2.7.6.20.2 被験者の内訳

Core Study における被験者の内訳を表 2.7.6.20-4 に示した。

本治験では 214 例がスクリーニングされ，うち 63 例が本治験に登録され無作為化された。このうち 1 例は誤って無作為化された被験者（5 mg 群）であり，当該被験者は治験薬を投与されなかった。残り 62 例は Core Study で規定された 4 週間の治験薬投与を完了した。

表 2.7.6.20-4　被験者の内訳（国際共同 202 試験，Core Study）

	プラセボ群	レンボレキサント投与群				
		2.5 mg 群	5 mg 群	10 mg 群	15 mg 群	合計
無作為化例	12	12	14	13	12	51
未投与例	0	0	1	0	0	1
投与例	12 (100.0)	12 (100.0)	13 (100.0)	13 (100.0)	12 (100.0)	50 (100.0)
完了例	12 (100.0)	12 (100.0)	13 (100.0)	13 (100.0)	12 (100.0)	50 (100.0)
中止例	0	0	0	0	0	0

数字は例数，（　）内は投与例に対する割合（%）

（添付資料 5.3.5.4.1 の Table 7 を引用）

継続期には 25 例（Core Study の投与群別の例数はプラセボ 3 例，2.5 mg 群 6 例，5 mg 群 5 例，10 mg 群 6 例，15 mg 群 5 例）が登録された。これらの被験者の本治験全体（Core Study 及び継続期のデータカットオフ日 2019 年 1 月 11 日まで）における最頻投与量は，≤5 mg（すなわち 2.5 mg 又は 5 mg）が 5 例，10 mg が 15 例，15 mg が 5 例であった。データカットオフ時点で 10 例が治験を中止しており，中止の主な理由は被験者都合が 4 例，有害事象及び効果不十分が各 2 例，同意撤回及び介護者喪失が各 1 例であった。

2.7.6.20.3 解析対象集団

Core Study においては，治験薬が投与された 62 例（プラセボ群 12 例，2.5 mg 群 12 例，5 mg 群 13 例，10 mg 群 13 例，15 mg 群 12 例）の全例が安全性解析対象集団，FAS 及び PK/PD 解析対象集団に採用された。未投与例 1 例はいずれの解析対象集団にも採用されなかった。なお，PK 解析対象集団には，レンボレキサント投与例のうち，薬物動態解析用の血液検体を Visit 5 で採取されなかった 1 例（2.5 mg 群）を除いた 49 例が採用された。

継続期においては，継続期に登録されてレンボレキサントを投与された 25 例全例が安全性解析対象集団に採用された。

2.7.6.20.4 被験者背景

Core Study における FAS（安全性解析対象集団と同一）の被験者背景の要約を表 2.7.6.20-5 に示した。

5 投与群における被験者背景は概して類似していたが，女性の割合は 15 mg 群（83.3%）で他の投与群（46.2%～61.5%）と比べてやや高かった。5 投与群における apnea-hypopnea index（AHI）の中央値は 3.60～7.05 イベント／時間であり，軽度の睡眠時無呼吸（5 イベント／時間以上 15 イベント／時間未満）を有する被験者が本治験に多く組み入れられていた。人種別では，日本人は白人に次いで多く，プラセボ群，2.5 mg 群，5 mg 群及び 15 mg 群に各 2 例，10 mg 群に 3 例が割り付けられた。なお，継続期の被験者背景は Core Study と大きく異ならなかった。

表 2.7.6.20-5　被験者背景（安全性解析対象集団）（国際共同 202 試験，Core Study）

	プラセボ群（12 例）	レンボレキサント投与群			
		2.5 mg 群（12 例）	5 mg 群（13 例）	10 mg 群（13 例）	15 mg 群（12 例）	合計（50 例）
年齢（歳）[a]						
例数	12	12	13	13	12	50
平均値（標準偏差）	75.3 (6.15)	76.5 (6.32)	76.9 (7.98)	71.8 (7.05)	71.9 (6.11)	74.3 (7.16)
中央値	75.5	76.0	81.0	71.0	73.5	74.0
最小値，最大値	65, 84	67, 89	64, 87	64, 85	64, 81	64, 89
年齢分類，例数(%)						
60～64 歳	0	0	1 (7.7)	1 (7.7)	2 (16.7)	4 (8.0)
65～74 歳	4 (33.3)	4 (33.3)	4 (30.8)	9 (69.2)	4 (33.3)	21 (42.0)
75～84 歳	8 (66.7)	7 (58.3)	7 (53.8)	2 (15.4)	6 (50.0)	22 (44.0)
85～90 歳	0	1 (8.3)	1 (7.7)	1 (7.7)	0	3 (6.0)
性別，例数(%)						
男性	5 (41.7)	6 (50.0)	5 (38.5)	7 (53.8)	2 (16.7)	20 (40.0)
女性	7 (58.3)	6 (50.0)	8 (61.5)	6 (46.2)	10 (83.3)	30 (60.0)
人種，例数(%)						
White	8 (66.7)	9 (75.0)	8 (61.5)	9 (69.2)	9 (75.0)	35 (70.0)
Black or African American	2 (16.7)	1 (8.3)	2 (15.4)	1 (7.7)	1 (8.3)	5 (10.0)
Japanese	2 (16.7)	2 (16.7)	2 (15.4)	3 (23.1)	2 (16.7)	9 (18.0)
Other	0	0	1 (7.7)	0	0	1 (2.0)
身長（cm）						
例数	12	12	13	13	12	50
平均値（標準偏差）	166.86 (14.449)	162.46 (10.138)	162.98 (11.322)	165.10 (8.779)	154.38 (13.749)	161.34 (11.507)
体重（kg）						
例数	12	12	13	13	12	50
平均値（標準偏差）	81.89 (20.217)	69.44 (15.521)	65.58 (12.236)	72.41 (19.812)	70.33 (18.417)	69.42 (16.416)
Body mass index (kg/m^2)						
例数	12	12	13	13	12	50
平均値（標準偏差）	29.34 (6.243)	26.11 (4.208)	24.66 (3.757)	26.30 (5.663)	30.45 (11.578)	26.82 (7.074)
Apnea-hypopnea index						
例数	12	12	13	12	11	48
欠測例[b]	0	0	0	1	1	2
平均値（標準偏差）	6.28 (3.963)	7.03 (4.185)	5.06 (4.134)	5.08 (4.045)	6.72 (5.389)	5.94 (4.395)
中央値	5.35	7.05	3.60	5.10	5.40	5.30
最小値，最大値	0, 13.7	0.2, 13.6	0, 12.7	0, 13.4	0, 14.9	0, 14.9

BMI = body mass index.
a: 同意取得時の年齢
b: 当該被験者についても apnea-hypopnea index が選択基準を満たすことを確認した。

（添付資料 5.3.5.4.1 の Table 9 を引用）

2.7.6.20.5 治験薬の暴露状況

Core Study では，治験薬を投与された全被験者で服薬コンプライアンスが 89%～118%であった。約 30%の被験者で服薬コンプライアンスが 100%を超過していたが，これは本来返却すべき治験薬を紛失してしまった等の理由によるものであり，過量投与は報告されなかった。各投与群の暴露期間の中央値は 28.0～28.5 日であり，全ての被験者が Core Study で予定された治験薬の投与を完了した。

本治験の継続期投与例（安全性解析対象集団）において，Core Study を含むレンボレキサント投与時（On treatment）を対象とした解析では，最頻投与量群別の服薬コンプライアンスの中央値は≤5 mg 群で 73.1%（範囲 64%～99%），10 mg 群で 96.2%（範囲 70%～101%）及び 15 mg 群で 100.1%（73%及び 101%）であった。継続期においても過量投与は報告されなかった。最頻投与量群別の暴露期間の中央値は≤5 mg 群で 119.0 日（範囲 28～256 日），10 mg 群で 288.0 日（範囲 89～336 日）及び 15 mg 群で 265.0 日（41～324 日）であった。

2.7.6.20.6 薬物動態の結果

血漿中レンボレキサント濃度測定のための採血は Visit 5 で実施し，特定の認知症治療剤（ドネペジル，メマンチン及びガランタミン）濃度測定のための採血は Visit 3 及び Visit 5 で実施した。ドネペジル及びメマンチンの血漿中濃度の要約統計量はレンボレキサント投与前後で類似していた。また，ガランタミンに関しては，併用している被験者が 1 名だったため，要約統計量が算出できず，レンボレキサント投与前後での比較はできなかった。

なお，本治験で得られた血漿中レンボレキサント濃度は，他試験のデータと併合し，母集団薬物動態／薬力学解析に利用した。

2.7.6.20.7 有効性の結果

本治験では，レンボレキサントの投与量として 2.5 mg，5 mg，10 mg 及び 15 mg を検討した。このうち，5 mg では睡眠，覚醒，概日リズム関連の各アクチグラフィパラメータにおいて改善が認められた。なお，睡眠又は覚醒に関連するアクチグラフィパラメータについては，事前に調査した上で規定した「習慣的な夜間睡眠時間帯（habitual time）」に基づく解析に加え，「実際に記録された夜間睡眠時間帯（logged time）」に基づく解析も実施した。本治験の総括報告書では，このうち logged time に基づく解析結果を主に示し，本項にもその結果を示した。以下に各評価項目の結果の概要を示す。

<u>睡眠関連の評価項目</u>

actigraphy sleep efficiency（aSE）：投与最終週における平均 aSE のベースラインからの変化量について，MCP-Mod 手法を用いて用量反応関係を検討したが，傾向性に対する検定結果が統計学的に有意となったモデルは無かった。ベースライン時の各投与群の平均 aSE は 76.34%～78.45%であった。aSE のベースラインからの変化量の最小二乗平均のプラセボ群との差（95%信頼区間）は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 3.177%（–0.741%，7.096%），2.802%（–1.119%，6.723%），–0.960%（–4.777%，2.857%），及び 0.713%（–3.160%，4.585%）であった。レンボレキサント 2.5 mg 群及び 5 mg 群では，4 週間の投与期

間中に一貫して夜間の睡眠効率の増加が認められた。

sleep fragmentation index（SFI）：ベースライン時の各投与群の平均 SFI は 50.07～58.51 であった。SFI のベースラインからの変化量の最小二乗平均のプラセボ群との差（95%信頼区間）は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ–5.098（–12.240，2.045），–6.105（–13.332，1.122），0.680（–6.262，7.623），及び–3.140（–10.178，3.897）であった（低いほど，夜間の睡眠の断片化が少なく連続した睡眠であることを示す）。レンボレキサント 2.5 mg 群，5 mg 群及び 15 mg 群では，4 週間の投与期間中に一貫してより連続した睡眠が認められた。

mean duration of wake bouts：ベースライン時の各投与群の平均値は 20.32～21.94 であった。mean duration of wake bouts のベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 1.932，3.386，1.337 及び 4.320 であった（高いほど wake bouts が長いことを示す）。aSE や SFI と異なり，いずれの投与量においても一貫した改善は認められなかった。

<u>覚醒関連の評価項目</u>

actigraphy wake efficiency（aWE）：投与最終週における平均 aWE のベースラインからの変化量について，MCP-Mod 手法を用いて用量反応関係を検討したが，傾向性に対する検定結果が統計学的に有意となったモデルは無かった。ベースライン時の各投与群の平均 aWE は 67.19%～72.53%であった。aSE のベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ–3.437%，1.458%，–4.994%，及び–2.593%であった。レンボレキサント 5 mg 群では，4 週間の投与期間中に一貫して日中の覚醒効率の増加が認められた。

wake fragmentation index（WFI）：ベースライン時の各投与群の平均 WFI は 85.72～94.76 であった。WFI のベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 4.845，–3.872，6.776 及び 3.017 であった（低いほど，日中の覚醒の断片化が少なく連続した覚醒であることを示す）。レンボレキサント 5 mg 群では，4 週間の投与期間中に一貫してより連続した覚醒が認められた。

mean duration of sleep bouts：ベースライン時の各投与群の平均値は 18.36～23.30 であった。mean duration of sleep bouts のベースラインからの変化量の最小二乗平均のプラセボ群との差（95%信頼区間）は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 0.063（–2.452，2.579），–0.238（–2.817，2.342），–0.293（–2.745，2.160）及び–1.557（–4.113，1.000）であった（高いほど sleep bouts が長いことを示す）。レンボレキサント 5 mg 群，10 mg 群及び 15 mg 群では，4 週間の投与期間中に一貫して日中の 10 分間以上連続した居眠りの短縮が認められた。

概日リズム関連の評価項目

interdaily stability（IS）：睡眠－覚醒リズムの日間の安定性の指標であり，0（安定性が低い）から1（安定性が高い）の値をとる。ベースライン時の各投与群の平均ISは0.41～0.49であった。ISのベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント2.5 mg群，5 mg群，10 mg群及び15 mg群でそれぞれ–0.032，0.033，–0.052及び0.005であった。レンボレキサント5 mg群では，4週間の投与期間中に一貫して睡眠－覚醒リズムの日間変動の安定化が認められた。

intradaily variability（IV）：休息時間帯（rest bouts）と活動時間帯（activity bouts）の転換の数及び強さを定量的に評価したもので，値が大きいほど断片化の程度が大きいことを示す。ベースライン時の各投与群の平均IVは0.90～1.10であった。IVのベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント2.5 mg群，5 mg群，10 mg群及び15 mg群でそれぞれ0.086，–0.012，0.057及び0.025であった。レンボレキサント5 mg群では，断片化の改善が認められた。

least active 5-hour period（L5）：24時間において最も活動性の低い5時間における活動性の平均値であり，高値は不穏であることを示す。ベースライン時の各投与群の平均L5は1163.2～1490.4 activity countsであった。L5のベースラインからの変化量の最小二乗平均のプラセボ群との差（95%信頼区間）は，レンボレキサント2.5 mg群，5 mg群，10 mg群及び15 mg群でそれぞれ–389.873（–739.177，–40.569），–402.994（–751.670，–54.319），–141.026（–489.805，207.752）及び–367.845（–717.870，–17.820）activity countsであり，全てのレンボレキサント投与群で，4週間の投与期間中に一貫して夜間のより静止した状態の睡眠が認められた。さらに，レンボレキサント2.5 mg群，5 mg群及び15 mg群ではプラセボ群と比較して統計学的に有意（それぞれ，*P*=0.0294，0.0243及び0.0398）なL5の減少が認められた。

most active 10-hour period（M10）：24時間において最も活動性の高い10時間の活動性の平均値であり，低値は不活発であることを示す。ベースライン時の各投与群の平均M10は8560.4～12158.1 activity countsであった。M10のベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント2.5 mg群，5 mg群，10 mg群及び15 mg群でそれぞれ–1276.180，227.464，–620.581及び–577.820 activity countsであり，レンボレキサント5 mg群で，日中の活発な状態が認められた。

amplitude of the rest-activity rhythm（AMP）：M10及びL5の差として計算され，休息－活動リズムの振幅を示す。ベースライン時の各投与群の平均AMPは7396.9～10994.8 activity countsであった。AMPのベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント2.5 mg群，5 mg群，10 mg群及び15 mg群でそれぞれ–839.088，651.922，–447.245及び–130.603 activity countsであり，レンボレキサント5 mg群で休息－活動リズムの振幅の改善（増加）が認められた。

relative amplitude of the rest-activity rhythm（RA）：M10 及び L5 の差を M10 及び L5 の和で除した値として計算され，休息－活動リズムの相対的な振幅を示す。ベースライン時の各投与群の平均 RA は 0.73～0.82 であった。RA のベースラインからの変化量の最小二乗平均のプラセボ群との差（95%信頼区間）は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 2.0%（–3.4%，7.4%），6.0%（0.5%，11.5%），0.3%（–5.1%，5.6%）及び 5.7%（0.4%，11.0%）であり，全てのレンボレキサント投与群で休息－活動リズムの相対的な振幅の改善（増加）が認められた。さらに，レンボレキサント 5 mg 群及び 15 mg 群ではプラセボ群と比較して統計学的に有意な RA の増加が認められた（それぞれ，*P*=0.0322 及び 0.0364）。

<u>その他の有効性評価項目</u>

夜間 TST：ベースライン時の各投与群の平均夜間 TST は 399.13～415.49 分であった。夜間 TST のベースラインからの変化量の最小二乗平均のプラセボ群との差（95%信頼区間）は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ–0.586（–32.916，31.744），10.726（–21.409，42.860），–1.253（–32.857，30.352）及び 16.460（–15.654，48.574）分であり，レンボレキサント 5 mg 群及び 15 mg 群で，4 週間の投与期間中に一貫して夜間の総睡眠時間の増加が認められた。

日中 TST：ベースライン時の各投与群の平均日中 TST は 258.49～292.02 分であった。日中 TST のベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 43.585，–10.341，48.065 及び 25.591 分であり，レンボレキサント 5 mg 群で，4 週間の投与期間中に一貫して日中の総睡眠時間の減少が認められた。

CGIC-ISWRD：本治験における原データ及び本治験で実施した他の精神症状の検査のスコアを閲覧することができない独立した評価者により，ISWRD の症状に特化した全般的臨床評価を行った。CGIC-ISWRD の総合判定スコアのプラセボに対するオッズ比は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 0.50，1.00，1.00 及び 0.38 であり，用量増加に応じた改善は認められなかった。

aSE 及び aWE に基づく反跳性の睡眠－覚醒断片化：aSE に基づく睡眠効率の反跳性は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 66.7%，23.8%，23.1%，52.0%及び 50.0%の被験者に認められ，プラセボ群と比べてレンボレキサント各投与群では低かった。一方，aWE に基づく覚醒効率の反跳性は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 37.5%，47.6%，42.3%，58.3%及び 54.2%の被験者に認められ，プラセボ群と比べてレンボレキサント各投与群では高かった。

ADAS-cog：AD 患者を対象とした臨床試験で最も広く用いられている認知機能評価スケールである。0～85 点のスコアで評価し，0 点は障害なし，85 点は障害の程度が最大であることを示す。ベースラインからの変化量の最小二乗平均は，プラセボ群，レンボレキサント 2.5 mg 群，

5 mg 群，10 mg 群及び 15 mg 群で–0.33，–4.81，0.01，–1.92 及び 1.18 であり，いずれの投与群でも認知機能の明らかな悪化は認められなかった。ベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ –4.48，0.34，–1.59 及び 1.51 であり，2.5 mg 群ではプラセボ群と比較して統計学的に有意な認知機能の改善が認められた（*P*=0.0227）。なお，他の投与群については，プラセボ群との統計学的に有意な差は認められなかった。

MMSE：スクリーニングを目的として広く用いられている認知機能検査である。合計スコアは 30 点であり，スコアが高いほど認知機能障害の程度が低く，スコアが低いほど障害の程度が高いことが示唆される。ベースラインからの変化量の最小二乗平均は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群で 1.88，1.96，1.01，1.15 及び–0.27 であり，いずれの投与群でも認知機能の明らかな悪化は認められなかった。ベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 0.08，–0.86，–0.73 及び–2.14 であり，いずれの投与群においても，プラセボ群との統計学的に有意な差は認められなかった。

被験者の自己評価に基づく EQ-5D-5L VAS スコア：ヘルスケアに関する臨床評価及び経済評価に用いることのできる一般的な評価尺度であり，患者の生活の質及び嗜好／有用性に関するデータの収集に用いた。VAS スコアは，0=「想像できる最も悪い健康状態」，100=「想像できる最も良い健康状態」としたアナログスケールである。ベースラインからの変化量の最小二乗平均は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 7.38，–9.33，6.41，6.13 及び 5.93 であり，2.5 mg 群以外の投与群では，被験者は自身の健康状態を高く評価していた。なお，ベースラインからの変化量の最小二乗平均は，レンボレキサント 2.5 mg 群ではプラセボと比較して統計学的に有意に減少しており，健康状態の悪化が示唆された。

介護者の代理評価に基づく EQ-5D-5L VAS スコア：ベースラインからの変化量の最小二乗平均は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ –5.42，–3.70，–2.62，2.66 及び–0.70 であり，10 mg 群以外の投与群で介護者は患者の健康状態がやや悪化したと評価していた。ベースラインからの変化量の最小二乗平均のプラセボ群との差は，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ 1.72，2.80，8.07 及び 4.72 であり，レンボレキサント 10 mg 群では健康状態の改善が示唆された。

NPI-10 合計スコア：認知症において認められる広範な行動を頻度及び重症度の双方から評価する手法である。点数が低いほど精神神経状態が良いことを示している。ベースラインからの変化量の最小二乗平均は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ–6.50，–3.77，–2.01，–6.16 及び 0.64 であり，15 mg 群以外の投与群では精神神経状態が改善している（ただし，プラセボ群と比べて優越性は認められない）ことが示唆された。

SDI スコア：NPI のうち睡眠障害項目について評価するための 7 つの質問項目群からなる。点数が低いほど睡眠障害の程度が低いことを示している。ベースラインからの変化量の最小二乗平均は，プラセボ群，レンボレキサント 2.5 mg 群，5 mg 群，10 mg 群及び 15 mg 群でそれぞれ–0.46，–0.16，–0.30，–0.06 及び–0.59 であり，睡眠障害の状態が改善している（ただし，プラセボ群と比べて優越性は認められない）ことが示唆された。

介護者における効果

介護者におけるレンボレキサント投与の効果を評価するため，PSQI（介護者の睡眠の質及びパターン），ZBI-short form（介護者の負担）及び EQ-5D-5L（介護者の健康状態）を用いた評価を実施したが，被験者の投与群（プラセボ群及びレンボレキサント各群）で明らかな差は認められなかった。

