Table 14.3.1-1.4
Treatment Emergent Adverse Events: Number of Participants by Treatment Group, System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
ノロウイルス性胃腸炎	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
ウイルス性胃腸炎	1 (0.5)	0	1 (0.5)	1 (0.5)	2 (2.3)	0
Mild	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Moderate	0	0	1 (0.5)	0	1 (1.2)	0
Severe	0	0	0	0	0	0
歯肉炎	0	0	2 (1.1)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	1 (0.5)	0	0	0
膿痂疹	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
咬傷感染	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
伝染性軟属腫	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
爪真菌症	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

Participants counted only once within each system organ class and preferred term for the most severe occurrence.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

Table 14.3.1-1.4
Treatment Emergent Adverse Events: Number of Participants by Treatment Group, System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
口腔ヘルペス	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
外耳炎	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
中耳炎	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
咽頭炎	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
レンサ球菌性咽頭炎	0	0	3 (1.6)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	3 (1.6)	0	0	0
Severe	0	0	0	0	0	0
肺炎	0	0	3 (1.6)	0	1 (1.2)	0
Mild	0	0	0	0	0	0
Moderate	0	0	3 (1.6)	0	1 (1.2)	0
Severe	0	0	0	0	0	0
処置後感染	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0

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Table 14.3.1-1.4
Treatment Emergent Adverse Events: Number of Participants by Treatment Group, System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
膿尿	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
ブドウ球菌皮膚感染	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
股部白癬	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
歯膿瘍	3 (1.6)	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	3 (1.6)	0	0	0	0	0
Severe	0	0	0	0	0	0
歯感染	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
尿管炎	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	1 (0.5)	0	0	0
腟感染 +	0	0	0	0	1 (1.4)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	1 (1.4)	0
Severe	0	0	0	0	0	0

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ウイルス血症	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
ウイルス感染	0	1 (1.1)	0	2 (1.1)	1 (1.2)	0
Mild	0	1 (1.1)	0	1 (0.5)	0	0
Moderate	0	0	0	1 (0.5)	1 (1.2)	0
Severe	0	0	0	0	0	0
ウイルス性咽頭炎	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
トリコモナス外陰腟炎 +	0	0	1 (0.6)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.6)	0	0	0
Severe	0	0	0	0	0	0
傷害、中毒および処置合併症	10 (5.4)	6 (6.5)	10 (5.5)	13 (7.0)	2 (2.3)	7 (7.7)
Mild	5 (2.7)	4 (4.3)	3 (1.6)	7 (3.8)	0	4 (4.4)
Moderate	5 (2.7)	2 (2.2)	5 (2.7)	5 (2.7)	2 (2.3)	3 (3.3)
Severe	0	0	2 (1.1)	1 (0.5)	0	0
肉離れ	1 (0.5)	1 (1.1)	2 (1.1)	1 (0.5)	0	2 (2.2)
Mild	1 (0.5)	1 (1.1)	2 (1.1)	1 (0.5)	0	0
Moderate	0	0	0	0	0	2 (2.2)
Severe	0	0	0	0	0	0
節足動物咬傷	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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Table 14.3.1-1.4
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挫傷	2 (1.1)	0	0	0	0	1 (1.1)
Mild	2 (1.1)	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
転倒	1 (0.5)	0	2 (1.1)	0	1 (1.2)	1 (1.1)
Mild	1 (0.5)	0	1 (0.5)	0	0	1 (1.1)
Moderate	0	0	0	0	1 (1.2)	0
Severe	0	0	1 (0.5)	0	0	0
処置による疼痛	2 (1.1)	1 (1.1)	0	0	0	1 (1.1)
Mild	0	1 (1.1)	0	0	0	0
Moderate	2 (1.1)	0	0	0	0	1 (1.1)
Severe	0	0	0	0	0	0
製品使用の苦情	0	0	0	1 (0.5)	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
蛇咬傷	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
足関節部骨折	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	1 (0.5)	0	0	0
脳振盪	0	0	2 (1.1)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0

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角膜擦過傷	0	0	0	1 (0.5)	1 (1.2)	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	1 (1.2)	0
Severe	0	0	0	0	0	0
上顆炎	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
足骨折	1 (0.5)	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
関節脱臼	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
関節損傷	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
裂傷	0	0	0	2 (1.1)	0	0
Mild	0	0	0	2 (1.1)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
靭帯捻挫	5 (2.7)	2 (2.2)	2 (1.1)	1 (0.5)	0	0
Mild	3 (1.6)	1 (1.1)	1 (0.5)	1 (0.5)	0	0
Moderate	2 (1.1)	1 (1.1)	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0

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口唇損傷	0	1 (1.1)	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	1 (1.1)	0	0	0	0
Severe	0	0	0	0	0	0
筋断裂	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
爪損傷	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
過量投与	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	1 (0.5)	0	0
外傷後疼痛	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
肋骨骨折	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
交通事故	0	0	1 (0.5)	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	1 (0.5)	0	0
Severe	0	0	0	0	0	0

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皮膚擦過傷	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Mild	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
熱傷	1 (0.5)	0	0	1 (0.5)	0	0
Mild	1 (0.5)	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
歯牙破折	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
各種物質毒性	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
外傷性血腫	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
尺骨骨折	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	1 (0.5)	0	0	0
臨床検査	14 (7.5)	8 (8.6)	8 (4.4)	14 (7.5)	8 (9.3)	9 (9.9)
Mild	9 (4.8)	6 (6.5)	5 (2.7)	8 (4.3)	7 (8.1)	6 (6.6)
Moderate	5 (2.7)	2 (2.2)	1 (0.5)	4 (2.2)	1 (1.2)	3 (3.3)
Severe	0	0	2 (1.1)	2 (1.1)	0	0

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血中クレアチンホスホキナーゼ増加	3 (1.6)	4 (4.3)	3 (1.6)	2 (1.1)	6 (7.0)	2 (2.2)
Mild	3 (1.6)	4 (4.3)	2 (1.1)	0	5 (5.8)	1 (1.1)
Moderate	0	0	0	2 (1.1)	1 (1.2)	1 (1.1)
Severe	0	0	1 (0.5)	0	0	0
体重減少	1 (0.5)	0	0	2 (1.1)	0	2 (2.2)
Mild	0	0	0	1 (0.5)	0	1 (1.1)
Moderate	1 (0.5)	0	0	1 (0.5)	0	1 (1.1)
Severe	0	0	0	0	0	0
アラニンアミノトランスフェラーゼ増加	3 (1.6)	2 (2.2)	2 (1.1)	4 (2.2)	0	1 (1.1)
Mild	2 (1.1)	0	0	2 (1.1)	0	0
Moderate	1 (0.5)	2 (2.2)	1 (0.5)	0	0	1 (1.1)
Severe	0	0	1 (0.5)	2 (1.1)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	2 (1.1)	2 (2.2)	2 (1.1)	3 (1.6)	1 (1.2)	1 (1.1)
Mild	1 (0.5)	1 (1.1)	1 (0.5)	1 (0.5)	0	0
Moderate	1 (0.5)	1 (1.1)	1 (0.5)	1 (0.5)	1 (1.2)	1 (1.1)
Severe	0	0	0	1 (0.5)	0	0
血中カリウム増加	1 (0.5)	0	0	0	0	1 (1.1)
Mild	1 (0.5)	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
腎クレアチニン・クリアランス減少	1 (0.5)	0	0	0	0	1 (1.1)
Mild	1 (0.5)	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
心拍数増加	1 (0.5)	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0

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尿中白血球陽性	0	0	1 (0.5)	0	1 (1.2)	1 (1.1)
Mild	0	0	0	0	1 (1.2)	1 (1.1)
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
血中アルカリホスファターゼ増加	0	0	1 (0.5)	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
血中クレアチニン増加	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
血中ブドウ糖増加	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
血中乳酸脱水素酵素増加	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
血中リン減少	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
尿中血陽性	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 0:44

Table 14.3.1-1.4
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Safety Population

System Organ Class Preferred Term Severity	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
心雑音	0	0	1 (0.5)	1 (0.5)	0	0
Mild	0	0	1 (0.5)	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
腎クレアチニン・クリアランス増加	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
心電図異常T波	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
糸球体濾過率減少	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Mild	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
起立時心拍数増加	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
血小板数減少	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
尿中蛋白陽性	0	1 (1.1)	0	1 (0.5)	0	0
Mild	0	1 (1.1)	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 0:44

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尿中赤血球	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
尿中赤血球陽性	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
体重増加	4 (2.2)	0	0	2 (1.1)	0	0
Mild	3 (1.6)	0	0	2 (1.1)	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
白血球数増加	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
代謝および栄養障害	5 (2.7)	3 (3.2)	6 (3.3)	11 (5.9)	1 (1.2)	4 (4.4)
Mild	4 (2.2)	3 (3.2)	5 (2.7)	10 (5.4)	0	3 (3.3)
Moderate	1 (0.5)	0	1 (0.5)	1 (0.5)	1 (1.2)	1 (1.1)
Severe	0	0	0	0	0	0
食欲減退	1 (0.5)	3 (3.2)	4 (2.2)	7 (3.8)	0	4 (4.4)
Mild	0	3 (3.2)	3 (1.6)	6 (3.2)	0	3 (3.3)
Moderate	1 (0.5)	0	1 (0.5)	1 (0.5)	0	1 (1.1)
Severe	0	0	0	0	0	0
脱水	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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痛風	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
高コレステロール血症	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	1 (1.2)	0
Severe	0	0	0	0	0	0
高カリウム血症	1 (0.5)	0	0	1 (0.5)	0	0
Mild	1 (0.5)	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
高脂血症	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
低カリウム血症	1 (0.5)	0	0	1 (0.5)	0	0
Mild	1 (0.5)	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
食欲亢進	2 (1.1)	0	1 (0.5)	0	0	0
Mild	2 (1.1)	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
多飲症	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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ビタミンＢ１２欠乏	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
筋骨格系および結合組織障害	12 (6.5)	5 (5.4)	13 (7.1)	13 (7.0)	3 (3.5)	3 (3.3)
Mild	3 (1.6)	3 (3.2)	5 (2.7)	3 (1.6)	1 (1.2)	1 (1.1)
Moderate	8 (4.3)	2 (2.2)	7 (3.8)	10 (5.4)	2 (2.3)	2 (2.2)
Severe	1 (0.5)	0	1 (0.5)	0	0	0
側腹部痛	1 (0.5)	0	0	0	0	3 (3.3)
Mild	0	0	0	0	0	2 (2.2)
Moderate	0	0	0	0	0	1 (1.1)
Severe	1 (0.5)	0	0	0	0	0
背部痛	4 (2.2)	2 (2.2)	3 (1.6)	4 (2.2)	0	1 (1.1)
Mild	0	1 (1.1)	0	1 (0.5)	0	0
Moderate	4 (2.2)	1 (1.1)	3 (1.6)	3 (1.6)	0	1 (1.1)
Severe	0	0	0	0	0	0
関節痛	1 (0.5)	1 (1.1)	4 (2.2)	2 (1.1)	2 (2.3)	0
Mild	0	0	2 (1.1)	0	0	0
Moderate	1 (0.5)	1 (1.1)	2 (1.1)	2 (1.1)	2 (2.3)	0
Severe	0	0	0	0	0	0
関節炎	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
肋軟骨炎	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0

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外骨腫	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
骨折痛	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	1 (0.5)	0	0	0
筋痙縮	0	1 (1.1)	2 (1.1)	1 (0.5)	0	0
Mild	0	1 (1.1)	2 (1.1)	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
筋骨格系胸痛	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
筋骨格不快感	1 (0.5)	0	1 (0.5)	0	0	0
Mild	1 (0.5)	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
筋骨格痛	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
筋肉痛	3 (1.6)	0	1 (0.5)	2 (1.1)	0	0
Mild	2 (1.1)	0	0	0	0	0
Moderate	1 (0.5)	0	1 (0.5)	2 (1.1)	0	0
Severe	0	0	0	0	0	0

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頚部痛	0	1 (1.1)	1 (0.5)	2 (1.1)	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	1 (0.5)	2 (1.1)	0	0
Severe	0	0	0	0	0	0
骨壊死	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
四肢痛	1 (0.5)	0	1 (0.5)	2 (1.1)	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	1 (0.5)	2 (1.1)	0	0
Severe	0	0	0	0	0	0
腱炎	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	1 (0.5)	0	0	0	0	0
ホジキン病	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	1 (0.5)	0	0	0	0	0
脂肪腫	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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神経系障害	13 (7.0)	4 (4.3)	15 (8.2)	16 (8.6)	9 (10.5)	5 (5.5)
Mild	8 (4.3)	3 (3.2)	8 (4.4)	10 (5.4)	5 (5.8)	3 (3.3)
Moderate	3 (1.6)	1 (1.1)	6 (3.3)	6 (3.2)	4 (4.7)	2 (2.2)
Severe	2 (1.1)	0	1 (0.5)	0	0	0
浮動性めまい	2 (1.1)	1 (1.1)	4 (2.2)	3 (1.6)	1 (1.2)	3 (3.3)
Mild	2 (1.1)	1 (1.1)	3 (1.6)	3 (1.6)	1 (1.2)	1 (1.1)
Moderate	0	0	1 (0.5)	0	0	2 (2.2)
Severe	0	0	0	0	0	0
過眠症	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
錯感覚	1 (0.5)	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
失神寸前の状態	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
注意力障害	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
体位性めまい	1 (0.5)	0	1 (0.5)	0	0	0
Mild	1 (0.5)	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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味覚異常	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
頭部不快感	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
頭痛	1 (0.5)	0	1 (0.5)	2 (1.1)	1 (1.2)	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	1 (0.5)	2 (1.1)	1 (1.2)	0
Severe	0	0	0	0	0	0
感覚鈍麻	0	0	0	2 (1.1)	1 (1.2)	0
Mild	0	0	0	2 (1.1)	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
頭蓋内動脈瘤	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
記憶障害	0	0	1 (0.5)	0	1 (1.2)	0
Mild	0	0	1 (0.5)	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
精神的機能障害	0	0	0	2 (1.1)	0	0
Mild	0	0	0	2 (1.1)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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片頭痛	3 (1.6)	0	3 (1.6)	1 (0.5)	1 (1.2)	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	2 (1.1)	1 (0.5)	1 (1.2)	0
Severe	2 (1.1)	0	1 (0.5)	0	0	0
前兆を伴う片頭痛	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
睡眠の質低下	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
坐骨神経痛	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	1 (1.2)	0
Severe	0	0	0	0	0	0
鎮静	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Mild	1 (0.5)	0	0	1 (0.5)	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
傾眠	2 (1.1)	2 (2.2)	4 (2.2)	6 (3.2)	1 (1.2)	0
Mild	2 (1.1)	1 (1.1)	3 (1.6)	3 (1.6)	1 (1.2)	0
Moderate	0	1 (1.1)	1 (0.5)	3 (1.6)	0	0
Severe	0	0	0	0	0	0
片頭痛発作重積	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	1 (1.2)	0
Severe	0	0	0	0	0	0

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失神	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
緊張性頭痛	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
振戦	1 (0.5)	0	0	1 (0.5)	0	0
Mild	1 (0.5)	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
妊娠、産褥および周産期の状態	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
流産 +	0	0	0	1 (0.6)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.6)	0	0
Severe	0	0	0	0	0	0
精神障害	7 (3.8)	5 (5.4)	10 (5.5)	10 (5.4)	5 (5.8)	6 (6.6)
Mild	6 (3.2)	1 (1.1)	5 (2.7)	6 (3.2)	2 (2.3)	6 (6.6)
Moderate	1 (0.5)	4 (4.3)	5 (2.7)	3 (1.6)	3 (3.5)	0
Severe	0	0	0	1 (0.5)	0	0
不眠症	3 (1.6)	2 (2.2)	1 (0.5)	2 (1.1)	0	2 (2.2)
Mild	3 (1.6)	1 (1.1)	0	2 (1.1)	0	2 (2.2)
Moderate	0	1 (1.1)	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0

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Table 14.3.1-1.4
Treatment Emergent Adverse Events: Number of Participants by Treatment Group, System Organ Class, Preferred Term, and Severity
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感情不安定	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
不安	2 (1.1)	1 (1.1)	1 (0.5)	0	1 (1.2)	1 (1.1)
Mild	2 (1.1)	0	1 (0.5)	0	0	1 (1.1)
Moderate	0	1 (1.1)	0	0	1 (1.2)	0
Severe	0	0	0	0	0	0
初期不眠症	1 (0.5)	1 (1.1)	0	1 (0.5)	0	1 (1.1)
Mild	1 (0.5)	0	0	0	0	1 (1.1)
Moderate	0	1 (1.1)	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
中期不眠症	1 (0.5)	0	0	1 (0.5)	0	1 (1.1)
Mild	1 (0.5)	0	0	0	0	1 (1.1)
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
異常な夢	0	0	0	1 (0.5)	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
激越	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
快感消失	0	1 (1.1)	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	1 (1.1)	0	0	0	0
Severe	0	0	0	0	0	0

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抑うつ気分	0	0	2 (1.1)	0	0	0
Mild	0	0	2 (1.1)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
うつ病	1 (0.5)	1 (1.1)	2 (1.1)	3 (1.6)	2 (2.3)	0
Mild	1 (0.5)	1 (1.1)	1 (0.5)	2 (1.1)	0	0
Moderate	0	0	1 (0.5)	1 (0.5)	2 (2.3)	0
Severe	0	0	0	0	0	0
抑うつ症状	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
情動障害	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
易刺激性	0	0	2 (1.1)	2 (1.1)	0	0
Mild	0	0	2 (1.1)	2 (1.1)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
大うつ病	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	1 (0.5)	0	0
悪夢	1 (0.5)	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0

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強迫性障害	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
身体疾患による睡眠障害、不眠症型	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
腎および尿路障害	3 (1.6)	3 (3.2)	7 (3.8)	1 (0.5)	5 (5.8)	0
Mild	1 (0.5)	3 (3.2)	4 (2.2)	0	2 (2.3)	0
Moderate	0	0	2 (1.1)	1 (0.5)	3 (3.5)	0
Severe	2 (1.1)	0	1 (0.5)	0	0	0
肋骨脊柱角圧痛	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
排尿困難	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
糖尿	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
血尿	1 (0.5)	0	2 (1.1)	0	0	0
Mild	1 (0.5)	0	2 (1.1)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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水腎症	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
尿意切迫	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	1 (1.2)	0
Severe	0	0	0	0	0	0
腎結石症	0	0	0	0	2 (2.3)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	2 (2.3)	0
Severe	0	0	0	0	0	0
頻尿	0	2 (2.2)	1 (0.5)	0	1 (1.2)	0
Mild	0	2 (2.2)	0	0	1 (1.2)	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
蛋白尿	0	1 (1.1)	3 (1.6)	1 (0.5)	1 (1.2)	0
Mild	0	1 (1.1)	3 (1.6)	0	1 (1.2)	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
尿管結石症	2 (1.1)	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	2 (1.1)	0	1 (0.5)	0	0	0
生殖系および乳房障害	1 (0.5)	1 (1.1)	1 (0.5)	3 (1.6)	2 (2.3)	2 (2.2)
Mild	1 (0.5)	1 (1.1)	1 (0.5)	1 (0.5)	1 (1.2)	0
Moderate	0	0	0	2 (1.1)	1 (1.2)	2 (2.2)
Severe	0	0	0	0	0	0

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無月経 +	0	0	0	0	0	1 (1.2)
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	1 (1.2)
Severe	0	0	0	0	0	0
月経過多 +	0	0	0	1 (0.6)	0	1 (1.2)
Mild	0	0	0	1 (0.6)	0	0
Moderate	0	0	0	0	0	1 (1.2)
Severe	0	0	0	0	0	0
乳房痛	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
月経困難症 +	0	0	1 (0.6)	1 (0.6)	0	0
Mild	0	0	1 (0.6)	0	0	0
Moderate	0	0	0	1 (0.6)	0	0
Severe	0	0	0	0	0	0
頻発月経 +	0	0	0	1 (0.6)	0	0
Mild	0	0	0	1 (0.6)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
子宮出血 +	0	0	0	1 (0.6)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.6)	0	0
Severe	0	0	0	0	0	0
子宮ポリープ +	0	1 (1.2)	0	0	0	0
Mild	0	1 (1.2)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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子宮脱 +	0	0	0	0	1 (1.4)	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	1 (1.4)	0
Severe	0	0	0	0	0	0
腟出血 +	1 (0.6)	0	0	0	0	0
Mild	1 (0.6)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
呼吸器、胸郭および縦隔障害	7 (3.8)	1 (1.1)	7 (3.8)	4 (2.2)	1 (1.2)	5 (5.5)
Mild	3 (1.6)	1 (1.1)	5 (2.7)	3 (1.6)	1 (1.2)	4 (4.4)
Moderate	4 (2.2)	0	1 (0.5)	1 (0.5)	0	1 (1.1)
Severe	0	0	1 (0.5)	0	0	0
息詰まり	1 (0.5)	0	2 (1.1)	1 (0.5)	0	2 (2.2)
Mild	0	0	2 (1.1)	1 (0.5)	0	2 (2.2)
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
喘息	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	0
Moderate	0	0	0	0	0	1 (1.1)
Severe	0	0	0	0	0	0
口腔咽頭痛	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
副鼻腔うっ血	2 (1.1)	0	0	1 (0.5)	0	1 (1.1)
Mild	2 (1.1)	0	0	1 (0.5)	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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運動誘発喘息	0	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
咳嗽	1 (0.5)	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
咽喉乾燥	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
鼻出血	1 (0.5)	0	1 (0.5)	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	1 (0.5)	0	0	0
鼻閉	1 (0.5)	0	3 (1.6)	1 (0.5)	0	0
Mild	1 (0.5)	0	2 (1.1)	0	0	0
Moderate	0	0	1 (0.5)	1 (0.5)	0	0
Severe	0	0	0	0	0	0
鼻乾燥	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
咽頭潰瘍	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

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アレルギー性鼻炎	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
上気道咳症候群	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
皮膚および皮下組織障害	8 (4.3)	5 (5.4)	5 (2.7)	4 (2.2)	2 (2.3)	5 (5.5)
Mild	3 (1.6)	5 (5.4)	4 (2.2)	1 (0.5)	2 (2.3)	5 (5.5)
Moderate	5 (2.7)	0	1 (0.5)	3 (1.6)	0	0
Severe	0	0	0	0	0	0
アトピー性皮膚炎	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
多汗症	1 (0.5)	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
全身性そう痒症	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
発疹	2 (1.1)	1 (1.1)	0	2 (1.1)	0	1 (1.1)
Mild	2 (1.1)	1 (1.1)	0	0	0	1 (1.1)
Moderate	0	0	0	2 (1.1)	0	0
Severe	0	0	0	0	0	0

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酒さ	0	0	0	0	0	1 (1.1)
Mild	0	0	0	0	0	1 (1.1)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
ざ瘡	1 (0.5)	0	1 (0.5)	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	1 (0.5)	0	0	0
Severe	0	0	0	0	0	0
皮膚嚢腫	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
皮膚炎	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
接触皮膚炎	1 (0.5)	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0
湿疹	0	1 (1.1)	0	0	0	0
Mild	0	1 (1.1)	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
皮膚疼痛	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

Participants counted only once within each system organ class and preferred term for the most severe occurrence.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

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Table 14.3.1-1.4
Treatment Emergent Adverse Events: Number of Participants by Treatment Group, System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
そう痒症	0	2 (2.2)	2 (1.1)	0	0	0
Mild	0	2 (2.2)	2 (1.1)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
アレルギー性そう痒症	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
乾癬	0	0	0	0	1 (1.2)	0
Mild	0	0	0	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
紅斑性皮疹	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
そう痒性皮疹	1 (0.5)	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
皮膚病変	0	0	1 (0.5)	0	0	0
Mild	0	0	1 (0.5)	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
蕁麻疹	1 (0.5)	0	0	0	0	0
Mild	0	0	0	0	0	0
Moderate	1 (0.5)	0	0	0	0	0
Severe	0	0	0	0	0	0

Participants counted only once within each system organ class and preferred term for the most severe occurrence.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

Table 14.3.1-1.4
Treatment Emergent Adverse Events: Number of Participants by Treatment Group, System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
血管障害	1 (0.5)	0	2 (1.1)	2 (1.1)	2 (2.3)	1 (1.1)
Mild	1 (0.5)	0	1 (0.5)	1 (0.5)	1 (1.2)	0
Moderate	0	0	1 (0.5)	1 (0.5)	1 (1.2)	1 (1.1)
Severe	0	0	0	0	0	0
高血圧	0	0	1 (0.5)	0	1 (1.2)	1 (1.1)
Mild	0	0	0	0	0	0
Moderate	0	0	1 (0.5)	0	1 (1.2)	1 (1.1)
Severe	0	0	0	0	0	0
深部静脈血栓症	0	0	0	1 (0.5)	0	0
Mild	0	0	0	0	0	0
Moderate	0	0	0	1 (0.5)	0	0
Severe	0	0	0	0	0	0
血腫	0	0	1 (0.5)	0	1 (1.2)	0
Mild	0	0	1 (0.5)	0	1 (1.2)	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
ほてり	1 (0.5)	0	0	0	0	0
Mild	1 (0.5)	0	0	0	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
起立性低血圧	0	0	0	1 (0.5)	0	0
Mild	0	0	0	1 (0.5)	0	0
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

Participants counted only once within each system organ class and preferred term for the most severe occurrence.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

Allergan
Protocol CGP-MD-01

Atogepant (AGN-241689)
Page 1 of 1

Table 14.3.1-2.1.A
On-Therapy Serious Adverse Events: Number of Participants by Treatment Group and Preferred Term Safety Population

Preferred Term	Placebo (N=186) n (%)[Related]	Atogepant 10-mg QD (N=93) n (%)[Related]	Atogepant 30-mg QD (N=183) n (%)[Related]	Atogepant 60-mg QD (N=186) n (%)[Related]	Atogepant 30-mg BID (N=86) n (%)[Related]	Atogepant 60-mg BID (N=91) n (%)[Related]
Any term	2 (1.1) [0]	1 (1.1) [0]	2 (1.1) [0]	2 (1.1) [0]	0	0
流産 +	0	0	0	1 (0.6) [0]	0	0
胆嚢炎	0	1 (1.1) [0]	0	0	0	0
ホジキン病	1 (0.5) [0]	0	0	0	0	0
大うつ病	0	0	0	1 (0.5) [0]	0	0
片頭痛	0	0	1 (0.5) [0]	0	0	0
過量投与	0	0	0	1 (0.5) [0]	0	0
尿管炎	0	0	1 (0.5) [0]	0	0	0
尿管結石症	1 (0.5) [0]	0	0	0	0	0

Includes SAEs that occurred on or after the study treatment start date and within 30 days of the study treatment end date or Visit 8 whichever comes later.
Related = Causally related to study treatment.
Participants are counted only once within each preferred term.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

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Table 14.3.1-2.3
Adverse Events Associated with Premature Discontinuation: Number of Participants by Treatment Group and Preferred Term
Safety Population

Preferred Term	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
Any term	5 (2.7)	4 (4.3)	11 (6.0)	6 (3.2)	5 (5.8)	7 (7.7)
疲労	0	0	0	0	0	3 (3.3)
浮動性めまい	0	0	1 (0.5)	0	0	2 (2.2)
感情不安定	0	0	0	0	0	1 (1.1)
卵巣良性腫瘍 +	0	0	0	0	0	1 (1.2)
胸痛	0	0	0	0	0	1 (1.1)
便秘	0	0	1 (0.5)	1 (0.5)	0	1 (1.1)
食欲減退	0	0	0	0	0	1 (1.1)
不眠症	0	0	0	0	0	1 (1.1)
悪心	0	0	3 (1.6)	0	0	1 (1.1)
失神寸前の状態	0	0	0	0	0	1 (1.1)
製品使用の苦情	0	0	0	1 (0.5)	0	1 (1.1)
腹部不快感	0	0	1 (0.5)	0	0	0
腹痛	0	1 (1.1)	0	0	0	0
アラニンアミノトランスフェラーゼ増加	0	0	1 (0.5)	1 (0.5)	0	0
関節痛	1 (0.5)	0	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	1 (0.5)	0	0
血中クレアチンホスホキナーゼ増加	0	1 (1.1)	0	0	0	0
脳振盪	0	0	1 (0.5)	0	0	0
抑うつ症状	0	0	1 (0.5)	0	0	0
注意力障害	0	0	0	0	1 (1.2)	0
胃食道逆流性疾患	0	0	1 (0.5)	0	0	0
ホジキン病	1 (0.5)	0	0	0	0	0
聴覚過敏	0	0	0	1 (0.5)	0	0
高血圧	0	0	0	0	1 (1.2)	0
過敏性腸症候群	0	0	0	1 (0.5)	0	0
片頭痛	1 (0.5)	0	1 (0.5)	1 (0.5)	0	0
筋肉痛	1 (0.5)	0	1 (0.5)	0	0	0
腎結石症	0	0	0	0	1 (1.2)	0
悪夢	1 (0.5)	0	0	0	0	0
食道痙攣	0	0	0	0	1 (1.2)	0
動悸	0	0	0	0	1 (1.2)	0
発疹	0	0	0	1 (0.5)	0	0

Only includes AEs leading to discontinuation during the study.
Participants are counted only once within each preferred term.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 0:45

Table 14.3.1-2.3
Adverse Events Associated with Premature Discontinuation: Number of Participants by Treatment Group and Preferred Term
Safety Population

Preferred Term	Placebo (N=186) n (%)	Atogepant 10-mg QD (N=93) n (%)	Atogepant 30-mg QD (N=183) n (%)	Atogepant 60-mg QD (N=186) n (%)	Atogepant 30-mg BID (N=86) n (%)	Atogepant 60-mg BID (N=91) n (%)
副鼻腔炎	0	1 (1.1)	0	0	0	0
嘔吐	0	1 (1.1)	0	0	0	0
体重増加	0	0	1 (0.5)	0	0	0

Only includes AEs leading to discontinuation during the study.
Participants are counted only once within each preferred term.
For sex-specific AEs, percentages are relative to the number of participants of the appropriate sex.

