redacted] (99)	MODERATE	1	RESOLVED	2	NO
					NAUSEA	[redacted] (116)	[redacted] (118)	MODERATE	1	RESOLVED	2	NO
					NAUSEA	[redacted] (131)	[redacted] (133)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		NAUSEA	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	3	NO
			[redacted]		NAUSEA	[redacted] (245)	[redacted] (247)	MILD	7/2	RESOLVED	2	NO
				[redacted]	NAUSEA	[redacted] (0)	[redacted] (1)	MODERATE	3	RESOLVED	2	NO
				[redacted]	NAUSEA	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
					NAUSEA	[redacted] (136)	[redacted] (136)	MODERATE	1	RESOLVED	2	NO
			[redacted]		NAUSEA	[redacted] (0)	[redacted] (19)	MILD	1	RESOLVED	3	NO
			[redacted]		NAUSEA	[redacted] (1)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
			[redacted]		NAUSEA	[redacted] (116)	[redacted] (121)	MODERATE	3	RESOLVED	3	NO
					NAUSEA	[redacted] (127)	[redacted] (132)	MODERATE	3	RESOLVED	3	NO
					NAUSEA	[redacted] (136)	[redacted] (139)	MODERATE	3	RESOLVED	3	NO
					NAUSEA	[redacted] (208)	[redacted] (209)	MODERATE	1	RESOLVED	3	NO
	食道逆流	20	[redacted]		ACID REFLUX	[redacted] (141)		MILD	7	PERSISTS	1	NO
		40	[redacted]		ACID REFLUX	[redacted] (4)	[redacted] (4)	MILD	7	PERSISTS	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
胃腸障害	口腔内痛	20	[redacted]		ORAL PAIN ASSOCIATED W/ROOT CANAL	[redacted] (37)	[redacted] (41)	MILD	7	RESOLVED	1	NO
					ORAL PAIN ASSOCIATED W/PERIODONTAL SURGERY	[redacted] (64)	[redacted] (71)	MILD	7	RESOLVED	1	NO
	直腸出血	40	[redacted]		RECTAL BLEEDING	[redacted] (198)	[redacted] (332)	MODERATE	1	RESOLVED	1	NO
	悪心	40	[redacted]		DRY HEAVES	[redacted] (74)	[redacted] (74)	MODERATE	1	RESOLVED	1	NO
	咽喉痛NOS	0	[redacted]		SORE-THROAT	[redacted] (0)	[redacted] (3)	MODERATE	4	RESOLVED	1	NO
					SORE THROAT	[redacted] (42)		MILD	1	PERSISTS	1	NO
		5	[redacted]		SORE THROAT	[redacted] (79)	[redacted] (83)	MILD	7	RESOLVED	1	NO
	咽喉刺激感	40	[redacted]		THROAT BURNING	[redacted] (74)	[redacted] (75)	SEVERE	1	RESOLVED	1	NO
	舌障害NOS	0	[redacted]		1/2 INCH SQUARED AREA OF REDNESS ON TONGUE	[redacted] (78)	[redacted] (148)	MILD	1	RESOLVED	1	NO
	歯痛	0	[redacted]		TOOTH PAIN	[redacted] (81)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]		TOOTHACHE	[redacted] (353)		MODERATE	7/8	PERSISTS	1	NO
		40	[redacted]		INTERMITTENT TOOTHACHE	[redacted] (2)	[redacted] (10)	MILD	7	RESOLVED	1	NO
	嘔吐NOS	0	[redacted]		VOMITING	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
			[redacted]		NAUSEA VOMITING	[redacted] (48)	[redacted] (50)	MODERATE	3	RESOLVED	1	NO
			[redacted]		NAUSEA, VOMITING	[redacted] (19)	[redacted] (20)	MODERATE	1	RESOLVED	1	NO
		5	[redacted]		NAUSEA & VOMITING	[redacted] (1)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
			[redacted]		NAUSEA & VOMITING	[redacted] (18)	[redacted] (18)	SEVERE	3/6	RESOLVED	1	NO
			[redacted]		VOMITING	[redacted] (355)	[redacted] (356)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		INTERMITTENT VOMITING	[redacted] (102)	[redacted] (109)	MODERATE	2	RESOLVED	3	NO
			[redacted]		VOMITING	[redacted] (381)	[redacted] (381)	MILD	4	RESOLVED	1	NO
			[redacted]		VOMITING	[redacted] (21)	[redacted] (22)	MODERATE	1	RESOLVED	1	NO
		40	[redacted]		VOMITING	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	3	NO
			[redacted]		VOMITING	[redacted] (141)	[redacted] (141)	MILD	4	RESOLVED	2	NO
			[redacted]		VOMITING	[redacted] (4)	[redacted] (4)	SEVERE	1	RESOLVED	2	NO
					VOMITING	[redacted] (159)	[redacted] (160)	MODERATE	7	RESOLVED	2	NO
			[redacted]		VOMITING	[redacted] (37)	[redacted] (37)	SEVERE	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	アルコールによる宿酔	0	[redacted]		HANGOVER	[redacted] (46)	[redacted] (47)	SEVERE	7	RESOLVED	1	NO
			[redacted]		HANGOVER	[redacted] (58)	[redacted] (58)	MILD	1	RESOLVED	1	NO
		5	[redacted]		HANGOVERS WORSE	[redacted] (1)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
					HANGOVERS WORSE	[redacted] (4)	[redacted] (7)	MODERATE	1	RESOLVED	2	NO
					HEADACHE/HANGOVER	[redacted] (46)	[redacted] (46)	SEVERE	7	RESOLVED	1	NO
					HEADACHE/HANGOVER	[redacted] (58)	[redacted] (58)	SEVERE	7	RESOLVED	1	NO
	胸痛NEC	0	[redacted]		CHEST PAIN	[redacted] (180)	[redacted] (194)	MODERATE	2	RESOLVED	3	NO
		20	[redacted]		CHEST PAIN W/ON HOSPITALIZATION	[redacted] (63)	[redacted] (64)	MODERATE	7/5/3	RESOLVED	1	YES
			[redacted]		CHEST PAIN	[redacted] (215)		MILD	7	RESOLVED	1	NO
		40	[redacted]		CHEST PAIN	[redacted] (62)	[redacted] (62)	SEVERE	6	RESOLVED	2	NO
			[redacted]		HYPERTENSION/CHEST DISCOMFORT	[redacted] (87)	[redacted] (88)	SEVERE	3/5/7	RESOLVED	2	YES
			[redacted]		CHEST PAIN	[redacted] (65)	[redacted] (65)	SEVERE	7	RESOLVED	1	NO
					CHEST PAIN	[redacted] (74)	[redacted] (74)	MODERATE	7	RESOLVED	1	NO
	胸部絞扼感	5	[redacted]		CHEST TIGHTNESS	[redacted] (128)	[redacted] (129)	MODERATE	1	RESOLVED	1	NO
	活力増進	0	[redacted]		INCREASED ENERGY	[redacted] (82)		MILD	1	PERSISTS	1	NO
	疲労	0	[redacted]		FATIGUE	[redacted] (0)	[redacted] (82)	MODERATE	1	RESOLVED	2	NO
			[redacted]		FATIGUE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	2	NO
			[redacted]		FATIGUE	[redacted] (49)	[redacted] (114)	MODERATE	4	RESOLVED	2	NO
					FATIGUE	[redacted] (291)	[redacted] (316)	MODERATE	1	RESOLVED	3	NO
			[redacted]		FATIGUE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	1	NO
			[redacted]		FATIGUE	[redacted] (1)		MODERATE	8	PERSISTS	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	疲労	5	[redacted]	[redacted]	FATIGUE	[redacted] (0)	[redacted] (3)	SEVERE	1	RESOLVED	3	NO
					FATIGUE	[redacted] (236)	[redacted] (239)	MODERATE	1	RESOLVED	3	NO
					TIREDNESS	[redacted] (21)	[redacted] (161)	MILD	1	RESOLVED	2	NO
					TIREDNESS	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
					FATIGUED	[redacted] (66)		MILD	1	PERSISTS	2	NO
					TIREDNESS	[redacted] (1)	[redacted] (4)	MILD	1	RESOLVED	3	NO
					FATIGUE	[redacted] (2)		MODERATE	3	RESOLVED	2	NO
					LOW ENERGY	[redacted] (310)		SEVERE	7	PERSISTS	1	NO
					FATIGUE	[redacted] (64)		MODERATE	1	PERSISTS	2	NO
		20	[redacted]	[redacted]	FATIGUE	[redacted] (0)	[redacted] (8)	SEVERE	1	RESOLVED	2	NO
					FATIGUE	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	2	NO
					FATIGUE	[redacted] (110)	[redacted] (116)	MILD	1	RESOLVED	1	NO
					FATIGUE	[redacted] (219)	[redacted] (224)	MILD	1	RESOLVED	3	NO
		40	[redacted]	[redacted]	FATIGUE	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	3	NO
					FATIGUE	[redacted] (5)	[redacted] (12)	MILD	1	RESOLVED	2	NO
					TIREDNESS	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
	酩酊感	40	[redacted]	[redacted]	ALCOHOL-LIKE EFFECTS	[redacted] (0)	[redacted] (19)	MODERATE	1	RESOLVED	2	NO
	びくびく感	40	[redacted]	[redacted]	FEELING JITTERY	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
	インフルエンザ様疾患	0	[redacted]	[redacted]	FLU SYMPTOMS	[redacted] (179)	[redacted] (188)	MILD	1	RESOLVED	1	NO
					FLU	[redacted] (91)		MILD	7	PERSISTS	1	NO
					COUGH, COLD, CONGESTION	[redacted] (4)	[redacted] (6)	MODERATE	7	RESOLVED	2	NO
					HEAD COLD	[redacted] (64)	[redacted] (66)	MILD	1	RESOLVED	1	NO
					FLU	[redacted] (192)	[redacted] (234)	SEVERE	7	RESOLVED	1	NO
					COLD SYMPTOMS	[redacted] (194)	[redacted] (199)	MODERATE	7	RESOLVED	1	NO
					UPPER RESPIRATORY INFECTION	[redacted] (309)	[redacted] (322)	MODERATE	1	RESOLVED	1	NO
					UPPER RESPIRATORY INFECTION	[redacted] (95)	[redacted] (107)	MILD	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	インフルエンザ様疾患	5	[redacted]	[redacted]	UPPER RESPIRATORY INFECTION	[redacted] (60)	[redacted] (67)	MODERATE	1	RESOLVED	1	NO
				[redacted]	FLU SYMPTOMS	[redacted] (78)	[redacted] (98)	MODERATE	7	RESOLVED	1	NO
				[redacted]	COLD	[redacted] (257)	[redacted] (259)	MILD	7	RESOLVED	1	NO
				[redacted]	COLD	[redacted] (35)	[redacted] (43)	MODERATE	3/7	RESOLVED	1	NO
				[redacted]	COLD / CONGESTION	[redacted] (87)	[redacted] (104)	MILD	7	RESOLVED	1	NO
				[redacted]	COLD SXS	[redacted] (47)	[redacted] (50)	SEVERE	7	RESOLVED	1	NO
				[redacted]	FLU	[redacted] (24)	[redacted] (28)	MODERATE	7	RESOLVED	1	NO
				[redacted]	COLD	[redacted] (298)	[redacted] (300)	MODERATE	7	RESOLVED	1	NO
				[redacted]	COLD SX	[redacted] (177)	[redacted] (182)	MILD	7	RESOLVED	1	NO
				[redacted]	FLU SX: N,V,D	[redacted] (266)	[redacted] (270)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]	[redacted]	URI	[redacted] (132)	[redacted] (133)	MILD	7	RESOLVED	1	NO
				[redacted]	FLU SYMPTOMS	[redacted] (147)	[redacted] (150)	MODERATE	7	RESOLVED	1	NO
				[redacted]	UPPER RESPIRATORY INFECTION	[redacted] (38)	[redacted] (44)	MILD	1	RESOLVED	1	NO
				[redacted]	CONGESTION	[redacted] (106)	[redacted] (122)	MILD	7	RESOLVED	1	NO
		40	[redacted]	[redacted]	FLU	[redacted] (257)	[redacted] (263)	MILD	7	RESOLVED	1	NO
			[redacted]	[redacted]	CHEST COLD	[redacted] (90)	[redacted] (92)	MILD	7	RESOLVED	1	NO
					SINUS COLD	[redacted] (45)	[redacted] (48)	MILD	7	RESOLVED	1	NO
			[redacted]	[redacted]	UPPER RESPIRATORY INFECTION	[redacted] (96)	[redacted] (105)	SEVERE	7	RESOLVED	2	NO
				[redacted]	HEAD COLD, CONGESTION	[redacted] (129)	[redacted] (144)	MODERATE	7	RESOLVED	1	NO
					UPPER RESPIRATORY INFECTION (COUGH INCLUDED)	[redacted] (284)	[redacted] (296)	MODERATE	7	RESOLVED	1	NO
				[redacted]	FLU	[redacted] (339)	[redacted] (348)	SEVERE	6/7	RESOLVED	1	NO
			[redacted]	[redacted]	CHEST COLD	[redacted] (92)	[redacted] (99)	MILD	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	インフルエンザ様疾患	40	[redacted]	[redacted]	URI	[redacted] (56)	[redacted] (62)	MODERATE	7	RESOLVED	1	NO
				[redacted]	HA, NASAL CONGESTION, CLOGGED EAR - MYALGIA, URI	[redacted] (131)	[redacted] (145)	MODERATE	6/7	RESOLVED	1	NO
					URI - NASAL CONGESTION, COUGH, SNEEZING	[redacted] (177)	[redacted] (184)	MODERATE	6	RESOLVED	1	NO
					URI - SNEEZING, COUGH, CHEST CONGESTION	[redacted] (200)	[redacted] (210)	MODERATE	1	RESOLVED	1	NO
					VIRAL FLU - NAUSEA, FEVER, MYALGIA, HEAD CONGESTION	[redacted] (248)	[redacted] (256)	MODERATE	7	RESOLVED	1	NO
			[redacted]		CONGESTION	[redacted] (181)	[redacted] (188)	MODERATE	7	RESOLVED	1	NO
					COLD SXS	[redacted] (181)	[redacted] (188)	MODERATE	7	RESOLVED	1	NO
				[redacted]	URI	[redacted] (243)	[redacted] (249)	MODERATE	7	RESOLVED	1	NO
			[redacted]		FLU SYMPTOMS	[redacted] (137)	[redacted] (151)	SEVERE	7	RESOLVED	1	NO
				[redacted]	COLD SYMPTOMS	[redacted] (154)		MILD	7	PERSISTS	1	NO
			[redacted]		UPPER RESPIRATORY INFECTION	[redacted] (145)	[redacted] (152)	MILD	7	RESOLVED	1	NO
	嗜眠	5	[redacted]		FEELS HUNG OVER IN MORNING (QUEASY, LOW ENERGY)	[redacted] (96)		MODERATE	1	PERSISTS	1	NO
			[redacted]		"DRAINED" FEELING	[redacted] (0)	[redacted] (87)	MILD	1	RESOLVED	2	NO
		20	[redacted]		DECREASED ENERGY	[redacted] (7)		MILD	1	PERSISTS	2	NO
		40	[redacted]		LETHARGY	[redacted] (160)	[redacted] (207)	MILD	1	RESOLVED	1	NO
				[redacted]	LACK OF ENERGY	[redacted] (1)	[redacted] (27)	MILD	1	RESOLVED	2	NO
					LETHARGY	[redacted] (116)	[redacted] (116)	MODERATE	3	RESOLVED	3	NO
					LETHARGY	[redacted] (127)	[redacted] (132)	MODERATE	3	RESOLVED	3	NO
					LETHARGY	[redacted] (136)	[redacted] (139)	MODERATE	3	RESOLVED	3	NO
					LETHARGY	[redacted] (208)	[redacted] (209)	MODERATE	1	RESOLVED	3	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
全身障害および投与局所様態	倦怠感	20	[redacted]		MALAISE	[redacted] (97)	[redacted] (99)	MODERATE	1	RESOLVED	2	NO
					MALAISE	[redacted] (116)	[redacted] (118)	MODERATE	1	RESOLVED	2	NO
					MALAISE	[redacted] (131)	[redacted] (133)	MODERATE	1	RESOLVED	2	NO
	下肢浮腫	20	[redacted]		SWELLING/PAIN IN ANKLE	[redacted] (320)		MODERATE	6/7	PERSISTS	1	NO
			[redacted]		SWELLING OF (RT) POSTERIOR HEEL	[redacted] (58)		MODERATE	7	PERSISTS	1	NO
	疼痛NOS	5	[redacted]		PAIN IN (LEFT) SIDE	[redacted] (41)	[redacted] (43)	MODERATE	1	RESOLVED	1	NO
		40	[redacted]		BODYACHE	[redacted] (103)	[redacted] (103)	MODERATE	7	RESOLVED	2	NO
	発熱	20	[redacted]		FEVER	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	1	NO
	悪寒	0	[redacted]		CHILLS	[redacted] (32)	[redacted] (32)	MILD	1	RESOLVED	1	NO
		20	[redacted]		CHILLS	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	1	NO
	不活発	20	[redacted]		SLUGGISHNESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
	口渇	40	[redacted]		SEVERE THIRST	[redacted] (19)	[redacted] (19)	SEVERE	6	RESOLVED	2	NO
	脱力	0	[redacted]		PHYSICALLY WEAK	[redacted] (4)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
肝・胆道系障害	肝腫大	5	[redacted]		HEPATOMEGALY	[redacted] (364)		MILD	1	PERSISTS	1	NO
		20	[redacted]		1" LIVER ENLARGEMENT	[redacted] (105)		MODERATE	1	PERSISTS	2	NO
		40	[redacted]		HEPATAMEGALY	[redacted] (84)		MILD	1	PERSISTS	1	NO
免疫系障害	虫刺されアレルギー	0	[redacted]		WASP STING - SWELLING & REDNESS	[redacted] (33)	[redacted] (35)	MODERATE	1	RESOLVED	1	NO
	複合アレルギー	0	[redacted]		ALLERGIES	[redacted] (41)		MILD	7	PERSISTS	1	NO
	季節性アレルギー	20	[redacted]		SEASONAL ALLERGIES	[redacted] (46)	[redacted] (137)	MODERATE	7	RESOLVED	1	NO
感染症および寄生虫症	気管支炎NOS	0	[redacted]		BRONCHITIS	[redacted] (36)	[redacted] (38)	MODERATE	7	RESOLVED	2	NO
		5	[redacted]		BRONCHITIS	[redacted] (31)	[redacted] (39)	MODERATE	7	RESOLVED	1	NO
			[redacted]		BRONCHITIS	[redacted] (58)	[redacted] (67)	SEVERE	6	RESOLVED	1	NO
		20	[redacted]		BRONCHITIS	[redacted] (13)	[redacted] (74)	MILD	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
感染症および寄生虫症	デング熱	20	[redacted]		DENGUE FEVER	[redacted] (209)	[redacted] (222)	MODERATE	1	RESOLVED	1	NO
	耳の感染症NOS	5	[redacted]		(LEFT) EAR INFECTION (INNER AND OUTER)	[redacted] (51)	[redacted] (110)	MODERATE	7	RESOLVED	1	NO
		20	[redacted]		EAR INFECTION	[redacted] (13)	[redacted] (74)	MILD	7	RESOLVED	1	NO
			[redacted]		EAR INFECTION	[redacted] (219)	[redacted] (228)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		EAR INFECTION	[redacted] (11)	[redacted] (17)	MODERATE	7	RESOLVED	1	NO
			[redacted]		EAR INFECTION (UNDIAGNOSED)	[redacted] (348)	[redacted] (354)	MODERATE	7	RESOLVED	1	NO
	ウイルス性胃腸炎NOS	20	[redacted]		GASTROINTESTINAL VIRUS	[redacted] (180)	[redacted] (182)	SEVERE	1	RESOLVED	1	NO
		40	[redacted]		STOMACH VIRUS	[redacted] (358)	[redacted] (363)	MILD	1	RESOLVED	1	NO
			[redacted]		GI "VIRUS" NAUSEA/DIARRHEA	[redacted] (384)	[redacted] (385)	MODERATE	1	RESOLVED	1	NO
	C型肝炎	20	[redacted]		HEPATITIS C	[redacted] (110)		MILD	1	PERSISTS	1	NO
	単純ヘルペス	20	[redacted]		HERPES SIMPLEX	[redacted] (3)	[redacted] (7)	MILD	7	RESOLVED	1	NO
		40	[redacted]		COLD SORE - TONGUE	[redacted] (47)	[redacted] (63)	MILD	1	RESOLVED	1	NO
	帯状疱疹	5	[redacted]		SHINGLES	[redacted] (333)	[redacted] (358)	MODERATE	7	RESOLVED	1	NO
	インフルエンザ	5	[redacted]		INFLUENZA	[redacted] (13)	[redacted] (14)	MODERATE	7	RESOLVED	1	NO
	限局性感染	20	[redacted]		FOOT INFECTION	[redacted] (54)	[redacted] (64)	MILD	7	RESOLVED	1	NO
	ウイルス性髄膜炎NEC	20	[redacted]		MENINGITIS (VIRAL)	[redacted] (338)	[redacted] (354)	SEVERE	5	RESOLVED	1	YES
	外耳炎（外耳道のせつを除く）NOS	20	[redacted]		ERYTHEMA RIGHT EXTERNAL CANAL	[redacted] (83)	[redacted] (95)	MILD	1	RESOLVED	1	NO
	咽頭炎NOS	40	[redacted]		SCRATCHY THROAT	[redacted] (103)	[redacted] (103)	MODERATE	1	RESOLVED	2	NO
	レンサ球菌性咽頭炎	40	[redacted]		STREP THROAT	[redacted] (11)	[redacted] (17)	MODERATE	7	RESOLVED	1	NO
	気道感染NOS	0	[redacted]		RESPIRATORY INFECTION	[redacted] (121)	[redacted] (145)	SEVERE	7	RESOLVED	1	NO
	副鼻腔炎NOS	5	[redacted]		SINUS INFECTION	[redacted] (133)	[redacted] (141)	MILD	7	RESOLVED	1	NO
			[redacted]		SINUS INFECTION	[redacted] (191)	[redacted] (203)	MILD	7	RESOLVED	1	NO
		40	[redacted]		SINUS INFECTION	[redacted] (18)	[redacted] (27)	SEVERE	7	RESOLVED	2	NO
			[redacted]		ACUTE SINUSITIS	[redacted] (251)	[redacted] (259)	SEVERE	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
感染症および寄生虫症	皮膚感染症NOS	5	[redacted]		INFECTION RT ELBOW	[redacted] (342)	[redacted] (371)	MODERATE	7	RESOLVED	1	NO
	歯膿瘍	40	[redacted]		TOOTH ABSCESS	[redacted] (141)	[redacted] (278)	SEVERE	6/7	RESOLVED	1	NO
	歯感染	5	[redacted]		TOOTH INFECTION	[redacted] (23)	[redacted] (36)	MODERATE	7	RESOLVED	1	NO
	上気道感染NOS	40	[redacted]		VIRAL UPPER RESPIRATORY INFECTION	[redacted] (363)		MILD	1	PERSISTS	1	NO
			[redacted]		URI/SINUS INFECTION	[redacted] (118)	[redacted] (147)	SEVERE	7	RESOLVED	1	NO
	尿路感染NOS	20	[redacted]		URINARY TRACT INFECTION	[redacted] (138)	[redacted] (204)	MILD	7	RESOLVED	1	NO
	ウイルス感染NOS	0	[redacted]		VIRUS & BACTERIA INFECTION	[redacted] (250)	[redacted] (276)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]		VIRAL INFECTION	[redacted] (2)	[redacted] (19)	MODERATE	7	RESOLVED	1	NO
傷害および中毒	事故NOS	0	[redacted]		SLIGHT TENDERNESS LEFT LOWER ANTERIOR CHEST (RIB) SECONDARY TO FALL	[redacted] (81)		MILD	1	PERSISTS	1	NO
	急性アルコール中毒	5	[redacted]		ALCOHOL INTOXIFICATION	[redacted] (38)	[redacted] (39)	SEVERE	5/6	RESOLVED	1	YES
		20	[redacted]		ALCOHOL INTOXICATION	[redacted] (147)	[redacted] (151)	SEVERE	5/7	RESOLVED	1	YES
	足関節部骨折	20	[redacted]		BROKEN FOOT	[redacted] (143)	[redacted] (169)	SEVERE	7	RESOLVED	1	NO
			[redacted]		BROKEN ANKLE	[redacted] (219)	[redacted] (220)	SEVERE	5/7	RESOLVED	1	YES
	節足動物咬傷	20	[redacted]		TICK BITE	[redacted] (288)	[redacted] (288)	MILD	7	RESOLVED	1	NO
	咬刺傷NOS	0	[redacted]		CAT BITE INFECTION	[redacted] (236)	[redacted] (246)	MILD	7	RESOLVED	1	NO
	熱傷NOS	0	[redacted]		BURN ON (RIGHT) NECK	[redacted] (7)	[redacted] (8)	MODERATE	7	RESOLVED	1	NO
	上顆炎	40	[redacted]		TENNIS ELBOW	[redacted] (335)	[redacted] (344)	MODERATE	7	RESOLVED	1	NO
	顔面骨骨折	40	[redacted]		BROKEN NOSE	[redacted] (243)	[redacted] (275)	MODERATE	1	RESOLVED	1	NO
	頭部損傷	40	[redacted]		INJURED HEAD & CHIN	[redacted] (73)	[redacted] (74)	MILD	1	RESOLVED	1	NO
	損傷NOS	0	[redacted]		CUT ON (RIGHT) EAR LOBE	[redacted] (98)	[redacted] (113)	MILD	1	RESOLVED	1	NO
		40	[redacted]		CUT RT. THUMB	[redacted] (358)	[redacted] (358)	SEVERE	6	RESOLVED	1	NO
	関節脱臼NEC	0	[redacted]		DISLOCATED SHOULDER	[redacted] (119)	[redacted] (334)	SEVERE	7	RESOLVED	1	NO
	関節捻挫	40	[redacted]		TWISTED KNEE	[redacted] (4)	[redacted] (13)	MODERATE	7	RESOLVED	1	NO
	裂傷	0	[redacted]		(RIGHT) ELBOW LACERATION	[redacted] (10)	[redacted] (13)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		CUT ON LOWER LIP	[redacted] (369)		MILD	1	PERSISTS	1	NO
				[redacted]	WOUND IN FOREHEAD	[redacted] (243)	[redacted] (275)	MODERATE	8	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
傷害および中毒	四肢損傷NOS	5	[redacted]		KNEE INJURY	[redacted] (186)		MILD	1		1	NO
			[redacted]		JAMMED FINGER	[redacted] (87)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		INJURED KNEE	[redacted] (73)		MILD	1	PERSISTS	1	NO
	筋肉損傷NOS	5	[redacted]		PULLED BACK MUSCLE	[redacted] (171)	[redacted] (171)	SEVERE	7	RESOLVED	1	NO
	肋骨骨折	40	[redacted]		TWO BROKEN RIBS	[redacted] (243)	[redacted] (275)	MODERATE	1	RESOLVED	1	NO
	交通事故	0	[redacted]		CAR ACCIDENT	[redacted] (64)	[redacted] (64)	MILD	1	RESOLVED	1	NO
	サンバーン	20	[redacted]		SUNBURN	[redacted] (84)	[redacted] (145)	MILD	1	RESOLVED	1	NO
	腱損傷	40	[redacted]		TORN ACHILLES TENDON	[redacted] (243)	[redacted] (358)	SEVERE	7	RESOLVED	1	NO
	腱断裂	40	[redacted]		TORN RIGHT BICEP TENDON	[redacted] (345)		SEVERE	6/7	PERSISTS	1	NO
臨床検査	血中コレステロール増加	0	[redacted]		HIGH CHOLESTEROL	[redacted] (344)		MILD	7	PERSISTS	1	NO
			[redacted]		ELEVATED CHOLESTEROL	[redacted] (312)		MODERATE	7		1	NO
	血中ブドウ糖増加	20	[redacted]		INCREASE IN BLOOD SUGAR	[redacted] (42)		MODERATE	1	PERSISTS	2	NO
	血圧上昇	0	[redacted]		ELEVATED BLOOD PRESSURE	[redacted] (44)	[redacted] (83)	MILD	1	RESOLVED	2	NO
			[redacted]		ELEVATED BLOOD PRESSURE	[redacted] (7)		MODERATE	1	PERSISTS	1	NO
			[redacted]		INCREASE IN BLOOD PRESSURE	[redacted] (61)		MODERATE	6/7	PERSISTS	2	NO
		20	[redacted]		ELEVATED B.P.	[redacted] (136)		MILD	1	PERSISTS	1	NO
		40	[redacted]		INCREASED BLOOD PRESSURE	[redacted] (42)		MILD	1	PERSISTS	2	NO
			[redacted]		INCREASED BLOOD PRESSURE	[redacted] (12)	[redacted] (28)	MILD	1	RESOLVED	1	NO
					INCREASED BLOOD PRESSURE	[redacted] (140)		MODERATE	1	PERSISTS	1	NO
	血中トリグリセリド増加	40	[redacted]		ELEVATED TRIGLYCERIDES	[redacted] (86)		SEVERE	6	PERSISTS	2	NO
	心電図異常NOS	0	[redacted]		ABN ECG, ABN - STRESS TEST, CARDIAC CATH - NORMAL	[redacted] (542)		MODERATE	8	RESOLVED	1	NO
	心拍数増加	40	[redacted]		INCREASED HEART RATE	[redacted] (7)		MILD	1	PERSISTS	2	NO
	心音異常	5	[redacted]		S4 (HEART)	[redacted] (360)		MILD	1	PERSISTS	1	NO
		20	[redacted]		HEART SOUNDS SOFT/DIFFICULT TO HEAR	[redacted] (382)		MILD	1	PERSISTS	1	NO
	肝機能検査NOS異常	5	[redacted]		ELEVATED LFTS	[redacted] (88)		MODERATE	2	PERSISTS	2	NO
		20	[redacted]		ELEVATED LIVER FUNCTION	[redacted] (379)		MILD	1	PERSISTS	1	NO
		40	[redacted]		ELEVATED LFT'S	[redacted] (90)	[redacted] (98)	SEVERE	3	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
臨床検査	血小板数減少	5	[redacted]		DECREASED PLATELETS	[redacted] (88)	[redacted] (98)	MODERATE	2	RESOLVED	2	NO
	ロンベルグ徴候陽性	0	[redacted]		SWAY ON ROMBERG	[redacted] (98)		MILD	1	PERSISTS	2	NO
		40	[redacted]		SWAY ON ROMBERG	[redacted] (88)	[redacted] (368)	MODERATE	1	RESOLVED	2	NO
	子宮頚部スミア異常	40	[redacted]		ABNORMAL PAP SMEAR	[redacted] (46)		MODERATE	7/8	RESOLVED	1	NO
	体重減少	5	[redacted]		WEIGHT LOSS	[redacted] (141)		MODERATE	1	PERSISTS	2	NO
		40	[redacted]		WEIGHT LOSS	[redacted] (82)	[redacted] (217)	MILD	1	RESOLVED	1	NO
	体重増加	5	[redacted]		INCREASED WEIGHT (10 LBS)	[redacted] (130)	[redacted] (169)	MILD	1	RESOLVED	1	NO
代謝および栄養障害	食欲不振	20	[redacted]		LOSS OF APPETITE	[redacted] (1)	[redacted] (61)	MODERATE	1	RESOLVED	3	NO
			[redacted]		LOSS OF APPETITE	[redacted] (23)	[redacted] (42)	MILD	1	RESOLVED	1	NO
	食欲減退NOS	5	[redacted]		APPETITE SUPPRESSED	[redacted] (0)	[redacted] (2)	MILD	8	RESOLVED	2	NO
			[redacted]		APPETITE DECREASE	[redacted] (1)	[redacted] (66)	MODERATE	1	RESOLVED	2	NO
					DECREASED APPETITE	[redacted] (93)		MODERATE	1	PERSISTS	1	NO
			[redacted]		DECREASED APPETITE	[redacted] (2)	[redacted] (9)	SEVERE	3	RESOLVED	2	NO
			[redacted]		DECREASED APPETITE	[redacted] (310)		SEVERE	7	PERSISTS	1	NO
		40	[redacted]		DECREASED APPETITE	[redacted] (10)	[redacted] (321)	MILD	1	RESOLVED	2	NO
			[redacted]		DECREASED APPETITE	[redacted] (34)	[redacted] (126)	MILD	1	RESOLVED	2	NO
	食欲亢進NOS	0	[redacted]		INCREASED CRAVING FOR SNACKS AND SWEETS	[redacted] (52)		MODERATE	1	PERSISTS	2	NO
		5	[redacted]		APPETITE INCREASE	[redacted] (12)	[redacted] (12)	MILD	1	RESOLVED	2	NO
		40	[redacted]		INCREASED APPETITE FOR SUGAR	[redacted] (28)	[redacted] (349)	MODERATE	1	RESOLVED	2	NO
			[redacted]		INCREASED APPETITE	[redacted] (20)	[redacted] (104)	MILD	4	RESOLVED	2	NO
	糖尿病NOS	20	[redacted]		DIABETES	[redacted] (141)	[redacted] (343)	MILD	1	RESOLVED	1	NO
	体液貯留	20	[redacted]		WATER RETENTION "BLOATING"	[redacted] (28)	[redacted] (28)	MILD	7	RESOLVED	1	NO
					WATER RETENTION "BLOATING"	[redacted] (280)		MODERATE	7	PERSISTS	1	NO
	ヘモクロマトーシス	0	[redacted]		HEMOCHROMATOSIS	[redacted] (240)		MODERATE	6	PERSISTS	1	NO
	高血糖NOS	20	[redacted]		ELEVATED GLUCOSE	[redacted] (41)	[redacted] (195)	MILD	8	RESOLVED	1	NO
	高脂血症NOS	5	[redacted]		HYPERLIPIDEMIA	[redacted] (305)		MILD	7	PERSISTS	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
筋骨格、結合組織および骨障害	関節痛	0	[redacted]		JOINT PAIN	[redacted] (18)	[redacted] (18)	MILD	7	RESOLVED	1	NO
					ARTHRITIC PAIN	[redacted] (19)	[redacted] (19)	MILD	7	RESOLVED	1	NO
		5	[redacted]		SHOULDER PAIN - RIGHT	[redacted] (78)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
			[redacted]		ELBOW PAIN	[redacted] (83)		MODERATE	7	PERSISTS	1	NO
		20	[redacted]		HIP PAIN	[redacted] (55)	[redacted] (56)	MODERATE	7	RESOLVED	1	NO
			[redacted]		JOINT PAIN	[redacted] (85)		MILD	7	PERSISTS	2	NO
			[redacted]		PAIN IN ANKLE	[redacted] (221)	[redacted] (271)	SEVERE	7	RESOLVED	1	NO
		40	[redacted]		RIGHT WRIST PAIN	[redacted] (318)		MODERATE	7	PERSISTS	1	NO
			[redacted]		LEFT SHOULDER PAIN	[redacted] (364)		MODERATE	7	PERSISTS	1	NO
	背部痛	0	[redacted]		BACK PAIN	[redacted] (7)	[redacted] (84)	MODERATE	7	RESOLVED	1	NO
			[redacted]		BACK PAIN / POSSIBLE BROKEN RIB	[redacted] (213)	[redacted] (237)	SEVERE	7	RESOLVED	1	NO
					BACK PAIN / RIB PAIN	[redacted] (156)	[redacted] (158)	MODERATE	7	RESOLVED	1	NO
			[redacted]		LEFT BACK PAIN	[redacted] (70)		MODERATE	1	PERSISTS	1	NO
			[redacted]		LOW BACK PAIN	[redacted] (5)	[redacted] (9)	MILD	7	RESOLVED	1	NO
		5	[redacted]		SHARP PAINS IN BACK	[redacted] (15)	[redacted] (15)	MODERATE	1	RESOLVED	1	NO
					BACK ACHE	[redacted] (144)	[redacted] (144)		7	RESOLVED	1	NO
			[redacted]		BACK PAIN	[redacted] (4)	[redacted] (17)	SEVERE	6/7	RESOLVED	1	NO
			[redacted]		LOW BACK PAIN	[redacted] (166)	[redacted] (169)	MODERATE	7	RESOLVED	1	NO
		20	[redacted]		BACK MUSCLE PAIN	[redacted] (246)		SEVERE	6	PERSISTS	1	NO
			[redacted]		BACK PAIN	[redacted] (45)	[redacted] (46)	SEVERE	7	RESOLVED	1	NO
			[redacted]		BACK PAIN	[redacted] (46)	[redacted] (46)	MILD	7	RESOLVED	1	NO
					BACK PAIN	[redacted] (70)	[redacted] (70)	MODERATE	7	RESOLVED	1	NO
					BACKACHE	[redacted] (157)	[redacted] (157)	MODERATE	7	RESOLVED	1	NO
					BACKACHE	[redacted] (166)	[redacted] (166)	MODERATE	7	RESOLVED	1	NO
					BACKACHE	[redacted] (276)	[redacted] (276)	MODERATE	7	RESOLVED	1	NO
					BACK PAIN	[redacted] (379)	[redacted] (379)	MODERATE	7	RESOLVED	1	NO
			[redacted]		BACK PAIN	[redacted] (34)	[redacted] (41)	MILD	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
筋骨格、結合組織および骨障害	背部痛	40	[redacted]		BACK PAIN	[redacted] (55)	[redacted] (57)	MODERATE	7	RESOLVED	1	NO
					BACK PAIN	[redacted] (76)	[redacted] (91)	MODERATE	7	RESOLVED	1	NO
			[redacted]		SORE BACK	[redacted] (7)		MODERATE	1	PERSISTS	1	NO
			[redacted]		BACK PAIN	[redacted] (60)	[redacted] (60)	MILD	7	RESOLVED	1	NO
			[redacted]		LOW BACK PAIN	[redacted] (297)	[redacted] (300)	MODERATE	7	RESOLVED	1	NO
	骨棘	5	[redacted]		BILATERAL HEEL SPURS	[redacted] (331)		MODERATE	7	PERSISTS	1	NO
	滑液包炎	5	[redacted]		BURSITIS LEFT ELBOW	[redacted] (286)	[redacted] (293)	MODERATE	7	RESOLVED	1	NO
	椎間板ヘルニア	40	[redacted]		HERNIATED DISK	[redacted] (278)			6/7	PERSISTS	1	NO
	関節運動範囲減少	40	[redacted]		LIMITED RANGE OF MOTION IN SHOULDER	[redacted] (104)		MILD	1	PERSISTS	2	NO
	関節硬直	40	[redacted]		JOINT STIFFNESS	[redacted] (106)	[redacted] (259)	MODERATE	1	RESOLVED	2	NO
	脊柱後弯症	0	[redacted]		KYPHOSIS	[redacted] (89)		MILD	1	PERSISTS	1	NO
	筋緊張	20	[redacted]		MUSCLE TENSION	[redacted] (219)	[redacted] (224)	MILD	1	RESOLVED	2	NO
			[redacted]		GENERALIZED MUSCLE TENSION	[redacted] (97)	[redacted] (99)	MODERATE	1	RESOLVED	2	NO
					GENERALIZED MUSCLE TENSION	[redacted] (116)	[redacted] (118)	MODERATE	1	RESOLVED	2	NO
					GENERALIZED MUSCLE TENSION	[redacted] (131)	[redacted] (133)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		MUSCLE TENSION INCREASED SEVERITY	[redacted] (88)		MODERATE	7	RESOLVED	1	NO
			[redacted]		MUSCLE TENSION	[redacted] (197)	[redacted] (201)	MODERATE	6	RESOLVED	2	NO
	筋攣縮	5	[redacted]		TWITCHING (RIGHT) EYE	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	1	NO
	筋痛	0	[redacted]		MUSCLE ACHES	[redacted] (49)	[redacted] (114)	MODERATE	4	RESOLVED	2	NO
					MUSCLE ACHES	[redacted] (291)	[redacted] (316)	MILD	1	RESOLVED	3	NO
		5	[redacted]		MUSCLE ACHES	[redacted] (9)	[redacted] (19)	MODERATE	7	RESOLVED	1	NO
			[redacted]		MUSCLE ACHES/TENSION	[redacted] (19)		MILD	7	PERSISTS	1	NO
		20	[redacted]		MUSCLE ACHES	[redacted] (206)	[redacted] (206)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		ACHING MUSCLES	[redacted] (180)	[redacted] (180)	MODERATE	7	RESOLVED	1	NO
			[redacted]		MUSCLE ACHES	[redacted] (200)	[redacted] (205)	MILD	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
筋骨格、結合組織および骨障害	頚部痛	5	[redacted]		NECK PAIN / SHOULDER PAIN	[redacted] (60)		MODERATE	7	PERSISTS	1	NO
	頚部硬直	40	[redacted]		STIFF NECK/BACK/ARM	[redacted] (36)		MILD	7	PERSISTS	1	NO
			[redacted]		STIFF NECK	[redacted] (59)	[redacted] (62)	MODERATE	7	RESOLVED	1	NO
	四肢痛	20	[redacted]		PAIN IN UPPER LEFT LEG	[redacted] (63)	[redacted] (143)	MODERATE	7	RESOLVED	1	NO
			[redacted]		PAIN OF POSTERIOR HEEL (RIGHT)	[redacted] (54)		MODERATE	7	PERSISTS	1	NO
					(LEFT) BICEP TENDON PAIN	[redacted] (58)		MODERATE	1	PERSISTS	1	NO
			[redacted]		HEEL SPUR PAIN	[redacted] (106)	[redacted] (106)	MODERATE	7	RESOLVED	1	NO
			[redacted]		SORE THUMB	[redacted] (21)	[redacted] (43)	MILD	7	RESOLVED	1	NO
			[redacted]		(RIGHT) HEEL PAIN	[redacted] (21)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		SORENESS IN ARM	[redacted] (62)	[redacted] (76)	MODERATE	6	RESOLVED	2	NO
良性および悪性新生物（嚢胞およびポリープを含む）	嚢胞NOS	5	[redacted]		CYST (RIGHT) LOWER LEG	[redacted] (70)	[redacted] (70)	MODERATE	3/8	RESOLVED	1	NO
神経系障害	失調NEC	5	[redacted]		ATAXIA - HEEL-TOE WALK	[redacted] (83)		MILD	1	PERSISTS	2	NO
	手根管症候群	5	[redacted]		WORSENING OF CARPAL TUNNEL SYNDROME	[redacted] (98)	[redacted] (196)	MODERATE	1	RESOLVED	1	NO
	小脳症候群	40	[redacted]		DYSMETRIA	[redacted] (84)		MILD	1	PERSISTS	1	NO
	意識レベルの低下	40	[redacted]		SLOWED REACTIONS	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
	注意力障害NEC	20	[redacted]		DIFFICULTY FOCUSING	[redacted] (0)	[redacted] (28)	MILD	1	RESOLVED	2	NO
		40	[redacted]		DECREASED CONCENTRATION	[redacted] (0)	[redacted] (11)	MILD	1	RESOLVED	2	NO
	浮動性めまい（回転性眩暈を除く）	0	[redacted]		DIZZINESS	[redacted] (236)	[redacted] (261)	MODERATE	1	RESOLVED	1	NO
			[redacted]		DIZZINESS	[redacted] (10)	[redacted] (11)	MODERATE	1	RESOLVED	3	NO
			[redacted]		LIGHTHEADEDNESS	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
					LIGHTHEADEDNESS	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treatment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Action	Outcome	Rel	SAE
神経系障害	浮動性めまい（回転性眩暈を除く）	5	[redacted]	[redacted]	DIZZINESS	[redacted] (0)	[redacted] (3)	SEVERE	1	RESOLVED	3	NO
				[redacted]	DIZZINESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
				[redacted]	DIZZINESS	[redacted] (0)		MILD	1	PERSISTS	2	NO
				[redacted]	LIGHTHEADNESS	[redacted] (299)	[redacted] (300)	MODERATE	1	RESOLVED	2	NO
				[redacted]	DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	3	NO
					DIZZINESS	[redacted] (11)	[redacted] (11)	MODERATE	1	RESOLVED	3	NO
				[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (21)	MILD	1	RESOLVED	2	NO
				[redacted]	DIZZINESS, LIGHTHEADED	[redacted] (0)	[redacted] (11)	SEVERE	8	RESOLVED	3	NO
				[redacted]	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (5)	MILD	1	RESOLVED	3	NO
				[redacted]	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO
					GIDDY	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
				[redacted]	DIZZINESS	[redacted] (4)	[redacted] (4)	MILD	1	RESOLVED	3	NO
				[redacted]	DIZZINESS	[redacted] (0)	[redacted] (1)	MILD	1	RESOLVED	2	NO
				[redacted]	DIZZINESS	[redacted] (0)	[redacted] (5)	MILD	1	RESOLVED	2	NO
		20	[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (10)	[redacted] (25)	MILD	1	RESOLVED	2	NO
				[redacted]	LIGHTHEADED	[redacted] (0)		MILD	1	PERSISTS	2	NO
				[redacted]	VERY MILD DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
				[redacted]	SLIGHT DIZZINESS	[redacted] (349)		MILD	4	PERSISTS	1	NO
				[redacted]	DIZZINESS	[redacted] (341)		MILD	1	PERSISTS	1	NO
				[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
				[redacted]	LIGHTHEADED	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	3	NO
				[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (11)	MILD	1	RESOLVED	3	NO
				[redacted]	LIGHTHEADED, DISCONNECTED	[redacted] (0)	[redacted] (6)	SEVERE	1	RESOLVED	3	NO
				[redacted]	LIGHTHEADEDNESS	[redacted] (35)	[redacted] (36)	MILD	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treatment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Action	Outcome	Rel	SAE
神経系障害	浮動性めまい（回転性眩暈を除く）	20	[redacted]	[redacted]	DIZZINESS	[redacted] (11)	[redacted] (12)	SEVERE	1	RESOLVED	1	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	DIZZINESS	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	INTERMITTENT DIZZINESS	[redacted] (110)	[redacted] (116)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
		40	[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (7)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	DIZZINESS	[redacted] (0)	[redacted] (1)	MILD	8	RESOLVED	3	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (0)	[redacted] (4)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	LIGHTHEADED	[redacted] (4)	[redacted] (6)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	DIZZINESS	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	DIZZINESS	[redacted] (0)	[redacted] (1)	MODERATE	3	RESOLVED	2	NO
			[redacted]	[redacted]	DIZZINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	3	NO
			[redacted]	[redacted]	DIZZY, SPACEY	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (2)	[redacted] (63)	MILD	7	RESOLVED	2	NO
			[redacted]	[redacted]	DIZZINESS	[redacted] (1)	[redacted] (5)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (1)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	LIGHTHEADEDNESS	[redacted] (147)	[redacted] (151)	MILD	1	RESOLVED	3	NO
	構語障害	40	[redacted]	[redacted]	SLURRED SPEECH	[redacted] (0)	[redacted] (1)	MILD	3	RESOLVED	2	NO
			[redacted]	[redacted]	SLURRED SPEECH	[redacted] (2)	[redacted] (3)	MODERATE	1	RESOLVED	2	NO
	頭痛NOS	0	[redacted]	[redacted]	HEADACHE	[redacted] (3)	[redacted] (24)	MILD	7	RESOLVED	2	NO
			[redacted]	[redacted]	HEADACHE	[redacted] (51)	[redacted] (51)	MILD	7	RESOLVED	1	NO
			[redacted]	[redacted]	HEADACHE	[redacted] (116)	[redacted] (116)	MILD	7	RESOLVED	1	NO
			[redacted]	[redacted]	HEADACHE	[redacted] (6)	[redacted] (6)	MILD	1	RESOLVED	1	NO
			[redacted]	[redacted]	HEADACHES	[redacted] (3)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	HEADACHE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	HEADACHE	[redacted] (12)	[redacted] (13)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	HEADACHE	[redacted] (19)		MILD	7	PERSISTS	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	0	[redacted]		HEADACHE	[redacted] (0)	[redacted] (84)	MODERATE	7	RESOLVED	2	NO
					HEADACHE - "TENSION"	[redacted] (85)		MILD	7	PERSISTS	1	NO
					H/A	[redacted] (2)	[redacted] (3)	MILD	1	RESOLVED	1	NO
					HEADACHE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	1	NO
					HEADACHES	[redacted] (0)	[redacted] (2)	MILD	1	RESOLVED	2	NO
					HEADACHES - INTERMITTENT	[redacted] (33)	[redacted] (83)	MILD	1	RESOLVED	2	NO
					HEADACHES	[redacted] (2)	[redacted] (16)	MILD	1	RESOLVED	1	NO
					HEADACHE	[redacted] (0)	[redacted] (0)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (20)	[redacted] (20)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (51)	[redacted] (51)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]		HEADACHE	[redacted] (4)	[redacted] (5)	SEVERE	7	RESOLVED	3	NO
					HEADACHE	[redacted] (236)	[redacted] (239)	MILD	1	RESOLVED	3	NO
					HEADACHE	[redacted] (257)	[redacted] (263)	MODERATE	1	RESOLVED	3	NO
					HEADACHE	[redacted] (3)	[redacted] (3)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (21)	[redacted] (21)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (39)	[redacted] (39)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (25)	[redacted] (26)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (44)	[redacted] (44)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (74)	[redacted] (74)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (78)	[redacted] (78)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (80)	[redacted] (80)	MODERATE	7	RESOLVED	2	NO
					HEADACHES	[redacted] (0)	[redacted] (1)	MODERATE	7	RESOLVED	2	NO
					HEADACHES	[redacted] (5)	[redacted] (5)	MODERATE	7	RESOLVED	2	NO
					PAINS IN HEAD	[redacted] (2)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
					SHARP PAINS IN HEAD	[redacted] (5)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
					HEADACHE	[redacted] (189)	[redacted] (189)	SEVERE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (221)	[redacted] (222)		7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	5	[redacted]		HEADACHE	[redacted] (1)	[redacted] (5)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (28)	[redacted] (28)	MILD	7	RESOLVED	2	NO
				[redacted]	HEADACHE	[redacted] (55)	[redacted] (55)	MILD	7	RESOLVED	2	NO
				[redacted]	HEADACHE	[redacted] (92)		MILD	6/7	PERSISTS	1	NO
				[redacted]	HEADACHE	[redacted] (18)	[redacted] (18)	SEVERE	7	RESOLVED	1	NO
				[redacted]	HEADACHE	[redacted] (20)	[redacted] (20)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (28)	[redacted] (28)	MILD	7	RESOLVED	1	NO
					H/A	[redacted] (67)	[redacted] (67)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (262)	[redacted] (262)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (297)	[redacted] (297)	MODERATE	7	RESOLVED	1	NO
				[redacted]	INTERMITTENT H/A	[redacted] (50)	[redacted] (235)	MODERATE	7	RESOLVED	1	NO
				[redacted]	H/A	[redacted] (3)	[redacted] (6)	MILD	1	RESOLVED	2	NO
					HEADACHE	[redacted] (316)	[redacted] (353)	SEVERE	8	RESOLVED	1	NO
					HEADACHE	[redacted] (353)		MODERATE	7	PERSISTS	1	NO
				[redacted]	HEADACHE	[redacted] (56)	[redacted] (56)	MODERATE	7	RESOLVED	1	NO
				[redacted]	HEADACHE	[redacted] (0)	[redacted] (0)	MILD	7	RESOLVED	1	NO
				[redacted]	HEADACHE	[redacted] (0)	[redacted] (8)	MILD	7	RESOLVED	2	NO
		20	[redacted]		HEADACHE	[redacted] (20)	[redacted] (21)	MODERATE	7	RESOLVED	2	NO
			[redacted]		HEADACHE	[redacted] (350)		MILD	7	PERSISTS	1	NO
			[redacted]		HEADACHE	[redacted] (10)	[redacted] (10)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (175)	[redacted] (176)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (199)	[redacted] (199)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (68)	[redacted] (68)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (280)	[redacted] (281)	MODERATE	7	RESOLVED	2	NO
				[redacted]	HEADACHE	[redacted] (5)	[redacted] (5)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (12)	[redacted] (12)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (21)	[redacted] (21)	MODERATE	7	RESOLVED	2	NO
				[redacted]	HEADACHE	[redacted] (1)	[redacted] (1)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	20	[redacted]		HEADACHES	[redacted] (4)	[redacted] (4)	SEVERE	7	RESOLVED	2	NO
					HEADACHES	[redacted] (19)	[redacted] (22)	MILD	1	RESOLVED	2	NO
					HEADACHES	[redacted] (66)	[redacted] (81)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (142)		MILD	7	PERSISTS	1	NO
					HA	[redacted] (81)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
					HEADACHE X3	[redacted] (150)	[redacted] (208)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (25)	[redacted] (25)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (42)	[redacted] (42)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (53)	[redacted] (53)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (57)	[redacted] (57)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (87)	[redacted] (87)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (126)	[redacted] (126)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (161)	[redacted] (161)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (218)	[redacted] (218)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (268)	[redacted] (268)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (332)	[redacted] (332)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (346)	[redacted] (346)	MODERATE	7	RESOLVED	1	NO
			[redacted]		HEADACHE	[redacted] (2)	[redacted] (2)	MILD	1	RESOLVED	1	NO
		40	[redacted]		HEADACHE	[redacted] (1)	[redacted] (6)	MODERATE	7	RESOLVED	2	NO
			[redacted]		HEADACHES	[redacted] (14)	[redacted] (38)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (37)	[redacted] (37)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (84)	[redacted] (85)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (41)	[redacted] (41)	MODERATE	7	RESOLVED	2	NO
					MILD HEADACHES	[redacted] (21)	[redacted] (60)	MILD	1	RESOLVED	2	NO
					HEADACHE	[redacted] (216)	[redacted] (216)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (87)	[redacted] (87)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (16)	[redacted] (17)	MODERATE	1	RESOLVED	2	NO
					HEADACHE	[redacted] (22)	[redacted] (26)	SEVERE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (337)	[redacted] (339)	SEVERE	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	頭痛NOS	40	[redacted]		HEADACHE	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
					HEADACHE	[redacted] (52)	[redacted] (52)	MILD	1	RESOLVED	2	NO
					HEADACHE	[redacted] (34)	[redacted] (34)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (5)	[redacted] (7)	MODERATE	7	RESOLVED	2	NO
					HEADACHE	[redacted] (200)	[redacted] (205)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (7)	[redacted] (8)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (15)	[redacted] (15)	MILD	1	RESOLVED	1	NO
					HEADACHE	[redacted] (19)	[redacted] (19)	MILD	1	RESOLVED	1	NO
					HEADACHE	[redacted] (21)	[redacted] (21)	MILD	7	RESOLVED	1	NO
					H/A	[redacted] (202)	[redacted] (202)	MILD	1	RESOLVED	1	NO
					H/A	[redacted] (42)	[redacted] (84)	MILD	7	RESOLVED	1	NO
					HEADACHE (RIGHT TEMPORAL)	[redacted] (18)	[redacted] (54)	MODERATE	7	RESOLVED	2	NO
					HEADACHE (FRONTAL)	[redacted] (22)	[redacted] (22)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (40)	[redacted] (40)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (73)	[redacted] (73)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	2	NO
					HEADACHE	[redacted] (6)	[redacted] (6)	MILD	7	RESOLVED	1	NO
					HEADACHE	[redacted] (22)	[redacted] (22)	MODERATE	7	RESOLVED	1	NO
					HEADACHE	[redacted] (48)	[redacted] (77)	MILD	7	RESOLVED	2	NO
					HEADACHE	[redacted] (3)	[redacted] (3)	MILD	1	RESOLVED	2	NO
					HEADACHE	[redacted] (7)	[redacted] (7)	MILD	1	RESOLVED	2	NO
					"SHARP PAIN RT SIDE OF HEAD" LASTED X 2 SEC.	[redacted] (19)	[redacted] (19)	MODERATE	1	RESOLVED	1	NO
	知覚過敏	20	[redacted]		DECREASED PAIN THRESHOLD	[redacted] (19)		MILD	1	PERSISTS	1	NO
	反射亢進	20	[redacted]		HYPERREFLEXIC PATELLAR REFLEX	[redacted] (86)		MILD	1	PERSISTS	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	筋緊張亢進	20	[redacted]		JAW TENSION/CLENCHING RT SIDE ONLY	[redacted] (70)	[redacted] (72)	MILD	1	RESOLVED	1	NO
		40	[redacted]		INCREASED MUSCLE TENSION	[redacted] (210)	[redacted] (210)	MODERATE	1	RESOLVED	3	NO
					INCREASED MUSCLE TENSION	[redacted] (222)	[redacted] (222)	MODERATE	1	RESOLVED	3	NO
					INCREASED MUSCLE TENSION	[redacted] (237)	[redacted] (237)	MODERATE	1	RESOLVED	3	NO
	感覚減退	40	[redacted]		NUMBNESS IN FACE	[redacted] (0)	[redacted] (1)	MODERATE	3	RESOLVED	2	NO
	舌下神経障害NOS	0	[redacted]		TONGUE DEVIATES TO LEFT	[redacted] (89)		MILD	1	PERSISTS	1	NO
	反射減弱	5	[redacted]		HYPOACTIVE DTR'S	[redacted] (83)		MODERATE	1	PERSISTS	2	NO
		20	[redacted]		DECREASED REFLEX (R) KNEE	[redacted] (307)		MODERATE	8	PERSISTS	1	NO
	活動亢進	5	[redacted]		"HYPER" FEELING	[redacted] (0)	[redacted] (87)	MILD	1	RESOLVED	2	NO
	不眠症NEC	0	[redacted]		SLEEP PROBLEMS	[redacted] (79)	[redacted] (153)	MILD	7	RESOLVED	2	NO
			[redacted]		DIFFICULTY FALLING ASLEEP	[redacted] (40)	[redacted] (47)	MILD	1	RESOLVED	1	NO
			[redacted]		INSOMNIA INTERMITTENT	[redacted] (361)		MILD	7	PERSISTS	1	NO
			[redacted]		NOT SLEEPING WELL	[redacted] (0)	[redacted] (85)	MILD	1	RESOLVED	2	NO
			[redacted]		INSOMNIA	[redacted] (2)	[redacted] (256)	MILD	7	RESOLVED	2	NO
			[redacted]		SLEEP PX'S	[redacted] (158)	[redacted] (158)	MILD	7	RESOLVED	1	NO
		5	[redacted]		INSOMNIA	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]		INSOMNIA	[redacted] (0)	[redacted] (5)	MODERATE	1	RESOLVED	2	NO
			[redacted]		INSOMNIA	[redacted] (1)	[redacted] (12)	MODERATE	7/8	RESOLVED	3	NO
			[redacted]		INSOMNIA	[redacted] (1)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		TROUBLE SLEEPING	[redacted] (4)	[redacted] (4)	MILD	7	RESOLVED	1	NO
			[redacted]		INSOMNIA	[redacted] (310)		SEVERE	7	PERSISTS	1	NO
			[redacted]		INSOMNIA	[redacted] (3)	[redacted] (6)	MILD	1	RESOLVED	1	NO
			[redacted]		INSOMNIA	[redacted] (1)	[redacted] (21)	MODERATE	1	RESOLVED	1	NO
			[redacted]		INSOMNIA	[redacted] (85)	[redacted] (100)	MILD	7	RESOLVED	3	NO
					INSOMNIA	[redacted] (163)	[redacted] (179)	MILD	7	RESOLVED	3	NO
			[redacted]		INSOMNIA	[redacted] (33)	[redacted] (33)	MODERATE	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	不眠症NEC	20	[redacted]	[redacted]	NOT SLEEPING WELL	[redacted] (34)	[redacted] (46)	SEVERE	7	RESOLVED	2	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (0)	[redacted] (219)	SEVERE	7	RESOLVED	3	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (0)	[redacted] (5)	MODERATE	7	RESOLVED	2	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (141)	[redacted] (141)	SEVERE	1	RESOLVED	2	NO
					INSOMNIA	[redacted] (145)	[redacted] (145)	SEVERE	1	RESOLVED	2	NO
					INSOMNIA	[redacted] (149)	[redacted] (149)	SEVERE	1	RESOLVED	2	NO
					INSOMNIA	[redacted] (341)	[redacted] (354)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (2)	[redacted] (2)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	RESTLESS SLEEP	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (22)	[redacted] (22)	MILD	7	RESOLVED	1	NO
			[redacted]	[redacted]	INSOMNIA, SLEEPLESSNESS	[redacted] (0)	[redacted] (1)	SEVERE	3/7	RESOLVED	3	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (2)	[redacted] (16)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (146)		MODERATE	1	PERSISTS	1	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (30)	[redacted] (30)	MODERATE	7	RESOLVED	1	NO
					INSOMNIA	[redacted] (38)	[redacted] (38)	MODERATE	7	RESOLVED	1	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (189)	[redacted] (190)	MILD	1	RESOLVED	2	NO
					INSOMNIA	[redacted] (198)	[redacted] (200)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (10)	[redacted] (42)	MILD	7	RESOLVED	2	NO
			[redacted]	[redacted]	INSOMNIA	[redacted] (0)	[redacted] (3)	MODERATE	1	RESOLVED	3	NO
					DECREASED SLEEP	[redacted] (97)	[redacted] (99)	MODERATE	1	RESOLVED	2	NO
					DECREASED SLEEP	[redacted] (116)	[redacted] (118)	MODERATE	1	RESOLVED	2	NO
					DECREASED SLEEP	[redacted] (131)	[redacted] (133)	MODERATE	1	RESOLVED	2	NO
			[redacted]	[redacted]	DECREASED SLEEP	[redacted] (65)	[redacted] (65)	MODERATE	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	不眠症NEC	40	[redacted]		DECREASED SLEEP	[redacted] (0)	[redacted] (63)	MODERATE	8	RESOLVED	2	NO
			[redacted]		INSOMNIA	[redacted] (158)	[redacted] (178)		7	RESOLVED	1	NO
			[redacted]		INSOMNIA	[redacted] (2)	[redacted] (3)	MODERATE	7	RESOLVED	1	NO
			[redacted]		LOSS OF SLEEP	[redacted] (0)	[redacted] (6)	SEVERE	1	RESOLVED	2	NO
					INSOMNIA	[redacted] (140)	[redacted] (140)	SEVERE	1	RESOLVED	2	NO
				[redacted]	INSOMNIA	[redacted] (43)	[redacted] (349)	MILD	1	RESOLVED	2	NO
				[redacted]	SLEEPLESSNESS	[redacted] (20)	[redacted] (104)	MODERATE	4/3	RESOLVED	2	NO
				[redacted]	INSOMNIA	[redacted] (1)	[redacted] (5)	SEVERE	1	RESOLVED	2	NO
					INSOMNIA	[redacted] (19)	[redacted] (19)	SEVERE	1	RESOLVED	2	NO
			[redacted]		INSOMNIA	[redacted] (59)		MILD	7	PERSISTS	1	NO
			[redacted]		INSOMNIA	[redacted] (105)	[redacted] (105)	MILD	1	RESOLVED	3	NO
					INSOMNIA	[redacted] (121)	[redacted] (121)	MILD	1	RESOLVED	3	NO
					INSOMNIA	[redacted] (123)	[redacted] (123)	MILD	1	RESOLVED	3	NO
					INSOMNIA	[redacted] (125)	[redacted] (125)	MILD	1	RESOLVED	3	NO
					INSOMNIA	[redacted] (133)	[redacted] (133)	MILD	1	RESOLVED	3	NO
					INSOMNIA	[redacted] (194)	[redacted] (195)	MILD	1	RESOLVED	2	NO
				[redacted]	RESTLESS SLEEP	[redacted] (6)	[redacted] (34)	MILD	1	RESOLVED	2	NO
				[redacted]	INSOMNIA	[redacted] (208)	[redacted] (209)	MODERATE	1	RESOLVED	3	NO
			[redacted]		DIFFICULTY SLEEPING	[redacted] (363)	[redacted] (363)	MILD	7	RESOLVED	1	NO
	中期不眠症	0	[redacted]		AWAKENING DURING SLEEP	[redacted] (0)		MODERATE	1	PERSISTS	2	NO
		20	[redacted]		MIDDLE INSOMNIA	[redacted] (0)	[redacted] (91)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		MIDDLE INSOMNIA	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
	片頭痛NOS	20	[redacted]		MIGRAINE	[redacted] (2)	[redacted] (2)	SEVERE	1	RESOLVED	2	NO
					MIGRAINE	[redacted] (104)	[redacted] (107)	SEVERE	1	RESOLVED	1	NO
		40	[redacted]		MIGRAINE HEADACHE	[redacted] (81)	[redacted] (82)	MODERATE	7	RESOLVED	1	NO
	不随意性筋収縮	5	[redacted]		MUSCLE CONTRACTIONS IN CHEST	[redacted] (75)	[redacted] (80)	MILD	1	RESOLVED	2	NO
	神経圧迫	0	[redacted]		LT ELBOW SURGERY (COMPRESSED NERVE)	[redacted] (213)	[redacted] (213)	MODERATE	5	RESOLVED	1	NO
		40	[redacted]		"PINCHED NERVE" RT ELBOW	[redacted] (45)	[redacted] (130)	SEVERE	3/7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	錯感覚NEC	5	[redacted]		TINGLING IN HANDS BILATERALLY X APPROX 2 HOURS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	1	NO
			[redacted]		NECK/ARM PAIN/TINGLING	[redacted] (293)	[redacted] (330)	MILD	7	RESOLVED	1	NO
		40	[redacted]		FACE TINGLING ARM TINGLING	[redacted] (2)	[redacted] (3)	MILD	1	RESOLVED	2	NO
	末梢性ニューロパシーNEC	40	[redacted]		NEUROPATHY	[redacted] (297)		MODERATE	7	PERSISTS	2	NO
	橈骨神経麻痺	0	[redacted]		LEFT HAND PALSY	[redacted] (93)	[redacted] (195)	SEVERE	1	RESOLVED	1	NO
	鎮静	40	[redacted]		SEDATION	[redacted] (1)	[redacted] (18)	MODERATE	1	RESOLVED	2	NO
			[redacted]		SEDATED	[redacted] (0)	[redacted] (1)	SEVERE	3	RESOLVED	2	NO
	副鼻腔炎に伴う頭痛	0	[redacted]		SINUS DRAINAGE	[redacted] (138)	[redacted] (140)	MILD	7	RESOLVED	1	NO
			[redacted]		SINUS HEADACHE	[redacted] (7)	[redacted] (7)	SEVERE	7	RESOLVED	1	NO
		20	[redacted]		SINUS HEADACHE	[redacted] (35)	[redacted] (40)	SEVERE	7	RESOLVED	1	NO
		40	[redacted]		SINUS HEADACHE	[redacted] (96)			7	PERSISTS	2	NO
	傾眠	0	[redacted]		DROWSINESS	[redacted] (0)		MILD	1	PERSISTS	2	NO
		5	[redacted]		EXCESSIVE SLEEPINESS	[redacted] (236)	[redacted] (239)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DROWSINESS	[redacted] (0)		SEVERE	1	PERSISTS	3	NO
			[redacted]		DROWSINESS	[redacted] (0)	[redacted] (41)	MILD	1	RESOLVED	2	NO
		20	[redacted]		DROWSINESS	[redacted] (1)		MODERATE	1	PERSISTS	1	NO
			[redacted]		SLEEPINESS	[redacted] (107)		MILD	1	PERSISTS	2	NO
			[redacted]		DROWSINESS	[redacted] (8)	[redacted] (84)	MILD	1	RESOLVED	3	NO
		40	[redacted]		DROWSINESS	[redacted] (0)	[redacted] (1)	MODERATE	8	RESOLVED	3	NO
			[redacted]		DROWSINESS	[redacted] (1)	[redacted] (12)	MODERATE	1	RESOLVED	3	NO
			[redacted]		DROWSINESS	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
			[redacted]		DROWSINESS	[redacted] (15)	[redacted] (15)	MILD	1	RESOLVED	2	NO
	失神	0	[redacted]		SYNCOPAL EPISODE	[redacted] (229)	[redacted] (229)	SEVERE	8	RESOLVED	2	NO
	味覚障害	0	[redacted]		ODD TASTE IN MOUTH	[redacted] (3)		MILD	1	RESOLVED	3	NO
		20	[redacted]		"DULL" TASTE IN MOUTH	[redacted] (0)	[redacted] (42)	MILD	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
神経系障害	振戦NEC	0	[redacted]	[redacted]	INCREASED SHAKING	[redacted] (156)		SEVERE	7/2	PERSISTS	2	NO
		5	[redacted]	[redacted]	BILATERAL HAND TREMOR	[redacted] (96)		MILD	1	PERSISTS	1	NO
			[redacted]	[redacted]	SHAKINESS / TREMORS	[redacted] (7)	[redacted] (8)	MODERATE	3	RESOLVED	2	NO
			[redacted]	[redacted]	TREMOR	[redacted] (42)	[redacted] (56)	MILD	1	RESOLVED	2	NO
		40	[redacted]	[redacted]	SHAKING	[redacted] (74)	[redacted] (74)	MILD	1	RESOLVED	1	NO
精神障害	異常な夢	0	[redacted]	[redacted]	STRANGE DREAMS	[redacted] (24)	[redacted] (85)	MILD	1	RESOLVED	2	NO
		5	[redacted]	[redacted]	VIVID DREAMS	[redacted] (0)	[redacted] (58)	MODERATE	1	RESOLVED	2	NO
		20	[redacted]	[redacted]	BAD DREAMS	[redacted] (32)	[redacted] (41)	SEVERE	1	RESOLVED	2	NO
		40	[redacted]	[redacted]	DREAMING	[redacted] (7)		MILD	1	PERSISTS	2	NO
	アルコール離脱症状	40	[redacted]	[redacted]	ALCOHOL WITHDRAWAL	[redacted] (63)	[redacted] (65)	MILD	1	RESOLVED	1	NO
	不安NEC	0	[redacted]	[redacted]	EDGY, ANXIOUS	[redacted] (0)	[redacted] (85)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	ANXIETY	[redacted] (26)		MODERATE	7	PERSISTS	1	NO
			[redacted]	[redacted]	ANXIETY	[redacted] (32)	[redacted] (32)	MILD	1	RESOLVED	1	NO
		20	[redacted]	[redacted]	ANXIETY	[redacted] (10)	[redacted] (12)	SEVERE	3/4/7	RESOLVED	2	NO
				[redacted]	ANXIETY	[redacted] (25)	[redacted] (26)	MILD	1	RESOLVED	2	NO
			[redacted]	[redacted]	ANXIETY	[redacted] (10)	[redacted] (12)	SEVERE	1	RESOLVED	2	NO
				[redacted]	ANXIETY	[redacted] (30)		MILD	7	PERSISTS	2	NO
		40	[redacted]	[redacted]	ANXIETY	[redacted] (116)		MODERATE	6	PERSISTS	1	NO
			[redacted]	[redacted]	ANXIETY	[redacted] (18)	[redacted] (19)	MILD	7	RESOLVED	1	NO
	注意欠陥多動性障害	40	[redacted]	[redacted]	ATTENTION DEFICIT	[redacted] (218)			7	PERSISTS	1	NO
	錯乱	5	[redacted]	[redacted]	FOGGY HEAD	[redacted] (0)	[redacted] (0)	MODERATE	1	RESOLVED	2	NO
		20	[redacted]	[redacted]	SPACEY	[redacted] (0)	[redacted] (1)	MODERATE	1	RESOLVED	3	NO
			[redacted]	[redacted]	LACK OF MENTAL CLARITY	[redacted] (0)	[redacted] (2)	MODERATE	1	RESOLVED	3	NO
		40	[redacted]	[redacted]	"CLOUDY HEAD"	[redacted] (2)	[redacted] (5)	MILD	1	RESOLVED	2	NO
	泣き	5	[redacted]	[redacted]	CRYING	[redacted] (2)	[redacted] (7)	MODERATE	1	RESOLVED	1	NO
	抑うつ気分	5	[redacted]	[redacted]	DEPRESSED MOOD	[redacted] (310)		SEVERE	7	PERSISTS	1	NO
		20	[redacted]	[redacted]	MILDLY DEPRESSED MOOD	[redacted] (280)		MILD	7	PERSISTS	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
精神障害	うつ病NEC	0	[redacted]		DEPRESSION	[redacted] (219)		MODERATE	7	PERSISTS	1	NO
		0	[redacted]		DEPRESSION	[redacted] (44)	[redacted] (44)	SEVERE	6	RESOLVED	2	NO
					DEPRESSION	[redacted] (54)	[redacted] (54)	SEVERE	6	RESOLVED	2	NO
					DEPRESSION	[redacted] (56)	[redacted] (57)	SEVERE	6	RESOLVED	2	NO
					DEPRESSION	[redacted] (151)	[redacted] (245)	SEVERE	1	RESOLVED	1	NO
					DEPRESSION	[redacted] (298)	[redacted] (305)	SEVERE	2/6	RESOLVED	1	NO
					DEPRESSION	[redacted] (329)		MODERATE	7	PERSISTS	1	NO
			[redacted]		MILD DEPRESSION	[redacted] (201)	[redacted] (277)	MILD	7	RESOLVED	1	NO
		5	[redacted]		DEPRESSION	[redacted] (266)	[redacted] (344)	MODERATE	7	RESOLVED	1	NO
		20	[redacted]		DEPRESSION	[redacted] (304)		MODERATE	7	PERSISTS	1	NO
		40	[redacted]		DEPRESSION	[redacted] (12)	[redacted] (16)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DEPRESSED	[redacted] (1)		MILD	6	PERSISTS	2	NO
				[redacted]	DEPRESSION	[redacted] (245)	[redacted] (361)	MODERATE	7	RESOLVED	1	NO
	失見当識	40	[redacted]		UNAWARE - DISORIENTED	[redacted] (0)	[redacted] (1)	SEVERE	3	RESOLVED	2	NO
	解離	20	[redacted]		UNFOCUSED DETACHED FEELING	[redacted] (0)	[redacted] (1)	SEVERE	3	RESOLVED	3	NO
		40	[redacted]		DISCONNECTED FEELING	[redacted] (91)		MILD	1	PERSISTS	3	NO
	不安増強	5	[redacted]		INCREASED ANXIETY	[redacted] (93)		MODERATE	8	PERSISTS	1	NO
		40	[redacted]		INCREASED ANXIETY	[redacted] (6)	[redacted] (59)	MODERATE	1	RESOLVED	1	NO
	幻覚NOS	40	[redacted]		HALLUCINATIONS	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
	せっかち	40	[redacted]		IMPATIENT	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO
	易刺激性	5	[redacted]		IRRITABILITY	[redacted] (3)	[redacted] (5)	MILD	1	RESOLVED	2	NO
			[redacted]		IRRITABLE	[redacted] (59)	[redacted] (81)	MODERATE	1	RESOLVED	1	NO
			[redacted]		IRRITABILITY	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	2	NO
		20	[redacted]		"BAD MOOD"	[redacted] (198)	[redacted] (200)	MILD	1	RESOLVED	3	NO
		40	[redacted]		IRRITABLE	[redacted] (0)	[redacted] (1)	SEVERE	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
精神障害	リビドー減退	0	[redacted]		DECREASED LIBIDO	[redacted] (68)	[redacted] (82)	MODERATE	1	RESOLVED	1	NO
		5	[redacted]		DECREASED LIBIDO	[redacted] (5)		MODERATE	1	PERSISTS	2	NO
		20	[redacted]		DECREASED LIBIDO	[redacted] (1)	[redacted] (39)	MODERATE	1	RESOLVED	2	NO
			[redacted]		DECREASED LIBIDO	[redacted] (19)		MILD	1	PERSISTS	2	NO
	気分変動NOS	20	[redacted]		SLIGHT ALTERATION OF MOOD	[redacted] (4)	[redacted] (38)	MILD	1	RESOLVED	1	NO
	気分障害NOS	5	[redacted]		MOOD DISORDER	[redacted] (365)		MODERATE	7	PERSISTS	1	NO
	気分動揺	40	[redacted]		MOOD CHANGES	[redacted] (0)	[redacted] (0)	SEVERE	1	RESOLVED	2	NO
	神経過敏	20	[redacted]		TREMULOUSNESS	[redacted] (6)	[redacted] (9)	MILD	1	RESOLVED	2	NO
	悪夢	0	[redacted]		NIGHTMARES	[redacted] (277)		MILD	1	PERSISTS	1	NO
		20	[redacted]		INTENSE NIGHTMARES	[redacted] (6)	[redacted] (19)	MODERATE	1	RESOLVED	2	NO
	パニック発作	0	[redacted]		PANIC ATTACK	[redacted] (140)	[redacted] (159)	SEVERE	1	RESOLVED	1	NO
		40	[redacted]		PANIC ATTACK	[redacted] (179)	[redacted] (179)	MODERATE	7	RESOLVED	1	NO
	妄想症	0	[redacted]		PARANOIA	[redacted] (12)	[redacted] (13)	MODERATE	1	RESOLVED	1	NO
	人格変化	5	[redacted]		PERSONALITY CHANGE	[redacted] (1)		MILD	1	PERSISTS	2	NO
	早漏	5	[redacted]		PREMATURE EJACULATION	[redacted] (45)	[redacted] (52)	MODERATE	1	RESOLVED	1	NO
	落ち着きのなさ	5	[redacted]		RESTLESSNESS	[redacted] (1)	[redacted] (31)	MILD	1	RESOLVED	2	NO
	睡眠障害NOS	5	[redacted]		CHANGE IN SLEEP PATTERN	[redacted] (15)	[redacted] (19)	MODERATE	1	RESOLVED	2	NO
	自殺念慮	0	[redacted]		SUICIDE IDEATION	[redacted] (210)	[redacted] (211)	SEVERE	6	RESOLVED	1	NO
					SUICIDAL IDEATION	[redacted] (303)	[redacted] (306)	MILD	2/6	RESOLVED	1	NO
腎および尿路障害	排尿困難	0	[redacted]		DIFFICULTY URINATING	[redacted] (236)	[redacted] (261)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		PROBLEM W/URINATION	[redacted] (188)		MODERATE	7	PERSISTS	1	NO
	夜間頻尿	20	[redacted]		NOCTURIA	[redacted] (215)	[redacted] (259)	MODERATE	1	RESOLVED	1	NO
	頻尿	5	[redacted]		FREQUENT URINATION	[redacted] (287)	[redacted] (299)	MODERATE	1	RESOLVED	2	NO
			[redacted]		URINARY FREQUENCY (INCREASED)	[redacted] (5)	[redacted] (31)	MILD	1	RESOLVED	1	NO
					URINARY FREQUENCY	[redacted] (186)	[redacted] (210)	SEVERE	7	RESOLVED	1	NO
	尿変色	20	[redacted]		"GOLDEN" URINE	[redacted] (10)	[redacted] (13)	SEVERE	1	RESOLVED	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
生殖系および乳房障害	良性前立腺肥大症	20	[redacted]		PROSTATE (BPH)	[redacted] (344)		MILD	7	PERSISTS	1	NO
	月経困難症	0	[redacted]		MENSTRUAL CRAMPS	[redacted] (48)	[redacted] (49)	MODERATE	7	RESOLVED	1	NO
		5	[redacted]		MENSTRUAL CRAMPS	[redacted] (6)	[redacted] (6)	MODERATE	7	RESOLVED	1	NO
					MENSTRUAL CRAMPS	[redacted] (66)	[redacted] (66)	MODERATE	7	RESOLVED	1	NO
					MENSTRUAL CRAMPS	[redacted] (103)	[redacted] (103)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		MENSTRUAL CRAMPS	[redacted] (31)	[redacted] (35)	MILD	7	RESOLVED	1	NO
			[redacted]		MENSTRUAL CRAMPS	[redacted] (349)	[redacted] (349)	MILD	7	RESOLVED	1	NO
	射精障害NOS	20	[redacted]		DIFFICULTY WITH EJACULATION	[redacted] (1)		MODERATE	1	RESOLVED	2	NO
	勃起力減退	40	[redacted]		ERECTILE DYSFUNCTION	[redacted] (25)	[redacted] (85)	SEVERE	6/7	RESOLVED	2	NO
	月経前症候群	0	[redacted]		PMS	[redacted] (43)		MODERATE	7	PERSISTS	1	NO
	精巣嚢胞	40	[redacted]		TESTICULAR CYST	[redacted] (42)	[redacted] (58)	MILD	6	RESOLVED	1	NO
	腟分泌物	20	[redacted]		VAGINAL DISCHARGE	[redacted] (155)	[redacted] (315)	MILD	1	RESOLVED	1	NO
呼吸器、胸郭および縦隔障害	咳嗽	5	[redacted]		COUGH	[redacted] (79)	[redacted] (83)	MILD	7	RESOLVED	1	NO
		5	[redacted]		COUGH	[redacted] (296)	[redacted] (331)	MODERATE	7	RESOLVED	1	NO
			[redacted]		COUGH	[redacted] (6)	[redacted] (15)	MODERATE	6/8/7	RESOLVED	1	NO
		20	[redacted]		COUGH	[redacted] (42)	[redacted] (43)	MILD	7	RESOLVED	1	NO
	鼻閉	0	[redacted]		NASAL CONGESTION	[redacted] (26)	[redacted] (26)	MILD	1	RESOLVED	1	NO
		5	[redacted]		SEVERE NASAL CONGESTION	[redacted] (51)	[redacted] (74)	SEVERE	7	RESOLVED	1	NO
		20	[redacted]		STUFFY NOSE	[redacted] (35)	[redacted] (42)	MILD	1	RESOLVED	1	NO
	後鼻漏	20	[redacted]		POST NASAL DRIP	[redacted] (84)		MILD	1	PERSISTS	1	NO
				[redacted]	POST NASAL DRIP	[redacted] (82)	[redacted] (92)	MILD	1	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
呼吸器、胸郭および縦隔障害	鼻炎NOS	5	[redacted]		REDDENED & IRRITATED NASAL MUCOSA	[redacted] (357)		MILD	1	PERSISTS	2	NO
	副鼻腔うっ血	0	[redacted]		SINUS CONGESTION	[redacted] (115)	[redacted] (139)	MILD	7	RESOLVED	1	NO
			[redacted]		SINUS CONGESTION	[redacted] (215)	[redacted] (218)	MILD	7	RESOLVED	1	NO
		5	[redacted]		SINUS CONGESTION	[redacted] (203)		MILD	7	PERSISTS	1	NO
		40	[redacted]		SINUS CONGESTION	[redacted] (27)	[redacted] (27)	MODERATE	7	RESOLVED	1	NO
	副鼻腔痛	0	[redacted]		SINUS PROBLEM	[redacted] (0)		MODERATE	7	PERSISTS	2	NO
		5	[redacted]		SINUS PROBLEMS	[redacted] (1)		MODERATE	7	PERSISTS	2	NO
	喘鳴音	5	[redacted]		RHONCHI AND WHEEZES BILATERALLY	[redacted] (96)		MILD	1	PERSISTS	1	NO
皮膚および皮下組織障害	ざ瘡様皮膚炎	5	[redacted]		ACNE / RASH	[redacted] (17)		MILD	1	PERSISTS	2	NO
	接触性皮膚炎	0	[redacted]		POISON IVY	[redacted] (74)	[redacted] (86)	MILD	1	RESOLVED	1	NO
		5	[redacted]		ALLERGIC DERMATITIS "POISON IVY"	[redacted] (2)	[redacted] (14)	MILD	7	RESOLVED	1	NO
	皮膚炎NOS	0	[redacted]		RASH	[redacted] (56)		MILD	7	PERSISTS	2	NO
					RASH	[redacted] (77)	[redacted] (84)	SEVERE	8	RESOLVED	2	NO
					RASH	[redacted] (98)		MODERATE	1	PERSISTS	1	NO
				[redacted]	RASH	[redacted] (362)		MILD	1	PERSISTS	1	NO
				[redacted]	RASH	[redacted] (31)		MILD	7	RESOLVED	2	NO
			[redacted]		RASH	[redacted] (86)	[redacted] (93)	MILD	1	RESOLVED	1	NO
			[redacted]		WORSENING OF SKIN RASH - UPPER AND LOWER EXTREMITIES	[redacted] (50)		MODERATE	7	RESOLVED	1	NO
		5	[redacted]		SKIN RASH ON FACE	[redacted] (1)	[redacted] (13)	MILD	6	RESOLVED	2	NO
		20	[redacted]		RASH ON ARMS	[redacted] (205)	[redacted] (286)	MODERATE	7	RESOLVED	1	NO
		40	[redacted]		FACIAL RASH	[redacted] (1)	[redacted] (34)	MODERATE	1	RESOLVED	1	NO
			[redacted]		RASH ON BUTTOCKS	[redacted] (35)	[redacted] (86)	MODERATE	7	RESOLVED	1	NO
				[redacted]	RASH	[redacted] (13)	[redacted] (14)	MODERATE	1	RESOLVED	1	NO
			[redacted]		RASH	[redacted] (275)		MODERATE	7	PERSISTS	2	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
皮膚および皮下組織障害	紅斑性単純性皮膚炎	40	[redacted]		ERYTHEMATOUS ECZEMA	[redacted] (92)		MILD	1	PERSISTS	1	NO
	過角化	5	[redacted]		RAISED HYPERKERATOTIC LESIONS ON CHEEKS	[redacted] (371)		MILD	1	PERSISTS	1	NO
	寝汗	20	[redacted]		NIGHT SWEATS	[redacted] (3)	[redacted] (20)	MODERATE	1	RESOLVED	2	NO
		40	[redacted]		NIGHT SWEATS	[redacted] (27)	[redacted] (104)	SEVERE	4	RESOLVED	1	NO
	そう痒症NOS	5	[redacted]		ITCHING	[redacted] (1)	[redacted] (3)	MODERATE	1	RESOLVED	1	NO
		20	[redacted]		ITCHY SOLES OF FEET	[redacted] (2)	[redacted] (359)	MODERATE	7	RESOLVED	2	NO
	斑状丘疹状皮疹	40	[redacted]		MACULAR, PAPULAR RASH	[redacted] (83)	[redacted] (85)	MILD	1	RESOLVED	1	NO
	ひび・あかぎれ	40	[redacted]		DRY CHAPPED SKIN OVERALL	[redacted] (369)		MILD	1	PERSISTS	1	NO
	皮膚色素過剰	20	[redacted]		MULTIPLE HYPER PIGMENTED SKIN LESIONS	[redacted] (382)		MILD	1	PERSISTS	1	NO
	多汗	5	[redacted]		SWEATING	[redacted] (0)	[redacted] (0)	MILD	1	RESOLVED	1	NO
	蕁麻疹NOS	40	[redacted]		HIVES	[redacted] (22)	[redacted] (23)	MODERATE	7	RESOLVED	2	NO
			[redacted]		BUTTOCK RASH	[redacted] (116)	[redacted] (244)	MILD	7	RESOLVED	1	NO
社会環境	薬物乱用	0	[redacted]		INCREASED USE OF COCAINE	[redacted] (42)	[redacted] (42)	MILD	1	RESOLVED	1	NO
外科および内科処置	足首手術	20	[redacted]		ANKLE SURGERY	[redacted] (251)	[redacted] (252)	SEVERE	5/7	RESOLVED	1	YES
	膀胱腫瘍切除	20	[redacted]		TUMOR REMOVED FROM BLADDER	[redacted] (243)	[redacted] (243)	SEVERE	6/5/7	RESOLVED	1	YES
	関節注入	0	[redacted]		1ST AND SECOND MCP - BILAT STEROID INJECTION	[redacted] (210)	[redacted] (210)	MODERATE	7	RESOLVED	1	NO
	整形外科的処置	5	[redacted]		ORTHOPEDIC SURGERY (R) SHOULDER	[redacted] (200)	[redacted] (565)	MILD	3	RESOLVED	1	NO
	抜歯NOS	5	[redacted]		DENTAL EXTRACTIONS	[redacted] (68)	[redacted] (69)	MODERATE	1	RESOLVED	1	NO
	疣贅切除	0	[redacted]		PLANTAR WART REMOVAL	[redacted] (132)	[redacted] (132)	MODERATE	7	RESOLVED	1	NO