2.7.6.20.8 安全性の結果

本治験の Core Study における有害事象の概要を表 2.7.6.20-6 に示した。

安全性解析対象集団における有害事象の発現率は，プラセボ群 33.3%（4/12 例），レンボレキサント 2.5 mg 群 25.0%（3/12 例），5 mg 群 23.1%（3/13 例），10 mg 群 30.8%（4/13 例），15 mg 群 50.0%（6/12 例）であった。副作用の発現率は，レンボレキサント 5 mg 群 7.7%（1/13 例），10 mg 群 23.1%（3/13 例），15 mg 群 33.3%（4/12 例）であり，プラセボ群及び 2.5 mg 群では副作用の発現は認められなかった。重症度が高度の有害事象は 15 mg 群で 1 例に認められた。当該被験者は Day 17 に重症度が高度の関節痛を発現した。治験薬との因果関係は医師により「関連なし」と判定された。

死亡例及び重篤な有害事象の発現は認められなかった。

表 2.7.6.20-6　有害事象の概要（安全性解析対象集団）（国際共同 202 試験，Core Study）

		レンボレキサント投与群			
	プラセボ群（12 例）	2.5 mg 群（12 例）	5 mg 群（13 例）	10 mg 群（13 例）	15 mg 群（12 例）
有害事象	4 (33.3)	3 (25.0)	3 (23.1)	4 (30.8)	6 (50.0)
副作用 [a]	0	0	1 (7.7)	3 (23.1)	4 (33.3)
重症度が高度の有害事象	0	0	0	0	1 (8.3)
重篤な有害事象	0	0	0	0	0
治験薬投与中止に至った有害事象	0	0	0	0	0

数値は発現例数，（　）内は解析対象例数（安全性解析対象集団）に対する発現率（%）
治験薬投与開始日から最終投与の 14 日後までに発現した有害事象を対象として集計した。
a: 治験薬との因果関係が「関連あり」又は因果関係の情報が欠測であった有害事象。
（添付資料 5.3.5.4.1 の Table 34 を引用）

本治験の継続期投与例（安全性解析対象集団）を対象とし，Core Study を含むレンボレキサント投与時（On treatment）における有害事象の概要を表 2.7.6.20-7 に示した。

安全性解析対象集団における有害事象の発現率は，レンボレキサント投与例全体で 56.0%（14/25 例），副作用の発現率は，20.0%（5/25 例）であった。重症度が高度の有害事象は 2 例に認められた。上述の関節痛を発現した 1 例の他，1 例が Day 106 に挫傷及び上肢骨折を発現した。いずれの事象も治験薬との因果関係は医師により「関連なし」と判定された。

死亡例は認められなかったものの，重篤な有害事象の発現が 2 例に認められた。1 例は Day 47（同日レンボレキサント 5 mg を服用）に虚血性脳卒中を発現し，入院するとともに，治験薬の投与を中止した。当該事象の重症度は中等度，治験薬との因果関係は医師により「関連なし」と判定され，Day 56 に回復が確認された。別の 1 例はレンボレキサント 10 mg を服用中の Day 188 に起立性低血圧を発現し，入院した。当該事象の重症度は中等度，治験薬との因果関係は医師により「関連なし」と判定され，Day 190 に回復が確認された。治験薬投与中止に至った有害事象は前述の虚血性脳卒中のほか，別の 1 例でレンボレキサント 5 mg を服用中に上肢骨折及び譫妄が認められた。重症度は上肢骨折が高度，譫妄が軽度であり，いずれも治験薬との因果関係は医師により「関連なし」と判定され，回復が確認された。

また，継続投与期には 4 例で減量に至った有害事象（3 例で傾眠，別の 1 例で鎮静）の発現が認められた。いずれも治験薬との因果関係は医師により「関連あり」と判定され，いずれの被験者においても投与量が 10 mg から 5 mg に減量された。このほか，1 例が治験薬投与中断に至った有害事象（性器分泌物及び性器損傷）を発現した。これらの事象の重症度はいずれも軽度，治験薬との因果関係は医師により「関連あり」と判定された。

表 2.7.6.20-7　有害事象の概要（安全性解析対象集団）（国際共同 202 試験，On Treatment）

	レンボレキサント最頻投与量			
	≤5 mg 群（5 例）	10 mg 群（15 例）	15 mg 群（5 例）	全体（25 例）
有害事象	4 (80.0)	7 (46.7)	3 (60.0)	14 (56.0)
副作用 [a]	4 (80.0)	1 (6.7)	0	5 (20.0)
重症度が高度の有害事象	1 (20.0)	0	1 (20.0)	2 (8.0)
重篤な有害事象	1 (20.0)	1 (6.7)	0	2 (8.0)
死亡	0	0	0	0
その他の重篤な有害事象	1 (20.0)	1 (6.7)	0	2 (8.0)
入院又は入院期間の延長	1 (20.0)	1 (6.7)	0	2 (8.0)
治験薬投与調節に至った有害事象	4 (80.0)	1 (6.7)	0	5 (20.0)
治験薬投与中止に至った有害事象	2 (40.0)	0	0	2 (8.0)
治験薬投与量減量に至った有害事象	4 (80.0)	0	0	4 (16.0)
治験薬投与中断に至った有害事象	0	1 (6.7)	0	1 (4.0)

数値は発現例数，（　）内は解析対象例数（安全性解析対象集団）に対する発現率（%）
本治験の継続期投与例（安全性解析対象集団）を対象に，Core Study を含むレンボレキサント投与開始日から最終投与の 14 日後までに発現した有害事象を集計した。
a: 治験薬との因果関係が「関連あり」又は因果関係の情報が欠測であった有害事象。
（添付資料 5.3.5.4.2 の Table 2 を引用）

本治験の Core Study における有害事象の発現例数（発現率）を表 2.7.6.20-8 に示した。

いずれかのレンボレキサント投与群で複数の被験者に発現した有害事象は，便秘（15 mg 群 2

例［16.7%］，10 mg群1例［7.7%］），傾眠（15 mg群2例［16.7%］，10 mg群1例［7.7%］），関節炎（15 mg群2例［16.7%］），頭痛（15 mg群2例［16.7%］）及び悪夢（10 mg群2例［15.4%］）であった。また，いずれかのレンボレキサント投与群で複数の被験者に発現した副作用は，傾眠（15 mg群2例［16.7%］，10 mg群1例［7.7%］）であった。

表 2.7.6.20-8　有害事象（安全性解析対象集団）（国際共同 202 試験，Core Study）

MedDRA SOC PT	プラセボ群 （12 例）	レンボレキサント投与群			
		2.5 mg 群 （12 例）	5 mg 群 （13 例）	10 mg 群 （13 例）	15 mg 群 （12 例）
有害事象	4 (33.3)	3 (25.0)	3 (23.1)	4 (30.8)	6 (50.0)
心臓障害	0	0	1 (7.7)	0	2 (16.7)
第一度房室ブロック	0	0	1 (7.7)	0	0
徐脈	0	0	0	0	1 (8.3)
動悸	0	0	0	0	1 (8.3)
胃腸障害	0	1 (8.3)	0	1 (7.7)	2 (16.7)
便秘	0	0	0	1 (7.7)	2 (16.7)
下痢	0	0	0	0	1 (8.3)
口内乾燥	0	0	0	0	1 (8.3)
腸閉塞	0	1 (8.3)	0	0	0
感染症および寄生虫症	3 (25.0)	1 (8.3)	2 (15.4)	0	0
気管支炎	0	0	1 (7.7)	0	0
蜂巣炎	0	1 (8.3)	0	0	0
上咽頭炎	1 (8.3)	0	1 (7.7)	0	0
眼感染	1 (8.3)	0	0	0	0
尿路感染	1 (8.3)	0	0	0	0
筋骨格系および結合組織障害	0	0	0	0	2 (16.7)
関節炎	0	0	0	0	2 (16.7)
筋骨格痛	0	0	0	0	1 (8.3)
神経系障害	0	1 (8.3)	1 (7.7)	1 (7.7)	3 (25.0)
傾眠	0	0	0	1 (7.7)	2 (16.7)
頭痛	0	0	0	0	2 (16.7)
浮動性めまい	0	1 (8.3)	0	0	0
鎮静	0	0	1 (7.7)	0	0
精神障害	0	0	1 (7.7)	2 (15.4)	0
悪夢	0	0	0	2 (15.4)	0
リビドー亢進	0	0	1 (7.7)	0	0
腎および尿路障害	1 (8.3)	0	0	0	0
腎結石症	1 (8.3)	0	0	0	0
血管障害	0	0	0	0	1 (8.3)
高血圧	0	0	0	0	1 (8.3)

MedDRA = Medical Dictionary for Regulatory Activities, PT = preferred term, SOC = system organ class.
MedDRA Version 21.0
数値は発現例数，（　）内は解析対象例数（安全性解析対象集団）に対する発現率（%）
治験薬投与開始日から最終投与の 14 日後までに発現した有害事象を対象として集計した。
（添付資料 5.3.5.4.1 の Table 35 を引用）

本治験の継続期投与例（安全性解析対象集団）25 例において，Core Study を含むレンボレキサント投与時（On treatment）に複数の被験者に発現した有害事象は，傾眠，転倒（各 3 例［12.0%］），下痢，上咽頭炎及び上気道感染（各 2 例［8.0%］）であり，複数の被験者に発現した副作用は傾眠（3 例［12.0%］）であった。

本治験の Core Study 及び継続期において，臨床検査値，バイタルサイン，心電図，eC-SSRS の結果から，臨床的に重要な異常は認められなかった。

Core Study の投与期の最初及び最後の各 3 日間における翌日の持ち越し効果の評価においては，15 mg 群においてのみ，ベースラインと比較して投与後では起床時刻後 3 時間における合計 activity counts の一貫した減少が認められ，翌朝の眠気が示唆された。ただし，投与期の最初及び最後の各 3 日間の起床時刻後 3 時間における 10 分を超える sleep bouts（睡眠）の数については，いずれの投与群でもベースラインと比較して投与後における一貫した増加又は減少は認められなかった。

2.7.6.21 付録

付録 2.7.6-1
SOC/PT 別の有害事象発現率
外国 003 試験
安全性解析対象集団

	Japanese					White	
System Organ Class Preferred Term	Placebo N = 6 n (%)	2.5 mg N = 6 n (%)	10 mg N = 6 n (%)	25 mg N = 6 n (%)	Overall-Japanese E2006 N = 18 n (%)	Placebo N = 2 n (%)	10 mg N = 6 n (%)
Subjects with any TEAE	2 (33.3)	1 (16.7)	0	2 (33.3)	3 (16.7)	1 (50.0)	3 (50.0)
胃腸障害	1 (16.7)	0	0	0	0	0	0
鼓腸	1 (16.7)	0	0	0	0	0	0
一般・全身障害および投与部位の状態	0	1 (16.7)	0	0	1 (5.6)	1 (50.0)	0
適用部位皮膚炎	0	0	0	0	0	1 (50.0)	0
疲労	0	1 (16.7)	0	0	1 (5.6)	0	0
感染症および寄生虫症	1 (16.7)	0	0	1 (16.7)	1 (5.6)	0	0
歯肉炎	0	0	0	1 (16.7)	1 (5.6)	0	0
麦粒腫	1 (16.7)	0	0	0	0	0	0
神経系障害	1 (16.7)	1 (16.7)	0	2 (33.3)	3 (16.7)	0	1 (16.7)
傾眠	1 (16.7)	1 (16.7)	0	2 (33.3)	3 (16.7)	0	1 (16.7)

N: Number of subjects dosed with each treatment (or any treatment as applicable); n: Number of subjects with adverse event; %: Calculated using the number of subjects treated with each treatment (or any treatment as applicable) as the denominator (n/N*100).
MedDRA Version 16.1

付録 2.7.6-1
SOC/PT 別の有害事象発現率
外国 003 試験
安全性解析対象集団

	Japanese					White	
System Organ Class Preferred Term	Placebo N = 6 n (%)	2.5 mg N = 6 n (%)	10 mg N = 6 n (%)	25 mg N = 6 n (%)	Overall-Japanese E2006 N = 18 n (%)	Placebo N = 2 n (%)	10 mg N = 6 n (%)
精神障害	0	0	0	1 (16.7)	1 (5.6)	0	2 (33.3)
異常な夢	0	0	0	1 (16.7)	1 (5.6)	0	2 (33.3)

N: Number of subjects dosed with each treatment (or any treatment as applicable); n: Number of subjects with adverse event; %: Calculated using the number of subjects treated with each treatment (or any treatment as applicable) as the denominator (n/N*100).
MedDRA Version 16.1

付録 2.7.6-2
SOC/PT 別の副作用発現率
外国 003 試験
安全性解析対象集団

	Japanese					White	
System Organ Class Preferred Term	Placebo N = 6 n (%)	2.5 mg N = 6 n (%)	10 mg N = 6 n (%)	25 mg N = 6 n (%)	Overall-Japanese E2006 N = 18 n (%)	Placebo N = 2 n (%)	10 mg N = 6 n (%)
Subjects with any treatment-related TEAE	2 (33.3)	1 (16.7)	0	2 (33.3)	3 (16.7)	0	3 (50.0)
胃腸障害	1 (16.7)	0	0	0	0	0	0
鼓腸	1 (16.7)	0	0	0	0	0	0
一般・全身障害および投与部位の状態	0	1 (16.7)	0	0	1 (5.6)	0	0
疲労	0	1 (16.7)	0	0	1 (5.6)	0	0
神経系障害	1 (16.7)	1 (16.7)	0	2 (33.3)	3 (16.7)	0	1 (16.7)
傾眠	1 (16.7)	1 (16.7)	0	2 (33.3)	3 (16.7)	0	1 (16.7)
精神障害	0	0	0	1 (16.7)	1 (5.6)	0	2 (33.3)
異常な夢	0	0	0	1 (16.7)	1 (5.6)	0	2 (33.3)

N: Number of subjects dosed with each treatment (or any treatment as applicable); n: Number of subjects with adverse event; %: Calculated using the number of subjects treated with each treatment (or any treatment as applicable) as the denominator (n/N*100).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly related to study drug or TEAEs with a missing causality.
MedDRA Version 16.1

付録 2.7.6-3
SOC/PT 別の有害事象発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
Subjects with any TEAE	19 (39.6)	18 (37 5)	12 (37.5)	8 (25.0)	17 (53.1)	28 (58.3)
神経系障害	10 (20.8)	13 (27 1)	8 (25.0)	6 (18.8)	12 (37.5)	22 (45.8)
傾眠	3 (6.3)	8 (16.7)	3 (9.4)	3 (9.4)	10 (31.3)	15 (31.3)
頭痛	8 (16.7)	1 (2.1)	4 (12.5)	3 (9.4)	2 (6.3)	9 (18.8)
浮動性めまい	1 (2.1)	3 (6.3)	2 (6.3)	0	0	2 (4.2)
注意力障害	0	1 (2.1)	1 (3.1)	0	0	1 (2.1)
頭部不快感	0	0	1 (3.1)	0	0	1 (2.1)
記憶障害	0	0	0	0	1 (3.1)	1 (2.1)
睡眠時麻痺	0	0	0	0	1 (3.1)	1 (2.1)
味覚異常	1 (2.1)	7 (14.6)	0	0	0	0
胃腸障害	2 (4.2)	5 (10.4)	3 (9.4)	2 (6.3)	6 (18.8)	10 (20.8)
口内乾燥	1 (2.1)	2 (4.2)	3 (9.4)	1 (3.1)	3 (9.4)	6 (12.5)
下痢	1 (2.1)	0	0	1 (3.1)	1 (3.1)	2 (4.2)
悪心	0	0	0	0	2 (6.3)	2 (4.2)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).

付録 2.7.6-3
SOC/PT 別の有害事象発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
胃腸障害 (Cont.)						
腹痛	0	1 (2.1)	0	0	0	0
上腹部痛	0	1 (2.1)	0	0	0	0
鼓腸	0	1 (2.1)	0	0	0	0
一般・全身障害および投与部位の状態	1 (2.1)	0	0	3 (9.4)	3 (9.4)	6 (12.5)
疲労	1 (2.1)	0	0	2 (6.3)	2 (6.3)	4 (8.3)
発熱	0	0	0	1 (3.1)	1 (3.1)	2 (4.2)
感染症および寄生虫症	4 (8.3)	2 (4.2)	3 (9.4)	1 (3.1)	2 (6.3)	6 (12.5)
インフルエンザ	0	0	2 (6.3)	1 (3.1)	2 (6.3)	5 (10.4)
ボレリア感染	0	0	1 (3.1)	0	0	1 (2.1)
膀胱炎	1 (2.1)	0	0	0	0	0
歯肉炎	0	1 (2.1)	0	0	0	0
鼻咽頭炎	2 (4.2)	1 (2.1)	0	0	0	0
創傷感染	1 (2.1)	0	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).

付録 2.7.6-3
SOC/PT 別の有害事象発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
筋骨格系および結合組織障害	2 (4.2)	1 (2.1)	0	0	2 (6.3)	2 (4.2)
背部痛	1 (2.1)	0	0	0	2 (6.3)	2 (4.2)
四肢痛	1 (2.1)	1 (2.1)	0	0	0	0
精神障害	1 (2.1)	3 (6.3)	2 (6.3)	0	1 (3.1)	2 (4.2)
異常な夢	0	1 (2.1)	1 (3.1)	0	1 (3.1)	2 (4.2)
性的興奮障害	0	0	1 (3.1)	0	0	1 (2.1)
落ち着きのなさ	0	0	1 (3.1)	0	0	1 (2.1)
妄想	1 (2.1)	0	0	0	0	0
易刺激性	0	2 (4.2)	0	0	0	0
皮膚および皮下組織障害	0	1 (2.1)	2 (6.3)	0	0	2 (4.2)
光線過敏性反応	0	1 (2.1)	1 (3.1)	0	0	1 (2.1)
発疹	0	0	1 (3.1)	0	0	1 (2.1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).

付録 2.7.6-3
SOC/PT 別の有害事象発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
耳および迷路障害	1 (2.1)	0	0	0	1 (3.1)	1 (2.1)
耳鳴	0	0	0	0	1 (3.1)	1 (2.1)
耳不快感	1 (2.1)	0	0	0	0	0
腎および尿路障害	0	0	0	0	1 (3.1)	1 (2.1)
腎仙痛	0	0	0	0	1 (3.1)	1 (2.1)
生殖系および乳房障害	0	0	0	0	1 (3.1)	1 (2.1)
月経困難症	0	0	0	0	1 (3.1)	1 (2.1)
呼吸器、胸郭および縦隔障害	0	1 (2.1)	1 (3.1)	0	0	1 (2.1)
口腔咽頭痛	0	0	1 (3.1)	0	0	1 (2.1)
咳嗽	0	1 (2.1)	0	0	0	0
血管障害	0	0	1 (3.1)	0	0	1 (2.1)
静脈炎	0	0	1 (3.1)	0	0	1 (2.1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).

付録 2.7.6-3
SOC/PT 別の有害事象発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
免疫系障害	1 (2.1)	1 (2.1)	0	0	0	0
過敏症	1 (2.1)	1 (2.1)	0	0	0	0
傷害、中毒および処置合併症	2 (4.2)	1 (2.1)	0	0	0	0
背部損傷	1 (2.1)	0	0	0	0	0
上顆炎	1 (2.1)	0	0	0	0	0
靭帯捻挫	1 (2.1)	0	0	0	0	0
肉離れ	0	1 (2.1)	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).

付録 2.7.6-4
SOC/PT 別の副作用発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
Subjects with any treatment-related TEAE	12 (25.0)	14 (29 2)	10 (31.3)	7 (21.9)	13 (40.6)	24 (50.0)
神経系障害	10 (20.8)	13 (27 1)	8 (25.0)	6 (18.8)	11 (34.4)	21 (43.8)
傾眠	3 (6.3)	8 (16.7)	3 (9.4)	3 (9.4)	10 (31.3)	15 (31.3)
頭痛	8 (16.7)	1 (2.1)	4 (12.5)	3 (9.4)	2 (6.3)	9 (18.8)
浮動性めまい	1 (2.1)	3 (6.3)	2 (6.3)	0	0	2 (4.2)
注意力障害	0	1 (2.1)	1 (3.1)	0	0	1 (2.1)
頭部不快感	0	0	1 (3.1)	0	0	1 (2.1)
記憶障害	0	0	0	0	1 (3.1)	1 (2.1)
味覚異常	1 (2.1)	7 (14.6)	0	0	0	0
胃腸障害	2 (4.2)	5 (10.4)	3 (9.4)	2 (6.3)	5 (15.6)	9 (18.8)
口内乾燥	1 (2.1)	2 (4.2)	3 (9.4)	1 (3.1)	3 (9.4)	6 (12.5)
悪心	0	0	0	0	2 (6.3)	2 (4.2)
下痢	1 (2.1)	0	0	1 (3.1)	0	1 (2.1)
腹痛	0	1 (2.1)	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly related to study drug or TEAEs with a missing causality.

付録 2.7.6-4
SOC/PT 別の副作用発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
胃腸障害 (Cont.)						
上腹部痛	0	1 (2.1)	0	0	0	0
鼓腸	0	1 (2.1)	0	0	0	0
一般・全身障害および投与部位の状態	0	0	0	2 (6.3)	2 (6.3)	4 (8.3)
疲労	0	0	0	2 (6.3)	2 (6.3)	4 (8.3)
感染症および寄生虫症	0	0	0	1 (3.1)	0	1 (2.1)
インフルエンザ	0	0	0	1 (3.1)	0	1 (2.1)
精神障害	1 (2.1)	3 (6.3)	1 (3.1)	0	0	1 (2.1)
異常な夢	0	1 (2.1)	1 (3.1)	0	0	1 (2.1)
落ち着きのなさ	0	0	1 (3.1)	0	0	1 (2.1)
妄想	1 (2.1)	0	0	0	0	0
易刺激性	0	2 (4.2)	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly related to study drug or TEAEs with a missing causality.