3101-301-002 試験［参考資料］

治験の標題： A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-controlled, Parallel-group Study to Evaluate the Efficacy, Safety, and Tolerability of Oral Atogepant for the Prevention of Migraine in Participants with Episodic Migraine (ADVANCE)	
施設数 / 実施国名： 136 施設 / 米国	
治験調整医師： [redacted], MD, MBA	
公表文献（参考資料）： なし	
治験期間： 治験開始日（最初の被験者の初回来院日）：2018 年 12 月 14 日 治験終了日（最後の被験者の最終来院日）：2020 年 6 月 19 日	開発のフェーズ： 第 III 相
治験の種類： 多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験	
目的： ● 反復性片頭痛（以下「EM」）被験者を対象として，片頭痛予防を目的としたアトゲパント水和物（以下「アトゲパント」）10 mg 1 日 1 回（以下「QD」），30 mg QD，及び 60 mg QD の安全性及び忍容性を評価する。 ● EM 被験者を対象として，片頭痛予防を目的としたアトゲパント 10 mg QD，30 mg QD，及び 60 mg QD のプラセボに対する優越性を前向き試験により検証する。	
被験者数（計画時と解析時）： 計画時：約 872 例 解析時：910 例（プラセボ群 223 例，アトゲパント 10 mg QD 群 222 例，アトゲパント 30 mg QD 群 230 例，アトゲパント 60 mg QD 群 235 例） 設定根拠 各投与群に無作為に割り付ける被験者のサンプルサイズを 218 例とすると，主要有効性評価項目で得られる，3 つのアトゲパント用量（各用量の有効性は同等と想定）とプラセボとの投与群間差の検出力は 98%以上となる。下表に示すように，有効性の主要評価項目及び 3 つの副次評価項目について十分な検出力が得られるようサンプルサイズを決定した。検出力は以下の推定に基づき nQuery Advisor 7.0 を使用して算出した： 1）本試験でのアトゲパント各用量とプラセボとの投与群間差は，過去の片頭痛予防効果が評価された試験（アトゲパント［第 II / III 相 CGP-MD-01 試験］，telcagepant[1]，モノクローナル抗体[2–4]）で得られた平均値と同程度になると推定される。各評価項目の標準偏差（以下「SD」）は，約 800 例を対象にした無作為化試験をもとに推定した。12 週間の投与期間での平均月間片頭痛日数（以下「MMD」）のベースラインからの変化量については，投与群間差は–1.5 日，SD は 3.5 日と推定した。投与群間差及び SD の推定値の詳細を下表に示す。 2）本試験の統計解析計画では，全体の第 I 種の過誤率を有意水準 5%で制御する。主要評価項目及び副次評価項目の検出力の算出では多重比較を考慮し，アトゲパント各用量とプラセボを両側有意水準 0.0167 で検定する。各用量の主要評価項目が 0.0167（両側）で有意であると判定された場合に，副次評価項目を順次検定する。	

仮説検定	評価項目	プラセボ群との投与群間差	SD	検出力
主要評価項目	12 週間の投与期間での平均 MMD のベースラインからの変化量	–1.5	3.5[a]	98%
第 1 副次評価項目	12 週間の投与期間での平均月間頭痛日数のベースラインからの変化量	–1.5	3.8[a]	95%[b]
第 2 副次評価項目	12 週間の投与期間での急性期治療薬の平均月間使用日数のベースラインからの変化量	–1.2	3.2[a]	93%[b]
第 3 副次評価項目	12 週間の投与期間での平均 MMD が 50%以上減少した被験者の割合	アトゲパント群の割合：50% プラセボ群の割合：33%	–	89%[b]

a. 約 800 例を対象とした無作為化試験をもとに算出
b. 副次評価項目の統計学的検出力は，各用量とプラセボとの比較順序で先行する評価項目は有意であるという条件下での検出力である（各評価項目は独立と仮定）。

診断と組入れ基準：

以下の選択基準をすべて満たした患者を組入れ可能とした。

選択基準

1. 本試験に関する手順が開始される前に文書同意及び患者のプライバシーに関する情報（Written Authorization for Use and Release of Health and Research Study Information）を得られた患者。
2. Visit 1 の時点で 18 歳以上 80 歳以下の男性患者又は女性患者。
3. 国際頭痛分類第 3 版（以下「ICHD-3」）に基づく診断と一致する前兆のある片頭痛又は前兆のない片頭痛を 1 年以上有する患者。
4. 片頭痛の発症年齢が 50 歳未満の患者。
5. 治験責任医師の判断による Visit 1 前 3 ヵ月間の平均 MMD が 4–14 日である患者。
6. 電子日誌（以下「eDiary」）で 28 日間のベースライン期間に片頭痛の日数が 4–14 日である患者。
7. ベースライン期間 28 日間のうち 20 日間以上 eDiary への入力があり，治験質問票及び eDiary を読解し，入力することができると治験責任医師が判断した患者。
8. 本試験参加期間中，治験実施計画書に規定された医学的に許容され，効果の高い避妊法を使用できる患者。

除外基準

以下の除外基準のいずれかに該当する患者は本試験から除外した。

1. 片頭痛を緊張型頭痛又はその他の頭痛と区別することが困難な患者。
2. 複視若しくは意識レベルの低下を伴う片頭痛，又は ICHD-3 に定義されている網膜片頭痛の既往歴を有する患者。
3. ICHD-3 に定義されている慢性片頭痛，新規発症持続性連日性頭痛，三叉神経・自律神経性頭痛（群発頭痛など），又は有痛性脳神経ニューロパチーと現在診断されている患者。
4. 治験責任医師の判断による Visit 1 前 3 ヵ月間の平均月間頭痛日数が 15 日以上である患者。
5. eDiary で 28 日間のベースライン期間の頭痛日数が 15 日以上である患者。
6. 片頭痛予防目的で処方された 4 種類超の治療薬（そのうち 2 種類は作用機序が異なる）に対して効果不十分であった患者。
7. 併用禁止薬若しくは併用禁止療法の一覧（治験実施計画書で規定）に記載されている薬剤，食事（グレープ

フルーツジュースなど），又は非薬物療法が必要であり，それらを中止できない若しくは許容される別の薬剤や治療法への切り替えができない患者。これには片頭痛予防への有効性が示されている併用薬（アミトリプチリン，トピラマート，プロプラノロールなど）も含まれる。

8. オピオイド鎮痛剤若しくはバルビツール酸系薬剤を 1 ヵ月あたり 2 日超，トリプタン系薬剤若しくはエルゴタミン製剤を 1 ヵ月あたり 10 日以上，又は単一成分の鎮痛薬（アスピリン，非ステロイド性抗炎症薬［以下「NSAIDs」］，アセトアミノフェンなど）を 1 ヵ月あたり 15 日以上，Visit 1 前の 3 ヵ月間に使用したと治験責任医師が判断した，若しくはベースライン期間に使用した患者（スクリーニングの 30 日前から本試験期間を通じてバルビツール酸系薬剤の使用は認められない）。
9. 妊娠している，本試験期間中に妊娠を計画している，又は現在授乳中の女性患者。妊娠可能な女性患者は，Visit 1 及び Visit 2 の尿妊娠検査が陰性であること。
10. スクリーニング（Visit 1）時に心電図（以下「ECG」）に臨床的に重大な異常を有すると治験責任医師により判断された患者。
11. ECG の最終報告書に基づき，Visit 1 の Fridericia 補正法を用いて心拍数で補正した QT 間隔（QTcF）が男性は 450 msec 超，女性は 470 msec 超の患者。
12. 臨床的に重大な心血管疾患又は脳血管疾患を有すると治験責任医師が判断した患者。これには以下の疾患を含むが，これらに限定されない。
    - 臨床的に重大な虚血性心疾患（不安定狭心症など）。
    - 臨床的に重大な心調律異常若しくは心伝導異常（心房細動，第 2 度又は第 3 度心ブロックなど）又はトルサードドポアントの危険因子（心不全，低カリウム血症，徐脈など）。
    - Visit 1 前 6 ヵ月以内の心筋梗塞，一過性脳虚血発作，又は脳卒中。
    - ニューヨーク心臓協会の心機能分類（NYHA 分類）で III 度又は IV 度と定義される心不全。
13. Visit 1 又は Visit 2 の座位収縮期血圧が 160 mm Hg 超又は座位拡張期血圧が 100 mm Hg 超の高血圧の患者。これらの上限を超えた場合，バイタルサインを一回のみ再測定可能とした。
14. Visit 1 に臨床的に重大な臨床検査値又は以下のいずれかの臨床検査値が認められた患者。
    - アラニンアミノトランスフェラーゼ（以下「ALT」）値又はアスパラギン酸アミノトランスフェラーゼ（以下「AST」）値が基準値の上限（以下「ULN」）の 1 倍超。
    - 総ビリルビン値が ULN の 1 倍超（ジルベール症候群と診断された患者を除く）。
    - 血清アルブミン値が 2.8 g/dL 未満。
15. 臨床的に重大な血液疾患，内分泌疾患，肺疾患，腎疾患，肝疾患，消化管疾患，又は神経疾患を有する患者。
    - これらの疾患の既往歴を有するものの，Visit 1 前 1 年超，状態が安定しており，本試験への参加に支障をきたすおそれはないと治験責任医師が判断した患者は組入れ可能とした。
    - 腎不全による透析中の患者は組入れ不可とした。
16. スクリーニング（Visit 1）前 6 ヵ月以内の急性肝炎の既往歴若しくは慢性肝疾患（非アルコール性脂肪性肝炎を含む）を有する，又は抗 A 型肝炎 IgM 抗体，B 型肝炎表面抗原，抗 C 型肝炎抗体，若しくは抗 E 型肝炎 IgM 抗体の検査で陽性であった患者。
17. 混合した精神状態，認知症，てんかん，又は片頭痛以外の重大な神経障害を有すると治験責任医師が判断した患者。
18. 現在の頭痛障害に重大な影響を及ぼす可能性がある他の疼痛疾患（線維筋痛症，顔面痛など）を併発していると治験責任医師が判断した患者。
19. 臨床面接及びコロンビア自殺評価スケール（以下「C-SSRS」）の回答により自傷行為の重大なリスクが認められた患者，又は他害行為の重大なリスクがあると治験責任医師が判断した患者。過去 6 ヵ月以内に実行する意思のある自殺念慮（計画の有無は問わない）（C-SSRS でタイプ 4 又は 5）を報告した患者，又は Visit 1 若しくは Visit 2 の評価前 6 ヵ月以内に何らかの自殺行動を報告した患者は除外することとした。
20. Visit 1 前 5 年間に悪性腫瘍の既往歴を有する患者（適切に治療された基底細胞癌，扁平上皮癌，又は子宮頸部上皮内癌は除く）。

21. 治験薬の吸収又は代謝に影響を及ぼす可能性のある消化管への処置又は消化管疾患（下痢症候群，炎症性腸疾患など）の既往歴を有する患者。肥満症に対する胃への処置（ラップバンドなど）を受けたものの，その処置を元に戻した患者は組入れ可能とした。
22. Visit 1 にレクリエーショナルドラッグ又は違法薬物の使用者であった患者，又は過去 1 年以内に薬物若しくはアルコールの乱用若しくは依存の既往歴を有する患者。
23. Visit 1 の尿中薬物検査が陽性であった患者（片頭痛のために処方されたオピオイド鎮痛剤などで説明できる併用は除く）。
24. 治験薬又は治験機器を用いた試験（市販の製剤又は機器を用いた試験も含む）に現在参加中，又は Visit 1 前 30 日以内に参加していた患者。
25. 以下の薬剤への曝露歴がある患者。
    - アトゲパント
    - 過去 6 ヵ月以内でのカルシトニン遺伝子関連ペプチド（以下「CGRP」）経路を遮断する注射用モノクローナル抗体
    - ubrogepant（3 回超投与）
    - リメゲパント（3 回超投与）
26. CGRP 受容体拮抗薬に対する過敏症又は臨床的に重大な副作用の既往歴を有する患者。
27. 治験責任医師，治験スタッフ，治験依頼者のいずれかに雇用されている，又はその近親者（両親，配偶者，兄弟姉妹，又は子供）。
28. 患者を重大なリスクにさらす，試験結果を混乱させる，又は患者の本試験の参加で著しく支障をきたす可能性があると治験責任医師が判断した状態又は状況にあった患者。
29. 医学的又はその他の理由（試験手順や来院予約を遵守しない可能性がある，本試験期間中に転居する予定があるなど）で本試験に不適格と治験責任医師が判断した患者。

治験方法：

本試験は，多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験であり，米国の 136 施設で実施した。910 例の被験者を 4 つの投与群（プラセボ群，アトゲパント 10 mg QD 群，アトゲパント 30 mg QD 群，アトゲパント 60 mg QD 群）のいずれかに 1：1：1：1 の割合で無作為に割り付けた。

治験実施計画書に従い，無作為化される被験者の約 70%は，有効性が証明されている片頭痛予防薬の投与歴が 1 回以上あることとした。無作為化は，有効性が証明されている片頭痛予防薬の使用歴（あり / なし）に基づいて層別化した。層に基づいてブロック全体を各施設に動的に割り当て，ブロック内で順番に投与群を割り付けた。

本試験は，4 週間のスクリーニング / ベースライン期間，12 週間の二重盲検期間，及び 4 週間の安全性追跡調査期間で構成された。予定された治験実施医療機関への来院は 8 回（Visit 1［スクリーニング / ベースライン］，Visit 2［無作為化］，Visit 3［2 週時］，Visit 4［4 週時］，Visit 5［6 週時］，Visit 6［8 週時］，Visit 7 / 早期中止［12 週時］，及び Visit 8［安全性追跡調査］）であった。

本試験の二重盲検期間を完了し，適格性を満たした被験者は，長期継続安全性試験である 3101-309-002 試験への継続参加が可能であった。継続試験に組み入れられた被験者では，継続試験で追跡調査が実施されるため，3101-301-002 試験の Visit 8 は不要とし，継続試験に組み入れられなかった被験者では，Visit 8 を実施した。COVID-19 パンデミックのために遠隔で Visit 7 を実施した被験者は 3101-309-002 試験に参加できず，遠隔で Visit 8（追跡調査 / 治験終了）を実施した。

非盲検下で安全性データ及び要約報告書をレビューし，安全性の問題及び傾向を特定し，未知の臨床的に重大な有害事象を示すデータが得られた場合に試験の計画変更又は早期中止などを治験依頼者に提言するために，独立したデータ安全性モニタリング委員会を設置した。

判定手順を策定し，臨床判定委員会による治験薬投与開始後の ULN の 3 倍以上の ALT 及び / 又は AST 上昇の盲検下での監視，モニタリング，及び判定のプロセスを規定した。この手順の目的は，ALT 及び / 又は AST 上昇とアトゲパントの因果関係を判定するための標準化したプロセスを提供することであった。

被験薬，用量，投与方法及びバッチ番号：

アトゲパント 10 mg，錠剤，経口投与，バッチ番号：[redacted]

アトゲパント 30 mg，錠剤，経口投与，バッチ番号：[redacted]，[redacted]，[redacted] アトゲパント 60 mg，錠剤，経口投与，バッチ番号：[redacted]，[redacted]
対照薬，用量，投与方法及びバッチ番号： アトゲパント 10 mg のプラセボ，錠剤，経口投与，バッチ番号：[redacted] アトゲパント 30 mg のプラセボ，錠剤，経口投与，バッチ番号：[redacted]，[redacted] アトゲパント 60 mg のプラセボ，錠剤，経口投与，バッチ番号：[redacted]，[redacted]
治療期間：12 週間
評価基準： 有効性： 主要評価項目： • 12 週間の投与期間での平均 MMD のベースラインからの変化量 副次評価項目： • 12 週間の投与期間での平均月間頭痛日数のベースラインからの変化量 • 12 週間の投与期間での急性期治療薬の平均月間使用日数のベースラインからの変化量 • 12 週間の投与期間での平均 MMD が 50%以上減少した被験者の割合 • 12 週時の片頭痛特有の生活の質に関する質問票第 2.1 版（以下「MSQ v2.1」）の日常役割機能制限（以下「RFR」）ドメインスコアのベースラインからの変化量 • 12 週間の投与期間での片頭痛による活動障害－ダイアリー（以下「AIM-D」）の日常活動機能ドメイン平均月間スコアのベースラインからの変化量 • 12 週間の投与期間での AIM-D の身体障害ドメイン平均月間スコアのベースラインからの変化量 その他の評価項目： • 4 週間隔（1–4 週，5–8 週，9–12 週）及び 12 週間の投与期間でのトリプタンの平均月間使用日数のベースラインからの変化量 • 12 週間の投与期間での平均月間累積頭痛時間のベースラインからの変化量 • 4 週間隔（1–4 週，5–8 週，9–12 週）及び 12 週間の投与期間での重度の平均月間頭痛日数のベースラインからの変化量 • 4 週間隔（1–4 週，5–8 週，9–12 週）及び 12 週間の投与期間での中等度 / 重度の平均月間頭痛日数のベースラインからの変化量 ヘルスアウトカム： Headache Impact Test（HIT-6），患者の全般的印象度－変化（PGIC），治験薬に対する患者の満足度（PSSM），仕事の生産性及び活動障害に関する質問票：片頭痛第 2.0 版（WPAI: MIGRAINE），Migraine Disability Assessment（MIDAS），患者の全般的印象度－重症度（PGIS），MSQ v2.1，AIM-D，Activity Level and Activity Limitation，European Quality of Life - 5-Dimensional - 5 Level（EQ-5D-5L），患者報告転帰測定情報システム 痛みによる支障－簡易版 6a（PROMIS-PI） 安全性： 有害事象，臨床検査値，バイタルサイン，ECG，C-SSRS
統計手法： 有効性： すべての有効性解析は，modified intent-to-treat（以下「mITT」）集団を用いて実施した。mITT 集団は，治験薬を 1 回以上投与され，評価可能なベースライン期間の eDiary データを有し，二重盲検期間の評価可能なベースライン後の 4 週間隔（1–4 週，5–8 週，9–12 週）の eDiary データを 1 つ以上有する，無作為化されたすべての被

験者で構成された。

主要評価項目及び重要な副次評価項目は，米国及び欧州連合（以下「EU」）とで同一とした。EU 申請を裏付ける主要 estimand は，off-treatment hypothetical estimand（以下「OTHE」）である。関連する解析は，OTHE 集団を対象に実施した。この解析対象集団は，無作為化されたすべての被験者のうち，治験薬を 1 回以上投与され，評価可能なベースライン期間の eDiary データを有し，二重盲検期間及び追跡調査期間中の評価可能なベースライン後の 4 週間隔（1–4 週，5–8 週，9–12 週）の eDiary データを 1 つ以上有する，無作為化されたすべての被験者（治験薬の投与中かどうかを問わない）と定義した。

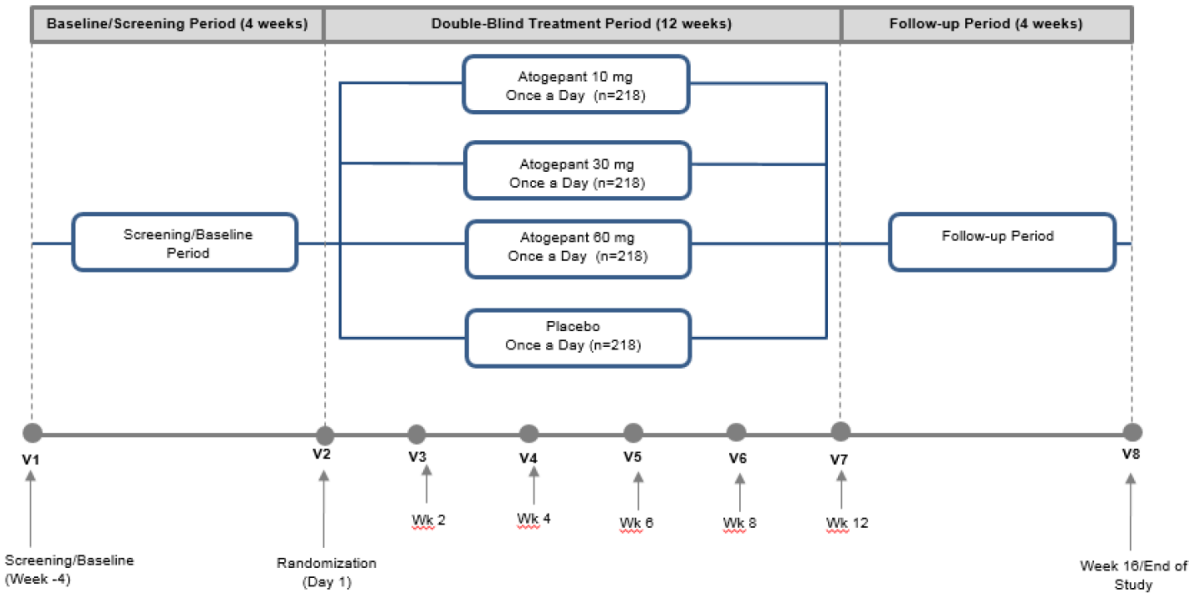
投与群間の主な比較では，ベースラインからの変化量に反復測定混合効果モデル（以下「MMRM」）を用いた。統計モデルには，投与群，来院，有効性が証明されている片頭痛予防薬の使用歴の有無，及び投与群と来院の交互作用をカテゴリー変数の固定効果として，ベースラインスコアとベースラインと来院の交互作用を共変量として含めた。無構造共分散行列を使用して，被験者内反復測定の共分散をモデル化した。Kenward-Roger 近似を使用して分母の自由度を推定した。解析には，ベースライン後のすべての値の観測値のみを用い，欠測値は補完しなかった。MMRM モデルで対比を用いて，各アトゲパント群とプラセボ群の対比較を行った。12 週間の投与期間での平均 MMD の 50%以上の減少は，ロジスティック回帰モデルを用いて解析した。その他の副次有効性評価項目は，主要評価項目と同じ方法で解析した。

主要評価項目及び副次評価項目の各アトゲパント群とプラセボ群との比較では，ファミリーワイズエラー率を $\alpha = 0.05$ で制御した。具体的には，アトゲパントの 3 用量と主要評価項目及び副次評価項目の多重比較の全体の第 I 種過誤率を，重み付きボンフェローニ検定手順を用いたグラフィカルアプローチによって，有意水準 0.05 で制御した。

安全性：

すべての安全性解析は，安全性解析対象集団を用いて実施した。安全性解析対象集団は，治験薬を 1 回以上投与されたすべての被験者で構成された。連続変数は，記述統計を用いて要約した。カテゴリー変数は，被験者数及び割合で要約した。

図 1. 試験デザインの概略（3101-301-002 試験）



n = 各投与群に無作為に割り付けられると予想された被験者数，V = Visit，Wk = Week

Cross reference: 3101-301-002 final CSR Figure 9-1

試験結果

被験者の内訳

被験者の内訳を表 1 に示す。

合計 910 例の被験者が無作為化され，902 例が治験薬を 1 回以上投与された（安全性解析対象集団）。mITT 集団は 873 例，OTHE 集団は 882 例であり，両集団の差は 9 例であった。無作為化された被験者全体の 88.5%（805 例）が治験を完了し，11.5%（105 例）が二重盲検期間中に投与を中止した。投与中止に至った主な理由は，同意撤回（3.8%），有害事象（2.7%），治験実施計画書からの逸脱（2.6%）であった。

人口統計学的及び他のベースラインの特性

人口統計学的特性，ベースライン特性及び原疾患のベースライン特性をそれぞれ表 2，表 3 及び表 4 に示す。

ベースラインの人口統計学的特性は，安全性解析対象集団の投与群間で同様で，片頭痛患者の集団として典型的なものであった。平均年齢は 41.6 歳で，ほとんどの被験者は女性（88.8%）であった。被験者の大半は白人（83.4%）及び非ヒスパニック系（91.5%）であった。ベースラインの体重及び体格指数（以下「BMI」）の平均値は投与群間で同様であった。安全性解析対象集団でのベースラインの平均体重は 84.20 kg，平均 BMI は 30.56 kg/m^2 であった。被験者の 25%は体重が 96.40 kg 以上で，BMI が 34.96 kg/m^2 以上であった。

片頭痛の既往歴は，安全性解析対象集団の投与群間で同様であった。全体で，前兆のある片頭痛のみが 16.2%，前兆のない片頭痛が 45.0%，前兆のある片頭痛と前兆のない片頭痛の混在が 38.8%であった。片頭痛の平均罹病期間は 21.2 年であった。スクリーニング時，片頭痛の急性期治療薬を被験者の 99.3%が使用していた。このうち NSAID が 63.1%，トリプタンが 48.8%，その他の薬剤（最も一般的なものはアセトアミノフェン，又はエキセドリンや BC 散剤などの併用薬）が 63.2%であった。全体で，被験者の 70.3%に過去に片頭痛予防薬（有効性が証明されているか否かを問わない）の使用歴があった。スクリーニング前 3 ヵ月間の平均 MMD は，アトゲパント群（7.2–7.3 日）とプラセボ群（7.7 日）で同程度であり，平均月間頭痛日数も同様であった（全アトゲパント群：9.1–9.3 日，プラセボ群：9.5 日）。

曝露状況

曝露状況を表 5 に示す。

合計 902 例の被験者が治験薬を 1 回以上投与され，そのうちアトゲパントが 680 例，プラセボが 222 例であった。

各投与群の平均投与期間は同程度であり，プラセボ群で 80.9 日，アトゲパント群で 78.2–80.9 日であった。

有効性の結果

mITT 集団（表 6）と OTHE 集団の両集団について，以下に示す有効性の結論を得た。

- EM 被験者での片頭痛予防を目的としたアトゲパント 10 mg QD，30 mg QD 及び 60 mg QD がプラセボより優れていることが示された。
- 主要評価項目：12 週間の投与期間での平均 MMD のベースラインからの変化量は，プラセボ群と比較してすべてのアトゲパント群で統計学的に有意かつ臨床的に意義のある投与群間差を示した（いずれも $P < 0.0001$，多重性調整済み）。
- 第 1 副次評価項目：12 週間の投与期間での平均月間頭痛日数のベースラインからの変化量は，プラセボ群と比較してすべてのアトゲパント群で統計学的に有意に大きかった（いずれも $P < 0.0001$，多重性調整済み）。
- 第 2 副次評価項目：12 週間の投与期間での急性期治療薬の平均月間使用日数のベースラインからの変化量は，プラセボ群と比較してすべてのアトゲパント群で統計学的に有意に大きかった（いずれも $P < 0.0001$，多重性調整済み）。
- 第 3 副次評価項目：12 週間の投与期間での平均 MMD が 50%以上減少した被験者の割合は，プラセボ群と比較してすべてのアトゲパント群で有意に高かった（いずれも $P < 0.0001$，多重性調整済み）。
- 第 4 副次評価項目：12 週時の MSQ v2.1 の RFR ドメインスコアのベースラインからの変化量は，プラセボ群と比較してすべてのアトゲパント群で統計学的に有意に改善した（いずれも $P < 0.0001$，多重性調整済み）。
- 第 5 副次評価項目：12 週間の投与期間での AIM-D の日常活動機能ドメイン平均月間スコアのベースラインからの変化量は，プラセボ群と比較してアトゲパント 30 mg QD 群及び 60 mg QD 群で統計学的に有意に改善した（いずれも $P \leq 0.0005$，多重性調整済み）。アトゲパント 10 mg QD 群はプラセボ群と比較して統計学的に有意な差はなかったものの，改善が認められた。
- 第 6 副次評価項目：12 週間の投与期間での AIM-D の身体障害ドメイン平均月間スコアのベースラインからの変化量は，プラセボ群と比較してアトゲパント 30 mg QD 群及び 60 mg QD 群で統計学的に有意に改善した（いずれも $P \leq 0.0021$，多重性調整済み）。アトゲパント 10 mg QD 群はプラセボ群と比較して統計学的に有意な差はなかったものの，改善が認められた。
- すべての有効性の主要評価項目及び副次評価項目において，アトゲパント 30 mg QD 群及び 10 mg QD 群と比較してアトゲパント 60 mg QD 群で一貫して大幅な改善が認められ，明らかな用量反応関係が認められた。
- 有効性のその他の追加評価項目の結果は，主要評価項目及び副次評価項目の結果と一致していた。

安全性の結果

アトゲパント 10 mg QD，30 mg QD，及び 60 mg QD の忍容性は良好であった。

有害事象

有害事象の発現状況を以下に示す。

有害事象の発現割合は，アトゲパント 60 mg QD 群 53.7%（124/231 例），アトゲパント 30 mg QD 群 52.2%（119/228 例），アトゲパント 10 mg QD 群 52.9%（117/221 例），プラセボ群 56.8%（126/222 例）であった。

いずれかの投与群で発現割合が 5.0%以上の有害事象は，便秘（アトゲパント 60 mg QD 群 6.9%［16 例］，アトゲパント 30 mg QD 群 7.0%［16 例］，アトゲパント 10 mg QD 群 7.7%［17 例］，プラセボ群 0.5%［1 例］，以下同順），悪心（6.1%［14 例］，4.4%［10 例］，5.0%［11 例］，1.8%［4 例］）及び上気道感染（3.9%［9 例］，5.7%［13 例］，4.1%［9 例］，4.5%［10 例］）であった。

治験薬と関連ありの有害事象の発現割合は，アトゲパント 60 mg QD 群 19.5%（45 例），アトゲパント 30 mg QD 群 14.9%（34 例），アトゲパント 10 mg QD 群 23.1%（51 例），プラセボ群 9.0%（20 例）であった。

いずれかの投与群で発現割合が 2.0%以上の治験薬と関連ありの有害事象は，便秘（アトゲパント 60 mg QD 群 5.2%［12 例］，アトゲパント 30 mg QD 群 4.4%［10 例］，アトゲパント 10 mg QD 群 5.9%［13 例］，プラセボ群 0.5%［1 例］，以下同順），悪心（4.3%［10 例］，2.2%［5 例］，3.2%［7 例］，0.5%［1 例］），疲労（2.2%［5 例］，1.8%［4 例］，1.4%［3 例］，0.5%［1 例］）及び傾眠（1.3%［3 例］，1.3%［3 例］，2.7%［6 例］，0.9%［2 例］）であった。

高度の有害事象の発現割合は，アトゲパント 60 mg QD 群 0.9%（2 例），アトゲパント 30 mg QD 群 0.4%（1 例），アトゲパント 10 mg QD 群 1.8%（4 例），プラセボ群 4.1%（9 例）であった。

いずれかの投与群で発現割合が 1.0%以上の高度の有害事象は，片頭痛（アトゲパント 60 mg QD 群 0%，アトゲパント 30 mg QD 群 0%，アトゲパント 10 mg QD 群 0%，プラセボ群 1.4%［3 例］）であった。

投与終了後の有害事象の発現割合は，アトゲパント 60 mg QD 群 2.6%（6 例），アトゲパント 30 mg QD 群 2.6%（6 例），アトゲパント 10 mg QD 群 3.2%（7 例），プラセボ群 4.1%（9 例）であった。

いずれかの投与群で 2 例以上の被験者に発現した投与終了後の有害事象は，上咽頭炎（アトゲパント 60 mg QD 群 0.4%［1 例］，アトゲパント 30 mg QD 群 0.9%［2 例］，アトゲパント 10 mg QD 群 0%，プラセボ群 0.5%［1 例］，以下同順），アラニンアミノトランスフェラーゼ増加（0%，0%，0.5%［1 例］，0.9%［2 例］）及びアスパラギン酸アミノトランスフェラーゼ増加（0%，0%，0.5%［1 例］，0.9%［2 例］）であった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の発現割合は，アトゲパント 60 mg QD 群 0%，アトゲパント 30 mg QD 群 0%，アトゲパント 10 mg QD 群 0.9%（2 例），プラセボ群 0.9%（2 例）であった。

重篤な有害事象は少なく，アトゲパント 10 mg QD 群とプラセボ群でそれぞれ 2 例の被験者（0.9%）に発現し，アトゲパント 30 mg QD 群又は 60 mg QD 群で発現した被験者はいなかった。

重篤な有害事象は，出血性胃潰瘍（アトゲパント 60 mg QD 群 0%，アトゲパント 30 mg QD 群 0%，アトゲパント 10 mg QD 群 0%，プラセボ群 0.5%［1 例］，以下同順），脳損傷（0%，0%，0%，0.5%［1 例］），視神経炎（0%，0%，0.5%［1 例］，0%），喘息（0%，0%，0.5%［1 例］，0%）及び陰圧性肺水腫（0%，0%，0%，0.5%［1 例］）であった。

治験薬の投与中止に至った有害事象の発現割合は，アトゲパント 60 mg QD 群 2.6%（6 例），アトゲパント 30 mg QD 群 1.8%（4 例），アトゲパント 10 mg QD 群 4.1%（9 例），プラセボ群 2.7%（6 例）であった。

有害事象が発現し，中止に至った被験者の割合は，全アトゲパント群で 1.8%–4.1%，プラセボ群で 2.7%であった。中止に至った有害事象については，用量反応関係は認められなかった。

治験薬の投与中止に至った有害事象は，耳痛（アトゲパント 60 mg QD 群 0.4%［1 例］，アトゲパント 30 mg QD 群 0%，アトゲパント 10 mg QD 群 0%，プラセボ群 0%，以下同順），回転性めまい（0%，0%，0.5%［1 例］，0%），便秘（0.4%［1 例］，0.9%［2 例］，0.5%［1 例］，0%），悪心（0.4%［1 例］，0%，0.5%［1 例］，0%），腹痛（0%，0%，0%，0.5%［1 例］），疲労（0.4%［1 例］，0%，0.5%［1 例］，0%），食欲減退（0.4%［1 例］，0%，0%，0%），糖尿病（0.4%［1 例］，0%，0%，0%），筋痙縮（0.4%［1 例］，0%，0%，0%），筋骨格系胸痛（0%，0%，0%，0.5%［1 例］），脳損傷（0%，0%，0%，0.5%［1 例］），浮動性めまい（0%，0.4%［1 例］，0%，0%），頭痛（0%，0%，0.5%［1 例］，0%），片頭痛（0%，0%，0%，0.5%［1 例］），視神経炎（0%，0%，0.5%［1 例］，0%），傾眠（0%，0%，0.5%［1 例］，0%），激越（0.4%［1 例］，0%，0%，0%），不眠症（0.4%［1 例］，0%，0%，0%），異常な夢（0%，0%，0.5%［1 例］，0%），双極性障害（0%，0.4%［1 例］，0%，0%），自殺念慮（0%，0%，0%，0.5%［1 例］），血尿（0%，0%，0.5%［1 例］，0%），腎仙痛（0%，0%，0%，0.5%［1 例］），骨盤痛（0%，0%，0.5%［1 例］，0%），陰圧性肺水腫（0%，0%，0%，0.5%［1 例］），多汗症（0.4%［1 例］，0%，0%，0%），全身性そう痒症（0.4%［1 例］，0%，0%，0%），発疹（0.4%［1 例］，0%，0%，0%）及び丘疹性皮疹（0%，0%，0.5%［1 例］，0%）であった。

便秘の発現割合は，プラセボ群（0.5%）と比較してアトゲパント群（約 7%）で高かったが，用量反応関係は認められなかった。また，重篤な便秘は認められず，ほとんどの事象は軽度で（高度は 1 例），投与中止に至った便秘の発現割合は低かった（アトゲパント群のいずれにおいても 1%未満）。

2 例の妊娠が報告された（いずれもアトゲパント 10 mg QD 群の被験者であった）。2 例とも健康な正期産児を出産した。

特に注目すべき有害事象

潜在的な Hy’s Law 基準に該当した被験者は認められず，ULN の 3 倍以上の ALT 及び / 又は AST の上昇及び ULN の 1.5 倍以上の総ビリルビンの上昇が同時に認められた被験者はいなかっ

た。ULN の 3 倍以上の ALT 又は AST の上昇は，プラセボ群の 1.8%，各アトゲパント群の 1%未満に認められた。ULN の 3 倍以上の ALT 又は AST の上昇は 9 例に認められた。これらの被験者について盲検下で治験薬との因果関係を臨床判定委員会が判定した結果，おそらく関連なしが 7 例，おそらく関連ありが 1 例（アトゲパント 30 mg QD 群），関連あるかもしれないが 1 例（アトゲパント 30 mg QD 群）であった。被験者ごとの評価，臨床判定委員会による盲検下での判定，及び被験者全体のパターン及び / 又は傾向の評価に基づき，アトゲパントに関連する肝臓への安全性の問題は確認されなかった。その他の臨床検査値に臨床的に関連する変化は認められなかった。

C-SSRS 評価による二重盲検期間中の実行する意思のある自殺念慮は，アトゲパント群では認められなかった。プラセボ群の 1 例が，自殺念慮の有害事象により試験を中止した。当該被験者は，C-SSRS 評価で自殺念慮及び自殺行動（中断した自殺企図）が認められた。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団
有害事象の要約	表 7（Table 14.3-2.1.1）
すべての有害事象	表 8（Table 14.3-2.1.2）
因果関係「関連あり」の有害事象	表 9（Table 14.3-2.1.5）
重症度別有害事象	表 10（Table 14.3-2.1.4）
重篤な有害事象	表 11（Table 14.3-2.2.1）
治験薬の投与中止に至った有害事象	表 12（Table 14.3-2.2.2）

臨床検査

臨床検査値に臨床的に意義のあるベースラインからの変化は認められなかった。

バイタルサイン

バイタルサインのパラメータの平均変化量及び臨床的に意義がある可能性のあるバイタルサイン値が認められた被験者の割合は体重を除いて概して小さく，投与群間で同様であった。過体重集団（ベースラインの平均 BMI が 30.56 kg/m^2）の平均体重は，アトゲパントの用量が高いほど減少量が大きかった。ベースラインから投与終了時までの体重の平均変化量は，プラセボ群で 0.32 kg，アトゲパント 10 mg QD 群で 0.10 kg，アトゲパント 30 mg QD 群で–0.52 kg，アトゲパント 60 mg QD 群で–1.06 kg であった。この傾向は，臨床的に意義がある可能性のあるベースラインからの体重減少が 7%以上であった被験者の割合にも反映されていた（プラセボ群：3.2%，アトゲパント 10 mg QD 群：4.1%，アトゲパント 30 mg QD 群：2.7%，アトゲパント 60 mg QD 群：5.7%）。

ECG

ECG の結果に意味のある変化は認められなかった。

結論

- EM 被験者の片頭痛予防に対するアトゲパント 10 mg QD，30 mg QD，及び 60 mg QD は，プラセボと比較して統計学的に有意で臨床的に意義のある改善を示した。
- 明らかな用量反応関係が認められ，有効性の主要評価項目及び副次評価項目のすべてにおいて，30 mg QD 及び 10 mg QD と比較してアトゲパント 60 mg QD で一貫して大幅な改善が認められた。
- 片頭痛予防を目的とした本試験でのアトゲパント 10 mg QD，30 mg QD，及び 60 mg QD の忍容性は良好であり，安全性に関する懸念は認められなかった。

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Allergan
Protocol 3101-301-002

Atogepant

Table 14.1-1.4
Participant Disposition
All Randomized Participants

Phase Disposition	Placebo (N=223) n (%)	Atogepant 10 mg QD (N=222) n (%)	Atogepant 30 mg QD (N=230) n (%)	Atogepant 60 mg QD (N=235) n (%)	Total (N=910) n (%)
Number of Participants Randomized	223 (100.0)	222 (100.0)	230 (100.0)	235 (100.0)	910 (100.0)
Number of Participants Treated	222 (99.6)	221 (99.5)	228 (99.1)	231 (98.3)	902 (99.1)
Double-Blind Treatment Period					
Number of Participants Entered	223 (100.0)	222 (100.0)	230 (100.0)	235 (100.0)	910 (100.0)
Number of Participants Completed	201 (90.1)	193 (86.9)	207 (90.0)	204 (86.8)	805 (88.5)
Number of Participants Discontinued	22 (9.9)	29 (13.1)	23 (10.0)	31 (13.2)	105 (11.5)
Reason for Discontinuation					
Adverse Event	6 (2.7)	9 (4.1)	4 (1.7)	6 (2.6)	25 (2.7)
Lack of efficacy	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.2)
Withdrawal by subject	8 (3.6)	9 (4.1)	8 (3.5)	10 (4.3)	35 (3.8)
Lost to Follow-Up	3 (1.3)	3 (1.4)	4 (1.7)	5 (2.1)	15 (1.6)
Pregnancy	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.1)
Protocol Deviation	4 (1.8)	5 (2.3)	7 (3.0)	8 (3.4)	24 (2.6)
Non-compliance with study drug	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.4)	3 (0.3)
Follow-Up Period					
Number of Participants Entered	46 (20.6)	54 (24.3)	38 (16.5)	45 (19.1)	183 (20.1)
Number of Participants Completed	41 (18.4)	49 (22.1)	32 (13.9)	36 (15.3)	158 (17.4)
Number of Participants Discontinued	5 (2.2)	5 (2.3)	6 (2.6)	9 (3.8)	25 (2.7)
Reason for Discontinuation					
Adverse Event	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	5 (2.2)	3 (1.4)	4 (1.7)	5 (2.1)	17 (1.9)
Lost to Follow-Up	0 (0.0)	1 (0.5)	0 (0.0)	3 (1.3)	4 (0.4)
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Protocol Deviation	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)	2 (0.2)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

N = Number of randomized participants.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
* Majority of participants who rolled over into Open-Label Safety Extension Study 3101-309-002 did not enter the Follow-Up Period for Study 3101-301-002.