表 2.7.6.5.7-31　有害事象一覧表－継続投与期－（無作為化例）（続き）

System organ class	Primary preferred term	Treat-ment (mg)	Inv #	Pat #	Event	Start date (Day)	End date (Day)	Severity	Ac-tion	Outcome	Rel	SAE
血管障害	ほてりNOS	20	[redacted]		INCREASED HOT FLASHES	[redacted] (2)		MODERATE	1	PERSISTS	2	NO
			[redacted]		HOT FLASHES	[redacted] (289)	[redacted] (318)	MILD	1	RESOLVED	2	NO
			[redacted]		"HOT FLASHES"	[redacted] (280)		MODERATE	7	PERSISTS	1	NO
	高血圧NOS	0	[redacted]		HYPERTENSION	[redacted] (245)		MILD	7	PERSISTS	1	NO
		20	[redacted]		HTN	[redacted] (292)		MILD	7	PERSISTS	1	NO
			[redacted]		HIGH BLOOD PRESSURE	[redacted] (35)		MILD	7	PERSISTS	1	NO
		40	[redacted]		HYPERTENSION	[redacted] (64)		SEVERE	8	PERSISTS	2	NO
			[redacted]		HYPERTENSION	[redacted] (0)		SEVERE	4/7	PERSISTS	2	NO
	不安定血圧	20	[redacted]		LABILE BLOOD PRESSURE	[redacted] (10)		MODERATE	3/4/7	PERSISTS	2	NO
	リンパ浮腫NOS	5	[redacted]		FIRM, IMMOBILE LYMPHNODE	[redacted] (99)		MODERATE	1	PERSISTS	1	NO

MedDRA Version 3.3

Action: 1 = None, 2 = Study drug permanently discontinued, 3 = Study drug temporarily discontinued, 4 = Dose reduced, 5 = Hospitalized, 6 = Supportive, 7 = Medication, 8 = Other

Rel = Relationship: 1 = Unlikely, 2 = Possible, 3 = Probable

SAE = Serious adverse event

＜資料番号 5.3.5.1-07：15.3.1.3.7＞

2.7.6.5.8　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（外国人：CPH-101-0399 試験，添付資料番号 5.3.5.1-08）【参考資料】

2.7.6.5.8.1　試験方法の概略

項目	内容
試験の目的	1.　多量飲酒者を対象にナルメフェンの飲酒量低減に対する有効性及び用量反応性を検討する。 2.　多量飲酒者を対象にナルメフェンの安全性及び忍容性を評価する。
試験デザイン	無作為化，二重盲検，プラセボ対照，多施設共同，並行群間比較
対象	多量飲酒者
選択基準	1)　飲酒量の低減又は飲酒のコントロールを常に望んでいる患者 2)　飲酒をコントロールすることが難しい患者 • 意図したよりも多量又は長時間飲酒することが多い患者 3)　スクリーニング来院前 1 ヵ月以内に，HDD が 8 日以上である患者（HDD は男性で 5 ドリンク以上，女性で 4 ドリンク以上のアルコールを消費した日とした） 4)　同意文書に署名した患者 5)　組入れ時に飲酒状態ではない患者 6)　18 歳以上の男性又は女性患者 7)　連絡可能な住所及び電話番号を有する患者
除外基準	1)　治験治療を妨げるか治療遵守に支障を来す恐れのある精神障害（精神病，統合失調症，中等度又は高度のうつ病，摂食障害，双極性感情障害，不安障害など），人格障害，又は他の障害を有する患者 2)　せん妄又は高度の離脱症状が認められる患者 3)　入院での解毒治療が必要な患者 4)　高度の肝障害又は腎障害を有する患者 5)　認知症，てんかん発作，精神遅滞，脳症を有する患者 6)　飲酒問題に優先して治療が必要な未治療の医療上の障害又は問題（アルコール関連問題を除く）を有する患者 7)　薬物依存の患者又は違法薬物を使用している患者 8)　現在又は過去にナルトレキソンによる治療を受けている患者 9)　現在又は過去 3 ヵ月以内で，ジスルフィラムによる治療を受けている患者 10)　現在又は過去 1 週間以内で，オピオイドの刺激薬による治療を受けている患者 11)　妊娠又は授乳中の患者

<table>
<tr><td>項目</td><td>内容</td></tr>
<tr><td></td><td>12) 妊娠可能な女性で，適切な避妊法を使用していない患者
13) 組入れ前 3 ヵ月以内に何らかの治験に参加したことがある患者
14) 治験の通院に支障を来す恐れのある制限された環境（例：病院，刑務所など）に入る予定がある患者，旅行又は転居の予定がある患者</td></tr>
<tr><td>使用薬剤，
ロット番号</td><td>被験薬
ナルメフェン塩酸塩錠 5 mg：[redacted]
ナルメフェン塩酸塩錠 20 mg：[redacted]
対照薬
プラセボ錠：[redacted]</td></tr>
<tr><td>用量及び投与方法</td><td>被験者は治験薬を 1 日 1 回連日服用した。最初の 1 週間（Week 1 来院まで）は，ナルメフェン塩酸塩 5 mg 又はプラセボを 1 日 1 回服用した。残りの 15 週間は，以下のとおりナルメフェン塩酸塩 10 mg，40 mg 又はプラセボを 1 日 1 回服用した。
<table>
<tr><th>Treatment Allocation</th><th>Tablets in one dose</th></tr>
<tr><td>Placebo</td><td>Two placebo tablets</td></tr>
<tr><td>Nalmefene 10 mg</td><td>Two 5 mg nalmefene hydrochloride tablets</td></tr>
<tr><td>Nalmefene 40 mg</td><td>Two 20 mg nalmefene hydrochloride tablets</td></tr>
</table></td></tr>
<tr><td>投与期間</td><td>16 週間</td></tr>
<tr><td>目標被験者数</td><td>150 例（ナルメフェン 10 mg 群：50 例，40 mg 群：50 例，プラセボ群：50 例）</td></tr>
<tr><td>目標被験者数の
設定根拠</td><td>被験者内相関を0.5，平均6週，最大16週の測定，プラセボ群の多量飲酒率を70%と仮定すると，検出力80%，両側有意水準5%，120例（各群40例）で多量飲酒がなしに対するありの割合の差35%を検出できる。脱落率を20%と推定し，150例（各群50例）を組入れる計画とした。</td></tr>
<tr><td>主な併用薬の規定</td><td>併用禁止薬/療法
• オピオイドの刺激薬
• ナルトレキソン，ジスルフィラムなどの薬物療法を含む精神療法又は他のアルコール依存症治療</td></tr>
<tr><td>評価項目</td><td>有効性
主要評価項目：HDD 数
HDD 数は 1 日のアルコール消費量が男性で 5 ドリンク以上，女性で 4 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した（1 ドリンクはエタノールとして 12 g を含む）。
アルコール消費量に関する副次的評価項目：
• TAC（Total Consumption）
TAC は 1 週間当たりの平均アルコール消費量（ドリンク/週）と</td></tr>
</table>

項目	内容
	定義した。 • VHDD 数 VHDD 数は 1 日のアルコール消費量が男性で 10 ドリンク以上，女性で 8 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した。 • 飲酒日当たりのアルコール消費量 • 飲酒日数に対する HDD 数の割合 • NDD 数（Number of Abstinence days） • 1 日アルコール消費量の最大値 1 日アルコール消費量の最大値は 1 ヵ月間で最も多く飲酒した日のアルコール消費量（ドリンク数）と定義した。 その他の副次的評価項目： • MCV，ALT，γ-GTP，%CDT • ADS，DrInC，OCDS • 近親者による被験者の飲酒パターン及びアルコール中毒の頻度の評価 **安全性** 有害事象，臨床検査値，バイタルサイン
解析方法	統計解析は ITT 集団を用いて実施した。統計モデルでは，投与群，性別，及び施設を独立変数とした。ノンパラメトリック検定では，投与群のみを説明変数として使用した。ベースラインのカテゴリカル変数は一般化ロジット関数を用いて，連続変数は分散分析を用いて解析した。投与群，性別，及び施設と共に反復測定に対する時間の効果を評価した際には，反復測定による分散分析を用いた。差の解析には単純比較を行った。正規性の仮定は残差から視覚的に確認し，裏付けとして Shapiro-Wilk 検定を用いた。 有効性主要評価項目である HDD 数は，反復測定による分散分析で解析した。
治験依頼者	Oy Contral Pharma Ltd
治験実施医療機関	フィンランド 6 施設
治験期間	20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日

2.7.6.5.8.2　治験スケジュール

治験スケジュールを表 2.7.6.5.8-1 に示した。

表 2.7.6.5.8-1　　治験スケジュール

			Week					
	Screening	Inclusion	1	3	6	9	12	16
Initial interview and information on study	X							
Discussion on treatment goals & expectations	X							
Informed consent	X							
AUDIT	X							
Social history	X							
Medical history	X	X			X			X
Alcohol use with TLFB	X	X	X	X	X	X	X	X
Physical examination	X	X			X			X
Psychiatric status	X							
Blood pressure and heart rate	X	X	X	X	X	X	X	X
Clinical Laboratory	X				X			X
ECG	X							
Drug screen	X							
Breath Alcohol	X	X	X	X	X	X	X	X
Check of inclusion and exclusion criteria	X	X						
Assignment of subject number		X						
DrInC		X						X
ADS		X						X
OCDS	X				X			X
Instructions and subject diary to the subject		X						
Dispensing/ checking of study drugs		X	X	X	X	X	X	X
Adverse events			X	X	X	X	X	X
Prior and concomitant medication	X	X	X	X	X	X	X	X
Prior and concomitant treatment	X	X	X	X	X	X	X	X
Spouse/ significant other estimate		X						X

AUDIT : World Health Organization により開発された，飲酒量が健康に有害かつ危険な飲酒者を見極める 10 項目の質問票。うち 3 項目は飲酒量及び頻度に関する質問，3 項目はアルコール依存に関する質問，4 項目はアルコール関連問題に関する質問。

TLFB：TLFB より導出される評価項目は HDD 数，TAC，VHDD 数，飲酒日当たりのアルコール消費量，飲酒日数に対する HDD 数の割合，NDD 数，1 日アルコール消費量の最大値

＜資料番号 5.3.5.1-08：8.1.1 項＞

2.7.6.5.8.3　試験結果

(1)　被験者の内訳

被験者の内訳を表 2.7.6.5.8-2 に，中止例の内訳を表 2.7.6.5.8-3 に示した。

179 例がスクリーニングを受け，そのうち 150 例（ナルメフェン 10 mg 群 50 例，40 mg 群 50 例，プラセボ群 50 例）に治験薬が投与された。

ナルメフェン 10 mg 群 39 例，40 mg 群 40 例，プラセボ群 41 例が治験薬の投与を完了した。ナルメフェン 10 mg 群 11 例，40 mg 群 10 例，プラセボ群 9 例が治験薬の投与を中止した。主な中止理由は，ナルメフェン群では有害事象（ナルメフェン 10 mg 群及び 40 mg 群で各 6 例），プラセボ群では有害事象（3 例），効果不十分又は臨床状態の悪化（3 例）であった。

表 2.7.6.5.8-2　　被験者の内訳

Screened				***All***
All Sites				**179**
21[redacted]				19
22				24
23				25
24				48
25				49
26				14
Received Study Medication	***Placebo***	***NMF 10***	***NMF 40***	***All***
All Sites	**50**	**50**	**50**	**150**
21[redacted]	6	6	6	18
22	6	6	6	18
23	8	8	8	24
24	12	12	12	36
25	14	14	14	42
26	4	4	4	12
Discontinued Medication				
All Sites	**9**	**11**	**10**	**30**
21[redacted]	1	-	-	1
22	3	1	5	9
23	1	3	1	5
24	1	1	2	4
25	1	5	2	8
26	2	1	-	3
Completed Medication				
All Sites	**41**	**39**	**40**	**120**
21[redacted]	5	6	6	17
22	3	5	1	9
23	7	5	7	19
24	11	11	10	32
25	13	9	12	34
26	2	3	4	9
TLFB Complete				
All Sites	**45**	**45**	**46**	**136**
21[redacted]	5	6	6	17
22	4	5	5	14
23	7	8	7	22
24	12	12	10	34
25	14	11	14	39
26	3	3	4	10

＜資料番号 5.3.5.1-08：Table 1＞

表 2.7.6.5.8-3　　中止例の内訳

Reason	Placebo	Nalmefene 10	Nalmefene 40	All
N	9	11	10	30
Adverse event	3	6	6	15
Lack of efficacy/clinical deterioration	3	1	1	5
Lost to follow up	1	2	1	4
Consent withdrawal	1	2	2	5
Other	1	-	-	1

＜資料番号 5.3.5.1-08：Table 3＞

(2)　解析したデータセット

統計解析は ITT 集団を用いて行った。ITT 集団は 150 例（ナルメフェン 10 mg 群 50 例，40 mg 群 50 例，プラセボ群 50 例）であった（資料番号 5.3.5.1-08：13.2 参照）。

(3)　人口統計学的及び他の基準値の特性

人口統計学的特性（年齢及び性別）を表 2.7.6.5.8-4 に，スクリーニング時の身長，体重，BMI を表 2.7.6.5.8-5 に示した。飲酒歴を表 2.7.6.5.8-6 に，アルコール関連問題の治療歴を表 2.7.6.5.8-7 に示した。また，有効性評価項目のベースライン値（1）を表 2.7.6.5.8-8 に，有効性評価項目のベースライン値（2）を表 2.7.6.5.8-9 に示した。

全例が白人，平均年齢は 49.2 歳（範囲：29.0～67.0 歳）であった（資料番号 5.3.5.1-08：Table 18.a.1.4, Table 18.a.5 参照）。年齢，性別に群間差は認められなかった（資料番号 5.3.5.1-08：Table 18.a.2 参照）。

被験者の約 63%がアルコール関連問題の家族歴を有していた。初回飲酒の平均年齢は 16.9 歳，アルコール関連問題の平均初発年齢は 36.7 歳であった（資料番号 5.3.5.1-08：Table 18.a.14，Table 18.a.15.4，Table 18.a.16.4 参照）。アルコール関連問題の治療歴では，プラセボ群が 36%と最も低く，ナルメフェン 10 mg 群が 54%と最も高かった。アルコール関連問題の平均治療開始年齢は 42.7 歳であった（資料番号 5.3.5.1-08：Table 18.a.18.4 参照）。

スクリーニング来院前 12 週間での HDD 数，VHDD 数，NDD 数（Number of Abstinence days），TAC（Total Consumption）に，投与群間，性別及び施設間で差は認められなかった。1 日アルコール消費量の最大値では，ほとんどの被験者が「Very Heavy」に分類され，群間で差は認められなかった。

表 2.7.6.5.8-4　　人口統計学的特性［男女別の年齢（歳）］（ITT）

	Placebo	*NMF 10*	*NMF 40*
Male			
n	39	39	44
Mean	49.1	49.0	50.4
SD	8.8	8.0	9.0
Median	49.0	47.0	50.5
Q1 to Q3	43.0 to 55.0	43.0 to 57.0	42.0 to 57.0
Min – Max	29 – 66	34 -- 63	32 – 67
Female			
n	11	11	6
Mean	44.3	50.8	49.0
SD	10.5	7.5	5.0
Median	43.0	51.0	50.0
Q1 to Q3	36.0 to 49.0	44.0 to 58.0	46.0 to 53.0
Min – Max	29 – 64	41 – 63	41 – 54

＜資料番号 5.3.5.1-08：Table 4＞

表 2.7.6.5.8-5　　スクリーニング時の身長，体重，BMI（ITT）

	Placebo	*NMF 10*	*NMF 40*
N	50	50	50
Height (cm)			
Mean	174.9	175.2	174.9
SD	9.0	8.1	10.6
Median	176.0	175.5	176.0
Q1 to Q3	168.0 to 182.0	170.0 to 180.0	173.0 to 180.0
Min – Max	154 – 191	160 – 197	120 – 192
Weight (kg)			
Mean	84.4	87.3	84.6
SD	17.7	17.4	12.6
Median	85.5	83.5	83.0
Q1 to Q3	74.0 to 96.0	75.0 to 94.0	76.0 to 92.0
Min – Max	47.0 – 146.0	59.0 – 147.0	61.0 – 113.0
BMI (kg/m^2)			
Mean	27.4	28.4	27.9
SD	4.6	5.2	5.5
Median	26.8	27.3	27.1
Q1 to Q3	24.4 to 29.6	24.9 to 29.7	24.4 to 29.8
Min – Max	19.3 – 40.2	21.0 – 47.5	19.7 – 55.6

＜資料番号 5.3.5.1-08：Table 13＞

表 2.7.6.5.8-6　　飲酒歴（ITT）

	Placebo	*NMF 10*	*NMF 40*
n	50	50	50
History of Alcohol Problems in Family			
Father	16 (32%)	22 (44%)	18 (36%)
Mother	1 (2%)	2 (4%)	3 (6%)
Grandparents	7 (14%)	5 (10%)	4 (8%)
Siblings	13 (26%)	6 (12%)	9 (18%)
Uncles	13 (26%)	11 (22%)	14 (28%)
Aunts	-	1 (2%)	-
Total	32 (64%)	32 (64%)	31 (62%)
Age at First Drinking Experience			
Mean	16.5	17.2	17.0
SD	4.8	4.8	3.6
Median	16.0	16.0	16.5
Q1 to Q3	15.0 to 17.0	15.0 to 18.0	15.0 to 18.0
Min – Max	10.0 – 45.0	8.0 – 30.0	11.0 – 29.0
Age at the Onset of Problem Drinking			
Mean	36.8	37.3	36.0
SD	10.9	10.6	11.4
Median	38.0	35.0	35.0
Q1 to Q3	30.0 to 44.0	30.0 to 45.0	27.0 to 42.0
Min – Max	16.0 – 66.0	12.0 – 61.0	18 – 60.0

＜資料番号 5.3.5.1-08：Table 6＞

表 2.7.6.5.8-7　　アルコール関連問題の治療歴（ITT）

	Placebo	*NMF 10*	*NMF 40*
Any Previous Treatment for Alcohol Problems	18 (36%)	27 (54%)	22 (44%)
Previous Detoxifications	6 (12%)	9 (18%)	10 (20%)
Previous Attendance at AA/Self-help groups	18 (36%)	27 (54%)	22 (44%)