付録 2.7.6-4
SOC/PT 別の副作用発現率
外国 106 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=48) n (%)	Zopiclone 7.5 mg (N=48) n (%)	Lemborexant 2.5 mg (N=32) n (%)	Lemborexant 5 mg (N=32) n (%)	Lemborexant 10 mg (N=32) n (%)	Lemborexant Total (N=48) n (%)
免疫系障害	0	1 (2.1)	0	0	0	0
過敏症	0	1 (2.1)	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (Baseline) or 1) reemerges during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 19.1
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly related to study drug or TEAEs with a missing causality.

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
Subjects with any TEAE	21 (37.5)	11 (34.4)	11 (40.7)	16 (42 1)
神経系障害	8 (14.3)	5 (15.6)	5 (18.5)	8 (21 1)
傾眠	0	1 (3.1)	1 (3.7)	2 (5.3)
頭痛	3 (5.4)	3 (9.4)	3 (11.1)	3 (7.9)
睡眠時麻痺	0	0	0	1 (2.6)
浮動性めまい	3 (5.4)	0	1 (3.7)	2 (5.3)
失神	0	1 (3.1)	0	0
健忘	0	0	0	0
カタプレキシー	0	0	0	0
注意力障害	0	0	0	0
味覚異常	0	0	0	1 (2.6)
大発作痙攣	0	0	0	0
鎮静	0	0	0	0
睡眠期リズム障害	0	0	0	0
平衡障害	1 (1.8)	0	0	0
片頭痛	1 (1.8)	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.

For each row category, a subject with two or more adverse events in that category is counted only once.

MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
Subjects with any TEAE	19 (59.4)	31 (55.4)	30 (60.0)	118 (50.2)
神経系障害	10 (31.3)	20 (35.7)	17 (34.0)	65 (27.7)
傾眠	4 (12.5)	10 (17.9)	11 (22.0)	29 (12 3)
頭痛	3 (9.4)	6 (10.7)	5 (10.0)	23 (9.8)
睡眠時麻痺	3 (9.4)	4 (7.1)	2 (4.0)	10 (4.3)
浮動性めまい	0	2 (3.6)	1 (2.0)	6 (2.6)
失神	0	0	1 (2.0)	2 (< 1)
健忘	0	0	1 (2.0)	1 (< 1)
カタプレキシー	0	1 (1.8)	0	1 (< 1)
注意力障害	0	0	1 (2.0)	1 (< 1)
味覚異常	0	0	0	1 (< 1)
大発作痙攣	0	0	1 (2.0)	1 (< 1)
鎮静	0	0	1 (2.0)	1 (< 1)
睡眠期リズム障害	0	0	1 (2.0)	1 (< 1)
平衡障害	0	0	0	0
片頭痛	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
神経系障害	8 (14.3)	5 (15.6)	5 (18.5)	8 (21 1)
錯感覚	1 (1.8)	0	0	0
精神障害	5 (8.9)	4 (12.5)	2 (7.4)	4 (10 5)
レム睡眠異常	2 (3.6)	0	2 (7.4)	1 (2.6)
悪夢	0	0	0	1 (2.6)
異常な夢	0	2 (6.3)	0	1 (2.6)
入眠時幻覚	0	0	0	1 (2.6)
不安	1 (1.8)	0	0	2 (5.3)
高揚状態	0	1 (3.1)	0	0
怒り	0	0	0	0
歯ぎしり	0	0	0	0
うつ病	0	0	0	0
多幸気分	0	0	0	0
過覚醒	2 (3.6)	1 (3.1)	0	0
落ち着きのなさ	0	0	0	0
ねごと	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.

For each row category, a subject with two or more adverse events in that category is counted only once.

MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
神経系障害	10 (31.3)	20 (35.7)	17 (34.0)	65 (27.7)
錯感覚	0	0	0	0
精神障害	7 (21.9)	11 (19.6)	5 (10.0)	33 (14.0)
レム睡眠異常	1 (3.1)	3 (5.4)	2 (4.0)	9 (3.8)
悪夢	3 (9.4)	4 (7.1)	0	8 (3.4)
異常な夢	3 (9.4)	0	0	6 (2.6)
入眠時幻覚	1 (3.1)	2 (3.6)	1 (2.0)	5 (2.1)
不安	1 (3.1)	0	1 (2.0)	4 (1.7)
高揚状態	0	0	1 (2.0)	2 (< 1)
怒り	0	1 (1.8)	0	1 (< 1)
歯ぎしり	0	1 (1.8)	0	1 (< 1)
うつ病	1 (3.1)	0	0	1 (< 1)
多幸気分	0	1 (1.8)	0	1 (< 1)
過覚醒	0	0	0	1 (< 1)
落ち着きのなさ	0	0	1 (2.0)	1 (< 1)
ねごと	0	1 (1.8)	0	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.

For each row category, a subject with two or more adverse events in that category is counted only once.

MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
胃腸障害	6 (10.7)	1 (3.1)	1 (3.7)	1 (2.6)
口内乾燥	2 (3.6)	1 (3.1)	0	0
下痢	0	0	0	1 (2.6)
悪心	3 (5.4)	0	1 (3.7)	0
腹痛	0	0	0	0
胃食道逆流性疾患	0	0	0	0
腹部不快感	1 (1.8)	0	0	0
腹部膨満	0	0	0	0
便秘	0	0	0	0
食中毒	0	0	0	0
歯痛	1 (1.8)	0	0	0
嘔吐	1 (1.8)	0	0	0
筋骨格系および結合組織障害	4 (7.1)	0	1 (3.7)	4 (10 5)
背部痛	0	0	1 (3.7)	0
筋肉痛	0	0	0	3 (7.9)
筋攣縮	0	0	1 (3.7)	1 (2.6)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.

For each row category, a subject with two or more adverse events in that category is counted only once.

MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
胃腸障害	1 (3.1)	8 (14.3)	6 (12.0)	18 (7.7)
口内乾燥	1 (3.1)	2 (3.6)	2 (4.0)	6 (2.6)
下痢	1 (3.1)	1 (1.8)	1 (2.0)	4 (1.7)
悪心	0	1 (1.8)	1 (2.0)	3 (1.3)
腹痛	1 (3.1)	1 (1.8)	0	2 (< 1)
胃食道逆流性疾患	0	2 (3.6)	0	2 (< 1)
腹部不快感	0	1 (1.8)	0	1 (< 1)
腹部膨満	0	1 (1.8)	0	1 (< 1)
便秘	0	0	1 (2.0)	1 (< 1)
食中毒	0	0	1 (2.0)	1 (< 1)
歯痛	0	0	0	0
嘔吐	0	0	0	0
筋骨格系および結合組織障害	2 (6.3)	5 (8.9)	3 (6.0)	15 (6.4)
背部痛	1 (3.1)	3 (5.4)	0	5 (2.1)
筋肉痛	1 (3.1)	1 (1.8)	0	5 (2.1)
筋攣縮	0	1 (1.8)	0	3 (1.3)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
筋骨格系および結合組織障害	4 (7.1)	0	1 (3.7)	4 (10 5)
筋力低下	0	0	0	0
筋痙縮	1 (1.8)	0	0	1 (2.6)
筋骨格痛	0	0	0	0
関節痛	1 (1.8)	0	0	0
筋骨格不快感	1 (1.8)	0	0	0
筋骨格硬直	1 (1.8)	0	0	0
一般・全身障害および投与部位の状態	1 (1.8)	1 (3.1)	0	2 (5.3)
酩酊感	0	0	0	0
悪寒	0	0	0	0
発熱	0	0	0	0
適用部位皮膚炎	0	1 (3.1)	0	0
無力症	0	0	0	0
活力増進	0	0	0	0
疲労	0	0	0	1 (2.6)
易刺激性	0	0	0	0
倦怠感	0	0	0	1 (2.6)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
筋骨格系および結合組織障害	2 (6.3)	5 (8.9)	3 (6.0)	15 (6.4)
筋力低下	0	0	2 (4.0)	2 (< 1)
筋痙縮	0	0	0	1 (< 1)
筋骨格痛	0	0	1 (2.0)	1 (< 1)
関節痛	0	0	0	0
筋骨格不快感	0	0	0	0
筋骨格硬直	0	0	0	0
一般・全身障害および投与部位の状態	1 (3.1)	1 (1.8)	7 (14.0)	12 (5.1)
酩酊感	0	0	3 (6.0)	3 (1.3)
悪寒	1 (3.1)	1 (1.8)	0	2 (< 1)
発熱	0	0	2 (4.0)	2 (< 1)
適用部位皮膚炎	0	0	0	1 (< 1)
無力症	0	0	1 (2.0)	1 (< 1)
活力増進	0	0	1 (2.0)	1 (< 1)
疲労	0	0	0	1 (< 1)
易刺激性	0	0	1 (2.0)	1 (< 1)
倦怠感	0	0	0	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.

For each row category, a subject with two or more adverse events in that category is counted only once.

MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
一般・全身障害および投与部位の状態	1 (1.8)	1 (3.1)	0	2 (5.3)
適用部位内出血	1 (1.8)	0	0	0
感染症および寄生虫症	1 (1.8)	2 (6.3)	1 (3.7)	1 (2.6)
上気道感染	0	0	1 (3.7)	0
ウイルス性上気道感染	0	1 (3.1)	0	0
インフルエンザ	0	0	0	0
鼻咽頭炎	0	0	0	1 (2.6)
副鼻腔炎	0	0	0	0
歯膿瘍	0	1 (3.1)	0	0
急性副鼻腔炎	1 (1.8)	0	0	0
臨床検査	0	0	2 (7.4)	0
アラニンアミノトランスフェラーゼ増加	0	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0
好中球数減少	0	0	1 (3.7)	0
血圧上昇	0	0	0	0
血中トリグリセリド増加	0	0	1 (3.7)	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
一般・全身障害および投与部位の状態	1 (3.1)	1 (1.8)	7 (14.0)	12 (5.1)
適用部位内出血	0	0	0	0
感染症および寄生虫症	2 (6.3)	1 (1.8)	1 (2.0)	8 (3.4)
上気道感染	1 (3.1)	1 (1.8)	0	3 (1.3)
ウイルス性上気道感染	1 (3.1)	0	0	2 (< 1)
インフルエンザ	0	0	1 (2.0)	1 (< 1)
鼻咽頭炎	0	0	0	1 (< 1)
副鼻腔炎	0	0	1 (2.0)	1 (< 1)
歯膿瘍	0	0	0	1 (< 1)
急性副鼻腔炎	0	0	0	0
臨床検査	1 (3.1)	0	4 (8.0)	7 (3.0)
アラニンアミノトランスフェラーゼ増加	1 (3.1)	0	1 (2.0)	2 (< 1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (3.1)	0	1 (2.0)	2 (< 1)
好中球数減少	0	0	1 (2.0)	2 (< 1)
血圧上昇	0	0	1 (2.0)	1 (< 1)
血中トリグリセリド増加	0	0	0	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
臨床検査	0	0	2 (7.4)	0
白血球数減少	0	0	0	0
眼障害	1 (1.8)	0	0	1 (2.6)
眼痛	0	0	0	1 (2.6)
霧視	0	0	0	0
眼の異常感	0	0	0	0
眼瞼痙攣	0	0	0	0
瞬目過多	1 (1.8)	0	0	0
代謝および栄養障害	2 (3.6)	0	1 (3.7)	0
高コレステロール血症	0	0	1 (3.7)	0
高カリウム血症	1 (1.8)	0	0	0
高トリグリセリド血症	0	0	0	0
食欲亢進	0	0	0	0
食欲減退	1 (1.8)	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
臨床検査	1 (3.1)	0	4 (8.0)	7 (3.0)
白血球数減少	0	0	1 (2.0)	1 (< 1)
眼障害	0	2 (3.6)	2 (4.0)	5 (2.1)
眼痛	0	0	1 (2.0)	2 (< 1)
霧視	0	1 (1.8)	1 (2.0)	2 (< 1)
眼の異常感	0	1 (1.8)	0	1 (< 1)
眼瞼痙攣	0	0	1 (2.0)	1 (< 1)
瞬目過多	0	0	0	0
代謝および栄養障害	0	2 (3.6)	1 (2.0)	4 (1.7)
高コレステロール血症	0	0	0	1 (< 1)
高カリウム血症	0	1 (1.8)	0	1 (< 1)
高トリグリセリド血症	0	0	1 (2.0)	1 (< 1)
食欲亢進	0	1 (1.8)	0	1 (< 1)
食欲減退	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
皮膚および皮下組織障害	2 (3.6)	0	0	1 (2.6)
光線過敏性反応	0	0	0	1 (2.6)
そう痒症	0	0	0	0
斑状丘疹状皮疹	0	0	0	0
皮膚色素過剰	0	0	0	0
爪破損	1 (1.8)	0	0	0
発疹	1 (1.8)	0	0	0
耳および迷路障害	0	0	0	1 (2.6)
耳痛	0	0	0	0
聴覚過敏	0	0	0	1 (2.6)
回転性めまい	0	0	0	0
傷害、中毒および処置合併症	0	1 (3.1)	0	0
挫傷	0	1 (3.1)	0	0
擦過傷	0	0	0	0
関節脱臼	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
皮膚および皮下組織障害	2 (6.3)	0	1 (2.0)	4 (1.7)
光線過敏性反応	0	0	0	1 (< 1)
そう痒症	1 (3.1)	0	0	1 (< 1)
斑状丘疹状皮疹	0	0	1 (2.0)	1 (< 1)
皮膚色素過剰	1 (3.1)	0	0	1 (< 1)
爪破損	0	0	0	0
発疹	0	0	0	0
耳および迷路障害	0	0	2 (4.0)	3 (1.3)
耳痛	0	0	1 (2.0)	1 (< 1)
聴覚過敏	0	0	0	1 (< 1)
回転性めまい	0	0	1 (2.0)	1 (< 1)
傷害、中毒および処置合併症	1 (3.1)	0	1 (2.0)	3 (1.3)
挫傷	0	0	0	1 (< 1)
擦過傷	1 (3.1)	0	0	1 (< 1)
関節脱臼	0	0	1 (2.0)	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
呼吸器、胸郭および縦隔障害	2 (3.6)	0	0	1 (2.6)
咳嗽	0	0	0	0
横隔膜障害	0	0	0	0
口腔咽頭痛	0	0	0	1 (2.6)
肺うっ血	0	0	0	0
喘息	1 (1.8)	0	0	0
鼻漏	1 (1.8)	0	0	0
腎および尿路障害	0	0	0	0
尿意切迫	0	0	0	0
頻尿	0	0	0	0
心臓障害	1 (1.8)	0	0	0
洞性徐脈	1 (1.8)	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-5
SOC/PT 別の有害事象発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
呼吸器、胸郭および縦隔障害	1 (3.1)	1 (1.8)	0	3 (1.3)
咳嗽	0	1 (1.8)	0	1 (< 1)
横隔膜障害	1 (3.1)	0	0	1 (< 1)
口腔咽頭痛	0	0	0	1 (< 1)
肺うっ血	1 (3.1)	0	0	1 (< 1)
喘息	0	0	0	0
鼻漏	0	0	0	0
腎および尿路障害	0	1 (1.8)	1 (2.0)	2 (< 1)
尿意切迫	0	0	1 (2.0)	1 (< 1)
頻尿	0	1 (1.8)	0	1 (< 1)
心臓障害	0	0	0	0
洞性徐脈	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
Subjects with any treatment-related TEAE	11 (19.6)	8 (25.0)	9 (33.3)	12 (31.6)
神経系障害	6 (10.7)	4 (12.5)	4 (14.8)	5 (13 2)
傾眠	0	1 (3.1)	1 (3.7)	2 (5.3)
頭痛	2 (3.6)	2 (6.3)	2 (7.4)	1 (2.6)
睡眠時麻痺	0	0	0	1 (2.6)
浮動性めまい	2 (3.6)	0	1 (3.7)	1 (2.6)
健忘	0	0	0	0
カタプレキシー	0	0	0	0
注意力障害	0	0	0	0
味覚異常	0	0	0	1 (2.6)
大発作痙攣	0	0	0	0
鎮静	0	0	0	0
睡眠期リズム障害	0	0	0	0
失神	0	1 (3.1)	0	0
平衡障害	1 (1.8)	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
Subjects with any treatment-related TEAE	15 (46.9)	24 (42.9)	24 (48.0)	92 (39 1)
神経系障害	8 (25.0)	16 (28.6)	15 (30.0)	52 (22 1)
傾眠	3 (9.4)	9 (16.1)	11 (22.0)	27 (11 5)
頭痛	2 (6.3)	3 (5.4)	3 (6.0)	13 (5.5)
睡眠時麻痺	3 (9.4)	4 (7.1)	2 (4.0)	10 (4.3)
浮動性めまい	0	2 (3.6)	1 (2.0)	5 (2.1)
健忘	0	0	1 (2.0)	1 (< 1)
カタプレキシー	0	1 (1.8)	0	1 (< 1)
注意力障害	0	0	1 (2.0)	1 (< 1)
味覚異常	0	0	0	1 (< 1)
大発作痙攣	0	0	1 (2.0)	1 (< 1)
鎮静	0	0	1 (2.0)	1 (< 1)
睡眠期リズム障害	0	0	1 (2.0)	1 (< 1)
失神	0	0	0	1 (< 1)
平衡障害	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
神経系障害	6 (10.7)	4 (12.5)	4 (14.8)	5 (13 2)
錯感覚	1 (1.8)	0	0	0
精神障害	5 (8.9)	4 (12.5)	2 (7.4)	3 (7.9)
レム睡眠異常	2 (3.6)	0	2 (7.4)	1 (2.6)
悪夢	0	0	0	1 (2.6)
異常な夢	0	2 (6.3)	0	1 (2.6)
入眠時幻覚	0	0	0	1 (2.6)
不安	1 (1.8)	0	0	1 (2.6)
高揚状態	0	1 (3.1)	0	0
怒り	0	0	0	0
歯ぎしり	0	0	0	0
多幸気分	0	0	0	0
過覚醒	2 (3.6)	1 (3.1)	0	0
落ち着きのなさ	0	0	0	0
ねごと	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
神経系障害	8 (25.0)	16 (28.6)	15 (30.0)	52 (22 1)
錯感覚	0	0	0	0
精神障害	6 (18.8)	11 (19.6)	5 (10.0)	31 (13 2)
レム睡眠異常	1 (3.1)	3 (5.4)	2 (4.0)	9 (3.8)
悪夢	3 (9.4)	4 (7.1)	0	8 (3.4)
異常な夢	2 (6.3)	0	0	5 (2.1)
入眠時幻覚	1 (3.1)	2 (3.6)	1 (2.0)	5 (2.1)
不安	0	0	1 (2.0)	2 (< 1)
高揚状態	0	0	1 (2.0)	2 (< 1)
怒り	0	1 (1.8)	0	1 (< 1)
歯ぎしり	0	1 (1.8)	0	1 (< 1)
多幸気分	0	1 (1.8)	0	1 (< 1)
過覚醒	0	0	0	1 (< 1)
落ち着きのなさ	0	0	1 (2.0)	1 (< 1)
ねごと	0	1 (1.8)	0	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
胃腸障害	5 (8.9)	1 (3.1)	1 (3.7)	1 (2.6)
口内乾燥	2 (3.6)	1 (3.1)	0	0
下痢	0	0	0	1 (2.6)
胃食道逆流性疾患	0	0	0	0
悪心	2 (3.6)	0	1 (3.7)	0
腹痛	0	0	0	0
便秘	0	0	0	0
腹部不快感	1 (1.8)	0	0	0
歯痛	1 (1.8)	0	0	0
筋骨格系および結合組織障害	2 (3.6)	0	1 (3.7)	2 (5.3)
筋肉痛	0	0	0	2 (5.3)
筋攣縮	0	0	1 (3.7)	0
筋力低下	0	0	0	0
関節痛	1 (1.8)	0	0	0
筋骨格硬直	1 (1.8)	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
胃腸障害	1 (3.1)	4 (7.1)	5 (10.0)	13 (5.5)
口内乾燥	1 (3.1)	2 (3.6)	2 (4.0)	6 (2.6)
下痢	1 (3.1)	1 (1.8)	1 (2.0)	4 (1.7)
胃食道逆流性疾患	0	2 (3.6)	0	2 (< 1)
悪心	0	0	1 (2.0)	2 (< 1)
腹痛	1 (3.1)	0	0	1 (< 1)
便秘	0	0	1 (2.0)	1 (< 1)
腹部不快感	0	0	0	0
歯痛	0	0	0	0
筋骨格系および結合組織障害	0	2 (3.6)	2 (4.0)	7 (3.0)
筋肉痛	0	1 (1.8)	0	3 (1.3)
筋攣縮	0	1 (1.8)	0	2 (< 1)
筋力低下	0	0	2 (4.0)	2 (< 1)
関節痛	0	0	0	0
筋骨格硬直	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
一般・全身障害および投与部位の状態	0	0	0	2 (5.3)
酩酊感	0	0	0	0
無力症	0	0	0	0
活力増進	0	0	0	0
疲労	0	0	0	1 (2.6)
倦怠感	0	0	0	1 (2.6)
眼障害	1 (1.8)	0	0	1 (2.6)
眼痛	0	0	0	1 (2.6)
霧視	0	0	0	0
眼の異常感	0	0	0	0
瞬目過多	1 (1.8)	0	0	0
臨床検査	0	0	1 (3.7)	0
アラニンアミノトランスフェラーゼ増加	0	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
一般・全身障害および投与部位の状態	0	0	4 (8.0)	6 (2.6)
酩酊感	0	0	2 (4.0)	2 (< 1)
無力症	0	0	1 (2.0)	1 (< 1)
活力増進	0	0	1 (2.0)	1 (< 1)
疲労	0	0	0	1 (< 1)
倦怠感	0	0	0	1 (< 1)
眼障害	0	2 (3.6)	2 (4.0)	5 (2.1)
眼痛	0	0	1 (2.0)	2 (< 1)
霧視	0	1 (1.8)	1 (2.0)	2 (< 1)
眼の異常感	0	1 (1.8)	0	1 (< 1)
瞬目過多	0	0	0	0
臨床検査	1 (3.1)	0	3 (6.0)	5 (2.1)
アラニンアミノトランスフェラーゼ増加	1 (3.1)	0	1 (2.0)	2 (< 1)
アスパラギン酸アミノトランスフェラーゼ増加	1 (3.1)	0	1 (2.0)	2 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
臨床検査	0	0	1 (3.7)	0
好中球数減少	0	0	1 (3.7)	0
白血球数減少	0	0	0	0
耳および迷路障害	0	0	0	1 (2.6)
聴覚過敏	0	0	0	1 (2.6)
回転性めまい	0	0	0	0
代謝および栄養障害	0	0	0	0
高トリグリセリド血症	0	0	0	0
食欲亢進	0	0	0	0
皮膚および皮下組織障害	0	0	0	1 (2.6)
光線過敏性反応	0	0	0	1 (2.6)
そう痒症	0	0	0	0