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Table 14.1-1.4
Participant Disposition
All Randomized Participants

Phase Disposition	Placebo (N=223) n (%)	Atogepant 10 mg QD (N=222) n (%)	Atogepant 30 mg QD (N=230) n (%)	Atogepant 60 mg QD (N=235) n (%)	Total (N=910) n (%)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	2 (0.2)
Number of participants who signed informed consent for 3101-309-002	173 (77.6)	161 (72.5)	182 (79.1)	179 (76.2)	695 (76.4)

N = Number of randomized participants.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
* Majority of participants who rolled over into Open-Label Safety Extension Study 3101-309-002 did not enter the Follow-Up Period for Study 3101-301-002.

表2

Allergan
Protocol 3101-301-002

Table 14.1-3.1.1
Demographics
Safety Population

Parameter	Placebo (N=222)	Atogepant 10 mg QD (N=221)	Atogepant 30 mg QD (N=228)	Atogepant 60 mg QD (N=231)	Total (N=902)
Age (years)					
Mean (SD)	40.3 (12.81)	41.4 (12.05)	42.1 (11.68)	42.5 (12.41)	41.6 (12.25)
Median	38.5	41.0	42.0	42.0	41.0
Q1, Q3	30.0, 50.0	33.0, 50.0	33.0, 50.0	32.0, 51.0	32.0, 50.0
Min, Max	18, 69	18, 73	19, 70	18, 72	18, 73
n	222	221	228	231	902
Age Group, n (%)					
< 20	6 (2.7)	3 (1.4)	1 (0.4)	4 (1.7)	14 (1.6)
20-29	46 (20.7)	37 (16.7)	36 (15.8)	38 (16.5)	157 (17.4)
30-39	63 (28.4)	62 (28.1)	62 (27.2)	61 (26.4)	248 (27.5)
40-49	48 (21.6)	61 (27.6)	70 (30.7)	60 (26.0)	239 (26.5)
50-59	41 (18.5)	40 (18.1)	42 (18.4)	43 (18.6)	166 (18.4)
60-69	18 (8.1)	16 (7.2)	16 (7.0)	23 (10.0)	73 (8.1)
>= 70	0 (0.0)	2 (0.9)	1 (0.4)	2 (0.9)	5 (0.6)
Sex, n (%)					
Male	24 (10.8)	21 (9.5)	24 (10.5)	32 (13.9)	101 (11.2)
Female	198 (89.2)	200 (90.5)	204 (89.5)	199 (86.1)	801 (88.8)
Race, n (%)					
White	194 (87.4)	181 (81.9)	185 (81.1)	192 (83.1)	752 (83.4)
Black or African American	24 (10.8)	34 (15.4)	38 (16.7)	28 (12.1)	124 (13.7)
Asian	2 (0.9)	2 (0.9)	1 (0.4)	7 (3.0)	12 (1.3)
American Indian Or Alaska Native	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)	3 (0.3)
Native Hawaiian Or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Multiple[1]	2 (0.9)	3 (1.4)	3 (1.3)	2 (0.9)	10 (1.1)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.1)

Age is relative to informed consent date.
[1] Participants who reported multiple races are only included in multiple category.
N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

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Table 14.1-3.1.1
Demographics
Safety Population

Parameter	Placebo (N=222)	Atogepant 10 mg QD (N=221)	Atogepant 30 mg QD (N=228)	Atogepant 60 mg QD (N=231)	Total (N=902)
Race Group, n (%)					
White	194 (87.4)	181 (81.9)	185 (81.1)	192 (83.1)	752 (83.4)
All Other Races	28 (12.6)	40 (18.1)	43 (18.9)	38 (16.5)	149 (16.5)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.1)
Ethnicity, n (%)					
Hispanic	23 (10.4)	21 (9.5)	19 (8.3)	14 (6.1)	77 (8.5)
Non-Hispanic	199 (89.6)	200 (90.5)	209 (91.7)	217 (93.9)	825 (91.5)

Age is relative to informed consent date.
[1] Participants who reported multiple races are only included in multiple category.
N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

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Allergan
Protocol 3101-301-002

Atogepant
Page 1 of 1

Table 14.1-3.1.4
Baseline Characteristics
Safety Population

Parameter	Placebo (N=222)	Atogepant 10 mg QD (N=221)	Atogepant 30 mg QD (N=228)	Atogepant 60 mg QD (N=231)	Total (N=902)
Weight (kg)					
Mean (SD)	84.68 (24.638)	83.63 (22.939)	85.86 (22.686)	82.65 (21.966)	84.20 (23.058)
Median	80.65	81.20	82.60	78.30	80.75
Q1, Q3	68.00, 96.00	68.20, 96.30	67.35, 98.85	65.90, 95.10	67.60, 96.40
Min, Max	44.7, 226.0	45.6, 198.9	47.9, 180.5	42.2, 176.1	42.2, 226.0
n	222	221	228	231	902
Height (cm)					
Mean (SD)	165.69 (7.535)	165.79 (8.479)	165.86 (7.730)	166.10 (8.683)	165.86 (8.112)
Median	165.10	165.10	165.10	165.10	165.10
Q1, Q3	160.00, 170.20	160.00, 170.20	160.95, 170.20	160.00, 171.00	160.00, 170.20
Min, Max	147.3, 186.7	147.0, 198.5	146.1, 195.6	148.1, 203.5	146.1, 203.5
n	222	221	228	231	902
BMI (kg/m^2)					
Mean (SD)	30.83 (8.713)	30.35 (7.597)	31.15 (7.631)	29.91 (7.318)	30.56 (7.828)
Median	28.93	29.01	30.25	28.26	29.01
Q1, Q3	24.51, 35.72	24.87, 34.00	25.24, 36.01	24.66, 33.82	24.87, 34.96
Min, Max	16.9, 82.0	16.4, 60.3	17.1, 66.2	16.3, 57.3	16.3, 82.0
n	222	221	228	231	902

Allergan
Protocol 3101-301-002

Atogepant

Table 14.1-3.2.2
Migraine History
Safety Population

Parameter Category Statistics	Placebo (N=222)	Atogepant 10 mg QD (N=221)	Atogepant 30 mg QD (N=228)	Atogepant 60 mg QD (N=231)	Total (N=902)
Migraine Diagnosis, n1 (%)					
With Aura	35 (15.8)	38 (17.2)	37 (16.2)	36 (15.6)	146 (16.2)
Without Aura	104 (46.8)	100 (45.2)	105 (46.1)	97 (42.0)	406 (45.0)
Both	83 (37.4)	83 (37.6)	86 (37.7)	98 (42.4)	350 (38.8)
Migraine Disorder Duration in Years					
Mean (SD)	20.0 (12.01)	20.7 (13.13)	21.6 (12.38)	22.5 (12.91)	21.2 (12.63)
Median	18.1	19.0	20.0	20.0	19.3
Q1, Q3	10.1, 26.0	10.0, 28.0	12.0, 30.0	12.0, 31.0	11.0, 29.3
Min, Max	2, 57	1, 57	1, 53	2, 64	1, 64
n	222	221	228	231	902
Migraine Prevention Medication in the Past, n1 (%)					
Yes	160 (72.1)	150 (67.9)	163 (71.5)	161 (69.7)	634 (70.3)
No	62 (27.9)	71 (32.1)	65 (28.5)	70 (30.3)	268 (29.7)
Average Number of Migraine Days per Month in Last 3 Months					
Mean (SD)	7.7 (2.57)	7.2 (2.47)	7.3 (2.40)	7.3 (2.43)	7.4 (2.47)
Median	8.0	7.0	7.0	7.0	7.0
Q1, Q3	5.0, 10.0	5.0, 9.0	5.0, 9.0	5.0, 9.0	5.0, 9.0
Min, Max	4, 14	4, 14	4, 14	4, 13	4, 14
n	222	221	228	231	902
Average Number of Headache Days per Month in Last 3 Months					
Mean (SD)	9.5 (2.76)	9.3 (2.69)	9.2 (2.69)	9.1 (2.71)	9.3 (2.71)
Median	10.0	10.0	9.0	10.0	10.0
Q1, Q3	8.0, 12.0	7.0, 12.0	7.0, 11.0	7.0, 11.0	7.0, 12.0
Min, Max	4, 14	4, 14	4, 14	4, 14	4, 14
n	222	221	228	231	902

N = Number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).
n = Number of participants with non-missing values in the specific category.
[1] Medication(s) that the subject usually takes to treat migraine headaches.

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Allergan
Protocol 3101-301-002

Atogepant

Table 14.1-3.2.2
Migraine History
Safety Population

Parameter Category Statistics	Placebo (N=222)	Atogepant 10 mg QD (N=221)	Atogepant 30 mg QD (N=228)	Atogepant 60 mg QD (N=231)	Total (N=902)
Acute Medication Treatment [1], n1 (%)					
Yes	221 (99.5)	220 (99.5)	224 (98.2)	231 (100.0)	896 (99.3)
Triptan	114 (51.4)	105 (47.5)	106 (46.5)	115 (49.8)	440 (48.8)
Ergot or Ergot Combinations	0 (0.0)	0 (0.0)	2 (0.9)	1 (0.4)	3 (0.3)
NSAID	142 (64.0)	147 (66.5)	143 (62.7)	137 (59.3)	569 (63.1)
Opiate or Opiate Combination	10 (4.5)	7 (3.2)	5 (2.2)	13 (5.6)	35 (3.9)
Antiemetic Agent	25 (11.3)	17 (7.7)	15 (6.6)	16 (6.9)	73 (8.1)
Barbiturates	2 (0.9)	2 (0.9)	0 (0.0)	2 (0.9)	6 (0.7)
Other	140 (63.1)	135 (61.1)	149 (65.4)	146 (63.2)	570 (63.2)
No	1 (0.5)	1 (0.5)	4 (1.8)	0 (0.0)	6 (0.7)
Advice on Lifestyle Alterations, n1 (%)					
Yes	157 (70.7)	158 (71.5)	142 (62.3)	150 (64.9)	607 (67.3)
No	65 (29.3)	63 (28.5)	86 (37.7)	81 (35.1)	295 (32.7)

N = Number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).
n = Number of participants with non-missing values in the specific category.
[1] Medication(s) that the subject usually takes to treat migraine headaches.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:11

Allergan
Protocol 3101-301-002

Atogepant

Table 14.3-1.1
Treatment Duration
Safety Population

Treatment Duration (Days)	Placebo (N=222)	Atogepant 10 mg QD (N=221)	Atogepant 30 mg QD (N=228)	Atogepant 60 mg QD (N=231)
Treatment Duration (Days), n1 (%)				
>= 1	222 (100.0)	221 (100.0)	228 (100.0)	231 (100.0)
>= 7	220 (99.1)	217 (98.2)	226 (99.1)	226 (97.8)
>= 14	215 (96.8)	213 (96.4)	226 (99.1)	224 (97.0)
>= 21	215 (96.8)	210 (95.0)	222 (97.4)	222 (96.1)
>= 28	214 (96.4)	205 (92.8)	222 (97.4)	220 (95.2)
>= 35	211 (95.0)	203 (91.9)	219 (96.1)	217 (93.9)
>= 42	211 (95.0)	201 (91.0)	219 (96.1)	215 (93.1)
>= 49	209 (94.1)	198 (89.6)	213 (93.4)	210 (90.9)
>= 56	206 (92.8)	197 (89.1)	212 (93.0)	208 (90.0)
>= 63	203 (91.4)	194 (87.8)	208 (91.2)	205 (88.7)
>= 70	202 (91.0)	193 (87.3)	207 (90.8)	204 (88.3)
>= 77	202 (91.0)	192 (86.9)	206 (90.4)	204 (88.3)
>= 84	190 (85.6)	175 (79.2)	185 (81.1)	185 (80.1)
Mean (SD)	80.9 (16.61)	78.2 (20.66)	80.9 (15.64)	79.3 (19.14)
Median	85.0	85.0	85.0	85.0
Q1, Q3	84.0, 86.0	84.0, 86.0	84.0, 86.0	84.0, 86.0
Min, Max	3, 94	1, 105	1, 103	1, 110
n	222	221	228	231
Participant-Years	49.2	47.3	50.5	50.2

Treatment Duration = last study treatment date - first study treatment date + 1.
Participant-Years = (total treatment duration in days)/365.25.
N = Number of Participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).

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Allergan
Protocol 3101-301-002

Atogepant
Page 1 of 2

Table 14.2-1.1.A
Summary of Primary and Secondary Efficacy Analyses with Multiplicity Adjustment
Modified Intent-to-Treat Population

Decision Sequence	Atogepant 10 mg QD (N=214)	Atogepant 30 mg QD (N=223)	Atogepant 60 mg QD (N=222)
P1: Change from baseline in mean monthly migraine days across the 12-week treatment period			
LSMD (95% CI), Atogepant vs. Placebo	-1.21 (-1.78, -0.64)	-1.38 (-1.94, -0.82)	-1.72 (-2.28, -1.15)
Model p-value	<.0001	<.0001	<.0001
Adjusted p-value	<.0001	<.0001	<.0001
S1: Change from baseline in mean monthly headache days across the 12-week treatment period			
LSMD (95% CI), Atogepant vs. Placebo	-1.42 (-2.03, -0.81)	-1.53 (-2.13, -0.92)	-1.71 (-2.32, -1.10)
Model p-value	<.0001	<.0001	<.0001
Adjusted p-value	<.0001	<.0001	<.0001
S2: Change from baseline in mean monthly acute medication use days across the 12-week treatment period			
LSMD (95% CI), Atogepant vs. Placebo	-1.31 (-1.81, -0.82)	-1.33 (-1.82, -0.83)	-1.50 (-2.00, -1.01)
Model p-value	<.0001	<.0001	<.0001
Adjusted p-value	<.0001	<.0001	<.0001
S3: >= 50% reduction in 3-month average of monthly migraine days			
Odds ratio (95% CI), Atogepant vs. Placebo	3.06 (2.05, 4.56)	3.53 (2.37, 5.26)	3.82 (2.56, 5.71)
Model p-value	<.0001	<.0001	<.0001
Adjusted p-value	<.0001	<.0001	<.0001
S4: Change from baseline in MSQ v2.1 Role Function Restrictive domain score at week 12			
LSMD (95% CI), Atogepant vs. Placebo	9.90 (5.45, 14.36)	10.08 (5.71, 14.46)	10.80 (6.42, 15.18)
Model p-value	<.0001	<.0001	<.0001
Adjusted p-value	<.0001	<.0001	<.0001

Adjusted p-values: using graphical approach to control the overall type I error rate for multiple comparisons. Refer to statistical analysis plan for details.
P1 model results are from Table 14.2-1.2; S1 model results are from Table 14.2-2.1; S2 model results are from Table 14.2-2.4; S3 model results are from Table 14.2-2.7; S4 model results are from Table 14.2-3.1; S5 model results are from Table 14.2-3.3; S6 model results are from Table 14.2-3.5.
LSMD = least squares mean difference. CI = confidence interval.

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Table 14.2-1.1.A
Summary of Primary and Secondary Efficacy Analyses with Multiplicity Adjustment
Modified Intent-to-Treat Population

Decision Sequence	Atogepant 10 mg QD (N=214)	Atogepant 30 mg QD (N=223)	Atogepant 60 mg QD (N=222)
S5: Change from baseline in mean monthly performance of daily activities domain score of the AIM-D across the 12-week treatment period			
LSMD (95% CI), Atogepant vs. Placebo	-1.19 (-2.56, 0.17)	-2.54 (-3.91, -1.18)	-3.32 (-4.68, -1.96)
Model p-value	0.0856	0.0003	<.0001
Adjusted p-value	0.0856	0.0005	<.0001
S6: Change from baseline in mean monthly physical impairment domain score of the AIM-D across the 12-week treatment period			
LSMD (95% CI), Atogepant vs. Placebo	-1.08 (-2.27, 0.11)	-1.99 (-3.18, -0.80)	-2.46 (-3.65, -1.28)
Model p-value	0.0743	0.0011	<.0001
Adjusted p-value	0.0856	0.0021	0.0002

Adjusted p-values: using graphical approach to control the overall type I error rate for multiple comparisons. Refer to statistical analysis plan for details.
P1 model results are from Table 14.2-1.2; S1 model results are from Table 14.2-2.1; S2 model results are from Table 14.2-2.4; S3 model results are from Table 14.2-2.7; S4 model results are from Table 14.2-3.1; S5 model results are from Table 14.2-3.3; S6 model results are from Table 14.2-3.5.
LSMD = least squares mean difference. CI = confidence interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:13:32

Allergan
Protocol 3101-301-002

Atogepant

Table 14.3-2.1.1
Number (%) of Participants with Adverse Events: Overall Summary
Safety Population

	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Treatment-emergent adverse events (TEAE)	126 (56.8)	117 (52.9)	119 (52.2)	124 (53.7)
Treatment-related TEAE	20 (9.0)	51 (23.1)	34 (14.9)	45 (19.5)
Deaths	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Treatment-emergent serious adverse events (TESAE)	2 (0.9)	2 (0.9)	0 (0.0)	0 (0.0)
Treatment-related TESAE	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
TEAE Leading to Treatment Discontinuation	6 (2.7)	9 (4.1)	4 (1.8)	6 (2.6)

Participants are counted only once within each category.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

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Allergan Atogepant
Protocol 3101-301-002 Page 1 of 12

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Participants with at least one TEAE	126 (56.8)	117 (52.9)	119 (52.2)	124 (53.7)
血液およびリンパ系障害	1 (0.5)	3 (1.4)	1 (0.4)	0 (0.0)
貧血	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
失血性貧血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
白血球増加症	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
リンパ節症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
心臓障害	3 (1.4)	2 (0.9)	0 (0.0)	2 (0.9)
左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
第一度房室ブロック	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
第二度房室ブロック	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
左房拡大	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
耳および迷路障害	3 (1.4)	4 (1.8)	2 (0.9)	3 (1.3)
耳鳴	1 (0.5)	0 (0.0)	0 (0.0)	2 (0.9)
耳痛	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
耳不快感	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	1 (0.5)	3 (1.4)	2 (0.9)	0 (0.0)
内分泌障害	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
甲状腺腫	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
甲状腺機能低下症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	3 (1.4)	3 (1.4)	4 (1.8)	0 (0.0)
眼瞼痙攣	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
ドライアイ	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:48

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
眼刺激	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
眼痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
強膜充血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
霧視	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
視力障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
硝子体浮遊物	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	21 (9.5)	38 (17.2)	34 (14.9)	32 (13.9)
便秘	1 (0.5)	17 (7.7)	16 (7.0)	16 (6.9)
悪心	4 (1.8)	11 (5.0)	10 (4.4)	14 (6.1)
下痢	4 (1.8)	3 (1.4)	2 (0.9)	4 (1.7)
消化不良	1 (0.5)	3 (1.4)	1 (0.4)	3 (1.3)
嘔吐	4 (1.8)	3 (1.4)	0 (0.0)	3 (1.3)
口内乾燥	3 (1.4)	1 (0.5)	2 (0.9)	1 (0.4)
食中毒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
埋伏歯	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
腹部膨満	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
腹痛	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)
上腹部痛	1 (0.5)	1 (0.5)	2 (0.9)	0 (0.0)
嚥下障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
鼓腸	0 (0.0)	2 (0.9)	1 (0.4)	0 (0.0)
出血性胃潰瘍	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	1 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)
口の感覚鈍麻	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
メレナ	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
膵不全	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
歯痛	0 (0.0)	2 (0.9)	2 (0.9)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:48

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
一般・全身障害および投与部位の状態	7 (3.2)	9 (4.1)	12 (5.3)	13 (5.6)
疲労	4 (1.8)	3 (1.4)	7 (3.1)	9 (3.9)
無力症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
非心臓性胸痛	1 (0.5)	3 (1.4)	0 (0.0)	1 (0.4)
疼痛	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
ワクチン接種部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
血管穿刺部位内出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
顔面痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
空腹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)
発熱	1 (0.5)	2 (0.9)	2 (0.9)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
肝胆道系障害	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
胆道ジスキネジア	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
胆嚢炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
免疫系障害	1 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
感染症および寄生虫症	46 (20.7)	32 (14.5)	53 (23.2)	51 (22.1)
上気道感染	10 (4.5)	9 (4.1)	13 (5.7)	9 (3.9)
尿路感染	8 (3.6)	3 (1.4)	9 (3.9)	9 (3.9)
上咽頭炎	8 (3.6)	4 (1.8)	8 (3.5)	8 (3.5)
インフルエンザ	2 (0.9)	3 (1.4)	2 (0.9)	5 (2.2)
副鼻腔炎	3 (1.4)	4 (1.8)	3 (1.3)	5 (2.2)

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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
胃腸炎	4 (1.8)	2 (0.9)	5 (2.2)	3 (1.3)
蜂巣炎	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.9)
レンサ球菌性咽頭炎	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
急性副鼻腔炎	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
体部白癬	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
結膜炎	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
ウイルス性胃腸炎	1 (0.5)	2 (0.9)	4 (1.8)	1 (0.4)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
喉頭炎	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
限局性感染	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
急性中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
咽頭炎	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
膿尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
細菌性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
歯感染	1 (0.5)	1 (0.5)	2 (0.9)	1 (0.4)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
外陰腟真菌感染 [f]	2 (1.0)	0 (0.0)	0 (0.0)	1 (0.5)
四肢膿瘍	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
細菌性腟症 [f]	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
気管支炎	1 (0.5)	1 (0.5)	3 (1.3)	0 (0.0)
膀胱炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
耳感染	1 (0.5)	2 (0.9)	2 (0.9)	0 (0.0)
皮膚真菌感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
淋疾	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:48

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
腎感染	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
肺炎	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性肺炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
処置後感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
ライノウイルス感染	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
皮下組織膿瘍	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
歯膿瘍	1 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)
ウイルス感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
外陰部腟カンジダ症 [f]	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
クラミジア外陰腟炎 [f]	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
傷害、中毒および処置合併症	13 (5.9)	10 (4.5)	12 (5.3)	13 (5.6)
足骨折	0 (0.0)	0 (0.0)	1 (0.4)	3 (1.3)
転倒	3 (1.4)	1 (0.5)	1 (0.4)	2 (0.9)
皮膚擦過傷	2 (0.9)	1 (0.5)	0 (0.0)	2 (0.9)
サンバーン	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)
挫傷	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
靱帯断裂	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
靱帯捻挫	2 (0.9)	3 (1.4)	0 (0.0)	1 (0.4)
肉離れ	1 (0.5)	3 (1.4)	3 (1.3)	1 (0.4)
術後血栓症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
皮膚裂傷	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
ワクチン接種合併症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
労働災害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
節足動物咬傷	3 (1.4)	0 (0.0)	2 (0.9)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:48

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
上顎炎	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
頭部損傷	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
関節脱臼	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
四肢損傷	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
筋断裂	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
処置による悪心	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
瘢痕	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
臨床検査	19 (8.6)	13 (5.9)	7 (3.1)	17 (7.4)
血中クレアチンホスホキナーゼ増加	2 (0.9)	5 (2.3)	2 (0.9)	7 (3.0)
アラニンアミノトランスフェラーゼ増加	6 (2.7)	3 (1.4)	2 (0.9)	2 (0.9)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
体重減少	2 (0.9)	1 (0.5)	0 (0.0)	2 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	6 (2.7)	2 (0.9)	2 (0.9)	1 (0.4)
拡張期血圧上昇	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
痛覚閾値低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
尿量減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
白血球数増加	2 (0.9)	0 (0.0)	0 (0.0)	1 (0.4)
血中アルカリホスファターゼ増加	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
血中クレアチニン増加	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
血中乳酸脱水素酵素増加	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
血中カリウム増加	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:48

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
血圧上昇	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
心電図T波逆転	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
エプスタイン・バーウイルス抗体陽性	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
糸球体濾過率減少	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
心拍数増加	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
国際標準比増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
体重増加	1 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)
代謝および栄養障害	6 (2.7)	4 (1.8)	1 (0.4)	6 (2.6)
食欲減退	0 (0.0)	2 (0.9)	0 (0.0)	3 (1.3)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
脱水	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
耐糖能障害	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	1 (0.5)	1 (0.5)	1 (0.4)	0 (0.0)
高脂血症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD欠乏	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	12 (5.4)	13 (5.9)	11 (4.8)	11 (4.8)
背部痛	2 (0.9)	4 (1.8)	2 (0.9)	2 (0.9)
筋骨格痛	3 (1.4)	1 (0.5)	1 (0.4)	2 (0.9)
腱炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
筋肉痛	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:48

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
頚部痛	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
関節痛	1 (0.5)	2 (0.9)	2 (0.9)	0 (0.0)
滑液包炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
肋軟骨炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
椎間板突出	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
関節雑音	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
関節硬直	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
筋骨格硬直	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)
顎痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
肩回旋筋腱板症候群	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
シェーグレン症候群	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
異形成母斑	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
脂肪腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	16 (7.2)	19 (8.6)	16 (7.0)	16 (6.9)
傾眠	2 (0.9)	7 (3.2)	4 (1.8)	4 (1.7)
浮動性めまい	0 (0.0)	4 (1.8)	4 (1.8)	3 (1.3)
片頭痛	4 (1.8)	1 (0.5)	2 (0.9)	3 (1.3)
頭痛	2 (0.9)	1 (0.5)	2 (0.9)	2 (0.9)
注意力障害	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.4)
片側錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
嗜眠	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)

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Table 14.3-2.1.2
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精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
緊張性頭痛	1 (0.5)	0 (0.0)	1 (0.4)	1 (0.4)
平衡障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
脳損傷	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
異常感覚	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
過眠症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
感覚鈍麻	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
腰髄神経根障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
神経圧迫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
視神経炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
錯感覚	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
下肢静止不能症候群	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
鎮静	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
副鼻腔炎に伴う頭痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
製品の問題	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
医療機器破損	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
医療機器材質の問題	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	11 (5.0)	11 (5.0)	10 (4.4)	14 (6.1)
不安	2 (0.9)	2 (0.9)	1 (0.4)	5 (2.2)
不眠症	0 (0.0)	3 (1.4)	1 (0.4)	4 (1.7)
異常な夢	0 (0.0)	2 (0.9)	1 (0.4)	2 (0.9)
激越	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
易刺激性	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
感情不安定	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
双極性障害	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
歯ぎしり	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
抑うつ気分	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
うつ病	3 (1.4)	0 (0.0)	1 (0.4)	0 (0.0)
情動障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
全般性不安障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
大うつ病	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
中期不眠症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
悪夢	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
ねごと	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
自殺念慮	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
腎および尿路障害	6 (2.7)	2 (0.9)	3 (1.3)	1 (0.4)
排尿困難	1 (0.5)	1 (0.5)	1 (0.4)	1 (0.4)
血尿	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
腎結石症	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
蛋白尿	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
腎仙痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	0 (0.0)	6 (2.7)	4 (1.8)	2 (0.9)
不正子宮出血 [f]	0 (0.0)	1 (0.5)	1 (0.5)	2 (1.0)
乳房分泌	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
月経過多 [f]	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
不規則月経 [f]	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
希発月経 [f]	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
骨盤痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
腟出血 [f]	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
呼吸器、胸郭および縦隔障害	13 (5.9)	12 (5.4)	7 (3.1)	8 (3.5)
副鼻腔うっ血	5 (2.3)	1 (0.5)	2 (0.9)	4 (1.7)
喘息	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
慢性閉塞性肺疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
咳嗽	2 (0.9)	3 (1.4)	1 (0.4)	1 (0.4)
呼吸困難	1 (0.5)	2 (0.9)	0 (0.0)	1 (0.4)
鼻閉	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
鼻出血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
下気道うっ血	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
陰圧性肺水腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	2 (0.9)	2 (0.9)	3 (1.3)	0 (0.0)
鼻痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
上気道咳症候群	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	4 (1.8)	6 (2.7)	3 (1.3)	6 (2.6)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)
発疹	2 (0.9)	2 (0.9)	0 (0.0)	2 (0.9)
接触皮膚炎	0 (0.0)	1 (0.5)	2 (0.9)	1 (0.4)
多汗症	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
ざ瘡	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
水疱	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
紅斑	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
そう痒症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
丘疹性皮疹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
血管障害	2 (0.9)	3 (1.4)	3 (1.3)	2 (0.9)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
血圧変動	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
高血圧	0 (0.0)	1 (0.5)	3 (1.3)	0 (0.0)
リンパ浮腫	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Protocol 3101-301-002

Atogepant

Table 14.3-2.1.5
Number (%) of Participants with Treatment Related Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Participants with at least one treatment related TEAE	20 (9.0)	51 (23.1)	34 (14.9)	45 (19.5)
心臓障害	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
第一度房室ブロック	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
耳痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
回転性めまい	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
眼障害	1 (0.5)	1 (0.5)	1 (0.4)	0 (0.0)
眼瞼痙攣	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
眼痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
胃腸障害	7 (3.2)	22 (10.0)	19 (8.3)	20 (8.7)
便秘	1 (0.5)	13 (5.9)	10 (4.4)	12 (5.2)
悪心	1 (0.5)	7 (3.2)	5 (2.2)	10 (4.3)
消化不良	1 (0.5)	0 (0.0)	0 (0.0)	2 (0.9)
口内乾燥	2 (0.9)	1 (0.5)	2 (0.9)	1 (0.4)
腹部膨満	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
腹痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
下痢	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
鼓腸	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
胃食道逆流性疾患	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)
口の感覚鈍麻	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants counted only once within each system organ class and preferred term for the most related occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.5
Number (%) of Participants with Treatment Related Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
口の錯感覚	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
嘔吐	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	1 (0.5)	4 (1.8)	4 (1.8)	5 (2.2)
疲労	1 (0.5)	3 (1.4)	4 (1.8)	5 (2.2)
異常感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
疼痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
感染症および寄生虫症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
上気道感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
臨床検査	2 (0.9)	4 (1.8)	3 (1.3)	6 (2.6)
アラニンアミノトランスフェラーゼ増加	0 (0.0)	2 (0.9)	2 (0.9)	2 (0.9)
血中クレアチンホスホキナーゼ増加	0 (0.0)	1 (0.5)	1 (0.4)	2 (0.9)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.5)	2 (0.9)	1 (0.4)
痛覚閾値低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
体重増加	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
白血球数増加	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	0 (0.0)	2 (0.9)	0 (0.0)	4 (1.7)
食欲減退	0 (0.0)	2 (0.9)	0 (0.0)	3 (1.3)
高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
筋骨格系および結合組織障害	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)