AA: Alcoholics Anonymous

＜資料番号 5.3.5.1-08：Table 7＞

表 2.7.6.5.8-8　　有効性評価項目のベースライン値（1）（ITT）

	Placebo	*NMF 10*	*NMF 40*
N	50	50	50
Number of HDDs			
Mean	14.3	15.2	14.9
SD	6.5	7.3	6.7
Median	12.2	13.0	12.5
Q1 to Q3	9.3 to 18.3	9.3 to 22.3	10.0 to 19.3
Min – Max	5.3 – 28	3.0 – 28	6.7 – 28
Number of VHDDs			
Mean	6.7	8.2	7.5
SD	5.2	6.9	6.6
Median	6.0	6.3	7.2
Q1 to Q3	3.0 to 9.0	3.7 to 10.3	2.3 to 10.3
Min – Max	0.0 – 24.7	0.0 – 27.7	0.0 – 27.7
Number of Abstinence days			
Mean	10.0	10.1	9.7
SD	6.6	7.2	7.2
Median	11.2	10.0	9.3
Q1 to Q3	3.3 to 16.0	3.3 to 16.3	2.3 to 16.3
Min – Max	0.0 – 22.0	0.0 – 24.0	0.0 – 21.3
Total Consumption (drinks/week)			
Mean	38.6	42.0	38.9
SD	18.4	23.6	18.3
Median	36.4	35.8	34.7
Q1 to Q3	25.1 to 50.2	23.9 to 60.8	25.3 to 48.8
Min – Max	14.7 – 92.7	6.5 – 104.2	15.0 - 89.9

＜資料番号 5.3.5.1-08：Table 8＞

表 2.7.6.5.8-9　　有効性評価項目のベースライン値（2）（ITT）

	Placebo	*NMF 10*	*NMF 40*
N	50	50	50
Proportion of HDDs of all drinking days			
>20-40%	3 (6%)	2 (4%)	-
>40-60%	4 (8%)	4 (8%)	9 (18%)
>60-80%	15 (30%)	6 (12%)	6 (12%)
>80%	28 (56%)	38 (76%)	35 (70%)
Mean weekly drinking[1]			
Moderate	5 (10%)	7 (14%)	5 (10%)
Heavy	15 (30%)	18 (36%)	19 (38%)
Very Heavy	30 (60%)	25 (50%)	26 (52%)
Maximum intensity of drinking[2]***)***			
Moderate	-	-	-
Heavy	2 (4%)	2 (4%)	5 (10%)
Very Heavy	48 (96%)	48 (96%)	45 (90%)
Average intensity of drinking[2]			
Moderate	-	1 (2%)	-
Heavy	35 (70%)	21 (42%)	27 (54%)
Very Heavy	15 (30%)	28 (56%)	23 (46%)

[1] Mean weekly drinking (drinks/week): moderate: male > 0-21, female > 0-14; heavy: male > 21-35, female > 14-28; very heavy: male > 35, female > 28

[2] Intensity of drinking (drinks/drinking day): moderate: male 1-4, female 1-3; heavy: male >4-9, female > 3-7; very heavy: male > 9, female > 7

＜資料番号 5.3.5.1-08：Table 9＞

(4)　有効性

(a)　主要評価項目

HDD 数の推移を表 2.7.6.5.8-10 及び図 2.7.6.5.8-1 に，HDD 数のベースラインから各時期の変化量を表 2.7.6.5.8-11 に示した。

HDD 数は，ナルメフェン 40 mg 群でプラセボ群に対し統計学的に有意に減少した（p = 0.0103，反復測定による分散分析）（資料番号 5.3.5.1-08：Table 18.b.2.2 参照）。最初の 1 ヵ月で飲酒量への効果が認められ，その後試験期間を通してベースラインより 29.2%～38.7%低い HDD 数を維持した。ナルメフェン 10 mg 群では，HDD 数が最初の 1 ヵ月で 29.5%減少したが，ベースラインからの減少の割合は 3 ヵ月目に低下した。ナルメフェン 10 mg 群のプラセボ群に対する優越性は示されなかった。プラセボ群では，HDD 数はゆるやかに減少し，治験終了時にはベースラインを 24.0%下回った。

表 2.7.6.5.8-10　　HDD 数の推移（ITT）

	Baseline	Month 1	Month 2	Month 3	Month 4
Placebo					
N	50	48	45	45	45
Mean	14.3	12.1	11.1	10.5	10.6
SD	6.5	7.7	7.1	7.3	8.5
Median	12.2	10.5	10.0	10.0	9.0
Q1 to Q3	9.3 to 18.3	7.5 to 16.5	6.0 to 16.0	6.0 to 15.0	4.0 to 17.0
Min – Max	5.3 – 28	0.0 – 28	0.0 – 28	0.0 – 28	0.0 – 28
NMF 10					
N	50	50	48	46	45
Mean	15.2	11.0	11.3	12.6	12.4
SD	7.3	8.3	7.7	7.8	7.7
Median	13.0	9.5	9.0	12.0	12.0
Q1 to Q3	9.3 to 22.3	4.0 to 16.0	5.0 to 17.5	6.0 to 17.0	6.0 to 17.0
Min – Max	3.0 – 28	0.0 – 28	0.0 – 28	0.0 – 28	0.0 – 28
NMF 40					
N	50	48	48	47	46
Mean	14.9	9.1	9.2	10.2	9.3
SD	6.7	7.4	8.2	7.5	8.5
Median	12.5	7.5	8.0	9.0	8.5
Q1 to Q3	10.0 to 19.3	4.0 to 13.0	2.0 to 13.0	5.0 to 14.0	1.0 to 14.0
Min – Max	6.7 – 28	0.0 – 28	0.0 – 28	0.0 – 28	0.0 – 28

＜資料番号 5.3.5.1-08：Table 17＞

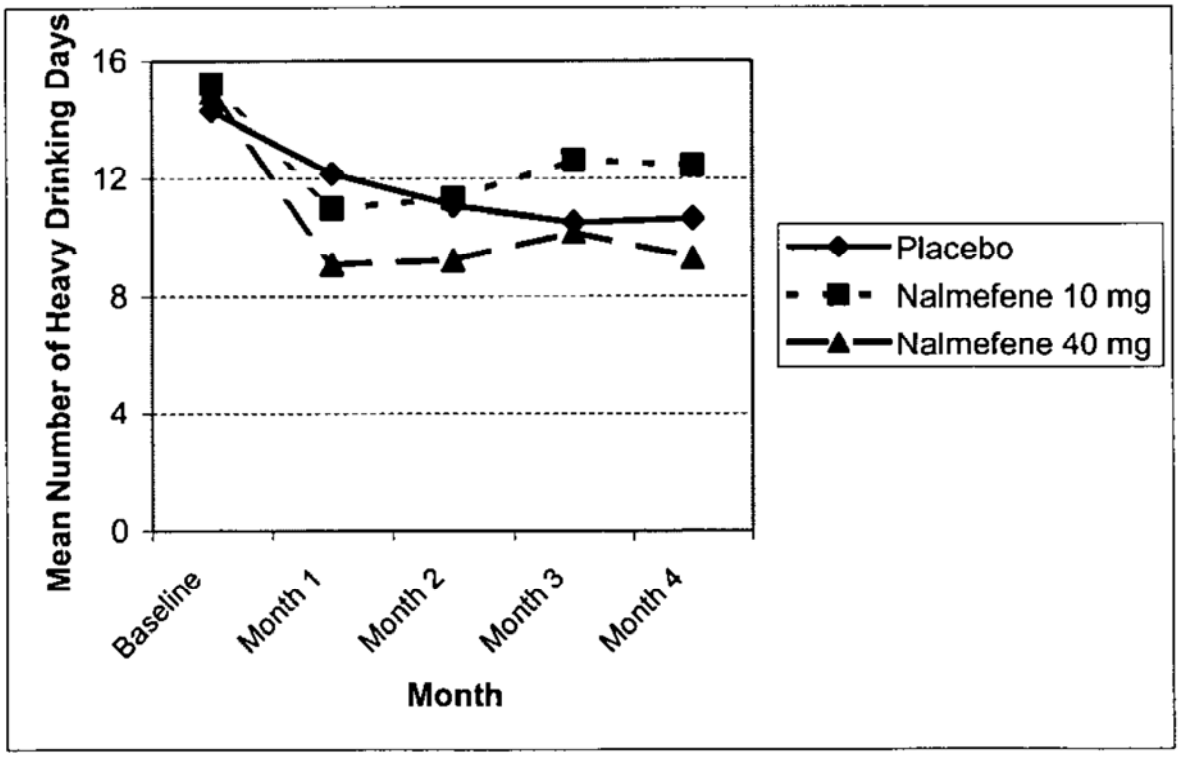


図 2.7.6.5.8-1　　HDD 数の推移（ITT）

＜資料番号 5.3.5.1-08：Figure 1＞

表 2.7.6.5.8-11　　HDD 数のベースラインから各時期の変化量（ITT）

	Month 1	Month 2	Month 3	Month 4
Placebo				
N	48	45	45	45
Absolute change	-2.2 (5.9)	-3.2 (5.5)	-3.8 (6.1)	-3.6 (7.6)
% change	-14.4 (47.1)	-22.1 (41.5)	-25.5 (47.1)	–24.0 (58.0)
NMF10 mg				
N	50	48	46	45
Absolute change	-4.2 (5.7)	-4.0 (6.3)	-2.6 (6.5)	-2.9 (5.4)
% change	-29.5 (36.1)	-25.1 (38.3)	–13.4 (45.6)	-17.4 (42.2)
NMF 40				
N	48	48	47	46
Absolute change	-5.6 (6.8)	–5.4 (6.7)	–4.5 (6.7)	-5.6 (7.8)
% change	-36.4 (42.5)	-38.7 (48.5)	–29.2 (45.0)	-37.3 (56.9)

平均値（SD）
＜資料番号 5.3.5.1-08：Table 18＞

(b)　副次的評価項目

i)　TAC

TAC の推移を表 2.7.6.5.8-12 に示した。

TAC はいずれの投与群でも減少し，群間で差は認められなかった。Month 1 から Month 4 でのベースラインからの減少割合の範囲は，ナルメフェン 10 mg 群で 13.7%～23.2%，40 mg 群で 26.2%～37.6%，プラセボ群で 12.9%～16.1%であった。

表 2.7.6.5.8-12　　TAC の推移（ITT）

	Baseline	Month 1	Month 2	Month 3	Month 4
Placebo					
N	50	48	45	45	45
Mean (SD)	38.6 (18.4)	32.4 (21.2)	30.6 (20.9)	29.7 (20.5)	28.6 (22.2)
Change from baseline		-6.2 (17.3)	-7.4 (18.1)	-8.4 (20.0)	-9.4 (25.7)
% change from baseline		-12.9 (42.9)	-14.4 (44.2)	-16.1 (52.3)	-14.9 (62.4)
NMF 10					
N	50	50	48	46	45
Mean (SD)	42 (23.6)	30.9 (24.4)	31.0 (22.2) 1.0 (5.8)	32. (19.6)	29.8 (18.3)
Change from baseline		-11.1 (19.9)	-10.8 (20.1)	-9.1 (18.9)	-11.7 (17.6)
% change from baseline		-23.2 (46.1)	-21.4 (42.4)	-13.7 (50.1)	-20.1 (50.0)
NMF 40					
N	50	48	48	47	46
Mean (SD)	38.9 (18.3)	24.6 (17.3)	24.1 (20.6)	27.5 (19.0)	24.2 (20.1)
Change from baseline		-13.6 (18.4)	-14.1 (17.8)	-10.7 (17.8)	-14.3 (19.6)
% change from baseline		-31.8 (43.8)	-37.6 (46.4)	-26.2 (48.0)	-35.3 (55.7)

＜資料番号 5.3.5.1-08：Table 24＞

ii)　VHDD 数

VHDD 数は HDD 数と同様にいずれの投与群でも減少し，群間に差は認められなかった。

iii)　飲酒日数に対する HDD 数の割合

治験期間中，被験者は多量飲酒を控える傾向が認められた。この傾向は特にナルメフェン 40 mg 群で顕著であり，Month 4 では，10 例が多量飲酒を全くしなかった又は飲酒機会のうち多量飲酒をした割合が 20%未満であった（資料番号 5.3.5.1-08：Table 23 参照）。また，ナルメフェン 40 mg 群で，HDD 数の減少は NDD 数の増加よりも大きかった。

iv)　NDD 数

NDD 数のベースラインから各時期の変化量を表 2.7.6.5.8-13 に示した。

NDD 数は，ナルメフェン 40 mg 群でプラセボ群と比較して増加した（p = 0.0089）（資料番号 5.3.5.1-08：Table 18.b.7.2 参照）。

表 2.7.6.5.8-13　NDD 数のベースラインから各時期の変化量（ITT）

	Month 1	Month 2	Month 3	Month 4
Placebo				
N	48	45	45	45
Mean (SD)	0.6 (4.2)	0.9 (4.5)	1.6 (5.5)	0.9 (7.4)
NMF 10				
N	50	48	46	45
Mean (SD)	2.3 (6.3)	2.3 (6.1)	0.4 (6.8)	1.0 (5.8)
NMF 40				
N	48	48	47	46
Mean (SD)	4.0 (6.6)	4.2 (7.2)	2.8 (6.8)	3.3 (8.1)

＜資料番号 5.3.5.1-08：Table 22＞

v)　その他のアルコール消費量に関する副次的評価項目

その他のアルコール消費量に関する副次的評価項目では，群間で差は認められなかった。

(c)　その他の副次的評価項目

その他の副次的評価項目では，アルコール消費量に関する副次的評価項目と同様に，群間で差は認められなかった。

(5)　安全性

(a)　治験薬の曝露状況

被験者はナルメフェン 10 mg 群，40 mg 群，又はプラセボ群に 50 例ずつ割付けられ，16 週間（112 日間）治験薬を投与された。ナルメフェン群の被験者は最初の 1 週間にナルメフェン 5 mg を連日投与された。30 例（20%）が治験期間中に治験薬の投与を中止した（資料番号 5.3.5.1-08：Table 18.d.2 参照）。

(b)　有害事象

いずれかの投与群で発現割合が 5%以上の有害事象を表 2.7.6.5.8-14 に，有害事象の器官別大分類を表 2.7.6.5.8-17 に，すべての有害事象を表 2.7.6.5.8-18 に，重症度別有害事象を表 2.7.6.5.8-19 に示した。

ナルメフェン群で 92%の被験者に，プラセボ群で 88%の被験者に有害事象が発現した（資料番号 5.3.5.1-08：Table 18.c.1 参照）。発現割合が高かった有害事象の器官別大分類は，神経系障害，全身障害および投与局所様態，及び胃腸障害であった。

発現割合が高かった有害事象は，浮動性めまい（回転性眩暈を除く）（ナルメフェン 10 mg 群 32%，40 mg 群 28%，プラセボ群 6%，以下同順），インフルエンザ様疾患（18%，28%，18%），頭痛 NOS（20%，16%，26%），不眠症 NEC（18%，24%，16%），下痢 NOS（8%，24%，12%），嘔気（22%，14%，6%），疲労（10%，14%，6%），倦怠感（12%，2%，6%），耳鳴（6%，10%，2%）であった。

有害事象は，主に投与期間の初期に発現した。長期毒性を示唆する有害事象はなかった。

表 2.7.6.5.8-14　いずれかの投与群で発現割合が 5%以上の有害事象（ITT）

Adverse event[a]	Placebo	Nalmefene 10	Nalmefene 40
浮動性めまい（回転性眩暈を除く）	3 (6%)	16 (32%)	14 (28%)
インフルエンザ様疾患	9 (18%)	9 (18%)	14 (28%)
頭痛NOS	13 (26%)	10 (20%)	8 (16%)
不眠症NEC	8 (16%)	9 (18%)	12 (24%)
下痢NOS	6 (12%)	4 (8%)	12 (24%)
嘔気	3 (6%)	11 (22%)	7 (14%)
疲労	3 (6%)	5 (10%)	7 (14%)
倦怠感	3 (6%)	6 (12%)	1 (2%)
耳鳴	1 (2%)	3 (6%)	5 (10%)
口内乾燥	2 (4%)	3 (6%)	4 (8%)
嘔吐NOS	2 (4%)	4 (8%)	3 (6%)
アルコールによる宿酔	1 (2%)	5 (10%)	2 (4%)
腹痛NOS	2 (4%)	5 (10%)	-
不眠増悪	1 (2%)	2 (4%)	4 (8%)
多汗	2 (4%)	2 (4%)	3 (6%)
便秘	-	1 (2%)	5 (10%)
状態悪化	1 (2%)	2 (4%)	3 (6%)
食欲減退NOS	-	5 (10%)	1 (2%)
うつ病NEC	3 (6%)	2 (4%)	1 (2%)
易刺激性	-	2 (4%)	3 (6%)
リビドー減退	-	2 (4%)	3 (6%)
動悸	-	3 (6%)	1 (2%)
消化不良	-	1 (2%)	3 (6%)
味覚障害	1 (2%)	-	3 (6%)
不安NEC	-	3 (6%)	1 (2%)
過敏症NOS	-	-	3 (6%)
傾眠	-	3 (6%)	-

n (%)
MedDRA Version 3.1
[a]MedDRA Preferred term
＜資料番号 5.3.5.1-08：Table 39＞

(c)　治験薬との関連性が否定できない有害事象（副作用）

副作用を表 2.7.6.5.8-20 に示した。

(d)　死亡，その他の重篤な有害事象

i)　死亡

本治験で死亡は報告されなかった。

ii)　その他の重篤な有害事象

重篤な有害事象を表 2.7.6.5.8-15 に，重篤な有害事象一覧表を表 2.7.6.5.8-16 に示した。

9 例に重篤な有害事象が発現した。これらはすべて治験薬との関連性が否定された。重篤な有害事象はプラセボ群 5 例，ナルメフェン 10 mg 群 4 例に発現し，40 mg 群には発現しなかっ

た。

表 2.7.6.5.8-15　重篤な有害事象（ITT）

System organ class Preferred term	Placebo	Nalmefene 10 mg	Total
	n	n	n
胃腸障害			
腹部ヘルニアNOS	1		1
胃炎NOS	1		1
イレウス		1	1
全身障害および投与局所様態			
アルコールによる宿酔		1	1
状態悪化	2	1	3
傷害および中毒			
頭部損傷	1		1
臨床検査			
関節鏡検査		1	1
外科および内科処置			
鼡径部ヘルニア修復		1	1
手術NOS	1		1

MedDRA Version 3.1

The angioplasty for subject #[redacted] and the 2 alcohol detoxifications for subject # [redacted] were not recorded on Adverse Event Form by the investigator but on concomitant treatment CRF page. Therefore, these events do not appear as SAEs in the database.

＜資料番号 5.3.5.1-08：Table 18.c.13.1，Table 18.c.13.2＞

表 2.7.6.5.8-16　重篤な有害事象一覧表（ITT）

Subj. no	System organ class	Preferred term	Reported event	Treatment group	Onset of event[a] from start of study medication (days)
[redacted]	外科および内科処置	手術NOS	Tendon rupture shoulder	Placebo	65
[redacted]	外科および内科処置	血管形成	Angioplasty	Placebo	2
[redacted]	傷害および中毒	頭部損傷	Light head trauma	Placebo	14
[redacted]	全身障害および投与局所様態	状態悪化	Inpatient detoxification	Placebo	6
[redacted]	全身障害および投与局所様態	状態悪化	Inpatient detoxification	Placebo	9
[redacted]	胃腸障害	胃炎NOS	Gastritis	Placebo	24
[redacted]	胃腸障害	腹部ヘルニアNOS	Hernia Umbilicalis incarcerata	Placebo	25
[redacted]	外科および内科処置	アルコールの解毒[b]	Inpatient detoxification	Placebo	64
[redacted]	外科および内科処置	アルコールの解毒[b]	Inpatient detoxification	Placebo	69
[redacted]	胃腸障害	イレウス	Ileus	Nalmefene 10	27
[redacted]	外科および内科処置	鼠径部ヘルニア修復	Inguinal hernia operation	Nalmefene 10	40
[redacted][a]	全身障害および投与局所様態	状態悪化 アルコールによる宿酔	Inpatient detoxification	Nalmefene 10	42
[redacted]	臨床検査	関節鏡検査	Arthroscopy of the left knee	Nalmefene 10	57

MedDRA Version 3.1

[a]One SAE report with inpatient detoxification was completed for subject [redacted], however two events were recorded on AE CRF pages.

[b]MedDRA Version.3.3 で変換

＜資料番号 5.3.5.1-08：Table 49＞

(e)　投与中止に至った有害事象

投与中止に至った有害事象を表 2.7.6.5.8-21 に示した。

15 例（ナルメフェン 10 mg 群 6 例，40 mg 群 6 例，プラセボ群 3 例）が有害事象により投与を中止した。

(f)　臨床検査

i)　治験期間を通しての臨床検査値

いずれの投与群でも臨床検査値に臨床的に重要な変動は認められなかった。

ナルメフェンの臓器毒性は示唆されなかった。

ii)　個々の臨床的に重要な異常

個々の臨床的に重要な臨床検査値の変動は認められなかった。

(g)　バイタルサイン

バイタルサインに重要な群間差は認められなかった。

(6)　結論

- ナルメフェン 40 mg の 1 日 1 回連日投与により多量飲酒を抑制する効果が認められた。
- ナルメフェン 10 mg の 1 日 1 回連日投与による多量飲酒の抑制効果はわずかで，経時的に効果は減少すると考えられた。
- ナルメフェンの安全性上の問題は示唆されなかった。

2.7.6.5.8.4　付録

(1)　有害事象

表 2.7.6.5.8-17　　有害事象の器官別大分類（ITT）

System organ class	Placebo	Nalmefene 10	Nalmefene 40
Any adverse events reported	44 (88%)	46 (92%)	46 (92%)
神経系障害	20 (40%)	26 (52%)	32 (64%)
全身障害および投与局所様態	18 (36%)	23 (46%)	27 (54%)
胃腸障害	14 (28%)	25 (50%)	26 (52%)
精神障害	6 (12%)	14 (28%)	9 (18%)
皮膚および皮下組織障害	9 (18%)	8 (16%)	7 (14%)
筋骨格、結合組織および骨障害	8 (16%)	5 (10%)	6 (12%)
耳および迷路障害	1 (2%)	3 (6%)	5 (10%)
臨床検査	2 (4%)	4 (8%)	4 (8%)
免疫系障害	-	-	3 (6%)
代謝および栄養障害	2 (4%)	6 (12%)	3 (6%)
心臓障害	1 (2%)	4 (8%)	2 (4%)
眼障害	3 (6%)	1 (2%)	2 (4%)
感染症および寄生虫症	5 (10%)	8 (16%)	2 (4%)
傷害および中毒	3 (6%)	2 (4%)	2 (4%)
腎および尿路障害	2 (4%)	-	2 (4%)
呼吸器、胸郭および縦隔障害	4 (8%)	2 (4%)	2 (4%)
生殖系および乳房障害	1 (2%)	-	1 (2%)
血液およびリンパ系障害	2 (4%)	-	-
外科および内科処置	1 (2%)	2 (4%)	-
血管障害	1 (2%)	1 (2%)	-

MedDRA Version 3.1

＜資料番号 5.3.5.1-08：Table 38＞

表 2.7.6.5.8-18　すべての有害事象（ITT）

System organ class	Placebo				Nalmefene 10 mg				Nalmefene 40 mg			
Preferred term			Low 95%	High 95%			Low 95%	High 95%			Low 95%	High 95%
	n	%	CI	CI	n	%	CI	CI	n	%	CI	CI
血液およびリンパ系障害												
貧血NOS	1	2										
白血球増加症NOS	1	2										
心臓障害												
狭心症									1	2		
下肢浮腫	1	2										
動悸					3	6			1	2		
頻脈NOS					2	4						
耳および迷路障害												
耳鳴	1	2			3	6			5	10	2	18
回転性眩暈NEC									1	2		
眼障害												
結膜出血	1	2										
結膜炎NEC	2	4			1	2						
羞明									1	2		
視覚異常NEC									1	2		
胃腸障害												
腹部膨満	1	2										
腹部ヘルニアNOS	1	2										
腹痛NOS	2	4			5	10	2	18				
上腹部痛	1	2			1	2			2	4		
便秘					1	2			5	10	2	18
下痢NOS	6	12	3	21	4	8			12	24	12	36
口内乾燥	2	4			3	6			4	8		
消化不良					1	2			3	6		
鼓腸									1	2		
胃炎NOS	1	2			1	2						
歯肉炎					1	2						
痔核									1	2		
胃腸障害												
イレウス					1	2						
嘔気	3	6			11	22	11	33	7	14	4	24
咽喉痛NOS	1	2			1	2						
嘔吐NOS	2	4			4	8			3	6		

表 2.7.6.5.8-18　すべての有害事象（ITT）（続き）

System organ class	Placebo				Nalmefene 10 mg				Nalmefene 40 mg			
Preferred term			Low 95%	High 95%			Low 95%	High 95%			Low 95%	High 95%
	n	%	CI	CI	n	%	CI	CI	n	%	CI	CI
全身障害および投与局所様態												
アルコールによる宿酔	1	2			5	10	2	18	2	4		
胸痛NEC	1	2			2	4			1	2		
状態悪化	1	2			2	4			3	6		
疲労	3	6			5	10	2	18	7	14	4	24
異常感					2	4						
酩酊感					1	2			1	2		
インフルエンザ様疾患	9	18	7	29	9	18	7	29	14	28	16	40
嗜眠									1	2		
倦怠感	3	6			6	12	3	21	1	2		
疼痛NOS									1	2		
発熱	2	4							1	2		
悪寒									1	2		
口渇	1	2										
脱力					1	2						
免疫系障害												
過敏症NOS									3	6		
感染症および寄生虫症												
急性気管支炎NOS					1	2						
気管支炎NOS	2	4			1	2						
耳の感染症NOS	1	2										
外耳感染NOS					1	2						
真菌感染NOS					1	2						
胃腸炎NOS					1	2						
感染症および寄生虫症												
虹彩炎					1	2						
限局性感染					1	2						
腎盂腎炎NOS	1	2										
副鼻腔炎NOS	1	2										
急性扁桃炎NOS	1	2										
扁桃炎NOS					1	2			1	2		
膣感染NOS					1	2						
歯感染	1	2			1	2			1	2		
傷害および中毒												
頭部損傷	1	2										
損傷NOS	2	4							1	2		
四肢損傷NOS					1	2			1	2		
筋肉損傷NOS	1	2										
歯牙損傷					1	2						

表 2.7.6.5.8-18　すべての有害事象（ITT）（続き）

System organ class Preferred term	Placebo				Nalmefene 10 mg				Nalmefene 40 mg			
			Low 95% CI	High 95% CI			Low 95% CI	High 95% CI			Low 95% CI	High 95% CI
	n	%			n	%			n	%		
臨床検査												
関節鏡検査					1	2						
血中ビリルビン増加									1	2		
血中コレステロール増加									1	2		
血中ブドウ糖増加	1	2							1	2		
血便					1	2						
血圧上昇									1	2		
血中トリグリセリド増加					2	4						
糖尿陽性	1	2										
肝機能検査NOS異常									2	4		
蛋白尿陽性	1	2										
代謝および栄養障害												
食欲減退NOS					5	10	2	18	1	2		
食欲障害NOS									1	2		
食欲亢進NOS	2	4			2	4						
痛風									1	2		
筋骨格、結合組織および骨障害												
関節痛	2	4							1	2		
関節症NOS					1	2						
背部痛	1	2			1	2						
筋痙攣	1	2										
筋痛	2	4							1	2		
頚部痛	1	2										
頚部硬直	1	2			2	4			1	2		
四肢痛	1	2			2	4			2	4		
背部痛増悪	1	2							1	2		
神経系障害												
灼熱感NOS					1	2						
小脳性運動失調					1	2						
痙攣NOS	1	2										
注意力障害NEC					2	4						
浮動性めまい（回転性眩暈を除く）	3	6			16	32	19	45	14	28	16	40
ジスキネジーNEC									1	2		
頭痛NOS	13	26	14	38	10	20	9	31	8	16	6	26
反射減弱					1	2						
活動亢進					1	2						
不眠増悪	1	2			2	4			4	8		
不眠症NEC	8	16	6	26	9	18	7	29	12	24	12	36
記憶障害									2	4		
筋固縮	1	2							1	2		

表 2.7.6.5.8-18　すべての有害事象（ITT）（続き）

System organ class Preferred term	Placebo				Nalmefene 10 mg				Nalmefene 40 mg			
			Low 95% CI	High 95% CI			Low 95% CI	High 95% CI			Low 95% CI	High 95% CI
	n	%			n	%			n	%		
神経系障害												
筋痙直増悪									1	2		
錯感覚NEC					1	2						
嗅覚錯誤	1	2										
傾眠					3	6						
味覚障害	1	2							3	6		
振戦NEC									1	2		
精神障害												
アルコール離脱症状					1	2						
不安NEC					3	6			1	2		
うつ病の増悪					1	2						
うつ病NEC	3	6			2	4			1	2		
錯覚					1	2						
易刺激性					2	4			3	6		
リビドー減退					2	4			3	6		
精神障害NEC					1	2						
神経過敏	2	4			1	2			1	2		
落ち着きのなさ	2	4							1	2		
自殺念慮	1	2										
思考異常NEC					1	2						
不安増悪	1	2										
過覚醒					1	2						
腎および尿路障害												
頻尿	1	2							2	4		
排尿異常NOS	1	2										
生殖系および乳房障害												
インポテンス									1	2		
卵巣嚢胞	1	2										
呼吸器、胸郭および縦隔障害												
喘息増悪	1	2										
呼吸困難NOS	1	2							1	2		
鼻炎NOS					1	2						
季節性鼻炎	1	2										
鼻漏									1	2		
副鼻腔痛	1	2			1	2			1	2		

表 2.7.6.5.8-18　すべての有害事象（ITT）（続き）

System organ class Preferred term	Placebo				Nalmefene 10 mg				Nalmefene 40 mg			
			Low 95% CI	High 95% CI			Low 95% CI	High 95% CI			Low 95% CI	High 95% CI
	n	%			n	%			n	%		
皮膚および皮下組織障害												
ざ瘡増悪					1	2						
冷湿					1	2						
皮膚炎NOS	2	4			1	2			1	2		
皮膚炎NOS増悪									1	2		
斑状出血	2	4			1	2						
立毛	1	2										
そう痒症NOS	2	4							1	2		
酒さ					1	2						
皮膚異常臭	1	2										
日光蕁麻疹	1	2										
多汗	2	4			2	4			3	6		
蕁麻疹NOS					1	2			1	2		
外科および内科処置												
鼠径部ヘルニア修復					1	2						
針穿刺					1	2						
手術NOS	1	2										
血管障害												
潮紅	1	2										
高血圧NOS					1	2						

MedDRA Version 3.1

＜資料番号 5.3.5.1-08：Table 18.c.5＞

(2) 重症度別有害事象

表 2.7.6.5.8-19 重症度別有害事象（ITT）

System organ class Preferred term	Placebo			Nalmefene 10 mg			Nalmefene 40 mg		
	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re
血液およびリンパ系障害									
貧血NOS		1							
白血球増加症NOS	1								
心臓障害									
狭心症							1		
下肢浮腫		1							
動悸				2	1		1		
頻脈NOS				1	2				
耳および迷路障害									
耳鳴	1			3			5		
回転性眩暈NEC							1		
眼障害									
結膜出血	1								
結膜炎NEC	2			1					
羞明							1		
視覚異常NEC								1	
胃腸障害									
腹部膨満		1							
腹部ヘルニアNOS			1						
腹痛NOS	1	1		4	1				
上腹部痛	1			1			2		
便秘				1			3	2	
下痢NOS	3	2	1	3	1		9	3	
口内乾燥	1	1		2	1		4		
消化不良				1			2	1	
鼓腸								1	
胃炎NOS		1	1			1			
歯肉炎				1					
痔核								1	
イレウス						1			
嘔気	2	3		7	5	1	4	3	1
咽喉痛NOS	1			1					
嘔吐NOS	1	1		2	2			1	2

表 2.7.6.5.8-19　重症度別有害事象（ITT）（続き）

System organ class Preferred term	Placebo			Nalmefene 10 mg			Nalmefene 40 mg		
	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re
全身障害および投与局所様態									
アルコールによる宿酔			1	3	2		1	1	
胸痛NEC		1		1	1			2	
状態悪化	2				2			5	
疲労	3			3	2	1	7	1	
異常感				1	1				
酩酊感					1		1		
インフルエンザ様疾患	8	4		4	5		14	4	
嗜眠							1		
倦怠感	3			5	1		1		
疼痛NOS							1		
発熱	1		1					1	
悪寒							1		
口渇	1								
脱力					1				
免疫系障害									
過敏症NOS							1	1	1
感染症および寄生虫症									
急性気管支炎NOS					2				
気管支炎NOS	1	1		1					
耳の感染症NOS	1								
外耳感染NOS					1				
真菌感染NOS				1					
胃腸炎NOS				1					
虹彩炎					1				
限局性感染					1				
腎盂腎炎NOS		1							
副鼻腔炎NOS	1								
急性扁桃炎NOS	1								
扁桃炎NOS					1		2		
腟感染NOS					1				
歯感染		1			1			1	
傷害および中毒									
頭部損傷	1								
損傷NOS	1	1					1		
四肢損傷NOS				1			1		
筋肉損傷NOS		1							
歯牙損傷					1				

表 2.7.6.5.8-19　重症度別有害事象（ITT）（続き）

System organ class Preferred term	Placebo			Nalmefene 10 mg			Nalmefene 40 mg		
	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re
臨床検査									
関節鏡検査				1					
血中ビリルビン増加								1	
血中コレステロール増加							1		
血中ブドウ糖増加	1						1		
血便				1					
血圧上昇								1	
血中トリグリセリド増加				2					
糖尿陽性		1							
肝機能検査NOS異常								2	
蛋白尿陽性		1							
代謝および栄養障害									
食欲減退NOS				5			1		
食欲障害NOS							1		
食欲亢進NOS	1	1		2					
痛風							1		
筋骨格、結合組織および骨障害									
関節痛	2						1		
関節症NOS					1				
背部痛	1			1					
筋痙攣	3								
筋痛	1	1						1	
頚部痛	1								
頚部硬直	1			2			1		
四肢痛		1	1		2		1	1	
背部痛増悪		1						1	
神経系障害									
灼熱感NOS				1					
小脳性運動失調					1				
痙攣NOS		2							
注意力障害NEC				2					

表 2.7.6.5.8-19　重症度別有害事象（ITT）（続き）

System organ class Preferred term	Placebo			Nalmefene 10 mg			Nalmefene 40 mg		
	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re
神経系障害									
浮動性めまい（回転性眩暈を除く）	4			12	5	2	16	1	2
ジスキネジーNEC								1	
頭痛NOS	11	2	1	7	1	2	5	2	1
反射減弱					1				
活動亢進					1				
不眠増悪	1			1	1		2	1	1
不眠症NEC	7	3		4	4	2	9	4	
記憶障害							2		
筋固縮	1						1		
筋痙直増悪							1		
錯感覚NEC				1					
嗅覚錯誤	1								
傾眠				2	1				
味覚障害	1						1	2	
振戦NEC							1		
精神障害									
アルコール離脱症状					1				
不安NEC				1	2		1		
うつ病の増悪					1				
うつ病NEC	1	2		2	1			1	
錯覚						1			
易刺激性				2			2	1	
リビドー減退				2			3		
精神障害NEC					1				
神経過敏	1	1		1				1	
落ち着きのなさ	1	1					1		
自殺念慮			1						
思考異常NEC				1					
不安増悪		1							
過覚醒				1					
腎および尿路障害									
頻尿	1						2		
排尿異常NOS	1								
生殖系および乳房障害									
インポテンス								1	
卵巣嚢胞		1							

表 2.7.6.5.8-19　重症度別有害事象（ITT）（続き）

System organ class Preferred term	Placebo			Nalmefene 10 mg			Nalmefene 40 mg		
	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re	Mild	Mode-rate	Seve-re
呼吸器、胸郭および縦隔障害									
喘息増悪		1							
呼吸困難NOS		1					1		
鼻炎NOS					1				
季節性鼻炎	1								
鼻漏								1	
副鼻腔痛	1			1			1		
皮膚および皮下組織障害									
ざ瘡増悪					1				
冷湿					1				
皮膚炎NOS	1	1		1			1		
皮膚炎NOS増悪								1	
斑状出血		2			1				
立毛		1							
そう痒症NOS		2					1		
酒さ				1					
皮膚および皮下組織障害									
皮膚異常臭		1							
日光蕁麻疹		2							
多汗	1	1		2			4		
蕁麻疹NOS				1			1		
外科および内科処置									
針穿刺				1					
手術NOS		1							
血管障害									
潮紅	1								
高血圧NOS					1				

MedDRA Version 3.1

＜資料番号 5.3.5.1-08：Table 18.c.6.1＞

(3) 副作用

表 2.7.6.5.8-20　副作用（ITT）

System organ class Preferred term	Placebo	Nalmefene 10 mg	Nalmefene 40 mg
	n	n	n
血液およびリンパ系障害			
白血球増加症NOS	1		
心臓障害			
狭心症			1
頻脈NOS		1	
耳および迷路障害			
耳鳴	1	3	2
回転性眩暈NEC			1
眼障害			
羞明			1
胃腸障害			
腹部膨満	1		
腹痛NOS		2	
上腹部痛	1	1	2
便秘		1	3
下痢NOS	1	1	7
口内乾燥	2	3	4
消化不良		1	2
鼓腸			1
嘔気	5	10	8
嘔吐NOS	1	2	3
全身障害および投与局所様態			
アルコールによる宿酔		1	2
胸痛NEC		1	
疲労	2	5	5
異常感		2	
酩酊感		1	1
嗜眠			1
倦怠感		3	1
口渇	1		
脱力		1	
免疫系障害			
過敏症NOS			2
臨床検査			
血圧上昇			1
肝機能検査NOS異常			2
代謝および栄養障害			
食欲減退NOS		4	1
食欲障害NOS			1
食欲亢進NOS	2	1	
筋骨格、結合組織および骨障害			
筋痛	1		
頚部硬直		1	

表 2.7.6.5.8-20　副作用（ITT）（続き）

System organ class Preferred term	Placebo	Nalmefene 10 mg	Nalmefene 40 mg
	n	n	n
神経系障害			
灼熱感NOS		1	
注意力障害NEC		2	
浮動性めまい（回転性眩暈を除く）	4	19	17
ジスキネジーNEC			1
頭痛NOS	8	6	5
活動亢進		1	
不眠増悪	1	2	3
不眠症NEC	8	10	6
記憶障害			2
筋固縮	1		
筋痙直増悪			1
錯感覚NEC		1	
傾眠		2	
味覚障害	1		2
精神障害			
不安NEC		3	
うつ病NEC	1		1
錯覚		1	
精神障害			
易刺激性		2	3
リビドー減退		2	3
精神障害NEC		1	
神経過敏	2	1	
落ち着きのなさ			1
過覚醒		1	
腎および尿路障害			
頻尿	1		1
生殖系および乳房障害			
インポテンス			1
呼吸器、胸郭および縦隔障害			
鼻漏			1
副鼻腔痛	1		1
皮膚および皮下組織障害			
冷湿		1	
皮膚炎NOS		1	
立毛	1		
そう痒症NOS	2		1
皮膚異常臭	1		
日光蕁麻疹	2		
多汗	1	2	3
蕁麻疹NOS		1	1
血管障害			
潮紅	1		

MedDRA Version 3.1

＜資料番号 5.3.5.1-08：Table 18.c.10＞

(4) 投与中止に至った有害事象

表 2.7.6.5.8-21　投与中止に至った有害事象（ITT）

Treatment group	Subject number	Adverse event
Placebo	[redacted]	Headache, insomnia, myalgia, frequent urination
	[redacted]	Gas in the stomach
	[redacted]	Nausea
Nalmefene 10	[redacted]	Dizziness
	[redacted]	Nausea
	[redacted]	Malaise
	[redacted]	Insomnia
	[redacted]	Nausea
	[redacted]	Dizziness
Nalmefene 40	[redacted]	Lightheadedness
	[redacted]	Allergic reaction
	[redacted]	Diarrhea
	[redacted]	Dizziness
	[redacted]	Allergic reaction
	[redacted]	Headache, nausea

MedDRA Version 3.1

＜資料番号 5.3.5.1-08：Table 50＞

2.7.6.5.9　アルコール依存症患者を対象とした継続長期試験（日本人：339-14-002 試験，添付資料番号 5.3.5.2-01）【評価資料】

2.7.6.5.9.1　試験方法の概略

項目	内容
試験の目的	アルコール依存症患者を対象として，ナルメフェン塩酸塩 20 mg の長期の安全性及び有効性を検討する。
試験デザイン	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
対象	アルコール依存症患者
選択基準	1) 339-14-001 試験を完了した患者 2) 339-14-002 試験の同意文書に署名した患者
除外基準	339-14-001 試験の治療期終了日の検査時に，以下の除外基準のいずれかに抵触する患者は除外した。 1) 臨床的に重大かつ安定していない疾患（たとえば NYHA 心機能分類クラス III 度以上の心不全・狭心症の合併，eGFR が 30 mL/min/1.73 m^2 未満の腎機能障害，肝不全，腫瘍性疾患）を合併する患者 2) 臨床的に意義があり，本治験参加に不適切であると治験責任又は分担医師が判断した心電図異常を有する患者 3) 下記のいずれかを満たす自殺リスクを有する患者 • C-SSRS 自殺念慮項目 4（実行する意思がややあるが，具体的に計画されていない積極的な自殺念慮）又は C-SSRS 自殺念慮項目 5（具体的な計画及び実行する意思のある積極的な自殺念慮）に対して「ある」と回答し，かついずれかの基準に合致するエピソードが過去 6 ヵ月以内に起こった • C-SSRS 自殺行動の 5 項目（非致死の自殺企図，中断された自殺企図，中断した自殺企図，予備行動，自殺既遂）のいずれかに対して「ある」と回答し，自殺行動の 5 項目のいずれかの基準に合致する直近のエピソードが過去 2 年以内に起こった • その他，治験責任又は分担医師が重大な自殺リスクがあると判断した 4) 臨床検査値で以下のいずれかを有する患者 • 赤血球数 300 万/mm^3 未満，ヘモグロビン 9.5 g/dL 未満，白血球数 3000/mm^3 未満，血小板数 75000/mm^3 未満 • ALT 又は AST が基準範囲上限の 3 倍を超える値 5) 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

項目	内容
	作，高所作業など危険を伴う職業に従事する患者 6) 妊婦，授乳中の女性患者，妊娠している可能性のある女性患者，本治験期間中及び治験薬最終投与後4週間以内に妊娠を希望する女性患者。男性患者においては，本治験期間中及び治験薬最終投与後4週間以内にパートナーが妊娠を希望している場合。また，本人及びパートナーが避妊を実施できない患者 7) その他，治験責任又は分担医師が対象として不適切と判断した患者
使用薬剤， ロット番号	**被験薬** ナルメフェン塩酸塩錠 20 mg：[redacted]，[redacted] **対照薬** プラセボ錠：[redacted]
用量及び投与方法	治療期では全被験者にナルメフェン塩酸塩錠 20 mg を投与し，退薬期ではナルメフェン塩酸塩錠 20 mg 又はプラセボ錠 1 錠を投与した。ナルメフェン塩酸塩錠 20 mg 又はプラセボ錠 1 錠を，飲酒のおそれがある場合に，飲酒の 1～2 時間前に頓用した。なお，服薬せずに飲酒し始めた場合は，できる限り早く 1 錠服薬することとした。1 日（午前 0 時から翌日の午前 0 時まで）1 錠を限度とした。錠剤の分割投与はしないこととした。 （試験デザインの概要，図 2.7.6.5.9-1 参照）
投与期間	治療期：24 週間，退薬期：4 週間
目標被験者数	339-14-001 試験からの移行例として約 400 例
目標被験者数の 設定根拠	本治験では，先行する 339-14-001 試験を完了し本治験への参加を希望した被験者を登録対象とし，その見込みとして約 400 例と推定した。見込みの算出に際しては，12013A 試験（投与期間 52 週間）での「ベースライン時及び無作為化時の双方で DRL が High 又は Very high の患者」の完了率（ナルメフェン 20 mg 群で 0.53，プラセボ群で 0.67）を参考にし，先行する 339-14-001 試験を完了した被験者が本治験へ移行する率を 0.8 と想定した。
主な併用薬の規定	**併用禁止薬/療法** 併用禁止及び併用制限薬を表 2.7.6.5.9-25 に示す。
評価項目	**安全性** 有害事象，臨床検査値，バイタルサイン，体重，12 誘導心電図，身体学的検査，POMS，C-SSRS，依存性調査 **有効性** HDD 数，TAC，DRL のベースラインは，TLFB 法により収集した 339-14-001 試験のスクリーニング来院前 4 週間とする。また，本治験で

項目	内容
	は 1 ヵ月を 4 週間（28 日間）とした。 • HDD 数のベースラインからの変化量 HDD 数は 1 日のアルコール消費量が男性で 60 g，女性で 40 g を超えた日の 1 ヵ月当たりの日数（日/月）と定義した。 • TAC のベースラインからの変化量 TAC は 1 ヵ月当たりの平均アルコール消費量(g/日)と定義した。 • RSDRL の被験者の割合 : DRL が 2 段階以上低下した被験者の割合 • RLDRL の被験者の割合：DRL が Low 以下となった被験者の割合 • TAC の 70%有効率：TAC が 70%以上低下した被験者の割合 • HDD 数の有効率：HDD 数が 4 日以下となった被験者の割合 • CGI-S • CGI-I • SF-36 • EQ-5D • AQoLS • γ-GTP • ALT • RUMQ-ADP
解析方法	先行する二重盲検試験である 339-14-001 試験及びその継続長期試験である本治験のデータを用いて集計･解析した。治療期のベースラインは，指定がない場合，339-14-001 試験のベースラインとし，退薬期及び後観察期のベースライン（以降，ベースライン II）は本治験の治療期 24 週（V10 の来院）とした。 **安全性** 339-14-001 試験及び本治験全体，治療期［治療期全体及び時期（339-14-001 試験，本治験）別］，退薬期及び後観察期で集計した。治療期は 339-14-001 試験の投与群ごとに，退薬期及び後観察期は退薬期の投与群ごとに集計した。 有害事象： 全体，器官別大分類及び基本語ごとに発現例数と発現割合を求め，更に重症度別で集計した。関連性が否定できない有害事象も同様に集計した。 臨床検査，バイタルサイン，体重，12 誘導心電図，POMS，C-SSRS：

項目	内容
	各時期の記述統計量の算出又は頻度集計を行った。ベースラインからの変化量は記述統計量を算出，又はベースラインに対するシフトテーブルを作成した。 依存性調査： 退薬期終了時の依存性調査 A，後観察終了時の依存性調査 B について，本治験の退薬期の投与群ごとに頻度集計を行った。 **有効性** HDD 数： 339-14-001 試験及び本治験の治療期の各時期の HDD 数及びベースラインからの変化量について，339-14-001 試験の投与群ごとに，記述統計量を求めた。
治験依頼者	大塚製薬株式会社
治験実施医療機関	日本，合計 82 施設
治験期間	2015 年 7 月 13 日～2017 年 1 月 18 日

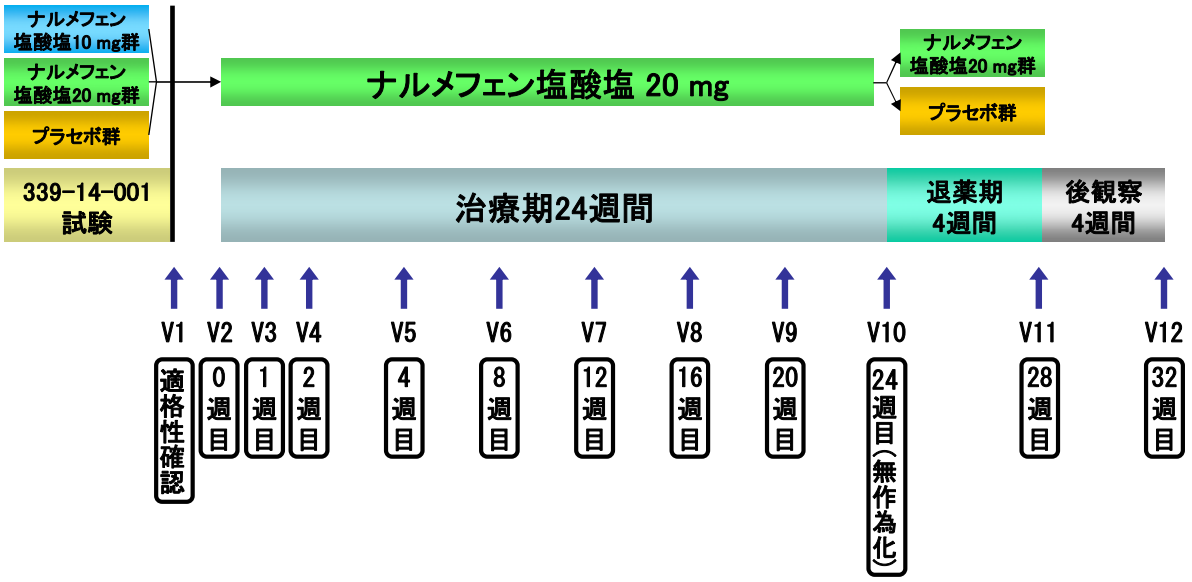


図 2.7.6.5.9-1　　試験デザイン

V：visit（来院日），後観察は退薬期完了例のみ実施した。
＜資料番号 5.3.5.2-01：図 9.1-1＞

2.7.6.5.9.2　治験スケジュール

治験スケジュールを表 2.7.6.5.9-1 に示した。

表 2.7.6.5.9-1　　治験スケジュール

来院		治療期									退薬期	後観察	中止時 [b]
	V1[a] (適格性確認)	V2	V3	V4	V5	V6	V7	V8	V9	V10 (無作為化)	V11	V12	
基準週		0	1	2	4	8	12	16	20	24	28	32	
基準日		1	8	15	29	57	85	113	141	169	197	225	
来院日の許容範囲[c] (基準日からの許容範囲)	-7	0	±3	±3	±7	±7	±7	±7	±7	±7	±7	±7	
同意文書取得[d]	●												
被験者背景の調査	■												
呼気中アルコール濃度の測定[e]		●	●	●	●	●	●	●	●	●	●	●	●
選択基準・除外基準の確認	●												
無作為化										●			
有効性評価													
TLFB[f,g]		●	●	●	●	●	●	●	●	●	●		●
CGI-S[g]		●	●	●	●	●	●	●	●	●	●		●
CGI-I		●	●	●	●	●	●	●	●	●	●		●
SF-36[g]							●			●	●		●
EQ-5D[g]							●			●	●		●
AQoLS[g]							●			●	●		●
RUMQ-ADP[g]							●			●	●		●
γ-GTP[g]	■						●			●	●		●
ALT[g]	■						●			●	●		●
安全性評価													
有害事象	◄	―	―	―	―	―	―	―	―	―	―	―	►
臨床検査[g]	■						●			●	●	●	●
血圧・脈拍数，体重[g]		●	●	●	●	●	●	●	●	●	●	●	●
12 誘導心電図検査[g]	■						●			●	●	●	●
身体学的検査[g]							●			●	●	●	●
POMS[g]							●			●	●	●	●
C-SSRS[g]	■	●	●	●	●	●	●	●	●	●	●	●	●
依存性調査 A											●		
依存性調査 B												●	
その他													
BRENDA		●	●	●	●	●	●	●	●	●	●	●	●
治験薬の配布		●	●	●	●	●	●	●	●	●			
治験薬の返却及び管理記録			●	●	●	●	●	●	●	●	●		●
併用薬・併用療法の確認	◄	―	―	―	―	―	―	―	―	―	―	―	►
新たに開始したアルコール依存症の治療の調査												●	●
妊娠検査[h]	■	●	●	●	●	●	●	●	●	●	●	●	●

■ 339-14-001 試験の治療期終了時来院（V10 の来院）のデータを用いた。

[a] 339-14-002 試験の V1 の来院は，339-14-001 試験の治療期終了時来院（V10 の来院）と同時に実施した。

[b] 治験中止時の来院は，中止が決定してからできるだけ早く実施した。治療期開始前に脱落した場合，中止時検査は実施せず，339-14-001 試験の治療期終了 4 週後調査を行った。なお，退薬期完了以降に中止した場合の有効性評価（TLFB，CGI-S，CGI-I，SF-36，EQ-5D，AQoLS，RUMQ-ADP）は実施不要とした。

[c] ある来院日が規定日の許容範囲から外れた場合でも，次回以降の来院は 0 週（治療期開始日，V2 の来院）を基準にして設定された来院日スケジュールを遵守した。

[d] 本治験への同意取得は 339-14-001 試験終了時までに取得した。

[e] アルコール濃度の測定は，呼気テストを用い，各来院時に最初の検査として実施した。呼気中アルコール濃度が 0.1 mg/L 以上の場合は，後日許容範囲内で再来院させ，観察・検査・評価を行った。

[f] TLFB 法により，各来院時に前回来院以降の飲酒量データを収集した。飲酒行動を思い出す際に，被験者は自

分用又は治験実施医療機関が被験者に配布したカレンダー等の TLFB の補助資料を用いてもよいこととした。TLFB の補助資料は記憶を補助する目的で使用し，原資料とはしなかった。注意：TLFB は，トレーニングを受け，修了の基準を満たした評価者のみが実施した。

[g] これらの評価項目に関するベースラインデータは，339-14-001 試験のスクリーニング来院（V1 の来院）のデータを用いた。

[h] 妊娠する可能性のある女性被験者のみ実施した。なお，子宮摘出，両側卵巣摘出の外科的処置などにより妊娠の可能性がない被験者，又は閉経後 12 ヵ月以上経過している被験者は実施不要とした。