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
臨床検査	1 (3.1)	0	3 (6.0)	5 (2.1)
好中球数減少	0	0	1 (2.0)	2 (< 1)
白血球数減少	0	0	1 (2.0)	1 (< 1)
耳および迷路障害	0	0	1 (2.0)	2 (< 1)
聴覚過敏	0	0	0	1 (< 1)
回転性めまい	0	0	1 (2.0)	1 (< 1)
代謝および栄養障害	0	1 (1.8)	1 (2.0)	2 (< 1)
高トリグリセリド血症	0	0	1 (2.0)	1 (< 1)
食欲亢進	0	1 (1.8)	0	1 (< 1)
皮膚および皮下組織障害	1 (3.1)	0	0	2 (< 1)
光線過敏性反応	0	0	0	1 (< 1)
そう痒症	1 (3.1)	0	0	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=56) n (%)	E2006 1 mg (N=32) n (%)	E2006 2.5 mg (N=27) n (%)	E2006 5 mg (N=38) n (%)
腎および尿路障害	0	0	0	0
頻尿	0	0	0	0
呼吸器、胸郭および縦隔障害	0	0	0	1 (2.6)
口腔咽頭痛	0	0	0	1 (2.6)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-6
SOC/PT 別の副作用発現率
外国 201 試験
安全性解析対象集団

MedDRA System Organ Class Preferred Term	E2006 10 mg (N=32) n (%)	E2006 15 mg (N=56) n (%)	E2006 25 mg (N=50) n (%)	E2006 Total (N=235) n (%)
腎および尿路障害	0	1 (1.8)	0	1 (< 1)
頻尿	0	1 (1.8)	0	1 (< 1)
呼吸器、胸郭および縦隔障害	0	0	0	1 (< 1)
口腔咽頭痛	0	0	0	1 (< 1)

A TEAE is defined as an AE that emerges during treatment, having been absent at pretreatment (baseline) or 1) reemerges during treatment, having been present at pretreatment (baseline) but stopped before treatment, or 2) worsens in severity during treatment relative to the pretreatment state, when the AE is continuous. Adverse events that occur up to the last dose day plus 7 days (including placebo dosing) are included as treatment-emergent events.
For each row category, a subject with two or more adverse events in that category is counted only once.
MedDRA Version 16.1
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.

付録 2.7.6-7　死亡又は重篤な有害事象の被験者ごとの叙述（外国 201 試験）

死亡又は重篤な有害事象が認められた被験者に関する叙述を以下に示した。

被験者識別コード	投与群	死亡に至った有害事象	死亡以外の重篤な有害事象
10021003	プラセボ群		X
10081004	レンボレキサント 25 mg 群		X

Subject ID:	10021003
Age, race, sex, actual treatment group:	28 years, WHITE, Female, Placebo
Medical history: (MedDRA Preferred Term)	–
Current medical conditions: (MedDRA Preferred Term)	–
Concomitant medications:	–
Date of first dose/last dose of study drug:	05 DEC 2013 / 21 DEC 2013
Other events: (MedDRA Preferred Term)	口内乾燥, 錯感覚

Serious adverse events (Investigator term/MedDRA preferred term):	hyperkalemia / 高カリウム血症
Start date of adverse event (Study Day)/outcome date of adverse event (Study Day):	07 DEC 2013 (Study Day 3) / 13 DEC 2013 (Study Day 9)
TEAE	Yes
Serious criteria:	Important medical event
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DOSE NOT CHANGED / NONE
Concomitant medications (used until/on the start date of adverse event):	–
Relationship of event:	NOT RELATED

Subject ID:	10081004
Age, race, sex, actual treatment group:	63 years, WHITE, Female, Lemborexant 25 mg
Medical history: (MedDRA Preferred Term)	胆石症, 閉経後, 胆嚢切除
Current medical conditions: (MedDRA Preferred Term)	–
Concomitant medications:	–
Date of first dose/last dose of study drug:	04 FEB 2014 / 05 FEB 2014
Other events: (MedDRA Preferred Term)	–

Serious adverse events (Investigator term/MedDRA preferred term):	Generalized tonic-clonic seizure / 大発作痙攣
Start date of adverse event (Study Day)/outcome date of adverse event (Study Day):	05 FEB 2014 (Study Day 2) / 06 FEB 2014 (Study Day 3)
TEAE	Yes
Serious criteria:	Important medical event
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG WITHDRAWN / Withdrawn from study
Concomitant medications (used until/on the start date of adverse event):	–
Relationship of event:	POSSIBLY RELATED