AE dictionary: MedDRA22.0
Participants counted only once within each system organ class and preferred term for the most related occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.5
Number (%) of Participants with Treatment Related Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
筋肉痛	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
関節雑音	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
神経系障害	7 (3.2)	14 (6.3)	8 (3.5)	8 (3.5)
傾眠	2 (0.9)	6 (2.7)	3 (1.3)	3 (1.3)
浮動性めまい	0 (0.0)	3 (1.4)	2 (0.9)	2 (0.9)
頭痛	1 (0.5)	1 (0.5)	1 (0.4)	1 (0.4)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
片頭痛	2 (0.9)	0 (0.0)	1 (0.4)	1 (0.4)
緊張性頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
注意力障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
異常感覚	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
過眠症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
嗜眠	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
視神経炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
錯感覚	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
鎮静	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
精神障害	3 (1.4)	5 (2.3)	2 (0.9)	4 (1.7)
異常な夢	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.4)
激越	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
不安	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
不眠症	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.4)
双極性障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
抑うつ気分	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
情動障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
初期不眠症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants counted only once within each system organ class and preferred term for the most related occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.5
Number (%) of Participants with Treatment Related Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
中期不眠症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
悪夢	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
ねごと	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
自殺念慮	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
不正子宮出血 [f]	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
希発月経 [f]	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)
呼吸器、胸郭および縦隔障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
呼吸困難	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
皮膚および皮下組織障害	0 (0.0)	3 (1.4)	0 (0.0)	4 (1.7)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)
多汗症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
ざ瘡	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
丘疹性皮疹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
血管障害	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
ほてり	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants counted only once within each system organ class and preferred term for the most related occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Participants with at least one TEAE	126 (56.8)	117 (52.9)	119 (52.2)	124 (53.7)
Mild	66 (29.7)	62 (28.1)	67 (29.4)	62 (26.8)
Moderate	51 (23.0)	51 (23.1)	51 (22.4)	60 (26.0)
Severe	9 (4.1)	4 (1.8)	1 (0.4)	2 (0.9)
血液およびリンパ系障害	1 (0.5)	3 (1.4)	1 (0.4)	0 (0.0)
Mild	1 (0.5)	2 (0.9)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
貧血	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失血性貧血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球増加症	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	3 (1.4)	2 (0.9)	0 (0.0)	2 (0.9)
Mild	2 (0.9)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左脚ブロック	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第二度房室ブロック	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左房拡大	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	3 (1.4)	4 (1.8)	2 (0.9)	3 (1.3)
Mild	2 (0.9)	4 (1.8)	2 (0.9)	3 (1.3)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	1 (0.5)	0 (0.0)	0 (0.0)	2 (0.9)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
回転性めまい	1 (0.5)	3 (1.4)	2 (0.9)	0 (0.0)
Mild	1 (0.5)	3 (1.4)	2 (0.9)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能低下症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	3 (1.4)	3 (1.4)	4 (1.8)	0 (0.0)
Mild	2 (0.9)	2 (0.9)	4 (1.8)	0 (0.0)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼痙攣	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
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Percentages are calculated as 100 x (n/N).
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ドライアイ	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼刺激	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
強膜充血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
霧視	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硝子体浮遊物	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	21 (9.5)	38 (17.2)	34 (14.9)	32 (13.9)
Mild	15 (6.8)	29 (13.1)	24 (10.5)	20 (8.7)
Moderate	6 (2.7)	8 (3.6)	10 (4.4)	12 (5.2)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
便秘	1 (0.5)	17 (7.7)	16 (7.0)	16 (6.9)
Mild	0 (0.0)	14 (6.3)	11 (4.8)	10 (4.3)
Moderate	1 (0.5)	2 (0.9)	5 (2.2)	6 (2.6)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
悪心	4 (1.8)	11 (5.0)	10 (4.4)	14 (6.1)
Mild	4 (1.8)	9 (4.1)	8 (3.5)	10 (4.3)
Moderate	0 (0.0)	2 (0.9)	2 (0.9)	4 (1.7)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下痢	4 (1.8)	3 (1.4)	2 (0.9)	4 (1.7)
Mild	3 (1.4)	3 (1.4)	1 (0.4)	2 (0.9)
Moderate	1 (0.5)	0 (0.0)	1 (0.4)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
消化不良	1 (0.5)	3 (1.4)	1 (0.4)	3 (1.3)
Mild	0 (0.0)	2 (0.9)	1 (0.4)	3 (1.3)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	4 (1.8)	3 (1.4)	0 (0.0)	3 (1.3)
Mild	3 (1.4)	2 (0.9)	0 (0.0)	2 (0.9)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内乾燥	3 (1.4)	1 (0.5)	2 (0.9)	1 (0.4)
Mild	3 (1.4)	0 (0.0)	2 (0.9)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
埋伏歯	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	1 (0.5)	1 (0.5)	2 (0.9)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	2 (0.9)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚥下障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼓腸	0 (0.0)	2 (0.9)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性胃潰瘍	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	1 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

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Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の感覚鈍麻	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メレナ	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵不全	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	0 (0.0)	2 (0.9)	2 (0.9)	0 (0.0)
Mild	0 (0.0)	2 (0.9)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
一般・全身障害および投与部位の状態	7 (3.2)	9 (4.1)	12 (5.3)	13 (5.6)
Mild	7 (3.2)	6 (2.7)	8 (3.5)	7 (3.0)
Moderate	0 (0.0)	3 (1.4)	4 (1.8)	6 (2.6)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疲労	4 (1.8)	3 (1.4)	7 (3.1)	9 (3.9)
Mild	4 (1.8)	2 (0.9)	5 (2.2)	6 (2.6)
Moderate	0 (0.0)	1 (0.5)	2 (0.9)	3 (1.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無力症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	1 (0.5)	3 (1.4)	0 (0.0)	1 (0.4)
Mild	1 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疼痛	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ワクチン接種部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管穿刺部位内出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
空腹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	0 (0.0)	0 (0.0)	2 (0.9)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
発熱	1 (0.5)	2 (0.9)	2 (0.9)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	2 (0.9)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆道ジスキネジア	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆嚢炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害	1 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	46 (20.7)	32 (14.5)	53 (23.2)	51 (22.1)
Mild	26 (11.7)	14 (6.3)	28 (12.3)	25 (10.8)
Moderate	19 (8.6)	18 (8.1)	25 (11.0)	26 (11.3)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	10 (4.5)	9 (4.1)	13 (5.7)	9 (3.9)
Mild	8 (3.6)	3 (1.4)	6 (2.6)	6 (2.6)
Moderate	2 (0.9)	6 (2.7)	7 (3.1)	3 (1.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	8 (3.6)	3 (1.4)	9 (3.9)	9 (3.9)
Mild	3 (1.4)	1 (0.5)	8 (3.5)	6 (2.6)
Moderate	5 (2.3)	2 (0.9)	1 (0.4)	3 (1.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上咽頭炎	8 (3.6)	4 (1.8)	8 (3.5)	8 (3.5)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	5 (2.3)	4 (1.8)	4 (1.8)	6 (2.6)
Moderate	3 (1.4)	0 (0.0)	4 (1.8)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	2 (0.9)	3 (1.4)	2 (0.9)	5 (2.2)
Mild	1 (0.5)	1 (0.5)	1 (0.4)	3 (1.3)
Moderate	1 (0.5)	2 (0.9)	1 (0.4)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	3 (1.4)	4 (1.8)	3 (1.3)	5 (2.2)
Mild	3 (1.4)	2 (0.9)	1 (0.4)	2 (0.9)
Moderate	0 (0.0)	2 (0.9)	2 (0.9)	3 (1.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	4 (1.8)	2 (0.9)	5 (2.2)	3 (1.3)
Mild	2 (0.9)	1 (0.5)	4 (1.8)	1 (0.4)
Moderate	2 (0.9)	1 (0.5)	1 (0.4)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.9)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レンサ球菌性咽頭炎	0 (0.0)	2 (0.9)	0 (0.0)	2 (0.9)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
急性副鼻腔炎	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体部白癬	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	1 (0.5)	2 (0.9)	4 (1.8)	1 (0.4)
Mild	0 (0.0)	1 (0.5)	2 (0.9)	1 (0.4)
Moderate	1 (0.5)	1 (0.5)	2 (0.9)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性中耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膿尿	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性副鼻腔炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯感染	1 (0.5)	1 (0.5)	2 (0.9)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	1 (0.5)	1 (0.5)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰膣真菌感染[f]	2 (1.0)	0 (0.0)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Moderate	2 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢膿瘍	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性膣症[f]	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	1 (0.5)	1 (0.5)	3 (1.3)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	2 (0.9)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳感染	1 (0.5)	2 (0.9)	2 (0.9)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚真菌感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
淋疾	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎感染	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
中耳炎	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺炎	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性肺炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ライノウイルス感染	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮下組織膿瘍	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯膿瘍	1 (0.5)	0 (0.0)	2 (0.9)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腟カンジダ症[f]	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
クラミジア外陰腟炎[f]	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	13 (5.9)	10 (4.5)	12 (5.3)	13 (5.6)
Mild	7 (3.2)	6 (2.7)	6 (2.6)	6 (2.6)
Moderate	5 (2.3)	3 (1.4)	6 (2.6)	7 (3.0)
Severe	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
足骨折	0 (0.0)	0 (0.0)	1 (0.4)	3 (1.3)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	3 (1.4)	1 (0.5)	1 (0.4)	2 (0.9)
Mild	3 (1.4)	0 (0.0)	0 (0.0)	2 (0.9)
Moderate	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚擦過傷	2 (0.9)	1 (0.5)	0 (0.0)	2 (0.9)
Mild	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
靭帯断裂	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
靭帯捻挫	2 (0.9)	3 (1.4)	0 (0.0)	1 (0.4)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
肉離れ	1 (0.5)	3 (1.4)	3 (1.3)	1 (0.4)
Mild	1 (0.5)	3 (1.4)	2 (0.9)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
術後血栓症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚裂傷	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ワクチン接種合併症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
労働災害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	3 (1.4)	0 (0.0)	2 (0.9)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	2 (0.9)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手骨折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
関節脱臼	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢損傷	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋断裂	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による悪心	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
瘢痕	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	19 (8.6)	13 (5.9)	7 (3.1)	17 (7.4)
Mild	13 (5.9)	6 (2.7)	4 (1.8)	9 (3.9)
Moderate	6 (2.7)	7 (3.2)	3 (1.3)	7 (3.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
血中クレアチンホスホキナーゼ増加	2 (0.9)	5 (2.3)	2 (0.9)	7 (3.0)
Mild	2 (0.9)	2 (0.9)	2 (0.9)	5 (2.2)
Moderate	0 (0.0)	3 (1.4)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
アラニンアミノトランスフェラーゼ増加	6 (2.7)	3 (1.4)	2 (0.9)	2 (0.9)
Mild	3 (1.4)	1 (0.5)	1 (0.4)	2 (0.9)
Moderate	3 (1.4)	2 (0.9)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	2 (0.9)	1 (0.5)	0 (0.0)	2 (0.9)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	6 (2.7)	2 (0.9)	2 (0.9)	1 (0.4)
Mild	2 (0.9)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	4 (1.8)	1 (0.5)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛覚閾値低下	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量減少	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
白血球数増加	2 (0.9)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ビリルビン増加	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中乳酸脱水素酵素増加	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
エプスタイン・バーウイルス抗体陽性	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糸球体濾過率減少	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心拍数増加	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
国際標準比増加	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	1 (0.5)	2 (0.9)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	6 (2.7)	4 (1.8)	1 (0.4)	6 (2.6)
Mild	6 (2.7)	2 (0.9)	1 (0.4)	3 (1.3)
Moderate	0 (0.0)	2 (0.9)	0 (0.0)	3 (1.3)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	0 (0.0)	2 (0.9)	0 (0.0)	3 (1.3)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.9)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高カリウム血症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耐糖能障害	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	1 (0.5)	1 (0.5)	1 (0.4)	0 (0.0)

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n = number of participants within a specific category.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	1 (0.5)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高脂血症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食欲亢進	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンD欠乏	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	12 (5.4)	13 (5.9)	11 (4.8)	11 (4.8)
Mild	9 (4.1)	8 (3.6)	7 (3.1)	9 (3.9)
Moderate	3 (1.4)	4 (1.8)	4 (1.8)	2 (0.9)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
背部痛	2 (0.9)	4 (1.8)	2 (0.9)	2 (0.9)
Mild	1 (0.5)	3 (1.4)	2 (0.9)	1 (0.4)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
筋骨格痛	3 (1.4)	1 (0.5)	1 (0.4)	2 (0.9)
Mild	2 (0.9)	0 (0.0)	1 (0.4)	2 (0.9)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱炎	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頚部痛	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節痛	1 (0.5)	2 (0.9)	2 (0.9)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑液包炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋軟骨炎	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
関節雑音	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節硬直	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	2 (0.9)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顎痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足底筋膜炎	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肩回旋筋腱板症候群	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シェーグレン症候群	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
異形成母斑	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂肪腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	16 (7.2)	19 (8.6)	16 (7.0)	16 (6.9)
Mild	7 (3.2)	14 (6.3)	10 (4.4)	9 (3.9)
Moderate	5 (2.3)	4 (1.8)	5 (2.2)	7 (3.0)
Severe	4 (1.8)	1 (0.5)	1 (0.4)	0 (0.0)
傾眠	2 (0.9)	7 (3.2)	4 (1.8)	4 (1.7)
Mild	2 (0.9)	4 (1.8)	4 (1.8)	3 (1.3)
Moderate	0 (0.0)	3 (1.4)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	0 (0.0)	4 (1.8)	4 (1.8)	3 (1.3)
Mild	0 (0.0)	3 (1.4)	2 (0.9)	2 (0.9)
Moderate	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
片頭痛	4 (1.8)	1 (0.5)	2 (0.9)	3 (1.3)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Moderate	1 (0.5)	1 (0.5)	2 (0.9)	1 (0.4)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	2 (0.9)	1 (0.5)	2 (0.9)	2 (0.9)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Moderate	2 (0.9)	0 (0.0)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	2 (0.9)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片側錯感覚	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神的機能障害	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前兆を伴う片頭痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)

AE dictionary: MedDRA22.0
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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	1 (0.5)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳損傷	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常感覚	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
過眠症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰髄神経根障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経圧迫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視神経炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
錯感覚	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鎮静	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎に伴う頭痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
製品の問題	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
医療機器破損	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
医療機器材質の問題	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	11 (5.0)	11 (5.0)	10 (4.4)	14 (6.1)
Mild	5 (2.3)	6 (2.7)	7 (3.1)	10 (4.3)
Moderate	5 (2.3)	5 (2.3)	3 (1.3)	3 (1.3)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
不安	2 (0.9)	2 (0.9)	1 (0.4)	5 (2.2)
Mild	2 (0.9)	1 (0.5)	1 (0.4)	3 (1.3)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.9)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	0 (0.0)	3 (1.4)	1 (0.4)	4 (1.7)
Mild	0 (0.0)	3 (1.4)	1 (0.4)	3 (1.3)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
異常な夢	0 (0.0)	2 (0.9)	1 (0.4)	2 (0.9)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	2 (0.9)
Moderate	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
激越	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意欠陥多動性障害	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
易刺激性	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感情不安定	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
双極性障害	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯ぎしり	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	3 (1.4)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
情動障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全般性不安障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
初期不眠症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
大うつ病	0 (0.0)	2 (0.9)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中期不眠症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪夢	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ねごと	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自殺念慮	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害	6 (2.7)	2 (0.9)	3 (1.3)	1 (0.4)
Mild	3 (1.4)	2 (0.9)	3 (1.3)	1 (0.4)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	1 (0.5)	1 (0.5)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎結石症	3 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	1 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎仙痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	0 (0.0)	6 (2.7)	4 (1.8)	2 (0.9)
Mild	0 (0.0)	4 (1.8)	3 (1.3)	2 (0.9)
Moderate	0 (0.0)	2 (0.9)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不正子宮出血[f]	0 (0.0)	1 (0.5)	1 (0.5)	2 (1.0)
Mild	0 (0.0)	1 (0.5)	1 (0.5)	2 (1.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房分泌	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経過多[f]	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
不規則月経[f]	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
希発月経[f]	0 (0.0)	1 (0.5)	1 (0.5)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腟出血[f]	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	13 (5.9)	12 (5.4)	7 (3.1)	8 (3.5)
Mild	6 (2.7)	7 (3.2)	4 (1.8)	5 (2.2)
Moderate	6 (2.7)	4 (1.8)	3 (1.3)	3 (1.3)
Severe	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
副鼻腔うっ血	5 (2.3)	1 (0.5)	2 (0.9)	4 (1.7)
Mild	2 (0.9)	0 (0.0)	1 (0.4)	3 (1.3)

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Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Moderate	3 (1.4)	1 (0.5)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘息	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
慢性閉塞性肺疾患	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	2 (0.9)	3 (1.4)	1 (0.4)	1 (0.4)
Mild	2 (0.9)	2 (0.9)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	1 (0.5)	2 (0.9)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
Moderate	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	1 (0.5)	1 (0.5)	0 (0.0)	1 (0.4)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
鼻出血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下気道うっ血	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰圧性肺水腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	2 (0.9)	2 (0.9)	3 (1.3)	0 (0.0)
Mild	2 (0.9)	1 (0.5)	2 (0.9)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠時無呼吸症候群	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くしゃみ	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	4 (1.8)	6 (2.7)	3 (1.3)	6 (2.6)
Mild	4 (1.8)	5 (2.3)	2 (0.9)	5 (2.2)
Moderate	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.3)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	2 (0.9)	2 (0.9)	0 (0.0)	2 (0.9)
Mild	2 (0.9)	2 (0.9)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触皮膚炎	0 (0.0)	1 (0.5)	2 (0.9)	1 (0.4)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:51

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Mild	0 (0.0)	1 (0.5)	1 (0.4)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ざ瘡	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
そう痒症	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹性皮疹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	2 (0.9)	3 (1.4)	3 (1.3)	2 (0.9)
Mild	2 (0.9)	3 (1.4)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	3 (1.3)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢冷感	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Mild	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧変動	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Mild	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ほてり	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	0 (0.0)	1 (0.5)	3 (1.3)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	3 (1.3)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ浮腫	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Mild	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Allergan
Protocol 3101-301-002

Atogepant

Table 14.3-2.2.1
Number (%) of Participants with Treatment-Emergent Serious Adverse Events (TESAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Participants with at least one TESAE	2 (0.9)	2 (0.9)	0 (0.0)	0 (0.0)
胃腸障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
出血性胃潰瘍	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
脳損傷	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
視神経炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
喘息	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
陰圧性肺水腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Allergan
Protocol 3101-301-002

Atogepant

Table 14.3-2.2.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) Leading to Treatment Discontinuation by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
Participants with at least one TEAE leading to treatment discontinuation	6 (2.7)	9 (4.1)	4 (1.8)	6 (2.6)
耳および迷路障害	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
耳痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
回転性めまい	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
胃腸障害	1 (0.5)	1 (0.5)	2 (0.9)	1 (0.4)
便秘	0 (0.0)	1 (0.5)	2 (0.9)	1 (0.4)
悪心	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
腹痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
疲労	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.4)
代謝および栄養障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
食欲減退	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
糖尿病	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
筋骨格系および結合組織障害	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)
筋痙縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
筋骨格系胸痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	2 (0.9)	3 (1.4)	1 (0.4)	0 (0.0)
脳損傷	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

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Table 14.3-2.2.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) Leading to Treatment Discontinuation by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=222) n (%)	Atogepant 10 mg QD (N=221) n (%)	Atogepant 30 mg QD (N=228) n (%)	Atogepant 60 mg QD (N=231) n (%)
頭痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
片頭痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
視神経炎	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
傾眠	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
精神障害	1 (0.5)	1 (0.5)	1 (0.4)	2 (0.9)
激越	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
不眠症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
異常な夢	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
双極性障害	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
自殺念慮	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
血尿	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
腎仙痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
骨盤痛	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
陰圧性肺水腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.9)
多汗症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
全身性そう痒症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
丘疹性皮疹	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

AE dictionary: MedDRA22.0
Participants are counted only once within each preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:55

3101-304-002 試験［参考資料］

治験の標題： A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy, Safety, and Tolerability of Oral Atogepant for the Prophylaxis of Migraine in Participants with Episodic Migraine Who Have Previously Failed 2 to 4 Classes of Oral Prophylactic Treatments (ELEVATE)	
施設数 / 実施国名： 73 施設 / カナダ，チェコ，デンマーク，フランス，ドイツ，ハンガリー，イタリア，オランダ，ポーランド，ロシア，スペイン，イギリス，及び米国	
治験調整医師： [redacted], MD, [redacted]	
公表文献（参考資料）： なし	
治験期間： 治験開始日（最初の被験者の初回来院日）：2021 年 3 月 5 日 治験終了日（最後の被験者の最終来院日）：2022 年 8 月 4 日	開発のフェーズ： 第 III 相
治験の種類： 多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験	
目的： 過去に 2–4 種類の経口片頭痛予防薬で効果不十分であった反復性片頭痛（以下「EM」）被験者を対象として，片頭痛予防を目的としたアトゲパント水和物（以下「アトゲパント」）60 mg 1 日 1 回（以下「QD」）経口投与の有効性，安全性，及び忍容性を評価する。	
被験者数（計画時と解析時）： 計画時： 約 300 例の被験者を 2 つの投与群（アトゲパント 60 mg QD 群及びプラセボ群）のいずれかに 1：1 の比率で無作為に割り付けることとした。 解析時： • intent-to-treat（以下「ITT」）集団：アトゲパント 60 mg QD 群 157 例，プラセボ群 158 例 • 安全性解析対象集団：アトゲパント 60 mg QD 群 156 例，プラセボ群 157 例， • modified ITT（以下「mITT」）集団：アトゲパント 60 mg QD 群 151 例，プラセボ群 154 例 • off-treatment hypothetical estimand（以下「OTHE」）集団：アトゲパント 60 mg QD 群 154 例，プラセボ群 155 例 <u>設定根拠</u> 各投与群に無作為に割り付ける被験者のサンプルサイズを 150 例とし，米国の場合の投与群間差を–1.7 日，欧州連合（以下「EU」）の場合の投与群間差を–1.6 日と想定すると，主要有効性評価項目で得られるアトゲパント 60 mg QD とプラセボとの投与群間差を検出するための検出力は，それぞれ 97%及び 95%となる。下表に示すように，米国及び EU での有効性の各副次評価項目に対しても十分な検出力が得られるようサンプルサイズを決定した。 検出力は以下の推定に基づき算出した： 1） 主要評価項目でのアトゲパント 60 mg QD とプラセボとの投与群間差は，過去のアトゲパントの片頭痛予防効果が評価された試験（3101-301-002 試験）で得られた相対的に保守的な推定値とした。主要評価項目の標準偏差（以下「SD」）は過去の片頭痛予防効果が評価された試験（Liberty 試験［エレヌマブ］[1]，3101-301-002 試験［アトゲパント］）をもとに，副次評価項目の SD は 3101-301-002 試験をもとに推定した。	

2） 多重比較には固定順序法を用い，ファミリーワイズエラー率を有意水準 0.05 で制御する。主要評価項目が両側有意水準 0.05 で有意であると判定された場合に副次評価項目を検定することとし，各副次評価項目の検出力は，先行する副次評価項目で有意差が認められることを条件とした（各評価項目間は独立と仮定）。

米国の主要評価項目及び副次評価項目に対する統計学的検出力

仮説検定	評価項目	プラセボ群との投与群間差	SD	検出力
主要評価項目	12 週間の投与期間での平均 MMD のベースラインからの変化量	–1.7	3.5	97%
第 1 副次評価項目	12 週間の投与期間での平均 MMD が 50%以上減少した被験者の割合	アトゲパント群の割合：60% プラセボ群の割合：29%,	–	99%
第 2 副次評価項目	12 週間の投与期間での平均月間頭痛日数のベースラインからの変化量	–1.7	3.7	95%
第 3 副次評価項目	12 週間の投与期間での急性期治療薬の平均月間使用日数のベースラインからの変化量	–1.5	3.1	97%
第 4 副次評価項目	12 週時の MSQ v2.1 の RFR ドメインスコアのベースラインからの変化量	10.8	22.6	96%
第 5 副次評価項目	12 週間の投与期間での AIM-D の日常活動機能ドメイン平均月間スコアのベースラインからの変化量	–3.3	7.3	93%
第 6 副次評価項目	12 週間の投与期間での AIM-D の身体障害ドメイン平均月間スコアのベースラインからの変化量	–2.4	6.4	81%

EU の主要評価項目及び副次評価項目に対する統計学的検出力

仮説検定	評価項目	プラセボ群との投与群間差[a]	SD[a]	検出力
主要評価項目	12 週間の投与期間での平均 MMD のベースラインからの変化量	–1.6	3.5	95%
第 1 副次評価項目	12 週間の投与期間での平均 MMD が 50%以上減少した被験者の割合	アトゲパント群の割合：59%, プラセボ群の割合：30%	–	99%
第 2 副次評価項目	12 週間の投与期間での平均月間頭痛日数のベースラインからの変化量	–1.6	3.7	92%
第 3 副次評価項目	12 週間の投与期間での急性期治療薬の平均月間使用日数のベースラインからの変化量	–1.4	3.2	93%

第 4 副次評価項目	12 週時の HIT-6 合計スコアのベースラインからの変化量	–3.9	7.6	98%
第 5 副次評価項目	12 週時の MSQ v2.1 の RFR ドメインスコアのベースラインからの変化量	10.9	22.8	96%

a. EU に適用した推定は，事前調査データに基づき，OTHE アプローチを使用した。

診断と組入れ基準：

<u>選択基準</u>

以下の選択基準をすべて満たした患者を組入れ可能とした。

1.	年齢
1.01	Visit 1 時点で 18 歳（又は法的成年年齢）以上 80 歳以下の男性患者又は女性患者。
2.	患者のタイプ及び片頭痛の特徴
2.01	国際頭痛分類第 3 版（以下「ICHD-3」）に基づく診断と一致する前兆のある片頭痛又は前兆のない片頭痛を 1 年以上有する患者。
2.02	片頭痛の発症年齢が 50 歳未満の患者。
2.03	治験責任医師の判断による Visit 1 前 3 ヵ月間の平均月間片頭痛日数（以下「MMD」）が 4–14 日である患者。
2.04	電子日誌（以下「eDiary」）で 28 日間のベースライン期間に片頭痛の日数が 4–14 日である患者（注意：無作為化の上限を 20%に設定し，ベースライン時の片頭痛日数が 4 日以上 8 日未満の被験者が無作為化予定の被験者の 20%を超えないようにする）。
2.05	ベースライン期間 28 日間のうち 20 日間以上 eDiary への入力があり，治験質問票及び eDiary を読解し，入力することができると治験責任医師が判断した患者。
2.06	患者は以下の基準をすべて満たす必要がある。 a. 以下に示す薬剤クラスの経口片頭痛予防薬のうち 2–4 種類で効果がなかった： i. プロプラノロール，メトプロロール，アテノロール，ビソプロロール，チモロール，又はナドロール ii. トピラマート iii. フルナリジン iv. バルプロ酸又は divalproex v. アミトリプチリン又はノルトリプチリン vi. ベンラファキシン又はデスベンラファキシン vii. リシノプリル viii. カンデサルタン ix. 各地域で承認された製品（oxeterone 又は pizotifen など） b. 以下に示す薬剤のうち 1 種類以上で効果がなかった： i. プロプラノロール又はメトプロロール ii. トピラマート iii. フルナリジン iv. アミトリプチリン （注意：予防薬の効果の有無は，治験責任医師の判断に基づく忍容性又は有効性を根拠とする。効果がなかった各予防薬を記録に残す必要がある。）
3.	避妊

3.01	妊娠のリスクを最小限に抑える意思のある男性患者： 男性患者は，治験薬の投与期間中，及び治験薬の最終投与後 3 日間，治験実施計画書に記載されている避妊法を使用することに同意し，この期間中，精子の提供を控える必要がある。 妊娠のリスクを最小限に抑える意思のある女性患者： 女性患者は，妊娠しておらず（スクリーニング［Visit 1］時及び無作為化［Visit 2］時の尿妊娠検査が陰性），本試験期間中に妊娠を計画しておらず，授乳しておらず，かつ以下の条件の 1 つ以上を満たす場合に組入れ可能とした。 a. 治験実施計画書に定義されている妊娠可能な女性でない。 b. 治験薬の投与期間中及び治験薬の最終投与後 3 日間は，治験実施計画書に定義されている避妊ガイダンス（医学的に許容され，効果の高い避妊方法を使用する）に従うことに同意する妊娠可能な女性。
4.	同意説明
4.01	本試験に関する手順が開始される前に文書同意及び患者のプライバシーに関する情報（Written Authorization for Use and Release of Health and Research Study Information［米国の施設の場合］及び written Data Protection consent［EU の施設の場合］など）を得られた患者。

除外基準

以下の除外基準のいずれかに該当する患者は本試験から除外した。

1.	健康状態
1.01	臨床的に重大な血液疾患，内分泌疾患，肺疾患，肝疾患，消化管疾患，又は神経疾患を有する患者。 • これらの疾患の既往歴を有するものの，Visit 1 前 1 年超，状態が安定しており，本試験への参加に支障をきたすおそれはないと治験責任医師が判断した患者は組入れ可能とした。
1.02	現在の頭痛障害に重大な影響を及ぼす可能性がある他の疼痛疾患（線維筋痛症，顔面痛など）を併発していると治験責任医師が判断した患者。
1.03	混合した精神状態，認知症，てんかん，又は片頭痛以外の重大な神経障害を有すると治験責任医師が判断した患者。
1.04	Visit 1 前 5 年間に悪性腫瘍の既往歴を有する患者（適切に治療された基底細胞癌，扁平上皮癌，又は子宮頚部上皮内癌は除く）。
1.05	治験薬の吸収又は代謝に影響を及ぼす可能性のある消化管処置又は消化管疾患（下痢症候群，炎症性腸疾患など）の既往歴を有する患者。肥満症に対する胃への処置（ラップバンドなど）を受けたものの，その処置を元に戻した患者は組入れ可能とした。
1.06	臨床的に重大な心血管疾患又は脳血管疾患を有すると治験責任医師が判断した患者。これには以下の疾患を含むが，これらに限定されない。 • 臨床的に重大な虚血性心疾患（不安定狭心症など）。 • 臨床的に重大な心調律異常若しくは心伝導異常（心房細動，第 2 度又は第 3 度心ブロックなど）又はトルサードドポアントの危険因子（心不全，低カリウム血症，徐脈など）。 • Visit 1 前 6 ヵ月以内の心筋梗塞，一過性脳虚血発作，又は脳卒中。 • ニューヨーク心臓協会の心機能分類（NYHA 分類）で III 度又は IV 度と定義される心不全。
1.07	臨床面接及びコロンビア自殺評価スケール（以下「C-SSRS」）の回答により自傷行為の重大なリスクが認められた患者，又は他害行為の重大なリスクがあると治験責任医師が判断した患者。過去 6 ヵ月以内に実行する意思のある自殺念慮（計画の有無は問わない）（C-SSRS でタイプ 4 又は 5）

	を報告した患者，又は Visit 1 若しくは Visit 2 の評価前 6 ヵ月以内に何らかの自殺行動を報告した患者は除外することとした。
1.08	Visit 1 にレクリエーショナルドラッグ又は違法薬物（合法・非合法に関わらず大麻を含む）の使用者であった患者，又は過去 1 年以内に薬物若しくはアルコールの乱用若しくは依存の既往歴を有する患者。
2.	片頭痛の特徴
2.01	治験責任医師の判断による Visit 1 前 3 ヵ月間の平均月間頭痛日数が 15 日以上である患者。
2.02	eDiary で 28 日間のベースライン期間の頭痛日数が 15 日以上である患者。
2.03	片頭痛を緊張型頭痛又はその他の頭痛と区別することが困難な患者。
2.04	複視若しくは意識レベルの低下を伴う片頭痛，又は ICHD-3 に定義されている網膜片頭痛の既往歴を有する患者。
2.05	ICHD-3 に定義されている慢性片頭痛，新規発症持続性連日性頭痛，薬物乱用頭痛，三叉神経・自律神経性頭痛（群発頭痛など），又は有痛性脳神経ニューロパチーと現在診断されている患者。
3.	前治療 / 併用療法
3.01	Visit 1 前の 30 日間（別途指定がない限り）及び本試験期間中に，併用禁止薬若しくは併用禁止療法の一覧（治験実施計画書で規定）に記載されている薬剤，食事（グレープフルーツジュースなど），又は非薬物療法を使用しており，それらを中止できない若しくは許容される別の薬剤や治療法への切り替えができない患者。これには，適応に関わらず，片頭痛予防への有効性が示されている併用薬（アミトリプチリン，トピラマート，プロプラノロールなど）も含まれる。
3.02	Visit 1 前 6 ヵ月間及び本試験期間中に頭部，顔面，又は頸部に治療又は美容目的でボツリヌス毒素の注射（Dysport®，BOTOX®，Xeomin®，Myobloc®，Jeuveau™ など）を使用した，又は使用する患者。
3.03	バルビツール酸系薬剤若しくはオピオイド鎮痛剤を 1 ヵ月あたり 2 日超，トリプタン系薬剤若しくはエルゴタミン製剤を 1 ヵ月あたり 10 日以上，又は単一成分の鎮痛薬（アスピリン，非ステロイド性抗炎症薬［以下「NSAIDs」］，アセトアミノフェンなど）を 1 ヵ月あたり 15 日以上，Visit 1 前の 3 ヵ月間に使用したと治験責任医師が判断した，若しくはベースライン期間に使用した患者。（注意：スクリーニングの 30 日前から本試験期間を通じてバルビツール酸系薬剤の使用は認められない。オピオイド鎮痛剤は，スクリーニング / ベースライン期間中及び本試験期間中の使用は認められないが，片頭痛又は頭痛とは関係のない目的［手術など］での一時使用は可能とした。）
3.04	以下の薬剤への曝露歴がある患者。 • アトゲパント • Visit 1 前 6 ヵ月以内でのカルシトニン遺伝子関連ペプチド（以下「CGRP」）経路を遮断する注射用モノクローナル抗体 • 治験中のその他の CGRP 受容体拮抗薬
3.05	CGRP 受容体拮抗薬に対する過敏症若しくは臨床的に重大な副作用の既往歴，又は治験薬（アトゲパント又はプラセボ）の成分に対する過敏症の既往歴を有する患者。
4.	臨床試験への参加歴（以前 / 現在）
4.01	治験薬又は治験機器を用いた試験（市販の製剤又は機器を用いた試験も含む）に現在参加中，又は Visit 1 前 30 日以内に参加していた患者。
5.	診断評価
5.01	Visit 1 又は Visit 2 の座位収縮期血圧が 160 mm Hg 超又は座位拡張期血圧が 100 mm Hg 超の高血圧の患者。これらの上限を超えた場合，バイタルサインを 1 回のみ再測定可能とした。

5.02	スクリーニング時（Visit 1）に心電図（以下「ECG」）に臨床的に重大な異常を有すると治験責任医師により判断された患者。
5.03	中央審査機関の ECG 報告に基づき，Visit 1 の Fridericia 補正法を用いて心拍数で補正した QT 間隔（QTcF）が男性は 450 msec 超，女性は 470 msec 超の患者。
5.04	Visit 1 に臨床的に重大な臨床検査値又は以下のいずれかの臨床検査値が認められた患者。 ● アラニンアミノトランスフェラーゼ（以下「ALT」）値又はアスパラギン酸アミノトランスフェラーゼ（以下「AST」）値が基準値の上限（以下「ULN」）の 1 倍超。 ● 総ビリルビン値が ULN の 1 倍超（ジルベール症候群と診断された患者を除く）。 ● 血清アルブミン値が 2.8 g/dL（4.06 μmol/L）未満。
5.05	Visit 1 の尿中薬物検査が陽性であった患者（片頭痛以外の症状に対して処方されたオピオイド鎮痛剤，不眠症治療のためのベンゾジアゼピン系薬剤などで説明できる併用は除く）。
5.06	スクリーニング（Visit 1）前 6 ヵ月以内の急性肝炎の既往歴若しくは慢性肝疾患（非アルコール性脂肪性肝炎を含む）を有する，又はスクリーニング時（Visit 1）に抗 A 型肝炎 IgM 抗体，B 型肝炎表面抗原，抗 C 型肝炎抗体，若しくは抗 E 型肝炎 IgM 抗体の検査で陽性であった患者。
6.	その他
6.01	治験責任医師，治験スタッフ，治験依頼者のいずれかに雇用されている，又はその近親者（両親，配偶者，兄弟姉妹，又は子供）。
6.02	患者を重大なリスクにさらす，試験結果を混乱させる，又は患者の本試験の参加で著しく支障をきたす可能性があると治験責任医師が判断した状態又は状況にあった患者。
6.03	医学的又はその他の理由（試験手順や来院予約を遵守しない可能性がある，本試験期間中に転居する予定があるなど）で本試験に不適格と治験責任医師が判断した患者。