＜資料番号 5.3.5.2-01：表 9.5.1.1-1＞

2.7.6.5.9.3 試験結果

治療期の結果では，339-14-001 試験のナルメフェン塩酸塩 20 mg 群，10 mg 群，又はプラセボ群からの移行例を，それぞれナルメフェン 20 mg 群，10 mg 群，又はプラセボ群からの移行例と記載した。また，20 mg 群及び 10 mg 群からの移行例をナルメフェン投与群全体からの移行例と記載した。退薬期の結果では，ナルメフェン塩酸塩 20 mg 群をナルメフェン 20 mg 群と記載した。時期は 339-14-001 試験の投与開始からの通算で記載した（たとえば，本治験の治療期 24 週を治療期 48 週と示した）。

(1) 被験者の内訳

本治験の治療期の被験者の内訳及び中止理由を全体及び 339-14-001 試験の投与群ごとに表 2.7.6.5.9-2 に示した。また，退薬期及び後観察期の被験者の内訳及び中止理由を全体及び退薬期の投与群ごとに表 2.7.6.5.9-3 に示した。

339-14-001 試験から本治験に 405 例（ナルメフェン 20 mg 群からの移行例 139 例，10 mg 群からの移行例 94 例，プラセボ群からの移行例 172 例，以下同順）が移行し，403 例（137 例，94 例，172 例）に治験薬が 1 回以上投与された。このうち，343 例（126 例，84 例，133 例）が治療期を完了し，退薬期に移行した。退薬期への移行例 343 例のうち，20 mg 群に 172 例，プラセボ群に 171 例が無作為に割付けされた。342 例（20 mg 群 171 例，プラセボ群 171 例，以下同順）は退薬期を完了し，後観察期へ移行した。339 例（169 例，170 例）は後観察期を完了し，治験を完了した。

本治験の治療期の中止例の割合は，20 mg 群からの移行例で 8.0%，10 mg 群からの移行例で 10.6%，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，20 mg 群及びプラセボ群からの移行例では有害事象，10 mg 群からの移行例では被験者の中止の申し出であった。退薬期の中止例は 20 mg 群の 1 例のみで，プラセボ群ではなかった。後観察期の中止例は，20 mg 群で 2 例，プラセボ群で 1 例であった。

表 2.7.6.5.9-2　　被験者の内訳及び中止理由－本治験の治療期－

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 with treated in study 339-14-002

＜資料番号 5.3.5.2-01：Table 14.1.1.1-2＞

表 2.7.6.5.9-3　　被験者の内訳及び中止理由－退薬期及び後観察期－

Treatment group of run-out period Subjects	Placebo N (%)[a]	Nalmefene 20 mg N (%)[a]	Total 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)
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＞

(2)　解析したデータセット

解析対象集団を全体及び 339-14-001 試験の投与群ごとに表 2.7.6.5.9-4 に示した。また，退薬期及び後観察期の解析対象集団を全体及び退薬期の投与群ごとに表 2.7.6.5.9-5 に示した。

本治験への移行例のうち治験薬が 1 回以上投与された被験者を SS とした。SS のうち，339-14-001 試験のベースライン時及び本治験の治験薬投与後 1 回以上 HDD 数のデータを有する被験者を FAS とした。FAS を有効性解析対象とした。

SS は 403 例（ナルメフェン 20 mg 群からの移行例 137 例，10 mg 群からの移行例 94 例，プラ

セボ群からの移行例 172 例，以下同順），FAS は 400 例（137 例，94 例，169 例）であった。

SS 及び FAS のうち，退薬期に移行した被験者は，いずれも 343 例（20 mg 群 172 例，プラセボ群 171 例，以下同順），後観察期に移行した被験者は，いずれも 342 例（171 例，171 例）であった。

表 2.7.6.5.9-4　　解析対象集団

Treatment group of study 339-14-001		Placebo	Nalmefene			Total
			20 mg	10 mg	Total	
Analysis set		N (%)[a]	N (%)[a]	N (%)[a]	N (%)[a]	N (%)[a]
Advanced to study 339-14-002		172	139	94	233	405
Safety set	Included	172 (100.0)	137 (98.6)	94 (100.0)	231 (99.1)	403 (99.5)
	Excluded	0 (0.0)	2 (1.4)	0 (0.0)	2 (0.9)	2 (0.5)
	Reason for Excluded					
	Not IMP intake	0	2	0	2	2
Full analysis set	Included	169 (98.3)	137 (98.6)	94 (100.0)	231 (99.1)	400 (98.8)
	Excluded	3 (1.7)	2 (1.4)	0 (0.0)	2 (0.9)	5 (1.2)
	Reason for Excluded					
	Not IMP intake	0	2	0	2	2
	No HDD data at baseline in the study 339-14-001 or after the initial IMP administration in study 339-14-002	3	0	0	0	3

[a]Percentages calculated vs number of subjects advanced to study 339-14-002

＜資料番号 5.3.5.2-01：Table 14.1.1.1-5＞

表 2.7.6.5.9-5　　解析対象集団－退薬期及び後観察期－

Treatment group of run-out period	Placebo	Nalmefene 20 mg	Total
	N (%)[a]	N (%)[a]	N (%)[a]
Advanced to study 339-14-002			405
Safety set			403
Advanced to run-out period	171 (42.4)	172 (42.7)	343 (85.1)
Advanced to posttreatment observation	171 (42.4)	171 (42.4)	342 (84.9)
Full analysis set			400
Advanced to run-out period	171 (42.8)	172 (43.0)	343 (85.8)
Advanced to posttreatment observation	171 (42.8)	171 (42.8)	342 (85.5)

[a]Percentages calculated vs number of subjects in each analysis set

＜資料番号 5.3.5.2-01：Table 14.1.1.1-6＞

(3)　人口統計学的及び他の基準値の特性

人口統計学的及び他の基準値の特性を表 2.7.6.5.9-6 に，飲酒歴を表 2.7.6.5.9-7 に，アルコール関連問題の治療歴を表 2.7.6.5.9-8 に，全体及び 339-14-001 試験の投与群ごとに示した。また，退薬期移行例の人口統計学的及び他の基準値の特性を表 2.7.6.5.9-26 に，飲酒歴を表 2.7.6.5.9-27

に，アルコール関連問題の治療歴を表 2.7.6.5.9-28 に，全体及び退薬期の投与群ごとに示した。

SS の人口統計学的及び他の基準値の特性は，各投与群からの移行例で，男性の割合は 62.8%～79.8%，年齢（平均値，以下同様）は 48.5～50.1 歳であり，45～54 歳が最も多かった。体重は 64.54～67.76 kg，BMI は 22.81～23.69 kg/m^2 であった。喫煙歴は，最も多かったのが「過去に喫煙していた」で 41.9%～52.1%であった。

飲酒を開始した年齢は 18.6～19.0 歳，飲酒の問題が発現した年齢は 36.7～37.6 歳，問題のある飲酒の家族歴を有する被験者の割合は 7.4%～15.3%であった。飲酒問題に対する治療を開始した年齢は 41.0～43.6 歳，アルコール依存に対する治療がある被験者の割合は 1.1%～2.9%であり，アルコール離脱症状に対する治療がある被験者はいなかった。

退薬期では被験者をナルメフェン 20 mg 群又はプラセボ群に無作為割付けした。退薬期での人口統計学的及び他の基準値の特性は，性別を除き，各投与群で同様であった。

表 2.7.6.5.9-6　　人口統計学的及び他の基準値の特性（SS）

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 1 (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)
Age categorization 2 (n [%])	< 25	2 (1.2)	2 (1.5)	1 (1.1)	3 (1.3)	5 (1.2)
	25 <= - < 35	13 (7.6)	12 (8.8)	9 (9.6)	21 (9.1)	34 (8.4)
	35 <= - < 45	47 (27.3)	31 (22.6)	18 (19.1)	49 (21.2)	96 (23.8)
	45 <= - < 55	65 (37.8)	43 (31.4)	34 (36.2)	77 (33.3)	142 (35.2)
	55 <= - < 65	27 (15.7)	32 (23.4)	23 (24.5)	55 (23.8)	82 (20.3)
	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
Weight categorization 1 (n [%])	< 65	89 (51.7)	73 (53.3)	37 (39.4)	110 (47.6)	199 (49.4)
	65 <=	83 (48.3)	64 (46.7)	57 (60.6)	121 (52.4)	204 (50.6)
Weight categorization 2 (n [%])	< 80	157 (91.3)	120 (87.6)	79 (84.0)	199 (86.1)	356 (88.3)
	80 <=	15 (8.7)	17 (12.4)	15 (16.0)	32 (13.9)	47 (11.7)
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)

表 2.7.6.5.9-6　　人口統計学的及び他の基準値の特性（SS）（続き）

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)
Important medical history related to alcohol dependence	Yes	10 (5.8)	10 (7.3)	7 (7.4)	17 (7.4)	27 (6.7)
	No	162 (94.2)	127 (92.7)	87 (92.6)	214 (92.6)	376 (93.3)
Complication	Yes	129 (75.0)	105 (76.6)	72 (76.6)	177 (76.6)	306 (75.9)
	No	43 (25.0)	32 (23.4)	22 (23.4)	54 (23.4)	97 (24.1)
Smoking history	Current smoker	55 (32.0)	39 (28.5)	14 (14.9)	53 (22.9)	108 (26.8)
	Occasional smoker	4 (2.3)	3 (2.2)	4 (4.3)	7 (3.0)	11 (2.7)
	Past smoker	72 (41.9)	59 (43.1)	49 (52.1)	108 (46.8)	180 (44.7)
	Never smoked	41 (23.8)	36 (26.3)	27 (28.7)	63 (27.3)	104 (25.8)
Drug abuse history	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Prior drugs	Yes	57 (33.1)	41 (29.9)	30 (31.9)	71 (30.7)	128 (31.8)
	No	115 (66.9)	96 (70.1)	64 (68.1)	160 (69.3)	275 (68.2)
Prior therapies other than BRENDA	Yes	3 (1.7)	3 (2.2)	3 (3.2)	6 (2.6)	9 (2.2)
	No	169 (98.3)	134 (97.8)	91 (96.8)	225 (97.4)	394 (97.8)
Concomitant drugs	Yes	116 (67.4)	90 (65.7)	65 (69.1)	155 (67.1)	271 (67.2)
	No	56 (32.6)	47 (34.3)	29 (30.9)	76 (32.9)	132 (32.8)
Concomitant therapies other than BRENDA	Yes	13 (7.6)	12 (8.8)	12 (12.8)	24 (10.4)	37 (9.2)
	No	159 (92.4)	125 (91.2)	82 (87.2)	207 (89.6)	366 (90.8)
CIWA-Ar summary score at the screening[b]	n	172	137	94	231	403
	Mean	0.6	0.5	0.5	0.5	0.5
	SD	1.3	1.0	1.2	1.1	1.2
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	7	6	6	6	7
CIWA-Ar summary score at the randomize[b]	n	172	137	94	231	403
	Mean	0.5	0.4	0.3	0.4	0.4
	SD	1.0	1.1	0.8	1.0	1.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	5	8	4	8	8

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

[b]If subject has at least one missing value, summary score is not calculated.

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＞

表 2.7.6.5.9-7　　飲酒歴（SS）

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 at first drinking experience	n	172	137	94	231	403
	Mean	18.6	18.6	19.0	18.8	18.7
	SD	2.5	2.1	2.1	2.1	2.3
	Min	6	8	12	8	6
	Median	19.0	19.0	19.5	19.0	19.0
	Max	30	25	30	30	30
Age categorization 1 at first drinking experience (n [%])	< 15	4 (2.3)	4 (2.9)	1 (1.1)	5 (2.2)	9 (2.2)
	15 <= - < 18	40 (23.3)	26 (19.0)	12 (12.8)	38 (16.5)	78 (19.4)
	18 <=	128 (74.4)	107 (78.1)	81 (86.2)	188 (81.4)	316 (78.4)
Age categorization 2 at first drinking experience (n [%])	< 20	91 (52.9)	82 (59.9)	47 (50.0)	129 (55.8)	220 (54.6)
	20 <=	81 (47.1)	55 (40.1)	47 (50.0)	102 (44.2)	183 (45.4)
Age at the onset of drinking problem	n	172	137	94	231	403
	Mean	36.7	37.4	37.6	37.5	37.1
	SD	11.7	13.9	12.0	13.1	12.5
	Min	17	15	18	15	15
	Median	36.5	35.0	35.0	35.0	35.0
	Max	68	80	64	80	80
Age categorization at the onset of drinking problem (n [%])	< 20	4 (2.3)	6 (4.4)	2 (2.1)	8 (3.5)	12 (3.0)
	20 <=	168 (97.7)	131 (95.6)	92 (97.9)	223 (96.5)	391 (97.0)
Problems of alcohol drinking history of family (n [%])	Yes	26 (15.1)	21 (15.3)	7 (7.4)	28 (12.1)	54 (13.4)
	No	146 (84.9)	116 (84.7)	87 (92.6)	203 (87.9)	349 (86.6)

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

＜資料番号 5.3.5.2-01：Table 14.1.1.1-9＞

表 2.7.6.5.9-8　　アルコール関連問題の治療歴（SS）

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 at first treatment period for alcohol problems	n	5	2	0	2	7
	Mean	43.6	41.0	-	41.0	42.9
	SD	6.7	8.5	-	8.5	6.6
	Min	37	35	-	35	35
	Median	41.0	41.0	-	41.0	41.0
	Max	54	47	-	47	54
Treated for alcohol dependence (n [%])	Yes	5 (2.9)	2 (1.5)	1 (1.1)	3 (1.3)	8 (2.0)
	No	167 (97.1)	135 (98.5)	93 (98.9)	228 (98.7)	395 (98.0)
Inpatient treatment (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Number of inpatient treatment	n	172	137	94	231	403
	Mean	0.0	0.0	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0	0.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	0	0	0	0	0
Inpatient treatment for psychiatrist (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Number of inpatient treatment for psychiatrist	n	172	137	94	231	403
	Mean	0.0	0.0	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0	0.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	0	0	0	0	0
Inpatient treatment other than psychiatrist (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Number of inpatient treatment other than psychiatrist	n	172	137	94	231	403
	Mean	0.0	0.0	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0	0.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	0	0	0	0	0
Outpatient treatment (n [%])	Yes	5 (2.9)	2 (1.5)	1 (1.1)	3 (1.3)	8 (2.0)
	No	167 (97.1)	135 (98.5)	93 (98.9)	228 (98.7)	395 (98.0)
Number of outpatient treatment	n	172	137	94	231	403
	Mean	0.2	0.1	0.0	0.1	0.1
	SD	1.9	0.9	0.3	0.7	1.4
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	25	10	3	10	25
Outpatient treatment for psychiatrist (n [%])	Yes	5 (2.9)	2 (1.5)	1 (1.1)	3 (1.3)	8 (2.0)
	No	167 (97.1)	135 (98.5)	93 (98.9)	228 (98.7)	395 (98.0)

表 2.7.6.5.9-8　　アルコール関連問題の治療歴（SS）（続き）

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)
Treated for alcohol dependence						
Number of outpatient treatment for psychiatrist	n	172	137	94	231	403
	Mean	0.2	0.1	0.0	0.1	0.1
	SD	1.9	0.9	0.3	0.7	1.4
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	25	10	3	10	25
Outpatient treatment other than psychiatrist (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Number of outpatient treatment other than psychiatrist	n	172	137	94	231	403
	Mean	0.0	0.0	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0	0.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	0	0	0	0	0
Treated for alcohol withdrawal symptoms (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Inpatient treatment (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Number of inpatient treatment	n	172	137	94	231	403
	Mean	0.0	0.0	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0	0.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	0	0	0	0	0
Outpatient treatment (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	No	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
Number of outpatient treatment	n	172	137	94	231	403
	Mean	0.0	0.0	0.0	0.0	0.0
	SD	0.0	0.0	0.0	0.0	0.0
	Min	0	0	0	0	0
	Median	0.0	0.0	0.0	0.0	0.0
	Max	0	0	0	0	0
Treated for alcohol dependence or alcohol withdrawal symptoms (n [%])	Yes	5 (2.9)	2 (1.5)	1 (1.1)	3 (1.3)	8 (2.0)
	No	167 (97.1)	135 (98.5)	93 (98.9)	228 (98.7)	395 (98.0)
Participated in alcoholics anonymous or other self help groups (n [%])	Never	172 (100.0)	137 (100.0)	94 (100.0)	231 (100.0)	403 (100.0)
	Currently	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Previously - within last 4 weeks	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Previously - greater than 4 weeks ago	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Assessment time point is baseline in study 339-14-001.
＜資料番号 5.3.5.2-01：Table 14.1.1.1-11＞

(4) 有効性

(a) HDD 数

339-14-001 試験及び本治験の治療期での HDD 数のベースラインからの変化量を表 2.7.6.5.9-9 に，HDD 数のベースラインから各時期の変化量の推移を図 2.7.6.5.9-2 に，339-14-001 試験の投与群ごとに示した。また，退薬期での HDD 数のベースライン II からの変化量を退薬期の投与群ごとに表 2.7.6.5.9-10 に示した。なお，339-14-001 試験の結果より，ナルメフェン 10 mg 及び 20 mg が有効用量であったため，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。

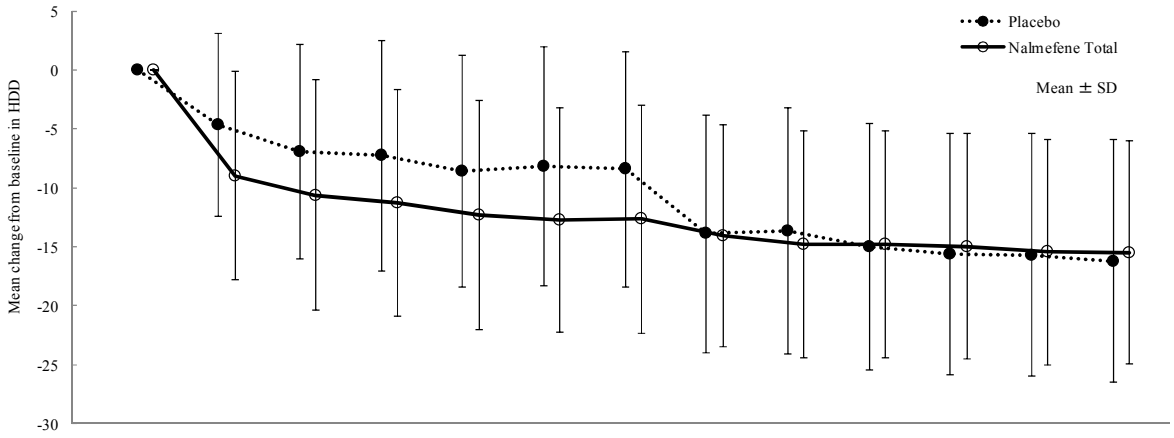
339-14-001 試験及び本治験の治療期での HDD 数のベースラインからの変化量（平均値 ± 標準偏差，以下同様）は，ナルメフェン投与群全体からの移行例で治療期 4 週に−8.94 ± 8.84 日/月，治療期 24 週に−12.62 ± 9.66 日/月，治療期 48 週に−15.46 ± 9.47 日/月であり，治療期 4 週に HDD 数が減少し，その効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週に−8.39 ± 9.97 日/月，治療期 28 週に−13.88 ± 10.07 日/月，治療期 48 週に−16.18 ± 10.31 日/月であり，本治験でナルメフェン投与開始後，HDD 数が減少し，その効果は治療期 48 週まで持続した。なお，ナルメフェン 20 mg 群からの移行例と 10 mg 群からの移行例の HDD 数の推移に大きな違いはなかった。

退薬期では，被験者を 20 mg 群又はプラセボ群のいずれかに 1:1 の割合で無作為割付けした。退薬期での HDD 数は，20 mg 群で維持され，プラセボ群で大きく悪化することはなかった。

表 2.7.6.5.9-9　HDD 数のベースラインからの変化量（FAS，OC）－339-14-001 試験及び本治験の治療期－

Study	Timepoint	Treatment group of study 339-14-001	Value			Change from Baseline		
			n	Mean	SD	n	Mean	SD
339-14-001	Baseline	Placebo	169	22.70	6.54			
		Nalmefene Total	231	23.29	6.16			
	Week 4	Placebo	169	18.10	8.19	169	-4.60	7.77
		Nalmefene Total	231	14.35	8.99	231	-8.94	8.84
	Week 24	Placebo	169	14.31	10.01	169	-8.39	9.97
		Nalmefene Total	231	10.67	9.46	231	-12.62	9.66
339-14-002	Week 4	Placebo	169	8.82	8.52	169	-13.88	10.07
	(Week 28)	Nalmefene Total	231	9.26	9.02	231	-14.03	9.43
	Week 12	Placebo	143	7.90	8.76	143	-15.00	10.46
	(Week 36)	Nalmefene Total	225	8.62	9.33	225	-14.80	9.63
	Week 24	Placebo	136	6.73	8.42	136	-16.18	10.31
	(Week 48)	Nalmefene Total	217	7.83	9.19	217	-15.46	9.47

(Week x) : Total period from baseline in study 339-14-001 excluding screening period in study 339-14-002.
Nalmefene Total : Nalmefene 10 mg or 20 mg.
＜資料番号 5.3.5.2-01：Table 14.1.1.2-34 より作成＞



Study	339-14-001							339-14-002					
Timepoint	Baseline	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 4 (Week 28)	Week 8 (Week 32)	Week 12 (Week 36)	Week 16 (Week 40)	Week 20 (Week 44)	Week 24 (Week 48)
n													
Treatment group of study 339-14-001													
Placebo	169	169	169	169	169	169	169	169	153	143	139	137	136
Nalmefene Total	231	231	231	231	231	231	231	231	227	225	223	220	217

図 2.7.6.5.9-2　HDD 数のベースラインから各時期の変化量の推移（FAS，OC）－339-14-001 試験及び本治験の治療期－

(Week x) : Total period from baseline in study 339-14-001 excluding screening period in study 339-14-002.
Nalmefene Total : Nalmefene 10 mg or 20 mg.
＜資料番号 5.3.5.2-01：Figure 14.2.1.2-5＞

表 2.7.6.5.9-10　HDD 数のベースライン II からの変化量（FAS，OC）－退薬期－

Timepoint	Treatment group of run-out period	Value			Change from Baseline II		
		n	Mean	SD	n	Mean	SD
Baseline II	Placebo	171	7.67	9.16			
	Nalmefene 20 mg	172	7.06	8.66			
Week 28	Placebo	171	8.77	9.81	171	1.10	4.48
(Week 52)	Nalmefene 20 mg	172	7.68	9.10	172	0.62	4.68

(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 14.1.1.2-2 より作成＞

(b)　TAC

339-14-001 試験及び本治験の治療期での TAC のベースラインからの変化量を表 2.7.6.5.9-11 に，TAC のベースラインから各時期の変化量の推移を図 2.7.6.5.9-3 に，339-14-001 試験の投与群ごとに示した。また，退薬期での TAC のベースライン II からの変化量を退薬期の投与群ごとに表 2.7.6.5.9-12 に示した。なお, 339-14-001 試験の結果より, ナルメフェン 10 mg 及び 20 mg が有効用量であったため，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。

339-14-001 試験及び本治験の治療期での TAC のベースラインからの変化量（平均値 ± 標準偏差, 以下同様）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−28.45 ± 28.26 g/日，治療期 24 週に−41.64 ± 33.30 g/日，治療期 48 週に−52.06 ± 31.93 g/日であり，治療期 4 週に TAC が減少し，その効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週に

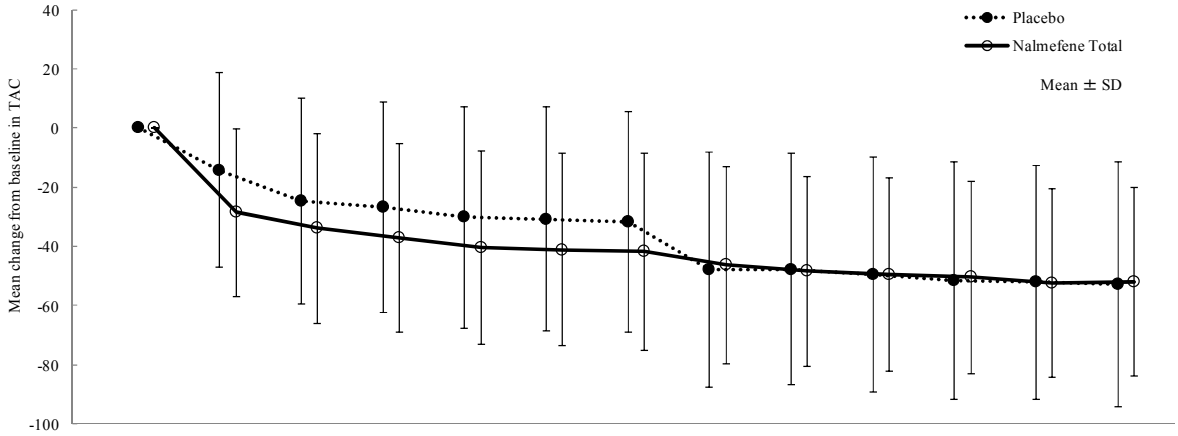
−31.62 ± 37.35 g/日, 治療期 28 週に−47.79 ± 39.55 g/日, 治療期 48 週に−52.87 ± 41.44 g/日であり, 本治験でナルメフェン投与開始後，TAC が減少し，その効果は治療期 48 週まで持続した。なお, ナルメフェン 20 mg 群からの移行例と 10 mg 群からの移行例の TAC の推移に大きな違いはなかった。

退薬期での TAC は，20 mg 群で維持され，プラセボ群で大きく悪化することはなかった。

表 2.7.6.5.9-11　TAC のベースラインからの変化量（FAS，OC）－339-14-001 試験及び本治験の治療期－

Study	Timepoint	Treatment group of study 339-14-001	Value			Change from Baseline		
			n	Mean	SD	n	Mean	SD
339-14-001	Baseline	Placebo	169	92.30	41.03			
		Nalmefene Total	231	94.13	33.63			
	Week 4	Placebo	169	78.06	37.43	169	-14.24	32.92
		Nalmefene Total	231	65.68	34.44	231	-28.45	28.26
	Week 24	Placebo	169	60.68	28.84	169	-31.62	37.35
		Nalmefene Total	231	52.48	33.39	231	-41.64	33.30
339-14-002	Week 4	Placebo	169	44.51	27.18	169	-47.79	39.55
	(Week 28)	Nalmefene Total	231	47.81	32.30	231	-46.31	33.43
	Week 12	Placebo	143	43.71	27.26	143	-49.63	39.73
	(Week 36)	Nalmefene Total	225	45.17	31.30	225	-49.48	32.60
	Week 24	Placebo	136	39.79	26.69	136	-52.87	41.44
	(Week 48)	Nalmefene Total	217	42.40	29.90	217	-52.06	31.93

(Week x) : Total period from baseline in study 339-14-001 excluding screening period in study 339-14-002.
Nalmefene Total : Nalmefene 10 mg or 20 mg.
＜資料番号 5.3.5.2-01：Table 14.1.1.2-35 より作成＞



Study	339-14-001							339-14-002					
Timepoint	Baseline	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 4 (Week 28)	Week 8 (Week 32)	Week 12 (Week 36)	Week 16 (Week 40)	Week 20 (Week 44)	Week 24 (Week 48)
n													
Treatment group of study 339-14-001													
Placebo	169	169	169	169	169	169	169	169	153	143	139	137	136
Nalmefene Total	231	231	231	231	231	231	231	231	227	225	223	220	217

図 2.7.6.5.9-3　TAC のベースラインから各時期の変化量の推移（FAS，OC）－339-14-001 試験及び本治験の治療期－

(Week x) : Total period from baseline in study 339-14-001 excluding screening period in study 339-14-002.
Nalmefene Total : Nalmefene 10 mg or 20 mg.
＜資料番号 5.3.5.2-01：Figure 14.2.1.2-7＞

表 2.7.6.5.9-12　TAC のベースライン II からの変化量（FAS，OC）－退薬期－

Timepoint	Treatment group of run-out period	Value n	Value Mean	Value SD	Change from Baseline II n	Change from Baseline II Mean	Change from Baseline II SD
Baseline II	Placebo	171	43.36	29.60			
	Nalmefene 20 mg	172	39.05	27.28			
Week 28 (Week 52)	Placebo	171	44.92	31.66	171	1.56	9.84
	Nalmefene 20 mg	172	38.96	28.60	172	-0.09	10.86

(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 14.1.1.2-4 より作成＞

(c)　RSDRL

RSDRL の被験者の割合は，ナルメフェン 20 mg 群及び 10 mg 群からの移行例で 339-14-001 試験の治療期に上昇し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で高かった（資料番号 5.3.5.2-01 : Table 14.1.1.2-5 参照）。

(d)　RLDRL

RLDRL の被験者の割合は，ナルメフェン 20 mg 群及び 10 mg 群からの移行例で 339-14-001 試験の治療期に上昇し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で高かった（資料番号 5.3.5.2-01 : Table

14.1.1.2-7 参照）。

(e) TAC の 70%有効率

TAC の 70%有効率は, ナルメフェン 20 mg 群及び 10 mg 群からの移行例で 339-14-001 試験の治療期に上昇し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で高かった（資料番号 5.3.5.2-01：Table 14.1.1.2-9 参照）。

(f) HDD 数の有効率

HDD 数の有効率は, ナルメフェン 20 mg 群及び 10 mg 群からの移行例で 339-14-001 試験の治療期に上昇し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で高かった（資料番号 5.3.5.2-01：Table 14.1.1.2-11 参照）。

(g) CGI-S

本治験の治療期での CGI-S スコアのベースラインからの変化量を 339-14-001 試験の投与群ごとに表 2.7.6.5.9-13 に，退薬期での CGI-S スコアのベースライン II からの変化量を退薬期の投与群ごとに表 2.7.6.5.9-14 に示した。

ナルメフェン 20 mg 群及び 10 mg 群からの移行例で，CGI-S スコアは 339-14-001 試験の治療期に減少し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で CGI-S スコアは減少した。

退薬期での CGI-S スコアは，20 mg 群で維持され，プラセボ群で大きく悪化することはなかった。

表 2.7.6.5.9-13　CGI-S スコアのベースラインからの変化量（FAS，OC）－本治験の治療期－

Study	Timepoint	Treatment group of study 339-14-001	Value			Change from Baseline		
			n	Mean	SD	n	Mean	SD
339-14-001	Baseline	Placebo	169	3.44	1.10			
		Nalmefene 20 mg	137	3.46	0.95			
		Nalmefene 10 mg	94	3.49	1.15			
339-14-002	Week 0	Placebo	169	3.08	1.10	169	-0.37	0.70
	(Week 24)	Nalmefene 20 mg	137	2.71	1.02	137	-0.75	0.87
		Nalmefene 10 mg	94	2.79	1.14	94	-0.70	1.05
	Week 24	Placebo	134	2.49	1.12	134	-0.89	1.12
	(Week 48)	Nalmefene 20 mg	131	2.34	1.02	131	-1.11	1.02
		Nalmefene 10 mg	85	2.48	1.06	85	-1.04	1.22

(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 14.1.1.2-13 より作成＞

表 2.7.6.5.9-14　CGI-S スコアのベースライン II からの変化量（FAS，OC）－退薬期－

		Value			Change from Baseline II		
Timepoint	Treatment group of run-out period	n	Mean	SD	n	Mean	SD
Baseline II	Placebo	171	2.41	1.07			
	Nalmefene 20 mg	172	2.45	1.08			
Week 28	Placebo	171	2.42	1.08	171	0.01	0.45
(Week 52)	Nalmefene 20 mg	172	2.41	1.09	172	-0.04	0.41

(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 14.1.1.2-14 より作成＞

(h)　CGI-I

本治験の治療期での CGI-I スコアを 339-14-001 試験の投与群ごとに表 2.7.6.5.9-15 に，退薬期での CGI-I スコアを退薬期の投与群ごとに表 2.7.6.5.9-16 に示した。

ナルメフェン 20 mg 群及び 10 mg 群からの移行例で，CGI-I スコアは 339-14-001 試験の治療期に減少し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で CGI-I スコアは減少した。

退薬期での CGI-I スコアは，20 mg 群で維持され，プラセボ群で大きく悪化することはなかった。

表 2.7.6.5.9-15　CGI-I スコア（FAS，OC）－本治験の治療期－

		Treatment group of	Value		
Study	Timepoint	study 339-14-001	n	Mean	SD
339-14-002	Week 0	Placebo	169	3.14	0.99
	(Week 24)	Nalmefene 20 mg	137	2.66	1.05
		Nalmefene 10 mg	94	2.57	1.15
	Week 24	Placebo	134	2.20	1.10
	(Week 48)	Nalmefene 20 mg	131	2.14	1.04
		Nalmefene 10 mg	84	2.10	1.05

(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 14.1.1.2-19 より作成＞

表 2.7.6.5.9-16　CGI-I スコア（FAS，OC）－退薬期－

		Value		
Timepoint	Treatment group of run-out period	n	Mean	SD
Baseline II	Placebo	171	2.16	1.08
	Nalmefene 20 mg	172	2.13	1.04
Week 28	Placebo	170	2.24	1.10
(Week 52)	Nalmefene 20 mg	172	2.13	1.06

(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 14.1.1.2-20 より作成＞

(i) SF-36

339-14-001 試験及び本治験の治療期での SF-36 の 8 つの健康概念［身体機能，日常役割機能（身体），体の痛み，全体的健康感，活力，心の健康，日常役割機能（精神），社会生活機能］及び 2 つのサマリースコア（Physical Component Summary，Mental Component Summary）は，いずれの投与群からの移行例でもベースラインとほぼ同様のスコアで推移した。

退薬期での SF-36 の 8 つの健康概念及び 2 つのサマリースコアは，いずれの投与群でもベースライン II と比較して変化はなかった。

(j) EQ-5D

339-14-001 試験及び本治験の治療期での EQ-5D の効用指標のスコア及び VAS による健康状態のスコアは，いずれの投与群からの移行例でもベースラインとほぼ同様のスコアで推移した。

退薬期での EQ-5D の効用指標のスコア及び VAS による健康状態のスコアは，いずれの投与群でもベースライン II と比較して変化はなかった。

(k) AQoLS

339-14-001 試験及び本治験の治療期での AQoLS 合計スコアは，ナルメフェン 20 mg 群及び 10 mg 群からの移行例で 339-14-001 試験の治療期に減少し，治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では治療期 24 週と比較して治療期 48 週で減少した。

退薬期での AQoLS 合計スコアは，いずれの投与群でもベースライン II と比較して変化はなかった。

(l) γ-GTP 及び ALT

γ-GTP 及び ALT は，ナルメフェン 20 mg 群及び 10 mg 群からの移行例では治療期 24 週に認められた効果が治療期 48 週まで持続した。プラセボ群からの移行例では，γ-GTP は治療期 24 週と比較して治療期 48 週で低かった。ALT の平均値は治療期 24 週と比較して治療期 48 週で高かったが，幾何平均値及び中央値で変化はなかった。

(m) RUMQ-ADP

直近の過去 12 週間に，何らかの医療資源を利用した被験者の割合，一般医，精神科医，又は他の専門医を受診した被験者の割合，及び病気休暇を取得した被験者の割合は，いずれの投与群からの移行例でもベースラインと比較して治療期 48 週で変化はなかった。

退薬期では，いずれの投与群でもベースライン II と比較して変化はなかった。

(5) 安全性

(a) 治験薬の曝露状況

339-14-001 試験及び本治験での治験薬の服薬状況を表 2.7.6.5.9-17 に，飲酒状況別の服薬状況を表 2.7.6.5.9-18 に示した。また，退薬期での治験薬の服薬状況を表 2.7.6.5.9-19 に，飲酒状況

別の服薬状況を表 2.7.6.5.9-20 に示した。

339-14-001 試験及び本治験での治験薬服薬日数の割合（平均値，以下同様）は，全体で 81.55%であった。1 ヵ月ごとにみても，339-14-001 試験及び本治験を通して 80%程度で推移した（資料番号 5.3.5.2-01：Table 14.1.1.3-4 参照）。治験薬を服薬して飲酒した日数の割合は，全体で 77.54%，治験薬を服薬せず飲酒した日数の割合は 3.19%，治験薬を服薬して飲酒しなかった日数の割合は 4.01%，治験薬を服薬せず飲酒しなかった日数の割合は 15.25%であった。頓用方法を遵守した日数の割合（治験薬を服薬して飲酒した日数，及び治験薬の服薬を問わず飲酒しなかった日数の合計の割合）は，全体で 96.8%であった。1 ヵ月ごとにみても，339-14-001 試験及び本治験を通して 95%程度で推移し，ナルメフェンを頓用したときの服薬遵守率は高かった（資料番号 5.3.5.2-01：Table 14.1.1.3-5 参照）。

退薬期での治験薬服薬日数の割合は，ナルメフェン 20 mg 群で 75.99%，プラセボ群で 77.82%であった。治験薬を服薬して飲酒した日数の割合は，20 mg 群で 70.79%，プラセボ群で 72.15%，治験薬を服薬せず飲酒した日数の割合は，20 mg 群で 2.68%，プラセボ群で 1.87%，治験薬を服薬して飲酒しなかった日数の割合は，20 mg 群で 5.20%，プラセボ群で 5.67%，治験薬を服薬せず飲酒しなかった日数の割合は，20 mg 群で 21.33%，プラセボ群で 20.31%であった。頓用方法を遵守した日数の割合は，20 mg 群で 97.32%，プラセボ群で 98.13%であった。

表 2.7.6.5.9-17　治験薬の服薬状況（SS）－339-14-001 試験及び本治験－

			IMP	
N	Summary statistics	TLFB days	Days	(%)
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

＜資料番号 5.3.5.2-01：Table 14.1.1.3-4 より作成＞

表 2.7.6.5.9-18　飲酒状況別の服薬状況（SS）－339-14-001 試験及び本治験－

			IMP intake and drinking		No IMP intake and drinking		IMP intake and no drinking		No IMP intake and no drinking	
N	Summary statistics	TLFB days	Days	%	Days	%	Days	%	Days	%
403	Mean	344.7	267.6	77.54	10.4	3.19	13.7	4.01	53.0	15.25
	SD	50.7	90.4	22.89	25.8	7.39	32.8	9.41	76.4	21.46
	Min	166	5	1.3	0	0.0	0	0.0	0	0.0
	Median	363.0	295.0	85.23	2.0	0.60	2.0	0.54	12.0	3.35
	Max	391	371	99.7	331	89.9	252	69.0	367	98.7
	P10	259.0	148.0	43.30	1.0	0.27	0.0	0.00	0.0	0.00
	P25	358.0	197.0	64.56	1.0	0.28	0.0	0.00	1.0	0.27
	P75	366.0	349.0	96.44	11.0	3.35	10.0	2.70	87.0	25.27
	P90	372.0	361.0	99.18	25.0	8.67	41.0	11.23	177.0	49.44

＜資料番号 5.3.5.2-01：Table 14.1.1.3-5 より作成＞

表 2.7.6.5.9-19　治験薬の服薬状況（SS）－退薬期－

				IMP	
Treatment group of run-out period	N	Summary statistics	TLFB days	Days	(%)
Placebo	171	Mean	28.0	21.6	77.82
		SD	5.6	9.3	30.34
		Min	14	0	0.0
		Median	28.0	24.0	93.33
		Max	42	42	100.0
Nalmefene 20 mg	172	Mean	27.9	21.4	75.99
		SD	5.3	10.2	31.88
		Min	11	0	0.0
		Median	28.0	25.0	92.86
		Max	42	42	100.0

＜資料番号 5.3.5.2-01：Table 14.1.1.3-16 より作成＞

表 2.7.6.5.9-20　飲酒状況別の服薬状況（SS）－退薬期－

				IMP intake and drinking		No IMP intake and drinking		IMP intake and no drinking		No IMP intake and no drinking	
Treatment group of run-out period	N	Summary statistics	TLFB days	Days	%	Days	%	Days	%	Days	%
Placebo	171	Mean	28.0	20.0	72.15	0.5	1.87	1.6	5.67	5.9	20.31
		SD	5.6	9.1	30.52	1.9	6.49	4.2	15.06	8.7	29.15
		Min	14	0	0.0	0	0.0	0	0.0	0	0.0
		Median	28.0	21.0	82.14	0.0	0.00	0.0	0.00	0.0	0.00
		Max	42	35	100.0	13	42.9	22	100.0	34	100.0
Nalmefene 20 mg	172	Mean	27.9	19.9	70.79	0.8	2.68	1.5	5.20	5.7	21.33
		SD	5.3	10.4	33.18	2.9	10.17	4.6	15.50	8.6	31.22
		Min	11	0	0.0	0	0.0	0	0.0	0	0.0
		Median	28.0	23.0	85.71	0.0	0.00	0.0	0.00	0.0	0.00
		Max	42	42	100.0	31	100.0	30	88.2	34	100.0

＜資料番号 5.3.5.2-01：Table 14.1.1.3-17 より作成＞

(b)　有害事象

339-14-001 試験及び本治験の治療期で，339-14-001 試験のいずれかの投与群からの移行例で発現割合が 2%以上の有害事象を表 2.7.6.5.9-29 に，本治験の治療期で発現したすべての有害事象を表 2.7.6.5.9-30 に，重症度別有害事象を表 2.7.6.5.9-32 に示した。また，退薬期で発現したすべての有害事象を表 2.7.6.5.9-31 に，重症度別有害事象を表 2.7.6.5.9-33 に示した。

本治験の治療期での有害事象の発現割合は，全体で 75.4%であった。発現した有害事象の多くは軽度又は中等度であった。全体で 5%以上に発現した有害事象は，悪心 19.6%，鼻咽頭炎 17.4%，浮動性めまい 9.9%，頭痛 7.2%，倦怠感及び傾眠各 6.5%，嘔吐 6.2%，腹部不快感 5.7%，不眠症 5.2%であった。

退薬期での有害事象の発現割合は，ナルメフェン 20 mg 群 17.4%，プラセボ群 11.7%であった。発現した有害事象の多くは軽度又は中等度であった。後観察期での有害事象の発現割合は，20 mg 群 18.7%，プラセボ群 12.9%であった。退薬期，後観察期のいずれでも，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（表 2.7.4.7.1-30 参照）。

339-14-001 試験又は本治験で，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検討した。初回発現時期の起点は，339-14-001 試験で 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，339-14-001 試験でプラセボ群であった被験者は本治験のナルメフェン投与開始日とした。

339-14-001 試験及び本治験での初回発現時期別有害事象の発現割合は，全体で Day 0～84 に最も高く 75.7%であり，Day 85～168 で 7.3%，Day 169～252 で 4.1%，Day 253～336 で 1.8%と推移し，Day 337 以降の発現はなかった。Day 169 以降（24 週超）に，全体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，Day 169～252 の鼻咽頭炎 6.0%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。339-14-001 試験及び本治験を通して，全体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。

本治験は継続長期試験であるため，339-14-001 試験の 10 mg 群からの移行例での 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，Day 0～84 に最も高く 67.0%であり，Day 85～168 で 11.7%，Day 169～252 で 9.6%，Day 253～336 で 2.2%，Day 337 以降の発現はなく，20 mg への増量後に発現割合が高くなることはなかった（表 2.7.4.7.1-15 参照）。

(c)　治験薬との関連性が否定できない有害事象（副作用）

本治験の治療期で発現したすべての副作用を表 2.7.6.5.9-34 に，重症度別副作用を表 2.7.6.5.9-36 に示した。また，退薬期で発現したすべての副作用を表 2.7.6.5.9-35 に，重症度別副作用を表 2.7.6.5.9-37 に示した。

本治験の治療期での副作用の発現割合は，全体で 52.4%であった。発現した副作用の多くは軽度又は中等度であった。全体で 5%以上に発現した副作用は，悪心 18.6%，浮動性めまい 8.9%，頭痛 6.0%，傾眠 5.7%，腹部不快感 5.2%であった。

退薬期での副作用の発現割合は，ナルメフェン 20 mg 群 5.8%，プラセボ群 5.3%であった。

発現した副作用の多くは軽度であった。後観察期での副作用の発現割合は，20 mg 群 4.7%，プラセボ群 1.8%であった。退薬期，後観察期のいずれでも，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副作用はなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-41 参照）。

(d) 死亡，その他の重篤な有害事象

i) 死亡

本治験で死亡は報告されなかった。

ii) その他の重篤な有害事象

本治験の治療期で発現した重篤な有害事象を表 2.7.6.5.9-21 に，退薬期で発現した重篤な有害事象を表 2.7.6.5.9-22 に，死亡以外の重篤な有害事象一覧表を表 2.7.6.5.9-38 に示した。更に，重篤な有害事象の叙述を 2.7.6.5.9.5 に示した。

本治験の治療期での重篤な有害事象の発現割合は，全体で 0.7%であった。重篤な有害事象は，ナルメフェン 20 mg 群からの移行例で脱水及び前立腺癌が各 1 例，10 mg 群からの移行例で胃腸炎 1 例であった。

退薬期での重篤な有害事象は，20 mg 群で血栓性脳梗塞，プラセボ群で器質化肺炎が各 1 例であった。

表 2.7.6.5.9-21　重篤な有害事象（SS）－本治験の治療期－

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	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 2.7.6.5.9-22　重篤な有害事象（SS）－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＞

(e)　投与中止に至った有害事象

本治験の治療期で発現した投与中止に至った有害事象を表 2.7.6.5.9-23 に, 退薬期で発現した投与中止に至った有害事象を表 2.7.6.5.9-24 に，投与中止に至った有害事象一覧表を表 2.7.6.5.9-39 に示した。

本治験の治療期での投与中止に至った有害事象の発現割合は，全体で 10.4%，ナルメフェン 20 mg 群からの移行例で 5.8%, 10 mg 群からの移行例で 2.1%, プラセボ群からの移行例で 18.6%であり，プラセボ群で高かった。プラセボ群からの移行例で，発現割合が 2%以上の投与中止に至った有害事象は，悪心 7.6%，浮動性めまい 5.8%，頭痛 2.9%，嘔吐及び食欲減退が各 2.3%であった。20 mg 群及び 10 mg 群からの移行例で，発現割合が 2%以上の投与中止に至った有害事象はなかった。

退薬期で投与中止に至った有害事象は，20 mg 群の 1 例で発現した。

表 2.7.6.5.9-23　投与中止に至った有害事象（SS）－本治験の治療期－

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 adverse events leading to discontinuation	32 (18.6)	8 (5.8)	2 (2.1)	10 (4.3)	42 (10.4)
心臓障害	3 (1.7)	0 (0.0)	1 (1.1)	1 (0.4)	4 (1.0)
動悸	3 (1.7)	0 (0.0)	1 (1.1)	1 (0.4)	4 (1.0)
胃腸障害	15 (8.7)	2 (1.5)	2 (2.1)	4 (1.7)	19 (4.7)
腹部不快感	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
悪心	13 (7.6)	1 (0.7)	1 (1.1)	2 (0.9)	15 (3.7)
嘔吐	4 (2.3)	0 (0.0)	1 (1.1)	1 (0.4)	5 (1.2)
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)
無力症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
悪寒	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
疲労	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
異常感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
熱感	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
倦怠感	3 (1.7)	1 (0.7)	1 (1.1)	2 (0.9)	5 (1.2)
口渇	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
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)
交通事故	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
臨床検査	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.4)	3 (0.7)
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)
血圧上昇	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
γ－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)
代謝および栄養障害	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.4)	5 (1.2)
脱水	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
食欲減退	4 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.0)
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)
骨端症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
骨粗鬆症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
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)
筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	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)
神経系障害	18 (10.5)	1 (0.7)	0 (0.0)	1 (0.4)	19 (4.7)
アカシジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
注意力障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
浮動性めまい	10 (5.8)	1 (0.7)	0 (0.0)	1 (0.4)	11 (2.7)
体位性めまい	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
頭痛	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.4)	6 (1.5)
麻痺	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
傾眠	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)

表 2.7.6.5.9-23　投与中止に至った有害事象（SS）－本治験の治療期－（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 (%)
精神障害	8 (4.7)	1 (0.7)	0 (0.0)	1 (0.4)	9 (2.2)
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)
多幸気分	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不眠症	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.4)	4 (1.0)
睡眠障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
精神障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
早朝覚醒型不眠症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
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)
勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
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)
冷汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
寝汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
全身性皮疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
蕁麻疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
血管障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
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 より作成＞

表 2.7.6.5.9-24　投与中止に至った有害事象（SS）－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 adverse events leading to discontinuation	0 (0.0)	1 (0.6)
臨床検査	0 (0.0)	1 (0.6)
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 より作成＞

(f)　注目すべき有害事象

注目すべき有害事象として，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及び日中の症状を検討した。その結果，本治験の治療期に全体で 5%以上の発現が認められたのは，睡眠障害に関連する夜間の症状 10.7%，睡眠障害に関連する日中の症状 8.2%であった（資料番号 5.3.5.2-01：Table 14.1.1.3-82，Table 14.1.1.3-83 参照）。

(g) 臨床検査

i) 治験期間を通しての臨床検査値

本治験の臨床検査で，安全性上問題となる変化は認められなかった。

ii) 個々の臨床的に重要な異常

本治験の治療期で臨床検査の PCS に該当した被験者の割合が全体で 5%以上であった項目は，尿潜血であったが，その割合は 339-14-001 試験の治療期と比較して低かった。退薬期で臨床検査の PCS に該当した被験者の割合は各投与群で大きく異ならなかった。

本治験の治療期で DILI のいずれかの基準に合致した被験者の割合は，全体で 1.7%であった（資料番号 5.3.5.2-01：Table 14.1.1.3-122 参照）。退薬期で DILI のいずれかの基準に合致した被験者の割合は，ナルメフェン 20 mg 群 1.7%，プラセボ群で 1.2%であり，いずれの投与群でも低かった（資料番号 5.3.5.2-01：Table 14.1.1.3-123 参照）。

(h) バイタルサイン及び体重

本治験のバイタルサイン及び体重で，安全性上問題となる変化は認められなかった。本治験の治療期で PCS に該当した被験者の割合が全体で 5%以上であった項目は，体重増加及び体重減少であった。退薬期で PCS に該当した被験者の割合は，いずれの投与群でも低かった。

(i) 心電図検査

本治験の心電図検査で，安全性上問題となる変化は認められなかった。本治験の治療期に，QTcB が 500 msec 以上又はベースラインから 60 msec 以上増加した被験者は 1 例（プラセボ群からの移行例）と少なかった。QTcF が 500 msec 以上又はベースラインから 60 msec 以上増加した被験者はいなかった。本治験の退薬期に QTcB が 500 msec 以上又はベースライン II から 60 msec 以上増加した被験者は，プラセボ群で 1 例であった。QTcF が 500 msec 以上又はベースライン II から 60 msec 以上増加した被験者はいなかった（資料番号 5.3.5.2-01：Table 14.1.1.3-144，Table 14.1.1.3-145 参照）。

(j) POMS

本治験の POMS 総スコア（TMD スコア）で，安全性上問題となる変化は認められなかった。

(k) C-SSRS

本治験の C-SSRS の評価で，自殺念慮及び自殺行動は認められなかった。

(l) 依存性調査

本治験では退薬期終了時に依存性調査票 A を用いてナルメフェンの依存性を評価し，後観察終了時に依存性調査票 B を用いてナルメフェンの離脱症状を評価した。依存性調査 A の結果を表 2.7.6.5.9-40 に，依存性調査 B の結果を表 2.7.6.5.9-41 に示した。

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は，ナルメフェン 20 mg 群で 96.5%（165/171 例），プラセボ群で 94.7%（162/171 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，20 mg 群で 3.5%（6/171 例），プラセボ群で 4.7%（8/171 例）であり，群間で大きく異ならなかった。プラセボ群で質問 8 に「非常に」と回答した被験者が 1 例認められたが，20 mg 群では「非常に」と回答した被験者は認められなかった。また，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群でも認められなかった。依存性調査 A の評価の結果，ナルメフェンに対する依存性は認められなかった。

依存性調査 B では，プラセボ群で質問 4 に「少し」と回答した被験者が 1 例認められたが，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 の評価の結果，ナルメフェンによる離脱症状は認められなかった。

(6) 結論

- ナルメフェン投与群全体からの移行例で，先行する 339-14-001 試験及び本治験の治療期 48 週間を通して飲酒量低減の効果を検討した結果，HDD 数及び TAC はともに治療期 4 週に減少し，その効果が治療期 48 週まで持続した。プラセボ群からの移行例では，ナルメフェン塩酸塩 20 mg の投与開始後，HDD 数及び TAC が減少し，その効果は治療期 48 週まで持続した。
- レスポンダーの評価（RSDRL，RLDRL，TAC の 70%有効率，HDD 数の有効率），CGI の評価，AQoLS，γ-GTP 及び ALT はナルメフェン 20 mg 群及び 10 mg 群からの移行例で治療期 24 週に認められた効果が治療期 48 週まで持続した。
- 本治験の治療期（24 週間）に全体で 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，頭痛，倦怠感，傾眠，嘔吐，腹部不快感，不眠症であった。本治験で発現した有害事象の重症度は，多くは軽度又は中等度であった。339-14-001 試験及び本治験を通して，全体で，投与期間の延長に伴い発現割合が明らかに高くなる有害事象は認められなかった。
- ナルメフェンの投与後に，依存性及び離脱症状は認められなかった。その他の安全性評価項目でも，長期投与に伴う安全性上の問題は認められなかった。

2.7.6.5.9.4　付録

(1)　併用禁止薬/療法

表 2.7.6.5.9-25　　併用禁止及び併用制限薬

分類	注意又は例外事項
アルコール依存症に対する治療薬	ナルトレキソンの経口剤及び注射剤，アカンプロサートカルシウム，トピラマート，ジスルフィラム及びシアナミドを含む。
何らかの治験薬又は国内未承認の医薬品	－
オピオイド系の鎮痛薬	オピオイド系以外の鎮痛薬は使用可。
オピオイド系の止瀉薬	オピオイド系以外の止瀉薬は使用可。
オピオイド系薬剤が含まれる鎮咳薬又は感冒薬	オピオイド系以外の鎮咳剤又は感冒薬は使用可。
抗うつ薬	－
抗精神病薬	－
抗てんかん薬	－
抗不安薬	頓用は可。
睡眠薬	頓用は可。
食欲抑制薬	－
その他の向精神薬（精神障害に対して使用される漢方薬を含む）	－
抗悪性腫瘍薬	－
筋弛緩薬	頓用は可。
インスリン	－
抗凝固薬	－
アルコールとの相互作用の可能性がある抗生剤（ニトロフラントイン，メトロニダゾール，チニダゾール）	－
抗真菌薬（全身用）	局所用抗真菌薬は使用可。
ステロイド剤	局所用及び吸入用ステロイド剤は使用可。経口避妊薬とホルモン補充療法も使用可。

＜資料番号 5.3.5.2-01：Table 9.4.7.1-1＞

(2) 退薬期移行例の人口統計学的及び他の基準値の特性

表 2.7.6.5.9-26　人口統計学的及び他の基準値の特性（SS）－退薬期－

Characteristics	Treatment group of run-out period	Placebo (N=171)	Nalmefene 20 mg (N=172)	Total (N=343)
Age (years)	n	171	172	343
	Mean	49.2	50.2	49.7
	SD	11.2	11.1	11.2
	Min	21	21	21
	Median	49.0	50.0	50.0
	Max	77	75	77
Age categorization 1 (n [%])	< 65	152 (88.9)	152 (88.4)	304 (88.6)
	65 <=	19 (11.1)	20 (11.6)	39 (11.4)
Age categorization 2 (n [%])	< 25	4 (2.3)	1 (0.6)	5 (1.5)
	25 <= - < 35	13 (7.6)	12 (7.0)	25 (7.3)
	35 <= - < 45	40 (23.4)	40 (23.3)	80 (23.3)
	45 <= - < 55	60 (35.1)	61 (35.5)	121 (35.3)
	55 <= - < 65	35 (20.5)	38 (22.1)	73 (21.3)
	65 <=	19 (11.1)	20 (11.6)	39 (11.4)
Sex (n [%])	Female	35 (20.5)	59 (34.3)	94 (27.4)
	Male	136 (79.5)	113 (65.7)	249 (72.6)
Body weight (kg)	n	171	172	343
	Mean	67.72	63.60	65.65
	SD	12.74	12.43	12.73
	Min	40.0	39.2	39.2
	Median	66.90	63.70	65.40
	Max	115.0	97.6	115.0
Weight categorization 1 (n [%])	< 65	73 (42.7)	90 (52.3)	163 (47.5)
	65 <=	98 (57.3)	82 (47.7)	180 (52.5)
Weight categorization 2 (n [%])	< 80	145 (84.8)	156 (90.7)	301 (87.8)
	80 <=	26 (15.2)	16 (9.3)	42 (12.2)
Height (cm)	n	171	172	343
	Mean	169.28	165.35	167.31
	SD	7.81	7.95	8.11
	Min	150.0	144.1	144.1
	Median	170.20	166.20	168.00
	Max	189.0	183.2	189.0
BMI (kg/m^2)[a]	n	171	172	343
	Mean	23.54	23.13	23.33
	SD	3.62	3.42	3.52
	Min	16.2	16.7	16.2
	Median	23.23	22.54	23.04
	Max	38.2	32.4	38.2
BMI categorization 1 (n [%])	< 18.5	10 (5.8)	10 (5.8)	20 (5.8)
	18.5 <= - < 25	110 (64.3)	111 (64.5)	221 (64.4)
	25 <= - < 30	42 (24.6)	44 (25.6)	86 (25.1)
	30 <= - < 40	9 (5.3)	7 (4.1)	16 (4.7)
	40 <=	0 (0.0)	0 (0.0)	0 (0.0)
BMI categorization 2 (n [%])	< 25	120 (70.2)	121 (70.3)	241 (70.3)
	25 <= - < 30	42 (24.6)	44 (25.6)	86 (25.1)
	30 <=	9 (5.3)	7 (4.1)	16 (4.7)

表 2.7.6.5.9-26　人口統計学的及び他の基準値の特性（SS）－退薬期－（続き）

Characteristics	Treatment group of run-out period	Placebo (N=171)	Nalmefene 20 mg (N=172)	Total (N=343)
Important medical history related to alcohol dependence	Yes	11 (6.4)	10 (5.8)	21 (6.1)
	No	160 (93.6)	162 (94.2)	322 (93.9)
Complication	Yes	128 (74.9)	130 (75.6)	258 (75.2)
	No	43 (25.1)	42 (24.4)	85 (24.8)
Smoking history	Current smoker	47 (27.5)	47 (27.3)	94 (27.4)
	Occasional smoker	7 (4.1)	4 (2.3)	11 (3.2)
	Past smoker	72 (42.1)	77 (44.8)	149 (43.4)
	Never smoked	45 (26.3)	44 (25.6)	89 (25.9)
Drug abuse history	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Prior drugs	Yes	47 (27.5)	58 (33.7)	105 (30.6)
	No	124 (72.5)	114 (66.3)	238 (69.4)
Prior therapies other than BRENDA	Yes	5 (2.9)	2 (1.2)	7 (2.0)
	No	166 (97.1)	170 (98.8)	336 (98.0)
Concomitant drugs	Yes	112 (65.5)	112 (65.1)	224 (65.3)
	No	59 (34.5)	60 (34.9)	119 (34.7)
Concomitant therapies other than BRENDA	Yes	13 (7.6)	17 (9.9)	30 (8.7)
	No	158 (92.4)	155 (90.1)	313 (91.3)
CIWA-Ar summary score at the screening[b]	n	171	172	343
	Mean	0.6	0.4	0.5
	SD	1.3	1.0	1.1
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	7	6	7
CIWA-Ar summary score at the randomize[b]	n	171	172	343
	Mean	0.5	0.3	0.4
	SD	1.1	0.8	1.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	8	7	8

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

[b]If subject has at least one missing value, summary score is not calculated.