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
Subjects with any TEAE	200 (62.7)	192 (61.1)	187 (59.6)	379 (60.4)
血液およびリンパ系障害	2 (0.6)	1 (0.3)	2 (0.6)	3 (0.5)
白血球減少症	0	0	1 (0.3)	1 (0.2)
血小板減少症	0	0	1 (0.3)	1 (0.2)
リンパ節症	0	1 (0.3)	0	1 (0.2)
貧血	2 (0.6)	0	0	0
心臓障害	2 (0.6)	11 (3.5)	5 (1.6)	16 (2.5)
動悸	1 (0.3)	2 (0.6)	3 (1.0)	5 (0.8)
頻脈	0	4 (1.3)	0	4 (0.6)
心筋症	0	0	2 (0.6)	2 (0.3)
狭心症	0	2 (0.6)	0	2 (0.3)
不整脈	0	2 (0.6)	0	2 (0.3)
僧帽弁閉鎖不全症	1 (0.3)	1 (0.3)	0	1 (0.2)
大動脈弁閉鎖不全症	1 (0.3)	0	0	0
心房細動	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
心臓障害 (Cont.)	2 (0.6)	11 (3.5)	5 (1.6)	16 (2.5)
左室肥大	1 (0.3)	0	0	0
三尖弁閉鎖不全症	1 (0.3)	0	0	0
耳および迷路障害	6 (1.9)	3 (1.0)	8 (2.5)	11 (1.8)
回転性めまい	3 (0.9)	2 (0.6)	3 (1.0)	5 (0.8)
耳鳴	0	0	3 (1.0)	3 (0.5)
耳管機能障害	0	0	1 (0.3)	1 (0.2)
中耳の炎症	0	0	1 (0.3)	1 (0.2)
頭位性回転性めまい	0	1 (0.3)	0	1 (0.2)
メニエール病	2 (0.6)	0	0	0
耳不快感	1 (0.3)	0	0	0
内分泌障害	2 (0.6)	1 (0.3)	0	1 (0.2)
甲状腺腫瘤	1 (0.3)	1 (0.3)	0	1 (0.2)
甲状腺腫	1 (0.3)	0	0	0
甲状腺機能低下症	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
眼障害	2 (0.6)	4 (1.3)	3 (1.0)	7 (1.1)
白内障	0	1 (0.3)	1 (0.3)	2 (0.3)
霰粒腫	0	0	1 (0.3)	1 (0.2)
眼そう痒症	0	0	1 (0.3)	1 (0.2)
霧視	1 (0.3)	1 (0.3)	0	1 (0.2)
深径覚の変化	0	1 (0.3)	0	1 (0.2)
糖尿病網膜症	0	1 (0.3)	0	1 (0.2)
眼のアレルギー	0	1 (0.3)	0	1 (0.2)
硝子体剥離	1 (0.3)	0	0	0
胃腸障害	19 (6.0)	26 (8.3)	23 (7.3)	49 (7.8)
悪心	3 (0.9)	8 (2.5)	4 (1.3)	12 (1.9)
下痢	5 (1.6)	2 (0.6)	5 (1.6)	7 (1.1)
嘔吐	0	1 (0.3)	4 (1.3)	5 (0.8)
上腹部痛	2 (0.6)	2 (0.6)	3 (1.0)	5 (0.8)
口内乾燥	1 (0.3)	2 (0.6)	3 (1.0)	5 (0.8)
腹痛	0	1 (0.3)	3 (1.0)	4 (0.6)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
胃腸障害 (Cont.)	19 (6.0)	26 (8.3)	23 (7.3)	49 (7.8)
歯痛	3 (0.9)	0	2 (0.6)	2 (0.3)
胃食道逆流性疾患	3 (0.9)	1 (0.3)	1 (0.3)	2 (0.3)
便秘	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
腹部不快感	0	0	1 (0.3)	1 (0.2)
鼓腸	0	0	1 (0.3)	1 (0.2)
胃炎	0	0	1 (0.3)	1 (0.2)
膵腫大	1 (0.3)	1 (0.3)	0	1 (0.2)
慢性胃炎	0	1 (0.3)	0	1 (0.2)
齲歯	0	1 (0.3)	0	1 (0.2)
消化不良	0	1 (0.3)	0	1 (0.2)
びらん性胃炎	0	1 (0.3)	0	1 (0.2)
胃腸障害	0	1 (0.3)	0	1 (0.2)
大腸ポリープ	0	1 (0.3)	0	1 (0.2)
口腔内潰瘍形成	0	1 (0.3)	0	1 (0.2)
歯周病	0	1 (0.3)	0	1 (0.2)
流涎過多	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
一般・全身障害および投与部位の状態	9 (2.8)	26 (8.3)	17 (5.4)	43 (6.8)
疲労	1 (0.3)	12 (3.8)	11 (3.5)	23 (3.7)
末梢性浮腫	2 (0.6)	5 (1.6)	0	5 (0.8)
異常感	0	3 (1.0)	0	3 (0.5)
口渇	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
発熱	1 (0.3)	0	1 (0.3)	1 (0.2)
無力症	0	0	1 (0.3)	1 (0.2)
不快感	0	0	1 (0.3)	1 (0.2)
疼痛	0	0	1 (0.3)	1 (0.2)
穿刺部位反応	0	0	1 (0.3)	1 (0.2)
ワクチン接種部位疼痛	0	0	1 (0.3)	1 (0.2)
胸痛	1 (0.3)	1 (0.3)	0	1 (0.2)
胸部不快感	0	1 (0.3)	0	1 (0.2)
悪寒	0	1 (0.3)	0	1 (0.2)
全身健康状態低下	0	1 (0.3)	0	1 (0.2)
倦怠感	0	1 (0.3)	0	1 (0.2)
非心臓性胸痛	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
一般・全身障害および投与部位の状態 (Cont.)	9 (2.8)	26 (8.3)	17 (5.4)	43 (6.8)
血管穿刺部位内出血	0	1 (0.3)	0	1 (0.2)
嚢胞	1 (0.3)	0	0	0
インフルエンザ様疾患	1 (0.3)	0	0	0
末梢腫脹	1 (0.3)	0	0	0
肝胆道系障害	1 (0.3)	4 (1.3)	2 (0.6)	6 (1.0)
脂肪肝	1 (0.3)	2 (0.6)	0	2 (0.3)
胆石症	0	2 (0.6)	0	2 (0.3)
胆汁うっ滞	0	0	1 (0.3)	1 (0.2)
肝嚢胞	0	0	1 (0.3)	1 (0.2)
肝毒性	0	0	1 (0.3)	1 (0.2)
胆嚢炎	0	1 (0.3)	0	1 (0.2)
胆嚢摘出術後症候群	0	1 (0.3)	0	1 (0.2)
免疫系障害	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.3)
過敏症	0	0	1 (0.3)	1 (0.2)
動物アレルギー	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
免疫系障害 (Cont.)	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.3)
薬物過敏症	1 (0.3)	0	0	0
季節性アレルギー	1 (0.3)	0	0	0
感染症および寄生虫症	97 (30.4)	86 (27.4)	82 (26.1)	168 (26.8)
上咽頭炎	40 (12.5)	30 (9.6)	29 (9.2)	59 (9.4)
インフルエンザ	15 (4.7)	15 (4.8)	16 (5.1)	31 (4.9)
上気道感染	10 (3.1)	13 (4.1)	11 (3.5)	24 (3.8)
尿路感染	7 (2.2)	4 (1.3)	9 (2.9)	13 (2.1)
胃腸炎	4 (1.3)	5 (1.6)	7 (2.2)	12 (1.9)
ウイルス性上気道感染	5 (1.6)	2 (0.6)	5 (1.6)	7 (1.1)
副鼻腔炎	8 (2.5)	4 (1.3)	3 (1.0)	7 (1.1)
気管支炎	4 (1.3)	6 (1.9)	1 (0.3)	7 (1.1)
歯感染	1 (0.3)	2 (0.6)	2 (0.6)	4 (0.6)
咽頭炎	3 (0.9)	3 (1.0)	1 (0.3)	4 (0.6)
結膜炎	0	1 (0.3)	2 (0.6)	3 (0.5)
蜂巣炎	0	2 (0.6)	1 (0.3)	3 (0.5)
消化管感染	1 (0.3)	0	2 (0.6)	2 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
感染症および寄生虫症 (Cont.)	97 (30.4)	86 (27.4)	82 (26.1)	168 (26.8)
肺炎	3 (0.9)	1 (0.3)	1 (0.3)	2 (0.3)
中耳炎	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.3)
ウイルス性胃腸炎	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
気道感染	0	1 (0.3)	1 (0.3)	2 (0.3)
鼻炎	0	1 (0.3)	1 (0.3)	2 (0.3)
口腔ヘルペス	0	2 (0.6)	0	2 (0.3)
四肢膿瘍	0	0	1 (0.3)	1 (0.2)
膀胱炎	0	0	1 (0.3)	1 (0.2)
歯肉炎	0	0	1 (0.3)	1 (0.2)
爪真菌症	0	0	1 (0.3)	1 (0.2)
耳下腺炎	0	0	1 (0.3)	1 (0.2)
皮下組織膿瘍	0	0	1 (0.3)	1 (0.2)
外陰部腟カンジダ症	0	0	1 (0.3)	1 (0.2)
せつ	1 (0.3)	1 (0.3)	0	1 (0.2)
感染性下痢	0	1 (0.3)	0	1 (0.2)
外耳蜂巣炎	0	1 (0.3)	0	1 (0.2)
眼感染	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
感染症および寄生虫症 (Cont.)	97 (30.4)	86 (27.4)	82 (26.1)	168 (26.8)
ヘリコバクター性胃炎	0	1 (0.3)	0	1 (0.2)
外耳炎	0	1 (0.3)	0	1 (0.2)
術後創感染	0	1 (0.3)	0	1 (0.2)
歯髄炎	0	1 (0.3)	0	1 (0.2)
唾液腺炎	0	1 (0.3)	0	1 (0.2)
歯膿瘍	0	1 (0.3)	0	1 (0.2)
耳感染	2 (0.6)	0	0	0
扁桃炎	2 (0.6)	0	0	0
アデノウイルス結膜炎	1 (0.3)	0	0	0
細菌性食中毒	1 (0.3)	0	0	0
細菌性気管支炎	1 (0.3)	0	0	0
慢性副鼻腔炎	1 (0.3)	0	0	0
毛嚢虫症	1 (0.3)	0	0	0
真菌感染	1 (0.3)	0	0	0
細菌性胃腸炎	1 (0.3)	0	0	0
麦粒腫	1 (0.3)	0	0	0
限局性感染	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
感染症および寄生虫症 (Cont.)	97 (30.4)	86 (27.4)	82 (26.1)	168 (26.8)
肺感染	1 (0.3)	0	0	0
乳腺炎	1 (0.3)	0	0	0
レンサ球菌性咽頭炎	1 (0.3)	0	0	0
化膿性分泌物	1 (0.3)	0	0	0
皮膚感染	1 (0.3)	0	0	0
傷害、中毒および処置合併症	27 (8.5)	20 (6.4)	18 (5.7)	38 (6.1)
転倒	10 (3.1)	5 (1.6)	5 (1.6)	10 (1.6)
挫傷	4 (1.3)	2 (0.6)	3 (1.0)	5 (0.8)
靭帯捻挫	1 (0.3)	0	3 (1.0)	3 (0.5)
処置による疼痛	0	1 (0.3)	2 (0.6)	3 (0.5)
関節損傷	3 (0.9)	1 (0.3)	1 (0.3)	2 (0.3)
動物咬傷	0	1 (0.3)	1 (0.3)	2 (0.3)
節足動物刺傷	0	1 (0.3)	1 (0.3)	2 (0.3)
下肢骨折	0	1 (0.3)	1 (0.3)	2 (0.3)
企図的過量投与	1 (0.3)	2 (0.6)	0	2 (0.3)
節足動物咬傷	0	2 (0.6)	0	2 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
傷害、中毒および処置合併症 (Cont.)	27 (8.5)	20 (6.4)	18 (5.7)	38 (6.1)
交通事故	1 (0.3)	0	1 (0.3)	1 (0.2)
歯牙破折	1 (0.3)	0	1 (0.3)	1 (0.2)
事故	0	0	1 (0.3)	1 (0.2)
動物による引っかき傷	0	0	1 (0.3)	1 (0.2)
関節脱臼	0	0	1 (0.3)	1 (0.2)
橈骨骨折	0	0	1 (0.3)	1 (0.2)
熱傷	0	0	1 (0.3)	1 (0.2)
上肢骨折	0	0	1 (0.3)	1 (0.2)
創傷	0	0	1 (0.3)	1 (0.2)
肉離れ	4 (1.3)	1 (0.3)	0	1 (0.2)
足骨折	1 (0.3)	1 (0.3)	0	1 (0.2)
靭帯断裂	1 (0.3)	1 (0.3)	0	1 (0.2)
手首関節骨折	1 (0.3)	1 (0.3)	0	1 (0.2)
靭帯損傷	0	1 (0.3)	0	1 (0.2)
半月板損傷	0	1 (0.3)	0	1 (0.2)
皮膚擦過傷	0	1 (0.3)	0	1 (0.2)
外傷性血腫	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
傷害、中毒および処置合併症 (Cont.)	27 (8.5)	20 (6.4)	18 (5.7)	38 (6.1)
背部損傷	1 (0.3)	0	0	0
軟骨損傷	1 (0.3)	0	0	0
上顆炎	1 (0.3)	0	0	0
筋断裂	1 (0.3)	0	0	0
骨盤骨折	1 (0.3)	0	0	0
肺挫傷	1 (0.3)	0	0	0
肋骨骨折	1 (0.3)	0	0	0
胸骨骨折	1 (0.3)	0	0	0
脛骨骨折	1 (0.3)	0	0	0
臨床検査	15 (4.7)	13 (4.1)	14 (4.5)	27 (4.3)
体重増加	4 (1.3)	3 (1.0)	6 (1.9)	9 (1.4)
アラニンアミノトランスフェラーゼ増加	1 (0.3)	3 (1.0)	2 (0.6)	5 (0.8)
血中トリグリセリド増加	2 (0.6)	3 (1.0)	0	3 (0.5)
肝機能検査値上昇	0	0	2 (0.6)	2 (0.3)
血中コレステロール増加	3 (0.9)	1 (0.3)	1 (0.3)	2 (0.3)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Total (N=628) n (%)
臨床検査 (Cont.)	15 (4.7)	13 (4.1)	14 (4.5)	27 (4.3)
血圧上昇	1 (0.3)	0	1 (0.3)	1 (0.2)
血中カリウム増加	0	0	1 (0.3)	1 (0.2)
トランスアミナーゼ上昇	0	0	1 (0.3)	1 (0.2)
尿中血陽性	0	1 (0.3)	0	1 (0.2)
心電図ＰＲ延長	0	1 (0.3)	0	1 (0.2)
心電図ＱＴ延長	0	1 (0.3)	0	1 (0.2)
尿中蛋白陽性	0	1 (0.3)	0	1 (0.2)
心雑音	2 (0.6)	0	0	0
血中乳酸脱水素酵素増加	1 (0.3)	0	0	0
好中球数減少	1 (0.3)	0	0	0
甲状腺機能検査異常	1 (0.3)	0	0	0
代謝および栄養障害	10 (3.1)	10 (3.2)	8 (2.5)	18 (2.9)
食欲亢進	1 (0.3)	3 (1.0)	3 (1.0)	6 (1.0)
食欲減退	1 (0.3)	2 (0.6)	1 (0.3)	3 (0.5)
ビタミンＤ欠乏	0	2 (0.6)	1 (0.3)	3 (0.5)
２型糖尿病	0	0	2 (0.6)	2 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
代謝および栄養障害 (Cont.)	10 (3.1)	10 (3.2)	8 (2.5)	18 (2.9)
ビタミンＢ群欠乏	0	0	2 (0.6)	2 (0.3)
糖尿病	0	0	1 (0.3)	1 (0.2)
体重減少不良	0	0	1 (0.3)	1 (0.2)
痛風	2 (0.6)	1 (0.3)	0	1 (0.2)
高尿酸血症	1 (0.3)	1 (0.3)	0	1 (0.2)
高脂血症	0	1 (0.3)	0	1 (0.2)
低カリウム血症	2 (0.6)	0	0	0
食欲障害	1 (0.3)	0	0	0
高コレステロール血症	1 (0.3)	0	0	0
鉄欠乏	1 (0.3)	0	0	0
筋骨格系および結合組織障害	35 (11.0)	45 (14.3)	20 (6.4)	65 (10.4)
背部痛	8 (2.5)	12 (3.8)	9 (2.9)	21 (3.3)
関節痛	9 (2.8)	14 (4.5)	3 (1.0)	17 (2.7)
変形性関節症	3 (0.9)	5 (1.6)	2 (0.6)	7 (1.1)
筋骨格痛	0	1 (0.3)	4 (1.3)	5 (0.8)
筋痙縮	1 (0.3)	4 (1.3)	1 (0.3)	5 (0.8)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
筋骨格系および結合組織障害 (Cont.)	35 (11.0)	45 (14.3)	20 (6.4)	65 (10.4)
頚部痛	1 (0.3)	4 (1.3)	1 (0.3)	5 (0.8)
筋力低下	0	1 (0.3)	1 (0.3)	2 (0.3)
筋肉痛	4 (1.3)	2 (0.6)	0	2 (0.3)
関節炎	0	2 (0.6)	0	2 (0.3)
筋緊張	0	2 (0.6)	0	2 (0.3)
筋骨格硬直	0	2 (0.6)	0	2 (0.3)
四肢痛	4 (1.3)	0	1 (0.3)	1 (0.2)
線維筋痛	0	0	1 (0.3)	1 (0.2)
変形性脊椎症	0	0	1 (0.3)	1 (0.2)
腱炎	0	0	1 (0.3)	1 (0.2)
滑液包炎	1 (0.3)	1 (0.3)	0	1 (0.2)
脊椎痛	1 (0.3)	1 (0.3)	0	1 (0.2)
筋拘縮	0	1 (0.3)	0	1 (0.2)
斜頚	0	1 (0.3)	0	1 (0.2)
椎間孔狭窄	0	1 (0.3)	0	1 (0.2)
筋骨格系胸痛	4 (1.3)	0	0	0
顎骨嚢胞	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
筋骨格系および結合組織障害 (Cont.)	35 (11.0)	45 (14.3)	20 (6.4)	65 (10.4)
顎下瘻	1 (0.3)	0	0	0
顎痛	1 (0.3)	0	0	0
軟部組織腫脹	1 (0.3)	0	0	0
滑液嚢腫	1 (0.3)	0	0	0
腱鞘炎	1 (0.3)	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）	2 (0.6)	2 (0.6)	3 (1.0)	5 (0.8)
悪性黒色腫	1 (0.3)	0	1 (0.3)	1 (0.2)
アクロコルドン	0	0	1 (0.3)	1 (0.2)
乳管内増殖性病変	0	0	1 (0.3)	1 (0.2)
平滑筋腫	0	0	1 (0.3)	1 (0.2)
基底細胞癌	1 (0.3)	1 (0.3)	0	1 (0.2)
脂肪腫	0	1 (0.3)	0	1 (0.2)
神経腫	1 (0.3)	0	0	0
神経系障害	40 (12.5)	64 (20.4)	77 (24.5)	141 (22.5)
傾眠	5 (1.6)	27 (8.6)	41 (13.1)	68 (10.8)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
神経系障害 (Cont.)	40 (12.5)	64 (20.4)	77 (24.5)	141 (22.5)
頭痛	21 (6.6)	28 (8.9)	21 (6.7)	49 (7.8)
浮動性めまい	6 (1.9)	5 (1.6)	4 (1.3)	9 (1.4)
睡眠時麻痺	0	0	5 (1.6)	5 (0.8)
錯感覚	1 (0.3)	0	3 (1.0)	3 (0.5)
頭部不快感	0	0	3 (1.0)	3 (0.5)
片頭痛	0	2 (0.6)	1 (0.3)	3 (0.5)
失神	0	2 (0.6)	1 (0.3)	3 (0.5)
注意力障害	0	0	2 (0.6)	2 (0.3)
味覚異常	0	0	2 (0.6)	2 (0.3)
感覚鈍麻	2 (0.6)	1 (0.3)	1 (0.3)	2 (0.3)
嗜眠	0	2 (0.6)	0	2 (0.3)
頭部動揺	1 (0.3)	0	1 (0.3)	1 (0.2)
坐骨神経痛	1 (0.3)	0	1 (0.3)	1 (0.2)
失語症	0	0	1 (0.3)	1 (0.2)
運動失調	0	0	1 (0.3)	1 (0.2)
頚動脈狭窄	0	0	1 (0.3)	1 (0.2)
カタプレキシー	0	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
神経系障害 (Cont.)	40 (12.5)	64 (20.4)	77 (24.5)	141 (22.5)
脳血管発作	0	0	1 (0.3)	1 (0.2)
構語障害	0	0	1 (0.3)	1 (0.2)
腰髄神経根障害	0	0	1 (0.3)	1 (0.2)
神経根圧迫	0	0	1 (0.3)	1 (0.2)
神経痛	0	0	1 (0.3)	1 (0.2)
鎮静	0	0	1 (0.3)	1 (0.2)
血管性脳症	0	0	1 (0.3)	1 (0.2)
頚腕症候群	1 (0.3)	1 (0.3)	0	1 (0.2)
糖尿病性ニューロパチー	0	1 (0.3)	0	1 (0.2)
副鼻腔炎に伴う頭痛	0	1 (0.3)	0	1 (0.2)
緊張性頭痛	0	1 (0.3)	0	1 (0.2)
三叉神経痛	0	1 (0.3)	0	1 (0.2)
頚動脈硬化症	1 (0.3)	0	0	0
記憶障害	1 (0.3)	0	0	0
モートン神経痛	1 (0.3)	0	0	0
睡眠の質低下	1 (0.3)	0	0	0
下肢静止不能症候群	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
神経系障害 (Cont.)	40 (12.5)	64 (20.4)	77 (24.5)	141 (22.5)
椎骨脳底動脈不全	1 (0.3)	0	0	0
製品の問題	0	1 (0.3)	0	1 (0.2)
医療機器内血栓	0	1 (0.3)	0	1 (0.2)
精神障害	14 (4.4)	22 (7.0)	21 (6.7)	43 (6.8)
悪夢	1 (0.3)	4 (1.3)	7 (2.2)	11 (1.8)
異常な夢	6 (1.9)	7 (2.2)	4 (1.3)	11 (1.8)
不安	3 (0.9)	4 (1.3)	1 (0.3)	5 (0.8)
錯乱状態	0	0	3 (1.0)	3 (0.5)
入眠時幻覚	0	1 (0.3)	2 (0.6)	3 (0.5)
うつ病	0	0	2 (0.6)	2 (0.3)
感情不安定	0	0	1 (0.3)	1 (0.2)
解離性障害	0	0	1 (0.3)	1 (0.2)
爆発頭部症候群	0	0	1 (0.3)	1 (0.2)
覚醒時幻覚	0	0	1 (0.3)	1 (0.2)
パニック発作	0	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
精神障害 (Cont.)	14 (4.4)	22 (7.0)	21 (6.7)	43 (6.8)
不眠症	2 (0.6)	1 (0.3)	0	1 (0.2)
全般性不安障害	1 (0.3)	1 (0.3)	0	1 (0.2)
抑うつ気分を伴う適応障害	0	1 (0.3)	0	1 (0.2)
自己像幻視	0	1 (0.3)	0	1 (0.2)
抑うつ気分	0	1 (0.3)	0	1 (0.2)
情動障害	0	1 (0.3)	0	1 (0.2)
易刺激性	0	1 (0.3)	0	1 (0.2)
リビドー減退	0	1 (0.3)	0	1 (0.2)
適応障害	1 (0.3)	0	0	0
腎および尿路障害	4 (1.3)	5 (1.6)	5 (1.6)	10 (1.6)
血尿	1 (0.3)	1 (0.3)	2 (0.6)	3 (0.5)
腎結石症	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
急性腎障害	0	0	1 (0.3)	1 (0.2)
腎嚢胞	0	0	1 (0.3)	1 (0.2)
排尿困難	0	1 (0.3)	0	1 (0.2)
水腎症	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
腎および尿路障害 (Cont.)	4 (1.3)	5 (1.6)	5 (1.6)	10 (1.6)
尿意切迫	0	1 (0.3)	0	1 (0.2)
蛋白尿	0	1 (0.3)	0	1 (0.2)
糖尿	1 (0.3)	0	0	0
夜間頻尿	1 (0.3)	0	0	0
生殖系および乳房障害	3 (0.9)	5 (1.6)	2 (0.6)	7 (1.1)
月経困難症	0	1 (0.3)	1 (0.3)	2 (0.3)
月経過多	0	1 (0.3)	1 (0.3)	2 (0.3)
良性前立腺肥大症	0	1 (0.3)	0	1 (0.2)
卵管水腫	0	1 (0.3)	0	1 (0.2)
外陰膣乾燥	0	1 (0.3)	0	1 (0.2)
乳房腫瘤	2 (0.6)	0	0	0
不正子宮出血	1 (0.3)	0	0	0
呼吸器、胸郭および縦隔障害	12 (3.8)	13 (4.1)	14 (4.5)	27 (4.3)
口腔咽頭痛	1 (0.3)	5 (1.6)	3 (1.0)	8 (1.3)
咳嗽	0	4 (1.3)	2 (0.6)	6 (1.0)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)	12 (3.8)	13 (4.1)	14 (4.5)	27 (4.3)
鼻閉	0	1 (0.3)	2 (0.6)	3 (0.5)
鼻漏	2 (0.6)	0	2 (0.6)	2 (0.3)
呼吸困難	0	0	2 (0.6)	2 (0.3)
喘息	4 (1.3)	0	1 (0.3)	1 (0.2)
慢性閉塞性肺疾患	1 (0.3)	0	1 (0.3)	1 (0.2)
過換気	0	0	1 (0.3)	1 (0.2)
鼻中隔弯曲	0	0	1 (0.3)	1 (0.2)
アレルギー性鼻炎	0	0	1 (0.3)	1 (0.2)
副鼻腔痛	0	0	1 (0.3)	1 (0.2)
咳払い	0	0	1 (0.3)	1 (0.2)
咽喉乾燥	0	1 (0.3)	0	1 (0.2)
副鼻腔不快感	0	1 (0.3)	0	1 (0.2)
湿性咳嗽	0	1 (0.3)	0	1 (0.2)
副鼻腔うっ血	0	1 (0.3)	0	1 (0.2)
くしゃみ	0	1 (0.3)	0	1 (0.2)
喘鳴	0	1 (0.3)	0	1 (0.2)
アレルギー性副鼻腔炎	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)	12 (3.8)	13 (4.1)	14 (4.5)	27 (4.3)
気管支痙攣	1 (0.3)	0	0	0
非感染性気管支炎	1 (0.3)	0	0	0
気胸	1 (0.3)	0	0	0
肺腫瘤	1 (0.3)	0	0	0
上気道の炎症	1 (0.3)	0	0	0
皮膚および皮下組織障害	14 (4.4)	10 (3.2)	18 (5.7)	28 (4.5)
多汗症	1 (0.3)	3 (1.0)	2 (0.6)	5 (0.8)
湿疹	1 (0.3)	1 (0.3)	2 (0.6)	3 (0.5)
皮膚炎	0	1 (0.3)	2 (0.6)	3 (0.5)
発疹	0	1 (0.3)	2 (0.6)	3 (0.5)
ざ瘡	0	1 (0.3)	1 (0.3)	2 (0.3)
蕁麻疹	3 (0.9)	0	1 (0.3)	1 (0.2)
寝汗	2 (0.6)	0	1 (0.3)	1 (0.2)
脱毛症	1 (0.3)	0	1 (0.3)	1 (0.2)
皮膚潰瘍	1 (0.3)	0	1 (0.3)	1 (0.2)
顔面腫脹	1 (0.3)	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
皮膚および皮下組織障害 (Cont.)	14 (4.4)	10 (3.2)	18 (5.7)	28 (4.5)
光線角化症	0	0	1 (0.3)	1 (0.2)
皮膚嚢腫	0	0	1 (0.3)	1 (0.2)
アレルギー性皮膚炎	0	0	1 (0.3)	1 (0.2)
爪破損	0	0	1 (0.3)	1 (0.2)
皮膚刺激	0	0	1 (0.3)	1 (0.2)
皮膚乾燥	1 (0.3)	1 (0.3)	0	1 (0.2)
接触皮膚炎	0	1 (0.3)	0	1 (0.2)
汗疹	0	1 (0.3)	0	1 (0.2)
そう痒症	0	1 (0.3)	0	1 (0.2)
全身性そう痒症	0	1 (0.3)	0	1 (0.2)
丘疹性皮疹	2 (0.6)	0	0	0
紅斑	1 (0.3)	0	0	0
結節性発疹	1 (0.3)	0	0	0
外科および内科処置	0	0	1 (0.3)	1 (0.2)
抜歯	0	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-8
SOC/PT 別の有害事象発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
血管障害	6 (1.9)	4 (1.3)	5 (1.6)	9 (1.4)
高血圧	4 (1.3)	3 (1.0)	3 (1.0)	6 (1.0)
深部静脈血栓症	0	0	1 (0.3)	1 (0.2)
潮紅	0	0	1 (0.3)	1 (0.2)
低血圧	0	1 (0.3)	0	1 (0.2)
不安定高血圧	1 (0.3)	0	0	0
末梢静脈疾患	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
Subjects with any TEAE	299 (66.9)	289 (66.1)	588 (66.5)
血液およびリンパ系障害	7 (1.6)	4 (0.9)	11 (1.2)
鉄欠乏性貧血	3 (0.7)	0	3 (0.3)
血小板減少症	1 (0.2)	1 (0.2)	2 (0.2)
貧血	2 (0.4)	0	2 (0.2)
低色素性貧血	0	1 (0.2)	1 (0.1)
白血球減少症	0	1 (0.2)	1 (0.1)
リンパ節炎	0	1 (0.2)	1 (0.1)
リンパ節症	1 (0.2)	0	1 (0.1)
正球性貧血	1 (0.2)	0	1 (0.1)
心臓障害	14 (3.1)	8 (1.8)	22 (2.5)
動悸	2 (0.4)	3 (0.7)	5 (0.6)
心房細動	3 (0.7)	1 (0.2)	4 (0.5)
頻脈	4 (0.9)	0	4 (0.5)
心筋症	1 (0.2)	2 (0.5)	3 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
心臓障害 (Cont.)	14 (3.1)	8 (1.8)	22 (2.5)
狭心症	2 (0.4)	0	2 (0.2)
不整脈	2 (0.4)	0	2 (0.2)
急性心筋梗塞	0	1 (0.2)	1 (0.1)
期外収縮	0	1 (0.2)	1 (0.1)
慢性心不全	1 (0.2)	0	1 (0.1)
僧帽弁閉鎖不全症	1 (0.2)	0	1 (0.1)
耳および迷路障害	8 (1.8)	11 (2.5)	19 (2.1)
回転性めまい	4 (0.9)	4 (0.9)	8 (0.9)
耳鳴	0	4 (0.9)	4 (0.5)
頭位性回転性めまい	1 (0.2)	1 (0.2)	2 (0.2)
耳管機能障害	0	1 (0.2)	1 (0.1)
中耳の炎症	0	1 (0.2)	1 (0.1)
耳不快感	1 (0.2)	0	1 (0.1)
聴力低下	1 (0.2)	0	1 (0.1)
鼓膜穿孔	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
内分泌障害	2 (0.4)	0	2 (0.2)
性腺機能低下	1 (0.2)	0	1 (0.1)
甲状腺腫瘤	1 (0.2)	0	1 (0.1)
眼障害	6 (1.3)	6 (1.4)	12 (1.4)
白内障	2 (0.4)	2 (0.5)	4 (0.5)
霰粒腫	0	1 (0.2)	1 (0.1)
眼そう痒症	0	1 (0.2)	1 (0.1)
眼瞼浮腫	0	1 (0.2)	1 (0.1)
黄斑変性	0	1 (0.2)	1 (0.1)
深径覚の変化	1 (0.2)	0	1 (0.1)
糖尿病網膜症	1 (0.2)	0	1 (0.1)
眼のアレルギー	1 (0.2)	0	1 (0.1)
フロッピー眼瞼症候群	1 (0.2)	0	1 (0.1)
緑内障	1 (0.2)	0	1 (0.1)
非感染性結膜炎	1 (0.2)	0	1 (0.1)
高血圧性網膜症	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
眼障害 (Cont.)	6 (1.3)	6 (1.4)	12 (1.4)
霧視	1 (0.2)	0	1 (0.1)
視力低下	1 (0.2)	0	1 (0.1)
胃腸障害	53 (11.9)	43 (9.8)	96 (10.9)
悪心	12 (2.7)	9 (2.1)	21 (2.4)
下痢	5 (1.1)	8 (1.8)	13 (1.5)
上腹部痛	5 (1.1)	5 (1.1)	10 (1.1)
嘔吐	4 (0.9)	4 (0.9)	8 (0.9)
腹痛	3 (0.7)	4 (0.9)	7 (0.8)
歯痛	3 (0.7)	4 (0.9)	7 (0.8)
口内乾燥	4 (0.9)	3 (0.7)	7 (0.8)
胃食道逆流性疾患	4 (0.9)	3 (0.7)	7 (0.8)
消化不良	2 (0.4)	4 (0.9)	6 (0.7)
便秘	5 (1.1)	1 (0.2)	6 (0.7)
胃炎	1 (0.2)	2 (0.5)	3 (0.3)
痔核	1 (0.2)	1 (0.2)	2 (0.2)
歯周病	1 (0.2)	1 (0.2)	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
胃腸障害 (Cont.)	53 (11.9)	43 (9.8)	96 (10.9)
口内炎	1 (0.2)	1 (0.2)	2 (0.2)
齲歯	2 (0.4)	0	2 (0.2)
大腸ポリープ	2 (0.4)	0	2 (0.2)
腹部不快感	0	1 (0.2)	1 (0.1)
小腸炎	0	1 (0.2)	1 (0.1)
鼓腸	0	1 (0.2)	1 (0.1)
胃腸出血	0	1 (0.2)	1 (0.1)
腹部ヘルニア	1 (0.2)	0	1 (0.1)
アルコール性膵炎	1 (0.2)	0	1 (0.1)
慢性胃炎	1 (0.2)	0	1 (0.1)
びらん性胃炎	1 (0.2)	0	1 (0.1)
胃腸障害	1 (0.2)	0	1 (0.1)
胃腸の炎症	1 (0.2)	0	1 (0.1)
裂孔ヘルニア	1 (0.2)	0	1 (0.1)
口腔内潰瘍形成	1 (0.2)	0	1 (0.1)
口腔内痛	1 (0.2)	0	1 (0.1)
膵腫大	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
胃腸障害 (Cont.)	53 (11.9)	43 (9.8)	96 (10.9)
流涎過多	1 (0.2)	0	1 (0.1)
一般・全身障害および投与部位の状態	36 (8.1)	30 (6.9)	66 (7.5)
疲労	14 (3.1)	17 (3.9)	31 (3.5)
末梢性浮腫	8 (1.8)	2 (0.5)	10 (1.1)
胸痛	1 (0.2)	2 (0.5)	3 (0.3)
倦怠感	2 (0.4)	1 (0.2)	3 (0.3)
異常感	3 (0.7)	0	3 (0.3)
無力症	0	2 (0.5)	2 (0.2)
発熱	0	2 (0.5)	2 (0.2)
胸部不快感	1 (0.2)	1 (0.2)	2 (0.2)
疼痛	1 (0.2)	1 (0.2)	2 (0.2)
口渇	1 (0.2)	1 (0.2)	2 (0.2)
非心臓性胸痛	2 (0.4)	0	2 (0.2)
不快感	0	1 (0.2)	1 (0.1)
顔面痛	0	1 (0.2)	1 (0.1)
インフルエンザ様疾患	0	1 (0.2)	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
一般・全身障害および投与部位の状態 (Cont.)	36 (8.1)	30 (6.9)	66 (7.5)
穿刺部位反応	0	1 (0.2)	1 (0.1)
ワクチン接種部位疼痛	0	1 (0.2)	1 (0.1)
悪寒	1 (0.2)	0	1 (0.1)
酩酊感	1 (0.2)	0	1 (0.1)
全身健康状態低下	1 (0.2)	0	1 (0.1)
炎症	1 (0.2)	0	1 (0.1)
体温調節障害	1 (0.2)	0	1 (0.1)
血管穿刺部位内出血	1 (0.2)	0	1 (0.1)
肝胆道系障害	5 (1.1)	2 (0.5)	7 (0.8)
脂肪肝	3 (0.7)	0	3 (0.3)
胆石症	2 (0.4)	0	2 (0.2)
胆汁うっ滞	0	1 (0.2)	1 (0.1)
肝嚢胞	0	1 (0.2)	1 (0.1)
肝毒性	0	1 (0.2)	1 (0.1)
胆嚢炎	1 (0.2)	0	1 (0.1)
胆嚢摘出術後症候群	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
免疫系障害	3 (0.7)	5 (1.1)	8 (0.9)
節足動物刺傷アレルギー	0	2 (0.5)	2 (0.2)
季節性アレルギー	2 (0.4)	0	2 (0.2)
アレルギー性浮腫	0	1 (0.2)	1 (0.1)
食物アレルギー	0	1 (0.2)	1 (0.1)
過敏症	0	1 (0.2)	1 (0.1)
動物アレルギー	1 (0.2)	0	1 (0.1)
感染症および寄生虫症	149 (33.3)	143 (32.7)	292 (33.0)
上咽頭炎	51 (11.4)	48 (11.0)	99 (11.2)
インフルエンザ	22 (4.9)	26 (5.9)	48 (5.4)
上気道感染	21 (4.7)	18 (4.1)	39 (4.4)
尿路感染	10 (2.2)	18 (4.1)	28 (3.2)
胃腸炎	8 (1.8)	10 (2.3)	18 (2.0)
副鼻腔炎	10 (2.2)	7 (1.6)	17 (1.9)
気管支炎	8 (1.8)	8 (1.8)	16 (1.8)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
感染症および寄生虫症 (Cont.)	149 (33.3)	143 (32.7)	292 (33.0)
ウイルス性上気道感染	6 (1.3)	8 (1.8)	14 (1.6)
歯感染	7 (1.6)	2 (0.5)	9 (1.0)
咽頭炎	4 (0.9)	3 (0.7)	7 (0.8)
膀胱炎	0	6 (1.4)	6 (0.7)
鼻炎	4 (0.9)	2 (0.5)	6 (0.7)
結膜炎	2 (0.4)	3 (0.7)	5 (0.6)
蜂巣炎	3 (0.7)	2 (0.5)	5 (0.6)
気道感染	2 (0.4)	2 (0.5)	4 (0.5)
中耳炎	3 (0.7)	1 (0.2)	4 (0.5)
肺炎	3 (0.7)	1 (0.2)	4 (0.5)
扁桃炎	1 (0.2)	2 (0.5)	3 (0.3)
喉頭炎	2 (0.4)	1 (0.2)	3 (0.3)
ウイルス性気道感染	2 (0.4)	1 (0.2)	3 (0.3)
ヘリコバクター性胃炎	3 (0.7)	0	3 (0.3)
四肢膿瘍	0	2 (0.5)	2 (0.2)
消化管感染	0	2 (0.5)	2 (0.2)
歯肉炎	0	2 (0.5)	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
感染症および寄生虫症 (Cont.)	149 (33.3)	143 (32.7)	292 (33.0)
外陰部腟カンジダ症	0	2 (0.5)	2 (0.2)
乳房膿瘍	1 (0.2)	1 (0.2)	2 (0.2)
眼感染	1 (0.2)	1 (0.2)	2 (0.2)
ウイルス性胃腸炎	1 (0.2)	1 (0.2)	2 (0.2)
爪真菌症	1 (0.2)	1 (0.2)	2 (0.2)
歯膿瘍	1 (0.2)	1 (0.2)	2 (0.2)
帯状疱疹	2 (0.4)	0	2 (0.2)
口腔ヘルペス	2 (0.4)	0	2 (0.2)
急性副鼻腔炎	0	1 (0.2)	1 (0.1)
カンジダ感染	0	1 (0.2)	1 (0.1)
遊走性紅斑	0	1 (0.2)	1 (0.1)
耳下腺炎	0	1 (0.2)	1 (0.1)
皮下組織膿瘍	0	1 (0.2)	1 (0.1)
細菌性腟症	1 (0.2)	0	1 (0.1)
ボレリア感染	1 (0.2)	0	1 (0.1)
細菌性気管支炎	1 (0.2)	0	1 (0.1)
クロストリジウム・ディフィシレ感染	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
感染症および寄生虫症 (Cont.)	149 (33.3)	143 (32.7)	292 (33.0)
感染性下痢	1 (0.2)	0	1 (0.1)
丹毒	1 (0.2)	0	1 (0.1)
外耳蜂巣炎	1 (0.2)	0	1 (0.1)
せつ	1 (0.2)	0	1 (0.1)
単純ヘルペス	1 (0.2)	0	1 (0.1)
下気道感染	1 (0.2)	0	1 (0.1)
外耳炎	1 (0.2)	0	1 (0.1)
急性中耳炎	1 (0.2)	0	1 (0.1)
歯周炎	1 (0.2)	0	1 (0.1)
百日咳	1 (0.2)	0	1 (0.1)
術後創感染	1 (0.2)	0	1 (0.1)
歯髄炎	1 (0.2)	0	1 (0.1)
猩紅熱	1 (0.2)	0	1 (0.1)
唾液腺炎	1 (0.2)	0	1 (0.1)
ブドウ球菌皮膚感染	1 (0.2)	0	1 (0.1)
創傷感染	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
傷害、中毒および処置合併症	40 (8.9)	34 (7.8)	74 (8.4)
転倒	12 (2.7)	10 (2.3)	22 (2.5)
挫傷	7 (1.6)	4 (0.9)	11 (1.2)
靱帯捻挫	1 (0.2)	7 (1.6)	8 (0.9)
処置による疼痛	4 (0.9)	4 (0.9)	8 (0.9)
企図的過量投与	4 (0.9)	0	4 (0.5)
節足動物咬傷	2 (0.4)	1 (0.2)	3 (0.3)
四肢損傷	2 (0.4)	1 (0.2)	3 (0.3)
手骨折	3 (0.7)	0	3 (0.3)
肉離れ	3 (0.7)	0	3 (0.3)
肋骨骨折	0	2 (0.5)	2 (0.2)
交通事故	0	2 (0.5)	2 (0.2)
歯牙破折	0	2 (0.5)	2 (0.2)
動物咬傷	1 (0.2)	1 (0.2)	2 (0.2)
足関節部骨折	1 (0.2)	1 (0.2)	2 (0.2)
節足動物刺傷	1 (0.2)	1 (0.2)	2 (0.2)
足骨折	1 (0.2)	1 (0.2)	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
傷害、中毒および処置合併症 (Cont.)	40 (8.9)	34 (7.8)	74 (8.4)
関節損傷	1 (0.2)	1 (0.2)	2 (0.2)
下肢骨折	1 (0.2)	1 (0.2)	2 (0.2)
半月板損傷	1 (0.2)	1 (0.2)	2 (0.2)
皮膚擦過傷	1 (0.2)	1 (0.2)	2 (0.2)
靭帯損傷	2 (0.4)	0	2 (0.2)
事故	0	1 (0.2)	1 (0.1)
動物による引っかき傷	0	1 (0.2)	1 (0.1)
関節脱臼	0	1 (0.2)	1 (0.1)
橈骨骨折	0	1 (0.2)	1 (0.1)
熱傷	0	1 (0.2)	1 (0.1)
上肢骨折	0	1 (0.2)	1 (0.1)
創傷	0	1 (0.2)	1 (0.1)
偶発的過量投与	1 (0.2)	0	1 (0.1)
筋膜断裂	1 (0.2)	0	1 (0.1)
靭帯断裂	1 (0.2)	0	1 (0.1)
外傷性血腫	1 (0.2)	0	1 (0.1)
手首関節骨折	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
臨床検査	32 (7.2)	27 (6.2)	59 (6.7)
体重増加	12 (2.7)	8 (1.8)	20 (2.3)
アラニンアミノトランスフェラーゼ増加	4 (0.9)	4 (0.9)	8 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	3 (0.7)	2 (0.5)	5 (0.6)
血中トリグリセリド増加	4 (0.9)	1 (0.2)	5 (0.6)
血中コレステロール増加	1 (0.2)	3 (0.7)	4 (0.5)
肝機能検査値上昇	1 (0.2)	2 (0.5)	3 (0.3)
体重減少	0	2 (0.5)	2 (0.2)
血圧上昇	1 (0.2)	1 (0.2)	2 (0.2)
血中尿酸増加	1 (0.2)	1 (0.2)	2 (0.2)
血中ビリルビン増加	0	1 (0.2)	1 (0.1)
血中鉄増加	0	1 (0.2)	1 (0.1)
血中カリウム増加	0	1 (0.2)	1 (0.1)
心電図異常	0	1 (0.2)	1 (0.1)
心電図変化	0	1 (0.2)	1 (0.1)
好中球数減少	0	1 (0.2)	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
臨床検査 (Cont.)	32 (7.2)	27 (6.2)	59 (6.7)
トランスアミナーゼ上昇	0	1 (0.2)	1 (0.1)
血中非抱合ビリルビン増加	1 (0.2)	0	1 (0.1)
尿中血陽性	1 (0.2)	0	1 (0.1)
尿中結晶陽性	1 (0.2)	0	1 (0.1)
心電図ＰＲ延長	1 (0.2)	0	1 (0.1)
心電図ＱＴ延長	1 (0.2)	0	1 (0.1)
尿中蛋白陽性	1 (0.2)	0	1 (0.1)
血清フェリチン減少	1 (0.2)	0	1 (0.1)
尿中ケトン体陽性	1 (0.2)	0	1 (0.1)
白血球数増加	1 (0.2)	0	1 (0.1)
代謝および栄養障害	20 (4.5)	12 (2.7)	32 (3.6)
食欲亢進	3 (0.7)	3 (0.7)	6 (0.7)
高尿酸血症	5 (1.1)	1 (0.2)	6 (0.7)
食欲減退	3 (0.7)	1 (0.2)	4 (0.5)
ビタミンＢ群欠乏	1 (0.2)	2 (0.5)	3 (0.3)
ビタミンＤ欠乏	2 (0.4)	1 (0.2)	3 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
代謝および栄養障害 (Cont.)	20 (4.5)	12 (2.7)	32 (3.6)
２型糖尿病	0	2 (0.5)	2 (0.2)
脂質異常症	1 (0.2)	1 (0.2)	2 (0.2)
肥満	1 (0.2)	1 (0.2)	2 (0.2)
高脂血症	2 (0.4)	0	2 (0.2)
糖尿病	0	1 (0.2)	1 (0.1)
低カリウム血症	0	1 (0.2)	1 (0.1)
体重減少不良	0	1 (0.2)	1 (0.1)
食物渇望	1 (0.2)	0	1 (0.1)
耐糖能障害	1 (0.2)	0	1 (0.1)
痛風	1 (0.2)	0	1 (0.1)
高トリグリセリド血症	1 (0.2)	0	1 (0.1)
筋骨格系および結合組織障害	64 (14.3)	46 (10.5)	110 (12.4)
背部痛	20 (4.5)	13 (3.0)	33 (3.7)
関節痛	20 (4.5)	10 (2.3)	30 (3.4)
変形性関節症	10 (2.2)	8 (1.8)	18 (2.0)
四肢痛	3 (0.7)	4 (0.9)	7 (0.8)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
筋骨格系および結合組織障害 (Cont.)	64 (14.3)	46 (10.5)	110 (12.4)
筋骨格痛	2 (0.4)	4 (0.9)	6 (0.7)
筋緊張	3 (0.7)	3 (0.7)	6 (0.7)
頚部痛	5 (1.1)	1 (0.2)	6 (0.7)
筋肉痛	3 (0.7)	2 (0.5)	5 (0.6)
筋痙縮	4 (0.9)	1 (0.2)	5 (0.6)
関節炎	3 (0.7)	1 (0.2)	4 (0.5)
脊椎痛	2 (0.4)	1 (0.2)	3 (0.3)
線維筋痛	1 (0.2)	1 (0.2)	2 (0.2)
筋力低下	1 (0.2)	1 (0.2)	2 (0.2)
滑液包炎	2 (0.4)	0	2 (0.2)
筋骨格硬直	2 (0.4)	0	2 (0.2)
関節腫脹	0	1 (0.2)	1 (0.1)
筋骨格障害	0	1 (0.2)	1 (0.1)
顎痛	0	1 (0.2)	1 (0.1)
関節リウマチ	0	1 (0.2)	1 (0.1)
変形性脊椎症	0	1 (0.2)	1 (0.1)
腱炎	0	1 (0.2)	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
筋骨格系および結合組織障害 (Cont.)	64 (14.3)	46 (10.5)	110 (12.4)
関節障害	1 (0.2)	0	1 (0.1)
筋拘縮	1 (0.2)	0	1 (0.1)
関節周囲炎	1 (0.2)	0	1 (0.1)
斜頸	1 (0.2)	0	1 (0.1)
椎間孔狭窄	1 (0.2)	0	1 (0.1)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3 (0.7)	6 (1.4)	9 (1.0)
皮膚有棘細胞癌	0	2 (0.5)	2 (0.2)
アクロコルドン	0	1 (0.2)	1 (0.1)
乳管内増殖性病変	0	1 (0.2)	1 (0.1)
平滑筋腫	0	1 (0.2)	1 (0.1)
悪性黒色腫	0	1 (0.2)	1 (0.1)
子宮平滑筋腫	0	1 (0.2)	1 (0.1)
基底細胞癌	1 (0.2)	0	1 (0.1)
乳癌	1 (0.2)	0	1 (0.1)
脂肪腫	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
神経系障害	105 (23.5)	113 (25.9)	218 (24.7)
傾眠	38 (8.5)	60 (13.7)	98 (11.1)
頭痛	43 (9.6)	32 (7.3)	75 (8.5)
浮動性めまい	14 (3.1)	8 (1.8)	22 (2.5)
睡眠時麻痺	8 (1.8)	8 (1.8)	16 (1.8)
錯感覚	1 (0.2)	4 (0.9)	5 (0.6)
失神	2 (0.4)	3 (0.7)	5 (0.6)
片頭痛	2 (0.4)	2 (0.5)	4 (0.5)
注意力障害	0	3 (0.7)	3 (0.3)
頭部不快感	0	3 (0.7)	3 (0.3)
感覚鈍麻	1 (0.2)	2 (0.5)	3 (0.3)
坐骨神経痛	2 (0.4)	1 (0.2)	3 (0.3)
嗜眠	3 (0.7)	0	3 (0.3)
味覚異常	0	2 (0.5)	2 (0.2)
腰髄神経根障害	0	2 (0.5)	2 (0.2)
平衡障害	1 (0.2)	1 (0.2)	2 (0.2)
糖尿病性ニューロパチー	2 (0.4)	0	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
神経系障害 (Cont.)	105 (23.5)	113 (25.9)	218 (24.7)
緊張性頭痛	2 (0.4)	0	2 (0.2)
失語症	0	1 (0.2)	1 (0.1)
運動失調	0	1 (0.2)	1 (0.1)
頚動脈狭窄	0	1 (0.2)	1 (0.1)
カタプレキシー	0	1 (0.2)	1 (0.1)
脳血管発作	0	1 (0.2)	1 (0.1)
構語障害	0	1 (0.2)	1 (0.1)
頭部動揺	0	1 (0.2)	1 (0.1)
過眠症	0	1 (0.2)	1 (0.1)
意識消失	0	1 (0.2)	1 (0.1)
神経根圧迫	0	1 (0.2)	1 (0.1)
神経痛	0	1 (0.2)	1 (0.1)
鎮静	0	1 (0.2)	1 (0.1)
血管性脳症	0	1 (0.2)	1 (0.1)
頚腕症候群	1 (0.2)	0	1 (0.1)
不随意性筋収縮	1 (0.2)	0	1 (0.1)
副鼻腔炎に伴う頭痛	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
神経系障害 (Cont.)	105 (23.5)	113 (25.9)	218 (24.7)
三叉神経痛	1 (0.2)	0	1 (0.1)
椎骨脳底動脈不全	1 (0.2)	0	1 (0.1)
製品の問題	1 (0.2)	0	1 (0.1)
医療機器内血栓	1 (0.2)	0	1 (0.1)
精神障害	29 (6.5)	30 (6.9)	59 (6.7)
異常な夢	9 (2.0)	7 (1.6)	16 (1.8)
悪夢	5 (1.1)	8 (1.8)	13 (1.5)
入眠時幻覚	1 (0.2)	5 (1.1)	6 (0.7)
不安	5 (1.1)	1 (0.2)	6 (0.7)
うつ病	1 (0.2)	4 (0.9)	5 (0.6)
錯乱状態	0	4 (0.9)	4 (0.5)
抑うつ気分を伴う適応障害	3 (0.7)	0	3 (0.3)
不眠症	2 (0.4)	0	2 (0.2)
感情不安定	0	1 (0.2)	1 (0.1)
解離性障害	0	1 (0.2)	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
精神障害 (Cont.)	29 (6.5)	30 (6.9)	59 (6.7)
爆発頭部症候群	0	1 (0.2)	1 (0.1)
覚醒時幻覚	0	1 (0.2)	1 (0.1)
パニック発作	0	1 (0.2)	1 (0.1)
睡眠時随伴症	0	1 (0.2)	1 (0.1)
睡眠障害	0	1 (0.2)	1 (0.1)
夢遊症	0	1 (0.2)	1 (0.1)
自己像幻視	1 (0.2)	0	1 (0.1)
抑うつ気分	1 (0.2)	0	1 (0.1)
情動障害	1 (0.2)	0	1 (0.1)
全般性不安障害	1 (0.2)	0	1 (0.1)
易刺激性	1 (0.2)	0	1 (0.1)
リビドー減退	1 (0.2)	0	1 (0.1)
腎および尿路障害	8 (1.8)	8 (1.8)	16 (1.8)
血尿	2 (0.4)	3 (0.7)	5 (0.6)
腎結石症	1 (0.2)	2 (0.5)	3 (0.3)
蛋白尿	1 (0.2)	1 (0.2)	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
腎および尿路障害 (Cont.)	8 (1.8)	8 (1.8)	16 (1.8)
排尿困難	2 (0.4)	0	2 (0.2)
尿意切迫	2 (0.4)	0	2 (0.2)
急性腎障害	0	1 (0.2)	1 (0.1)
腎嚢胞	0	1 (0.2)	1 (0.1)
水腎症	1 (0.2)	0	1 (0.1)
頻尿	1 (0.2)	0	1 (0.1)
生殖系および乳房障害	8 (1.8)	3 (0.7)	11 (1.2)
月経困難症	2 (0.4)	2 (0.5)	4 (0.5)
月経過多	1 (0.2)	1 (0.2)	2 (0.2)
良性前立腺肥大症	1 (0.2)	0	1 (0.1)
膀胱瘤	1 (0.2)	0	1 (0.1)
卵管水腫	1 (0.2)	0	1 (0.1)
外陰腟乾燥	1 (0.2)	0	1 (0.1)
外陰腟そう痒症	1 (0.2)	0	1 (0.1)
呼吸器、胸郭および縦隔障害	22 (4.9)	18 (4.1)	40 (4.5)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)	22 (4.9)	18 (4.1)	40 (4.5)
咳嗽	9 (2.0)	2 (0.5)	11 (1.2)
口腔咽頭痛	6 (1.3)	3 (0.7)	9 (1.0)
鼻閉	1 (0.2)	3 (0.7)	4 (0.5)
呼吸困難	1 (0.2)	2 (0.5)	3 (0.3)
鼻漏	0	2 (0.5)	2 (0.2)
喘息	1 (0.2)	1 (0.2)	2 (0.2)
慢性閉塞性肺疾患	0	1 (0.2)	1 (0.1)
鼻出血	0	1 (0.2)	1 (0.1)
過換気	0	1 (0.2)	1 (0.1)
喉頭の炎症	0	1 (0.2)	1 (0.1)
鼻中隔弯曲	0	1 (0.2)	1 (0.1)
アレルギー性鼻炎	0	1 (0.2)	1 (0.1)
副鼻腔痛	0	1 (0.2)	1 (0.1)
睡眠時無呼吸症候群	0	1 (0.2)	1 (0.1)
咳払い	0	1 (0.2)	1 (0.1)
咽喉乾燥	1 (0.2)	0	1 (0.1)
副鼻腔不快感	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
呼吸器、胸郭および縦隔障害 (Cont.)	22 (4.9)	18 (4.1)	40 (4.5)
湿性咳嗽	1 (0.2)	0	1 (0.1)
呼吸不全	1 (0.2)	0	1 (0.1)
副鼻腔うっ血	1 (0.2)	0	1 (0.1)
くしゃみ	1 (0.2)	0	1 (0.1)
上気道咳症候群	1 (0.2)	0	1 (0.1)
血管運動性鼻炎	1 (0.2)	0	1 (0.1)
喘鳴	1 (0.2)	0	1 (0.1)
皮膚および皮下組織障害	22 (4.9)	24 (5.5)	46 (5.2)
発疹	4 (0.9)	4 (0.9)	8 (0.9)
湿疹	3 (0.7)	4 (0.9)	7 (0.8)
多汗症	3 (0.7)	2 (0.5)	5 (0.6)
ざ瘡	1 (0.2)	2 (0.5)	3 (0.3)
皮膚炎	1 (0.2)	2 (0.5)	3 (0.3)
光線角化症	1 (0.2)	1 (0.2)	2 (0.2)
皮膚嚢腫	1 (0.2)	1 (0.2)	2 (0.2)
皮膚乾燥	2 (0.4)	0	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
皮膚および皮下組織障害 (Cont.)	22 (4.9)	24 (5.5)	46 (5.2)
汗疹	2 (0.4)	0	2 (0.2)
脱毛症	0	1 (0.2)	1 (0.1)
アレルギー性皮膚炎	0	1 (0.2)	1 (0.1)
びまん性脱毛症	0	1 (0.2)	1 (0.1)
寝汗	0	1 (0.2)	1 (0.1)
爪破損	0	1 (0.2)	1 (0.1)
皮膚刺激	0	1 (0.2)	1 (0.1)
皮膚潰瘍	0	1 (0.2)	1 (0.1)
顔面腫脹	0	1 (0.2)	1 (0.1)
蕁麻疹	0	1 (0.2)	1 (0.1)
接触皮膚炎	1 (0.2)	0	1 (0.1)
爪の障害	1 (0.2)	0	1 (0.1)
色素沈着障害	1 (0.2)	0	1 (0.1)
そう痒症	1 (0.2)	0	1 (0.1)
アレルギー性そう痒症	1 (0.2)	0	1 (0.1)
全身性そう痒症	1 (0.2)	0	1 (0.1)
日光皮膚炎	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-9
SOC/PT 別の有害事象発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
外科および内科処置	0	1 (0.2)	1 (0.1)
抜歯	0	1 (0.2)	1 (0.1)
血管障害	8 (1.8)	10 (2.3)	18 (2.0)
高血圧	5 (1.1)	6 (1.4)	11 (1.2)
低血圧	1 (0.2)	1 (0.2)	2 (0.2)
血栓症	1 (0.2)	1 (0.2)	2 (0.2)
深部静脈血栓症	0	1 (0.2)	1 (0.1)
潮紅	0	1 (0.2)	1 (0.1)
血圧変動	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
Subjects with any treatment-related TEAE	44 (13.8)	78 (24.8)	91 (29.0)	169 (26.9)
血液およびリンパ系障害	0	0	2 (0.6)	2 (0.3)
白血球減少症	0	0	1 (0.3)	1 (0.2)
血小板減少症	0	0	1 (0.3)	1 (0.2)
心臓障害	1 (0.3)	3 (1.0)	2 (0.6)	5 (0.8)
動悸	1 (0.3)	2 (0.6)	2 (0.6)	4 (0.6)
不整脈	0	1 (0.3)	0	1 (0.2)
心房細動	1 (0.3)	0	0	0
耳および迷路障害	1 (0.3)	2 (0.6)	5 (1.6)	7 (1.1)
回転性めまい	1 (0.3)	2 (0.6)	2 (0.6)	4 (0.6)
耳鳴	0	0	3 (1.0)	3 (0.5)
眼障害	0	1 (0.3)	1 (0.3)	2 (0.3)
眼そう痒症	0	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
眼障害 (Cont.)	0	1 (0.3)	1 (0.3)	2 (0.3)
眼のアレルギー	0	1 (0.3)	0	1 (0.2)
胃腸障害	2 (0.6)	8 (2.5)	7 (2.2)	15 (2.4)
口内乾燥	1 (0.3)	2 (0.6)	3 (1.0)	5 (0.8)
悪心	0	4 (1.3)	1 (0.3)	5 (0.8)
上腹部痛	0	1 (0.3)	1 (0.3)	2 (0.3)
下痢	1 (0.3)	0	1 (0.3)	1 (0.2)
便秘	0	0	1 (0.3)	1 (0.2)
嘔吐	0	0	1 (0.3)	1 (0.2)
消化不良	0	1 (0.3)	0	1 (0.2)
流涎過多	0	1 (0.3)	0	1 (0.2)
一般・全身障害および投与部位の状態	2 (0.6)	13 (4.1)	9 (2.9)	22 (3.5)
疲労	1 (0.3)	10 (3.2)	8 (2.5)	18 (2.9)
異常感	0	3 (1.0)	0	3 (0.5)
口渇	1 (0.3)	1 (0.3)	1 (0.3)	2 (0.3)
不快感	0	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
感染症および寄生虫症	1 (0.3)	2 (0.6)	0	2 (0.3)
咽頭炎	0	1 (0.3)	0	1 (0.2)
上気道感染	0	1 (0.3)	0	1 (0.2)
上咽頭炎	1 (0.3)	0	0	0
傷害、中毒および処置合併症	1 (0.3)	0	0	0
挫傷	1 (0.3)	0	0	0
臨床検査	7 (2.2)	8 (2.5)	10 (3.2)	18 (2.9)
体重増加	3 (0.9)	3 (1.0)	4 (1.3)	7 (1.1)
アラニンアミノトランスフェラーゼ増加	1 (0.3)	2 (0.6)	2 (0.6)	4 (0.6)
血中トリグリセリド増加	1 (0.3)	3 (1.0)	0	3 (0.5)
肝機能検査値上昇	0	0	2 (0.6)	2 (0.3)
血中コレステロール増加	2 (0.6)	0	1 (0.3)	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 (0.3)	0	1 (0.3)	1 (0.2)
血中カリウム増加	0	0	1 (0.3)	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
臨床検査 (Cont.)	7 (2.2)	8 (2.5)	10 (3.2)	18 (2.9)
心電図ＰＲ延長	0	1 (0.3)	0	1 (0.2)
血中乳酸脱水素酵素増加	1 (0.3)	0	0	0
代謝および栄養障害	2 (0.6)	4 (1.3)	4 (1.3)	8 (1.3)
食欲亢進	1 (0.3)	3 (1.0)	3 (1.0)	6 (1.0)
体重減少不良	0	0	1 (0.3)	1 (0.2)
食欲減退	0	1 (0.3)	0	1 (0.2)
食欲障害	1 (0.3)	0	0	0
筋骨格系および結合組織障害	2 (0.6)	5 (1.6)	1 (0.3)	6 (1.0)
筋力低下	0	1 (0.3)	1 (0.3)	2 (0.3)
筋痙縮	1 (0.3)	1 (0.3)	0	1 (0.2)
筋骨格硬直	0	1 (0.3)	0	1 (0.2)
頸部痛	0	1 (0.3)	0	1 (0.2)
変形性関節症	0	1 (0.3)	0	1 (0.2)
筋骨格系胸痛	1 (0.3)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
神経系障害	19 (6.0)	41 (13.1)	61 (19.4)	102 (16.2)
傾眠	4 (1.3)	27 (8.6)	40 (12.7)	67 (10.7)
頭痛	11 (3.4)	12 (3.8)	12 (3.8)	24 (3.8)
浮動性めまい	1 (0.3)	3 (1.0)	3 (1.0)	6 (1.0)
睡眠時麻痺	0	0	4 (1.3)	4 (0.6)
注意力障害	0	0	2 (0.6)	2 (0.3)
味覚異常	0	0	2 (0.6)	2 (0.3)
頭部不快感	0	0	2 (0.6)	2 (0.3)
頭部動揺	1 (0.3)	0	1 (0.3)	1 (0.2)
感覚鈍麻	1 (0.3)	0	1 (0.3)	1 (0.2)
カタプレキシー	0	0	1 (0.3)	1 (0.2)
構語障害	0	0	1 (0.3)	1 (0.2)
片頭痛	0	0	1 (0.3)	1 (0.2)
錯感覚	0	0	1 (0.3)	1 (0.2)
鎮静	0	0	1 (0.3)	1 (0.2)
嗜眠	0	1 (0.3)	0	1 (0.2)
失神	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
神経系障害 (Cont.)	19 (6.0)	41 (13.1)	61 (19.4)	102 (16.2)
緊張性頭痛	0	1 (0.3)	0	1 (0.2)
記憶障害	1 (0.3)	0	0	0
睡眠の質低下	1 (0.3)	0	0	0
下肢静止不能症候群	1 (0.3)	0	0	0
椎骨脳底動脈不全	1 (0.3)	0	0	0
精神障害	9 (2.8)	14 (4.5)	14 (4.5)	28 (4.5)
異常な夢	5 (1.6)	7 (2.2)	4 (1.3)	11 (1.8)
悪夢	1 (0.3)	3 (1.0)	7 (2.2)	10 (1.6)
入眠時幻覚	0	1 (0.3)	2 (0.6)	3 (0.5)
錯乱状態	0	0	2 (0.6)	2 (0.3)
爆発頭部症候群	0	0	1 (0.3)	1 (0.2)
不眠症	1 (0.3)	1 (0.3)	0	1 (0.2)
自己像幻視	0	1 (0.3)	0	1 (0.2)
抑うつ気分	0	1 (0.3)	0	1 (0.2)
情動障害	0	1 (0.3)	0	1 (0.2)
不安	2 (0.6)	0	0	0