治験方法：

本試験は，過去に 2–4 種類の経口片頭痛予防薬で効果不十分であった EM 被験者を対象に，片頭痛予防を目的としてアトゲパント 60 mg QD 経口投与の有効性，安全性，及び忍容性を評価する第 III 相，多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験であった。

約 300 例の被験者をプラセボ群又はアトゲパント 60 mg QD 群のいずれかに 1：1 の割合で無作為に割り付けた。治験実施計画書に従い，無作為化は，地域（北米，欧州，及びアジア / 太平洋）に基づいて層別化したが，アジア / 太平洋地域から本試験に組み入れられた被験者はいなかった。また，無作為化は，スクリーニング / ベースライン期間の片頭痛日数（4 日以上 8 日未満，8 日以上）及び過去の効果不十分であった片頭痛予防薬の種類（2 種類，2 種類超）でも層別化した。実際の層別データは，eDiary 及び電子症例報告書（eCRF）からのデータを使用した。

本試験は，4 週間のスクリーニング / ベースライン期間，12 週間の二重盲検期間，及び 4 週間の安全性追跡調査期間の合計 20 週間で構成された。予定された治験実施医療機関への来院は 8 回（Visit 1［スクリーニング / ベースライン］，Visit 2［無作為化］，Visit 3［2 週時］，Visit 4［4 週時］，Visit 5［6 週時］，Visit 6［8 週時］，Visit 7 / 早期中止［12 週時］，及び Visit 8［16 週時 / 試験終了 / 安全性追跡調査］）であった。3101-312-002 試験（長期安全性継続試験）に継続参加する被験者を除き，治験薬を 1 回以上投与されたすべての被験者は，Visit 8 を完了することとした。継続試験に参加する被験者は，継続試験で追跡調査が実施されるため本試験の Visit 8 は不要とした。

非盲検下で安全性データ及び要約報告書をレビューし，安全性の問題及び傾向を特定し，未知の臨床的に重大な有害事象を示すデータが得られた場合に試験の計画変更又は早期中止などを治験依頼者に提言するために，独立したデータ安全性モニタリング委員会を設置した。

判定手順を策定し，臨床判定委員会による治験薬投与開始後の ULN の 3 倍以上の ALT 及び / 又は AST 上昇の盲検下での監視，モニタリング，判定のプロセスを規定した。本手順の目的は，ALT 及び / 又は AST 上昇とアトゲパントの因果関係を判定するためにこれらの事象と関係のあるデータを判定する場合の標準化したプロセス

を提供することであった。

被験薬，用量，投与方法及びバルクロット番号：
アトゲパント 60 mg QD，12 週間経口投与

被験薬	製剤	製造者	バルクロット番号
アトゲパント	60 mg	[redacted]	[redacted]

対照薬，用量，投与方法及びバルクロット番号：
プラセボ，12 週間経口投与

対照薬	製剤	製造者	バルクロット番号
プラセボ	対応するプラセボ 60 mg	[redacted]	[redacted]

治療期間：本試験は，4 週間のスクリーニング / ベースライン期間，12 週間の二重盲検期間，及び 4 週間の安全性追跡調査期間の合計 20 週間で構成された。

評価基準：

有効性：

主要評価項目：

- 12 週間の投与期間での平均 MMD のベースラインからの変化量

副次評価項目：

米国申請では 6 つの副次評価項目，EU 申請では 5 つの副次評価項目を設定した。

- 12 週間の投与期間での平均 MMD が 50%以上減少した被験者の割合
- 12 週間の投与期間での平均月間頭痛日数のベースラインからの変化量
- 12 週間の投与期間での急性期治療薬の平均月間使用日数のベースラインからの変化量
- 12 週時の片頭痛特有の生活の質に関する質問票第 2.1 版（以下「MSQ v2.1」）の日常役割機能制限（RFR）ドメインスコアのベースラインからの変化量
- 12 週間の投与期間での片頭痛による活動障害－ダイアリー（以下「AIM-D」）の日常活動機能ドメイン平均月間スコアのベースラインからの変化量（米国のみ）
- 12 週間の投与期間での AIM-D の身体障害ドメイン平均月間スコアのベースラインからの変化量（米国のみ）
- 12 週時の Headache Impact Test（以下「HIT-6」）合計スコアのベースラインからの変化量（EU のみ）

有効性及びヘルスアウトカム：

有効性の評価（医療資源利用データ以外のヘルスアウトカム測定結果を含む）は，被験者が eDiary（自宅で毎日使用）に記録した頭痛の持続時間，特徴，症状，急性期治療薬の使用などの情報に基づいて行った。これら収集したデータを片頭痛日数及び頭痛日数の定義に当てはめた。医療資源利用データは，治験責任医師による問診に基づき収集された。有効性の評価には以下のヘルスアウトカム評価項目が含まれる：

AIM-D 及び Activity Level and Activity Limitation：eDiary を介して毎日収集

European Quality of Life - 5-Dimensional - 5 Level（EQ-5D-5L）：本試験期間中の異なる時点で eDiary を介して収集し，電子タブレットで管理

HIT-6，患者の全般的印象度－変化（PGIC），患者の全般的印象度－重症度（PGIS），仕事の生産性及び活動障害に関する質問票：片頭痛第 2.0 版（WPAI: MIGRAINE），治験薬に対する患者の満足度（PSSM），

Migraine Disability Assessment（MIDAS），MSQ v2.1，患者報告転帰測定情報システム 痛みによる支障－簡易版 6a（PROMIS-PI），及び患者健康質問票-9（PHQ-9）：決められた来院時に電子タブレットで実施
医療資源利用：各来院時に治験責任医師が書面にて収集

安全性：
有害事象（特に注目すべき有害事象を含む），バイタルサイン，身体所見，ECG，臨床検査値，C-SSRS

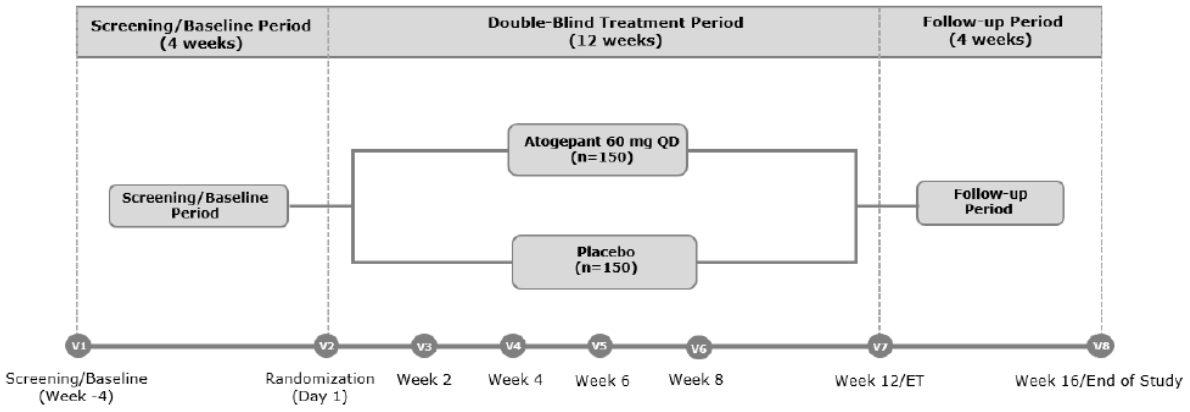
統計手法：
有効性及びヘルスアウトカム：
主要評価項目及び副次評価項目のアトゲパント 60 mg QD 群とプラセボ群との比較では，多重比較に固定順序法を用いて，ファミリーワイズエラー率を $\alpha = 0.05$ で制御した。
その他の有効性評価項目の解析は，mITT 集団及び OTHE 集団に基づき，多重性を調整せず，名目上の有意水準で実施した。
本試験では，2 つの有効性解析集団を以下のように定義した：

- mITT 集団：治験薬を 1 回以上投与され，評価可能なベースライン期間の eDiary データを有し，二重盲検期間中に評価可能なベースライン後の 4 週間隔（1–4 週，5–8 週，及び 9–12 週）の eDiary データを 1 つ以上有する，無作為化されたすべての被験者。
- OTHE 集団：治験薬を 1 回以上投与され，評価可能なベースライン期間の eDiary データを有し，評価可能なベースライン後の 4 週間隔（1–4 週，5–8 週，9–12 週）の eDiary データを 1 つ以上有する，無作為化されたすべての被験者（治験薬の投与中かどうかを問わない）。

すべての有効性解析（mITT 集団及び OTHE 集団）では，割り付けられた投与群に基づいて解析された。

安全性：
すべての安全性解析は，安全性解析対象集団を用いて実施した。安全性解析対象集団は，治験薬を 1 回以上投与されたすべての被験者で構成された。被験者は，実際に投与期間の大部分で投与された用量に対応する投与群に基づいて解析された。安全性パラメータ（臨床検査，バイタルサイン，ECG）について，治験薬の初回投与前の欠測値でない最後の測定値を，すべての安全性解析のベースライン値として使用した。連続変数は，被験者数，平均値，SD，中央値，第 1 四分位数，第 3 四分位数，最小値，及び最大値で要約した。カテゴリー変数は，被験者の人数と割合で要約した。

図 1. 試験デザインの概略（3101-304-002 試験）



Cross reference: 3101-304-002 final CSR Figure 1

試験結果

被験者の内訳

被験者の内訳を表 1 に示す。

合計 315 例の被験者が無作為化され，313 例（99.4%）が治験薬を 1 回以上投与された（安全性解析対象集団）。mITT 集団は 305 例，OTHE 集団は 309 例であった。無作為化された被験者全体の 93.7%（295 例）が二重盲検期間を完了し，6.3%（20 例）が二重盲検期間中に投与を中止した。投与中止に至った主な理由は，治験実施計画書からの逸脱（2.5%），有害事象（1.9%）及び同意撤回（1.3%）であった。

安全性追跡調査期間を完了したのは 86 例（27.3%）で，1 例が安全性追跡調査期間を中止した（同意撤回）。Visit 7，Visit 8，又は投与中断期間後に長期安全性継続試験（3101-312-002 試験）に 265 例（84.1%）が継続参加した。Visit 7 で継続参加した被験者は，本試験の安全性追跡調査期間に移行しなかった。

人口統計学的及び他のベースラインの特性

人口統計学的特性，ベースライン特性及び原疾患のベースライン特性をそれぞれ表 2，表 3 及び表 4 に示す。

ベースラインの人口統計学的特性は，安全性解析対象集団の投与群間で臨床的に意義のある差は認められなかった。平均年齢は 42.2 歳で，被験者の 89.5%が女性，95.8%が白人であった。ベースラインの体重及び体格指数（BMI）の平均値はそれぞれ 72.83 kg，25.86 kg/m^2 であった。

片頭痛の既往歴は，安全性解析対象集団の投与群間で臨床的に意義のある差は認められなかった。全体で，前兆のある片頭痛のみが 20.1%，前兆のない片頭痛が 62.0%，前兆のある片頭痛と前兆のない片頭痛の混在が 17.9%であり，片頭痛の平均罹病期間は 20.5 年であった。スクリーニング時，片頭痛の急性期治療薬を被験者の 99.0%が使用しており，いずれかの投与群の 20%以上で使用されていた薬剤は，トリプタン系薬剤（81.5%）及び NSAID（64.9%）であった。スクリーニング前 3 ヵ月間の平均 MMD は全体で 9.4 日（範囲：4–14），平均月間頭痛日数は全体で 10.1 日であった。

曝露状況

曝露状況を表 5 に示す。

合計 313 例の被験者が治験薬を 1 回以上投与され，そのうちアトゲパント 60 mg QD が 156 例，プラセボが 157 例であった。

平均投与期間は，アトゲパント 60 mg QD 群 81.7 日，プラセボ群 83.7 日であった。

有効性の結果

mITT 集団（表 6）と OTHE 集団の両集団について，以下に示す有効性の結論を得た。

- 主要評価項目：12 週間の投与期間での平均 MMD のベースラインからの変化量は，mITT 集団及び OTHE 集団でプラセボ群と比較してアトゲパント 60 mg QD 群で統計学的に有意かつ臨床的に意義のある群間差を示した（$P < 0.0001$，多重性調整済み）。
- 米国の 6 つの副次評価項目（mITT 集団）及び EU の 5 つの副次評価項目（OTHE 集団）のすべての評価項目で，ベースラインからの変化量は，プラセボ群と比較してアトゲパント 60 mg QD 群で統計学的に有意かつ臨床的に意義のある群間差を示した（いずれも $P < 0.0001$，多重性調整済み）。

全体として，有効性のその他の評価項目の結果は，主要評価項目及び副次評価項目の結果と一致していた。

安全性の結果

アトゲパント 60 mg QD は，過去に 2–4 種類の経口片頭痛予防薬で効果不十分であった EM 被験者で，許容可能な安全性及び忍容性プロファイルを示した。

有害事象

有害事象の発現状況を以下に示す。

有害事象の発現割合は，アトゲパント 60 mg QD 群 51.9%（81/156 例），プラセボ群 53.5%（84/157 例）であった。

いずれかの投与群で発現割合が 5%以上の有害事象は，便秘（アトゲパント 60 mg QD 群 10.3%［16 例］，プラセボ群 2.5%［4 例］，以下同順），COVID-19（8.3%［13 例］，9.6%［15 例］），悪心（7.1%［11 例］，3.2%［5 例］）及び上咽頭炎（5.1%［8 例］，7.6%［12 例］）であった。

治験薬と関連ありの有害事象の発現割合は，アトゲパント 60 mg QD 群 19.9%（31 例），プラセボ群 8.9%（14 例）であった。

いずれかの投与群で発現割合が 2%以上の治験薬と関連ありの有害事象は，便秘（アトゲパント 60 mg QD 群 8.3%［13 例］，プラセボ群 1.9%［3 例］，以下同順），悪心（5.1%［8 例］，1.9%［3 例］）及び食欲減退（3.2%［5 例］，0%）であった。

高度の有害事象の発現割合は，アトゲパント 60 mg QD 群 2.6%（4 例），プラセボ群 0.6%（1 例）であった。ほとんどの有害事象は，治験責任医師により軽度又は中等度と判断された。

いずれかの投与群で発現割合が 1%以上の高度の有害事象は認められなかった。

投与終了後の有害事象の発現割合は，アトゲパント 60 mg QD 群 15.9%（7 例），プラセボ群 11.6%（5 例）であった。

いずれかの投与群で発現割合が 5%以上の投与終了後の有害事象は，COVID-19（アトゲパント 60 mg QD 群 0%，プラセボ群 7.0%［3 例］）であった。全体として，投与終了後の有害事象の発現割合は，投与群間で同程度であり，COVID-19 及び片頭痛を除き，いずれの投与群でも 1 例以下であった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の発現割合は，アトゲパント 60 mg QD 群 2.6%（4 例），プラセボ群 0%であった。

重篤な有害事象は，人工流産（女性被験者のみ）（アトゲパント 60 mg QD 群 0.7%［1/139 例］，プラセボ群 0%［0/141 例］，以下同順），並びに心室性頻脈及び乳癌第 2 期及び浸潤性乳癌（各 0.6%［1/156 例］，各 0%）であった。治験責任医師が，アトゲパントと関連ありと判断した重篤な有害事象はなかった。

治験薬の投与中止に至った有害事象の発現割合は，アトゲパント 60 mg QD 群 1.9%（3 例），プラセボ群 1.3%（2 例）であった。

治験薬の投与中止に至った有害事象は，心室性頻脈，便秘，悪心及び傾眠（アトゲパント 60 mg QD 群各 0.6%［1 例］，プラセボ群各 0%，以下同順），並びに片頭痛，そう痒症及び皮膚剥脱（各 0%，各 0.6%［1 例］）であった。

特に注目すべき有害事象

潜在的な Hy's Law 基準に該当した被験者は認められなかった。

治験薬の投与後に ULN の 3 倍以上の ALT 又は AST 上昇が認められた被験者はいなかった。

C-SSRS 評価による二重盲検期間中の実行する意思のある自殺念慮及び自殺行動は，いずれの投与群でも認められなかった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団
有害事象の要約	表 7（Table 14.3-2.1.1）
すべての有害事象	表 8（Table 14.3-2.1.2）
因果関係「関連あり」の有害事象	表 9（Table 14.3-2.1.5）
重症度別有害事象	表 10（Table 14.3-2.1.4）
重篤な有害事象	表 11（Table 14.3-2.2.1）
治験薬の投与中止に至った有害事象	表 12（Table 14.3-2.2.2）

臨床検査

臨床検査値に臨床的に意義のあるベースラインからの変化は認められなかった。

バイタルサイン

12 週間の投与期間終了時の平均体重は，アトゲパント 60 mg QD 群ではベースラインから約 1 kg 減少したが，プラセボ群ではほぼ変化が認められなかった。この傾向は，臨床的に意義がある可能性のあるベースラインからの体重減少が 7%以上であった被験者の割合にも反映されていた（アトゲパント 60 mg QD 群 3.9%，プラセボ群 1.3%）。

その他のバイタルサインのベースラインからの変化量は投与群間で同様であった。

ECG

アトゲパント 60 mg QD 群の 1 例で，ベースライン時に正常な ECG パラメータであったが，二重盲検期間終了時に臨床的に重要な異常（150 msec 以上の QRS 延長）が認められた。当該被験者に発現した重篤な有害事象（心室性頻脈）は，治験責任医師によりアトゲパントとの関連なしと判断された。

結論

過去に 2–4 種類の経口片頭痛予防薬で効果不十分であった EM 被験者を対象に評価した，主要評価項目である 12 週間の投与期間での平均 MMD のベースラインからの変化量は，mITT 集団及び OTHE 集団でプラセボ群と比較してアトゲパント 60 mg QD 群で統計学的に有意な改善を示した（$P < 0.0001$，多重性調整済み）。すべての有効性の副次評価項目で，プラセボと比較してアトゲパント 60 mg QD は，ベースラインから統計学的に有意に改善した。

過去に 2–4 種類の経口片頭痛予防薬で効果不十分であった EM 被験者で，アトゲパント 60 mg QD は許容可能な安全性及び忍容性プロファイルを示した。本試験で認められた主な有害事象は，アトゲパントの既知の安全性プロファイルと一致しており，新たな安全性に関する懸念は認められなかった。

参考文献

1. Reuter U, Goadsby PJ, Lanteri-Minet M, et al. Efficacy and tolerability of erenumab in patients with episodic migraine in whom two-to-four previous preventive treatments were unsuccessful: a randomised, double-blind, placebo-controlled, Phase 3b study. Lancet. 2018;392(10161):2280-7.

表1

Table 14.1-1.4
Participant Disposition
Intent-to-Treat Population

Phase Disposition	Placebo (N=158) n (%)	Atogepant 60 mg QD (N=157) n (%)	Total (N=315) n (%)
Number of Participants Randomized	158 (100.0)	157 (100.0)	315 (100.0)
Number of Participants Treated	157 (99.4)	156 (99.4)	313 (99.4)
Double-Blind Treatment Period			
Number of Participants Entered	158 (100.0)	157 (100.0)	315 (100.0)
Number of Participants Completed	151 (95.6)	144 (91.7)	295 (93.7)
Number of Participants Discontinued	7 (4.4)	13 (8.3)	20 (6.3)
Reason for Discontinuation			
Adverse Event	2 (1.3)	4 (2.5)	6 (1.9)
Lack of efficacy	0 (0.0)	1 (0.6)	1 (0.3)
Withdrawal by subject	2 (1.3)	2 (1.3)	4 (1.3)
Lost to Follow-Up	0 (0.0)	0 (0.0)	0 (0.0)
Pregnancy	0 (0.0)	1 (0.6)	1 (0.3)
Protocol Deviation	3 (1.9)	5 (3.2)	8 (2.5)
Non-compliance with study drug	0 (0.0)	0 (0.0)	0 (0.0)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Follow-Up Period			
Number of Participants Entered	43 (27.2)	44 (28.0)	87 (27.6)
Number of Participants Completed	42 (26.6)	44 (28.0)	86 (27.3)
Number of Participants Discontinued	1 (0.6)	0 (0.0)	1 (0.3)
Reason for Discontinuation			
Adverse Event	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by subject	1 (0.6)	0 (0.0)	1 (0.3)
Lost to Follow-Up	0 (0.0)	0 (0.0)	0 (0.0)
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)
Protocol Deviation	0 (0.0)	0 (0.0)	0 (0.0)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

N = Number of randomized participants.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

Table 14.1-1.4
Participant Disposition
Intent-to-Treat Population

Phase Disposition	Placebo (N=158) n (%)	Atogepant 60 mg QD (N=157) n (%)	Total (N=315) n (%)
Number of participants who signed informed consent for 3101-312-002	138 (87.3)	127 (80.9)	265 (84.1)

N = Number of randomized participants.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

表2

Table 14.1-3.1.1
Demographics
Safety Population

Parameter	Placebo (N=157)	Atogepant 60 mg QD (N=156)	Total (N=313)
Age (years)			
Mean (SD)	43.4 (10.28)	40.9 (10.67)	42.2 (10.53)
Median	44.0	41.0	43.0
Q1, Q3	37.0, 49.0	33.0, 48.0	35.0, 49.0
Min, Max	18, 68	19, 67	18, 68
n	157	156	313
Age Group, n (%)			
< 20	1 (0.6)	1 (0.6)	2 (0.6)
20-29	14 (8.9)	23 (14.7)	37 (11.8)
30-39	34 (21.7)	42 (26.9)	76 (24.3)
40-49	69 (43.9)	57 (36.5)	126 (40.3)
50-59	28 (17.8)	26 (16.7)	54 (17.3)
60-69	11 (7.0)	7 (4.5)	18 (5.8)
>= 70	0 (0.0)	0 (0.0)	0 (0.0)
Sex, n (%)			
Male	16 (10.2)	17 (10.9)	33 (10.5)
Female	141 (89.8)	139 (89.1)	280 (89.5)

Age is relative to informed consent date.
[1] Participants who reported multiple races are only included in multiple category.
N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

Table 14.1-3.1.1
Demographics
Safety Population

Parameter	Placebo (N=157)	Atogepant 60 mg QD (N=156)	Total (N=313)
Race, n (%)			
White	151 (96.2)	149 (95.5)	300 (95.8)
Black or African American	4 (2.5)	3 (1.9)	7 (2.2)
Asian	2 (1.3)	2 (1.3)	4 (1.3)
American Indian Or Alaska Native	0 (0.0)	0 (0.0)	0 (0.0)
Native Hawaiian Or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)
Multiple [1]	0 (0.0)	2 (1.3)	2 (0.6)
Race Group, n (%)			
White	151 (96.2)	149 (95.5)	300 (95.8)
All Other Races	6 (3.8)	7 (4.5)	13 (4.2)
Ethnicity, n (%)			
Hispanic or Latino	4 (2.5)	7 (4.5)	11 (3.5)
Not Hispanic or Latino	153 (97.5)	149 (95.5)	302 (96.5)
Region, n (%)			
North America	20 (12.7)	20 (12.8)	40 (12.8)
Europe	137 (87.3)	136 (87.2)	273 (87.2)

Age is relative to informed consent date.
[1] Participants who reported multiple races are only included in multiple category.
N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

表3

Table 14.1-3.1.4
Baseline Characteristics
Safety Population

Parameter	Placebo (N=157)	Atogepant 60 mg QD (N=156)	Total (N=313)
Weight (kg)			
Mean (SD)	74.00 (16.091)	71.65 (14.778)	72.83 (15.471)
Median	71.50	69.20	70.50
Q1, Q3	63.00, 85.00	59.90, 82.40	61.00, 83.60
Min, Max	43.0, 132.5	46.1, 112.7	43.0, 132.5
n	157	156	313
Height (cm)			
Mean (SD)	167.93 (7.148)	167.32 (7.942)	167.62 (7.548)
Median	168.50	166.50	167.60
Q1, Q3	162.50, 172.50	162.00, 171.65	162.00, 172.00
Min, Max	150.0, 191.0	148.6, 196.0	148.6, 196.0
n	157	156	313
BMI (kg/m^2)			
Mean (SD)	26.16 (5.219)	25.56 (4.893)	25.86 (5.060)
Median	25.03	24.48	24.74
Q1, Q3	22.76, 28.63	22.03, 28.52	22.23, 28.53
Min, Max	16.8, 45.3	16.5, 41.6	16.5, 45.3
n	157	156	313

表4

Table 14.1-3.2.2
Migraine History
Safety Population

Parameter Category Statistics	Placebo (N=157)	Atogepant 60 mg QD (N=156)	Total (N=313)
Migraine Diagnosis, n1 (%)			
With Aura	33 (21.0)	30 (19.2)	63 (20.1)
Without Aura	91 (58.0)	103 (66.0)	194 (62.0)
Both	33 (21.0)	23 (14.7)	56 (17.9)
Migraine Disorder Duration in Years			
Mean (SD)	20.7 (11.20)	20.3 (11.64)	20.5 (11.41)
Median	20.5	18.0	20.0
Q1, Q3	10.5, 29.0	11.6, 26.5	11.4, 28.6
Min, Max	2, 53	1, 51	1, 53
n	157	156	313
Migraine Prevention Medication in the Past, n1 (%)			
Yes	157 (100.0)	156 (100.0)	313 (100.0)
No	0 (0.0)	0 (0.0)	0 (0.0)
Average Number of Migraine Days per Month in Last 3 Months			
Mean (SD)	9.4 (2.25)	9.4 (2.54)	9.4 (2.40)
Median	10.0	10.0	10.0
Q1, Q3	8.0, 11.0	8.0, 11.5	8.0, 11.0
Min, Max	4, 14	4, 14	4, 14
n	157	156	313
Average Number of Headache Days per Month in Last 3 Months			
Mean (SD)	10.1 (2.31)	10.2 (2.52)	10.1 (2.41)
Median	10.0	10.0	10.0
Q1, Q3	9.0, 12.0	8.0, 12.0	9.0, 12.0
Min, Max	4, 14	3, 14	3, 14
n	157	156	313

N = Number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).
n = Number of participants with non-missing values in the specific category.
[1] Current usual treatment for acute migraine.

Table 14.1-3.2.2
Migraine History
Safety Population

Parameter Category Statistics	Placebo (N=157)	Atogepant 60 mg QD (N=156)	Total (N=313)
Acute Medication Treatment [1], n1 (%)			
Yes	154 (98.1)	156 (100.0)	310 (99.0)
Triptan	128 (81.5)	127 (81.4)	255 (81.5)
Ergot or Ergot Combinations	3 (1.9)	6 (3.8)	9 (2.9)
NSAID	98 (62.4)	105 (67.3)	203 (64.9)
Opiate or Opiate Combination	1 (0.6)	1 (0.6)	2 (0.6)
Antiemetic Agent	4 (2.5)	3 (1.9)	7 (2.2)
Barbiturates	0 (0.0)	0 (0.0)	0 (0.0)
Other	25 (15.9)	25 (16.0)	50 (16.0)
No	3 (1.9)	0 (0.0)	3 (1.0)
Advice on Lifestyle Alterations, n1 (%)			
Yes	96 (61.1)	92 (59.0)	188 (60.1)
No	61 (38.9)	64 (41.0)	125 (39.9)

N = Number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).
n = Number of participants with non-missing values in the specific category.
[1] Current usual treatment for acute migraine.

表5

Table 14.3-1.1
Treatment Duration
Safety Population

	Placebo (N=157)	Atogepant 60 mg QD (N=156)
Treatment Duration (Days), n1 (%)		
>= 1	157 (100.0)	156 (100.0)
>= 7	155 (98.7)	154 (98.7)
>= 14	154 (98.1)	152 (97.4)
>= 21	154 (98.1)	151 (96.8)
>= 28	152 (96.8)	151 (96.8)
>= 35	152 (96.8)	150 (96.2)
>= 42	152 (96.8)	150 (96.2)
>= 49	151 (96.2)	149 (95.5)
>= 56	151 (96.2)	147 (94.2)
>= 63	151 (96.2)	145 (92.9)
>= 70	151 (96.2)	145 (92.9)
>= 77	151 (96.2)	145 (92.9)
>= 84	136 (86.6)	134 (85.9)
Mean (SD)	83.7 (13.64)	81.7 (15.49)
Median	85.0	85.0
Q1, Q3	84.0, 86.0	84.0, 86.0
Min, Max	5, 100	2, 97
n	157	156
Participant-Years	36.0	34.9

Treatment Duration = last study treatment date - first study treatment date + 1.
Participant-Years = (total treatment duration in days)/365.25.
N = Number of Participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).

表6

Table 14.2-1.1.A
Summary of Primary and Secondary Efficacy Analyses with Multiplicity Adjustment
Modified Intent-to-Treat Population

Decision Sequence	Atogepant 60 mg QD (N=151)
P1: Change from baseline in mean monthly migraine days across the 12-week treatment period	
LSMD (95% CI), atogepant vs. Placebo	-2.43 (-3.27, -1.59)
Model p-value	<.0001
Adjusted p-value	<.0001
S1: Achievement of at least a 50% reduction in mean monthly migraine days across the 12-week treatment period	
Odds ratio (95% CI), atogepant vs. Placebo	5.15 (3.02, 8.79)
Model p-value	<.0001
Adjusted p-value	<.0001
S2: Change from baseline in mean monthly headache days across the 12-week treatment period	
LSMD (95% CI), atogepant vs. Placebo	-2.28 (-3.15, -1.42)
Model p-value	<.0001
Adjusted p-value	<.0001
S3: Change from baseline in mean monthly acute medication use days across the 12-week treatment period	
LSMD (95% CI), atogepant vs. Placebo	-2.68 (-3.43, -1.93)
Model p-value	<.0001
Adjusted p-value	<.0001
S4: Change from baseline in MSQ v2.1 Role Function Restrictive domain score at week 12	
LSMD (95% CI), atogepant vs. Placebo	17.67 (13.05, 22.30)
Model p-value	<.0001
Adjusted p-value	<.0001

Adjusted p-values: using graphical approach to control the overall type I error rate for multiple comparisons. Refer to statistical analysis plan for details.
P1 model results are from Table 14.2-1.2; S1 model results are from Table 14.2-2.1.A; S2 model results are from Table 14.2-2.2.A; S3 model results are from Table 14.2-2.3.A; S4 model results are from Table 14.2-3.1.A; S5 model results are from Table 14.2-3.2; S6 model results are from Table 14.2-3.3.
LSMD = least squares mean difference. CI = confidence interval.

Table 14.2-1.1.A
Summary of Primary and Secondary Efficacy Analyses with Multiplicity Adjustment
Modified Intent-to-Treat Population

Decision Sequence	Atogepant 60 mg QD (N=151)
S5: Change from baseline in mean monthly performance of daily activities domain score of the AIM-D across the 12-week treatment period	
LSMD (95% CI), atogepant vs. Placebo	-4.71 (-6.37, -3.05)
Model p-value	<.0001
Adjusted p-value	<.0001
S6: Change from baseline in mean monthly physical impairment domain score of the AIM-D across the 12-week treatment period	
LSMD (95% CI), atogepant vs. Placebo	-4.39 (-5.94, -2.85)
Model p-value	<.0001
Adjusted p-value	<.0001

Adjusted p-values: using graphical approach to control the overall type I error rate for multiple comparisons. Refer to statistical analysis plan for details.
P1 model results are from Table 14.2-1.2; S1 model results are from Table 14.2-2.1.A; S2 model results are from Table 14.2-2.2.A; S3 model results are from Table 14.2-2.3.A; S4 model results are from Table 14.2-3.1.A; S5 model results are from Table 14.2-3.2; S6 model results are from Table 14.2-3.3.
LSMD = least squares mean difference. CI = confidence interval.