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

＜資料番号 5.3.5.2-01：Table 14.1.1.1-13＞

表 2.7.6.5.9-27　飲酒歴（SS）－退薬期－

Treatment group of run-out period Characteristics		Placebo (N=171)	Nalmefene 20 mg (N=172)	Total (N=343)
Age at first drinking experience	n	171	172	343
	Mean	18.7	18.8	18.7
	SD	2.4	2.0	2.2
	Min	6	12	6
	Median	19.0	19.0	19.0
	Max	30	30	30
Age categorization 1 at first drinking experience (n [%])	< 15	4 (2.3)	2 (1.2)	6 (1.7)
	15 <= - < 18	28 (16.4)	33 (19.2)	61 (17.8)
	18 <=	139 (81.3)	137 (79.7)	276 (80.5)
Age categorization 2 at first drinking experience (n [%])	< 20	95 (55.6)	95 (55.2)	190 (55.4)
	20 <=	76 (44.4)	77 (44.8)	153 (44.6)
Age at the onset of drinking problem	n	171	172	343
	Mean	36.5	38.1	37.3
	SD	12.4	12.0	12.2
	Min	15	17	15
	Median	35.0	39.0	36.0
	Max	66	67	67
Age categorization at the onset of drinking problem (n [%])	< 20	8 (4.7)	2 (1.2)	10 (2.9)
	20 <=	163 (95.3)	170 (98.8)	333 (97.1)
Problems of alcohol drinking history of family (n [%])	Yes	19 (11.1)	24 (14.0)	43 (12.5)
	No	152 (88.9)	148 (86.0)	300 (87.5)

Assessment time point is baseline in study 339-14-001.
＜資料番号 5.3.5.2-01：Table 14.1.1.1-15＞

表 2.7.6.5.9-28　アルコール関連問題の治療歴（SS）－退薬期－

Characteristics	Treatment group of run-out period	Placebo (N=171)	Nalmefene 20 mg (N=172)	Total (N=343)
Age at first treatment period for alcohol problems	n	3	3	6
	Mean	45.0	43.3	44.2
	SD	7.8	5.5	6.1
	Min	40	37	37
	Median	41.0	46.0	43.5
	Max	54	47	54
Treated for alcohol dependence (n [%])	Yes	4 (2.3)	3 (1.7)	7 (2.0)
	No	167 (97.7)	169 (98.3)	336 (98.0)
Inpatient treatment (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Number of inpatient treatment	n	171	172	343
	Mean	0.0	0.0	0.0
	SD	0.0	0.0	0.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	0	0	0
Inpatient treatment for psychiatrist (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Number of inpatient treatment for psychiatrist	n	171	172	343
	Mean	0.0	0.0	0.0
	SD	0.0	0.0	0.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	0	0	0
Treated for alcohol dependence				
Inpatient treatment other than psychiatrist (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Number of inpatient treatment other than psychiatrist	n	171	172	343
	Mean	0.0	0.0	0.0
	SD	0.0	0.0	0.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	0	0	0
Outpatient treatment (n [%])	Yes	4 (2.3)	3 (1.7)	7 (2.0)
	No	167 (97.7)	169 (98.3)	336 (98.0)
Number of outpatient treatment	n	171	172	343
	Mean	0.2	0.1	0.1
	SD	1.9	0.8	1.5
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	25	10	25

表 2.7.6.5.9-28　アルコール関連問題の治療歴（SS）－退薬期－（続き）

Characteristics	Treatment group of run-out period	Placebo (N=171)	Nalmefene 20 mg (N=172)	Total (N=343)
Treated for alcohol dependence				
Outpatient treatment for psychiatrist (n [%])	Yes	4 (2.3)	3 (1.7)	7 (2.0)
	No	167 (97.7)	169 (98.3)	336 (98.0)
Number of outpatient treatment for psychiatrist	n	171	172	343
	Mean	0.2	0.1	0.1
	SD	1.9	0.8	1.5
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	25	10	25
Outpatient treatment other than psychiatrist (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Number of outpatient treatment other than psychiatrist	n	171	172	343
	Mean	0.0	0.0	0.0
	SD	0.0	0.0	0.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	0	0	0
Treated for alcohol withdrawal symptoms (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Inpatient treatment (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Number of inpatient treatment	n	171	172	343
	Mean	0.0	0.0	0.0
	SD	0.0	0.0	0.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	0	0	0
Outpatient treatment (n [%])	Yes	0 (0.0)	0 (0.0)	0 (0.0)
	No	171 (100.0)	172 (100.0)	343 (100.0)
Number of outpatient treatment	n	171	172	343
	Mean	0.0	0.0	0.0
	SD	0.0	0.0	0.0
	Min	0	0	0
	Median	0.0	0.0	0.0
	Max	0	0	0
Treated for alcohol dependence or alcohol withdrawal symptoms (n [%])	Yes	4 (2.3)	3 (1.7)	7 (2.0)
	No	167 (97.7)	169 (98.3)	336 (98.0)

表 2.7.6.5.9-28　アルコール関連問題の治療歴（SS）－退薬期－（続き）

Characteristics	Treatment group of run-out period	Placebo (N=171)	Nalmefene 20 mg (N=172)	Total (N=343)
Participated in alcoholics anonymous or other self help groups (n [%])	Never	171 (100.0)	172 (100.0)	343 (100.0)
	Currently	0 (0.0)	0 (0.0)	0 (0.0)
	Previously - within last 4 weeks	0 (0.0)	0 (0.0)	0 (0.0)
	Previously - greater than 4 weeks ago	0 (0.0)	0 (0.0)	0 (0.0)

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

＜資料番号 5.3.5.2-01：Table 14.1.1.1-17＞

(3) 有害事象

表 2.7.6.5.9-29　339-14-001 試験及び本治験の治療期で，いずれかの投与群からの移行例で発現割合が 2%以上の有害事象（SS）

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)		
System organ class　Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	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)	74 (78.7)	67 (71.3)	85 (90.4)	191 (82.7)	163 (70.6)	210 (90.9)	326 (80.9)	304 (75.4)	371 (92.1)
心臓障害	3 (1.7)	8 (4.7)	10 (5.8)	5 (3.6)	1 (0.7)	6 (4.4)	3 (3.2)	8 (8.5)	11 (11.7)	8 (3.5)	9 (3.9)	17 (7.4)	11 (2.7)	17 (4.2)	27 (6.7)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	2 (2.1)	0 (0.0)	2 (0.9)	2 (0.9)	0 (0.0)	2 (0.5)	2 (0.5)
動悸	2 (1.2)	6 (3.5)	7 (4.1)	4 (2.9)	1 (0.7)	5 (3.6)	1 (1.1)	4 (4.3)	5 (5.3)	5 (2.2)	5 (2.2)	10 (4.3)	7 (1.7)	11 (2.7)	17 (4.2)
頻脈	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	1 (1.1)	3 (3.2)	2 (0.9)	1 (0.4)	3 (1.3)	3 (0.7)	2 (0.5)	5 (1.2)
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)	0 (0.0)	1 (1.1)	1 (1.1)	6 (2.6)	5 (2.2)	10 (4.3)	6 (1.5)	9 (2.2)	14 (3.5)
回転性めまい	0 (0.0)	2 (1.2)	2 (1.2)	5 (3.6)	1 (0.7)	6 (4.4)	0 (0.0)	1 (1.1)	1 (1.1)	5 (2.2)	2 (0.9)	7 (3.0)	5 (1.2)	4 (1.0)	9 (2.2)
眼障害	4 (2.3)	1 (0.6)	5 (2.9)	1 (0.7)	6 (4.4)	7 (5.1)	2 (2.1)	2 (2.1)	4 (4.3)	3 (1.3)	8 (3.5)	11 (4.8)	7 (1.7)	9 (2.2)	16 (4.0)
眼乾燥	1 (0.6)	1 (0.6)	2 (1.2)	0 (0.0)	1 (0.7)	1 (0.7)	1 (1.1)	1 (1.1)	2 (2.1)	1 (0.4)	2 (0.9)	3 (1.3)	2 (0.5)	3 (0.7)	5 (1.2)
胃腸障害	36 (20.9)	67 (39.0)	87 (50.6)	63 (46.0)	42 (30.7)	80 (58.4)	44 (46.8)	39 (41.5)	62 (66.0)	107 (46.3)	81 (35.1)	142 (61.5)	143 (35.5)	148 (36.7)	229 (56.8)
腹部不快感	4 (2.3)	9 (5.2)	13 (7.6)	6 (4.4)	9 (6.6)	12 (8.8)	4 (4.3)	5 (5.3)	7 (7.4)	10 (4.3)	14 (6.1)	19 (8.2)	14 (3.5)	23 (5.7)	32 (7.9)
腹部膨満	4 (2.3)	4 (2.3)	7 (4.1)	8 (5.8)	3 (2.2)	11 (8.0)	2 (2.1)	1 (1.1)	2 (2.1)	10 (4.3)	4 (1.7)	13 (5.6)	14 (3.5)	8 (2.0)	20 (5.0)
腹痛	0 (0.0)	2 (1.2)	2 (1.2)	3 (2.2)	1 (0.7)	4 (2.9)	5 (5.3)	1 (1.1)	5 (5.3)	8 (3.5)	2 (0.9)	9 (3.9)	8 (2.0)	4 (1.0)	11 (2.7)
上腹部痛	2 (1.2)	1 (0.6)	3 (1.7)	3 (2.2)	3 (2.2)	5 (3.6)	0 (0.0)	2 (2.1)	2 (2.1)	3 (1.3)	5 (2.2)	7 (3.0)	5 (1.2)	6 (1.5)	10 (2.5)
便秘	2 (1.2)	8 (4.7)	10 (5.8)	8 (5.8)	2 (1.5)	10 (7.3)	3 (3.2)	5 (5.3)	6 (6.4)	11 (4.8)	7 (3.0)	16 (6.9)	13 (3.2)	15 (3.7)	26 (6.5)
齲歯	1 (0.6)	2 (1.2)	3 (1.7)	3 (2.2)	1 (0.7)	4 (2.9)	3 (3.2)	0 (0.0)	3 (3.2)	6 (2.6)	1 (0.4)	7 (3.0)	7 (1.7)	3 (0.7)	10 (2.5)
下痢	2 (1.2)	2 (1.2)	4 (2.3)	4 (2.9)	6 (4.4)	7 (5.1)	4 (4.3)	1 (1.1)	5 (5.3)	8 (3.5)	7 (3.0)	12 (5.2)	10 (2.5)	9 (2.2)	16 (4.0)
消化不良	1 (0.6)	2 (1.2)	3 (1.7)	2 (1.5)	0 (0.0)	2 (1.5)	1 (1.1)	3 (3.2)	3 (3.2)	3 (1.3)	3 (1.3)	5 (2.2)	4 (1.0)	5 (1.2)	8 (2.0)
胃炎	2 (1.2)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.7)	1 (1.1)	1 (1.1)	2 (2.1)	2 (0.9)	1 (0.4)	3 (1.3)	4 (1.0)	1 (0.2)	5 (1.2)
悪心	9 (5.2)	41 (23.8)	46 (26.7)	38 (27.7)	21 (15.3)	50 (36.5)	27 (28.7)	17 (18.1)	32 (34.0)	65 (28.1)	38 (16.5)	82 (35.5)	74 (18.4)	79 (19.6)	128 (31.8)
歯痛	2 (1.2)	0 (0.0)	2 (1.2)	3 (2.2)	2 (1.5)	5 (3.6)	0 (0.0)	2 (2.1)	2 (2.1)	3 (1.3)	4 (1.7)	7 (3.0)	5 (1.2)	4 (1.0)	9 (2.2)
嘔吐	3 (1.7)	14 (8.1)	16 (9.3)	12 (8.8)	6 (4.4)	17 (12.4)	6 (6.4)	5 (5.3)	11 (11.7)	18 (7.8)	11 (4.8)	28 (12.1)	21 (5.2)	25 (6.2)	44 (10.9)

表 2.7.6.5.9-29　339-14-001 試験及び本治験の治療期で，いずれかの投与群からの移行例で発現割合が 2%以上の有害事象（続き）

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)		
System organ class　Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
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)	11 (11.7)	12 (12.8)	19 (20.2)	45 (19.5)	24 (10.4)	61 (26.4)	70 (17.4)	57 (14.1)	111 (27.5)
無力症	1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	1 (0.7)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	1 (0.4)	3 (1.3)	3 (0.7)	2 (0.5)	5 (1.2)
疲労	2 (1.2)	3 (1.7)	5 (2.9)	6 (4.4)	0 (0.0)	6 (4.4)	3 (3.2)	3 (3.2)	5 (5.3)	9 (3.9)	3 (1.3)	11 (4.8)	11 (2.7)	6 (1.5)	16 (4.0)
異常感	1 (0.6)	6 (3.5)	7 (4.1)	5 (3.6)	3 (2.2)	7 (5.1)	2 (2.1)	1 (1.1)	3 (3.2)	7 (3.0)	4 (1.7)	10 (4.3)	8 (2.0)	10 (2.5)	17 (4.2)
倦怠感	7 (4.1)	15 (8.7)	21 (12.2)	15 (10.9)	7 (5.1)	20 (14.6)	3 (3.2)	4 (4.3)	6 (6.4)	18 (7.8)	11 (4.8)	26 (11.3)	25 (6.2)	26 (6.5)	47 (11.7)
発熱	1 (0.6)	2 (1.2)	3 (1.7)	2 (1.5)	0 (0.0)	2 (1.5)	2 (2.1)	2 (2.1)	3 (3.2)	4 (1.7)	2 (0.9)	5 (2.2)	5 (1.2)	4 (1.0)	8 (2.0)
口渇	3 (1.7)	6 (3.5)	7 (4.1)	5 (3.6)	1 (0.7)	6 (4.4)	2 (2.1)	0 (0.0)	2 (2.1)	7 (3.0)	1 (0.4)	8 (3.5)	10 (2.5)	7 (1.7)	15 (3.7)
免疫系障害	0 (0.0)	4 (2.3)	4 (2.3)	2 (1.5)	0 (0.0)	2 (1.5)	2 (2.1)	3 (3.2)	5 (5.3)	4 (1.7)	3 (1.3)	7 (3.0)	4 (1.0)	7 (1.7)	11 (2.7)
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)	2 (2.1)	3 (3.2)	5 (5.3)	3 (1.3)	3 (1.3)	6 (2.6)	3 (0.7)	7 (1.7)	10 (2.5)
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)	22 (23.4)	21 (22.3)	39 (41.5)	64 (27.7)	50 (21.6)	101 (43.7)	134 (33.3)	91 (22.6)	192 (47.6)
膀胱炎	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	2 (1.5)	2 (1.5)	2 (2.1)	0 (0.0)	2 (2.1)	2 (0.9)	2 (0.9)	4 (1.7)	4 (1.0)	2 (0.5)	6 (1.5)
胃腸炎	1 (0.6)	3 (1.7)	4 (2.3)	2 (1.5)	0 (0.0)	2 (1.5)	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	1 (0.4)	4 (1.7)	4 (1.0)	4 (1.0)	8 (2.0)
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)	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	1 (0.4)	4 (1.7)	4 (1.0)	3 (0.7)	7 (1.7)
鼻咽頭炎	61 (35.5)	31 (18.0)	76 (44.2)	33 (24.1)	23 (16.8)	51 (37.2)	21 (22.3)	16 (17.0)	34 (36.2)	54 (23.4)	39 (16.9)	85 (36.8)	115 (28.5)	70 (17.4)	161 (40.0)
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)	2 (2.1)	2 (2.1)	4 (4.3)	8 (3.5)	12 (5.2)	20 (8.7)	24 (6.0)	20 (5.0)	43 (10.7)
靱帯捻挫	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	2 (1.5)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)	3 (1.3)	2 (0.5)	2 (0.5)	4 (1.0)
挫傷	3 (1.7)	2 (1.2)	5 (2.9)	0 (0.0)	2 (1.5)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)	3 (0.7)	4 (1.0)	7 (1.7)
臨床検査	17 (9.9)	12 (7.0)	24 (14.0)	21 (15.3)	13 (9.5)	28 (20.4)	12 (12.8)	7 (7.4)	18 (19.1)	33 (14.3)	20 (8.7)	46 (19.9)	50 (12.4)	32 (7.9)	70 (17.4)
アラニンアミノトランスフェラーゼ増加	0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	1 (0.7)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	1 (0.4)	3 (1.3)	3 (0.7)	1 (0.2)	3 (0.7)
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)	1 (1.1)	0 (0.0)	1 (1.1)	3 (1.3)	1 (0.4)	4 (1.7)	3 (0.7)	2 (0.5)	5 (1.2)
血圧上昇	2 (1.2)	3 (1.7)	4 (2.3)	2 (1.5)	2 (1.5)	4 (2.9)	3 (3.2)	0 (0.0)	3 (3.2)	5 (2.2)	2 (0.9)	7 (3.0)	7 (1.7)	5 (1.2)	11 (2.7)
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)	2 (2.1)	1 (1.1)	3 (3.2)	7 (3.0)	3 (1.3)	10 (4.3)	8 (2.0)	3 (0.7)	11 (2.7)
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)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)	6 (1.5)	0 (0.0)	6 (1.5)

表 2.7.6.5.9-29　339-14-001 試験及び本治験の治療期で，いずれかの投与群からの移行例で発現割合が 2%以上の有害事象（続き）

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)		
System organ class　Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	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	1 (0.6)	0 (0.0)	1 (0.6)	2 (1.5)	2 (1.5)	4 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.9)	4 (1.7)	3 (0.7)	2 (0.5)	5 (1.2)
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)	2 (2.1)	1 (1.1)	2 (2.1)	3 (1.3)	1 (0.4)	3 (1.3)	6 (1.5)	2 (0.5)	6 (1.5)
体重減少	0 (0.0)	1 (0.6)	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.7)	1 (1.1)	1 (1.1)	2 (2.1)	2 (0.9)	1 (0.4)	3 (1.3)	2 (0.5)	2 (0.5)	4 (1.0)
体重増加	0 (0.0)	2 (1.2)	2 (1.2)	2 (1.5)	1 (0.7)	3 (2.2)	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	2 (0.9)	5 (2.2)	3 (0.7)	4 (1.0)	7 (1.7)
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)	2 (2.1)	0 (0.0)	2 (2.1)	11 (4.8)	11 (4.8)	20 (8.7)	13 (3.2)	24 (6.0)	34 (8.4)
食欲減退	2 (1.2)	11 (6.4)	12 (7.0)	6 (4.4)	4 (2.9)	10 (7.3)	1 (1.1)	0 (0.0)	1 (1.1)	7 (3.0)	4 (1.7)	11 (4.8)	9 (2.2)	15 (3.7)	23 (5.7)
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)	9 (9.6)	9 (9.6)	18 (19.1)	25 (10.8)	24 (10.4)	46 (19.9)	40 (9.9)	43 (10.7)	77 (19.1)
関節痛	5 (2.9)	2 (1.2)	7 (4.1)	2 (1.5)	2 (1.5)	3 (2.2)	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	3 (1.3)	5 (2.2)	8 (2.0)	5 (1.2)	12 (3.0)
背部痛	4 (2.3)	7 (4.1)	11 (6.4)	3 (2.2)	8 (5.8)	11 (8.0)	5 (5.3)	4 (4.3)	9 (9.6)	8 (3.5)	12 (5.2)	20 (8.7)	12 (3.0)	19 (4.7)	31 (7.7)
筋肉痛	1 (0.6)	0 (0.0)	1 (0.6)	4 (2.9)	1 (0.7)	5 (3.6)	0 (0.0)	1 (1.1)	1 (1.1)	4 (1.7)	2 (0.9)	6 (2.6)	5 (1.2)	2 (0.5)	7 (1.7)
神経系障害	36 (20.9)	60 (34.9)	79 (45.9)	45 (32.8)	32 (23.4)	63 (46.0)	21 (22.3)	19 (20.2)	32 (34.0)	66 (28.6)	51 (22.1)	95 (41.1)	102 (25.3)	111 (27.5)	174 (43.2)
浮動性めまい	8 (4.7)	27 (15.7)	31 (18.0)	19 (13.9)	8 (5.8)	23 (16.8)	6 (6.4)	5 (5.3)	10 (10.6)	25 (10.8)	13 (5.6)	33 (14.3)	33 (8.2)	40 (9.9)	64 (15.9)
体位性めまい	1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	1 (0.7)	3 (2.2)	0 (0.0)	1 (1.1)	1 (1.1)	2 (0.9)	2 (0.9)	4 (1.7)	3 (0.7)	3 (0.7)	6 (1.5)
味覚異常	4 (2.3)	7 (4.1)	10 (5.8)	2 (1.5)	7 (5.1)	8 (5.8)	2 (2.1)	0 (0.0)	2 (2.1)	4 (1.7)	7 (3.0)	10 (4.3)	8 (2.0)	14 (3.5)	20 (5.0)
頭部不快感	1 (0.6)	3 (1.7)	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	2 (0.5)	3 (0.7)	5 (1.2)
頭痛	12 (7.0)	13 (7.6)	22 (12.8)	4 (2.9)	8 (5.8)	12 (8.8)	6 (6.4)	8 (8.5)	14 (14.9)	10 (4.3)	16 (6.9)	26 (11.3)	22 (5.5)	29 (7.2)	48 (11.9)
感覚鈍麻	2 (1.2)	2 (1.2)	3 (1.7)	3 (2.2)	0 (0.0)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	3 (1.3)	5 (1.2)	2 (0.5)	6 (1.5)
傾眠	12 (7.0)	12 (7.0)	24 (14.0)	26 (19.0)	9 (6.6)	29 (21.2)	8 (8.5)	5 (5.3)	11 (11.7)	34 (14.7)	14 (6.1)	40 (17.3)	46 (11.4)	26 (6.5)	64 (15.9)
睡眠の質低下	3 (1.7)	3 (1.7)	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	2 (0.9)	5 (1.2)	3 (0.7)	7 (1.7)
精神障害	10 (5.8)	37 (21.5)	46 (26.7)	21 (15.3)	10 (7.3)	28 (20.4)	9 (9.6)	10 (10.6)	15 (16.0)	30 (13.0)	20 (8.7)	43 (18.6)	40 (9.9)	57 (14.1)	89 (22.1)
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)	1 (1.1)	1 (1.1)	2 (2.1)	5 (2.2)	2 (0.9)	7 (3.0)	7 (1.7)	5 (1.2)	12 (3.0)
不眠症	1 (0.6)	13 (7.6)	14 (8.1)	9 (6.6)	2 (1.5)	11 (8.0)	6 (6.4)	6 (6.4)	9 (9.6)	15 (6.5)	8 (3.5)	20 (8.7)	16 (4.0)	21 (5.2)	34 (8.4)
中期不眠症	1 (0.6)	5 (2.9)	6 (3.5)	5 (3.6)	2 (1.5)	7 (5.1)	1 (1.1)	2 (2.1)	2 (2.1)	6 (2.6)	4 (1.7)	9 (3.9)	7 (1.7)	9 (2.2)	15 (3.7)
睡眠障害	0 (0.0)	5 (2.9)	5 (2.9)	1 (0.7)	1 (0.7)	1 (0.7)	1 (1.1)	0 (0.0)	1 (1.1)	2 (0.9)	1 (0.4)	2 (0.9)	2 (0.5)	6 (1.5)	7 (1.7)
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)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	1 (0.4)	2 (0.5)	6 (1.5)	7 (1.7)

表 2.7.6.5.9-29　339-14-001 試験及び本治験の治療期で，いずれかの投与群からの移行例で発現割合が 2%以上の有害事象（続き）

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)		
System organ class	Study	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total	339-14-001	339-14-002	Total
Preferred term		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
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)	1 (1.1)	1 (1.1)	2 (2.1)	7 (3.0)	2 (0.9)	8 (3.5)	8 (2.0)	4 (1.0)	11 (2.7)
勃起増強		0 (0.0)	1 (0.6)	1 (0.6)	3 (2.2)	0 (0.0)	3 (2.2)	1 (1.1)	0 (0.0)	1 (1.1)	4 (1.7)	0 (0.0)	4 (1.7)	4 (1.0)	1 (0.2)	5 (1.2)
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)	6 (6.4)	2 (2.1)	8 (8.5)	13 (5.6)	8 (3.5)	18 (7.8)	21 (5.2)	12 (3.0)	30 (7.4)
鼻出血		0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	2 (2.1)	0 (0.0)	2 (2.1)	3 (1.3)	0 (0.0)	3 (1.3)	3 (0.7)	0 (0.0)	3 (0.7)
口腔咽頭痛		1 (0.6)	1 (0.6)	2 (1.2)	2 (1.5)	3 (2.2)	4 (2.9)	1 (1.1)	1 (1.1)	2 (2.1)	3 (1.3)	4 (1.7)	6 (2.6)	4 (1.0)	5 (1.2)	8 (2.0)
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)	6 (6.4)	1 (1.1)	6 (6.4)	16 (6.9)	6 (2.6)	20 (8.7)	21 (5.2)	20 (5.0)	38 (9.4)
湿疹		0 (0.0)	0 (0.0)	0 (0.0)	3 (2.2)	1 (0.7)	4 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	1 (0.4)	4 (1.7)	3 (0.7)	1 (0.2)	4 (1.0)
発疹		1 (0.6)	3 (1.7)	4 (2.3)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	2 (0.5)	3 (0.7)	5 (1.2)
蕁麻疹		0 (0.0)	2 (1.2)	2 (1.2)	2 (1.5)	0 (0.0)	2 (1.5)	2 (2.1)	0 (0.0)	2 (2.1)	4 (1.7)	0 (0.0)	4 (1.7)	4 (1.0)	2 (0.5)	6 (1.5)
血管障害		6 (3.5)	2 (1.2)	7 (4.1)	4 (2.9)	4 (2.9)	6 (4.4)	4 (4.3)	5 (5.3)	7 (7.4)	8 (3.5)	9 (3.9)	13 (5.6)	14 (3.5)	11 (2.7)	20 (5.0)
高血圧		4 (2.3)	1 (0.6)	4 (2.3)	2 (1.5)	2 (1.5)	3 (2.2)	1 (1.1)	2 (2.1)	3 (3.2)	3 (1.3)	4 (1.7)	6 (2.6)	7 (1.7)	5 (1.2)	10 (2.5)
ほてり		2 (1.2)	1 (0.6)	3 (1.7)	1 (0.7)	1 (0.7)	1 (0.7)	2 (2.1)	3 (3.2)	3 (3.2)	3 (1.3)	4 (1.7)	4 (1.7)	5 (1.2)	5 (1.2)	7 (1.7)

MedDRA Ver. 19.0

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

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	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	141 (82.0)	96 (70.1)	67 (71.3)	163 (70.6)	304 (75.4)
血液およびリンパ系障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
貧血	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	8 (4.7)	1 (0.7)	8 (8.5)	9 (3.9)	17 (4.2)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
右脚ブロック	0 (0.0)	0 (0.0)	2 (2.1)	2 (0.9)	2 (0.5)
動悸	6 (3.5)	1 (0.7)	4 (4.3)	5 (2.2)	11 (2.7)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
心室性期外収縮	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害	4 (2.3)	4 (2.9)	1 (1.1)	5 (2.2)	9 (2.2)
一過性難聴	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
耳管開放	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
聴覚過敏	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
回転性めまい	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
内分泌障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
高プロラクチン血症	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
眼障害	1 (0.6)	6 (4.4)	2 (2.1)	8 (3.5)	9 (2.2)
眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
結膜出血	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
アレルギー性結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	1 (0.6)	1 (0.7)	1 (1.1)	2 (0.9)	3 (0.7)
上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜炎	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
視力障害	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
角膜障害	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
胃腸障害	67 (39.0)	42 (30.7)	39 (41.5)	81 (35.1)	148 (36.7)
腹部不快感	9 (5.2)	9 (6.6)	5 (5.3)	14 (6.1)	23 (5.7)
腹部膨満	4 (2.3)	3 (2.2)	1 (1.1)	4 (1.7)	8 (2.0)
腹痛	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	1 (0.6)	3 (2.2)	2 (2.1)	5 (2.2)	6 (1.5)
慢性胃炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
便秘	8 (4.7)	2 (1.5)	5 (5.3)	7 (3.0)	15 (3.7)
齲歯	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.4)	3 (0.7)
下痢	2 (1.2)	6 (4.4)	1 (1.1)	7 (3.0)	9 (2.2)
口内乾燥	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害					
消化不良	2 (1.2)	0 (0.0)	3 (3.2)	3 (1.3)	5 (1.2)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硬便	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
食中毒	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
胃ポリープ	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
胃潰瘍	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
胃炎	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
胃食道逆流性疾患	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	41 (23.8)	21 (15.3)	17 (18.1)	38 (16.5)	79 (19.6)
口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涎過多	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	2 (1.5)	2 (2.1)	4 (1.7)	4 (1.0)
嘔吐	14 (8.1)	6 (4.4)	5 (5.3)	11 (4.8)	25 (6.2)
口腔知覚不全	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
大腸ポリープ	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
口腔粘膜血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟便	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
一般・全身障害および投与部位の状態	33 (19.2)	12 (8.8)	12 (12.8)	24 (10.4)	57 (14.1)
無力症	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
悪寒	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
不快感	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
疲労	3 (1.7)	0 (0.0)	3 (3.2)	3 (1.3)	6 (1.5)
異常感	6 (3.5)	3 (2.2)	1 (1.1)	4 (1.7)	10 (2.5)
熱感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
宿酔	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
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)
注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	15 (8.7)	7 (5.1)	4 (4.3)	11 (4.8)	26 (6.5)
発熱	2 (1.2)	0 (0.0)	2 (2.1)	2 (0.9)	4 (1.0)
口渇	6 (3.5)	1 (0.7)	0 (0.0)	1 (0.4)	7 (1.7)
末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
ワクチン接種部位腫脹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝胆道系障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
アルコール性肝疾患	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
免疫系障害	4 (2.3)	0 (0.0)	3 (3.2)	3 (1.3)	7 (1.7)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	4 (2.3)	0 (0.0)	3 (3.2)	3 (1.3)	7 (1.7)
感染症および寄生虫症	41 (23.8)	29 (21.2)	21 (22.3)	50 (21.6)	91 (22.6)
口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アニサキス症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
気管支炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
結膜炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱炎	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
蓄膿	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	3 (1.7)	0 (0.0)	1 (1.1)	1 (0.4)	4 (1.0)
ウイルス性胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
帯状疱疹	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	2 (1.2)	0 (0.0)	1 (1.1)	1 (0.4)	3 (0.7)
鼻咽頭炎	31 (18.0)	23 (16.8)	16 (17.0)	39 (16.9)	70 (17.4)
食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液腺炎	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
副鼻腔炎	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
ウイルス性下痢	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉膿瘍	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
ヘリコバクター感染	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
ヘリコバクター性胃炎	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
感染性腸炎	0 (0.0)	1 (0.7)	1 (1.1)	2 (0.9)	2 (0.5)
ヘルペス性皮膚炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口腔ヘルペス	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
ノロウイルス性胃腸炎	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
傷害、中毒および処置合併症	8 (4.7)	10 (7.3)	2 (2.1)	12 (5.2)	20 (5.0)
偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アルコール中毒	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
節足動物刺傷	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
凍瘡	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓骨骨折	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症					
凍傷	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
手骨折	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯捻挫	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
交通事故	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
外傷性血腫	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
擦過傷	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
挫傷	2 (1.2)	2 (1.5)	0 (0.0)	2 (0.9)	4 (1.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
靱帯損傷	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚擦過傷	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
剥離骨折	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
熱中症	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
外傷後頚部症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	12 (7.0)	13 (9.5)	7 (7.4)	20 (8.7)	32 (7.9)
アラニン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)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
血圧上昇	3 (1.7)	2 (1.5)	0 (0.0)	2 (0.9)	5 (1.2)
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)
血中プロラクチン増加	0 (0.0)	2 (1.5)	1 (1.1)	3 (1.3)	3 (0.7)
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)
血中尿酸増加	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
C－反応性蛋白増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心電図QT延長	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
γ－グルタミルトランスフェラーゼ増加	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
尿中血陽性	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数減少	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
脂質異常	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	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					
体重減少	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
体重増加	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
尿中ケトン体陽性	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
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)
尿量増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
便潜血陽性	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
肝機能検査値上昇	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
代謝および栄養障害	13 (7.6)	11 (8.0)	0 (0.0)	11 (4.8)	24 (6.0)
脱水	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
糖尿病	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
痛風	1 (0.6)	2 (1.5)	0 (0.0)	2 (0.9)	3 (0.7)
高コレステロール血症	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
高トリグリセリド血症	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
高尿酸血症	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
ビタミン欠乏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	11 (6.4)	4 (2.9)	0 (0.0)	4 (1.7)	15 (3.7)
高脂血症	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
筋骨格系および結合組織障害	19 (11.0)	15 (10.9)	9 (9.6)	24 (10.4)	43 (10.7)
関節痛	2 (1.2)	2 (1.5)	1 (1.1)	3 (1.3)	5 (1.2)
関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	7 (4.1)	8 (5.8)	4 (4.3)	12 (5.2)	19 (4.7)
筋固縮	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	1 (0.6)	1 (0.7)	1 (1.1)	2 (0.9)	3 (0.7)
筋肉痛	0 (0.0)	1 (0.7)	1 (1.1)	2 (0.9)	2 (0.5)
頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
骨壊死	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
骨粗鬆症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
変形性脊椎症	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
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)
弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
椎間板突出	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
筋骨格硬直	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
指変形	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	2 (1.5)	0 (0.0)	2 (0.9)	3 (0.7)
皮膚乳頭腫	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
前立腺癌	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
神経系障害	60 (34.9)	32 (23.4)	19 (20.2)	51 (22.1)	111 (27.5)
アカシジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
健忘	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
浮動性めまい	27 (15.7)	8 (5.8)	5 (5.3)	13 (5.6)	40 (9.9)
体位性めまい	1 (0.6)	1 (0.7)	1 (1.1)	2 (0.9)	3 (0.7)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	7 (4.1)	7 (5.1)	0 (0.0)	7 (3.0)	14 (3.5)
ジスキネジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
頭部不快感	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
頭痛	13 (7.6)	8 (5.8)	8 (8.5)	16 (6.9)	29 (7.2)
知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
麻痺	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
坐骨神経痛	0 (0.0)	1 (0.7)	1 (1.1)	2 (0.9)	2 (0.5)
鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	12 (7.0)	9 (6.6)	5 (5.3)	14 (6.1)	26 (6.5)
嗅覚減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肘部管症候群	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
睡眠の質低下	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
精神障害	37 (21.5)	10 (7.3)	10 (10.6)	20 (8.7)	57 (14.1)
異常な夢	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
アルコールによる宿酔	3 (1.7)	1 (0.7)	1 (1.1)	2 (0.9)	5 (1.2)
アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.6)	1 (0.7)	1 (1.1)	2 (0.9)	3 (0.7)
抑うつ気分	2 (1.2)	0 (0.0)	1 (1.1)	1 (0.4)	3 (0.7)
不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多幸気分	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
幻聴	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不眠症	13 (7.6)	2 (1.5)	6 (6.4)	8 (3.5)	21 (5.2)
易刺激性	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
リビドー減退	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
中期不眠症	5 (2.9)	2 (1.5)	2 (2.1)	4 (1.7)	9 (2.2)
悪夢	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
落ち着きのなさ	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
精神障害					
睡眠障害	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.4)	6 (1.5)
緊張	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
無為	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
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)
抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
早朝覚醒型不眠症	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.4)	6 (1.5)
腎および尿路障害	0 (0.0)	2 (1.5)	1 (1.1)	3 (1.3)	3 (0.7)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
尿管結石症	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
生殖系および乳房障害	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
月経困難症	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
自発陰茎勃起	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	4 (2.3)	6 (4.4)	2 (2.1)	8 (3.5)	12 (3.0)
咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過換気	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
鼻の炎症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
鼻漏	0 (0.0)	1 (0.7)	1 (1.1)	2 (0.9)	2 (0.5)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.6)	3 (2.2)	1 (1.1)	4 (1.7)	5 (1.2)

表 2.7.6.5.9-30　すべての有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
皮膚および皮下組織障害	14 (8.1)	5 (3.6)	1 (1.1)	6 (2.6)	20 (5.0)
ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
冷汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚炎	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
アトピー性皮膚炎	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.4)	3 (0.7)
そう痒症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
乾癬	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
発疹	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
全身性皮疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
蕁麻疹	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
全身性そう痒症	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
血管障害	2 (1.2)	4 (2.9)	5 (5.3)	9 (3.9)	11 (2.7)
充血	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
高血圧	1 (0.6)	2 (1.5)	2 (2.1)	4 (1.7)	5 (1.2)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	1 (0.6)	1 (0.7)	3 (3.2)	4 (1.7)	5 (1.2)
製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
医療機器不具合	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

MedDRA Ver. 19.0

Total 0 例の有害事象は，本治験の SS で 339-14-001 試験のみで発現した。

＜資料番号 5.3.5.2-01：Table 14.1.1.3-27 より作成＞

表 2.7.6.5.9-31　すべての有害事象（SS）－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 adverse events	20 (11.7)	30 (17.4)
心臓障害	0 (0.0)	4 (2.3)
不整脈	0 (0.0)	1 (0.6)
左脚ブロック	0 (0.0)	1 (0.6)
右脚ブロック	0 (0.0)	1 (0.6)
心室性期外収縮	0 (0.0)	1 (0.6)
耳および迷路障害	0 (0.0)	1 (0.6)
回転性めまい	0 (0.0)	1 (0.6)
眼障害	1 (0.6)	2 (1.2)
眼精疲労	0 (0.0)	1 (0.6)
眼のアレルギー	0 (0.0)	1 (0.6)
視力低下	1 (0.6)	0 (0.0)
胃腸障害	2 (1.2)	2 (1.2)
便秘	0 (0.0)	1 (0.6)
下痢	0 (0.0)	1 (0.6)
消化不良	1 (0.6)	0 (0.0)
悪心	1 (0.6)	0 (0.0)
一般・全身障害および投与部位の状態	1 (0.6)	2 (1.2)
胸痛	0 (0.0)	1 (0.6)
異常感	1 (0.6)	0 (0.0)
宿酔	0 (0.0)	1 (0.6)
免疫系障害	1 (0.6)	0 (0.0)
季節性アレルギー	1 (0.6)	0 (0.0)
感染症および寄生虫症	2 (1.2)	8 (4.7)
結膜炎	1 (0.6)	0 (0.0)
憩室炎	0 (0.0)	1 (0.6)
鼻咽頭炎	1 (0.6)	7 (4.1)
傷害、中毒および処置合併症	2 (1.2)	1 (0.6)
節足動物刺傷	1 (0.6)	0 (0.0)
足骨折	0 (0.0)	1 (0.6)
擦過傷	1 (0.6)	0 (0.0)

表 2.7.6.5.9-31　すべての有害事象（SS）－退薬期－（続き）

Treatment group of run-out period System organ class Preferred term	Placebo (N=171) n (%)	Nalmefene 20 mg (N=172) n (%)
臨床検査	9 (5.3)	9 (5.2)
アラニンアミノトランスフェラーゼ増加	2 (1.2)	1 (0.6)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	0 (0.0)
血中重炭酸塩減少	1 (0.6)	0 (0.0)
血中コレステロール増加	0 (0.0)	1 (0.6)
血中ブドウ糖増加	1 (0.6)	0 (0.0)
血圧上昇	0 (0.0)	1 (0.6)
血中プロラクチン増加	2 (1.2)	1 (0.6)
血中トリグリセリド増加	2 (1.2)	2 (1.2)
心電図QT延長	0 (0.0)	2 (1.2)
γ－グルタミルトランスフェラーゼ増加	3 (1.8)	1 (0.6)
体重増加	1 (0.6)	0 (0.0)
血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)
代謝および栄養障害	0 (0.0)	1 (0.6)
脂質異常症	0 (0.0)	1 (0.6)
筋骨格系および結合組織障害	1 (0.6)	4 (2.3)
背部痛	0 (0.0)	1 (0.6)
関節周囲炎	1 (0.6)	1 (0.6)
筋骨格硬直	0 (0.0)	2 (1.2)
神経系障害	0 (0.0)	2 (1.2)
浮動性めまい	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)
皮膚および皮下組織障害	0 (0.0)	1 (0.6)
アトピー性皮膚炎	0 (0.0)	1 (0.6)
血管障害	0 (0.0)	1 (0.6)
高血圧	0 (0.0)	1 (0.6)