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
腎および尿路障害	0	1 (0.3)	0	1 (0.2)
尿意切迫	0	1 (0.3)	0	1 (0.2)
呼吸器、胸郭および縦隔障害	0	0	2 (0.6)	2 (0.3)
過換気	0	0	1 (0.3)	1 (0.2)
咳払い	0	0	1 (0.3)	1 (0.2)
皮膚および皮下組織障害	7 (2.2)	3 (1.0)	2 (0.6)	5 (0.8)
多汗症	1 (0.3)	2 (0.6)	2 (0.6)	4 (0.6)
皮膚乾燥	0	1 (0.3)	0	1 (0.2)
丘疹性皮疹	2 (0.6)	0	0	0
蕁麻疹	2 (0.6)	0	0	0
脱毛症	1 (0.3)	0	0	0
結節性発疹	1 (0.3)	0	0	0
血管障害	0	1 (0.3)	1 (0.3)	2 (0.3)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-10
SOC/PT 別の副作用発現率
国際共同 303 試験：投与第 1 期
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)	Lemborexant Total (N=628) n (%)
血管障害 (Cont.)	0	1 (0.3)	1 (0.3)	2 (0.3)
高血圧	0	0	1 (0.3)	1 (0.2)
低血圧	0	1 (0.3)	0	1 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
Subjects with any treatment-related TEAE	119 (26.6)	130 (29.7)	249 (28.2)
血液およびリンパ系障害	0	2 (0.5)	2 (0.2)
白血球減少症	0	1 (0.2)	1 (0.1)
血小板減少症	0	1 (0.2)	1 (0.1)
心臓障害	3 (0.7)	2 (0.5)	5 (0.6)
動悸	2 (0.4)	2 (0.5)	4 (0.5)
不整脈	1 (0.2)	0	1 (0.1)
耳および迷路障害	2 (0.4)	5 (1.1)	7 (0.8)
回転性めまい	2 (0.4)	2 (0.5)	4 (0.5)
耳鳴	0	3 (0.7)	3 (0.3)
眼障害	1 (0.2)	1 (0.2)	2 (0.2)
眼そう痒症	0	1 (0.2)	1 (0.1)
眼のアレルギー	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
胃腸障害	13 (2.9)	9 (2.1)	22 (2.5)
悪心	6 (1.3)	3 (0.7)	9 (1.0)
口内乾燥	4 (0.9)	3 (0.7)	7 (0.8)
上腹部痛	2 (0.4)	1 (0.2)	3 (0.3)
下痢	1 (0.2)	1 (0.2)	2 (0.2)
便秘	0	1 (0.2)	1 (0.1)
嘔吐	0	1 (0.2)	1 (0.1)
消化不良	1 (0.2)	0	1 (0.1)
流涎過多	1 (0.2)	0	1 (0.1)
一般・全身障害および投与部位の状態	16 (3.6)	16 (3.7)	32 (3.6)
疲労	12 (2.7)	14 (3.2)	26 (2.9)
異常感	3 (0.7)	0	3 (0.3)
口渇	1 (0.2)	1 (0.2)	2 (0.2)
無力症	0	1 (0.2)	1 (0.1)
不快感	0	1 (0.2)	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
一般・全身障害および投与部位の状態 (Cont.)	16 (3.6)	16 (3.7)	32 (3.6)
酩酊感	1 (0.2)	0	1 (0.1)
倦怠感	1 (0.2)	0	1 (0.1)
感染症および寄生虫症	2 (0.4)	1 (0.2)	3 (0.3)
上咽頭炎	0	1 (0.2)	1 (0.1)
咽頭炎	1 (0.2)	0	1 (0.1)
上気道感染	1 (0.2)	0	1 (0.1)
傷害、中毒および処置合併症	3 (0.7)	1 (0.2)	4 (0.5)
転倒	2 (0.4)	1 (0.2)	3 (0.3)
挫傷	1 (0.2)	0	1 (0.1)
手骨折	1 (0.2)	0	1 (0.1)
処置による疼痛	1 (0.2)	0	1 (0.1)
臨床検査	13 (2.9)	16 (3.7)	29 (3.3)
体重増加	7 (1.6)	7 (1.6)	14 (1.6)
アラニンアミノトランスフェラーゼ増加	2 (0.4)	2 (0.5)	4 (0.5)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
臨床検査 (Cont.)	13 (2.9)	16 (3.7)	29 (3.3)
血中トリグリセリド増加	3 (0.7)	1 (0.2)	4 (0.5)
血中コレステロール増加	0	2 (0.5)	2 (0.2)
肝機能検査値上昇	0	2 (0.5)	2 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.2)	1 (0.1)
血中カリウム増加	0	1 (0.2)	1 (0.1)
好中球数減少	0	1 (0.2)	1 (0.1)
血中非抱合ビリルビン増加	1 (0.2)	0	1 (0.1)
心電図ＰＲ延長	1 (0.2)	0	1 (0.1)
代謝および栄養障害	7 (1.6)	4 (0.9)	11 (1.2)
食欲亢進	3 (0.7)	3 (0.7)	6 (0.7)
体重減少不良	0	1 (0.2)	1 (0.1)
食欲減退	1 (0.2)	0	1 (0.1)
食物渇望	1 (0.2)	0	1 (0.1)
高脂血症	1 (0.2)	0	1 (0.1)
高尿酸血症	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
筋骨格系および結合組織障害	5 (1.1)	3 (0.7)	8 (0.9)
筋力低下	1 (0.2)	1 (0.2)	2 (0.2)
筋肉痛	0	1 (0.2)	1 (0.1)
四肢痛	0	1 (0.2)	1 (0.1)
筋痙縮	1 (0.2)	0	1 (0.1)
筋骨格硬直	1 (0.2)	0	1 (0.1)
頚部痛	1 (0.2)	0	1 (0.1)
変形性関節症	1 (0.2)	0	1 (0.1)
神経系障害	67 (15.0)	86 (19.7)	153 (17.3)
傾眠	37 (8.3)	58 (13.3)	95 (10.7)
頭痛	20 (4.5)	16 (3.7)	36 (4.1)
睡眠時麻痺	7 (1.6)	7 (1.6)	14 (1.6)
浮動性めまい	8 (1.8)	6 (1.4)	14 (1.6)
注意力障害	0	3 (0.7)	3 (0.3)
味覚異常	0	2 (0.5)	2 (0.2)
頭部不快感	0	2 (0.5)	2 (0.2)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
神経系障害 (Cont.)	67 (15.0)	86 (19.7)	153 (17.3)
平衡障害	1 (0.2)	1 (0.2)	2 (0.2)
嗜眠	2 (0.4)	0	2 (0.2)
カタプレキシー	0	1 (0.2)	1 (0.1)
構語障害	0	1 (0.2)	1 (0.1)
頭部動揺	0	1 (0.2)	1 (0.1)
過眠症	0	1 (0.2)	1 (0.1)
感覚鈍麻	0	1 (0.2)	1 (0.1)
片頭痛	0	1 (0.2)	1 (0.1)
錯感覚	0	1 (0.2)	1 (0.1)
鎮静	0	1 (0.2)	1 (0.1)
失神	1 (0.2)	0	1 (0.1)
緊張性頭痛	1 (0.2)	0	1 (0.1)
精神障害	18 (4.0)	21 (4.8)	39 (4.4)
異常な夢	9 (2.0)	7 (1.6)	16 (1.8)
悪夢	4 (0.9)	8 (1.8)	12 (1.4)
入眠時幻覚	1 (0.2)	5 (1.1)	6 (0.7)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
精神障害 (Cont.)	18 (4.0)	21 (4.8)	39 (4.4)
錯乱状態	0	3 (0.7)	3 (0.3)
爆発頭部症候群	0	1 (0.2)	1 (0.1)
睡眠時随伴症	0	1 (0.2)	1 (0.1)
夢遊症	0	1 (0.2)	1 (0.1)
不安	1 (0.2)	0	1 (0.1)
自己像幻視	1 (0.2)	0	1 (0.1)
抑うつ気分	1 (0.2)	0	1 (0.1)
情動障害	1 (0.2)	0	1 (0.1)
不眠症	1 (0.2)	0	1 (0.1)
腎および尿路障害	1 (0.2)	0	1 (0.1)
尿意切迫	1 (0.2)	0	1 (0.1)
呼吸器、胸郭および縦隔障害	0	2 (0.5)	2 (0.2)
過換気	0	1 (0.2)	1 (0.1)
咳払い	0	1 (0.2)	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-11
SOC/PT 別の副作用発現率
国際共同 303 試験：レンボレキサント投与例
安全性解析対象集団