表7

Table 14.3-2.1.1
Number (%) of Participants with Adverse Events: Overall Summary
Safety Population

	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
Treatment-emergent adverse events (TEAE)	84 (53.5)	81 (51.9)
Treatment-related TEAE	14 (8.9)	31 (19.9)
Deaths	0 (0.0)	0 (0.0)
Treatment-emergent serious adverse events (TESAE)	0 (0.0)	4 (2.6)
Treatment-related TESAE	0 (0.0)	0 (0.0)
TEAE Leading to Treatment Discontinuation	2 (1.3)	3 (1.9)

Participants are counted only once within each category.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

表8

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
Participants with at least one TEAE	84 (53.5)	81 (51.9)
血液およびリンパ系障害	0 (0.0)	1 (0.6)
白血球減少症	0 (0.0)	1 (0.6)
心臓障害	0 (0.0)	1 (0.6)
心室性頻脈	0 (0.0)	1 (0.6)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.6)
皮様嚢腫	0 (0.0)	1 (0.6)
耳および迷路障害	0 (0.0)	1 (0.6)
耳鳴	0 (0.0)	1 (0.6)
内分泌障害	1 (0.6)	0 (0.0)
自己免疫性甲状腺炎	1 (0.6)	0 (0.0)
眼障害	2 (1.3)	1 (0.6)
アレルギー性結膜炎	0 (0.0)	1 (0.6)
複視	1 (0.6)	0 (0.0)
霧視	1 (0.6)	0 (0.0)
胃腸障害	19 (12.1)	28 (17.9)
便秘	4 (2.5)	16 (10.3)
悪心	5 (3.2)	11 (7.1)
腹痛	2 (1.3)	2 (1.3)
下痢	4 (2.5)	2 (1.3)
嘔吐	2 (1.3)	2 (1.3)
上腹部痛	0 (0.0)	1 (0.6)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
消化不良	4 (2.5)	1 (0.6)
食中毒	0 (0.0)	1 (0.6)
齲歯	1 (0.6)	0 (0.0)
口内乾燥	1 (0.6)	0 (0.0)
おくび	1 (0.6)	0 (0.0)
消化管運動過剰	1 (0.6)	0 (0.0)
血便排泄	1 (0.6)	0 (0.0)
歯痛	1 (0.6)	0 (0.0)
一般・全身障害および投与部位の状態	6 (3.8)	6 (3.8)
疲労	1 (0.6)	3 (1.9)
冷感	0 (0.0)	1 (0.6)
体温変動感	0 (0.0)	1 (0.6)
非心臓性胸痛	0 (0.0)	1 (0.6)
口渇	0 (0.0)	1 (0.6)
血管穿刺部位血腫	0 (0.0)	1 (0.6)
血管穿刺部位疼痛	0 (0.0)	1 (0.6)
注射部位疼痛	1 (0.6)	0 (0.0)
倦怠感	1 (0.6)	0 (0.0)
疼痛	1 (0.6)	0 (0.0)
発熱	2 (1.3)	0 (0.0)
恥骨上痛	1 (0.6)	0 (0.0)
肝胆道系障害	0 (0.0)	1 (0.6)
胆石症	0 (0.0)	1 (0.6)
免疫系障害	2 (1.3)	1 (0.6)
薬物過敏症	0 (0.0)	1 (0.6)
季節性アレルギー	2 (1.3)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
感染症および寄生虫	44 (28.0)	35 (22.4)
COVID-19	15 (9.6)	13 (8.3)
上咽頭炎	12 (7.6)	8 (5.1)
尿路感染	4 (2.5)	4 (2.6)
気管支炎	0 (0.0)	2 (1.3)
インフルエンザ	2 (1.3)	2 (1.3)
結膜炎	0 (0.0)	1 (0.6)
胃腸炎	1 (0.6)	1 (0.6)
ウイルス性胃腸炎	1 (0.6)	1 (0.6)
帯状疱疹	0 (0.0)	1 (0.6)
咽頭炎	0 (0.0)	1 (0.6)
歯髄炎	1 (0.6)	1 (0.6)
副鼻腔炎	2 (1.3)	1 (0.6)
扁桃炎	2 (1.3)	1 (0.6)
歯膿瘍	0 (0.0)	1 (0.6)
上気道感染	1 (0.6)	1 (0.6)
ウイルス性上気道感染	0 (0.0)	1 (0.6)
無症候性細菌尿	1 (0.6)	0 (0.0)
細菌性膣症 [f]	1 (0.7)	0 (0.0)
膀胱炎	1 (0.6)	0 (0.0)
憩室炎	1 (0.6)	0 (0.0)
陰部単純ヘルペス	1 (0.6)	0 (0.0)
中耳炎	1 (0.6)	0 (0.0)
レンサ球菌性咽頭炎	1 (0.6)	0 (0.0)
ウイルス性気道感染	1 (0.6)	0 (0.0)
傷害、中毒および処置合併症	3 (1.9)	6 (3.8)
挫傷	0 (0.0)	1 (0.6)
上顎炎	0 (0.0)	1 (0.6)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
眼挫傷	0 (0.0)	1 (0.6)
処置後炎症	0 (0.0)	1 (0.6)
外傷後疼痛	0 (0.0)	1 (0.6)
腱断裂	0 (0.0)	1 (0.6)
靭帯断裂	1 (0.6)	0 (0.0)
靭帯捻挫	1 (0.6)	0 (0.0)
肉離れ	1 (0.6)	0 (0.0)
臨床検査	6 (3.8)	5 (3.2)
血中カリウム増加	1 (0.6)	1 (0.6)
糸球体濾過率減少	0 (0.0)	1 (0.6)
心拍数増加	0 (0.0)	1 (0.6)
SARS-CoV-2 検査陽性	0 (0.0)	1 (0.6)
体重減少	1 (0.6)	1 (0.6)
血中ビリルビン増加	1 (0.6)	0 (0.0)
血中コレステロール増加	1 (0.6)	0 (0.0)
ヘマトクリット減少	1 (0.6)	0 (0.0)
Ｅ型肝炎抗体陽性	1 (0.6)	0 (0.0)
赤血球数減少	1 (0.6)	0 (0.0)
体重増加	1 (0.6)	0 (0.0)
代謝および栄養障害	3 (1.9)	7 (4.5)
食欲減退	2 (1.3)	5 (3.2)
食欲亢進	0 (0.0)	1 (0.6)
インスリン抵抗性	0 (0.0)	1 (0.6)
ビタミンＤ欠乏	1 (0.6)	0 (0.0)
筋骨格系および結合組織障害	13 (8.3)	4 (2.6)
関節痛	1 (0.6)	2 (1.3)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
四肢痛	0 (0.0)	2 (1.3)
頚部痛	3 (1.9)	1 (0.6)
弾発指	0 (0.0)	1 (0.6)
背部痛	2 (1.3)	0 (0.0)
側腹部痛	1 (0.6)	0 (0.0)
筋痙縮	1 (0.6)	0 (0.0)
筋緊張	1 (0.6)	0 (0.0)
筋肉痛	1 (0.6)	0 (0.0)
変形性関節症	1 (0.6)	0 (0.0)
脊椎痛	1 (0.6)	0 (0.0)
腱炎	1 (0.6)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	2 (1.3)
乳癌第２期	0 (0.0)	1 (0.6)
浸潤性乳癌	0 (0.0)	1 (0.6)
アクロコルドン	1 (0.6)	0 (0.0)
神経系障害	9 (5.7)	8 (5.1)
片頭痛	4 (2.5)	3 (1.9)
浮動性めまい	2 (1.3)	2 (1.3)
傾眠	0 (0.0)	2 (1.3)
頭痛	2 (1.3)	1 (0.6)
錯感覚	1 (0.6)	1 (0.6)
失神	0 (0.0)	1 (0.6)
注意力障害	1 (0.6)	0 (0.0)
味覚不全	1 (0.6)	0 (0.0)
精神障害	5 (3.2)	8 (5.1)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
不眠症	2 (1.3)	5 (3.2)
不安	0 (0.0)	1 (0.6)
易刺激性	0 (0.0)	1 (0.6)
季節性感情障害	0 (0.0)	1 (0.6)
気分動揺	1 (0.6)	0 (0.0)
睡眠障害	1 (0.6)	0 (0.0)
自殺念慮	1 (0.6)	0 (0.0)
腎および尿路障害	2 (1.3)	2 (1.3)
非感染性膀胱炎	0 (0.0)	1 (0.6)
血尿	0 (0.0)	1 (0.6)
尿路結石	1 (0.6)	0 (0.0)
尿意切迫	1 (0.6)	0 (0.0)
生殖系および乳房障害	0 (0.0)	1 (0.6)
過少月経 [f]	0 (0.0)	1 (0.7)
呼吸器、胸郭および縦隔障害	2 (1.3)	4 (2.6)
気管支痙攣	0 (0.0)	1 (0.6)
呼吸困難	0 (0.0)	1 (0.6)
鼻出血	0 (0.0)	1 (0.6)
口腔咽頭痛	1 (0.6)	1 (0.6)
アレルギー性鼻炎	0 (0.0)	1 (0.6)
鼻漏	1 (0.6)	0 (0.0)
皮膚および皮下組織障害	6 (3.8)	3 (1.9)
斑状出血	0 (0.0)	1 (0.6)
多汗症	0 (0.0)	1 (0.6)
そう痒症	2 (1.3)	1 (0.6)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
発疹	1 (0.6)	1 (0.6)
嵌入爪	1 (0.6)	0 (0.0)
口囲皮膚炎	1 (0.6)	0 (0.0)
皮膚剥脱	1 (0.6)	0 (0.0)
蕁麻疹	1 (0.6)	0 (0.0)
外科および内科処置	0 (0.0)	1 (0.6)
人工流産 [f]	0 (0.0)	1 (0.7)
血管障害	3 (1.9)	3 (1.9)
高血圧	3 (1.9)	3 (1.9)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表9

Table 14.3-2.1.5
Number (%) of Participants with Treatment Related Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
Participants with at least one treatment related TEAE	14 (8.9)	31 (19.9)
耳および迷路障害	0 (0.0)	1 (0.6)
耳鳴	0 (0.0)	1 (0.6)
胃腸障害	8 (5.1)	21 (13.5)
便秘	3 (1.9)	13 (8.3)
悪心	3 (1.9)	8 (5.1)
上腹部痛	0 (0.0)	1 (0.6)
下痢	0 (0.0)	1 (0.6)
消化不良	2 (1.3)	1 (0.6)
嘔吐	0 (0.0)	1 (0.6)
消化管運動過剰	1 (0.6)	0 (0.0)
一般・全身障害および投与部位の状態	1 (0.6)	2 (1.3)
疲労	0 (0.0)	1 (0.6)
口渇	0 (0.0)	1 (0.6)
倦怠感	1 (0.6)	0 (0.0)
感染症および寄生虫症	1 (0.6)	0 (0.0)
尿路感染	1 (0.6)	0 (0.0)
臨床検査	2 (1.3)	2 (1.3)
糸球体濾過率減少	0 (0.0)	1 (0.6)
心拍数増加	0 (0.0)	1 (0.6)
体重減少	1 (0.6)	0 (0.0)
体重増加	1 (0.6)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants counted only once within each system organ class and preferred term for the most related occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.5
Number (%) of Participants with Treatment Related Treatment-Emergent Adverse Events (TEAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
代謝および栄養障害	0 (0.0)	5 (3.2)
食欲減退	0 (0.0)	5 (3.2)
神経系障害	1 (0.6)	2 (1.3)
浮動性めまい	0 (0.0)	1 (0.6)
傾眠	0 (0.0)	1 (0.6)
注意力障害	1 (0.6)	0 (0.0)
精神障害	2 (1.3)	3 (1.9)
不眠症	1 (0.6)	3 (1.9)
気分動揺	1 (0.6)	0 (0.0)
呼吸器、胸郭および縦隔障害	0 (0.0)	1 (0.6)
鼻出血	0 (0.0)	1 (0.6)
皮膚および皮下組織障害	2 (1.3)	2 (1.3)
多汗症	0 (0.0)	1 (0.6)
発疹	0 (0.0)	1 (0.6)
そう痒症	1 (0.6)	0 (0.0)
皮膚剥脱	1 (0.6)	0 (0.0)
蕁麻疹	1 (0.6)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants counted only once within each system organ class and preferred term for the most related occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表10

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
Participants with at least one TEAE	84 (53.5)	81 (51.9)
Mild	50 (31.8)	52 (33.3)
Moderate	33 (21.0)	25 (16.0)
Severe	1 (0.6)	4 (2.6)
血液およびリンパ系障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
白血球減少症	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
心臓障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
心室性頻脈	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
先天性、家族性および遺伝性障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
皮様嚢腫	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
耳および迷路障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
内分泌障害	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
自己免疫性甲状腺炎	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
眼障害	2 (1.3)	1 (0.6)
Mild	2 (1.3)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
アレルギー性結膜炎	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
複視	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
霧視	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
胃腸障害	19 (12.1)	28 (17.9)
Mild	13 (8.3)	21 (13.5)
Moderate	6 (3.8)	6 (3.8)
Severe	0 (0.0)	1 (0.6)
便秘	4 (2.5)	16 (10.3)
Mild	3 (1.9)	12 (7.7)
Moderate	1 (0.6)	3 (1.9)
Severe	0 (0.0)	1 (0.6)
悪心	5 (3.2)	11 (7.1)
Mild	4 (2.5)	9 (5.8)
Moderate	1 (0.6)	2 (1.3)
Severe	0 (0.0)	0 (0.0)
腹痛	2 (1.3)	2 (1.3)
Mild	0 (0.0)	2 (1.3)
Moderate	2 (1.3)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
下痢	4 (2.5)	2 (1.3)
Mild	1 (0.6)	1 (0.6)
Moderate	3 (1.9)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
嘔吐	2 (1.3)	2 (1.3)
Mild	1 (0.6)	1 (0.6)
Moderate	1 (0.6)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
上腹部痛	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
消化不良	4 (2.5)	1 (0.6)
Mild	3 (1.9)	1 (0.6)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
齲歯	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
口内乾燥	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
おくび	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
消化管運動過剰	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
血便排泄	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
歯痛	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
一般・全身障害および投与部位の状態	6 (3.8)	6 (3.8)
Mild	5 (3.2)	6 (3.8)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
疲労	1 (0.6)	3 (1.9)
Mild	1 (0.6)	3 (1.9)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
冷感	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
体温変動感	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
非心臓性胸痛	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
口渴	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
血管穿刺部位血腫	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
血管穿刺部位疼痛	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
注射部位疼痛	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
倦怠感	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
疼痛	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
発熱	2 (1.3)	0 (0.0)
Mild	2 (1.3)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
恥骨上痛	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
肝胆道系障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
胆石症	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
免疫系障害	2 (1.3)	1 (0.6)
Mild	2 (1.3)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
季節性アレルギー	2 (1.3)	0 (0.0)
Mild	2 (1.3)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
感染症および寄生虫症	44 (28.0)	35 (22.4)
Mild	26 (16.6)	21 (13.5)
Moderate	18 (11.5)	14 (9.0)
Severe	0 (0.0)	0 (0.0)
COVID-19	15 (9.6)	13 (8.3)
Mild	12 (7.6)	9 (5.8)
Moderate	3 (1.9)	4 (2.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
上咽頭炎	12 (7.6)	8 (5.1)
Mild	8 (5.1)	6 (3.8)
Moderate	4 (2.5)	2 (1.3)
Severe	0 (0.0)	0 (0.0)
尿路感染	4 (2.5)	4 (2.6)
Mild	2 (1.3)	2 (1.3)
Moderate	2 (1.3)	2 (1.3)
Severe	0 (0.0)	0 (0.0)
気管支炎	0 (0.0)	2 (1.3)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
インフルエンザ	2 (1.3)	2 (1.3)
Mild	0 (0.0)	1 (0.6)
Moderate	2 (1.3)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
胃腸炎	1 (0.6)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
歯髄炎	1 (0.6)	1 (0.6)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
副鼻腔炎	2 (1.3)	1 (0.6)
Mild	1 (0.6)	0 (0.0)
Moderate	1 (0.6)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
扁桃炎	2 (1.3)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	2 (1.3)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
歯膿瘍	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
上気道感染	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
ウイルス性上気道感染	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
無症候性細菌尿	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
細菌性膣症 [f]	1 (0.7)	0 (0.0)
Mild	1 (0.7)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
膀胱炎	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
憩室炎	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
陰部単純ヘルペス	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
中耳炎	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
レンサ球菌性咽頭炎	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
ウイルス性気道感染	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	3 (1.9)	6 (3.8)
Mild	0 (0.0)	4 (2.6)
Moderate	3 (1.9)	2 (1.3)
Severe	0 (0.0)	0 (0.0)
挫傷	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
上顎炎	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
眼挫傷	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
処置後炎症	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
外傷後疼痛	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
腱断裂	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
靭帯断裂	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
靭帯捻挫	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
肉離れ	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
臨床検査	6 (3.8)	5 (3.2)
Mild	6 (3.8)	4 (2.6)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
血中カリウム増加	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
糸球体濾過率減少	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
心拍数増加	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
SARS-CoV-2 検査陽性	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
体重減少	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
血中ビリルビン増加	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
血中コレステロール増加	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
ヘマトクリット減少	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
E型肝炎抗体陽性	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
赤血球数減少	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
体重増加	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
代謝および栄養障害	3 (1.9)	7 (4.5)
Mild	2 (1.3)	5 (3.2)
Moderate	1 (0.6)	2 (1.3)
Severe	0 (0.0)	0 (0.0)
食欲減退	2 (1.3)	5 (3.2)
Mild	1 (0.6)	4 (2.6)
Moderate	1 (0.6)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
食欲亢進	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
インスリン抵抗性	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
ビタミンD欠乏	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
筋骨格系および結合組織障害	13 (8.3)	4 (2.6)
Mild	9 (5.7)	4 (2.6)
Moderate	4 (2.5)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
関節痛	1 (0.6)	2 (1.3)
Mild	1 (0.6)	2 (1.3)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
四肢痛	0 (0.0)	2 (1.3)
Mild	0 (0.0)	2 (1.3)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
頚部痛	3 (1.9)	1 (0.6)
Mild	3 (1.9)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
弾発指	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
背部痛	2 (1.3)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	2 (1.3)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
側腹部痛	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
筋痙縮	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
筋緊張	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
筋肉痛	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
変形性関節症	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
脊椎痛	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
腱炎	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	2 (1.3)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	2 (1.3)
乳癌第２期	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	1 (0.6)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
浸潤性乳癌	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	1 (0.6)
アクロコルドン	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
神経系障害	9 (5.7)	8 (5.1)
Mild	4 (2.5)	4 (2.6)
Moderate	4 (2.5)	4 (2.6)
Severe	1 (0.6)	0 (0.0)
片頭痛	4 (2.5)	3 (1.9)
Mild	1 (0.6)	1 (0.6)
Moderate	2 (1.3)	2 (1.3)
Severe	1 (0.6)	0 (0.0)
浮動性めまい	2 (1.3)	2 (1.3)
Mild	2 (1.3)	2 (1.3)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
傾眠	0 (0.0)	2 (1.3)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
頭痛	2 (1.3)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	2 (1.3)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
錯感覚	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
失神	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
注意力障害	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
味覚不全	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
精神障害	5 (3.2)	8 (5.1)
Mild	3 (1.9)	6 (3.8)
Moderate	2 (1.3)	2 (1.3)
Severe	0 (0.0)	0 (0.0)
不眠症	2 (1.3)	5 (3.2)
Mild	1 (0.6)	4 (2.6)
Moderate	1 (0.6)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
不安	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
易刺激性	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
季節性感情障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
気分動揺	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
睡眠障害	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
自殺念慮	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
腎および尿路障害	2 (1.3)	2 (1.3)
Mild	1 (0.6)	1 (0.6)
Moderate	1 (0.6)	1 (0.6)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
非感染性膀胱炎	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
血尿	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
尿路結石	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
尿意切迫	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
生殖系および乳房障害	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
過少月経 [f]	0 (0.0)	1 (0.7)
Mild	0 (0.0)	1 (0.7)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	2 (1.3)	4 (2.6)
Mild	2 (1.3)	3 (1.9)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
気管支痙攣	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
呼吸困難	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
口腔咽頭痛	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
アレルギー性鼻炎	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
鼻漏	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	6 (3.8)	3 (1.9)
Mild	2 (1.3)	3 (1.9)
Moderate	4 (2.5)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
斑状出血	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
多汗症	0 (0.0)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
そう痒症	2 (1.3)	1 (0.6)
Mild	0 (0.0)	1 (0.6)
Moderate	2 (1.3)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
発疹	1 (0.6)	1 (0.6)
Mild	1 (0.6)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
嵌入爪	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
口囲皮膚炎	1 (0.6)	0 (0.0)
Mild	1 (0.6)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
皮膚剥脱	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.6)	0 (0.0)
Mild	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)
Severe	0 (0.0)	0 (0.0)
外科および内科処置	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	1 (0.6)
人工流産 [f]	0 (0.0)	1 (0.7)
Mild	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	1 (0.7)
血管障害	3 (1.9)	3 (1.9)
Mild	3 (1.9)	3 (1.9)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-2.1.4
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class Preferred Term Severity	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
高血圧	3 (1.9)	3 (1.9)
Mild	3 (1.9)	3 (1.9)
Moderate	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each system organ class and preferred term for the most intense occurrence.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表11

Table 14.3-2.2.1
Number (%) of Participants with Treatment-Emergent Serious Adverse Events (TESAE) by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
Participants with at least one TESAE	0 (0.0)	4 (2.6)
心臓障害	0 (0.0)	1 (0.6)
心室性頻脈	0 (0.0)	1 (0.6)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0 (0.0)	2 (1.3)
乳癌第２期	0 (0.0)	1 (0.6)
浸潤性乳癌	0 (0.0)	1 (0.6)
外科および内科処置	0 (0.0)	1 (0.6)
人工流産 [f]	0 (0.0)	1 (0.7)

AE dictionary: MedDRA 24.0
Participants are counted only once within each preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表12

Table 14.3-2.2.2
Number (%) of Participants with Treatment-Emergent Adverse Events (TEAE) Leading to Treatment Discontinuation by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=157) n (%)	Atogepant 60 mg QD (N=156) n (%)
Participants with at least one TEAE leading discontinuation	2 (1.3)	3 (1.9)
心臓障害	0 (0.0)	1 (0.6)
心室性頻脈	0 (0.0)	1 (0.6)
胃腸障害	0 (0.0)	2 (1.3)
便秘	0 (0.0)	1 (0.6)
悪心	0 (0.0)	1 (0.6)
神経系障害	1 (0.6)	1 (0.6)
傾眠	0 (0.0)	1 (0.6)
片頭痛	1 (0.6)	0 (0.0)
皮膚および皮下組織障害	1 (0.6)	0 (0.0)
そう痒症	1 (0.6)	0 (0.0)
皮膚剥脱	1 (0.6)	0 (0.0)

AE dictionary: MedDRA 24.0
Participants are counted only once within each preferred term.
N = number of participants in the Safety Population.
n = number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

3101-306-002 試験［評価資料］

治験の標題： A Phase 3, Multicenter, Open-Label 52-Week Extension Study to Evaluate the Long-Term Safety and Tolerability of Oral Atogepant for the Prevention of Migraine in Japanese Participants with Chronic or Episodic Migraine	
施設数 / 実施国名： 24 施設 / 日本	
治験調整医師： [redacted], M.D., Ph.D.	
公表文献（参考資料）： なし	
治験期間： 治験開始日（最初の被験者の初回来院日）：2020 年 6 月 18 日 治験終了日（最後の被験者の最終来院日）：2024 年 6 月 11 日	開発のフェーズ： 第 III 相
治験の種類： 多施設共同，非盲検，52 週間，長期安全性継続投与，第 III 相試験	
目的： ・ 慢性片頭痛（以下「CM」）又は反復性片頭痛（以下「EM」）を有する日本人被験者を対象として，片頭痛予防に対しアトゲパント水和物（以下「アトゲパント」）60 mg 1 日 1 回（以下「QD」）を 52 週間投与したときの安全性及び忍容性を評価する。 ・ CM 又は EM を有する日本人被験者を対象として，片頭痛予防に対しアトゲパント 60 mg QD を 52 週間投与したときの有効性を評価する。	
被験者数（計画時と解析時）： 計画時：170 例以上（3101-303-002 試験［以下「導入試験」］を完了した被験者：140 例以上，新規 EM 被験者：約 30 例） 解析時：合計 186 例の被験者が治験薬を投与され，安全性解析対象集団に含まれた（導入試験を完了した被験者：155 例，新規 EM 被験者：31 例）。 設定根拠： 本試験の被験者数は，統計学的な観点ではなく，曝露した期間及び被験者数に関する規制当局の安全要件に基づいて決定した。アトゲパントを 1 年間投与された被験者が 100 例以上となるよう，導入試験から 140 例以上及び新規 EM 被験者（特定の実施医療機関からのみ）約 30 例以上を含む 170 例以上の被験者を本試験に組み入れることとした。	
診断と組入れ基準： 選択基準： 以下の選択基準をすべて満たした患者を組入れ可能とした。 <u>すべての患者</u> 1. 本試験に関するあらゆる手順が開始される前に文書同意及び患者のプライバシーに関する情報（国内の規制に則った Written Authorization for Use and Release of Health and Research Study Information 及び Written Data Protection Consent など）を得られた患者。 2. 本試験期間中に治験実施計画書に規定された医学的に許容され，効果の高い避妊法を使用している患者。 <u>導入試験を完了した患者のみ</u> 3. 導入試験の二重盲検投与期間の終了時（Visit 7）又は追跡調査期間の終了時（Visit 8）（本試験の開始時期に応じてどちらかの Visit）を完了し，重大な治験実施計画書からの逸脱（治験実施計画書に規定された手順の	

不遵守など）がなく，治験責任医師の判断により許容できない安全性リスクを示唆する有害事象が認められなかった患者。

新規 EM 患者のみ

4. Visit –1 に 18 歳以上 80 歳以下の男性患者又は女性患者。
5. 国際頭痛分類第 3 版（以下「ICHD-3」）に基づく診断と一致する前兆のある片頭痛又は前兆のない片頭痛を 1 年以上有する患者。
6. 片頭痛の発症年齢が 50 歳未満の患者。
7. 治験責任医師の判断による Visit –1 前 3 ヵ月間の平均月間片頭痛日数（以下「MMD」）が 4–14 日である患者。
8. 電子日誌（以下「eDiary」）で 28 日間のベースライン期間に片頭痛日数が 4–14 日である患者。
9. ベースライン期間 28 日間のうち 20 日間以上 eDiary への入力があり，治験質問票及び eDairy を読解し，入力することができると治験責任医師が判断した患者。

除外基準：

以下の除外基準のいずれかに該当する患者は本試験から除外した。

すべての患者

1. 併用禁止薬若しくは併用禁止療法の一覧（治験実施計画書で規定）に記載されている薬剤，食事（すなわちグレープフルーツ又はグレープフルーツジュース），又は非薬物療法が必要であり，それらを中止できない若しくは許容される別の薬剤や治療法への切り替えができない患者。片頭痛予防に有効性が証明されている 1 種類の薬剤を投与中の導入試験から移行した患者は，導入試験の Visit 1 前の 12 週間以上，用量が安定しており，その薬剤の忍容性が良好である場合，かつ患者が本試験期間中，安定した用量及び用法でその薬剤の投与を継続する意思があり，継続することができる場合に本試験に参加可能とした。
2. 妊娠している，本試験期間中に妊娠を計画している，又は現在授乳中の女性患者。妊娠可能な女性患者は，Visit –1（新規 EM 患者）及び Visit 1（すべての患者）の尿妊娠検査が陰性であること。
3. Visit –1（新規 EM 患者）又は Visit 1（導入試験を完了した患者）に心電図（以下「ECG」）に臨床的に重大な異常を有すると治験責任医師により判断された患者。
4. Visit –1（新規 EM 患者）又は Visit 1（すべての患者）に座位収縮期血圧が 160 mm Hg 超又は座位拡張期血圧が 100 mm Hg 超の高血圧の患者。これらの上限を超えた場合，バイタルサインを一回のみ再測定可能とした。
5. 臨床面接及びコロンビア自殺評価スケール（以下「C-SSRS」）の回答により自傷行為の重大なリスクが認められた患者，又は他害行為の重大なリスクがあると治験責任医師が判断した患者。実行する意思のある自殺念慮（計画の有無は問わない）（C-SSRS でタイプ 4 又は 5）を報告した患者，又は Visit –1 前 6 ヵ月以内（新規 EM 患者）若しくは Visit 1 で最終来院以降（すべての患者）に自殺行動を報告した患者は除外することとした。
6. 臨床的に重大な血液疾患，内分泌疾患，心血管疾患，肺疾患，腎疾患，肝疾患，消化管疾患，又は神経疾患を有する患者。
   - これらの疾患の既往歴を有するものの，Visit –1（新規 EM 患者）前 1 年超，状態が安定しており，本試験への参加に支障をきたすおそれはないと治験責任医師が判断した患者は組入れ可能とした。
   - 腎不全のため透析を受けている患者は組入れ不可とした。
7. 患者を重大なリスクにさらす，試験結果を混乱させる，又は患者の本試験の参加で著しく支障をきたす可能性があると治験責任医師が判断した状態又は状況にあった患者。
8. 医学的又はその他の理由（試験手順や来院予約を遵守しない可能性がある，本試験期間中に転居する予定があるなど）で本試験に不適格と治験責任医師が判断した患者。

新規 EM 患者のみ

9. 片頭痛を緊張型頭痛又はその他の頭痛と区別することが困難な患者。
10. 複視若しくは意識レベルの低下を伴う片頭痛，又は ICHD-3 に定義されている網膜片頭痛の既往歴を有する

患者。

11. ICHD-3 に定義されている CM，新規発症持続性連日性頭痛，三叉神経・自律神経性頭痛（群発頭痛など），又は有痛性脳神経ニューロパチーと現在診断されている患者。
12. 治験責任医師の判断で Visit –1 前 3 ヵ月間の平均月間頭痛日数が 15 日以上である患者。
13. eDiary で 28 日間のベースライン期間の頭痛日数が 15 日以上である患者。
14. 片頭痛予防目的で処方された 4 種類超の治療薬（そのうち 2 種類は作用機序が異なる）に対して効果不十分であった患者。
15. オピオイド鎮痛剤若しくはバルビツール酸系薬剤を 1 ヵ月あたり 2 日超，トリプタン系薬剤若しくはエルゴタミン製剤を 1 ヵ月あたり 10 日以上，又は単一成分の鎮痛薬（アスピリン，非ステロイド性抗炎症薬［NSAIDs］，アセトアミノフェンなど）を 1 ヵ月あたり 15 日以上，Visit –1 前の 3 ヵ月間に使用したと治験責任医師が判断した，若しくはベースライン期間に使用した患者（スクリーニング前の 30 日間及び本試験期間中のバルビツール酸系薬剤の使用は認められない）。
16. 中央検査機関による ECG についての最終報告で Visit –1 に Fridericia 補正法を用いて心拍数で補正した QT 間隔（QTcF）が男性は 450 msec 超，女性は 470 msec 超の患者。
17. 臨床的に重大な心血管疾患又は脳血管疾患を有すると治験責任医師が判断した患者。これには以下の疾患を含むが，これらに限定されない。
    - 臨床的に重大な虚血性心疾患（不安定狭心症など）。
    - 臨床的に重大な心調律異常若しくは心伝導異常（心房細動，第 2 度又は第 3 度心ブロックなど）又はトルサードドポアントの危険因子（心不全，低カリウム血症，徐脈など）。
    - Visit –1 前 6 ヵ月以内の心筋梗塞，一過性脳虚血発作，又は脳卒中。
    - ニューヨーク心臓協会（NYHA 分類）の心機能分類で III 度又は IV 度と定義される心不全。
18. Visit –1 に臨床的に重大な臨床検査値又は以下のいずれかの臨床検査値が認められた患者。
    - アラニンアミノトランスフェラーゼ（以下「ALT」）値又はアスパラギン酸アミノトランスフェラーゼ（以下「AST」）値が基準値の上限（以下「ULN」）の 1 倍超。
    - 総ビリルビン値が ULN の 1 倍超（ジルベール症候群と診断された被験者を除く）。
    - 血清アルブミン値が 2.8 g/dL 未満。
19. スクリーニング（Visit –1）前 6 ヵ月以内の急性肝炎若しくは慢性肝疾患（非アルコール性脂肪性肝炎，ウイルス性慢性肝炎，及び肝硬変を含む）の既往歴を有する，又は抗 A 型肝炎 IgM 抗体，B 型肝炎表面抗原，抗 C 型肝炎抗体，若しくは E 型肝炎 IgM 抗体の検査で陽性であった患者。
20. 混合した精神状態，認知症，てんかん，又は片頭痛以外の重大な神経障害を有すると治験責任医師が判断した患者。
21. 現在の頭痛障害に重大な影響を及ぼす可能性がある他の疼痛疾患（線維筋痛症，顔面痛など）を併発していると治験責任医師が判断した患者。
22. Visit –1 前 5 年間に悪性腫瘍の既往歴を有する患者（適切に治療された基底細胞癌，扁平上皮癌，又は子宮頚部上皮内癌は除く）。
23. 治験薬の吸収又は代謝に影響を及ぼす可能性のある消化管処置又は消化管疾患（下痢症候群，炎症性腸疾患など）の既往歴を有する患者。肥満症に対する胃への処置（ラップバンドなど）を受けたものの，その処置を元に戻した患者は組入れ可能とした。
24. Visit –1 にレクリエーショナルドラッグ又は違法薬物の使用者であった患者，又は過去 1 年以内に薬物若しくはアルコールの乱用若しくは依存の既往歴を有する患者。
25. Visit –1 の尿中薬物検査が陽性であった患者（片頭痛のために処方されたオピオイド鎮痛剤などの併用薬物で説明がつく場合は除く）。
26. 治験薬又は治験機器を用いた試験（市販の製剤又は機器を用いた試験も含む）に現在参加している，又は Visit –1 前 30 日以内に参加したことがある患者。
27. 以下の薬剤への曝露歴がある患者：

・ アトゲパント（AGN-241689 又は MK-8031）。
・ 過去 6 ヵ月以内のカルシトニン遺伝子関連ペプチド（以下「CGRP」）経路を遮断する注射用モノクローナル抗体。
・ その他の治験薬としての CGRP 受容体拮抗薬（以下「CGRP-RA」）。

28. CGRP-RA に対する過敏症若しくは臨床的に重大な副作用の既往歴，又は治験薬（アトゲパント）の成分に対する過敏症の既往歴を有する患者。
29. 活動性の重症急性呼吸器症候群コロナウイルス 2（以下「SARS-CoV-2」）感染者。患者が SARS-CoV-2 感染を示唆する徴候 / 症状を示している場合，分子（ポリメラーゼ連鎖反応［以下「PCR」］など）検査の結果が陰性であれば，試験への組入れの検討対象とした。
（注意：SARS-CoV-2 感染の適格基準を満たさない患者は，スクリーニング脱落となり，以下の SARS-CoV-2 感染ウイルス消失基準を満たした場合にのみ再スクリーニング可能とした：PCR 検査結果が初めて陰性になってから 14 日以上経過していること［無症候性の患者の場合］，又は回復［解熱剤を使用せずに解熱していること及び症状が改善していることと定義］から 14 日経過していること。）
30. SARS-CoV-2 感染による「新型コロナウイルス後遺症」の持続的な症状，又は患者を重大なリスクにさらす，試験結果を混乱させる，若しくは患者の本試験の参加で著しく支障をきたす可能性があると治験責任医師が判断したその他の持続的な症状を有する患者。

治験方法：

本試験は，国内で実施した多施設共同，非盲検，52 週間，長期安全性継続投与試験であった。被験者にアトゲパント 60 mg QD を経口投与した。本試験は，52 週間の非盲検投与期間及び 4 週間の安全性追跡調査期間で構成され，被験者は以下 2 つのコホートに組み入れられた。

導入試験を完了した CM 被験者：導入試験（CM 予防に対するアトゲパントの第 III 相，多施設共同，無作為化，二重盲検，プラセボ対照，並行群間比較試験）を完了した日本人被験者。導入試験を完了した CM 被験者が本試験の同意文書に署名した後，導入試験の Visit 7 を本試験の Visit 1 として実施した。Visit 1 以降，試験期間中の来院は 4 週ごととし，治験終了来院は，アトゲパントの最終投与から 4 週間後とした。本試験開始前に導入試験の Visit 7 が終了する被験者は，導入試験の来院及び手順のスケジュールに従い，Visit 7 / 早期中止及び Visit 8 / 治験終了来院（治験薬投与の中止を含む）を完了することとした。

新規 EM 被験者：選択された実施医療機関に新規に組み入れられた EM を有する日本人被験者。被験者の参加は Visit –1 で 4 週間のスクリーニング / ベースライン期間から開始した。4 週間のスクリーニング / ベースライン期間を完了し，すべての選択基準を満たした被験者が Visit 1 で 52 週間の非盲検投与期間に組み入れられた。
Visit 1 以降，本試験期間中の来院は 4 週ごととし，治験終了来院は，アトゲパントの最終投与から 4 週間後とした。

安全性データ及び要約報告書をレビューし，安全性の問題及び傾向を特定し，未知の臨床的に重大な有害事象を示すデータが得られた場合，試験の計画変更又は早期中止などを治験依頼者に提言するために，独立したデータ安全性モニタリング委員会を設置した。

判定手順を策定し，臨床判定委員会による治験薬投与終了後の ALT 及び / 又は AST が ULN の 3 倍以上上昇について，監視，モニタリング，及び判定のプロセスを規定した。この判定手順の目的は，ALT 及び / 又は AST の上昇とアトゲパントの因果関係を判定するための標準化したプロセスを提供することであった。

被験薬，用量，投与方法及びロット番号：

アトゲパント 60 mg QD，錠剤，経口投与，ロット番号：[redacted]，[redacted]