MedDRA Ver. 19.0

＜資料番号 5.3.5.2-01：Table 14.1.1.3-34 より作成＞

(4) 重症度別有害事象

表 2.7.6.5.9-32 重症度別有害事象（SS）－本治験の治療期－

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with adverse events	112 (65.1)	27 (15.7)	2 (1.2)	141 (82.0)	80 (58.4)	16 (11.7)	0 (0.0)	96 (70.1)	57 (60.6)	10 (10.6)	0 (0.0)	67 (71.3)	137 (59.3)	26 (11.3)	0 (0.0)	163 (70.6)	249 (61.8)	53 (13.2)	2 (0.5)	304 (75.4)
血液およびリンパ系障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
貧血	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	7 (4.1)	1 (0.6)	0 (0.0)	8 (4.7)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	8 (8.5)	0 (0.0)	0 (0.0)	8 (8.5)	9 (3.9)	0 (0.0)	0 (0.0)	9 (3.9)	16 (4.0)	1 (0.2)	0 (0.0)	17 (4.2)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
動悸	5 (2.9)	1 (0.6)	0 (0.0)	6 (3.5)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	4 (4.3)	0 (0.0)	0 (0.0)	4 (4.3)	5 (2.2)	0 (0.0)	0 (0.0)	5 (2.2)	10 (2.5)	1 (0.2)	0 (0.0)	11 (2.7)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
心室性期外収縮	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)	4 (2.9)	0 (0.0)	0 (0.0)	4 (2.9)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	5 (2.2)	0 (0.0)	0 (0.0)	5 (2.2)	9 (2.2)	0 (0.0)	0 (0.0)	9 (2.2)
一過性難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳管開放	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
聴覚過敏	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
回転性めまい	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
内分泌障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
高プロラクチン血症	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
眼障害	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	6 (4.4)	0 (0.0)	0 (0.0)	6 (4.4)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	8 (3.5)	0 (0.0)	0 (0.0)	8 (3.5)	8 (2.0)	1 (0.2)	0 (0.0)	9 (2.2)
眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
結膜出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
上強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼部腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
角膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
眼充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
角膜障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃腸障害	59 (34.3)	8 (4.7)	0 (0.0)	67 (39.0)	37 (27.0)	5 (3.6)	0 (0.0)	42 (30.7)	37 (39.4)	2 (2.1)	0 (0.0)	39 (41.5)	74 (32.0)	7 (3.0)	0 (0.0)	81 (35.1)	133 (33.0)	15 (3.7)	0 (0.0)	148 (36.7)
腹部不快感	7 (4.1)	2 (1.2)	0 (0.0)	9 (5.2)	9 (6.6)	0 (0.0)	0 (0.0)	9 (6.6)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	14 (6.1)	0 (0.0)	0 (0.0)	14 (6.1)	21 (5.2)	2 (0.5)	0 (0.0)	23 (5.7)
腹部膨満	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)	2 (1.5)	1 (0.7)	0 (0.0)	3 (2.2)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	1 (0.4)	0 (0.0)	4 (1.7)	7 (1.7)	1 (0.2)	0 (0.0)	8 (2.0)
腹痛	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.5)	1 (0.7)	0 (0.0)	3 (2.2)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	4 (1.7)	1 (0.4)	0 (0.0)	5 (2.2)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.5)
慢性胃炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
便秘	8 (4.7)	0 (0.0)	0 (0.0)	8 (4.7)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	7 (3.0)	0 (0.0)	0 (0.0)	7 (3.0)	15 (3.7)	0 (0.0)	0 (0.0)	15 (3.7)
齲歯	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害																				
下痢	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	5 (3.6)	1 (0.7)	0 (0.0)	6 (4.4)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	5 (2.2)	2 (0.9)	0 (0.0)	7 (3.0)	7 (1.7)	2 (0.5)	0 (0.0)	9 (2.2)
口内乾燥	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
消化不良	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硬便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
食中毒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃ポリープ	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃潰瘍	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃食道逆流性疾患	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	38 (22.1)	3 (1.7)	0 (0.0)	41 (23.8)	19 (13.9)	2 (1.5)	0 (0.0)	21 (15.3)	15 (16.0)	2 (2.1)	0 (0.0)	17 (18.1)	34 (14.7)	4 (1.7)	0 (0.0)	38 (16.5)	72 (17.9)	7 (1.7)	0 (0.0)	79 (19.6)
口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口内炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
嘔吐	11 (6.4)	3 (1.7)	0 (0.0)	14 (8.1)	5 (3.6)	1 (0.7)	0 (0.0)	6 (4.4)	3 (3.2)	2 (2.1)	0 (0.0)	5 (5.3)	8 (3.5)	3 (1.3)	0 (0.0)	11 (4.8)	19 (4.7)	6 (1.5)	0 (0.0)	25 (6.2)
口腔知覚不全	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
大腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔粘膜血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟便	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	28 (16.3)	5 (2.9)	0 (0.0)	33 (19.2)	10 (7.3)	2 (1.5)	0 (0.0)	12 (8.8)	12 (12.8)	0 (0.0)	0 (0.0)	12 (12.8)	22 (9.5)	2 (0.9)	0 (0.0)	24 (10.4)	50 (12.4)	7 (1.7)	0 (0.0)	57 (14.1)
無力症	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
悪寒	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
不快感	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
疲労	2 (1.2)	1 (0.6)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	5 (1.2)	1 (0.2)	0 (0.0)	6 (1.5)
異常感	6 (3.5)	0 (0.0)	0 (0.0)	6 (3.5)	3 (2.2)	0 (0.0)	0 (0.0)	3 (2.2)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	10 (2.5)	0 (0.0)	0 (0.0)	10 (2.5)
熱感	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
宿酔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位疼痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	13 (7.6)	2 (1.2)	0 (0.0)	15 (8.7)	5 (3.6)	2 (1.5)	0 (0.0)	7 (5.1)	4 (4.3)	0 (0.0)	0 (0.0)	4 (4.3)	9 (3.9)	2 (0.9)	0 (0.0)	11 (4.8)	22 (5.5)	4 (1.0)	0 (0.0)	26 (6.5)
発熱	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	1 (0.2)	0 (0.0)	4 (1.0)
口渇	6 (3.5)	0 (0.0)	0 (0.0)	6 (3.5)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ワクチン接種部位腫脹	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肝胆道系障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
脂肪肝	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
免疫系障害	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
感染症および寄生虫症	36 (20.9)	5 (2.9)	0 (0.0)	41 (23.8)	29 (21.2)	0 (0.0)	0 (0.0)	29 (21.2)	17 (18.1)	4 (4.3)	0 (0.0)	21 (22.3)	46 (19.9)	4 (1.7)	0 (0.0)	50 (21.6)	82 (20.3)	9 (2.2)	0 (0.0)	91 (22.6)
口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アニサキス症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
気管支炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
結膜炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膀胱炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
蓄膿	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	2 (1.2)	1 (0.6)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	2 (0.5)	2 (0.5)	0 (0.0)	4 (1.0)
ウイルス性胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
膿痂疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	2 (1.2)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	3 (0.7)	0 (0.0)	3 (0.7)
鼻咽頭炎	30 (17.4)	1 (0.6)	0 (0.0)	31 (18.0)	23 (16.8)	0 (0.0)	0 (0.0)	23 (16.8)	15 (16.0)	1 (1.1)	0 (0.0)	16 (17.0)	38 (16.5)	1 (0.4)	0 (0.0)	39 (16.9)	68 (16.9)	2 (0.5)	0 (0.0)	70 (17.4)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
唾液腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染症および寄生虫症																				
副鼻腔炎	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ウイルス性下痢	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
歯肉膿瘍	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ヘリコバクター感染	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
感染性腸炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
ヘルペス性皮膚炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口腔ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
ノロウイルス性胃腸炎	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	2 (0.5)	0 (0.0)	2 (0.5)
傷害、中毒および処置合併症	6 (3.5)	2 (1.2)	0 (0.0)	8 (4.7)	7 (5.1)	3 (2.2)	0 (0.0)	10 (7.3)	0 (0.0)	2 (2.1)	0 (0.0)	2 (2.1)	7 (3.0)	5 (2.2)	0 (0.0)	12 (5.2)	13 (3.2)	7 (1.7)	0 (0.0)	20 (5.0)
偶発的過量投与	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アルコール中毒	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
凍瘡	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
転倒	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腓骨骨折	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
凍傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
手骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
熱射病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節脱臼	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靭帯捻挫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
肋骨骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
傷害、中毒および処置合併症																				
交通事故	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
外傷性血腫	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
挫傷	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
創傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靭帯損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
胸部損傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳擦過傷	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚擦過傷	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
剥離骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
熱中症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	10 (5.8)	1 (0.6)	1 (0.6)	12 (7.0)	12 (8.8)	1 (0.7)	0 (0.0)	13 (9.5)	7 (7.4)	0 (0.0)	0 (0.0)	7 (7.4)	19 (8.2)	1 (0.4)	0 (0.0)	20 (8.7)	29 (7.2)	2 (0.5)	1 (0.2)	32 (7.9)
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)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中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)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
血圧上昇	1 (0.6)	1 (0.6)	1 (0.6)	3 (1.7)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	1 (0.2)	1 (0.2)	5 (1.2)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査																				
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿酸増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
C－反応性蛋白増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
尿中ブドウ糖	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
尿中血陽性	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
心拍数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
脂質異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
体重増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査																				
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
便潜血陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
代謝および栄養障害	11 (6.4)	2 (1.2)	0 (0.0)	13 (7.6)	10 (7.3)	1 (0.7)	0 (0.0)	11 (8.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	10 (4.3)	1 (0.4)	0 (0.0)	11 (4.8)	21 (5.2)	3 (0.7)	0 (0.0)	24 (6.0)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
痛風	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
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)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高尿酸血症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	9 (5.2)	2 (1.2)	0 (0.0)	11 (6.4)	4 (2.9)	0 (0.0)	0 (0.0)	4 (2.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	13 (3.2)	2 (0.5)	0 (0.0)	15 (3.7)
高脂血症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
筋骨格系および結合組織障害	18 (10.5)	1 (0.6)	0 (0.0)	19 (11.0)	13 (9.5)	2 (1.5)	0 (0.0)	15 (10.9)	8 (8.5)	1 (1.1)	0 (0.0)	9 (9.6)	21 (9.1)	3 (1.3)	0 (0.0)	24 (10.4)	39 (9.7)	4 (1.0)	0 (0.0)	43 (10.7)
関節痛	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
関節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	7 (4.1)	0 (0.0)	0 (0.0)	7 (4.1)	7 (5.1)	1 (0.7)	0 (0.0)	8 (5.8)	3 (3.2)	1 (1.1)	0 (0.0)	4 (4.3)	10 (4.3)	2 (0.9)	0 (0.0)	12 (5.2)	17 (4.2)	2 (0.5)	0 (0.0)	19 (4.7)
筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋攣縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格痛	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
筋骨格系および結合組織障害																				
筋肉痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
頚部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨端症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
骨壊死	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
骨粗鬆症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
四肢痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
変形性脊椎症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
弾発指	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
椎間板突出	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
筋骨格硬直	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
指変形	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
靭帯炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物(嚢胞およびポリープを含む)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
皮膚乳頭腫	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
前立腺癌	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
神経系障害	50 (29.1)	9 (5.2)	1 (0.6)	60 (34.9)	30 (21.9)	2 (1.5)	0 (0.0)	32 (23.4)	19 (20.2)	0 (0.0)	0 (0.0)	19 (20.2)	49 (21.2)	2 (0.9)	0 (0.0)	51 (22.1)	99 (24.6)	11 (2.7)	1 (0.2)	111 (27.5)
アカシジア	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
健忘	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
自律神経失調	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
浮動性めまい	19 (11.0)	7 (4.1)	1 (0.6)	27 (15.7)	7 (5.1)	1 (0.7)	0 (0.0)	8 (5.8)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	12 (5.2)	1 (0.4)	0 (0.0)	13 (5.6)	31 (7.7)	8 (2.0)	1 (0.2)	40 (9.9)
体位性めまい	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	6 (3.5)	1 (0.6)	0 (0.0)	7 (4.1)	7 (5.1)	0 (0.0)	0 (0.0)	7 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (3.0)	0 (0.0)	0 (0.0)	7 (3.0)	13 (3.2)	1 (0.2)	0 (0.0)	14 (3.5)
ジスキネジア	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
頭部不快感	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
頭痛	12 (7.0)	1 (0.6)	0 (0.0)	13 (7.6)	8 (5.8)	0 (0.0)	0 (0.0)	8 (5.8)	8 (8.5)	0 (0.0)	0 (0.0)	8 (8.5)	16 (6.9)	0 (0.0)	0 (0.0)	16 (6.9)	28 (6.9)	1 (0.2)	0 (0.0)	29 (7.2)
知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
単麻痺	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
麻痺	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
坐骨神経痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	12 (7.0)	0 (0.0)	0 (0.0)	12 (7.0)	8 (5.8)	1 (0.7)	0 (0.0)	9 (6.6)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	13 (5.6)	1 (0.4)	0 (0.0)	14 (6.1)	25 (6.2)	1 (0.2)	0 (0.0)	26 (6.5)
嗅覚減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肘部管症候群	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
睡眠の質低下	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
精神障害	33 (19.2)	4 (2.3)	0 (0.0)	37 (21.5)	9 (6.6)	1 (0.7)	0 (0.0)	10 (7.3)	9 (9.6)	1 (1.1)	0 (0.0)	10 (10.6)	18 (7.8)	2 (0.9)	0 (0.0)	20 (8.7)	51 (12.7)	6 (1.5)	0 (0.0)	57 (14.1)
異常な夢	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
アルコールによる宿酔	2 (1.2)	1 (0.6)	0 (0.0)	3 (1.7)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	1 (0.2)	0 (0.0)	5 (1.2)
アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
抑うつ気分	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多幸気分	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
幻聴	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不眠症	11 (6.4)	2 (1.2)	0 (0.0)	13 (7.6)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	5 (5.3)	1 (1.1)	0 (0.0)	6 (6.4)	7 (3.0)	1 (0.4)	0 (0.0)	8 (3.5)	18 (4.5)	3 (0.7)	0 (0.0)	21 (5.2)
易刺激性	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
リビドー減退	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
中期不眠症	3 (1.7)	2 (1.2)	0 (0.0)	5 (2.9)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	7 (1.7)	2 (0.5)	0 (0.0)	9 (2.2)
悪夢	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
落ち着きのなさ	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
睡眠障害	5 (2.9)	0 (0.0)	0 (0.0)	5 (2.9)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	6 (1.5)	0 (0.0)	0 (0.0)	6 (1.5)
緊張	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感情不安定	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
早朝覚醒型不眠症	5 (2.9)	0 (0.0)	0 (0.0)	5 (2.9)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	6 (1.5)	0 (0.0)	0 (0.0)	6 (1.5)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
尿路結石	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
尿管結石症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
生殖系および乳房障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.4)	0 (0.0)	2 (0.9)	3 (0.7)	1 (0.2)	0 (0.0)	4 (1.0)
月経困難症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不正子宮出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
自発陰茎勃起	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)	6 (4.4)	0 (0.0)	0 (0.0)	6 (4.4)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	8 (3.5)	0 (0.0)	0 (0.0)	8 (3.5)	12 (3.0)	0 (0.0)	0 (0.0)	12 (3.0)
咳嗽	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過換気	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
喉頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻の炎症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
気胸	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
呼吸器、胸郭および縦隔障害																				
鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	3 (2.2)	0 (0.0)	0 (0.0)	3 (2.2)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
皮膚および皮下組織障害	11 (6.4)	3 (1.7)	0 (0.0)	14 (8.1)	4 (2.9)	1 (0.7)	0 (0.0)	5 (3.6)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	5 (2.2)	1 (0.4)	0 (0.0)	6 (2.6)	16 (4.0)	4 (1.0)	0 (0.0)	20 (5.0)
ざ瘡	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管浮腫	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
冷汗	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
薬疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
紅斑	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
過角化	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
そう痒症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
乾癬	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
発疹	2 (1.2)	1 (0.6)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
全身性皮疹	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-32　重症度別有害事象（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
皮膚および皮下組織障害																				
脂漏性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
蕁麻疹	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
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)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	4 (2.9)	0 (0.0)	0 (0.0)	4 (2.9)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	9 (3.9)	0 (0.0)	0 (0.0)	9 (3.9)	11 (2.7)	0 (0.0)	0 (0.0)	11 (2.7)
充血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
高血圧	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)
製品の問題	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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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For an event occurring more than once in the same subject, the event with higher severity was used for tabulation.

Total 0 例の有害事象は，本治験の SS で 339-14-001 試験のみで発現した。

＜資料番号 5.3.5.2-01：Table 14.1.1.3-29 より作成＞

表 2.7.6.5.9-33　重症度別有害事象（SS）－退薬期－

Treatment group of run-out period	Placebo (N=171)				Nalmefene 20 mg (N=172)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with adverse events	18 (10.5)	1 (0.6)	1 (0.6)	20 (11.7)	28 (16.3)	2 (1.2)	0 (0.0)	30 (17.4)
心臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
心室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
耳および迷路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
回転性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
眼障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
眼精疲労	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
眼のアレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
視力低下	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
便秘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
下痢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
消化不良	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
胸痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
異常感	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
宿酔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)

表 2.7.6.5.9-33　重症度別有害事象（SS）－退薬期－（続き）

Treatment group of run-out period	Placebo (N=171)				Nalmefene 20 mg (N=172)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
免疫系障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	7 (4.1)	1 (0.6)	0 (0.0)	8 (4.7)
結膜炎	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)
鼻咽頭炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	7 (4.1)	0 (0.0)	0 (0.0)	7 (4.1)
傷害、中毒および処置合併症	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
節足動物刺傷	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
擦過傷	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	9 (5.3)	0 (0.0)	0 (0.0)	9 (5.3)	9 (5.2)	0 (0.0)	0 (0.0)	9 (5.2)
アラニンアミノトランスフェラーゼ増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	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	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中重炭酸塩減少	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血中ブドウ糖増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血中プロラクチン増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血中トリグリセリド増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
γ－グルタミルトランスフェラーゼ増加	3 (1.8)	0 (0.0)	0 (0.0)	3 (1.8)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
体重増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-33　重症度別有害事象（SS）－退薬期－（続き）

Treatment group of run-out period	Placebo (N=171)				Nalmefene 20 mg (N=172)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
代謝および栄養障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
脂質異常症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
筋骨格系および結合組織障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)
背部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
関節周囲炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
神経系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)
浮動性めまい	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血栓性脳梗塞	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)
呼吸器、胸郭および縦隔障害	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
器質化肺炎	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
アトピー性皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
高血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)

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For an event occurring more than once in the same subject, the event with higher severity was used for tabulation.

＜資料番号 5.3.5.2-01：Table 14.1.1.3-36 より作成＞

(5) 副作用

表 2.7.6.5.9-34　すべての副作用（SS）－本治験の治療期－

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	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 drug-related adverse events	109 (63.4)	59 (43.1)	43 (45.7)	102 (44.2)	211 (52.4)
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)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	7 (4.1)	1 (0.7)	4 (4.3)	5 (2.2)	12 (3.0)
右脚ブロック	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
動悸	5 (2.9)	1 (0.7)	2 (2.1)	3 (1.3)	8 (2.0)
頻脈	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
心室性期外収縮	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害	3 (1.7)	2 (1.5)	1 (1.1)	3 (1.3)	6 (1.5)
一過性難聴	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
聴覚過敏	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
回転性めまい	2 (1.2)	0 (0.0)	1 (1.1)	1 (0.4)	3 (0.7)
内分泌障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
高プロラクチン血症	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
眼障害	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
胃腸障害	59 (34.3)	35 (25.5)	26 (27.7)	61 (26.4)	120 (29.8)
腹部不快感	9 (5.2)	8 (5.8)	4 (4.3)	12 (5.2)	21 (5.2)
腹部膨満	2 (1.2)	2 (1.5)	1 (1.1)	3 (1.3)	5 (1.2)
腹痛	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	0 (0.0)	2 (1.5)	1 (1.1)	3 (1.3)	3 (0.7)
便秘	5 (2.9)	1 (0.7)	3 (3.2)	4 (1.7)	9 (2.2)
下痢	0 (0.0)	2 (1.5)	0 (0.0)	2 (0.9)	2 (0.5)
口内乾燥	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
消化不良	2 (1.2)	0 (0.0)	1 (1.1)	1 (0.4)	3 (0.7)
硬便	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
胃炎	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
悪心	41 (23.8)	19 (13.9)	15 (16.0)	34 (14.7)	75 (18.6)
口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涎過多	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
嘔吐	12 (7.0)	4 (2.9)	2 (2.1)	6 (2.6)	18 (4.5)
口腔知覚不全	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
大腸ポリープ	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-34　すべての副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害					
胃腸音異常	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
軟便	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
一般・全身障害および投与部位の状態	27 (15.7)	8 (5.8)	6 (6.4)	14 (6.1)	41 (10.2)
無力症	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪寒	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
不快感	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
疲労	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
異常感	4 (2.3)	3 (2.2)	1 (1.1)	4 (1.7)	8 (2.0)
熱感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
宿酔	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
倦怠感	12 (7.0)	3 (2.2)	3 (3.2)	6 (2.6)	18 (4.5)
発熱	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口渇	6 (3.5)	1 (0.7)	0 (0.0)	1 (0.4)	7 (1.7)
末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
肝胆道系障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝機能異常	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
食道カンジダ症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	8 (4.7)	7 (5.1)	3 (3.2)	10 (4.3)	18 (4.5)
アラニン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)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
血中ビリルビン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	3 (1.7)	2 (1.5)	0 (0.0)	2 (0.9)	5 (1.2)
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)
血中プロラクチン増加	0 (0.0)	2 (1.5)	1 (1.1)	3 (1.3)	3 (0.7)
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)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-34　すべての副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	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					
γ－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)
尿中ブドウ糖陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中血陽性	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
肝機能検査異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
体重増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
尿中ケトン体陽性	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
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)
肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	12 (7.0)	3 (2.2)	0 (0.0)	3 (1.3)	15 (3.7)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	11 (6.4)	3 (2.2)	0 (0.0)	3 (1.3)	14 (3.5)
高脂血症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
筋骨格系および結合組織障害	5 (2.9)	3 (2.2)	0 (0.0)	3 (1.3)	8 (2.0)
関節痛	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
背部痛	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.4)	2 (0.5)
筋固縮	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
筋緊張	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
神経系障害	56 (32.6)	28 (20.4)	13 (13.8)	41 (17.7)	97 (24.1)
アカシジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
注意力障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
浮動性めまい	25 (14.5)	7 (5.1)	4 (4.3)	11 (4.8)	36 (8.9)
体位性めまい	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	7 (4.1)	7 (5.1)	0 (0.0)	7 (3.0)	14 (3.5)
ジスキネジア	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
頭部不快感	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
頭痛	11 (6.4)	8 (5.8)	5 (5.3)	13 (5.6)	24 (6.0)
知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
ミオクローヌス	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
麻痺	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-34　すべての副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
神経系障害					
傾眠	10 (5.8)	9 (6.6)	4 (4.3)	13 (5.6)	23 (5.7)
嗅覚減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠の質低下	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
精神障害	30 (17.4)	6 (4.4)	6 (6.4)	12 (5.2)	42 (10.4)
異常な夢	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
アルコールによる宿酔	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.6)	0 (0.0)	1 (1.1)	1 (0.4)	2 (0.5)
抑うつ気分	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多幸気分	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
幻聴	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
不眠症	8 (4.7)	1 (0.7)	3 (3.2)	4 (1.7)	12 (3.0)
易刺激性	2 (1.2)	1 (0.7)	1 (1.1)	2 (0.9)	4 (1.0)
リビドー減退	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
中期不眠症	5 (2.9)	2 (1.5)	2 (2.1)	4 (1.7)	9 (2.2)
悪夢	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
落ち着きのなさ	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
睡眠障害	5 (2.9)	1 (0.7)	0 (0.0)	1 (0.4)	6 (1.5)
緊張	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
無為	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早朝覚醒型不眠症	3 (1.7)	1 (0.7)	0 (0.0)	1 (0.4)	4 (1.0)
腎および尿路障害	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
生殖系および乳房障害	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
自発陰茎勃起	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	1 (0.6)	1 (0.7)	1 (1.1)	2 (0.9)	3 (0.7)
咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過換気	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
鼻閉	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
鼻漏	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-34　すべての副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo	Nalmefene 20 mg	Nalmefene 10 mg	Nalmefene Total	Total
System organ class	(N=172)	(N=137)	(N=94)	(N=231)	(N=403)
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)
皮膚および皮下組織障害	8 (4.7)	2 (1.5)	1 (1.1)	3 (1.3)	11 (2.7)
冷汗	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.4)	1 (0.2)
多汗症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
寝汗	2 (1.2)	1 (0.7)	0 (0.0)	1 (0.4)	3 (0.7)
発疹	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
全身性皮疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)
全身性そう痒症	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	1 (0.2)
血管障害	2 (1.2)	1 (0.7)	5 (5.3)	6 (2.6)	8 (2.0)
高血圧	1 (0.6)	0 (0.0)	2 (2.1)	2 (0.9)	3 (0.7)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	1 (0.6)	1 (0.7)	3 (3.2)	4 (1.7)	5 (1.2)

MedDRA Ver. 19.0

Total 0 例の副作用は，本治験の SS で 339-14-001 試験のみで発現した。

＜資料番号 5.3.5.2-01：Table 14.1.1.3-28 より作成＞

表 2.7.6.5.9-35　すべての副作用（SS）－退薬期－

Treatment group of run-out period System organ class Preferred term	Placebo (N=171) n (%)	Nalmefene 20 mg (N=172) n (%)
Total number of subjects with drug-related adverse events	9 (5.3)	10 (5.8)
心臓障害	0 (0.0)	1 (0.6)
不整脈	0 (0.0)	1 (0.6)
胃腸障害	1 (0.6)	1 (0.6)
便秘	0 (0.0)	1 (0.6)
悪心	1 (0.6)	0 (0.0)
一般・全身障害および投与部位の状態	1 (0.6)	0 (0.0)
異常感	1 (0.6)	0 (0.0)
臨床検査	6 (3.5)	7 (4.1)
アラニンアミノトランスフェラーゼ増加	2 (1.2)	1 (0.6)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	0 (0.0)
血中コレステロール増加	0 (0.0)	1 (0.6)
血圧上昇	0 (0.0)	1 (0.6)
血中プロラクチン増加	2 (1.2)	1 (0.6)
血中トリグリセリド増加	2 (1.2)	1 (0.6)
心電図QT延長	0 (0.0)	2 (1.2)
γ－グルタミルトランスフェラーゼ増加	3 (1.8)	0 (0.0)
血中アルカリホスファターゼ増加	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)
血管障害	0 (0.0)	1 (0.6)
高血圧	0 (0.0)	1 (0.6)

MedDRA Ver. 19.0

＜資料番号 5.3.5.2-01：Table 14.1.1.3-35 より作成＞

(6) 重症度別副作用

表 2.7.6.5.9-36 重症度別副作用（SS）－本治験の治療期－

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with drug-related adverse events	88 (51.2)	19 (11.0)	2 (1.2)	109 (63.4)	51 (37.2)	8 (5.8)	0 (0.0)	59 (43.1)	42 (44.7)	1 (1.1)	0 (0.0)	43 (45.7)	93 (40.3)	9 (3.9)	0 (0.0)	102 (44.2)	181 (44.9)	28 (6.9)	2 (0.5)	211 (52.4)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	6 (3.5)	1 (0.6)	0 (0.0)	7 (4.1)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	4 (4.3)	0 (0.0)	0 (0.0)	4 (4.3)	5 (2.2)	0 (0.0)	0 (0.0)	5 (2.2)	11 (2.7)	1 (0.2)	0 (0.0)	12 (3.0)
右脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
動悸	4 (2.3)	1 (0.6)	0 (0.0)	5 (2.9)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	7 (1.7)	1 (0.2)	0 (0.0)	8 (2.0)
頻脈	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
心室性期外収縮	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳および迷路障害	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	6 (1.5)	0 (0.0)	0 (0.0)	6 (1.5)
一過性難聴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
聴覚過敏	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
耳鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
回転性めまい	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
内分泌障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
高プロラクチン血症	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
眼障害	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
眼の異常感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
眼刺激	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸障害	52 (30.2)	7 (4.1)	0 (0.0)	59 (34.3)	31 (22.6)	4 (2.9)	0 (0.0)	35 (25.5)	25 (26.6)	1 (1.1)	0 (0.0)	26 (27.7)	56 (24.2)	5 (2.2)	0 (0.0)	61 (26.4)	108 (26.8)	12 (3.0)	0 (0.0)	120 (29.8)
腹部不快感	7 (4.1)	2 (1.2)	0 (0.0)	9 (5.2)	8 (5.8)	0 (0.0)	0 (0.0)	8 (5.8)	4 (4.3)	0 (0.0)	0 (0.0)	4 (4.3)	12 (5.2)	0 (0.0)	0 (0.0)	12 (5.2)	19 (4.7)	2 (0.5)	0 (0.0)	21 (5.2)
腹部膨満	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	1 (0.4)	0 (0.0)	3 (1.3)	4 (1.0)	1 (0.2)	0 (0.0)	5 (1.2)
腹痛	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
下腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	1 (0.4)	0 (0.0)	3 (1.3)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
便秘	5 (2.9)	0 (0.0)	0 (0.0)	5 (2.9)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	9 (2.2)	0 (0.0)	0 (0.0)	9 (2.2)
下痢	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
口内乾燥	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
消化不良	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
硬便	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
胃炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
悪心	38 (22.1)	3 (1.7)	0 (0.0)	41 (23.8)	17 (12.4)	2 (1.5)	0 (0.0)	19 (13.9)	14 (14.9)	1 (1.1)	0 (0.0)	15 (16.0)	31 (13.4)	3 (1.3)	0 (0.0)	34 (14.7)	69 (17.1)	6 (1.5)	0 (0.0)	75 (18.6)
口腔内不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
流涎過多	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
嘔吐	10 (5.8)	2 (1.2)	0 (0.0)	12 (7.0)	3 (2.2)	1 (0.7)	0 (0.0)	4 (2.9)	1 (1.1)	1 (1.1)	0 (0.0)	2 (2.1)	4 (1.7)	2 (0.9)	0 (0.0)	6 (2.6)	14 (3.5)	4 (1.0)	0 (0.0)	18 (4.5)
口腔知覚不全	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
大腸ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口の錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸音異常	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
軟便	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
一般・全身障害および投与部位の状態	22 (12.8)	5 (2.9)	0 (0.0)	27 (15.7)	6 (4.4)	2 (1.5)	0 (0.0)	8 (5.8)	6 (6.4)	0 (0.0)	0 (0.0)	6 (6.4)	12 (5.2)	2 (0.9)	0 (0.0)	14 (6.1)	34 (8.4)	7 (1.7)	0 (0.0)	41 (10.2)
無力症	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
胸部不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪寒	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
不快感	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
疲労	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
異常感	4 (2.3)	0 (0.0)	0 (0.0)	4 (2.3)	3 (2.2)	0 (0.0)	0 (0.0)	3 (2.2)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	8 (2.0)	0 (0.0)	0 (0.0)	8 (2.0)
熱感	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
宿酔	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
倦怠感	10 (5.8)	2 (1.2)	0 (0.0)	12 (7.0)	1 (0.7)	2 (1.5)	0 (0.0)	3 (2.2)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	4 (1.7)	2 (0.9)	0 (0.0)	6 (2.6)	14 (3.5)	4 (1.0)	0 (0.0)	18 (4.5)
発熱	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
口渇	6 (3.5)	0 (0.0)	0 (0.0)	6 (3.5)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
末梢腫脹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肝胆道系障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
肝機能異常	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
免疫系障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
口角口唇炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
歯肉炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
臨床検査	6 (3.5)	1 (0.6)	1 (0.6)	8 (4.7)	7 (5.1)	0 (0.0)	0 (0.0)	7 (5.1)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	10 (4.3)	0 (0.0)	0 (0.0)	10 (4.3)	16 (4.0)	1 (0.2)	1 (0.2)	18 (4.5)
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)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	1 (0.6)	1 (0.6)	1 (0.6)	3 (1.7)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	1 (0.2)	1 (0.2)	5 (1.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中プロラクチン増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
γ－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)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中血陽性	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
赤血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
体重増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
白血球数減少	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査値上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
代謝および栄養障害	10 (5.8)	2 (1.2)	0 (0.0)	12 (7.0)	3 (2.2)	0 (0.0)	0 (0.0)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	13 (3.2)	2 (0.5)	0 (0.0)	15 (3.7)
食欲亢進	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	9 (5.2)	2 (1.2)	0 (0.0)	11 (6.4)	3 (2.2)	0 (0.0)	0 (0.0)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	12 (3.0)	2 (0.5)	0 (0.0)	14 (3.5)
高脂血症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋骨格系および結合組織障害	5 (2.9)	0 (0.0)	0 (0.0)	5 (2.9)	3 (2.2)	0 (0.0)	0 (0.0)	3 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	8 (2.0)	0 (0.0)	0 (0.0)	8 (2.0)
関節痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
背部痛	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
筋固縮	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
筋緊張	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
筋骨格硬直	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格不快感	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
神経系障害	46 (26.7)	9 (5.2)	1 (0.6)	56 (32.6)	26 (19.0)	2 (1.5)	0 (0.0)	28 (20.4)	13 (13.8)	0 (0.0)	0 (0.0)	13 (13.8)	39 (16.9)	2 (0.9)	0 (0.0)	41 (17.7)	85 (21.1)	11 (2.7)	1 (0.2)	97 (24.1)
アカシジア	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
注意力障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
浮動性めまい	17 (9.9)	7 (4.1)	1 (0.6)	25 (14.5)	6 (4.4)	1 (0.7)	0 (0.0)	7 (5.1)	4 (4.3)	0 (0.0)	0 (0.0)	4 (4.3)	10 (4.3)	1 (0.4)	0 (0.0)	11 (4.8)	27 (6.7)	8 (2.0)	1 (0.2)	36 (8.9)
体位性めまい	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
異常感覚	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚異常	6 (3.5)	1 (0.6)	0 (0.0)	7 (4.1)	7 (5.1)	0 (0.0)	0 (0.0)	7 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (3.0)	0 (0.0)	0 (0.0)	7 (3.0)	13 (3.2)	1 (0.2)	0 (0.0)	14 (3.5)
ジスキネジア	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
頭部不快感	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
頭痛	10 (5.8)	1 (0.6)	0 (0.0)	11 (6.4)	8 (5.8)	0 (0.0)	0 (0.0)	8 (5.8)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	13 (5.6)	0 (0.0)	0 (0.0)	13 (5.6)	23 (5.7)	1 (0.2)	0 (0.0)	24 (6.0)
知覚過敏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
記憶障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
神経系障害																				
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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
麻痺	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
鎮静	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	10 (5.8)	0 (0.0)	0 (0.0)	10 (5.8)	8 (5.8)	1 (0.7)	0 (0.0)	9 (6.6)	4 (4.3)	0 (0.0)	0 (0.0)	4 (4.3)	12 (5.2)	1 (0.4)	0 (0.0)	13 (5.6)	22 (5.5)	1 (0.2)	0 (0.0)	23 (5.7)
嗅覚減退	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠の質低下	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
精神障害	26 (15.1)	4 (2.3)	0 (0.0)	30 (17.4)	6 (4.4)	0 (0.0)	0 (0.0)	6 (4.4)	6 (6.4)	0 (0.0)	0 (0.0)	6 (6.4)	12 (5.2)	0 (0.0)	0 (0.0)	12 (5.2)	38 (9.4)	4 (1.0)	0 (0.0)	42 (10.4)
異常な夢	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
アルコールによる宿酔	2 (1.2)	1 (0.6)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	1 (0.2)	0 (0.0)	3 (0.7)
アルコール症	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不安	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
抑うつ気分	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
不快気分	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多幸気分	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
幻聴	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
不眠症	6 (3.5)	2 (1.2)	0 (0.0)	8 (4.7)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	10 (2.5)	2 (0.5)	0 (0.0)	12 (3.0)
易刺激性	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
リビドー減退	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
中期不眠症	3 (1.7)	2 (1.2)	0 (0.0)	5 (2.9)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	7 (1.7)	2 (0.5)	0 (0.0)	9 (2.2)
悪夢	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
落ち着きのなさ	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
睡眠障害	5 (2.9)	0 (0.0)	0 (0.0)	5 (2.9)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	6 (1.5)	0 (0.0)	0 (0.0)	6 (1.5)
緊張	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
無為	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
精神障害																				
抑うつ症状	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早朝覚醒型不眠症	3 (1.7)	0 (0.0)	0 (0.0)	3 (1.7)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	4 (1.0)	0 (0.0)	0 (0.0)	4 (1.0)
腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
排尿困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
生殖系および乳房障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
勃起増強	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
自発陰茎勃起	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
勃起不全	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
咽喉乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過換気	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻閉	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
鼻漏	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
喘鳴	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭不快感	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

表 2.7.6.5.9-36　重症度別副作用（SS）－本治験の治療期－（続き）

Treatment group of study 339-14-001	Placebo				Nalmefene 20 mg				Nalmefene 10 mg				Nalmefene Total				Total			
	(N=172)				(N=137)				(N=94)				(N=231)				(N=403)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
皮膚および皮下組織障害	6 (3.5)	2 (1.2)	0 (0.0)	8 (4.7)	2 (1.5)	0 (0.0)	0 (0.0)	2 (1.5)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	3 (1.3)	0 (0.0)	0 (0.0)	3 (1.3)	9 (2.2)	2 (0.5)	0 (0.0)	11 (2.7)
冷汗	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
皮膚炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
多汗症	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
寝汗	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
発疹	1 (0.6)	1 (0.6)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	2 (0.5)
全身性皮疹	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	1 (0.2)
丘疹性皮疹	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
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)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (0.2)
血管障害	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	5 (5.3)	0 (0.0)	0 (0.0)	5 (5.3)	6 (2.6)	0 (0.0)	0 (0.0)	6 (2.6)	8 (2.0)	0 (0.0)	0 (0.0)	8 (2.0)
高血圧	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.1)	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.9)	3 (0.7)	0 (0.0)	0 (0.0)	3 (0.7)
低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.7)	3 (3.2)	0 (0.0)	0 (0.0)	3 (3.2)	4 (1.7)	0 (0.0)	0 (0.0)	4 (1.7)	5 (1.2)	0 (0.0)	0 (0.0)	5 (1.2)

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For an event occurring more than once in the same subject, the event with higher severity was used for tabulation.

Total 0 例の副作用は，本治験の SS で 339-14-001 試験のみで発現した。

＜資料番号 5.3.5.2-01：Table 14.1.1.3-30 より作成＞

表 2.7.6.5.9-37　重症度別副作用（SS）－退薬期－

Treatment group of run-out period	Placebo (N=171)				Nalmefene 20 mg (N=172)			
System organ class	Mild	Moderate	Severe	Total	Mild	Moderate	Severe	Total
Preferred term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total number of subjects with drug-related adverse events	8 (4.7)	0 (0.0)	1 (0.6)	9 (5.3)	10 (5.8)	0 (0.0)	0 (0.0)	10 (5.8)
心臓障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
不整脈	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
胃腸障害	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
便秘	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
悪心	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	6 (3.5)	0 (0.0)	0 (0.0)	6 (3.5)	7 (4.1)	0 (0.0)	0 (0.0)	7 (4.1)
アラニンアミノトランスフェラーゼ増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	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	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血圧上昇	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血中プロラクチン増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
血中トリグリセリド増加	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	2 (1.2)
γ－グルタミルトランスフェラーゼ増加	3 (1.8)	0 (0.0)	0 (0.0)	3 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
器質化肺炎	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
高血圧	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)

MedDRA Ver. 19.0

For an event occurring more than once in the same subject, the event with higher severity was used for tabulation.

＜資料番号 5.3.5.2-01：Table 14.1.1.3-37 より作成＞

(7) 重篤な有害事象一覧表

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）

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]	20[redacted] 20[redacted] 20[redacted] 366, 190	20[redacted] 20[redacted] 20[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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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]	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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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

表 2.7.6.5.9-38　死亡以外の重篤な有害事象一覧表（SS）（続き）

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 10 mg, N20: Nalmefene 20 mg, P: Placebo.

＜資料番号 5.3.5.2-01：Table 14.1.1.3-189＞

(8) 投与中止に至った有害事象一覧表

表 2.7.6.5.9-39 投与中止に至った有害事象一覧表（SS）

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	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 188, 15	20[redacted]	中期不眠症	TREATMENT (339-14-002) 173, 0 0 RECOVERED/RESOLVED 16	RELATED MILD	N DOSE NOT CHANGED
					全身性皮疹	TREATMENT (339-14-002) 187, 14 0 NOT RECOVERED/NOT RESOLVED 2	RELATED MODERATE	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 193, 18	20[redacted]	鼻咽頭炎	TREATMENT (339-14-001) 17, - 0 RECOVERED/RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
					挫傷	TREATMENT (339-14-001) 163, - 0 NOT RECOVERED/NOT RESOLVED 6	NOT RELATED MODERATE	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					多幸気分	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					易刺激性	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-002) 186, 11 0 RECOVERED/RESOLVED 6	NOT RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-002) 191, 16 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				悪心	TREATMENT (339-14-002) 192, 17 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 170, 1	20[redacted]	便秘	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 169, 0 0 RECOVERING/RESOLVING 5	RELATED MODERATE	N DRUG WITHDRAWN
					食欲減退	TREATMENT (339-14-002) 169, 0 0 RECOVERING/RESOLVING 5	RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 169, 0 0 RECOVERING/RESOLVING 5	RELATED MODERATE	N DRUG WITHDRAWN
					麻痺	TREATMENT (339-14-002) 169, 0 0 RECOVERING/RESOLVING 5	RELATED MODERATE	N DRUG WITHDRAWN
P-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 177, 1	20[redacted]	過角化	TREATMENT (339-14-001) 78, - 0 RECOVERING/RESOLVING 92	NOT RELATED MILD	N DOSE NOT CHANGED
					倦怠感	TREATMENT (339-14-002) 176, 0 0 RECOVERED/RESOLVED 4	RELATED MODERATE	N DRUG WITHDRAWN
					食欲減退	TREATMENT (339-14-002) 176, 0 0 RECOVERED/RESOLVED 4	RELATED MODERATE	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				冷汗	TREATMENT (339-14-002) 176, 0 0 RECOVERED/RESOLVED 1	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 199, 32	20[redacted]-[redacted]-[redacted]	口腔知覚不全	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 55	RELATED MILD	N DOSE NOT CHANGED
					口渇	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 55	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 27, - 0 RECOVERED/RESOLVED 10	NOT RELATED MILD	N DOSE NOT CHANGED
					口腔知覚不全	TREATMENT (339-14-001) 83, - 0 NOT RECOVERED/NOT RESOLVED 78	RELATED MILD	N DOSE NOT CHANGED
					口渇	TREATMENT (339-14-001) 83, - 0 NOT RECOVERED/NOT RESOLVED 78	RELATED MILD	N DOSE NOT CHANGED
					口腔知覚不全	TREATMENT (339-14-002) 167, 0 0 NOT RECOVERED/NOT RESOLVED 36	RELATED MILD	N DOSE NOT CHANGED
					口渇	TREATMENT (339-14-002) 167, 0 0 NOT RECOVERED/NOT RESOLVED 36	RELATED MILD	N DOSE NOT CHANGED
					早朝覚醒型不眠症	TREATMENT (339-14-002) 176, 9 0 NOT RECOVERED/NOT RESOLVED 27	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				体位性めまい	TREATMENT (339-14-002) 197, 30 0 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
					寝汗	TREATMENT (339-14-002) 197, 30 0 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 186, 11	20[redacted]	感情不安定	TREATMENT (339-14-001) 76, - 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					上気道の炎症	TREATMENT (339-14-001) 79, - 0 RECOVERED/RESOLVED 11	NOT RELATED MILD	N DOSE NOT CHANGED
					膿痂疹	TREATMENT (339-14-001) 82, - 0 RECOVERED/RESOLVED 7	NOT RELATED MILD	N DOSE NOT CHANGED
					胃炎	TREATMENT (339-14-001) 165, - 0 NOT RECOVERED/NOT RESOLVED 4	NOT RELATED MODERATE	N DOSE NOT CHANGED
					高プロラクチン血症	TREATMENT (339-14-001) 168, - 1 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
					頭痛	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				精神障害	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 183, 1	20[redacted]-[redacted]-[redacted]	嘔吐	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 3	RELATED MODERATE	N DRUG WITHDRAWN
					食欲減退	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 4	RELATED MODERATE	N DRUG WITHDRAWN
					浮動性めまい	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 5	RELATED MODERATE	N DRUG WITHDRAWN
					頭痛	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 2	RELATED MODERATE	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 269, 95	20[redacted]-[redacted]-[redacted]	血圧上昇	TREATMENT (339-14-001) 0, - 0 NOT RECOVERED/NOT RESOLVED 168	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 175, 1 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-002) 175, 1 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 175, 1 0 RECOVERED/RESOLVED 44	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				悪心	TREATMENT (339-14-002) 256, 82 0 RECOVERED/RESOLVED 14	RELATED MILD	N DRUG WITHDRAWN
					浮動性めまい	TREATMENT (339-14-002) 256, 82 0 RECOVERED/RESOLVED 14	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 201, 28	20[redacted]	尿中血陽性	TREATMENT (339-14-001) 164, - 1 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					異常感	TREATMENT (339-14-002) 177, 4 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 189, 16 0 RECOVERED/RESOLVED 13	RELATED MILD	N DRUG WITHDRAWN
					倦怠感	TREATMENT (339-14-002) 189, 16 0 RECOVERED/RESOLVED 13	RELATED MILD	N DRUG WITHDRAWN
P-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 196, 22	20[redacted]	アルコールによる宿酔	TREATMENT (339-14-001) 132, - 0 RECOVERED/RESOLVED 16	RELATED MILD	N DOSE NOT CHANGED
					痔核	TREATMENT (339-14-001) 168, - 0 NOT RECOVERED/NOT RESOLVED 2	NOT RELATED MODERATE	N DOSE NOT CHANGED
					悪寒	TREATMENT (339-14-002) 174, 0 0 RECOVERED/RESOLVED 22	RELATED MODERATE	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				疲労	TREATMENT (339-14-002) 174, 0 0 RECOVERED/RESOLVED 22	RELATED MODERATE	N DRUG WITHDRAWN
					浮動性めまい	TREATMENT (339-14-002) 174, 0 0 RECOVERED/RESOLVED 22	RELATED MODERATE	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 202, 32	20[redacted]	上腹部痛	TREATMENT (339-14-001) 6, - 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					下痢	TREATMENT (339-14-001) 6, - 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-001) 6, - 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					睡眠障害	TREATMENT (339-14-002) 170, 0 0 RECOVERED/RESOLVED 3	RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-002) 171, 1 1 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					倦怠感	TREATMENT (339-14-002) 171, 1 1 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					倦怠感	TREATMENT (339-14-002) 177, 7 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				悪心	TREATMENT (339-14-002) 178, 8 1 RECOVERED/RESOLVED 1	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 185, 15 1 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 195, 25 1 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					悪心	TREATMENT (339-14-002) 202, 32 1 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 184, 16	20[redacted]	動悸	TREATMENT (339-14-001) 60, - 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					頻脈	TREATMENT (339-14-001) 60, - 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					血圧上昇	TREATMENT (339-14-001) 60, - 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED
					血圧上昇	TREATMENT (339-14-002) 170, 2 0 RECOVERED/RESOLVED 19	RELATED MODERATE	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 174, 5	20[redacted]	口内炎	TREATMENT (339-14-001) 5, - 0 RECOVERED/RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				鼻咽頭炎	TREATMENT (339-14-001) 5, - 0 RECOVERED/RESOLVED 7	NOT RELATED MILD	N DOSE NOT CHANGED
					口腔咽頭不快感	TREATMENT (339-14-001) 15, - 0 RECOVERED/RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED
					頭痛	TREATMENT (339-14-001) 43, - 0 RECOVERED/RESOLVED 43	NOT RELATED MILD	N DOSE NOT CHANGED
					高血圧	TREATMENT (339-14-001) 50, - 0 RECOVERED/RESOLVED 36	NOT RELATED MILD	N DOSE NOT CHANGED
					口腔咽頭不快感	TREATMENT (339-14-001) 138, - 0 NOT RECOVERED/NOT RESOLVED 25	NOT RELATED MILD	N DOSE NOT CHANGED
					高血圧	TREATMENT (339-14-001) 142, - 0 RECOVERED/RESOLVED 4	NOT RELATED MILD	N DOSE NOT CHANGED
					関節痛	TREATMENT (339-14-001) 152, - 1 NOT RECOVERED/NOT RESOLVED 11	NOT RELATED MILD	N DOSE NOT CHANGED
					関節痛	TREATMENT (339-14-001) 160, - 0 NOT RECOVERED/NOT RESOLVED 3	NOT RELATED MILD	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 7	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				悪心	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 7	RELATED MILD	N DRUG WITHDRAWN
					食欲減退	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 7	RELATED MILD	N DRUG WITHDRAWN
					不眠症	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 7	RELATED MILD	N DRUG WITHDRAWN
P-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 186, 1	20[redacted]	胸部不快感	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 7	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 26, - 0 RECOVERED/RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
					血中トリグリセリド増加	TREATMENT (339-14-001) 83, - 0 NOT RECOVERED/NOT RESOLVED 92	RELATED MILD	N DOSE NOT CHANGED
					白血球数増加	TREATMENT (339-14-001) 83, - 0 RECOVERED/RESOLVED 92	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 108, - 1 RECOVERED/RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 143, - 3 RECOVERED/RESOLVED 29	NOT RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				動悸	TREATMENT (339-14-002) 186, 1 1 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					悪心	TREATMENT (339-14-002) 186, 1 1 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					嘔吐	TREATMENT (339-14-002) 186, 1 1 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					不眠症	TREATMENT (339-14-002) 186, 1 1 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 231, 56	20[redacted]	食欲減退	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 148	RELATED MILD	N DOSE NOT CHANGED
					不眠症	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					蕁麻疹	TREATMENT (339-14-002) 209, 34 0 RECOVERED/RESOLVED 5	RELATED MILD	N DRUG WITHDRAWN
					鼻咽頭炎	TREATMENT (339-14-002) 224, 49 0 NOT RECOVERED/NOT RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED
	[redacted]		20[redacted] 20[redacted] 20[redacted] 170, 1	20[redacted]	傾眠	TREATMENT (339-14-001) 1, - 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				結膜炎	TREATMENT (339-14-001) 136, - 0 RECOVERED/RESOLVED 10	NOT RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 156, - 0 RECOVERED/RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
					異常感	TREATMENT (339-14-002) 170, 1 1 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
					多幸気分	TREATMENT (339-14-002) 170, 1 1 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
					悪心	TREATMENT (339-14-002) 171, 2 2 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 258, 82	20[redacted]	眼の異常感	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 10	RELATED MILD	N DOSE NOT CHANGED
					ヘルペスウイルス感染	TREATMENT (339-14-001) 78, - 2 RECOVERED/RESOLVED 17	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 78, - 2 RECOVERED/RESOLVED 17	NOT RELATED MILD	N DOSE NOT CHANGED
					尿中ブドウ糖陽性	TREATMENT (339-14-001) 171, - 2 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				腹部不快感	TREATMENT (339-14-002) 176, 0 0 RECOVERED/RESOLVED 5	RELATED MILD	N DOSE NOT CHANGED
					アルコールによる宿酔	TREATMENT (339-14-002) 176, 0 0 RECOVERED/RESOLVED 5	RELATED MILD	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-002) 183, 7 0 RECOVERED/RESOLVED 6	RELATED MILD	N DOSE NOT CHANGED
					アルコールによる宿酔	TREATMENT (339-14-002) 183, 7 0 RECOVERED/RESOLVED 6	RELATED MILD	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-002) 190, 14 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-002) 196, 20 0 RECOVERED/RESOLVED 32	RELATED MODERATE	N DOSE NOT CHANGED
					アルコールによる宿酔	TREATMENT (339-14-002) 196, 20 0 RECOVERED/RESOLVED 32	RELATED MODERATE	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-002) 232, 56 0 RECOVERED/RESOLVED 27	RELATED MILD	N DRUG WITHDRAWN
					アルコールによる宿酔	TREATMENT (339-14-002) 232, 56 0 RECOVERED/RESOLVED 27	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				尿中ブドウ糖陽性	TREATMENT (339-14-002) 262, 86 5 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N NOT APPLICABLE
	[redacted]		20[redacted] 20[redacted] 20[redacted] 178, 3	20[redacted]	便秘	TREATMENT (339-14-001) 1, - 0 RECOVERED/RESOLVED 168	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 11	RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 11	RELATED MILD	N DOSE NOT CHANGED
					味覚異常	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 104	RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 175, 0 0 NOT RECOVERED/NOT RESOLVED 8	RELATED MODERATE	N DRUG WITHDRAWN
					上腹部痛	TREATMENT (339-14-002) 182, 7 5 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N NOT APPLICABLE
	[redacted]		20[redacted] 20[redacted] 20[redacted] 186, 11	20[redacted]	動悸	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 12	RELATED MILD	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 196, 28	20[redacted]	歯肉炎	TREATMENT (339-14-001) 1, - 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				頭痛	TREATMENT (339-14-001) 4, - 1 RECOVERED/RESOLVED 158	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 27, - 1 RECOVERED/RESOLVED 3	NOT RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 31	RELATED MILD	N DRUG WITHDRAWN
					睡眠障害	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 31	RELATED MILD	N DRUG WITHDRAWN
					背部痛	TREATMENT (339-14-002) 173, 5 0 RECOVERED/RESOLVED 26	NOT RELATED MILD	N DOSE NOT CHANGED
	[redacted]		20[redacted] 20[redacted] 20[redacted] 192, 10	20[redacted]	悪心	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MILD	N DRUG WITHDRAWN
					倦怠感	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MILD	N DRUG WITHDRAWN
					口渇	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MILD	N DRUG WITHDRAWN
					筋骨格不快感	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				浮動性めまい	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MODERATE	N DRUG WITHDRAWN
					勃起増強	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MILD	N DRUG WITHDRAWN
					ほてり	TREATMENT (339-14-002) 182, 0 0 RECOVERED/RESOLVED 11	RELATED MILD	N DRUG WITHDRAWN
P-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 261, 66	20[redacted]	歯周炎	TREATMENT (339-14-001) 121, - 0 RECOVERING/RESOLVING 54	NOT RELATED MILD	N DOSE NOT CHANGED
					アルコール症	TREATMENT (339-14-001) 174, - 1 NOT RECOVERED/NOT RESOLVED 1	RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 210, 15 0 RECOVERED/RESOLVED 118	RELATED MILD	N DOSE NOT CHANGED
					頭痛	TREATMENT (339-14-002) 210, 15 0 RECOVERED/RESOLVED 118	RELATED MILD	N DRUG WITHDRAWN
					悪寒	TREATMENT (339-14-002) 216, 21 0 RECOVERED/RESOLVED 49	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 260, 65 0 RECOVERED/RESOLVED 68	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]		20[redacted] 20[redacted] 20[redacted] 182, 13	20[redacted]	胃炎	TREATMENT (339-14-001) 3, - 0 RECOVERED/RESOLVED 6	RELATED MILD	N DOSE NOT CHANGED
					咽頭炎	TREATMENT (339-14-001) 3, - 0 RECOVERED/RESOLVED 6	NOT RELATED MILD	N DOSE NOT CHANGED
					偶発的過量投与	TREATMENT (339-14-001) 13, - 0 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					ミオクローヌス	TREATMENT (339-14-001) 16, - 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					皮膚炎	TREATMENT (339-14-001) 16, - 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					外傷後頚部症候群	TREATMENT (339-14-001) 154, - 0 NOT RECOVERED/NOT RESOLVED 10	NOT RELATED MILD	N DOSE NOT CHANGED
					発疹	TREATMENT (339-14-001) 154, - 0 NOT RECOVERED/NOT RESOLVED 10	NOT RELATED MILD	N DOSE NOT CHANGED
					動悸	TREATMENT (339-14-002) 170, 1 0 RECOVERED/RESOLVED 13	RELATED MODERATE	N DRUG WITHDRAWN
					熱感	TREATMENT (339-14-002) 170, 1 0 RECOVERED/RESOLVED 13	RELATED MODERATE	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 257, 83	20[redacted]	悪心	TREATMENT (339-14-001) 108, - 1 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					骨端症	TREATMENT (339-14-002) 195, 21 0 NOT RECOVERED/NOT RESOLVED 64	NOT RELATED MILD	N DRUG WITHDRAWN
					骨粗鬆症	TREATMENT (339-14-002) 215, 41 0 NOT RECOVERED/NOT RESOLVED 44	NOT RELATED MILD	N DRUG WITHDRAWN
P-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 172, 1	20[redacted]	悪心	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 3	RELATED MILD	N DOSE NOT CHANGED
					下腹部痛	TREATMENT (339-14-001) 1, - 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					四肢痛	TREATMENT (339-14-001) 153, - 1 RECOVERING/RESOLVING 12	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 171, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					筋骨格不快感	TREATMENT (339-14-002) 171, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					注意力障害	TREATMENT (339-14-002) 171, 0 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 211, 43	20[redacted]	中期不眠症	TREATMENT (339-14-001) 23, - 0 RECOVERED/RESOLVED 59	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 111, - 1 RECOVERED/RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 154, - 0 RECOVERED/RESOLVED 4	NOT RELATED MILD	N DOSE NOT CHANGED
					倦怠感	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 4	RELATED MILD	N DOSE NOT CHANGED
					発熱	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 1	RELATED MODERATE	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 4	RELATED MODERATE	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 174, 6 0 RECOVERED/RESOLVED 9	RELATED MODERATE	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 184, 16 0 RECOVERED/RESOLVED 1	RELATED MODERATE	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 196, 28 0 RECOVERED/RESOLVED 1	RELATED MODERATE	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				浮動性めまい	TREATMENT (339-14-002) 202, 34 0 RECOVERED/RESOLVED 2	RELATED MODERATE	N DOSE NOT CHANGED
					無力症	TREATMENT (339-14-002) 210, 42 0 RECOVERED/RESOLVED 4	RELATED MODERATE	N DRUG WITHDRAWN
					浮動性めまい	TREATMENT (339-14-002) 210, 42 0 RECOVERED/RESOLVED 4	RELATED MODERATE	N DRUG WITHDRAWN
P-N20	[redacted]	[redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 171, 3	20[redacted]-[redacted]-[redacted]	頭痛	TREATMENT (339-14-002) 168, 0 0 NOT RECOVERED/NOT RESOLVED 12	RELATED MILD	N DRUG WITHDRAWN
					傾眠	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 12	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 20[redacted]-[redacted]-[redacted] 184, 9	20[redacted]-[redacted]-[redacted]	傾眠	TREATMENT (339-14-001) 91, - 0 NOT RECOVERED/NOT RESOLVED 78	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 140, - 1 RECOVERED/RESOLVED 11	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 175, 0 0 NOT RECOVERED/NOT RESOLVED 14	RELATED MILD	N DRUG WITHDRAWN
					嘔吐	TREATMENT (339-14-002) 175, 0 0 RECOVERED/RESOLVED 9	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				頭痛	TREATMENT (339-14-002) 175, 0 0 NOT RECOVERED/NOT RESOLVED 14	RELATED MILD	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 273, 91	20[redacted]	鼻咽頭炎	TREATMENT (339-14-001) 20, - 0 RECOVERED/RESOLVED 7	NOT RELATED MILD	N DOSE NOT CHANGED
					副鼻腔炎	TREATMENT (339-14-001) 116, - 0 RECOVERED/RESOLVED 60	NOT RELATED MILD	N DOSE NOT CHANGED
					副鼻腔炎	TREATMENT (339-14-002) 182, 0 0 NOT RECOVERED/NOT RESOLVED 127	NOT RELATED MILD	N DOSE NOT CHANGED
					腹部膨満	TREATMENT (339-14-002) 185, 3 0 RECOVERED/RESOLVED 124	RELATED MILD	N DOSE NOT CHANGED
					傾眠	TREATMENT (339-14-002) 185, 3 0 RECOVERED/RESOLVED 124	RELATED MILD	N DRUG WITHDRAWN
					多汗症	TREATMENT (339-14-002) 185, 3 0 RECOVERED/RESOLVED 124	RELATED MILD	N DOSE NOT CHANGED
					異常感	TREATMENT (339-14-002) 197, 15 1 RECOVERED/RESOLVED 112	RELATED MILD	N DRUG WITHDRAWN
					関節痛	TREATMENT (339-14-002) 266, 84 4 NOT RECOVERED/NOT RESOLVED 43	NOT RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				関節脱臼	TREATMENT (339-14-002) 272, 90 0 RECOVERED/RESOLVED 37	NOT RELATED MILD	N DOSE NOT CHANGED
					交通事故	TREATMENT (339-14-002) 272, 90 0 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DRUG WITHDRAWN
					挫傷	TREATMENT (339-14-002) 272, 90 0 RECOVERED/RESOLVED 37	NOT RELATED MILD	N DOSE NOT CHANGED
					注意力障害	TREATMENT (339-14-002) 272, 90 0 RECOVERED/RESOLVED 37	RELATED MILD	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 169, 1	20[redacted]	ほてり	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 11	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 109, - 0 RECOVERED/RESOLVED 46	NOT RELATED MILD	N DOSE NOT CHANGED
					血中トリグリセリド増加	TREATMENT (339-14-001) 161, - 1 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					血圧上昇	TREATMENT (339-14-002) 169, 1 1 RECOVERED/RESOLVED 3	RELATED SEVERE	N DRUG WITHDRAWN
					食欲減退	TREATMENT (339-14-002) 169, 1 1 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				浮動性めまい	TREATMENT (339-14-002) 169, 1 1 RECOVERED/RESOLVED 3	RELATED MODERATE	N DRUG WITHDRAWN
					不眠症	TREATMENT (339-14-002) 169, 1 1 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 190, 21	20[redacted]	脂漏性皮膚炎	TREATMENT (339-14-001) 49, - 0 RECOVERED/RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
					インフルエンザ	TREATMENT (339-14-001) 58, - 1 RECOVERED/RESOLVED 6	NOT RELATED MODERATE	N DOSE NOT CHANGED
					胸痛	TREATMENT (339-14-001) 153, - 0 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 7	RELATED MODERATE	N DOSE NOT CHANGED
					中期不眠症	TREATMENT (339-14-002) 169, 0 0 RECOVERED/RESOLVED 7	RELATED MODERATE	N DOSE NOT CHANGED
					アカシジア	TREATMENT (339-14-002) 178, 9 0 RECOVERED/RESOLVED 3	RELATED MODERATE	N DOSE NOT CHANGED
					アカシジア	TREATMENT (339-14-002) 190, 21 1 NOT RECOVERED/NOT RESOLVED 1	RELATED MODERATE	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 169, 1	20[redacted]	浮動性めまい	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 1	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 70, - 0 RECOVERED/RESOLVED 16	NOT RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-001) 86, - 0 RECOVERED/RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					膀胱炎	TREATMENT (339-14-001) 95, - 0 RECOVERED/RESOLVED 6	NOT RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 168, 0 0 RECOVERED/RESOLVED 2	RELATED SEVERE	N DRUG WITHDRAWN
					発疹	TREATMENT (339-14-002) 175, 7 7 NOT RECOVERED/NOT RESOLVED 1	RELATED MILD	N NOT APPLICABLE
N20-N20-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 350, 176	20[redacted] 20[redacted]	靭帯捻挫	TREATMENT (339-14-002) 249, 75 0 RECOVERED/RESOLVED 22	NOT RELATED MILD	N DOSE NOT CHANGED
					アスパラギン酸アミノトランスフェラーゼ増加	TREATMENT (339-14-002) 256, 82 0 NOT RECOVERED/NOT RESOLVED 99	RELATED MILD	N DRUG WITHDRAWN