MedDRA System Organ Class Preferred Term	Lemborexant 5 mg (N=447) n (%)	Lemborexant 10 mg (N=437) n (%)	Lemborexant Total (N=884) n (%)
皮膚および皮下組織障害	5 (1.1)	3 (0.7)	8 (0.9)
多汗症	2 (0.4)	2 (0.5)	4 (0.5)
湿疹	1 (0.2)	1 (0.2)	2 (0.2)
皮膚乾燥	2 (0.4)	0	2 (0.2)
血管障害	1 (0.2)	1 (0.2)	2 (0.2)
高血圧	0	1 (0.2)	1 (0.1)
低血圧	1 (0.2)	0	1 (0.1)

TEAE = Treatment-emergent Adverse Event.
A TEAE is defined as an AE with onset date on or after the first dose of study drug up to 14 days after the last dose of study drug.
Subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Treatment-related TEAEs include TEAEs that were considered by the Investigator to be reasonably possibly caused by the study drug or TEAEs with a missing causality.
MedDRA (Medical Dictionary for Regulatory Activities) Version 21.0

付録 2.7.6-12　死亡又は重篤な有害事象の被験者ごとの叙述（国際共同 303 試験）

死亡又は重篤な有害事象が認められた被験者に関する叙述を以下に示した。

被験者識別コード	投与群（投与第 1 期→投与第 2 期）	死亡に至った有害事象	死亡以外の重篤な有害事象
50021063	レンボレキサント 10 mg		X
50031045	レンボレキサント 10 mg→レンボレキサント 10 mg		X
50161022	プラセボ		X
50201018	レンボレキサント 5 mg		X
50211001	レンボレキサント 5 mg→レンボレキサント 5 mg		X
50241033	レンボレキサント 10 mg→レンボレキサント 10 mg		X
50251037	プラセボ→レンボレキサント 10 mg		X
50291009	レンボレキサント 5 mg→レンボレキサント 5 mg		X
50301012	プラセボ→レンボレキサント 5 mg		X
50311022	レンボレキサント 5 mg→レンボレキサント 5 mg		X
50321025	プラセボ→レンボレキサント 10 mg		X
50341061	レンボレキサント 5 mg→レンボレキサント 5 mg		X
50381001	プラセボ		X
51051014	プラセボ→レンボレキサント 10 mg		X
51071007	プラセボ→レンボレキサント 10 mg		X
51171004	レンボレキサント 5 mg→レンボレキサント 5 mg		X
52071003	プラセボ→レンボレキサント 5 mg		X
53041002	レンボレキサント 10 mg		X
55061007	プラセボ→レンボレキサント 5 mg		X
56021035	レンボレキサント 5 mg→レンボレキサント 5 mg		X
56051038	レンボレキサント 10 mg		X
56061008	プラセボ→レンボレキサント 5 mg		X
56061012	レンボレキサント 5 mg→レンボレキサント 5 mg		X
58011011	プラセボ→レンボレキサント 5 mg		X
58021004	レンボレキサント 10 mg→レンボレキサント 10 mg		X
58021006	レンボレキサント 5 mg→レンボレキサント 5 mg		X
58071021	レンボレキサント 5 mg→レンボレキサント 5 mg		X
59021005	プラセボ→レンボレキサント 5 mg		X
59021006	レンボレキサント 10 mg→レンボレキサント 10 mg		X
59021011	レンボレキサント 10 mg→レンボレキサント 10 mg		X
59021012	レンボレキサント 10 mg→レンボレキサント 10 mg		X
59021015	レンボレキサント 5 mg→レンボレキサント 5 mg		X
59021018	プラセボ→レンボレキサント 10 mg		X

被験者識別コード	投与群（投与第 1 期→投与第 2 期）	死亡に至った有害事象	死亡以外の重篤な有害事象
59021021	レンボレキサント 10 mg→レンボレキサント 10 mg		X
59021036	レンボレキサント 5 mg→レンボレキサント 5 mg		X
59021047	レンボレキサント 5 mg→レンボレキサント 5 mg		X
59021050	レンボレキサント 5 mg→レンボレキサント 5 mg		X
59021077	プラセボ→レンボレキサント 10 mg		X

Subject ID:	50021063
Age, race, sex, actual treatment group:	88 years, WHITE, Male, Lemborexant 10 mg
Medical history: (MedDRA Preferred Term)	大動脈弁疾患, 大動脈弁置換
Current medical conditions: (MedDRA Preferred Term)	冠動脈疾患, 心房細動, 良性前立腺肥大症, 2 型糖尿病, 湿疹, 高脂血症, 高血圧, 肺腫瘤, 変形性関節症
Concomitant medications:	ATORVASTATIN(01), LOSARTAN(02), ACETYLSALICYLIC ACID(03), METFORMIN(04), TAMSULOSIN(05), FOLIC ACID(07), TRIAMCINOLONE(08), METFORMIN(09), CLOPIDOGREL(10), APIXABAN(11), DOCUSATE(12)
Date of first dose/last dose of study drug (Study Day):	31 AUG 2017 / 11 SEP 2017 (Study Day 12)
Other events: (MedDRA Preferred Term)	急性腎障害, 運動失調, 失語症