対照薬，用量，投与方法及びロット番号：

該当なし

治療期間：52 週間の非盲検投与期間及び 4 週間の安全性追跡調査期間

評価基準：

有効性及びヘルスアウトカム：

有効性の評価は，被験者が eDiary（自宅で毎日使用）に記録した頭痛の持続時間，特徴，症状，及び急性期治療薬の使用などの情報に基づいて行った。これらの収集したデータを片頭痛日数，頭痛日数，急性期治療薬の使用日数，及びトリプタン系薬剤の使用日数の定義に当てはめた。片頭痛による活動障害–ダイアリー（以下「AIM-D」），Activity Level and Activity Limitation の測定は eDiary を通じて毎日収集した。片頭痛特有の生活の質に関する質問票第 2.1 版（以下「MSQ v2.1」），Headache Impact Test（以下「HIT-6」），治験薬に対する患者の満足度（PSSM），Migraine Disability Assessment（MIDAS），患者の全般的印象度–変化（PGIC），患者の全般的印象度–重症度（PGIS），仕事の生産性及び活動障害に関する質問票：片頭痛第 2.0 版（WPAI: MIRAINE）及び European Quality of Life - 5-Dimensional - 5 Level（EQ-5D-5L）の測定は決められた来院時に電子タブレットで実施した。

安全性：

有害事象（特に注目すべき有害事象を含む）のモニタリング，バイタルサイン，ECG，身体所見，臨床検査値，C-SSRS

統計手法：

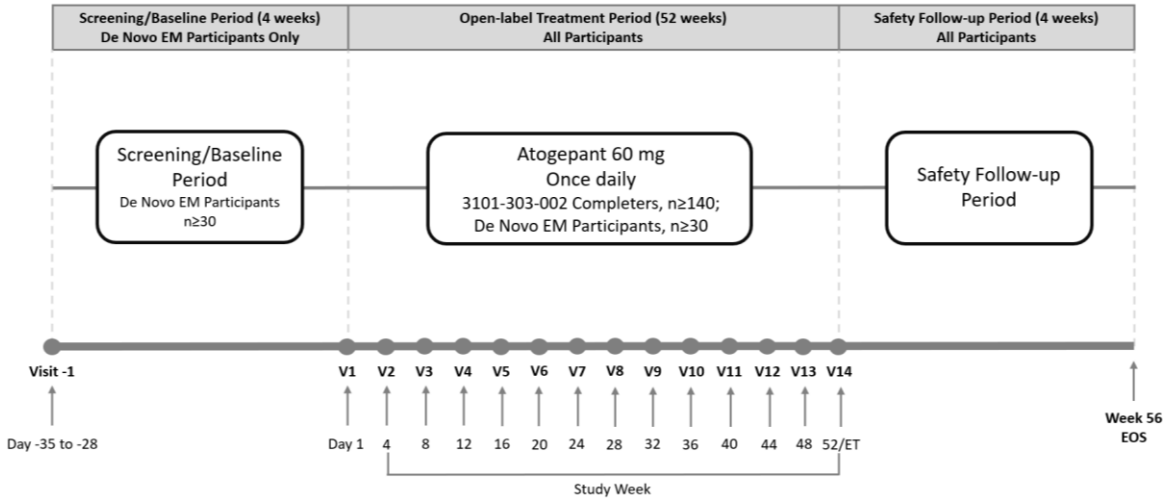
有効性：

本試験の主要目的はアトゲパントを 52 週間投与したときの安全性及び忍容性の評価であり，有効性の評価項目は「主要」，「副次」又は「追加」という分類は行わなかった。有効性の評価項目は，modified intent-to-treat（以下「mITT」）集団に基づき記述的に解析した。導入試験で定義された有効性の主要評価変数（MMD のベースラインからの変化量）及び導入試験に規定された有効性の重要な副次評価変数（月間頭痛日数のベースラインからの変化量，急性期治療薬の月間使用日数のベースラインからの変化量，MMD の 50%以上の改善［減少］，MSQ v2.1 の役割機能制限（以下「RFR」）ドメインスコアのベースラインからの変化量，AIM-D の日常活動機能ドメイン月間スコアのベースラインからの変化量，AIM-D の身体障害ドメイン月間スコアのベースラインからの変化量，及び HIT-6 合計スコアのベースラインからの変化量）について，点推定値及び 95%信頼区間（以下「CI」）を示した。連続変数の評価項目の 95% CI は，反復測定混合効果モデルに基づき，MMD 改善（減少）の割合の 95% CI は，二項分布の正規近似に基づいた。

安全性：

安全性解析は，安全性解析対象集団に基づき記述統計を用いて実施した。

図 1. 試験デザインの概略（3101-306-002 試験）



EOS = 治験終了，ET = 早期中止，V = Visit
Cross reference: 3101-306-002 final CSR Figure 1

試験結果

被験者の内訳

被験者の内訳を表 1 に示す。

全体で，本試験（安全性解析対象集団）では，CM 又は EM を有する被験者 186 例にアトゲパント 60 mg QD を投与した。導入試験を完了した CM を有する被験者 155 例が本試験に移行し，アトゲパントを 1 回以上投与された。新規 EM 被験者の 31 例が本試験に組み入れられ，アトゲパントを 1 回以上投与された。

大部分の被験者（84.9%［158 / 186 例］）が非盲検投与期間を完了した。主な中止理由（各コホート又は全体で被験者の 5%以上）は，有害事象及び Visit 1 での中止基準に該当であり，いずれも CM 被験者コホートのみであった。

人口統計学的及び他のベースラインの特性

人口統計学的特性，ベースラインの特性，及び原疾患のベースライン特性をそれぞれ表 2，表 3，及び表 4 に示す。

安全性解析対象集団の被験者の平均年齢は 43.2 歳であり，被験者の多くが女性であった。ベースラインの体重の平均値は 55.87 kg，ベースラインの体格指数の平均値は 21.96 kg/m^2 であった。ベースラインの人口統計学的特性及び身体的特性は，導入試験を完了した CM 被験者と新規 EM 被験者で同様であった。

また，mITT 集団のベースラインの人口統計学的特性及び身体的特性についても安全性解析対象集団と同様であった（3101-306-002 final CSR Table 14.1-4.1.2，Table 14.1-4.2.2）。

片頭痛の既往歴は，CM 被験者又は EM 被験者間でおおむね同様であった。ただし，片頭痛の診断の種類から予想されたとおり，スクリーニング前 3 ヵ月間の平均 MMD 及び平均月間頭痛日数は，導入試験を完了した CM 被験者コホートの方が新規 EM 被験者コホートよりも大幅に長かった。

曝露状況

曝露状況を表 5 に示す。

全体で，平均投与期間は 324.7 日であり，158 例（84.9%）の被験者は投与期間が 360 日以上であった。

有効性の結果

有効性評価項目の結果を表 6–表 12 に示す。

有効性のデータは探索的なものであり，毎日の eDiary 又は試験来院時に収集されたヘルスアウトカム測定に基づくものであった。

本試験では，MMD，月間頭痛日数，及び急性期治療薬の月間使用日数の減少，並びに MMD の 50%以上の減少など，CM 又は EM を有する日本人被験者の片頭痛予防に対するアトゲパント 60 mg QD の長期有効性が裏付けられた。

ヘルスアウトカム評価（MSQ v2.1 の RFR ドメインスコア，AIM-D の日常活動機能及び身体障害のドメインスコア，及び HIT-6 スコア）の結果は，ベースラインからの改善を示した。

アトゲパント 60 mg QD の有効性は，導入試験を完了した CM 被験者では 52 週間の投与期間中維持された。新規 EM 被験者では，アトゲパント 60 mg QD の有効性は，投与開始後 1 ヵ月（1–4 週）に認められ，52 週間の投与期間中持続した。

安全性の結果

CM 又は EM を有する日本人被験者を対象とした本試験では，アトゲパント 60 mg QD 経口投与の安全性及び忍容性は良好であった。

有害事象

有害事象の発現状況を以下に示す。

有害事象の発現割合は，アトゲパント 60 mg QD 群全体 88.7%（165 / 186 例）（CM 被験者 88.4%［137 / 155 例］，EM 被験者 90.3%［28 / 31 例］）であった。

発現割合が 10%以上の有害事象は，発熱（アトゲパント 60 mg QD 群全体 29.0%［54 例］：CM 被験者 33.5%［52 例］，EM 被験者 6.5%［2 例］，以下同順），上咽頭炎（16.1%［30

例］：11.6%［18 例］，38.7%［12 例］），及び便秘（11.3%［21 例］：11.0%［17 例］，12.9%［4 例］）であった。発熱のほとんどが COVID-19 ワクチン接種に関連していた。便秘は，すべて重症度が軽度であり，重篤な有害事象及び治験薬の投与中止に至った有害事象は認められなかった。

治験薬と関連ありの有害事象の発現割合は，アトゲパント 60 mg QD 群全体 16.7%（31 例）（CM 被験者 16.1%［25 例］，EM 被験者 19.4%［6 例］）であった。

発現割合が 5.0%以上の治験薬と関連ありの有害事象は，便秘（アトゲパント 60 mg QD 群全体 7.5%［14 例］：CM 被験者 7.1%［11 例］，EM 被験者 9.7%［3 例］）のみであった。

高度の有害事象の発現割合は，アトゲパント 60 mg QD 群全体 2.2%（4 例）（CM 被験者 2.6%［4 例］，EM 被験者 0%）であった。その内訳は，アラニンアミノトランスフェラーゼ増加，アスパラギン酸アミノトランスフェラーゼ増加，顔面麻痺及び意識消失（アトゲパント 60 mg QD 群全体各 0.5%［1 例］：CM 被験者各 0.6%［1 例］，EM 被験者各 0%，以下同順），並びに子宮平滑筋腫（女性被験者のみ）（0.6%［1 / 170 例］：0.7%［1 / 141 例］，0%［0 / 29 例］）であった。

投与終了後の有害事象の発現割合は，アトゲパント 60 mg QD 群全体 16.7%（31 例）（CM 被験者 17.4%［27 例］，EM 被験者 12.9%［4 例］）であった。

2 例以上に発現した投与終了後の有害事象の発現割合は，アラニンアミノトランスフェラーゼ増加（アトゲパント 60 mg QD 群全体 3.2%［6 例］：CM 被験者 2.6%［4 例］，EM 被験者 6.5%［2 例］，以下同順），発熱（2.7%［5 例］：3.2%［5 例］，0%），アスパラギン酸アミノトランスフェラーゼ増加（2.2%［4 例］：1.3%［2 例］，6.5%［2 例］），頭痛（1.6%［3 例］：1.9%［3 例］，0%），上咽頭炎（1.1%［2 例］：0.6%［1 例］，3.2%［1 例］），並びに下痢，ワクチン接種部位腫脹，血中アルカリホスファターゼ増加及び筋肉痛（各 1.1%［2 例］：各 1.3%［2 例］，各 0%）であった。

死亡に至った有害事象は認められなかった。

重篤な有害事象の発現割合は，アトゲパント 60 mg QD 群全体 3.8%［7 例］（CM 被験者 4.5%［7 / 155 例］，EM 被験者 0%，以下同順）であった。その内訳は，子宮平滑筋腫（女性被験者のみ）（0.6%［1 / 170 例］：0.7%［1 / 141 例］，0%），並びに回転性めまい，胆石症，虫垂炎，アラニンアミノトランスフェラーゼ増加，アスパラギン酸アミノトランスフェラーゼ増加，意識消失，片頭痛及びうつ病（各 0.5%［1 例］：各 0.6%［1 例］，各 0%［0 例］）であった。2 例以上に報告された重篤な有害事象はなく，いずれも治験責任医師に治験薬と関連なしと判断された。

治験薬の投与中止に至った有害事象の発現割合は，アトゲパント 60 mg QD 群全体 4.8%［9 例］（CM 被験者 5.8%［9 例］，EM 被験者 0%）であった。

2 例以上に発現した投与中止に至った有害事象の発現割合は，アラニンアミノトランスフェラーゼ増加（アトゲパント 60 mg QD 群全体 2.2%［4 例］：CM 被験者 2.6%［4 例］，EM 被験者 0%，以下同順）及びアスパラギン酸アミノトランスフェラーゼ増加（1.6%［3 例］：1.9%［3 例］，0%）であった。

3 ヵ月ごとの有害事象では，大部分の有害事象は本試験の投与開始後 3–6 ヵ月以内に発現する傾向にあった。例外は，一般・全身障害および投与部位の状態（発熱を含む），感染症および寄生虫症，筋骨格系および結合組織障害の器官別大分類に属する有害事象などであった。

特に注目すべき有害事象

臨床検査値が潜在的な Hy's law 基準に該当した被験者は認められなかった。ALT 及び / 又は AST が ULN の 3 倍以上の上昇が 9 例に認められた。9 例のうち 4 例は，臨床判定委員会によりアトゲパントとおそらく関連なしと判定された。アトゲパントと関連あるかもしれない又はおそらく関連ありと判定された 5 例は，いずれも非重篤であり，重症度は軽度又は中等度，総ビリルビンの同時上昇は認められず，アトゲパントの投与中止の有無にかかわらず回復した。アトゲパントと関連あるかもしれない又はおそらく関連ありと判定された 5 例のうち 4 例で交絡因子が特定された。

C-SSRS 評価による非盲検投与期間中及び安全性追跡調査期間中に実行する意思のある自殺念慮及び自殺行動は認められなかった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団
有害事象の要約	表 13（Table 14.3-1.1）
すべての有害事象	表 14（Table 14.3-1.2）
因果関係「関連あり」の有害事象	表 15（Table 14.3-1.4）
重症度別有害事象	表 16（Table 14.3-1.3）
重篤な有害事象	表 17（Table 14.3-2.1）
治験薬の投与中止に至った有害事象	表 18（Table 14.3-2.3）
3 ヵ月ごとの有害事象	表 19（Table 14.3-1.5.A）

臨床検査

その他の臨床検査値に臨床的に重大な変化の傾向は認められなかった。

バイタルサイン

ベースラインからの投与終了時までの体重の平均変化量は–1.78 kg であり，投与期間中に 31.7%の被験者に臨床的に意義がある可能性のある体重減少（ベースラインの体重から 7%以上の減少）が認められた。体重減少の有害事象は，2.7%の被験者に報告され，いずれも重症度は軽度かつ非重篤であり，治験薬の投与中止に至った被験者はいなかった。

血圧に臨床的に重大な変化の傾向は認められなかった。

ECG

ECG に臨床的に重大な変化の傾向は認められなかった。

結論

本試験では，CM 又は EM の予防を目的としたアトゲパント 60 mg QD 経口投与の安全性及び忍容性は良好であった。本試験での日本人被験者の安全性の結果は，アトゲパントの国際共同臨床開発プログラムで認められたアトゲパントの安全性プロファイルと一致していた。本試験では新たな安全性シグナルは特定されなかった。CM 被験者又は EM 被験者で臨床的有効性及びヘルスアウトカム評価項目の改善について同様の傾向が認められた。

CM を有する導入試験を完了した被験者では，MMD の減少，MMD の 50%以上減少の達成，月間頭痛日数の減少，及び急性期治療薬の使用日数の減少のアトゲパント投与の有効性は，1 年間のアトゲパント投与期間中良好に維持された。新規 EM 被験者では，アトゲパント 60 mg QD の有効性は，投与開始後 1 ヵ月（1–4 週）に認められ，52 週間の投与期間中持続した。

ヘルスアウトカムの評価では，非盲検投与期間中，ベースラインと比較して，被験者の日常的な社会活動及び仕事関連の活動の改善，日常活動機能の向上，身体障害の軽減，頭痛による影響の軽減が示された。

表1

Table 14.1-1.2
Disposition of Participants
Safety Population

Disposition	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Number of Participants Treated	155 (100.0)	31 (100.0)	186 (100.0)
Number Of Participants Completed Open-Label Treatment Period	130 (83.9)	28 (90.3)	158 (84.9)
Number of Participants Discontinued Before End of Open-Label Treatment Period	25 (16.1)	3 (9.7)	28 (15.1)
Reasons for Discontinuation			
Met Withdrawal Criteria at Visit 1	8 (5.2)	0 (0.0)	8 (4.3)
Lab	7 (4.5)	0 (0.0)	7 (3.8)
ECG	1 (0.6)	0 (0.0)	1 (0.5)
Adverse Event	9 (5.8)	0 (0.0)	9 (4.8)
Lack of Efficacy	4 (2.6)	0 (0.0)	4 (2.2)
Withdrawal by Participant	4 (2.6)	1 (3.2)	5 (2.7)
Lost to Follow-Up	0 (0.0)	0 (0.0)	0 (0.0)
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)
Protocol Deviation	0 (0.0)	1 (3.2)	1 (0.5)
Non-Compliance with Study Drug	0 (0.0)	0 (0.0)	0 (0.0)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (3.2)	1 (0.5)
Number of Participants Entered Safety Follow-Up Period	155 (100.0)	31 (100.0)	186 (100.0)
Number of Participants Completed Safety Follow-Up Period	155 (100.0)	31 (100.0)	186 (100.0)
Number of Participants Discontinued Safety Follow-Up Period	0 (0.0)	0 (0.0)	0 (0.0)
Reasons for Discontinuation			
Adverse Event	0 (0.0)	0 (0.0)	0 (0.0)
Withdrawal by Participant	0 (0.0)	0 (0.0)	0 (0.0)
Lost to Follow-Up	0 (0.0)	0 (0.0)	0 (0.0)
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)
Protocol Deviation	0 (0.0)	0 (0.0)	0 (0.0)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

表2

Table 14.1-4.1.1
Demographics
Safety Population

Parameter	3101-303-002 CM Completers (N=155)	De Novo EM Participants (N=31)	Total (N=186)
Age (years)			
Mean (SD)	43.4 (9.47)	42.4 (11.95)	43.2 (9.90)
Median	45.0	43.0	44.5
Q1, Q3	37.0, 50.0	32.0, 52.0	37.0, 50.0
Min, Max	20, 65	20, 74	20, 74
n	155	31	186
Age Group, n (%)			
< 20	0 (0.0)	0 (0.0)	0 (0.0)
20-29	14 (9.0)	7 (22.6)	21 (11.3)
30-39	35 (22.6)	4 (12.9)	39 (21.0)
40-49	63 (40.6)	10 (32.3)	73 (39.2)
50-59	39 (25.2)	9 (29.0)	48 (25.8)
60-69	4 (2.6)	0 (0.0)	4 (2.2)
>= 70	0 (0.0)	1 (3.2)	1 (0.5)
< 40	49 (31.6)	11 (35.5)	60 (32.3)
40-64	105 (67.7)	19 (61.3)	124 (66.7)
>= 65	1 (0.6)	1 (3.2)	2 (1.1)
< 75	155 (100.0)	31 (100.0)	186 (100.0)
>= 75	0 (0.0)	0 (0.0)	0 (0.0)
Sex, n (%)			
Male	14 (9.0)	2 (6.5)	16 (8.6)
Female	141 (91.0)	29 (93.5)	170 (91.4)
Race, n (%)			
Asian	155 (100.0)	31 (100.0)	186 (100.0)
All Other Races	0 (0.0)	0 (0.0)	0 (0.0)
Ethnicity, n (%)			
Hispanic or Latino	0 (0.0)	0 (0.0)	0 (0.0)
Not Hispanic or Latino	155 (100.0)	31 (100.0)	186 (100.0)

Notes: Age relative to informed consent date.

表3

Table 14.1-4.2.1
Baseline Characteristics
Safety Population

Parameter	3101-303-002 CM Completers (N=155)	De Novo EM Participants (N=31)	Total (N=186)
Weight (kg)			
Mean (SD)	55.74 (8.827)	56.50 (13.869)	55.87 (9.805)
Median	54.40	53.10	53.95
Q1, Q3	49.50, 60.50	47.20, 64.00	49.10, 60.50
Min, Max	38.4, 89.4	37.8, 102.4	37.8, 102.4
n	155	31	186
Height (cm)			
Mean (SD)	159.56 (6.705)	158.83 (6.200)	159.44 (6.613)
Median	159.00	158.00	158.80
Q1, Q3	155.00, 163.70	154.00, 162.50	155.00, 163.50
Min, Max	141.8, 183.3	149.8, 173.7	141.8, 183.3
n	155	31	186
BMI (kg/m**2)			
Mean (SD)	21.88 (3.145)	22.36 (5.109)	21.96 (3.535)
Median	21.35	20.66	21.24
Q1, Q3	19.65, 23.50	19.49, 24.23	19.63, 23.50
Min, Max	16.5, 33.0	16.3, 36.0	16.3, 36.0
n	155	31	186
BMI Category, n (%)			
Underweight [<18.5]	16 (10.3)	6 (19.4)	22 (11.8)
Normal [>=18.5 - <25]	117 (75.5)	18 (58.1)	135 (72.6)
Overweight [>=25 - <30]	19 (12.3)	3 (9.7)	22 (11.8)
Obese [>=30]	3 (1.9)	4 (12.9)	7 (3.8)

表4

Table 14.1-4.3.2
Migraine History
Safety Population

Parameter Category Statistics	3101-303-002 CM Completers (N=155)	De Novo EM Participants (N=31)	Total (N=186)
Migraine Diagnosis, n1 (%)			
With Aura	25 (16.1)	5 (16.1)	30 (16.1)
Without Aura	107 (69.0)	21 (67.7)	128 (68.8)
Both	23 (14.8)	5 (16.1)	28 (15.1)
Migraine Disorder Duration in Years			
Mean (SD)	23.1 (10.24)	23.0 (13.26)	23.0 (10.76)
Median	23.0	19.0	23.0
Q1, Q3	14.0, 30.3	11.0, 34.0	13.8, 31.0
Min, Max	3, 50	5, 60	3, 60
n	155	31	186
Migraine Prevention Medication in the Past, n1 (%)			
Yes	138 (89.0)	24 (77.4)	162 (87.1)
No	17 (11.0)	7 (22.6)	24 (12.9)
Average Number of Migraine Days per Month in Last 3 Months Prior to Screening			
Mean (SD)	16.6 (5.96)	7.5 (2.25)	15.1 (6.49)
Median	15.0	7.0	15.0
Q1, Q3	12.0, 20.0	5.0, 10.0	10.0, 20.0
Min, Max	8, 30	4, 12	4, 30
n	155	31	186
Average Number of Headache Days per Month in Last 3 Months Prior to Screening			
Mean (SD)	20.4 (4.92)	8.0 (2.48)	18.3 (6.53)
Median	20.0	8.0	18.0
Q1, Q3	16.0, 24.0	6.0, 10.0	15.0, 22.0
Min, Max	15, 30	4, 14	4, 30
n	155	31	186

Migraine history as collected in the lead-in study for 3101-303-002 Completers and in 3101-306-002 screening period for De Novo EM Participants.
N = number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 * (n1/N).
[1] Current usual treatment for acute migraine.

Table 14.1-4.3.2
Migraine History
Safety Population

Parameter Category Statistics	3101-303-002 CM Completers (N=155)	De Novo EM Participants (N=31)	Total (N=186)
Acute Medication Treatment [1], n1 (%)			
Yes	154 (99.4)	31 (100.0)	185 (99.5)
Triptan	140 (90.3)	30 (96.8)	170 (91.4)
Ergot or Ergot Combinations	0 (0.0)	0 (0.0)	0 (0.0)
NSAID	106 (68.4)	19 (61.3)	125 (67.2)
Opiate or Opiate Combination	1 (0.6)	0 (0.0)	1 (0.5)
Antiemetic Agent	59 (38.1)	4 (12.9)	63 (33.9)
Barbiturates	0 (0.0)	0 (0.0)	0 (0.0)
Other	29 (18.7)	9 (29.0)	38 (20.4)
No	1 (0.6)	0 (0.0)	1 (0.5)
Advice on Lifestyle Alterations, n1 (%)			
Yes	107 (69.0)	15 (48.4)	122 (65.6)
No	48 (31.0)	16 (51.6)	64 (34.4)

Migraine history as collected in the lead-in study for 3101-303-002 Completers and in 3101-306-002 screening period for De Novo EM Participants.
N = number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 * (n1/N).
[1] Current usual treatment for acute migraine.

表5

Table 14.1-5.1
Extent of Exposure
Safety Population

	3101-303-002 CM Completers (N=155)	De Novo EM Participants (N=31)	Total (N=186)
Duration of Exposure (days), n (%)			
>= 1 day	155 (100.0)	31 (100.0)	186 (100.0)
>= 28 days	149 (96.1)	29 (93.5)	178 (95.7)
>= 56 days	146 (94.2)	29 (93.5)	175 (94.1)
>= 84 days	144 (92.9)	29 (93.5)	173 (93.0)
>= 90 days	142 (91.6)	29 (93.5)	171 (91.9)
>= 112 days	139 (89.7)	29 (93.5)	168 (90.3)
>= 140 days	138 (89.0)	29 (93.5)	167 (89.8)
>= 168 days	136 (87.7)	28 (90.3)	164 (88.2)
>= 180 days	136 (87.7)	28 (90.3)	164 (88.2)
>= 196 days	134 (86.5)	28 (90.3)	162 (87.1)
>= 224 days	134 (86.5)	28 (90.3)	162 (87.1)
>= 252 days	132 (85.2)	28 (90.3)	160 (86.0)
>= 270 days	132 (85.2)	28 (90.3)	160 (86.0)
>= 280 days	132 (85.2)	28 (90.3)	160 (86.0)
>= 360 days	130 (83.9)	28 (90.3)	158 (84.9)
Mean (SD)	322.5 (101.94)	335.6 (94.93)	324.7 (100.68)
Median	364.0	365.0	364.0
Q1, Q3	363.0, 364.0	364.0, 366.0	363.0, 364.0
Min, Max	1, 376	1, 368	1, 376
n	155	31	186
Participant-Years	136.9	28.5	165.3

Duration of Exposure = last study treatment date - first study treatment date + 1.
Participant-Years = (duration of exposure in days)/365.25.

表6

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Baseline			
Mean (SD)	18.15 (5.290)	7.48 (2.039)	16.37 (6.314)
Median	18.00	7.15	16.30
Q1, Q3	15.00, 22.00	6.00, 9.00	11.20, 21.00
Min, Max	8.0, 28.0	4.0, 12.0	4.0, 28.0
n	150	30	180
Week 1 - 4			
Mean (SD)	11.78 (8.049)	4.09 (4.664)	10.50 (8.107)
Median	10.00	2.00	8.00
Q1, Q3	5.00, 18.00	1.00, 6.22	4.00, 16.08
Min, Max	0.0, 28.0	0.0, 22.0	0.0, 28.0
n	150	30	180
Change from Baseline			
Mean (SD)	-6.36 (7.222)	-3.39 (4.630)	-5.87 (6.937)
LS Mean (SE) [1]	-6.38 (0.580)	-3.38 (0.842)	-5.86 (0.502)
95% CI [1]	-7.52, -5.23	-5.10, -1.65	-6.85, -4.87
Median	-6.00	-4.48	-5.00
Q1, Q3	-12.00, -1.00	-6.00, -1.00	-10.00, -1.00
Min, Max	-26.0, 12.4	-9.0, 17.0	-26.0, 17.0
n	150	30	180

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 5 - 8			
Mean (SD)	11.67 (8.150)	4.41 (4.391)	10.48 (8.113)
Median	10.00	3.00	8.00
Q1, Q3	5.00, 17.81	1.00, 6.00	3.23, 16.00
Min, Max	0.0, 28.0	0.0, 16.0	0.0, 28.0
n	148	29	177
Change from Baseline			
Mean (SD)	-6.48 (7.433)	-3.12 (4.054)	-5.93 (7.094)
LS Mean (SE) [1]	-6.38 (0.601)	-3.19 (0.752)	-5.83 (0.515)
95% CI [1]	-7.57, -5.19	-4.73, -1.65	-6.85, -4.81
Median	-6.87	-4.00	-6.00
Q1, Q3	-12.00, -0.41	-5.00, -1.00	-10.00, -1.00
Min, Max	-25.0, 12.5	-9.0, 11.0	-25.0, 12.5
n	148	29	177
Week 9 - 12			
Mean (SD)	12.05 (8.475)	4.01 (3.802)	10.72 (8.436)
Median	9.00	3.00	8.00
Q1, Q3	5.00, 18.00	1.00, 6.00	4.00, 16.59
Min, Max	0.0, 28.0	0.0, 13.0	0.0, 28.0
n	146	29	175
Change from Baseline			
Mean (SD)	-6.13 (7.291)	-3.51 (3.412)	-5.69 (6.864)
LS Mean (SE) [1]	-6.00 (0.597)	-3.55 (0.638)	-5.59 (0.508)
95% CI [1]	-7.18, -4.81	-4.86, -2.24	-6.59, -4.58
Median	-5.31	-4.00	-5.00
Q1, Q3	-11.44, -2.00	-5.84, -1.00	-10.00, -1.04
Min, Max	-23.9, 13.5	-9.0, 3.0	-23.9, 13.5
n	146	29	175

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 13 - 16			
Mean (SD)	12.26 (8.320)	4.00 (3.754)	10.86 (8.331)
Median	10.98	3.00	9.00
Q1, Q3	5.00, 18.00	2.00, 5.83	3.50, 17.00
Min, Max	0.0, 28.0	0.0, 17.0	0.0, 28.0
n	142	29	171
Change from Baseline			
Mean (SD)	-5.99 (7.874)	-3.53 (3.377)	-5.57 (7.359)
LS Mean (SE) [1]	-5.79 (0.631)	-3.55 (0.632)	-5.42 (0.535)
95% CI [1]	-7.04, -4.55	-4.85, -2.26	-6.48, -4.36
Median	-5.50	-4.00	-5.00
Q1, Q3	-12.00, 0.00	-6.00, -2.00	-11.00, -1.00
Min, Max	-22.9, 14.5	-8.0, 6.0	-22.9, 14.5
n	142	29	171
Week 17 - 20			
Mean (SD)	11.75 (8.088)	3.64 (3.259)	10.35 (8.080)
Median	11.00	3.00	9.00
Q1, Q3	5.00, 17.00	1.00, 5.00	3.30, 15.00
Min, Max	0.0, 28.0	0.0, 15.0	0.0, 28.0
n	139	29	168
Change from Baseline			
Mean (SD)	-6.53 (7.216)	-3.89 (3.228)	-6.07 (6.765)
LS Mean (SE) [1]	-6.21 (0.593)	-3.89 (0.580)	-5.83 (0.502)
95% CI [1]	-7.39, -5.04	-5.07, -2.70	-6.82, -4.84
Median	-7.00	-4.00	-6.00
Q1, Q3	-11.00, -1.00	-6.00, -1.69	-10.00, -1.22
Min, Max	-26.0, 13.9	-10.0, 4.0	-26.0, 13.9
n	139	29	168

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 21 - 24			
Mean (SD)	11.66 (8.094)	3.19 (3.939)	10.19 (8.188)
Median	10.00	2.33	8.00
Q1, Q3	5.00, 17.63	0.00, 4.00	3.00, 16.00
Min, Max	0.0, 28.0	0.0, 16.0	0.0, 28.0
n	138	29	167
Change from Baseline			
Mean (SD)	-6.60 (6.826)	-4.34 (3.462)	-6.21 (6.420)
LS Mean (SE) [1]	-6.29 (0.570)	-4.37 (0.652)	-5.97 (0.485)
95% CI [1]	-7.42, -5.16	-5.70, -3.03	-6.93, -5.01
Median	-6.80	-5.00	-6.00
Q1, Q3	-11.00, -1.00	-6.00, -4.00	-10.00, -1.00
Min, Max	-26.0, 11.0	-10.0, 4.0	-26.0, 11.0
n	138	29	167
Week 25 - 28			
Mean (SD)	11.62 (8.585)	2.63 (2.624)	10.08 (8.584)
Median	10.00	2.00	7.00
Q1, Q3	5.00, 18.00	1.00, 3.62	3.00, 15.08
Min, Max	0.0, 28.0	0.0, 12.0	0.0, 28.0
n	135	28	163
Change from Baseline			
Mean (SD)	-6.65 (7.475)	-4.76 (2.422)	-6.32 (6.906)
LS Mean (SE) [1]	-6.33 (0.622)	-4.68 (0.456)	-6.05 (0.522)
95% CI [1]	-7.56, -5.10	-5.61, -3.74	-7.08, -5.02
Median	-8.00	-5.00	-6.00
Q1, Q3	-12.00, 0.00	-6.02, -3.00	-11.00, -1.00
Min, Max	-25.0, 11.0	-10.0, 2.0	-25.0, 11.0
n	135	28	163

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 29 - 32			
Mean (SD)	11.66 (8.484)	3.24 (3.400)	10.21 (8.462)
Median	10.00	2.00	8.00
Q1, Q3	4.00, 18.67	0.50, 4.57	3.00, 16.00
Min, Max	0.0, 28.0	0.0, 12.0	0.0, 28.0
n	134	28	162
Change from Baseline			
Mean (SD)	-6.59 (7.913)	-4.14 (3.642)	-6.17 (7.404)
LS Mean (SE) [1]	-6.21 (0.646)	-4.12 (0.638)	-5.86 (0.548)
95% CI [1]	-7.49, -4.94	-5.43, -2.81	-6.94, -4.78
Median	-6.00	-4.00	-6.00
Q1, Q3	-12.00, -1.00	-6.36, -2.32	-10.44, -1.00
Min, Max	-26.0, 15.0	-10.0, 7.0	-26.0, 15.0
n	134	28	162
Week 33 - 36			
Mean (SD)	11.37 (8.399)	2.85 (2.796)	9.89 (8.368)
Median	9.00	2.00	7.26
Q1, Q3	4.00, 17.00	0.50, 4.55	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 11.0	0.0, 28.0
n	133	28	161
Change from Baseline			
Mean (SD)	-6.88 (7.785)	-4.54 (3.287)	-6.48 (7.254)
LS Mean (SE) [1]	-6.54 (0.634)	-4.44 (0.554)	-6.19 (0.536)
95% CI [1]	-7.79, -5.28	-5.58, -3.30	-7.25, -5.13
Median	-7.00	-5.00	-6.72
Q1, Q3	-12.44, -1.00	-7.00, -1.50	-11.00, -1.00
Min, Max	-26.0, 13.0	-11.0, 2.0	-26.0, 13.0
n	133	28	161