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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-N20	[redacted]				γ－グルタミルトランスフェラーゼ増加	TREATMENT (339-14-002) 256, 82 0 NOT RECOVERED/NOT RESOLVED 99	RELATED MILD	N DRUG WITHDRAWN
					アラニンアミノトランスフェラーゼ増加	RUN-OUT 343, 169 0 NOT RECOVERED/NOT RESOLVED 12	RELATED MILD	N DRUG WITHDRAWN
N20-N20	[redacted]	20[redacted] 20[redacted] 20[redacted] 317, 149		20[redacted]	筋肉痛	TREATMENT (339-14-001) 84, - 1 NOT RECOVERED/NOT RESOLVED 78	NOT RELATED MILD	N DOSE NOT CHANGED
					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
					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

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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]		20[redacted] 20[redacted] 20[redacted] 321, 146	20[redacted]	悪心	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 28	RELATED MILD	N DOSE NOT CHANGED
					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
					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
					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

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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]				挫傷	TREATMENT (339-14-002) 308, 133 0 RECOVERED/RESOLVED 17	NOT RELATED MILD	N DOSE NOT CHANGED
					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
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 173, 2	20[redacted]	体重増加	TREATMENT (339-14-001) 164, - 1 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					浮動性めまい	TREATMENT (339-14-002) 171, 0 0 RECOVERED/RESOLVED 3	RELATED MODERATE	N DRUG WITHDRAWN
					頭痛	TREATMENT (339-14-002) 171, 0 0 RECOVERED/RESOLVED 3	RELATED MILD	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 280, 98	20[redacted]	喉頭不快感	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 24	RELATED MILD	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-001) 28, - 0 RECOVERED/RESOLVED 55	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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]				高血圧	TREATMENT (339-14-001) 175, - 1 NOT RECOVERED/NOT RESOLVED 1	NOT RELATED MILD	N DOSE NOT CHANGED
					高血圧	TREATMENT (339-14-002) 266, 84 0 RECOVERED/RESOLVED 34	NOT RELATED MILD	N DOSE NOT CHANGED
					腹部不快感	TREATMENT (339-14-002) 273, 91 1 RECOVERED/RESOLVED 8	RELATED MILD	N DRUG WITHDRAWN
N20-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 180, 12	20[redacted]	倦怠感	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 141	RELATED MILD	N DOSE NOT CHANGED
					口渇	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 141	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 60	NOT RELATED MILD	N DOSE NOT CHANGED
					胃腸炎	TREATMENT (339-14-001) 62, - 7 RECOVERED/RESOLVED 9	NOT RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 126, - 2 RECOVERED/RESOLVED 17	NOT RELATED MILD	N DOSE NOT CHANGED
					倦怠感	TREATMENT (339-14-002) 171, 3 0 RECOVERED/RESOLVED 2	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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]				倦怠感	TREATMENT (339-14-002) 175, 7 0 RECOVERED/RESOLVED 7	RELATED MODERATE	N DRUG WITHDRAWN
	[redacted]		20[redacted] 20[redacted] 20[redacted] 237, 56	20[redacted]	発熱	TREATMENT (339-14-001) 11, - 1 RECOVERED/RESOLVED 5	NOT RELATED MILD	N DOSE NOT CHANGED
					紅斑	TREATMENT (339-14-001) 11, - 1 RECOVERED/RESOLVED 23	NOT RELATED MILD	N DOSE NOT CHANGED
					筋骨格痛	TREATMENT (339-14-001) 67, - 0 NOT RECOVERED/NOT RESOLVED 108	NOT RELATED MILD	N DOSE NOT CHANGED
					関節痛	TREATMENT (339-14-001) 146, - 0 NOT RECOVERED/NOT RESOLVED 29	NOT RELATED MILD	N DOSE NOT CHANGED
					全身性エリテマトーデス	TREATMENT (339-14-002) 223, 42 0 NOT RECOVERED/NOT RESOLVED 15	NOT RELATED MILD	N DRUG WITHDRAWN
N20-N20	[redacted]		20[redacted] 20[redacted] 20[redacted] 338, 170	20[redacted]	倦怠感	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 5	RELATED MILD	N DOSE NOT CHANGED
					鼻咽頭炎	TREATMENT (339-14-001) 41, - 0 RECOVERED/RESOLVED 4	NOT RELATED MILD	N DOSE NOT CHANGED
					背部痛	TREATMENT (339-14-001) 56, - 0 RECOVERED/RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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]				インフルエンザ	TREATMENT (339-14-001) 76, - 1 RECOVERED/RESOLVED 9	NOT RELATED MILD	N DOSE NOT CHANGED
					口腔ヘルペス	TREATMENT (339-14-001) 99, - 1 RECOVERED/RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED
					背部痛	TREATMENT (339-14-001) 154, - 1 RECOVERED/RESOLVED 8	NOT RELATED MILD	N DOSE NOT CHANGED
					痛風	TREATMENT (339-14-002) 177, 9 0 RECOVERED/RESOLVED 2	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 307, 139 0 NOT RECOVERED/NOT RESOLVED 32	RELATED MILD	N DRUG WITHDRAWN
					不眠症	TREATMENT (339-14-002) 307, 139 0 RECOVERED/RESOLVED 32	RELATED MILD	N DRUG WITHDRAWN
N10-N20	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 196, 20	20[redacted]	不眠症	TREATMENT (339-14-001) 0, - 0 NOT RECOVERED/NOT RESOLVED 170	RELATED MODERATE	N DOSE NOT CHANGED
					勃起増強	TREATMENT (339-14-001) 0, - 0 RECOVERED/RESOLVED 170	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-001) 1, - 1 RECOVERED/RESOLVED 1	RELATED MILD	N DOSE NOT CHANGED

表 2.7.6.5.9-39　投与中止に至った有害事象一覧表（SS）（続き）

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	[redacted]				鼻咽頭炎	TREATMENT (339-14-001) 4, - 0 RECOVERED/RESOLVED 13	NOT RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 176, 0 0 RECOVERED/RESOLVED 1	RELATED MILD	N DOSE NOT CHANGED
					嘔吐	TREATMENT (339-14-002) 178, 2 0 RECOVERED/RESOLVED 1	RELATED MILD	N DOSE NOT CHANGED
					悪心	TREATMENT (339-14-002) 192, 16 0 RECOVERED/RESOLVED 6	RELATED MODERATE	N DRUG WITHDRAWN
					嘔吐	TREATMENT (339-14-002) 194, 18 0 RECOVERED/RESOLVED 2	RELATED MODERATE	N DRUG WITHDRAWN
	[redacted]	[redacted]	20[redacted] 20[redacted] 20[redacted] 198, 27	20[redacted]	腹部不快感	TREATMENT (339-14-002) 187, 16 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					動悸	TREATMENT (339-14-002) 193, 22 0 RECOVERED/RESOLVED 2	RELATED MILD	N DRUG WITHDRAWN
					倦怠感	TREATMENT (339-14-002) 198, 27 1 RECOVERED/RESOLVED 3	RELATED MILD	N 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 10 mg, N20: Nalmefene 20 mg, P: Placebo.

＜資料番号 5.3.5.2-01：Table 14.1.1.3-191＞

(9) 依存性調査

表 2.7.6.5.9-40　依存性調査 A（SS）

	Treatment group of run-out period		Placebo (N=171)	Nalmefene 20 mg (N=172)
	Worst answer in all questions by subject	n	171	171
		Remarkable	1 (0.6)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	8 (4.7)	6 (3.5)
		None	162 (94.7)	165 (96.5)
1	Do you feel clear headed on this drug?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	2 (1.2)	0 (0.0)
		None	169 (98.8)	171 (100.0)
2	Do you feel indifferent to disliked persons or things on this drug?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	0 (0.0)
		None	170 (99.4)	171 (100.0)
3	Do you become hyperactive or talkative on this drug?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	0 (0.0)
		None	170 (99.4)	171 (100.0)
4	Do you become broad-minded on this drug?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	1 (0.6)
		None	170 (99.4)	170 (99.4)
5	Do you feel intoxicated on this drug?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	5 (2.9)	4 (2.3)
		None	166 (97.1)	167 (97.7)
6	Do you feel irritable or somewhat lonely when the drug effect runs out?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	0 (0.0)
		None	170 (99.4)	171 (100.0)
7	Do you want to continue taking this drug?	n	171	171
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	0 (0.0)
		None	170 (99.4)	171 (100.0)

表 2.7.6.5.9-40　依存性調査 A（続き）

Treatment group of run-out period		Placebo (N=171)	Nalmefene 20 mg (N=172)
8 Do you think this drug became less effective?	n	171	171
	Remarkable	1 (0.6)	0 (0.0)
	Moderate	0 (0.0)	0 (0.0)
	Slight	3 (1.8)	2 (1.2)
	None	167 (97.7)	169 (98.8)
9 Do you want to take this drug in a larger dose?	n	171	171
	Remarkable	0 (0.0)	0 (0.0)
	Moderate	0 (0.0)	0 (0.0)
	Slight	2 (1.2)	0 (0.0)
	None	169 (98.8)	171 (100.0)
10 Do you feel nauseated or tremulous when the drug effect runs out?	n	171	171
	Remarkable	0 (0.0)	0 (0.0)
	Moderate	0 (0.0)	0 (0.0)
	Slight	0 (0.0)	0 (0.0)
	None	171 (100.0)	171 (100.0)

1：この薬をのむと頭がかるくなって，回転が良くなるような感じがしますか
2：この薬をのむと嫌な人や事柄が気にならなくなりますか
3：この薬をのむと口数やからだの動きが多くなりますか
4：この薬をのむと気が大きくなりますか
5：この薬をのむと酔っぱらったようなフワフワした気分になりますか
6：この薬がきれる頃いらいらしたり，なんとなく淋しい気持になりますか
7：この薬をずっと続けてのみたいですか
8：段々，前程きかなくなったようですか
9：この薬をもっと多くのみたいですか
10：この薬がきれる頃嘔吐や手足のふるえなどがありますか
Remarkable：非常に，Moderate：かなり，Slight：少し，None：いいえ
＜資料番号 5.3.5.2-01：Table 14.1.1.3-184＞

表 2.7.6.5.9-41　依存性調査 B（SS）

	Treatment group of run-out period		Placebo (N=171)	Nalmefene 20 mg (N=171)
	Worst answer in all questions by subject	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	0 (0.0)
		None	169 (99.4)	169 (100.0)
1	Have you felt irritable or unstable after you were off this drug?	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	0 (0.0)	0 (0.0)
		None	170 (100.0)	169 (100.0)
2	Have you had more difficulty in sleeping after you were off this drug?	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	0 (0.0)	0 (0.0)
		None	170 (100.0)	169 (100.0)
3	Have you had nausea, vomiting, tremors of limb or perspiration after you were off this drug?	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	0 (0.0)	0 (0.0)
		None	170 (100.0)	169 (100.0)
4	Do you really want to take this drug again?	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	1 (0.6)	0 (0.0)
		None	169 (99.4)	169 (100.0)
5	Have you had convulsions after you were off this drug?	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	0 (0.0)	0 (0.0)
		None	170 (100.0)	169 (100.0)
6	Have you had clouded mind or heard or seen anything unusual after you were off this drug?	n	170	169
		Remarkable	0 (0.0)	0 (0.0)
		Moderate	0 (0.0)	0 (0.0)
		Slight	0 (0.0)	0 (0.0)
		None	170 (100.0)	169 (100.0)

1：あの薬をやめてから，いらいらして落ちつかなくなりましたか
2：あの薬をやめてから以前より眠れなくなりましたか
3：あの薬をやめてから嘔気，嘔吐，手足のふるえしびれ，発汗などがみられましたか
4：あの薬を是非又のみたいですか
5：あの薬をやめてから，ひきつけがありましたか
6：あの薬をやめてから，もうろうとしたり，変なものが見えたり聞えたりしましたか
Remarkable：非常に，Moderate：かなり，Slight：少し，None：いいえ
＜資料番号 5.3.5.2-01：Table 14.1.1.3-185＞

2.7.6.5.9.5　重篤な有害事象の叙述

Subject	[redacted]		**Category of Event**	Non-Fatal SAE	
Age	[redacted]	**Gender**	[redacted]	**Race**	[redacted]	**Ethnicity**	NOT HISPANIC OR LATINO

Treatment Exposure

Treatment	**Dose**	**Treatment Exposure Date (Study Day)**
Nalmefene	20 mg	20[redacted] (Study Day 1) to 20[redacted] (Study Day 160)
Nalmefene	20 mg	20[redacted] (Study Day 169) to 20[redacted] (Study Day 317)

Adverse Event

Investigator Term / Preferred Term	**SAE**	**Withdrawn from study**	**Start Date (Study Day)**	**End Date (Study Day)**	**Relationship**	**Severity**	**Action to Drug**	**Outcome**
MUSCLEPAINS / Myalgia 筋肉痛	No	No	20[redacted] (Study Day 85)	20[redacted] (Study Day 162)	NOT RELATED	MILD	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED
QUEASY / Nausea 悪心	No	No	20[redacted] (Study Day 169)	20[redacted] (Study Day 170)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
DIARRHOEA / Diarrhoea 下痢	No	No	20[redacted] (Study Day 172)	20[redacted] (Study Day 176)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
STING / Arthropod sting 節足動物刺傷	No	No	20[redacted] (Study Day 183)	20[redacted] (Study Day 225)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
DIZZINESS ON STANDING UP / Dizziness postural 体位性めまい	No	No	20[redacted] (Study Day 184)	20[redacted] (Study Day 197)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
PROSTATE CANCER / Prostate cancer 前立腺癌	Yes	Yes	20[redacted] (Study Day 310)	20[redacted] (Study Day 324)	NOT RELATED	MILD	DRUG WITHDRAWN	NOT RECOVERED/NOT RESOLVED

Relevant Medical History (Investigator Term / Preferred Name)	**Continuing**
ALCOHOL DEPENDENCE / Alcoholism	Yes
COSTIVENESS / Constipation	Yes
GOUT / Gout	Yes
HIGH LEVELS OF PSA / Prostatic specific antigen increased	Yes
HYPERTENSION / Hypertension	Yes
INSOMNIA / Insomnia	Yes
THYROID GLAUD DISORDERS / Thyroid disorder	Yes
URTICARIA CHRONIC / Urticaria chronic	Yes

Concomitant Medications (Investigator Term / Preferred Name)
ALLOPURINOL / ALLOPURINOL
BROTIZOLAM / BROTIZOLAM
EBASTINE / EBASTINE
HYDROXYZINE HYDROCHLORIDE / HYDROXYZINE HYDROCHLORIDE
ISEPAMICIN / ISEPAMICIN
LEVOFLOXACIN HYDRATE / LEVOFLOXACIN
LEVOTHYROXINE SODIUM HYDRATE / LEVOTHYROXINE SODIUM
MOMETASONE FUROATE / MOMETASONE FUROATE
PENTAZOCINE / PENTAZOCINE
PNEUMOCOCCAL VACCINE / PNEUMOCOCCAL VACCINE
SENNOSIDE / SENNOSIDE A+B CALCIUM

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被験者番号 [redacted] は，アルコール依存症を有する [redacted] 歳の[redacted]で，重篤と判断された前立腺癌を発現した。治験責任又は分担医師は，当該事象を軽度と判定し，ナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。治験依頼者は当該事象とナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。

被験者は先行する 339-14-001 試験で 20[redacted] 年 [redacted] 月 [redacted] 日から [redacted] 月 [redacted] 日までナルメフェン塩酸塩 20 mg の投与を受け，20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目）に本治験の治療期（ナルメフェン塩酸塩 20 mg）を開始した。

20[redacted] 年 [redacted] [redacted] 日，他院 A での定期受診で PSA 値の上昇が認められ，20[redacted] 年 [redacted] 月 [redacted] 日に検査のための入院が予定された。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 130 日目），他院 A で定期受診していたこと及び検査のための入院が予定されたことについて治験責任又は分担医師は報告を受けた。なお，他院 A での定期検診は，被験者が 20[redacted] 年に健康診断で PSA 高値（約 4.0 ng/mL）を指摘され，その後の経過を観察するための検診であった。20[redacted] 年当時の検査結果では臨床上の問題はなく，前立腺肥大や前立腺癌とは診断されなかった。その後の健康診断での PSA 値は，20[redacted] 年に約 4.0 ng/mL，20[redacted] 年に 7.0 ng/mL であり，20[redacted] 年には他院 A で精密検査も受けたが，検査結果に異常はなかった。その後，20[redacted] 年，20[redacted] 年，20[redacted] 年 [redacted] 月及び 20[redacted] 年 [redacted] 月の他院 A での定期受診でも，PSA 高値は継続していた。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 131 日目），前立腺生検検査のため，被験者は他院 A に入院した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 132 日目），被験者は他院 A を退院した。入院中に発現した有害事象はなかった。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 142 日目），生検検査の結果，前立腺癌と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 149 日目），治験責任又は分担医師は治験中止と判断し，ナルメフェン塩酸塩 20 mg の最終服薬日となった。

20[redacted] 年 [redacted] 月 [redacted] 日，前立腺癌に対する治療方針を判断するため，他院 A で画像検査を実施した。

20[redacted]年[redacted]月[redacted]日，前立腺摘除のため20[redacted]年[redacted]月[redacted]日に他院Bを受診予定であることについて，被験者より電話で連絡を受けた。

20[redacted]年[redacted]月[redacted]日，治験責任又は分担医師は他院Aから診療情報提供書を入手し，他院Aでの検査時に併用禁止薬であるペンタゾシン（オピオイド系鎮痛剤）が投与されたことを確認した。

20[redacted]年[redacted]月[redacted]日，被験者は他院Bに入院した。

20[redacted]年[redacted]月[redacted]日，他院Bで根治的前立腺摘除を受けた。

20[redacted]年[redacted]月[redacted]日，手術後の経過は順調であり，被験者は他院Bを退院した。治験責任又は分担医師は，寛解と診断するには5年以上の経過観察が必要であることから，前立腺癌の転帰を軽快と判断した。

治験責任又は分担医師は，前立腺癌の発生に関与するアンドロゲン，がん原生及び前立腺癌の発生について，ナルメフェン塩酸塩との関連性を否定した。また，癌の発生の時間的経過からも，ナルメフェン塩酸塩との関連性を否定できると判断した。

Subject	[redacted]		**Category of Event**	Non-Fatal SAE	
Age	[redacted]	**Gender**	[redacted]	**Race**	[redacted]	**Ethnicity**	NOT HISPANIC OR LATINO

Treatment Exposure		
Treatment	**Dose**	**Treatment Exposure Date (Study Day)**
Nalmefene	20 mg	20[redacted] (Study Day 1) to 20[redacted] (Study Day 167)
Nalmefene	20 mg	20[redacted] (Study Day 176) to 20[redacted] (Study Day 321)

Adverse Event

Investigator Term / Preferred Term	**SAE**	**Withdrawn from study**	**Start Date (Study Day)**	**End Date (Study Day)**	**Relationship**	**Severity**	**Action to Drug**	**Outcome**
QUEASY / Nausea 悪心	No	No	20[redacted] (Study Day 1)	20[redacted] (Study Day 28)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
VOMITING / Vomiting 嘔吐	No	No	20[redacted] (Study Day 5)	20[redacted] (Study Day 6)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
MALAISE / Malaise 倦怠感	No	No	20[redacted] (Study Day 7)	20[redacted] (Study Day 28)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
HYPOVITAMINOSIS / Hypovitaminosis ビタミン欠乏症	No	No	20[redacted] (Study Day 14)	20[redacted] (Study Day 56)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
DIARRHEA / Diarrhoea 下痢	No	No	20[redacted] (Study Day 23)	20[redacted] (Study Day 27)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
DIARRHEA / Diarrhoea 下痢	No	No	20[redacted] (Study Day 49)	20[redacted] (Study Day 52)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
QUEASY / Nausea 悪心	No	No	20[redacted] (Study Day 84)	20[redacted] (Study Day 169)	RELATED	MILD	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED
QUEASY / Nausea 悪心	No	No	20[redacted] (Study Day 177)	20[redacted] (Study Day 189)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
CONTUSION / Contusion 挫傷	No	No	20[redacted] (Study Day 309)	20[redacted] (Study Day 325)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
EXCORIATION / Excoriation 擦過傷	No	No	20[redacted] (Study Day 309)	20[redacted] (Study Day 325)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED

APPETITE IMPAIRED / Decreased appetite 食欲減退	No	No	20[redacted] (Study Day 320)	20[redacted] (Study Day 325)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
DEHYDRATION / Dehydration 脱水	Yes	Yes	20[redacted] (Study Day 322)	20[redacted] (Study Day 325)	NOT RELATED	MODERATE	DRUG WITHDRAWN	NOT RECOVERED/NOT RESOLVED
LIVER FUNCTION TEST INCREASED / Liver function test increased 肝機能検査値上昇	No	No	20[redacted] (Study Day 322)	20[redacted] (Study Day 325)	NOT RELATED	MILD	NOT APPLICABLE	NOT RECOVERED/NOT RESOLVED

Relevant Medical History (Investigator Term / Preferred Name)	**Continuing**
ALCOHOL DEPENDENCE / Alcoholism	Yes
DYSLIPIDAEMIA / Dyslipidaemia	Yes
HYPERTENSION / Hypertension	Yes
HYPERURICAEMIA / Hyperuricaemia	Yes
INSOMNIIA / Insomnia	Yes
OSSIFICATION OF POSTERIOR LONGITUDINAL LIGAMENT / Spinal ligament ossification	Yes

Concomitant Medications (Investigator Term / Preferred Name)
ALLOPURINOL / ALLOPURINOL
AMLODIPINE BESILATE / AMLODIPINE BESILATE
LIMAPROST ALFADEX / LIMAPROST ALFADEX
MECOBALAMIN / MECOBALAMIN
MOSAPRIDE CITRATE HYDRATE / MOSAPRIDE CITRATE
PAREPLUS / SOLUTIONS FOR PARENTERAL NUTRITION
VITADAN / VITANEURIN /02072701/
ZOLPIDEM TARTRATE / ZOLPIDEM TARTRATE

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被験者番号 [redacted] は，アルコール依存症を有する [redacted] 歳の[redacted]で，重篤と判断された脱水を発現した。治験責任又は分担医師は，当該事象を中等度と判定し，ナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。治験依頼者は当該事象とナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。

被験者は先行する 339-14-001 試験で 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日までナルメフェン塩酸塩 20 mg の投与を受け，20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目）に本治験の治療期（ナルメフェン塩酸塩 20 mg）を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 146 日目），ナルメフェン塩酸塩 20 mg の最終服薬日となった。

20[redacted] 年 [redacted] 月 [redacted] 日，Visit 9 来院時に，被験者は重篤な有害事象である脱水を発現した。治験責任又は分担医師の判断で，被験者は入院し，治験を中止した。

20[redacted]年[redacted]月[redacted]日，全身状態が改善し，被験者は退院した。治験責任又は分担医師は，脱水の転帰を回復と判断した。

治験責任又は分担医師は，脱水は加齢，来院前の活動量の増加，又は気温の上昇によるものと判断し，ナルメフェン塩酸塩との関連性を否定できると判断した。

Subject	[redacted]		**Category of Event**	Non-Fatal SAE	
Age	[redacted]	**Gender**	[redacted]	**Race**	[redacted]	**Ethnicity**	NOT HISPANIC OR LATINO

Treatment Exposure

Treatment	**Dose**	**Treatment Exposure Date (Study Day)**
Nalmefene	10 mg	20[redacted] (Study Day 1) to 20[redacted] (Study Day 163)
Nalmefene	20 mg	20[redacted] (Study Day 168) to 20[redacted] (Study Day 336)
Nalmefene	20 mg	20[redacted] (Study Day 337) to 20[redacted] (Study Day 364)

Adverse Event

Investigator Term / Preferred Term	**SAE**	**Withdrawn from study**	**Start Date (Study Day)**	**End Date (Study Day)**	**Relationship**	**Severity**	**Action to Drug**	**Outcome**
ABDOMINAL PAIN / Abdominal pain 腹痛	No	No	20[redacted] (Study Day 5)	20[redacted] (Study Day 5)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
ABDOMINAL PAIN / Abdominal pain 腹痛	No	No	20[redacted] (Study Day 144)	20[redacted] (Study Day 145)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
VOMITING / Vomiting 嘔吐	No	No	20[redacted] (Study Day 144)	20[redacted] (Study Day 145)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
ACUTE GATROENTERITIS / Gastroenteritis 胃腸炎	Yes	No	20[redacted] (Study Day 218)	20[redacted] (Study Day 221)	NOT RELATED	MODERATE	DOSE NOT CHANGED	RECOVERED/RESOLVED
PROLACTIN HIGH / Blood prolactin increased 血中プロラクチン増加	No	No	20[redacted] (Study Day 253)	20[redacted] (Study Day 337)	RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
PROLACTIM HIGH / Blood prolactin increased 血中プロラクチン増加	No	No	20[redacted] (Study Day 365)	20[redacted] (Study Day 393)	RELATED	MILD	NOT APPLICABLE	RECOVERED/RESOLVED

Relevant Medical History (Investigator Term / Preferred Name)	**Continuing**
ALCOHOL DEPENDENCE / Alcoholism	Yes
ASTHENOPIA / Asthenopia	Yes
COXALGIA / Arthralgia	Yes
HEPATIC FUNCTION DISORDER / Hepatic function abnormal	Yes
HYPERLIPIDAEMIA / Hyperlipidaemia	Yes

Concomitant Medications (Investigator Term / Preferred Name)
BIFIDOBACTERIUM / BIFIDOBACTERIUM NOS
CEFTRIAXONE SODIUM HYDRATE / CEFTRIAXONE SODIUM
ESOMEPRAZOLE MAGNESIUM HYDRATE / ESOMEPRAZOLE MAGNESIUM
SMILE 40 EX MILD / SMILE 40 EX

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被験者番号 [redacted]は，アルコール依存症を有する [redacted] 歳の[redacted]で，重篤と判断された胃腸炎を発現した。治験責任又は分担医師は，当該事象を中等度と判定し，ナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。治験依頼者は当該事象とナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。

被験者は先行する 339-14-001 試験で 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日までナルメフェン塩酸塩 10 mg の投与を受け，20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目）に本治験の治療期（ナルメフェン塩酸塩 20 mg）を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 50 日目），被験者は飲酒したが，体調に変化はなかった。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 51 日目），午前中に腹痛のため他院を受診した。血液検査の結果，炎症（白血球数 12030/mm^3，好中球数 78.9%，C 反応性タンパク質 0.07 mg/dL）が認められた。精密検査及び加療のため，被験者は他院に入院した。セフトリアキソンナトリウム 2 g/日，ビフィズス菌製剤 3 g/日，エソメプラゾールマグネシウム水和物カプセル 20 mg/日の投与を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 53 日目），血液検査の結果，白血球数が基準範囲内まで低下したことが確認された（白血球数 6640/mm^3，好中球数 61.9%，C 反応性タンパク質 0.16 mg/dL）。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 54 日目），抗生物質（セフトリアキソンナトリウム）の点滴を終了した。症状及び白血球数が改善したため，被験者は他院を退院した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 57 日目），ビフィズス菌製剤及びエソメプラゾールマグネシウム水和物カプセルの服薬を終了した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 58 日目），治験責任又は分担医師は，他院から診療情報提供書を入手し，被験者の退院をもって胃腸炎の転帰は回復と判断した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 170 日目），Visit 10 来院時に無作為割付けされ，ナルメフェン塩酸塩 20 mg の退薬期を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 197 日目），ナルメフェン塩酸塩 20 mg の最終服薬日となった。

他院からの診療情報提供書で診断名が急性胃腸炎であり偶発的な事象であること，また治験薬の作用機序から治験薬との関連性は考えにくいことから，治験責任又は分担医師は，ナルメフェン塩酸塩との関連性を否定できると判断した。

臨床検査結果

検査項目	基準範囲	20[redacted]年[redacted]月[redacted]日	20[redacted]年[redacted]月[redacted]日
白血球数（/mm^3）	3900～9800	12030	6640
好中球数（%）	40.0～74.0	78.9	61.9
C 反応性タンパク質（mg/dL）	0.30 未満	0.07	0.16

Subject	[redacted]		**Category of Event**	Non-Fatal SAE	
Age	[redacted]	**Gender**	[redacted]	**Race**	[redacted]	**Ethnicity**	NOT HISPANIC OR LATINO

Treatment Exposure

Treatment	**Dose**	**Treatment Exposure Date (Study Day)**
Placebo	0 mg	20[redacted] (Study Day 1) to 20[redacted] (Study Day 170)
Nalmefene	20 mg	20[redacted] (Study Day 177) to 20[redacted] (Study Day 344)
Nalmefene	20 mg	20[redacted] (Study Day 345) to 20[redacted] (Study Day 366)

Adverse Event

Investigator Term / Preferred Term	**SAE**	**Withdrawn from study**	**Start Date (Study Day)**	**End Date (Study Day)**	**Relationship**	**Severity**	**Action to Drug**	**Outcome**
COMMON COLD / Nasopharyngitis 鼻咽頭炎	No	No	20[redacted] (Study Day 117)	20[redacted] (Study Day 128)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
COMMON COLD / Nasopharyngitis 鼻咽頭炎	No	No	20[redacted] (Study Day 182)	20[redacted] (Study Day 197)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED
DYSLIPIDAEMIA / Dyslipidaemia 脂質異常症	No	No	20[redacted] (Study Day 348)	20[redacted] (Study Day 401)	NOT RELATED	MILD	DOSE NOT CHANGED	NOT RECOVERED/NOT RESOLVED
ATHEROTHROMBOTIC BRAIN INFARCTION / Thrombotic cerebral infarction 血栓性脳梗塞	Yes	No	20[redacted] (Study Day 348)	20[redacted] (Study Day 401)	NOT RELATED	MODERATE	DOSE NOT CHANGED	RECOVERED/RESOLVED WITH SEQUELAE
DIARRHOEA / Diarrhoea 下痢	No	No	20[redacted] (Study Day 358)	20[redacted] (Study Day 358)	NOT RELATED	MILD	DOSE NOT CHANGED	RECOVERED/RESOLVED

Relevant Medical History (Investigator Term / Preferred Name)	**Continuing**
ALCOHOL DEPENDENCE / Alcoholism	Yes
CONSTIPATION / Constipation	Yes
COPD / Chronic obstructive pulmonary disease	Yes
LOW BACK PAIN / Back pain	Yes

Concomitant Medications (Investigator Term / Preferred Name)

ADENOSINE TRIPHOSPHATE DISODIUM HYDRATE / ADENOSINE TRIPHOSPHATE, DISODIUM SALT
CARBOSYSTEINE / CARBOCISTEINE
CILOSTAZOL / CILOSTAZOL
CLOPIDOGREL SULFATE / CLOPIDOGREL BISULFATE
DIMEMORFAN PHOSPHATE / DIMEMORFAN PHOSPHATE
EDARAVONE / EDARAVONE
ETHYL ICOSAPENTATE / EICOSAPENTAENOIC ACID ETHYL ESTER
FAMOTIDINE / FAMOTIDINE

LANSOPRAZOLE / LANSOPRAZOLE
LEVOFLOXACIN HYDRATE / LEVOFLOXACIN
MAGNESIUM OXIDE / MAGNESIUM OXIDE
OZAGREL SODIUM / OZAGREL SODIUM
PITAVASTATIN CALCIUM HYDRATE / PITAVASTATIN CALCIUM
ULTIBRO INHALATION CAPSULES / ULTIBRO
VEEN-F / EUFUSOL

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被験者番号 [redacted] は，アルコール依存症を有する [redacted] 歳の[redacted]で，重篤と判断された血栓性脳梗塞を発現した。治験責任又は分担医師は，当該事象を中等度と判定し，ナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。治験依頼者は当該事象とナルメフェン塩酸塩 20 mg との因果関係を関連性は否定できると判断した。

被験者は先行する 339-14-001 試験で 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日までプラセボの投与を受け，20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目）に本治験の治療期（ナルメフェン塩酸塩 20 mg）を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 169 日目），Visit 10 来院時に無作為割付けされ，ナルメフェン塩酸塩 20 mg の退薬期を開始した。同日の収縮期/拡張期血圧は，140/74 mmHg であった。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 172 日目）23 時半頃，被験者は左上肢の筋力が低下し，腕を上げられないことに気が付いた。その後，左半身の麻痺及び会話機能障害も認められた。被験者は重篤な有害事象である血栓性脳梗塞を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 173 日目），起床時に症状が継続しており，頭重感もあったため，被験者は他院の脳外科を受診した。MRI の結果，右放射冠の分枝粥腫型梗塞と診断され，被験者は入院した。左半身の麻痺は軽度であり，増悪することなく継続した。プレタール OD 錠 50 mg 1 回 1 錠を 1 日 2 回，ピタバスタチンカルシウム錠 1 mg 1 回 1 錠を 1 日 1 回，エダラボン点滴静注 30 mg 1 日 2 回，オザペンバッグ注 80 mg 1 日 2 回，アデノシン P 注射液 20 mg，ヴィーン F 輸液 500 mL の投与を開始した。同日，被験者は脂質異常症と診断された。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 177 日目），アデノシン P 注射液 20 mg 及びヴィーン F 輸液 500 mL の投与を終了した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 179 日目），プレタール OD 錠 50 mg，エダラボン点滴静注 30 mg，及びオザペンバッグ注 80 mg の投与を終了した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 180 日目），プレタール OD 錠 50 mg 1 回 2 錠を 1 日 2 回，イコサペント酸エチル粒状カプセル 600 mg 1 回 1 カプセルを 1 日 3 回，ファモチジン D 錠 10 mg 1 回 1 錠を 1 日 2 回の投与を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 181 日目），後遺症として軽度の麻痺が認められたが，リハビリは不要と他院の医師が判断し，被験者は退院した（mRS = 1）。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 190 日目），ナルメフェン塩酸塩 20 mg の最終服薬日となった。

20[redacted]年[redacted]月[redacted]日,治験責任又は分担医師は被験者が入院したことについての報告を受け,血栓性脳梗塞の転帰を回復したが後遺症ありと判断した。

20[redacted]年[redacted]月[redacted]日，被験者は他院を受診し，血栓性脳梗塞は回復したが，後遺症である軽度の麻痺が継続していることを確認した。同日，プレタール OD 錠 50 mg，イコサペント酸エチル粒状カプセル 600 mg，ファモチジン D 錠 10 mg の投与を終了した。ピタバスタチンカルシウム錠 1 mg 1 回 1 錠を 1 日 1 回，ランソプラゾール OD 錠 15 mg 1 回 1 錠を 1 日 1 回，クロピドグレル錠 75 mg 1 回 1 錠を 1 日 1 回（20[redacted]年[redacted]月[redacted]日から投与開始），イコサペント酸エチル粒状カプセル 900 mg 1 回 1 カプセル 1 日 2 回による治療が継続された。

20[redacted]年[redacted]月[redacted]日，Visit 12 来院時に後遺症である麻痺が軽快していることを確認した。治療内容に変更はなかった。

被験者は多量飲酒，喫煙，及びコレステロール高値を含む危険因子を多く有しているため，治験責任又は分担医師はナルメフェン塩酸塩との関連性を否定できると判断した。

臨床検査結果

検査項目	基準範囲	20[redacted]/[redacted]/[redacted]	20[redacted]/[redacted]/[redacted]	20[redacted]/[redacted]/[redacted]
収縮期血圧（mm Hg）	－	140	－	－
拡張期血圧（mm Hg）	－	74	－	－
総コレステロール（mg/dL）	130～219	－	249	196
トリグリセリド（mg/dL）	30～150	－	197	135
高密度リポタンパク質（mg/dL）	41～64	－	57	68
低密度リポタンパク質（mg/dL）	70～139	－	153	101

Subject	[redacted]		**Category of Event**	Non-Fatal SAE	
Age	[redacted]	**Gender**	[redacted]	**Race**	[redacted]	**Ethnicity**	NOT HISPANIC OR LATINO

Treatment Exposure

Treatment	**Dose**	**Treatment Exposure Date (Study Day)**
Nalmefene	20 mg	20[redacted] (Study Day 1) to 20[redacted] (Study Day 170)
Nalmefene	20 mg	20[redacted] (Study Day 177) to 20[redacted] (Study Day 338)
Placebo	0 mg	20[redacted] (Study Day 339) to 20[redacted] (Study Day 373)

Adverse Event

Investigator Term / Preferred Term	**SAE**	**Withdrawn from study**	**Start Date (Study Day)**	**End Date (Study Day)**	**Relationship**	**Severity**	**Action to Drug**	**Outcome**
ORGANISING PNEUMONIA / Organising pneumonia 器質化肺炎	Yes	No	20[redacted] (Study Day 357)	20[redacted] (Study Day 422)	RELATED	SEVERE	NOT APPLICABLE	RECOVERING/RESOLVING
OSTEOPOROSIS / Osteoporosis 骨粗鬆症	No	No	20[redacted] (Study Day 397)	20[redacted] (Study Day 422)	NOT RELATED	MODERATE	NOT APPLICABLE	NOT RECOVERED/NOT RESOLVED
SUGAR BLOOD LEVEL INCREASED / Blood glucose increased 血中ブドウ糖増加	No	No	20[redacted] (Study Day 412)	20[redacted] (Study Day 422)	NOT RELATED	MODERATE	NOT APPLICABLE	NOT RECOVERED/NOT RESOLVED

Relevant Medical History (Investigator Term / Preferred Name)	**Continuing**
ALCOHOL DEPENDENCE / Alcoholism	Yes
POLINOSIS / Seasonal allergy	Yes

Concomitant Medications (Investigator Term / Preferred Name)

ADRENALINE / EPINEPHRINE
ALENDRONATE SODIUM HYDRATE / ALENDRONATE SODIUM
AZITHTROMYCIN HYDRATE / AZITHROMYCIN DIHYDRATE
BAKTAR / BACTRIM
FLUMAZENIL / FLUMAZENIL
HYDROXYZINE HYDROCHLORIDE / HYDROXYZINE HYDROCHLORIDE
LANSOPRAZOLE / LANSOPRAZOLE
LIDOCAINE / LIDOCAINE
MIDAZOLAM / MIDAZOLAM
PREDNISOLONE / PREDNISOLONE
PREDONISOLONE / PREDNISOLONE
SOLDEM3A / CARBOHYDRATES NOS W/POTASSIUM CHLORIDE/SODIUM
SULBACILLIN 1.5G FOR INJECTION / UNACID /00917901/
VOGLIBOSE / VOGLIBOSE

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被験者番号[redacted]は，アルコール依存症を有する[redacted]歳の[redacted]で，重篤と判断された器質化肺炎を発現した。治験責任又は分担医師は，当該事

象を高度と判定し，プラセボとの因果関係を関連性は否定できないと判断した。治験依頼者は当該事象とプラセボとの因果関係を関連性は否定できないと判断した。

被験者は先行する 339-14-001 試験で 20[redacted] 年 [redacted] 月 [redacted] 日から 20[redacted] 年 [redacted] 月 [redacted] 日までナルメフェン塩酸塩 20 mg の投与を受け，20[redacted] 年 [redacted] 月 [redacted] 日（投与 1 日目）に本治験の治療期（ナルメフェン塩酸塩 20 mg）を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 162 日目），ナルメフェン塩酸塩 20 mg の最終服薬日となった。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 163 日目），Visit 10 来院時に無作為割付けされ，プラセボの退薬期を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 181 日目），走ると息苦しさやだるさなどの症状が認められた。被験者は重篤な有害事象である器質化肺炎を発現した。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 193 日目），他院で胸部 X 線検査及びマイコプラズマ抗体検査を受け，ジスロマックが処方された。

20[redacted] 年 [redacted] 月 [redacted] 日（投与 197 日目），プラセボの最終服薬日となった。

20[redacted] 年 [redacted] 月 [redacted] 日，Visit 11 来院時に体調に変化は認められなかった。

20[redacted] 年 [redacted] 月 [redacted] 日，他院で胸部 X 線検査を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は健康診断で他院を受診し，20[redacted] 年 [redacted] 月下旬から胸部違和感があったことを訴えた。血液検査の結果，KL-6 1194 U/mL（基準範囲：500 U/mL 未満），リウマチ因子 16 IU/mL（基準範囲：15 IU/mL 以下），抗 ARS 抗体 123.4（基準範囲：25.0 未満）であった。胸部 X 線検査及び胸部 CT 検査の結果，両側下肺葉中心にすりガラス影を認めた。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は他院の呼吸器内科に入院した。

20[redacted] 年 [redacted] 月 [redacted] 日，気管支鏡検査が実施された。気管支肺胞洗浄液でリンパ球の上昇（72%）が認められ，器質化肺炎と診断された。プレドニゾロン 30 mg/日，ランソプラゾール，バクタ配合錠，及びアレンドロン酸の投与を開始した。治療経過は良好であり，胸部 X 線上の陰影に改善が認められた。

20[redacted] 年 [redacted] 月 [redacted] 日，治験実施医療機関は，被験者の入院について連絡を受けた。

20[redacted] 年 [redacted] 月 [redacted] 日，器質化肺炎及び抗 ARS 抗体陽性について精査するため，被験者はリウマチ・膠原病科に移された。治療経過は良好であった。

20[redacted] 年 [redacted] 月 [redacted] 日，治験実施医療機関は被験者に連絡し，被験者が退院していないこと及びリウマチ・膠原病科に移ったことを聴取した。治験責任又は分担医師は，治験の中止を判断した。

20[redacted] 年 [redacted] 月 [redacted] 日，被験者は他院を退院した。治験責任又は分担医師は，器質化肺炎の転帰を軽快と判断した。プレドニゾロン 25 mg/日に減量された。ランソプラゾール OD 錠 15 mg，バクタ配合錠，及びアレンドロン酸錠 35 mg の投与は継続され，ボグリボース OD 錠 0.3 mg の投与を開始した。

20[redacted] 年 [redacted] 月 [redacted] 日，中止時検査を実施した。治験責任又は分担医師は他院より診療情報提供書を入手した。被験者は抗 ARS 抗体陽性であり，抗

ARS 抗体症候群が器質化肺炎の原因と考えられたが，皮膚筋炎に特徴的な発疹や筋炎の症状が臨床経過で認められなかった。そのため，器質化肺炎は薬剤性肺炎に起因すると判断された。

20[redacted]年[redacted]月[redacted]日，プレドニゾロン 20 mg/日に減量された。

20[redacted]年[redacted]月[redacted]日，プレドニゾロン 15 mg/日に減量された。

20[redacted]年[redacted]月[redacted]日，プレドニゾロン 10 mg/日に減量された。

20[redacted]年[redacted]月[redacted]日，プレドニゾロン 9 mg/日に減量された。

20[redacted]年[redacted]月[redacted]日，プレドニゾロン 8 mg/日に減量された。今後，他院に 2 ヵ月ごとに来院し，1 mg/日ずつ減量される予定であることを治験責任又は分担医師は被験者より報告を受けた。胸痛及び息苦しさなどの自覚症状は軽減していたが，まだ継続していた。

臨床検査結果

検査項目	基準範囲	20[redacted]年[redacted]月[redacted]日	20[redacted]年[redacted]月[redacted]日	20[redacted]年[redacted]月[redacted]日	20[redacted]年[redacted]月[redacted]日	20[redacted]年[redacted]月[redacted]日
好塩基球（%）	0.0～2.0	1.4	0.0	1.0	1.2	1.0
C 反応性タンパク質（mg/dL）	0.5 未満	0.0	0.0	0.0	0.02	0.5
好酸球（%）	0.0～8.0	2.6	3.0	3.0	3.1	5.0
リンパ球（%）	18.0～49.0	36.2	25.0	22.0	25.9	21.0
単球（%）	2.0～10.0	7.1	8.0	6.0	7.1	5.0
好中球（%）	40.0～75.0	52.7	64.0	68.0	62.7	68.0
白血球数（/mm^3）	3300～9000	4400	4900	5100	4240	8300
KL-6（U/mL）	500 未満	－	－	－	1194	－
リウマチ因子（IU/mL）	15 以下	－	－	－	16	－
抗 ARS 抗体	25.0 未満	－	－	－	123.4	－

2.7.6.5.10　アルコール使用障害患者を対象とした可変用量での長期試験（外国人：CPH-101-0400 試験，添付資料番号 5.3.5.2-02）【参考資料】

2.7.6.5.10.1 試験方法の概略

項目	内容
試験の目的	多量飲酒者を対象にナルメフェン頓用投与の飲酒量低減に対する有効性及び安全性を予備的に検討する。
試験デザイン	多施設共同，非盲検，非対照
対象	多量飲酒者
選択基準	1) 飲酒をコントロールすることが難しい患者 • 意図したよりも多量又は長時間飲酒することが多い患者 2) スクリーニング来院前 12 週間に，HDD が 24 日以上かつ連続した断酒日が 14 日間以下である患者（HDD は男性で 5 ドリンク以上，女性で 4 ドリンク以上のアルコールを消費した日とした） 3) 組入れ時に飲酒状態ではなく，また，高度の離脱症状が認められない患者 4) 同意文書に署名した患者 5) 18 歳以上の男性又は女性患者 6) 定まった住所及び電話番号を有する患者
除外基準	1) 精神障害（精神病，統合失調症，中等度又は高度のうつ病，摂食障害，双極性感情障害，不安障害など），人格障害，飲酒問題に優先して治療が必要な障害，又は治験治療を妨げるか治療遵守に支障を来す恐れのある障害を有する患者 2) せん妄又は高度の離脱症状が認められる患者，又は入院での解毒治療が必要な患者 3) 高度の肝障害又は腎障害を有する患者 4) 認知症，てんかん発作，精神遅滞，脳症を有する患者 5) 飲酒問題に優先して治療が必要な未治療の医療上の問題（アルコール関連問題を除く）を有する患者 6) 薬物依存の患者又は違法薬物を使用している患者 7) 過去にナルメフェンの臨床試験に参加した患者 8) 現在又は過去 6 ヵ月以内で，ジスルフィラム又はナルトレキソンによる治療を受けている患者 9) 現在又は過去 1 週間以内で，オピオイドの刺激薬による治療を受けている患者 10) 妊娠又は授乳中の患者 11) 妊娠可能な女性で，適切な避妊法を使用していない患者

項目	内容
	12) 組入れ前 6 ヵ月以内に何らかの治験に参加した患者
使用薬剤, ロット番号	**被験薬** ナルメフェン塩酸塩錠 20 mg：[redacted], [redacted]
用量及び投与方法	ナルメフェン塩酸塩錠 20 mg を，飲酒の直前，可能であれば飲酒の 1 時間以上前に頓用で経口服用した。1 日 1 回までの服用とし，必要であれば，毎日服用可能であった。治療効果がみられない［被験者が評価した CGI スコアが 3 以上（軽度改善から重度悪化）である］場合は，組入れから 2 週間後以降に 40 mg（2 錠）に増量できることとした。忍容できない有害事象が発現した場合は，治験責任医師の判断で，一時的に又は治験期間終了まで，20 mg から 10 mg（1/2 錠）に，又は 40 mg から 20 mg に用量を減量できることとした。
投与期間	52 週間
目標被験者数	60 例
目標被験者数の 設定根拠	被験者数は，統計的検出力を算出して決定したものではなく，ナルメフェンの安全性及び有効性評価を適切に行うために必要な曝露量を考慮し，臨床的判断に基づき決定した。
主な併用薬の規定	**併用禁止薬/療法** • オピオイドの刺激薬 • ナルトレキソン • ジスルフィラム • 鎮痛薬
評価項目	**有効性** 主要評価項目：HDD 数 HDD 数は 1 日のアルコール消費量が男性で 5 ドリンク以上，女性で 4 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した（1 ドリンクはエタノールとして約 12 g を含む）。 アルコール消費量に関する副次的評価項目： • TAC TAC は 1 週間当たりの平均アルコール消費量（ドリンク/週）と定義した。 • VHDD 数 VHDD 数は，1 日のアルコール消費量が男性で 10 ドリンク以上，女性で 8 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した。 • 飲酒日当たりのアルコール消費量 • 飲酒日数に対する HDD 数の割合

項目	内容
	• 初回 HDD が認められるまでの期間 • 危険な飲酒日数 危険な飲酒日数は1日のアルコール消費量が男性で3ドリンク以上，女性で 2 ドリンク以上の日の 1 ヵ月当たりの日数（日/月）と定義した。 • 危険でない飲酒日の累積日数 危険でない飲酒日は1日のアルコール消費量が男性で3ドリンク未満，女性で 2 ドリンク未満の日と定義した。 • NDD 数 • No HDD の累積日数 No HDD は 1 日のアルコール消費量が男性で 5 ドリンク未満，女性で 4 ドリンク未満の日と定義した。 その他の副次的評価項目： • 血中アルコール濃度 • MCV，ALT，γ-GTP，%CDT • ADS • 強迫性飲酒尺度 • DrInC • CGI **安全性** 有害事象，臨床検査値，身体所見，バイタルサイン，12 誘導心電図，ベックのうつ病調査票及び不安調査票，曝露期間，1 日当たりの投与量
解析方法	統計学的モデルは，性別，施設，及びアルコール関連問題の家族歴の治療効果に対する影響を評価するために用いた。有効性主要評価項目である HDD 数は，ポアソン分布又は二項分布のいずれかを仮定した一般化線形混合効果モデルを用いて解析した。
治験依頼者	Biotie Therapies Corp.
治験実施医療機関	フィンランド 2 施設
治験期間	20[redacted]年[redacted]月[redacted]日～20[redacted]年[redacted]月[redacted]日