Serious adverse events (Investigator term/MedDRA preferred term):	cerebrovascular accident / 脳血管発作
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	12 SEP 2017 (Study Day 13, Follow-up/off-study) / 16 SEP 2017 (Study Day 17, Follow-up/off-study)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED WITH SEQUELAE
Study drug action taken/other action taken:	DRUG WITHDRAWN / WITHDRAWN FROM STUDY
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05
Relationship of event:	NOT RELATED

Subject ID:	50031045
Age, race, sex, actual treatment group:	61 years, WHITE, Male, Lemborexant 10 mg → Lemborexant 10 mg
Medical history: (MedDRA Preferred Term)	足変形, ヘルニア, バニオン手術, ヘルニア修復
Current medical conditions: (MedDRA Preferred Term)	変形性関節症, 高脂血症, バレット食道, 胃食道逆流性疾患, 筋肉痛, 良性前立腺肥大症, 頚部痛, 坐骨神経痛, 傾眠
Concomitant medications:	SIMVASTATIN(01), VITAMINS NOS(02), CALCIUM(03), CINNAMOMUM VERUM(04), POLYCARBOPHIL(05), LINUM USITATISSIMUM(06), CURCUMA LONGA(07), ESOMEPRAZOLE(08), ANACIN /00141001/(09), INFLUENZA VACCINE(10), MELOXICAM(11), NAPROXEN(12), IBUPROFEN(13), ANACIN /00141001/(14), NAPROXEN(15), OXYCODONE(16), VICODIN(17), TRIAMCINOLONE(18), PANTOPRAZOLE(19), ACETYLSALICYLIC ACID(20), CORTISONE(21)
Date of first dose/last dose of study drug (Study Day):	06 SEP 2017 / 09 SEP 2018 (Study Day 369)
Other events: (MedDRA Preferred Term)	頭痛, 神経痛, 節足動物咬傷, 失神

Serious adverse events (Investigator term/MedDRA preferred term):	Worsening Osteoarthritis of the Right Knee / 変形性関節症
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	20 NOV 2017 (Study Day 76, Period 1) / 01 MAY 2018 (Study Day 238, Period 2)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED WITH SEQUELAE
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 10, 14, 20
Relationship of event:	NOT RELATED

Subject ID:	50161022
Age, race, sex, actual treatment group:	38 years, WHITE, Female, Placebo→ Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	副鼻腔手術, 関節形成, 手首手術
Current medical conditions: (MedDRA Preferred Term)	口腔ヘルペス, アレルギー性鼻炎, 2 型糖尿病, 乾癬, 乾癬性関節症
Concomitant medications:	METFORMIN(01), GLIPIZIDE(02), CO-TYLENOL /00446801/(03), APREMILAST(04), GLUCOSAMINE(05), BUSPIRONE(06), CLINDAMYCIN(07), CYCLOBENZAPRINE(08), DOCUSATE(09), FLUTICASONE(10), INSULIN DETEMIR(11), INSULIN ASPART(12), MAGNESIUM HYDROXIDE(13), MAGNESIUM OXIDE(14), NAPROXEN(15), PANTOPRAZOLE(16), PROMETHAZINE(17), SACCHAROMYCES BOULARDII(18), VICODIN(19), SULFASALAZINE(20), NAPROXEN(21)
Date of first dose/last dose of study drug (Study Day):	24 OCT 2017 / 18 NOV 2018 (Study Day 391)
Other events: (MedDRA Preferred Term)	耳感染, 異常な夢, 転倒, 悪心, 胃食道逆流性疾患, 乾癬性関節症, 不安, 筋痙縮

Serious adverse events (Investigator term/MedDRA preferred term):	Proximal tibia fracture, left knee / 脛骨骨折
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	23 MAR 2018 (Study Day 151, Period 1) / 25 JUN 2018 (Study Day 245, Period 1)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	MILD
Outcome:	RECOVERED/RESOLVED WITH SEQUELAE
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Septic Arthritis / 細菌性関節炎
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	17 APR 2018 (Study Day 176, Period 1) / 12 JUN 2018 (Study Day 232, Period 1)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	MILD
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DOSE NOT CHANGED

Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 10, 19
Relationship of event:	NOT RELATED

Subject ID:	50201018
Age, race, sex, actual treatment group:	41 years, CHINESE, Female, Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	足関節部骨折, 四肢痛
Current medical conditions: (MedDRA Preferred Term)	貧血, 注意欠陥多動性障害
Concomitant medications:	OXYCOCET(01), DOCUSATE(02), ENOXAPARIN(03), CEFAZOLIN(05), SODIUM CHLORIDE(06), SIMETICONE(07), DIPHENHYDRAMINE(08), CYCLOBENZAPRINE(09)
Date of first dose/last dose of study drug (Study Day):	10 SEP 2017 / 07 JAN 2018 (Study Day 120)
Other events: (MedDRA Preferred Term)	企図的過量投与, 不安, 頻脈

Serious adverse events (Investigator term/MedDRA preferred term):	Fall / 転倒
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	08 JAN 2018 (Study Day 121, Follow-up/off-study) / 08 JAN 2018 (Study Day 121, Follow-up/off-study)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG WITHDRAWN
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 05, 06, 07, 08, 09
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Left type II open tibia-fibula shaft fracture / 下肢骨折
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	08 JAN 2018 (Study Day 121, Follow-up/off-study) / 13 JAN 2018 (Study Day 126, Follow-up/off-study)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG WITHDRAWN
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 05, 06, 07, 08, 09
Relationship of event:	NOT RELATED

Subject ID:	50211001
Age, race, sex, actual treatment group:	67 years, WHITE, Female, Lemborexant 5 mg → Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	扁桃摘出, 足関節部骨折, 骨折治療, 膝関節形成, 関節固定術, 眼瞼形成, 股関節形成
Current medical conditions: (MedDRA Preferred Term)	憩室, 椎間板障害, 変形性脊椎症, 変形性関節症, 血中コレステロール増加, 胃食道逆流性疾患, 高血圧, 2 型糖尿病, 閉経後, うつ病, 関節リウマチ
Concomitant medications:	METFORMIN(01), HYZAAR(02), SIMVASTATIN(03), OMEPRAZOLE(04), ACETYLSALICYLIC ACID(05), VENLAFAXINE(06), AMLODIPINE(07), LIRAGLUTIDE(08), HYDROXYCHLOROQUINE(09), HYDROMORPHONE(10), ACETYLSALICYLIC ACID(12), GLYCERYL TRINITRATE(13), ONDANSETRON(14)
Date of first dose/last dose of study drug (Study Day):	13 MAR 2017 / 04 MAR 2018 (Study Day 357)
Other events: (MedDRA Preferred Term)	大腸ポリープ

Serious adverse events (Investigator term/MedDRA preferred term):	Chest Pain of undetermined Etiology / 胸痛
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	03 MAY 2017 (Study Day 52, Period 1) / 04 MAY 2017 (Study Day 53, Period 1)
TEAE1/TEAE2	Yes / No
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 10, 12, 13, 14
Relationship of event:	NOT RELATED

Subject ID:	50241033
Age, race, sex, actual treatment group:	46 years, BLACK OR AFRICAN AMERICAN, Female, Lemborexant 10 mg → Lemborexant 10 mg
Medical history: (MedDRA Preferred Term)	乳房形成
Current medical conditions: (MedDRA Preferred Term)	尿路感染, 多嚢胞性卵巣, 女性不妊手術, 片頭痛, 高血圧, 子宮平滑筋腫
Concomitant medications:	LEVONORGESTREL(01), LISINOPRIL(02), TEMAZEPAM(03), THOMAPYRIN N(04), IBUPROFEN(05), OXYCODONE(08), PARACETAMOL(09), ALPRAZOLAM(10), CALCIUM CARBONATE(11), DIPHENHYDRAMINE(12), DOCUSATE(13), HYDRALAZINE(14), ONDANSETRON(15), RIVAROXABAN(16), RIVAROXABAN(17), TEMAZEPAM(18), ENOXAPARIN(19), PSEUDOEPHEDRINE(20)
Date of first dose/last dose of study drug (Study Day):	29 AUG 2017 / 03 SEP 2018 (Study Day 371)
Other events: (MedDRA Preferred Term)	インフルエンザ, 鼻漏

Serious adverse events (Investigator term/MedDRA preferred term):	Deep Vein Thrombosis left leg / 深部静脈血栓症
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	20 DEC 2017 (Study Day 114, Period 1) / 23 FEB 2018 (Study Day 179, Period 1)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DOSE NOT CHANGED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 10, 11, 12, 13, 14, 15
Relationship of event:	NOT RELATED

Subject ID:	50251037
Age, race, sex, actual treatment group:	71 years, WHITE, Female, Placebo → Lemborexant 10 mg
Medical history: (MedDRA Preferred Term)	扁桃摘出, 胆嚢切除, 胆嚢炎, 女性不妊手術, 胃潰瘍, 閉経後, 手根管除圧, 腱鞘切開, 上肢骨折, 胃バイパス
Current medical conditions: (MedDRA Preferred Term)	甲状腺機能低下症, 季節性アレルギー, 遠視, 老視, 糖尿病, 高血圧, 不安, 難聴, 高コレステロール血症, 乾癬, 黄斑変性, 関節痛
Concomitant medications:	PRAVASTATIN(01), LISINOPRIL(02), NIFEDIPINE(03), LEVOTHYROXINE(04), ATENOLOL(05), BETAMETHASONE(06), BIOTIN(07), CYANOCOBALAMIN(08), COLECALCIFEROL(09), VACCINIUM MACROCARPON(10), MACUHEALTH WITH LMZ3(11), NITROFURANTOIN(12), PANTOPRAZOLE(13), HYDRALAZINE(14), EVOFLOXACIN(15), CEFTRIAXONE(16), METRONIDAZOLE(17), ONDANSETRON(18), OMEPRAZOLE(19), AUGMENTIN/00756801/(20), LACTINEX/00203201/(21), DOCUSATE(22), FLUOXETINE(23), CIPROFLOXACIN(24), FLUOROURACIL(25)
Date of first dose/last dose of study drug (Study Day):	27 JUN 2017 / 09 FEB 2018 (Study Day 228)
Other events: (MedDRA Preferred Term)	尿路感染, 悪心, 小腸炎

Serious adverse events (Investigator term/MedDRA preferred term):	gastrointestinal bleed / 胃腸出血
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	10 FEB 2018 (Study Day 229, Follow-up/off-study) / 13 FEB 2018 (Study Day 232, Follow-up/off-study)
TEAE1/TEAE2	No / Yes
Serious criteria:	Life threatening, Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG WITHDRAWN
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 10, 11, 12, 13, 15, 16, 18, 19, 26
Relationship of event:	NOT RELATED

Subject ID:	50291009
Age, race, sex, actual treatment group:	42 years, BLACK OR AFRICAN AMERICAN, Male, Lemborexant 5 mg → Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	椎間板突出, 靭帯手術, 椎間板手術, 靭帯断裂, 転倒, 脊椎手術
Current medical conditions: (MedDRA Preferred Term)	薬物過敏症, 季節性アレルギー, 半月板損傷, 背部痛
Concomitant medications:	MORPHINE(01), OXYCODONE(02), BACTRIM(03), MEROPENEM(04), VANCOMYCIN(05), RIVAROXABAN(06), RIVAROXABAN(07)
Date of first dose/last dose of study drug (Study Day):	27 SEP 2017 / 23 SEP 2018 (Study Day 362)
Other events: (MedDRA Preferred Term)	外耳炎, 医療機器内血栓

Serious adverse events (Investigator term/MedDRA preferred term):	Bacterial infection of surgical incision / 術後創感染
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	22 NOV 2017 (Study Day 57, Period 1) / 02 DEC 2017 (Study Day 67, Period 1)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED WITH SEQUELAE
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	–
Relationship of event:	NOT RELATED

Subject ID:	50301012
Age, race, sex, actual treatment group:	56 years, BLACK OR AFRICAN AMERICAN, Female, Placebo → Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	女性不妊手術, 胆嚢切除, 高血圧, 不整脈, 心臓アブレーション, 胃切除, 高コレステロール血症, 肺炎
Current medical conditions: (MedDRA Preferred Term)	喘息, 肥満, 関節痛, 変形性関節症
Concomitant medications:	LOSARTAN (01), METOPROLOL (02), BUDESONIDE W/FORMOTEROL FUMARATE (03), VERAPAMIL (04), ERGOCALCIFEROL (05), ATORVASTATIN (06), MONTELUKAST (07), CYANOCOBALAMIN (08), BUDESONIDE W/FORMOTEROL FUMARATE (09), PREDNISONE (10), CEFDINIR (11), DOXYCYCLINE (12), SALBUTAMOL (13), VICODIN (14), TIZANIDINE (15), POTASSIUM (16), PARACETAMOL (17), METHYLPREDNISOLONE (18), ONDANSETRON (19), SODIUM CHLORIDE (20), ENOXAPARIN (21), CEFTRIAXONE (22), AZITHROMYCIN (23), PARACETAMOL (24), PARACETAMOL (25), PLANTAGO OVATA (26), DOCUSATE (27), POTASSIUM (28), LACTOBACILLUS NOS (29), HYDRALAZINE (30), LEVOSALBUTAMOL (31), TUSSIN DM (32), PANTOPRAZOLE (33), METHYLPREDNISOLONE (34), IBUPROFEN (35), HYDROMORPHONE (36), PARACETAMOL (37), ENOXAPARIN (38), ONDANSETRON (39), PROMETHAZINE (40), OSMOTAN (41), ACETYLSALICYLIC ACID (42), PANTOPRAZOLE (44), AMOXICILLIN (45), CLARITHROMYCIN (46), HYDROMORPHONE (47), DILTIAZEM (48), PREDNISONE (49), MOXIFLOXACIN (50), POTASSIUM (51), POTASSIUM (52), SALBUTAMOL (55), FISH OIL (57), TETRACYCLINE (62), METRONIDAZOLE (63), OMEPRAZOLE (64), PARACETAMOL (65), DIPHENHYDRAMINE (66), ENOXAPARIN (67), HYDROGEN PEROXIDE (68), HYDROMORPHONE (69), HYDROMORPHONE (70), FLEBOBAG RING LACT (71), METHOCARBAMOL (72), NALOXONE (73), ONDANSETRON (74), OXYCODONE (75), OXYCODONE (76), DOCUSATE W/SENNA (77), CEFAZOLIN (78), KETOROLAC (79), SODIUM CHLORIDE (80), ACETYLSALICYLIC ACID (81), OXYCOCET (82), BUPIVACAINE (84), TRIAMCINOLONE (85), LOSARTAN(86)
Date of first dose/last dose of study drug (Study Day):	06 JUL 2017 / 01 JUL 2018 (Study Day 361)
Other events: (MedDRA Preferred Term)	気管支痙攣, 胸痛, 高血圧, 低カリウム血症, 便秘, 喘息, ヘリコバクター性胃炎, 血小板減少症, 血尿, 正球性貧血

Serious adverse events (Investigator term/MedDRA preferred term):	Pneumonia / 肺炎
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	15 SEP 2017 (Study Day 72, Period 1) / 03 OCT 2017 (Study Day 90, Period 1)
TEAE1/TEAE2	Yes / No
Serious criteria:	Requires inpatient hospitalization or prolongation of existing

	hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 08, 12, 13, 48, 49, 55
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Worsened Hiatal Hernia / 裂孔ヘルニア
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	21 FEB 2018 (Study Day 231, Period 2) / 24 FEB 2018 (Study Day 234, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DOSE NOT CHANGED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 39, 40, 41, 44, 45, 46, 48, 49, 50, 51, 52, 55, 86
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Worsening of Pain of Right Hip Osteoarthritis / 変形性関節症
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	31 MAY 2018 (Study Day 330, Period 2) / 04 JUN 2018 (Study Day 334, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 44, 45, 46, 47, 48, 49, 50, 51, 52, 55, 57, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 84, 85, 86
Relationship of event:	NOT RELATED

Subject ID:	50311022
Age, race, sex, actual treatment group:	41 years, WHITE, Female, Lemborexant 5 mg → Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	胆嚢切除, 抜歯
Current medical conditions: (MedDRA Preferred Term)	筋肉痛, 傾眠, 肥満
Concomitant medications:	IBUPROFEN(01), CEFALEXIN(02), HYDROCHLOROTHIAZIDE(03), PANADEINE CO(04), CLINDAMYCIN(05), DOXYCYCLINE(06), TRAMADOL(07), BACLOFEN(08), MORPHINE(09), POTASSIUM(10), THIAMINE(11), VITAMINS NOS(12)
Date of first dose/last dose of study drug (Study Day):	07 SEP 2017 / 10 JUN 2018 (Study Day 277)
Other events: (MedDRA Preferred Term)	蜂巣炎, 末梢性浮腫, 霧視, 筋痙縮, 気管支炎, 白内障, 乳房膿瘍, 上気道咳症候群, 喉頭炎

Serious adverse events (Investigator term/MedDRA preferred term):	acute pancreatitis due to alcohol use / アルコール性膵炎
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	11 JUN 2018 (Study Day 278, Follow-up/off-study) / 14 JUN 2018 (Study Day 281, Follow-up/off-study)
TEAE1/TEAE2	No / Yes
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	SEVERE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG WITHDRAWN
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 08, 09, 10, 11, 12
Relationship of event:	NOT RELATED

Subject ID:	50321025
Age, race, sex, actual treatment group:	74 years, BLACK OR AFRICAN AMERICAN, Female, Placebo → Lemborexant 10 mg
Medical history: (MedDRA Preferred Term)	子宮摘出, 椎間板突出
Current medical conditions: (MedDRA Preferred Term)	高血圧, 2 型糖尿病, 外科的脊椎固定, 変形性関節症
Concomitant medications:	RISTFOR(01), AMLODIPINE(02), NAPROXEN(03), CO-DIOVAN(04), GLUCOSAMINE(05), MAGNESIUM(06), VICODIN(07), METHYLPREDNISOLONE(08), METHYLPREDNISOLONE(09), METHYLPREDNISOLONE(10), METHYLPREDNISOLONE(11), METHYLPREDNISOLONE(12), METHYLPREDNISOLONE(13), COLECALCIFEROL(14), BIOTIN(15), ACETYLSALICYLIC ACID(16), DOCUSATE(17), MACROGOL(18), ANESTHETICS, GENERAL(19)
Date of first dose/last dose of study drug (Study Day):	14 JUL 2017 / 15 JUL 2018 (Study Day 367)
Other events: (MedDRA Preferred Term)	–

Serious adverse events (Investigator term/MedDRA preferred term):	WORSENING OF OSTEOARTHRITIS OF THE LEFT KNEE / 変形性関節症
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	26 FEB 2018 (Study Day 228, Period 2) / 01 MAR 2018 (Study Day 231, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Requires inpatient hospitalization or prolongation of existing hospitalization
Severity:	MILD
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02, 03, 04, 05, 06, 07, 08, 09, 14, 15, 16, 19
Relationship of event:	NOT RELATED

Subject ID:	50341061
Age, race, sex, actual treatment group:	20 years, BLACK OR AFRICAN AMERICAN, Female, Lemborexant 5 mg → Lemborexant 5 mg
Medical history: (MedDRA Preferred Term)	–
Current medical conditions: (MedDRA Preferred Term)	鉄欠乏性貧血, 月経困難症, 片頭痛
Concomitant medications:	IBUPROFEN(01), NORLESTRIN FE(02)
Date of first dose/last dose of study drug (Study Day):	05 OCT 2017 / 01 OCT 2018 (Study Day 362)
Other events: (MedDRA Preferred Term)	呼吸困難

Serious adverse events (Investigator term/MedDRA preferred term):	overdose intentional 2 doses of IP / 企図的過量投与
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	07 APR 2018 (Study Day 185, Period 2) / 07 APR 2018 (Study Day 185, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Overdose intentional 2 doses of IP / 企図的過量投与
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	08 APR 2018 (Study Day 186, Period 2) / 08 APR 2018 (Study Day 186, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Overdose intentional 2 doses of IP / 企図的過量投与

Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	14 APR 2018 (Study Day 192, Period 2) / 14 APR 2018 (Study Day 192, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Overdose intentional 2 doses of IP / 企図的過量投与
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	15 APR 2018 (Study Day 193, Period 2) / 15 APR 2018 (Study Day 193, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Overdose intentional 2 doses of IP / 企図的過量投与
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	12 MAY 2018 (Study Day 220, Period 2) / 12 MAY 2018 (Study Day 220, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Overdose intentional 2 doses of IP / 企図的過量投与

Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	13 MAY 2018 (Study Day 221, Period 2) / 13 MAY 2018 (Study Day 221, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED

Serious adverse events (Investigator term/MedDRA preferred term):	Overdose intentional 2 doses of IP / 企図的過量投与
Start date of adverse event (Study Day, Period)/outcome date of adverse event (Study Day, Period):	16 JUN 2018 (Study Day 255, Period 2) / 16 JUN 2018 (Study Day 255, Period 2)
TEAE1/TEAE2	No / Yes
Serious criteria:	Important medical events
Severity:	MODERATE
Outcome:	RECOVERED/RESOLVED
Study drug action taken/other action taken:	DRUG INTERRUPTED
Concomitant medications (used until/on the start date of adverse event):	01, 02
Relationship of event:	NOT RELATED