2.7.6.5.10.2 治験スケジュール

治験スケジュールを表 2.7.6.5.10-1 に示した。

表 2.7.6.5.10-1　　治験スケジュール

	Screening	Inclusion	Weeks					
			1, 2, 4, 8	12	16, 20, 24	28	36, 44	52
Informed consent	x							
Medical history	x							
Physical examination	x							x
Breath alcohol	x	x	x	x	x	x	x	x
Structured clinical interview for DSM-IV	x							
Alcohol use disorders identification test	x							
Drinker inventory of consequences	x			x		x		x
Alcohol dependence scale	x			x		x		x
Timeline followback	x	x	x	x	x	x	x	x
Beck's depression inventory	x			x		x		x
Beck's anxiety inventory	x			x		x		x
Obsessive-compulsive drinking scale	x	x	x	x	x	x	x	x
Clinical laboratory	x			x		x		x
Pregnancy test	x							
Urine drug screen	x							
Electrocardiogram	x			x		x		x
Clinical global impression-subject			x	x	x	x	x	x
Adverse event questioning			x	x	x	x	x	x
Blood pressure and heart rate	x	x	x	x	x	x	x	x
Concomitant medication/treatment	x	x	x	x	x	x	x	x
Medication check			x	x	x	x	x	x

Timeline followback で導出される評価項目は，HDD 数，TAC，VHDD 数，飲酒日当たりのアルコール消費量，飲酒日数に対する HDD 数の割合，初回 HDD が認められるまでの期間，危険な飲酒日数，危険でない飲酒日の累積日数，NDD 数，No HDD の累積日数

＜資料番号 5.3.5.2-02：Text Table 2＞

2.7.6.5.10.3 試験結果

(1)　被験者の内訳

被験者の内訳を図 2.7.6.5.10-1 に，中止例の内訳を表 2.7.6.5.10-2 に，それぞれ示した。

73 例がスクリーニング検査を受け，60 例が組入れられた。28 例（46.7%）が 52 週間の治療期間を完了し（資料番号 5.3.5.2-02：14.4.3.1 参照），32 例（53.3%）が治験を中止した。主な中止理由は，同意撤回及び有害事象であった。

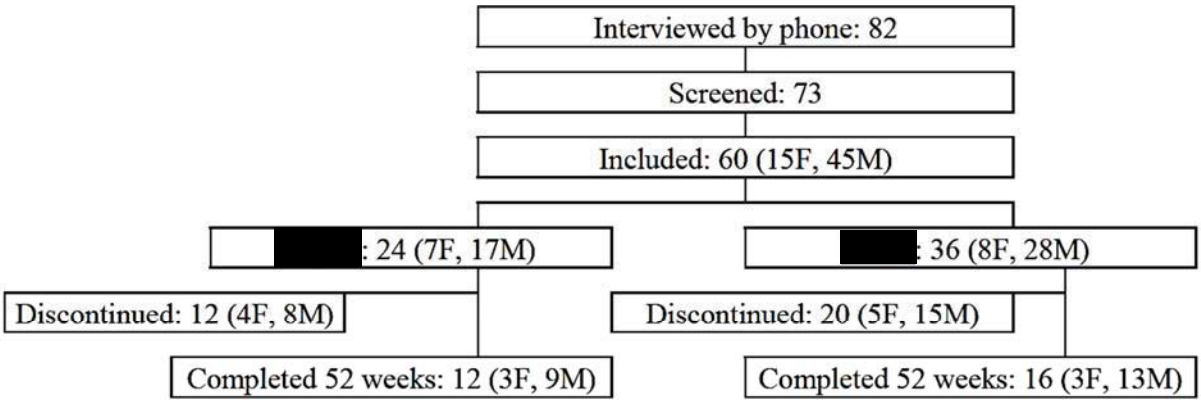


図 2.7.6.5.10-1　　被験者の内訳

[redacted], [redacted]：治験実施医療機関の名称

F: female, M: male

＜資料番号 5.3.5.2-02：Text Figure 1＞

表 2.7.6.5.10-2　　中止例の内訳

Reason	[redacted] N (%)	[redacted] N (%)	Total N (%)
Total	12 (50.0)	20 (55.6)	32 (53.3)
Consent withdrawn	5 (20.8)	10 (27.8)	15 (25.0)
Adverse event	3 (12.5)	7 (19.4)	10 (16.7)
Lost to follow-up	4 (16.7)	2 (5.6)	6 (10.0)
Other	-	1 (2.8)	1 (1.7)

[redacted], [redacted]：治験実施医療機関の名称

＜資料番号 5.3.5.2-02：Text Table 7＞

(2)　解析したデータセット

すべての解析は，本治験に組入れられた全被験者を含む ITT 集団 60 例で実施した。サブグループ解析又は per protocol 解析は実施しなかった。

(3)　人口統計学的及び他の基準値の特性

人口統計学的特性を表 2.7.6.5.10-3 に示した。

15 例が女性，45 例が男性であり，全例が白人であった（資料番号 5.3.5.2-02：14.1.1.3 参照）。平均年齢は 49.9 歳（範囲：32～75 歳），平均の BMI は 27.5 kg/m^2（範囲：18～38 kg/m^2）であった。20.0%が独居，43.3%が配偶者又はパートナーと暮らし，26.7%が配偶者又はパートナー及び子供と暮らし，8.3%が独身で子供と暮らしていた（資料番号 5.3.5.2-02：14.1.1.8 参照）。65.0%が在職中であり，18.3%が退職していた（資料番号 5.3.5.2-02：14.1.1.5 参照）。

66.7%がアルコール関連問題の家族歴を有していた（資料番号 5.3.5.2-02：14.1.2.1 参照）。初回飲酒の平均年齢は 15.4 歳（範囲 5～26 歳）（資料番号 5.3.5.2-02：14.1.2.3 参照），アルコール関連問題の平均初発年齢は 34.6 歳（範囲：16～60 歳）であった（資料番号 5.3.5.2-02：14.1.2.4 参照）。44 例（73.3%）にアルコール関連問題の治療歴があった（資料番号 5.3.5.2-02：14.1.2.5 参照）。半数近く（45.0%）の被験者が喫煙者であった（資料番号 5.3.5.2-02：14.1.3.1 参照）。

DSM-IV による判定で，全被験者が現行アルコール依存の基準及び現行アルコール乱用の基準を満たした（資料番号 5.3.5.2-02：14.1.5.2 参照）。

表 2.7.6.5.10-3　　人口統計学的特性（ITT）

	[redacted] (N=24)	[redacted] (N=36)	Total (N=60)
Females : Males	7 (29.2%) : 17 (70.8%)	8 (22.2%) : 28 (77.8%)	15 (25.0%) : 45 (75.0%)
Age (years)	49.5 (8.9; 34-69)	50.2 (8.8; 32-75)	49.9 (8.8; 32-75)
Body mass index (kg/m^2)	26.8 (4.7; 18-36)	28.0 (5.0; 20-38)	27.5 (4.9; 18-38)

Means (with standard deviation and range) are given.
＜資料番号 5.3.5.2-02：Text Table 9＞

(4)　有効性

(a)　主要評価項目

HDD 数の推移を図 2.7.6.5.10-2 及び表 2.7.6.5.10-4 に示した。

HDD 数の中央値は，治験期間後半で，ベースラインの 17 日/月から 3～6 日/月に減少し，ベースラインからの減少の割合の中央値は 68.8%～79.4%であった。HDD 数の減少は投与開始後 2 ヵ月間で最も大きかった。

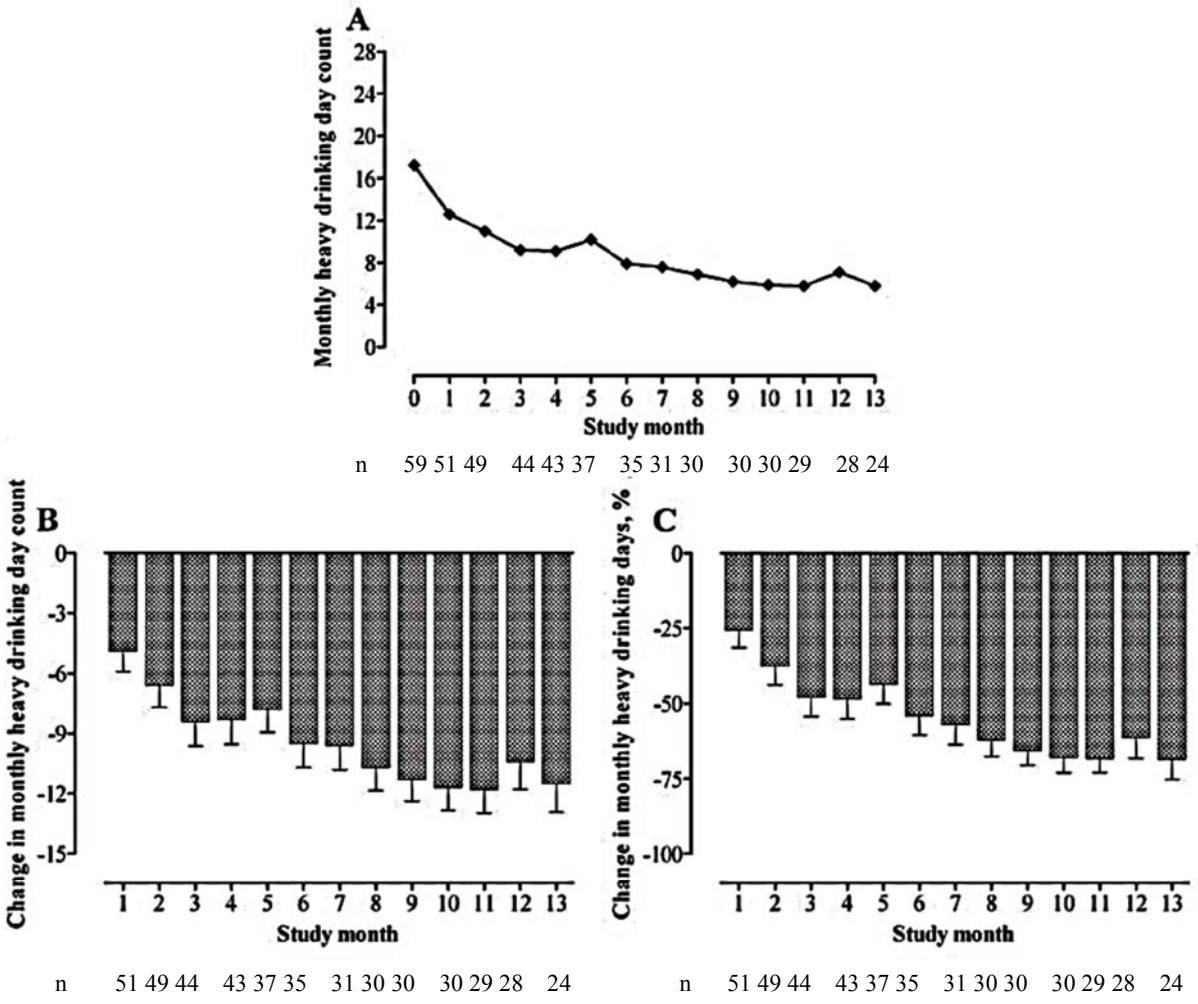


図 2.7.6.5.10-2　　HDD 数の推移（ITT）

A. Population mean. B. Mean change in the heavy drinking day count. C. Percent change in the heavy drinking day count. Error bars are standard errors of the mean.

＜資料番号 5.3.5.2-02：Text Figure 3，Text Table 16 より作成＞

表 2.7.6.5.10-4　　HDD 数の推移（ITT）

	Month	0	1	2	3	4	5	6	7	8	9	10	11	12	13
	N	59	51	49	44	43	37	35	31	30	30	30	29	28	24
Count	Median	17	12	10	6.5	5	11	6	6	5.5	6	4	4	5.5	3
	Mean	17.2	12.6	11.0	9.2	9.1	10.2	7.9	7.6	6.9	6.2	5.9	5.8	7.1	5.8
	SD	6.3	7.6	8.6	8.5	8.4	7.4	6.8	7.1	6.2	5.7	6.1	5.9	7.2	7.0
Change	Median		-4	-8	-8	-9	-9	-10	-10	-10	-11	-12	-11	-10	-10.5
	Mean		-4.9	-6.6	-8.4	-8.3	-7.8	-9.5	-9.6	-10.7	-11.3	-11.7	-11.8	-10.4	-11.5
	SD		7.2	7.8	8.1	8.1	7.0	7.1	6.8	6.3	5.9	6.2	6.3	7.3	7.0
Per cent change	Median		-22.2	-50.0	-58.6	-62.5	-45.5	-66.7	-68.8	-69.4	-68.9	-73.9	-75.0	-68.8	-79.4
	Mean		-25.5	-37.4	-47.9	-48.5	-43.6	-54.0	-56.9	-62.1	-65.6	-67.8	-68.2	-61.3	-68.4
	SD		41.8	45.1	42.7	43.5	39.4	38.2	37.2	30.1	27.1	29.1	26.1	36.3	33.9

Month 0 refers to baseline.

＜資料番号 5.3.5.2-02：Text Table 16＞

(b)　副次的評価項目

i)　TAC

TAC の推移を図 2.7.6.5.10-3 及び表 2.7.6.5.10-5 に示した。

TAC は治験開始後，比較的速やかに減少し，治験終了前の数ヵ月間は 15 ドリンク/週程度で推移した。

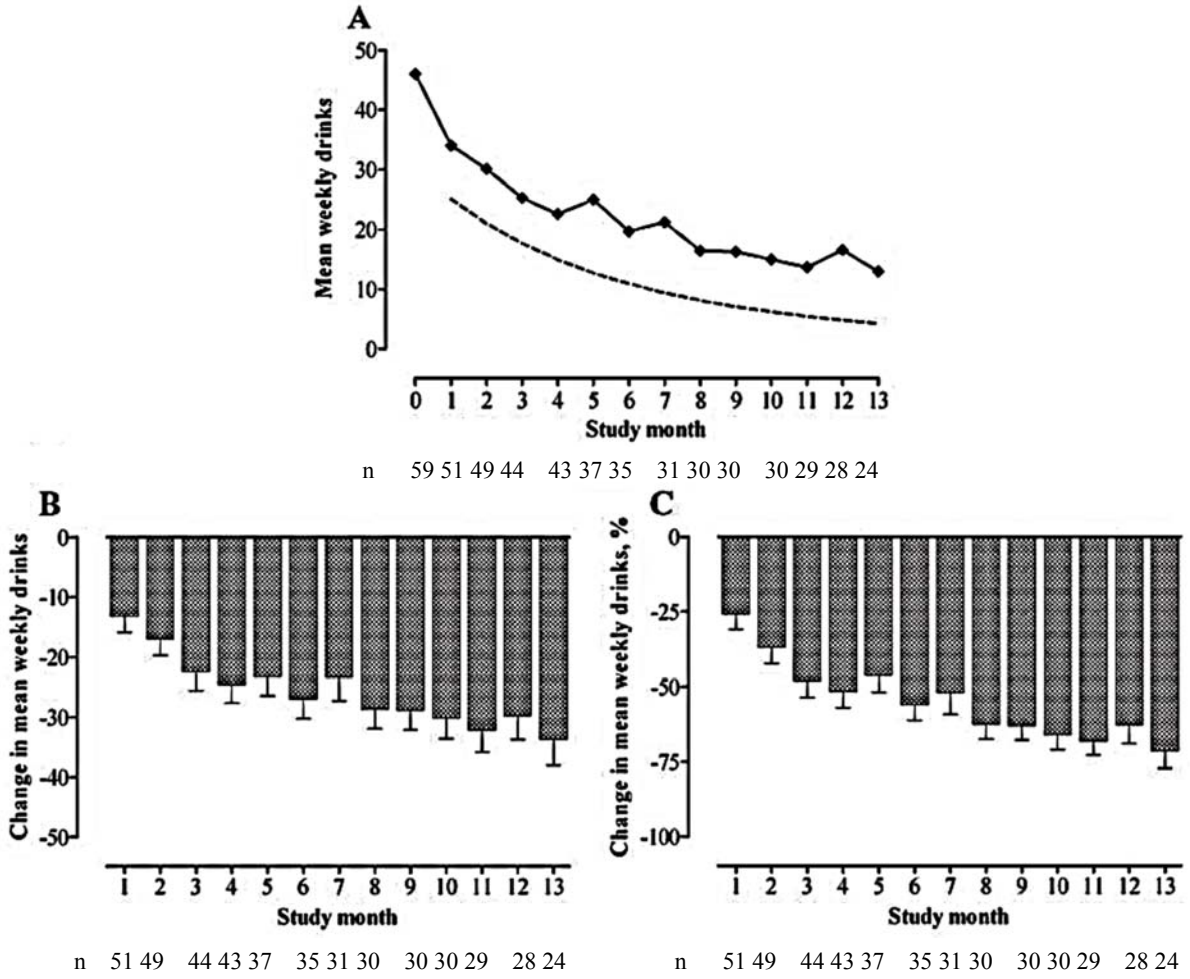


図 2.7.6.5.10-3　　TAC の推移（ITT）

A. Consumption as standard drinks per week observed (diamonds) and modeled (dashed line). B. Mean change in mean weekly drink consumption. C. Percent change in mean alcohol consumption. Error bars are standard error of the mean.

＜資料番号 5.3.5.2-02：Text Figure 13，Text Table 20 より作成＞

表 2.7.6.5.10-5　　TAC の推移（ITT）

Study month		0	1	2	3	4	5	6	7	8	9	10	11	12	13
Subject count		59	51	49	44	43	37	35	31	30	30	30	29	28	24
Weekly drinks	Median	43.8	31.9	22.1	15.3	16.3	21.0	16.0	17.8	13.7	13.2	11.5	10.3	13.2	8.4
	Mean	46.0	34.0	30.1	25.3	22.6	25.0	19.7	21.2	16.5	16.3	15.0	13.7	16.6	13.0
	SD	21.1	20.8	23.2	23.6	19.5	17.9	15.3	20.1	12.8	13.2	13.6	12.3	15.9	15.1
Change in the mean weekly drink count	Median		-9.2	-12.3	-19.6	-23.5	-19.4	-19.8	-21.2	-22.7	-25.1	-26.6	-26.5	-28.3	-27.5
	Mean		-13.2	-16.9	-22.4	-24.6	-23.2	-26.9	-23.3	-28.6	-28.8	-30.1	-32.1	-29.7	-33.6
	SD		19.2	19.9	20.9	19.8	19.5	19.4	22.1	17.9	17.8	18.8	19.7	21.0	21.5
Per cent change in the drink count	Median		-31.5	-35.9	-53.8	-59.5	-50.7	-61.9	-60.5	-64.3	-57.1	-70.0	-72.3	-67.8	-76.9
	Mean		-25.8	-36.9	-48.0	-51.5	-46.2	-56.0	-51.9	-62.4	-63.0	-66.0	-68.1	-62.6	-71.3
	SD		36.5	37.5	37.1	35.9	33.9	31.0	40.4	27.1	25.6	27.1	25.2	33.3	28.8

Month 0 refers to baseline.
＜資料番号 5.3.5.2-02：Text Table 20＞

ii)　アルコール消費量に関する副次的評価項目

その他のアルコール消費量に関する副次的評価項目の変化は，主要評価項目である HDD 数の結果と同様であった。

(c)　その他の副次的評価項目

MCV，ALT，γ-GTP，及び%CDT の推移を表 2.7.6.5.10-6 に示した。

ALT，γ-GTP，及び%CDT は，治験期間中に減少し改善が認められたが，MCV では変化が認められなかった。

表 2.7.6.5.10-6　　臨床検査値（ITT）

		Mean corpuscular volume, fl				Alanine amino-transferase, U l^{-1}				Gamma glutamyl-transferase, U l^{-1}				Carbohydrate-deficient trans-ferrin, %			
Study week		0	12	28	52	0	12	28	52	0	12	28	52	0	12	28	52
Female	Median	97	96	96	94.5	25	25	21	21	42	44	46.5	40.5	2.8	2.8	2.4	2.4
	Mean	94.5	95.0	95.5	96.0	25.9	25.2	23.1	22.2	41.9	45.5	44.9	47.0	3.7	3.7	2.6	2.5
	SD	6.0	6.0	4.8	5.1	7.8	6.2	9.6	7.6	16.0	21.3	14.1	21.0	1.9	2.4	0.7	0.6
	N	15	11	8	6	15	11	8	6	15	11	8	6	15	11	8	6
Male	Median	97	96	96	97	35	24	25	24.5	73	53	38.5	36	3.1	2.8	2.7	2.6
	Mean	96.8	96.6	96.0	96.3	51.4	47.1	33.0	36.4	124.8	92.4	51.8	68.6	3.8	3.5	3.1	3.1
	SD	3.7	3.8	3.5	3.6	52.4	53.8	24.5	36.9	143.7	106.1	57.9	127.8	2.1	1.8	1.4	1.5
	N	43	35	24	22	45	35	24	22	45	35	24	22	42	35	24	22
Total	Median	97	96	96	96.5	28.5	24.5	23	23.5	59	47.5	39	36	3.0	2.8	2.5	2.6
	Mean	96.2	96.2	95.8	96.3	45.0	41.8	30.6	33.3	104.0	81.2	50.1	64.0	3.7	3.5	3.0	3.0
	SD	4.5	4.4	3.8	3.9	46.7	47.8	22.0	33.2	129.5	94.9	50.4	113.4	2.0	2.0	1.3	1.4
	N	58	46	32	28	60	46	32	28	60	46	32	28	57	46	32	28

＜資料番号 5.3.5.2-02：Text Table 23＞

ADS，強迫性飲酒尺度，及び DrInC は，治験期間中に経時的に改善した。

最終評価時点の CGI を表 2.7.6.5.10-7 に示した。

CGI は，治験期間中に経時的に改善した。約 60%の被験者が最終評価時点で「Much improved」

又は「Very much improved」と評価した。

表 2.7.6.5.10-7　　最終評価時点の CGI（ITT）

	Females		Males		Total	
	N	%	N	%	N	%
Very much improved	3	21.4	10	23.3	13	22.8
Much improved	4	28.6	17	39.5	21	36.8
Minimally improved	4	28.6	9	20.9	13	22.8
Unchanged	2	14.3	6	14.0	8	14.0
Minimally worsened	.	0.0	.	0.0	.	0.0
Much worsened	1	7.1	.	0.0	1	1.8
Very much worsened	.	0.0	1	2.3	1	1.8
Total	14	100.0	43	100.0	57	100.0

Subjects' impression is shown.
＜資料番号 5.3.5.2-02：Text Table 22＞

(5)　安全性

(a)　治験薬の曝露状況

治験薬の 1 日当たりの平均投与量と曝露期間の関係を表 2.7.6.5.10-8 に示した。

治験薬の曝露期間の平均値（標準偏差，以下同様）は，212.7 日間（139.9 日間）で，1 日当たりの投与量の平均値は 11.7 mg（8.6 mg）であった（資料番号 5.3.5.2-02：14.3.6.13，14.3.6.14 参照）。

総飲酒日 6155 日のうち，88.7%（5458 日）で治験薬が服用された（資料番号 5.3.5.2-02：14.4.1.1 参照）。飲酒しなかった 6972 日を含めた服薬遵守率の平均値は 94.7%であった（資料番号 5.3.5.2-02：14.4.1.3 参照）。

表 2.7.6.5.10-8　　治験薬の 1 日当たりの投与量と曝露期間（ITT）

Duration, weeks	≤5 mg		5-10 mg		10-20 mg		20-30 mg		>30 mg		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
≤1	.	.	.	.	4	7.0	.	.	.	.	4	7.0
1-2	.	.	1	1.8	.	.	.	.	.	.	1	1.8
2-4	.	.	.	.	2	3.5	.	.	.	.	2	3.5
4-12	1	1.8	4	7.0	2	3.5	1	1.8	.	.	8	14.0
12-24	4	7.0	2	3.5	2	3.5	2	3.5	1	1.8	11	19.3
24-36	1	1.8	2	3.5	.	.	1	1.8	.	.	4	7.0
36-48	.	.	2	3.5	1	1.8	.	.	.	.	3	5.3
>48	6	10.5	9	15.8	5	8.8	3	5.3	1	1.8	24	42.1
Total	12	21.1	20	35.1	16	28.1	7	12.3	2	3.5	57	100.0

Duration and dose categories always upper limit inclusive.
＜資料番号 5.3.5.2-02：Text Table 29＞

(b)　有害事象

4 例以上に発現した有害事象を表 2.7.6.5.10-9 に，有害事象の器官別大分類を表 2.7.6.5.10-11

に，すべての有害事象を表 2.7.6.5.10-12 に，重症度別有害事象及び副作用を表 2.7.6.5.10-13 に示した。

有害事象の発現割合は 95.0%（57 例）であった。発現割合が高かった有害事象の器官別大分類は，全身障害および投与局所様態，胃腸障害，神経系障害，及び精神障害であった。発現割合が高かった有害事象は，倦怠感（38.3%），嘔気（28.3%），インフルエンザ様疾患（25.0%），頭痛 NOS（25.0%），不眠症（23.3%），疲労（21.7%），及び浮動性めまい（回転性眩暈を除く）（20.0%）であった。

食欲減退 NOS，浮動性めまい，疲労，不眠症，倦怠感，嘔気，多汗，嘔吐 NOS のほとんどで，投与 1 週目に初回発現が認められた（資料番号 5.3.5.2-02：Text Table 32 参照）。また，これらの有害事象のほとんどで持続期間が短かった（持続期間の中央値は 2～4 日）。不眠症及び多汗で持続期間が長くなる傾向があり，持続期間の中央値はそれぞれ 10.5 日及び 17.5 日であった（資料番号 5.3.5.2-02：Text Table 33 参照）。

有害事象のプロファイルは，これまでに報告されているもの及び Contral Pharm（現 Biotie Therapies）が実施した治験で認められたものと大きく異ならなかった。

表 2.7.6.5.10-9　4 例以上に発現した有害事象（ITT）

	Events	Subjects		95% CI limits	
Preferred term	N	N	Proportion	Lower	Upper
倦怠感	35	23	38.3%	26.0 %	50.6%
嘔気	20	17	28.3%	16.9 %	39.7%
インフルエンザ様疾患	24	15	25.0%	14.0 %	36.0%
頭痛NOS	17	15	25.0%	14.0 %	36.0%
不眠症	17	14	23.3%	12.6 %	34.0%
疲労	18	13	21.7%	11.2 %	32.1%
浮動性めまい（回転性眩暈を除く）	14	12	20.0%	9.9%	30.1%
嘔吐NOS	11	10	16.7%	7.2%	26.1%
多汗	9	9	15.0%	6.0%	24.0%
浮動性めまい	9	7	11.7%	3.5%	19.8%
下痢NOS	7	6	10.0%	2.4%	17.6%
腹痛NOS	5	5	8.3%		
食欲減退NOS	5	5	8.3%		
無感情	5	5	8.3%		
消化不良	4	4	6.7%		
関節痛	4	4	6.7%		
背部痛	4	4	6.7%		
下肢静止不能症候群	4	4	6.7%		

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CI: confidence interval

＜資料番号 5.3.5.2-02：Text Table 31＞

(c)　治験薬との関連性が否定できない有害事象（副作用）

重症度別有害事象及び副作用を表 2.7.6.5.10-13 に示した。

(d)　死亡，その他の重篤な有害事象

i)　死亡

本治験で死亡は報告されなかった。

ii)　その他の重篤な有害事象

重篤な有害事象を表 2.7.6.5.10-10 に，重篤及び重要な有害事象一覧表を表 2.7.6.5.10-14 に示した。

重篤な有害事象が 2 例で 4 件発現した。いずれの事象も，治験薬との関連性は否定された。

表 2.7.6.5.10-10　重篤な有害事象（ITT）

Subject	Event as reported	Preferred terms in adverse event database
[redacted]	Took excessive amount of alcohol and clonazepam	非偶発的過量投与
[redacted]	Took excessive amount of alcohol and clonazepam	非偶発的過量投与
[redacted]	Broken ankle	足関節部骨折
[redacted]	Wound due to operation on left ankle infected	術後創感染

MedDRA/J Version 4.0

＜資料番号 5.3.5.2-02：Text Table 34＞

(e)　投与中止に至った有害事象

重篤及び重要な有害事象一覧表（投与中止に至った有害事象を含む）を表 2.7.6.5.10-14 に示した。

10 例（16.7%）が有害事象により投与を中止した（表 2.7.6.5.10-2）。嘔気・嘔吐 NOS（3 例）による中止が最も多かった（資料番号 5.3.5.2-02：Text Table 35 参照）。

(f)　臨床検査

i)　治験期間を通しての臨床検査値

臨床検査値に明らかな変動は認められなかった。臨床検査値の解析からは，ナルメフェンの安全性の問題は示唆されなかった。

ii)　個々の臨床的に重要な異常

臨床的に重要な臨床検査値の変動が 2 例で 5 件認められた（資料番号 5.3.5.2-02：14.3.4 参照）。これらはいずれも，安全性の観点で問題となる変動ではなかった。

(g)　バイタルサイン

血圧の中央値から，被験者のほとんどが高血圧であることが示された。治験期間中に血圧の経時的な変化は認められなかった。心拍数に，特定の経時的な傾向は認められなかった。

(h) 心電図検査

6 例で心電図変化が認められた（資料番号 5.3.5.2-02：Text Table 44 参照）。これらの変化から，安全性上の問題は示唆されなかった。

(i) ベックのうつ病調査票及び不安調査票

ナルメフェンは不安及びうつ病を引き起こさなかった。不安及びうつ病のスコアは経時的に減少した。

(6) 結論

- ナルメフェンの頓用により，多量飲酒が明らかに減少し，心理的スコア（ADS，強迫性飲酒尺度，DrInC，及び CGI）の改善が認められた。
- ナルメフェンを頓用したときの服薬遵守率は高かった。
- 本治験で認められたナルメフェンの安全性プロファイルは，これまでに報告されているもの及び治験依頼者が実施した治験で認められたものと大きく異ならなかった。
- 有害事象は主に投与期間の初期に発現した。発現割合が高かった有害事象は，倦怠感，嘔気，インフルエンザ様疾患，頭痛 NOS，不眠症，疲労，浮動性めまい（回転性眩暈を除く）であった。不眠症を除き，これらの事象の持続期間は短かった。
- 臨床検査値からは，ナルメフェンの安全性上の問題は示唆されなかった。
- ナルメフェンは，本治験の被験者で不安及びうつ病を引き起こさなかった。
- 以上，多量飲酒者にナルメフェンを頓用した結果，ナルメフェンは多量飲酒を抑制した。また，多量飲酒者でナルメフェンは安全で，忍容性は良好であった。

2.7.6.5.10.4 付録

(1) 有害事象

表 2.7.6.5.10-11　有害事象の器官別大分類（ITT）

System organ class	95% CI for proportion		Total		
			Events	Subjects	
	Low	High	N	%	N
全身障害および投与局所様態	54.7%	78.6%	96	66.7%	40
胃腸障害	40.7%	66.0%	55	53.3%	32
神経系障害	39.0%	64.3%	52	51.7%	31
精神障害	27.6%	52.4%	37	40.0%	24
筋骨格系および結合組織障害	22.9%	47.1%	24	35.0%	21
皮膚および皮下組織障害	12.6%	34.0%	17	23.3%	14
感染症および寄生虫症	3.5%	19.8%	8	11.7%	7
呼吸器、胸郭および縦隔障害	3.5%	19.8%	7	11.7%	7
傷害、中毒および処置合併症			6	8.3%	5
眼障害			5	6.7%	4
代謝および栄養障害			5	8.3%	5
心臓障害			3	5.0%	3
腎および尿路障害			3	3.3%	2
生殖系および乳房障害			3	3.3%	2
血液およびリンパ系障害			2	3.3%	2
臨床検査			2	3.3%	2
血管障害			2	3.3%	2
耳および迷路障害			1	1.7%	1
外科および内科処置			1	1.7%	1

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CI: confidence interval

＜資料番号 5.3.5.2-02：Text Table 30＞

表 2.7.6.5.10-12　すべての有害事象（ITT）

	Number of patients		Total events
Preferred term	N	%	N
ANY EVENT	57	95.0%	329
倦怠感	23	38.3%	35
インフルエンザ様疾患	15	25.0%	24
嘔気	17	28.3%	20
疲労	13	21.7%	18
頭痛NOS	15	25.0%	17
不眠症	14	23.3%	17
浮動性めまい（回転性眩暈を除く）	12	20.0%	14
嘔吐NOS	10	16.7%	11
浮動性めまい	7	11.7%	9
多汗	9	15.0%	9
下痢NOS	6	10.0%	7
腹痛NOS	5	8.3%	5
無感情	5	8.3%	5
食欲減退NOS	5	8.3%	5
悪寒	3	5.0%	5
関節痛	4	6.7%	4
背部痛	4	6.7%	4
消化不良	4	6.7%	4
筋硬直	3	5.0%	4
眼部不快感	3	5.0%	4
そう痒症NOS	3	5.0%	4
下肢静止不能症候群	4	6.7%	4
アルコールによる宿酔	3	5.0%	3
うつ病NOS	3	5.0%	3
呼吸困難NOS	3	5.0%	3
四肢痛	3	5.0%	3
皮疹NOS	3	5.0%	3
圧迫感NOS	3	5.0%	3
頻尿	2	3.3%	3
胸部圧迫感	2	3.3%	2
便秘	2	3.3%	2
咳嗽	2	3.3%	2
易刺激性	2	3.3%	2
リビドー減退	2	3.3%	2
非偶発的過量投与	1	1.7%	2
疼痛NOS	1	1.7%	2
発熱	2	3.3%	2
アレルギー性鼻炎NOS	2	3.3%	2
副鼻腔炎NOS	2	3.3%	2
睡眠時無呼吸症候群	1	1.7%	2
腹部膨満	1	1.7%	1
激越	1	1.7%	1
アルコールの解毒	1	1.7%	1
貧血NOS	1	1.7%	1

表 2.7.6.5.10-12　すべての有害事象（ITT）（続き）

	Number of patients		Total events
Preferred term	N	%	N
足関節部骨折	1	1.7%	1
不安NEC	1	1.7%	1
不整脈NOS	1	1.7%	1
感染性関節炎NOS	1	1.7%	1
関節症NOS	1	1.7%	1
血圧上昇	1	1.7%	1
急性気管支炎NOS	1	1.7%	1
滑液包炎	1	1.7%	1
鎖骨骨折	1	1.7%	1
結膜充血	1	1.7%	1
妄想NOS	1	1.7%	1
注意力障害	1	1.7%	1
口内乾燥	1	1.7%	1
勃起機能不全NOS	1	1.7%	1
眼瞼浮腫	1	1.7%	1
異常感	1	1.7%	1
冷感	1	1.7%	1
熱感	1	1.7%	1
線維筋痛	1	1.7%	1
胃腸炎NOS	1	1.7%	1
高血圧NOS	1	1.7%	1
感覚減退	1	1.7%	1
口唇感覚鈍麻	1	1.7%	1
椎間板変性症NOS	1	1.7%	1
関節靭帯断裂	1	1.7%	1
臨床検査異常NOS	1	1.7%	1
月経障害NOS	1	1.7%	1
片頭痛NOS	1	1.7%	1
筋痙攣	1	1.7%	1
筋脱力NOS	1	1.7%	1
筋骨格痛	1	1.7%	1
爪真菌感染NOS	1	1.7%	1
悪夢	1	1.7%	1
動悸	1	1.7%	1
パニック障害NOS	1	1.7%	1
咽喉頭疼痛	1	1.7%	1
肺炎NOS	1	1.7%	1
術後創感染	1	1.7%	1
月経前症候群	1	1.7%	1
Restless legs syndrome	1	1.7%	1
肋骨骨折	1	1.7%	1
重感	1	1.7%	1
会話障害	1	1.7%	1
腫脹NOS	1	1.7%	1
頻脈NOS	1	1.7%	1
口渇	1	1.7%	1

表 2.7.6.5.10-12　すべての有害事象（ITT）（続き）

	Number of patients		Total events
Preferred term	N	%	N
血小板減少症	1	1.7%	1
血栓症NOS	1	1.7%	1
耳鳴	1	1.7%	1
舌障害NOS	1	1.7%	1
舌浮腫	1	1.7%	1
振戦	1	1.7%	1
脱力	1	1.7%	1

MedDRA/J Version 4.0

＜資料番号 5.3.5.2-02：14.3.1.1＞

(2) 重症度別有害事象

表 2.7.6.5.10-13 重症度別有害事象及び副作用（ITT）

SOC term	Number of patients		95% CI for proportion		Severity of events			Causality of events			Total events
Preferred term	N	%	Lower	Upper	Mild	Moderate	Severe	Unlike	Possible	Probable	N
血液およびリンパ系障害	2	3.3%			1	1	0	2	0	0	2
貧血NOS	1	1.7%			1	0	0	1	0	0	1
血小板減少症	1	1.7%			0	1	0	1	0	0	1
心臓障害	3	5.0%			2	1	0	1	2	0	3
不整脈NOS	1	1.7%			1	0	0	0	1	0	1
動悸	1	1.7%			0	1	0	0	1	0	1
頻脈NOS	1	1.7%			1	0	0	1	0	0	1
耳および迷路障害	1	1.7%			0	1	0	0	1	0	1
耳鳴	1	1.7%			0	1	0	0	1	0	1
眼障害	4	6.7%			4	1	0	2	3	0	5
結膜充血	1	1.7%			1	0	0	1	0	0	1
眼部不快感	3	5.0%			3	1	0	1	3	0	4
胃腸障害	32	53.3%	40.7%	66.0%	28	19	8	12	31	12	55
腹部膨満	1	1.7%			0	1	0	1	0	0	1
腹痛NOS	5	8.3%			3	2	0	1	4	0	5
便秘	2	3.3%			2	0	0	0	2	0	2
下痢NOS	6	10.0%	2.4%	17.6%	6	0	1	4	2	1	7
口内乾燥	1	1.7%			0	1	0	0	0	1	1
消化不良	4	6.7%			2	2	0	3	1	0	4
口唇感覚鈍麻	1	1.7%			1	0	0	0	1	0	1
嘔気	17	28.3%	16.9%	39.7%	9	8	3	1	14	5	20
咽喉頭疼痛	1	1.7%			0	0	1	0	1	0	1
舌障害NOS	1	1.7%			1	0	0	0	0	1	1
舌浮腫	1	1.7%			1	0	0	1	0	0	1
嘔吐NOS	10	16.7%	7.2%	26.1%	3	5	3	1	6	4	11

表 2.7.6.5.10-13　重症度別有害事象及び副作用（ITT）（続き）

SOC term	Number of patients		95% CI for proportion		Severity of events			Causality of events			Total events
Preferred term	N	%	Lower	Upper	Mild	Moderate	Severe	Unlike	Possible	Probable	N
全身障害および投与局所様態	40	66.7%	54.7%	78.6%	51	36	9	29	58	9	96
胸部圧迫感	2	3.3%			1	1	0	0	1	1	2
疲労	13	21.7%	11.2%	32.1%	7	8	3	1	15	2	18
異常感	1	1.7%			0	1	0	0	1	0	1
冷感	1	1.7%			1	0	0	1	0	0	1
熱感	1	1.7%			1	0	0	0	1	0	1
インフルエンザ様疾患	15	25.0%	14.0%	36.0%	17	7	0	24	0	0	24
倦怠感	23	38.3%	26.0%	50.6%	21	12	2	2	30	3	35
疼痛NOS	1	1.7%			0	2	0	0	2	0	2
発熱	2	3.3%			1	1	0	1	1	0	2
悪寒	3	5.0%			1	3	1	0	5	0	5
圧迫感NOS	3	5.0%			1	0	2	0	1	2	3
口渇	1	1.7%			0	0	1	0	0	1	1
脱力	1	1.7%			0	1	0	0	1	0	1
感染症および寄生虫症	7	11.7%	3.5%	19.8%	2	6	0	8	0	0	8
感染性関節炎NOS	1	1.7%			0	1	0	1	0	0	1
急性気管支炎NOS	1	1.7%			0	1	0	1	0	0	1
胃腸炎NOS	1	1.7%			1	0	0	1	0	0	1
爪真菌感染NOS	1	1.7%			1	0	0	1	0	0	1
肺炎NOS	1	1.7%			0	1	0	1	0	0	1
術後創感染	1	1.7%			0	1	0	1	0	0	1
副鼻腔炎NOS	2	3.3%			0	2	0	2	0	0	2

表 2.7.6.5.10-13　重症度別有害事象及び副作用（ITT）（続き）

SOC term	Number of patients		95% CI for proportion		Severity of events			Causality of events			Total events
Preferred term	N	%	Lower	Upper	Mild	Moderate	Severe	Unlike	Possible	Probable	N
傷害、中毒および処置合併症	5	8.3%			0	4	2	6	0	0	6
足関節部骨折	1	1.7%			0	0	1	1	0	0	1
鎖骨骨折	1	1.7%			0	1	0	1	0	0	1
関節靭帯断裂	1	1.7%			0	1	0	1	0	0	1
非偶発的過量投与	1	1.7%			0	1	1	2	0	0	2
肋骨骨折	1	1.7%			0	1	0	1	0	0	1
臨床検査	2	3.3%			0	1	1	2	0	0	2
血圧上昇	1	1.7%			0	1	0	1	0	0	1
臨床検査異常NOS	1	1.7%			0	0	1	1	0	0	1
代謝および栄養障害	5	8.3%			3	2	0	0	5	0	5
食欲減退NOS	5	8.3%			3	2	0	0	5	0	5
筋骨格系および結合組織障害	21	35.0%	22.9%	47.1%	10	13	1	17	6	1	24
関節痛	4	6.7%			1	3	0	4	0	0	4
関節症NOS	1	1.7%			0	1	0	1	0	0	1
背部痛	4	6.7%			2	2	0	4	0	0	4
滑液包炎	1	1.7%			0	1	0	1	0	0	1
線維筋痛	1	1.7%			0	1	0	0	1	0	1
椎間板変性症NOS	1	1.7%			0	1	0	1	0	0	1
筋痙攣	1	1.7%			1	0	0	0	1	0	1
筋硬直	3	5.0%			1	2	1	0	3	1	4
筋脱力NOS	1	1.7%			0	1	0	0	1	0	1
筋骨格痛	1	1.7%			1	0	0	1	0	0	1
四肢痛	3	5.0%			2	1	0	3	0	0	3
重感	1	1.7%			1	0	0	1	0	0	1
腫脹NOS	1	1.7%			1	0	0	1	0	0	1

表 2.7.6.5.10-13　重症度別有害事象及び副作用（ITT）（続き）

SOC term	Number of patients		95% CI for proportion		Severity of events			Causality of events			Total events
Preferred term	N	%	Lower	Upper	Mild	Moderate	Severe	Unlike	Possible	Probable	N
神経系障害	31	51.7%	39.0%	64.3%	32	15	5	13	34	5	52
注意力障害	1	1.7%			1	0	0	0	1	0	1
浮動性めまい	7	11.7%	3.5%	19.8%	5	4	0	0	8	1	9
浮動性めまい（回転性眩暈を除く）	12	20.0%	9.9%	30.1%	10	3	1	3	10	1	14
頭痛NOS	15	25.0%	14.0%	36.0%	10	6	1	6	10	1	17
感覚減退	1	1.7%			1	0	0	0	1	0	1
片頭痛NOS	1	1.7%			0	0	1	0	1	0	1
下肢静止不能症候群	4	6.7%			2	0	2	2	1	1	4
Restless legs syndrome	1	1.7%			1	0	0	0	0	1	1
睡眠時無呼吸症候群	1	1.7%			1	1	0	2	0	0	2
会話障害	1	1.7%			0	1	0	0	1	0	1
振戦	1	1.7%			1	0	0	0	1	0	1
精神障害	24	40.0%	27.6%	52.4%	16	17	4	13	22	2	37
激越	1	1.7%			1	0	0	0	1	0	1
アルコールによる宿酔	3	5.0%			3	0	0	3	0	0	3
不安NEC	1	1.7%			0	1	0	1	0	0	1
無感情	5	8.3%			4	1	0	4	1	0	5
妄想NOS	1	1.7%			0	1	0	0	1	0	1
うつ病NOS	3	5.0%			1	2	0	3	0	0	3
不眠症	14	23.3%	12.6%	34.0%	4	9	4	0	15	2	17
易刺激性	2	3.3%			0	2	0	1	1	0	2
リビドー減退	2	3.3%			2	0	0	0	2	0	2
悪夢	1	1.7%			1	0	0	0	1	0	1
パニック障害NOS	1	1.7%			0	1	0	1	0	0	1
腎および尿路障害	2	3.3%			1	2	0	0	3	0	3
頻尿	2	3.3%			1	2	0	0	3	0	3

表 2.7.6.5.10-13　重症度別有害事象及び副作用（ITT）（続き）

SOC term	Number of patients		95% CI for proportion		Severity of events			Causality of events			Total events
Preferred term	N	%	Lower	Upper	Mild	Moderate	Severe	Unlike	Possible	Probable	N
生殖系および乳房障害	2	3.3%			3	0	0	3	0	0	3
勃起機能不全NOS	1	1.7%			1	0	0	1	0	0	1
月経障害NOS	1	1.7%			1	0	0	1	0	0	1
月経前症候群	1	1.7%			1	0	0	1	0	0	1
呼吸器、胸郭および縦隔障害	7	11.7%	3.5%	19.8%	4	2	1	5	1	1	7
咳嗽	2	3.3%			1	1	0	2	0	0	2
呼吸困難NOS	3	5.0%			2	0	1	1	1	1	3
アレルギー性鼻炎NOS	2	3.3%			1	1	0	2	0	0	2
皮膚および皮下組織障害	14	23.3%	12.6%	34.0%	5	9	3	1	14	2	17
眼瞼浮腫	1	1.7%			1	0	0	0	1	0	1
そう痒症NOS	3	5.0%			0	2	2	0	3	1	4
皮疹NOS	3	5.0%			2	1	0	1	2	0	3
多汗	9	15.0%	6.0%	24.0%	2	6	1	0	8	1	9
外科および内科処置	1	1.7%			0	1	0	1	0	0	1
アルコールの解毒	1	1.7%			0	1	0	1	0	0	1
血管障害	2	3.3%			0	2	0	2	0	0	2
高血圧NOS	1	1.7%			0	1	0	1	0	0	1
血栓症NOS	1	1.7%			0	1	0	1	0	0	1

MedDRA/J Version 4.0

CI: confidence interval

＜資料番号 5.3.5.2-02：14.3.1.2＞

(3) 重篤な有害事象一覧表

表 2.7.6.5.10-14　重篤及び重要な有害事象一覧表（ITT）

Patient	SAE	SOC-term	Preferred term	Adverse events	Relationship to study drug	Severity	Action study	Medication	Start date (DDMMMYYYY)	Ongoing at week 28	End date (DDMMMYYYY)	Outcome
[redacted]	NO	胃腸障害	嘔気	nausea	PROBABLE	MILD	DIVIDED DOSE		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MODERATE	DISCONTINUED	TEMPORARILY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	皮膚および皮下組織障害	そう痒症NOS	itching	POSSIBLE	SEVERE	DISCONTINUED	TEMPORARILY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	神経系障害	浮動性めまい（回転性眩暈を除く）	dizziness	POSSIBLE	MILD	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	全身障害および投与局所様態	悪寒	chills	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	皮膚および皮下組織障害	多汗	sweating	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	眼障害	眼部不快感	unpleasant feeling in the eyes	POSSIBLE	MILD	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	精神障害	激越	agitation	POSSIBLE	MILD	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	神経系障害	浮動性めまい	lightheadedness	POSSIBLE	MILD	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]	ONGOING		NOT YET KNOWN
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MODERATE	DOSAGE REDUCED		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MODERATE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	胃腸障害	嘔気	nausea	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]	ONGOING		NOT YET KNOWN

表 2.7.6.5.10-14　重篤及び重要な有害事象一覧表（ITT）（続き）

Pat-ient	SAE	SOC-term	Preferred term	Adverse events	Relationship to study drug	Severity	Action study	Medication	Start date (DDMMMYYYY)	Ongoing at week 28	End date (DDMMMYYYY)	Outcome
[redacted]	NO	胃腸障害	嘔吐NOS	vomiting	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	筋骨格系および結合組織障害	筋硬直	muscle tension (lihasj?nnityst?, -kouristeluja)	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	皮膚および皮下組織障害	多汗	sweating	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	神経系障害	下肢静止不能症候群	feeling you have to stretch all the time	PROBABLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	胃腸障害	嘔吐NOS	vomiting	PROBABLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	精神障害	不眠症	insomnia	PROBABLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	神経系障害	頭痛NOS	headache	UNLIKELY	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	全身障害および投与局所様態	疲労	fatigue	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	精神障害	不眠症	insomnia	POSSIBLE	SEVERE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MODERATE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	悪寒	chills	POSSIBLE	SEVERE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE

表 2.7.6.5.10-14　重篤及び重要な有害事象一覧表（ITT）（続き）

Pat-ient	SAE	SOC-term	Preferred term	Adverse events	Relationship to study drug	Severity	Action study	Medication	Start date (DDMMMYYYY)	Ongoing at week 28	End date (DDMMMYYYY)	Outcome
[redacted]	NO	神経系障害	振戦	tremor	POSSIBLE	MILD	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	疲労	fatigue	POSSIBLE	MILD	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	SEVERE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	全身障害および投与局所様態	疲労	fatigue	POSSIBLE	MODERATE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	全身障害および投与局所様態	悪寒	chills	POSSIBLE	MODERATE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		RESOLVED WITHOUT SEQUELAE
	NO	筋骨格系および結合組織障害	筋硬直	muscle tension	POSSIBLE	MODERATE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	神経系障害	下肢静止不能症候群	need to stretch legs time after time	POSSIBLE	SEVERE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MODERATE	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN

表 2.7.6.5.10-14　重篤及び重要な有害事象一覧表（ITT）（続き）

Pat-ient	SAE	SOC-term	Preferred term	Adverse events	Relationship to study drug	Severity	Action study	Medication	Start date (DDMMMYYYY)	Ongoing at week 28	End date (DDMMMYYYY)	Outcome
[redacted]	NO	胃腸障害	嘔気	nausea	PROBABLE	SEVERE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	胃腸障害	嘔吐NOS	vomaiting	PROBABLE	SEVERE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	神経系障害	浮動性めまい（回転性眩暈を除く）	dizziness	PROBABLE	SEVERE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	疲労	fatigue	PROBABLE	SEVERE	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	胃腸障害	嘔気	nausea	PROBABLE	MILD	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]	ONGOING		NOT YET KNOWN
[redacted]	NO	呼吸器、胸郭および縦隔障害	呼吸困難NOS	difficulties in breathing.	PROBABLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	圧迫感NOS	Pressure in throat	PROBABLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	胃腸障害	嘔気	Nausea	PROBABLE	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	全身障害および投与局所様態	脱力	weakness	POSSIBLE	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	胸部圧迫感	pressure in the chest.	POSSIBLE	MILD	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE

表 2.7.6.5.10-14　重篤及び重要な有害事象一覧表（ITT）（続き）

Pat-ient	SAE	SOC-term	Preferred term	Adverse events	Relationship to study drug	Severity	Action study	Medication	Start date (DDMMMYYYY)	Ongoing at week 28	End date (DDMMMYYYY)	Outcome
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MILD	DOSAGE REDUCED		[redacted]20[redacted]	ONGOING		NOT YET KNOWN
[redacted]	NO	腎および尿路障害	頻尿	Acut temporary need to urinate.	POSSIBLE	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	胃腸障害	腹痛NOS	Abdominal pain	POSSIBLE	MILD	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	胃腸障害	嘔吐NOS	vomiting	POSSIBLE	MILD	DIVIDED DOSE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MILD	DOSAGE REDUCED		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	YES	傷害、中毒および処置合併症	非偶発的過量投与	The patient took an excessive amount of alcohol and clonazepam, called the ambulance and went to hospital for observatio	UNLIKELY	MODERATE	NONE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	YES	傷害、中毒および処置合併症	非偶発的過量投与	The patient took an excessive amount of alcohol and tablets of clonatsepam after a quarrel with his girlfriend.He was ta	UNLIKELY	SEVERE	NONE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	胃腸障害	腹部膨満	The feeling oh heaviness in the stomach.	UNLIKELY	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	血液およびリンパ系障害	血小板減少症	The amount of thrombocytes was falling.	UNLIKELY	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]	ONGOING		NOT YET KNOWN
	NO	臨床検査	臨床検査異常NOS	deterioration of laboratory values	UNLIKELY	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]	ONGOING		NOT YET KNOWN

表 2.7.6.5.10-14　重篤及び重要な有害事象一覧表（ITT）（続き）

Patient	SAE	SOC-term	Preferred term	Adverse events	Relationship to study drug	Severity	Action study	Medication	Start date (DDMMMYYYY)	Ongoing at week 28	End date (DDMMMYYYY)	Outcome
[redacted]	NO	全身障害および投与局所様態	圧迫感NOS	pressure in the throath	PROBABLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	胃腸障害	咽喉頭疼痛	pain in throat	POSSIBLE	SEVERE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	眼障害	眼部不快感	pressure in eyes	POSSIBLE	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
	NO	全身障害および投与局所様態	胸部圧迫感	Chest pressure	PROBABLE	MODERATE	DISCONTINUED	PERMANENTLY	[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MILD	DOSAGE REDUCED		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	NO	全身障害および投与局所様態	倦怠感	malaise	POSSIBLE	MILD	DOSAGE REDUCED		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE
[redacted]	YES	傷害、中毒および処置合併症	足関節部骨折	Broken left ankle	UNLIKELY	SEVERE	NONE		[redacted]20[redacted]		[redacted]20[redacted]	IMPROVING
	YES	感染症および寄生虫症	術後創感染	The wound due to operation on left ankle infected	UNLIKELY	MODERATE	NONE		[redacted]20[redacted]		[redacted]20[redacted]	RESOLVED WITHOUT SEQUELAE

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＜資料番号 5.3.5.2-02：14.3.2 より作成＞