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 37 - 40			
Mean (SD)	11.21 (8.175)	2.47 (3.206)	9.68 (8.240)
Median	10.19	1.00	7.28
Q1, Q3	4.57, 16.80	0.00, 3.50	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 14.0	0.0, 28.0
n	132	28	160
Change from Baseline			
Mean (SD)	-6.98 (7.709)	-4.92 (3.519)	-6.62 (7.189)
LS Mean (SE) [1]	-6.63 (0.627)	-4.80 (0.629)	-6.34 (0.532)
95% CI [1]	-7.87, -5.39	-6.10, -3.51	-7.39, -5.29
Median	-7.00	-5.66	-6.11
Q1, Q3	-12.48, -0.89	-7.00, -3.23	-11.00, -2.00
Min, Max	-24.0, 9.0	-11.0, 3.0	-24.0, 9.0
n	132	28	160
Week 41 - 44			
Mean (SD)	11.19 (8.291)	3.37 (4.505)	9.81 (8.304)
Median	10.00	2.00	8.00
Q1, Q3	5.00, 16.00	0.00, 4.69	3.00, 14.00
Min, Max	0.0, 28.0	0.0, 21.0	0.0, 28.0
n	131	28	159
Change from Baseline			
Mean (SD)	-6.95 (7.516)	-4.02 (4.168)	-6.43 (7.120)
LS Mean (SE) [1]	-6.59 (0.621)	-3.76 (0.843)	-6.14 (0.532)
95% CI [1]	-7.82, -5.36	-5.50, -2.02	-7.19, -5.09
Median	-7.00	-5.00	-6.00
Q1, Q3	-13.00, -1.00	-7.00, -2.31	-11.78, -1.00
Min, Max	-24.0, 8.0	-10.0, 9.0	-24.0, 9.0
n	131	28	159

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-1
Monthly Migraine Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 45 - 48			
Mean (SD)	11.26 (8.309)	3.09 (3.842)	9.81 (8.311)
Median	10.00	1.39	7.89
Q1, Q3	4.15, 16.00	0.00, 4.69	3.00, 14.52
Min, Max	0.0, 28.0	0.0, 15.0	0.0, 28.0
n	130	28	158
Change from Baseline			
Mean (SD)	-6.89 (7.769)	-4.30 (3.895)	-6.43 (7.293)
LS Mean (SE) [1]	-6.58 (0.638)	-4.13 (0.745)	-6.19 (0.543)
95% CI [1]	-7.84, -5.32	-5.66, -2.59	-7.26, -5.12
Median	-8.00	-4.99	-7.00
Q1, Q3	-12.94, -1.00	-7.00, -1.39	-11.00, -1.00
Min, Max	-24.0, 13.0	-10.0, 4.0	-24.0, 13.0
n	130	28	158
Week 49 - 52			
Mean (SD)	11.37 (8.468)	3.20 (3.757)	9.93 (8.435)
Median	9.67	3.00	7.26
Q1, Q3	4.31, 17.23	0.00, 5.00	3.11, 15.56
Min, Max	0.0, 28.0	0.0, 17.0	0.0, 28.0
n	130	28	158
Change from Baseline			
Mean (SD)	-6.77 (7.651)	-4.19 (3.500)	-6.32 (7.154)
LS Mean (SE) [1]	-6.45 (0.636)	-4.10 (0.665)	-6.06 (0.538)
95% CI [1]	-7.70, -5.19	-5.47, -2.74	-7.12, -4.99
Median	-7.63	-4.92	-6.87
Q1, Q3	-11.78, -0.48	-6.86, -1.93	-10.62, -1.00
Min, Max	-27.0, 12.0	-10.0, 5.0	-27.0, 12.0
n	130	28	158

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

表7

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 25%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 1 - 4			
Responder Rate, n/N1 [1] (%)	91/150 (60.7)	22/30 (73.3)	113/180 (62.8)
95% CI	(52.8, 68.5)	(57.5, 89.2)	(55.7, 69.8)
Week 5 - 8			
Responder Rate, n/N1 [1] (%)	92/148 (62.2)	21/29 (72.4)	113/177 (63.8)
95% CI	(54.3, 70.0)	(56.1, 88.7)	(56.8, 70.9)
Week 9 - 12			
Responder Rate, n/N1 [1] (%)	89/146 (61.0)	20/29 (69.0)	109/175 (62.3)
95% CI	(53.0, 68.9)	(52.1, 85.8)	(55.1, 69.5)
Week 13 - 16			
Responder Rate, n/N1 [1] (%)	81/144 (56.3)	23/29 (79.3)	104/173 (60.1)
95% CI	(48.1, 64.4)	(64.6, 94.1)	(52.8, 67.4)
Week 17 - 20			
Responder Rate, n/N1 [1] (%)	85/140 (60.7)	22/29 (75.9)	107/169 (63.3)
95% CI	(52.6, 68.8)	(60.3, 91.4)	(56.0, 70.6)
Week 21 - 24			
Responder Rate, n/N1 [1] (%)	86/139 (61.9)	24/29 (82.8)	110/168 (65.5)
95% CI	(53.8, 69.9)	(69.0, 96.5)	(58.3, 72.7)
Week 25 - 28			
Responder Rate, n/N1 [1] (%)	88/136 (64.7)	26/28 (92.9)	114/164 (69.5)
95% CI	(56.7, 72.7)	(83.3, 100.0)	(62.5, 76.6)
Week 29 - 32			
Responder Rate, n/N1 [1] (%)	84/134 (62.7)	22/28 (78.6)	106/162 (65.4)
95% CI	(54.5, 70.9)	(63.4, 93.8)	(58.1, 72.8)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 25%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 33 - 36			
Responder Rate, n/N1 [1] (%)	85/134 (63.4)	20/28 (71.4)	105/162 (64.8)
95% CI	(55.3, 71.6)	(54.7, 88.2)	(57.5, 72.2)
Week 37 - 40			
Responder Rate, n/N1 [1] (%)	84/132 (63.6)	23/28 (82.1)	107/160 (66.9)
95% CI	(55.4, 71.8)	(68.0, 96.3)	(59.6, 74.2)
Week 41 - 44			
Responder Rate, n/N1 [1] (%)	88/131 (67.2)	21/28 (75.0)	109/159 (68.6)
95% CI	(59.1, 75.2)	(59.0, 91.0)	(61.3, 75.8)
Week 45 - 48			
Responder Rate, n/N1 [1] (%)	83/130 (63.8)	21/28 (75.0)	104/158 (65.8)
95% CI	(55.6, 72.1)	(59.0, 91.0)	(58.4, 73.2)
Week 49 - 52			
Responder Rate, n/N1 [1] (%)	85/130 (65.4)	22/28 (78.6)	107/158 (67.7)
95% CI	(57.2, 73.6)	(63.4, 93.8)	(60.4, 75.0)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 30%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 1 - 4			
Responder Rate, n/N1 [1] (%)	84/150 (56.0)	21/30 (70.0)	105/180 (58.3)
95% CI	(48.1, 63.9)	(53.6, 86.4)	(51.1, 65.5)
Week 5 - 8			
Responder Rate, n/N1 [1] (%)	86/148 (58.1)	20/29 (69.0)	106/177 (59.9)
95% CI	(50.2, 66.1)	(52.1, 85.8)	(52.7, 67.1)
Week 9 - 12			
Responder Rate, n/N1 [1] (%)	83/146 (56.8)	19/29 (65.5)	102/175 (58.3)
95% CI	(48.8, 64.9)	(48.2, 82.8)	(51.0, 65.6)
Week 13 - 16			
Responder Rate, n/N1 [1] (%)	77/144 (53.5)	23/29 (79.3)	100/173 (57.8)
95% CI	(45.3, 61.6)	(64.6, 94.1)	(50.4, 65.2)
Week 17 - 20			
Responder Rate, n/N1 [1] (%)	80/140 (57.1)	21/29 (72.4)	101/169 (59.8)
95% CI	(48.9, 65.3)	(56.1, 88.7)	(52.4, 67.2)
Week 21 - 24			
Responder Rate, n/N1 [1] (%)	80/139 (57.6)	24/29 (82.8)	104/168 (61.9)
95% CI	(49.3, 65.8)	(69.0, 96.5)	(54.6, 69.2)
Week 25 - 28			
Responder Rate, n/N1 [1] (%)	82/136 (60.3)	24/28 (85.7)	106/164 (64.6)
95% CI	(52.1, 68.5)	(72.8, 98.7)	(57.3, 72.0)
Week 29 - 32			
Responder Rate, n/N1 [1] (%)	79/134 (59.0)	22/28 (78.6)	101/162 (62.3)
95% CI	(50.6, 67.3)	(63.4, 93.8)	(54.9, 69.8)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 30%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 33 - 36			
Responder Rate, n/N1 [1] (%)	81/134 (60.4)	20/28 (71.4)	101/162 (62.3)
95% CI	(52.2, 68.7)	(54.7, 88.2)	(54.9, 69.8)
Week 37 - 40			
Responder Rate, n/N1 [1] (%)	76/132 (57.6)	22/28 (78.6)	98/160 (61.3)
95% CI	(49.1, 66.0)	(63.4, 93.8)	(53.7, 68.8)
Week 41 - 44			
Responder Rate, n/N1 [1] (%)	81/131 (61.8)	21/28 (75.0)	102/159 (64.2)
95% CI	(53.5, 70.2)	(59.0, 91.0)	(56.7, 71.6)
Week 45 - 48			
Responder Rate, n/N1 [1] (%)	80/130 (61.5)	21/28 (75.0)	101/158 (63.9)
95% CI	(53.2, 69.9)	(59.0, 91.0)	(56.4, 71.4)
Week 49 - 52			
Responder Rate, n/N1 [1] (%)	82/130 (63.1)	22/28 (78.6)	104/158 (65.8)
95% CI	(54.8, 71.4)	(63.4, 93.8)	(58.4, 73.2)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 50%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 1 - 4			
Responder Rate, n/N1 [1] (%)	66/150 (44.0)	19/30 (63.3)	85/180 (47.2)
95% CI	(36.1, 51.9)	(46.1, 80.6)	(39.9, 54.5)
Week 5 - 8			
Responder Rate, n/N1 [1] (%)	63/148 (42.6)	17/29 (58.6)	80/177 (45.2)
95% CI	(34.6, 50.5)	(40.7, 76.5)	(37.9, 52.5)
Week 9 - 12			
Responder Rate, n/N1 [1] (%)	60/146 (41.1)	16/29 (55.2)	76/175 (43.4)
95% CI	(33.1, 49.1)	(37.1, 73.3)	(36.1, 50.8)
Week 13 - 16			
Responder Rate, n/N1 [1] (%)	60/144 (41.7)	16/29 (55.2)	76/173 (43.9)
95% CI	(33.6, 49.7)	(37.1, 73.3)	(36.5, 51.3)
Week 17 - 20			
Responder Rate, n/N1 [1] (%)	60/140 (42.9)	17/29 (58.6)	77/169 (45.6)
95% CI	(34.7, 51.1)	(40.7, 76.5)	(38.1, 53.1)
Week 21 - 24			
Responder Rate, n/N1 [1] (%)	60/139 (43.2)	22/29 (75.9)	82/168 (48.8)
95% CI	(34.9, 51.4)	(60.3, 91.4)	(41.3, 56.4)
Week 25 - 28			
Responder Rate, n/N1 [1] (%)	59/136 (43.4)	23/28 (82.1)	82/164 (50.0)
95% CI	(35.1, 51.7)	(68.0, 96.3)	(42.3, 57.7)
Week 29 - 32			
Responder Rate, n/N1 [1] (%)	61/134 (45.5)	17/28 (60.7)	78/162 (48.1)
95% CI	(37.1, 54.0)	(42.6, 78.8)	(40.5, 55.8)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 50%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 33 - 36			
Responder Rate, n/N1 [1] (%)	63/134 (47.0)	20/28 (71.4)	83/162 (51.2)
95% CI	(38.6, 55.5)	(54.7, 88.2)	(43.5, 58.9)
Week 37 - 40			
Responder Rate, n/N1 [1] (%)	63/132 (47.7)	21/28 (75.0)	84/160 (52.5)
95% CI	(39.2, 56.2)	(59.0, 91.0)	(44.8, 60.2)
Week 41 - 44			
Responder Rate, n/N1 [1] (%)	59/131 (45.0)	21/28 (75.0)	80/159 (50.3)
95% CI	(36.5, 53.6)	(59.0, 91.0)	(42.5, 58.1)
Week 45 - 48			
Responder Rate, n/N1 [1] (%)	65/130 (50.0)	19/28 (67.9)	84/158 (53.2)
95% CI	(41.4, 58.6)	(50.6, 85.2)	(45.4, 60.9)
Week 49 - 52			
Responder Rate, n/N1 [1] (%)	62/130 (47.7)	17/28 (60.7)	79/158 (50.0)
95% CI	(39.1, 56.3)	(42.6, 78.8)	(42.2, 57.8)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 75%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 1 - 4			
Responder Rate, n/N1 [1] (%)	30/150 (20.0)	13/30 (43.3)	43/180 (23.9)
95% CI	(13.6, 26.4)	(25.6, 61.1)	(17.7, 30.1)
Week 5 - 8			
Responder Rate, n/N1 [1] (%)	33/148 (22.3)	9/29 (31.0)	42/177 (23.7)
95% CI	(15.6, 29.0)	(14.2, 47.9)	(17.5, 30.0)
Week 9 - 12			
Responder Rate, n/N1 [1] (%)	29/146 (19.9)	11/29 (37.9)	40/175 (22.9)
95% CI	(13.4, 26.3)	(20.3, 55.6)	(16.6, 29.1)
Week 13 - 16			
Responder Rate, n/N1 [1] (%)	31/144 (21.5)	9/29 (31.0)	40/173 (23.1)
95% CI	(14.8, 28.2)	(14.2, 47.9)	(16.8, 29.4)
Week 17 - 20			
Responder Rate, n/N1 [1] (%)	27/140 (19.3)	9/29 (31.0)	36/169 (21.3)
95% CI	(12.8, 25.8)	(14.2, 47.9)	(15.1, 27.5)
Week 21 - 24			
Responder Rate, n/N1 [1] (%)	28/139 (20.1)	12/29 (41.4)	40/168 (23.8)
95% CI	(13.5, 26.8)	(23.5, 59.3)	(17.4, 30.3)
Week 25 - 28			
Responder Rate, n/N1 [1] (%)	33/136 (24.3)	15/28 (53.6)	48/164 (29.3)
95% CI	(17.1, 31.5)	(35.1, 72.0)	(22.3, 36.2)
Week 29 - 32			
Responder Rate, n/N1 [1] (%)	32/134 (23.9)	14/28 (50.0)	46/162 (28.4)
95% CI	(16.7, 31.1)	(31.5, 68.5)	(21.5, 35.3)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

Improvement: >= 75%

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 33 - 36			
Responder Rate, n/N1 [1] (%)	35/134 (26.1)	14/28 (50.0)	49/162 (30.2)
95% CI	(18.7, 33.6)	(31.5, 68.5)	(23.2, 37.3)
Week 37 - 40			
Responder Rate, n/N1 [1] (%)	32/132 (24.2)	17/28 (60.7)	49/160 (30.6)
95% CI	(16.9, 31.6)	(42.6, 78.8)	(23.5, 37.8)
Week 41 - 44			
Responder Rate, n/N1 [1] (%)	31/131 (23.7)	14/28 (50.0)	45/159 (28.3)
95% CI	(16.4, 30.9)	(31.5, 68.5)	(21.3, 35.3)
Week 45 - 48			
Responder Rate, n/N1 [1] (%)	31/130 (23.8)	15/28 (53.6)	46/158 (29.1)
95% CI	(16.5, 31.2)	(35.1, 72.0)	(22.0, 36.2)
Week 49 - 52			
Responder Rate, n/N1 [1] (%)	30/130 (23.1)	12/28 (42.9)	42/158 (26.6)
95% CI	(15.8, 30.3)	(24.5, 61.2)	(19.7, 33.5)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

100% Improvement

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 1 - 4			
Responder Rate, n/N1 [1] (%)	6/150 (4.0)	7/30 (23.3)	13/180 (7.2)
95% CI	(0.9, 7.1)	(8.2, 38.5)	(3.4, 11.0)
Week 5 - 8			
Responder Rate, n/N1 [1] (%)	3/148 (2.0)	4/29 (13.8)	7/177 (4.0)
95% CI	(0.0, 4.3)	(1.2, 26.3)	(1.1, 6.8)
Week 9 - 12			
Responder Rate, n/N1 [1] (%)	5/146 (3.4)	6/29 (20.7)	11/175 (6.3)
95% CI	(0.5, 6.4)	(5.9, 35.4)	(2.7, 9.9)
Week 13 - 16			
Responder Rate, n/N1 [1] (%)	3/144 (2.1)	4/29 (13.8)	7/173 (4.0)
95% CI	(0.0, 4.4)	(1.2, 26.3)	(1.1, 7.0)
Week 17 - 20			
Responder Rate, n/N1 [1] (%)	5/140 (3.6)	3/29 (10.3)	8/169 (4.7)
95% CI	(0.5, 6.6)	(0.0, 21.4)	(1.5, 7.9)
Week 21 - 24			
Responder Rate, n/N1 [1] (%)	7/139 (5.0)	8/29 (27.6)	15/168 (8.9)
95% CI	(1.4, 8.7)	(11.3, 43.9)	(4.6, 13.2)
Week 25 - 28			
Responder Rate, n/N1 [1] (%)	7/136 (5.1)	5/28 (17.9)	12/164 (7.3)
95% CI	(1.4, 8.9)	(3.7, 32.0)	(3.3, 11.3)
Week 29 - 32			
Responder Rate, n/N1 [1] (%)	6/134 (4.5)	7/28 (25.0)	13/162 (8.0)
95% CI	(1.0, 8.0)	(9.0, 41.0)	(3.8, 12.2)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

Table 14.2-2
Monthly Migraine Days: Number (%) of Participants with Improvement (Decrease)
Modified Intent-to-Treat Population

100% Improvement

Visit	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 33 - 36			
Responder Rate, n/N1 [1] (%)	7/134 (5.2)	7/28 (25.0)	14/162 (8.6)
95% CI	(1.5, 9.0)	(9.0, 41.0)	(4.3, 13.0)
Week 37 - 40			
Responder Rate, n/N1 [1] (%)	8/132 (6.1)	8/28 (28.6)	16/160 (10.0)
95% CI	(2.0, 10.1)	(11.8, 45.3)	(5.4, 14.6)
Week 41 - 44			
Responder Rate, n/N1 [1] (%)	6/131 (4.6)	9/28 (32.1)	15/159 (9.4)
95% CI	(1.0, 8.2)	(14.8, 49.4)	(4.9, 14.0)
Week 45 - 48			
Responder Rate, n/N1 [1] (%)	3/130 (2.3)	8/28 (28.6)	11/158 (7.0)
95% CI	(0.0, 4.9)	(11.8, 45.3)	(3.0, 10.9)
Week 49 - 52			
Responder Rate, n/N1 [1] (%)	8/130 (6.2)	10/28 (35.7)	18/158 (11.4)
95% CI	(2.0, 10.3)	(18.0, 53.5)	(6.4, 16.3)

[1] N1 = Number of participants available for analysis at a specific time point.
95% CI based on the normal approximation to the binomial.

表8

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Baseline			
Mean (SD)	21.46 (3.993)	8.57 (2.181)	19.31 (6.104)
Median	21.00	8.50	20.00
Q1, Q3	18.00, 25.00	7.00, 9.74	16.08, 24.00
Min, Max	15.0, 28.0	5.0, 13.0	5.0, 28.0
n	150	30	180
Week 1 - 4			
Mean (SD)	14.74 (8.231)	4.55 (4.734)	13.04 (8.633)
Median	14.50	3.50	12.00
Q1, Q3	8.00, 22.00	1.00, 7.00	6.22, 19.19
Min, Max	0.0, 28.0	0.0, 22.0	0.0, 28.0
n	150	30	180
Change from Baseline			
Mean (SD)	-6.72 (6.967)	-4.02 (4.811)	-6.27 (6.721)
LS Mean (SE) [1]	-6.72 (0.570)	-3.97 (0.864)	-6.26 (0.500)
95% CI [1]	-7.85, -5.59	-5.74, -2.20	-7.25, -5.27
Median	-5.00	-5.00	-5.00
Q1, Q3	-11.00, -1.00	-6.72, -2.00	-11.00, -1.00
Min, Max	-26.0, 11.0	-11.2, 16.0	-26.0, 16.0
n	150	30	180

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 5 - 8			
Mean (SD)	14.33 (8.247)	4.93 (4.508)	12.79 (8.497)
Median	14.00	3.00	12.00
Q1, Q3	7.00, 21.50	2.00, 7.00	6.00, 19.00
Min, Max	1.0, 28.0	0.0, 16.0	0.0, 28.0
n	148	29	177
Change from Baseline			
Mean (SD)	-7.13 (7.028)	-3.62 (4.253)	-6.56 (6.769)
LS Mean (SE) [1]	-7.06 (0.577)	-3.72 (0.788)	-6.50 (0.503)
95% CI [1]	-8.20, -5.92	-5.34, -2.11	-7.49, -5.51
Median	-6.74	-4.00	-6.00
Q1, Q3	-13.00, -1.44	-6.00, -2.00	-12.00, -2.00
Min, Max	-25.0, 11.0	-12.0, 10.0	-25.0, 11.0
n	148	29	177
Week 9 - 12			
Mean (SD)	14.67 (8.231)	4.84 (4.045)	13.04 (8.517)
Median	14.00	4.00	12.00
Q1, Q3	8.00, 22.00	1.00, 7.00	6.00, 20.00
Min, Max	0.0, 28.0	0.0, 15.0	0.0, 28.0
n	146	29	175
Change from Baseline			
Mean (SD)	-6.80 (6.956)	-3.72 (3.827)	-6.29 (6.633)
LS Mean (SE) [1]	-6.71 (0.570)	-3.76 (0.708)	-6.22 (0.494)
95% CI [1]	-7.83, -5.58	-5.22, -2.31	-7.20, -5.25
Median	-6.12	-4.00	-6.00
Q1, Q3	-12.00, -1.64	-6.72, -1.68	-11.00, -1.64
Min, Max	-23.9, 11.0	-12.0, 4.0	-23.9, 11.0
n	146	29	175

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 13 - 16			
Mean (SD)	14.83 (8.389)	4.32 (3.916)	13.05 (8.749)
Median	15.00	3.00	12.00
Q1, Q3	7.00, 22.00	2.00, 5.83	5.00, 20.00
Min, Max	0.0, 28.0	0.0, 18.0	0.0, 28.0
n	142	29	171
Change from Baseline			
Mean (SD)	-6.71 (7.341)	-4.24 (3.909)	-6.29 (6.934)
LS Mean (SE) [1]	-6.58 (0.604)	-4.27 (0.708)	-6.21 (0.518)
95% CI [1]	-7.78, -5.39	-5.72, -2.82	-7.23, -5.19
Median	-5.24	-5.89	-5.48
Q1, Q3	-13.00, -1.00	-6.00, -3.00	-11.00, -1.74
Min, Max	-22.9, 11.0	-11.0, 7.0	-22.9, 11.0
n	142	29	171
Week 17 - 20			
Mean (SD)	14.39 (8.249)	4.34 (3.786)	12.65 (8.552)
Median	14.00	3.36	12.00
Q1, Q3	8.00, 22.00	2.00, 5.00	5.00, 19.00
Min, Max	0.0, 28.0	0.0, 15.0	0.0, 28.0
n	139	29	168
Change from Baseline			
Mean (SD)	-7.11 (7.043)	-4.22 (3.831)	-6.61 (6.682)
LS Mean (SE) [1]	-6.93 (0.579)	-4.24 (0.687)	-6.49 (0.499)
95% CI [1]	-8.07, -5.78	-5.65, -2.83	-7.47, -5.50
Median	-7.00	-5.00	-6.00
Q1, Q3	-13.00, -1.00	-7.00, -1.00	-11.10, -1.00
Min, Max	-27.0, 11.0	-11.2, 3.0	-27.0, 11.0
n	139	29	168

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 21 - 24			
Mean (SD)	14.28 (8.270)	3.98 (4.027)	12.49 (8.632)
Median	14.00	3.00	12.00
Q1, Q3	7.37, 21.00	1.00, 5.00	5.00, 20.00
Min, Max	0.0, 28.0	0.0, 16.0	0.0, 28.0
n	138	29	167
Change from Baseline			
Mean (SD)	-7.19 (6.827)	-4.58 (3.540)	-6.73 (6.447)
LS Mean (SE) [1]	-6.97 (0.563)	-4.64 (0.665)	-6.58 (0.487)
95% CI [1]	-8.08, -5.85	-6.00, -3.27	-7.54, -5.62
Median	-7.00	-5.00	-6.00
Q1, Q3	-12.00, -1.00	-6.24, -4.00	-11.00, -2.00
Min, Max	-26.0, 11.0	-11.0, 4.0	-26.0, 11.0
n	138	29	167
Week 25 - 28			
Mean (SD)	14.22 (8.666)	3.17 (2.844)	12.32 (8.997)
Median	13.00	2.50	10.00
Q1, Q3	7.00, 23.00	1.15, 4.00	4.00, 20.46
Min, Max	0.0, 28.0	0.0, 13.0	0.0, 28.0
n	135	28	163
Change from Baseline			
Mean (SD)	-7.25 (7.147)	-5.25 (2.780)	-6.91 (6.642)
LS Mean (SE) [1]	-7.07 (0.585)	-5.17 (0.516)	-6.76 (0.502)
95% CI [1]	-8.23, -5.92	-6.23, -4.11	-7.75, -5.77
Median	-7.00	-5.38	-6.00
Q1, Q3	-13.00, -1.00	-6.86, -3.43	-12.00, -2.00
Min, Max	-25.0, 8.0	-11.0, 1.0	-25.0, 8.0
n	135	28	163

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 29 - 32			
Mean (SD)	14.28 (8.481)	4.16 (4.314)	12.53 (8.791)
Median	13.00	2.00	11.00
Q1, Q3	7.84, 22.81	1.00, 5.80	5.00, 19.00
Min, Max	0.0, 28.0	0.0, 16.0	0.0, 28.0
n	134	28	162
Change from Baseline			
Mean (SD)	-7.20 (7.510)	-4.26 (4.212)	-6.69 (7.128)
LS Mean (SE) [1]	-6.97 (0.616)	-4.35 (0.770)	-6.53 (0.529)
95% CI [1]	-8.19, -5.76	-5.93, -2.77	-7.58, -5.49
Median	-6.50	-5.00	-6.00
Q1, Q3	-13.00, -1.00	-6.86, -2.00	-11.85, -1.00
Min, Max	-27.0, 11.0	-12.0, 6.0	-27.0, 11.0
n	134	28	162
Week 33 - 36			
Mean (SD)	13.81 (8.680)	3.40 (2.920)	12.00 (8.904)
Median	13.00	2.54	10.00
Q1, Q3	7.00, 21.78	1.00, 6.00	4.00, 17.23
Min, Max	0.0, 28.0	0.0, 11.0	0.0, 28.0
n	133	28	161
Change from Baseline			
Mean (SD)	-7.68 (7.399)	-5.02 (2.912)	-7.21 (6.900)
LS Mean (SE) [1]	-7.44 (0.604)	-4.99 (0.520)	-7.03 (0.515)
95% CI [1]	-8.63, -6.24	-6.06, -3.92	-8.05, -6.02
Median	-8.00	-6.00	-6.72
Q1, Q3	-13.00, -1.00	-6.86, -3.00	-12.00, -1.00
Min, Max	-27.0, 10.0	-11.2, 1.0	-27.0, 10.0
n	133	28	161

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 37 - 40			
Mean (SD)	14.00 (8.291)	3.12 (3.239)	12.10 (8.697)
Median	13.00	2.00	11.00
Q1, Q3	7.13, 20.00	1.00, 5.00	5.00, 18.00
Min, Max	0.0, 28.0	0.0, 14.0	0.0, 28.0
n	132	28	160
Change from Baseline			
Mean (SD)	-7.43 (7.036)	-5.30 (3.721)	-7.06 (6.618)
LS Mean (SE) [1]	-7.17 (0.581)	-5.20 (0.642)	-6.86 (0.499)
95% CI [1]	-8.32, -6.02	-6.52, -3.88	-7.85, -5.88
Median	-8.00	-6.00	-7.00
Q1, Q3	-13.00, -2.00	-7.75, -3.00	-11.68, -2.00
Min, Max	-23.9, 8.0	-11.2, 2.0	-23.9, 8.0
n	132	28	160
Week 41 - 44			
Mean (SD)	13.92 (8.485)	3.80 (4.650)	12.14 (8.825)
Median	12.00	2.00	11.00
Q1, Q3	7.00, 21.00	1.02, 5.19	5.00, 19.00
Min, Max	0.0, 28.0	0.0, 21.0	0.0, 28.0
n	131	28	159
Change from Baseline			
Mean (SD)	-7.49 (7.240)	-4.62 (4.475)	-6.98 (6.911)
LS Mean (SE) [1]	-7.20 (0.601)	-4.34 (0.915)	-6.76 (0.523)
95% CI [1]	-8.39, -6.02	-6.23, -2.45	-7.80, -5.73
Median	-7.00	-5.00	-6.72
Q1, Q3	-13.00, -1.00	-7.00, -3.81	-12.00, -1.00
Min, Max	-23.0, 8.0	-11.2, 9.0	-23.0, 9.0
n	131	28	159

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-3.1
Monthly Headache Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 45 - 48			
Mean (SD)	14.15 (8.563)	3.81 (3.842)	12.32 (8.860)
Median	13.00	2.11	11.00
Q1, Q3	7.26, 22.00	1.00, 6.34	5.00, 19.00
Min, Max	0.0, 28.0	0.0, 15.0	0.0, 28.0
n	130	28	158
Change from Baseline			
Mean (SD)	-7.27 (7.475)	-4.61 (3.523)	-6.80 (7.006)
LS Mean (SE) [1]	-6.96 (0.620)	-4.47 (0.687)	-6.57 (0.529)
95% CI [1]	-8.19, -5.73	-5.89, -3.06	-7.62, -5.53
Median	-7.00	-5.46	-6.00
Q1, Q3	-13.00, -1.00	-6.92, -2.39	-12.00, -1.00
Min, Max	-24.0, 10.0	-12.0, 3.0	-24.0, 10.0
n	130	28	158
Week 49 - 52			
Mean (SD)	14.19 (8.417)	3.67 (3.761)	12.32 (8.768)
Median	13.48	3.00	10.37
Q1, Q3	7.26, 20.74	1.00, 5.50	5.19, 18.31
Min, Max	0.0, 28.0	0.0, 17.0	0.0, 28.0
n	130	28	158
Change from Baseline			
Mean (SD)	-7.24 (7.167)	-4.75 (3.248)	-6.80 (6.703)
LS Mean (SE) [1]	-6.95 (0.592)	-4.65 (0.627)	-6.59 (0.505)
95% CI [1]	-8.12, -5.78	-5.94, -3.36	-7.59, -5.59
Median	-6.74	-5.00	-6.27
Q1, Q3	-12.81, -1.44	-6.86, -3.14	-11.74, -1.77
Min, Max	-26.0, 10.0	-10.1, 5.0	-26.0, 10.0
n	130	28	158

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

表9

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Baseline			
Mean (SD)	16.53 (6.803)	6.76 (2.847)	14.90 (7.292)
Median	17.50	7.00	15.78
Q1, Q3	11.00, 21.00	5.00, 8.00	9.00, 20.00
Min, Max	0.0, 28.0	0.0, 13.0	0.0, 28.0
n	150	30	180
Week 1 - 4			
Mean (SD)	10.91 (7.990)	3.28 (3.194)	9.64 (7.933)
Median	9.00	2.00	8.00
Q1, Q3	4.15, 15.83	0.00, 6.00	3.00, 14.50
Min, Max	0.0, 28.0	0.0, 10.0	0.0, 28.0
n	150	30	180
Change from Baseline			
Mean (SD)	-5.62 (6.725)	-3.48 (4.066)	-5.26 (6.400)
LS Mean (SE) [1]	-5.66 (0.525)	-3.51 (0.591)	-5.28 (0.451)
95% CI [1]	-6.70, -4.62	-4.72, -2.30	-6.17, -4.39
Median	-5.00	-4.11	-5.00
Q1, Q3	-10.00, -1.00	-7.00, -1.00	-9.00, -1.00
Min, Max	-26.0, 15.0	-9.0, 6.0	-26.0, 15.0
n	150	30	180

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 5 - 8			
Mean (SD)	11.04 (8.171)	3.76 (3.462)	9.85 (8.060)
Median	9.00	2.00	8.00
Q1, Q3	4.00, 17.00	1.00, 5.00	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 14.0	0.0, 28.0
n	148	29	177
Change from Baseline			
Mean (SD)	-5.50 (7.081)	-3.02 (3.951)	-5.09 (6.724)
LS Mean (SE) [1]	-5.51 (0.550)	-3.11 (0.631)	-5.09 (0.471)
95% CI [1]	-6.59, -4.42	-4.40, -1.81	-6.02, -4.16
Median	-5.00	-3.00	-5.00
Q1, Q3	-10.00, 0.00	-6.00, 0.00	-9.00, 0.00
Min, Max	-22.9, 17.0	-12.0, 5.0	-22.9, 17.0
n	148	29	177
Week 9 - 12			
Mean (SD)	11.45 (7.753)	3.86 (3.612)	10.19 (7.759)
Median	9.35	3.00	8.00
Q1, Q3	5.00, 17.00	1.00, 6.00	4.00, 16.00
Min, Max	0.0, 28.0	0.0, 15.0	0.0, 28.0
n	146	29	175
Change from Baseline			
Mean (SD)	-5.14 (6.902)	-2.92 (4.159)	-4.77 (6.570)
LS Mean (SE) [1]	-5.11 (0.527)	-2.99 (0.667)	-4.74 (0.454)
95% CI [1]	-6.15, -4.07	-4.36, -1.62	-5.63, -3.84
Median	-4.45	-3.00	-4.00
Q1, Q3	-9.00, -1.00	-6.00, 0.00	-9.00, -0.84
Min, Max	-23.9, 18.0	-12.0, 4.0	-23.9, 18.0
n	146	29	175

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 13 - 16			
Mean (SD)	11.54 (8.087)	3.41 (3.296)	10.16 (8.087)
Median	11.00	3.00	8.00
Q1, Q3	5.00, 17.00	2.00, 4.00	3.00, 16.00
Min, Max	0.0, 28.0	0.0, 16.0	0.0, 28.0
n	142	29	171
Change from Baseline			
Mean (SD)	-5.19 (7.188)	-3.37 (3.940)	-4.88 (6.774)
LS Mean (SE) [1]	-5.10 (0.553)	-3.44 (0.608)	-4.81 (0.474)
95% CI [1]	-6.20, -4.01	-4.69, -2.20	-5.75, -3.88
Median	-4.65	-4.00	-4.07
Q1, Q3	-9.00, 0.00	-6.00, -2.00	-9.00, 0.00
Min, Max	-23.0, 18.0	-11.0, 5.0	-23.0, 18.0
n	142	29	171
Week 17 - 20			
Mean (SD)	11.43 (8.069)	3.11 (2.959)	10.00 (8.077)
Median	11.00	2.24	8.50
Q1, Q3	4.00, 17.00	1.00, 4.00	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 14.0	0.0, 28.0
n	139	29	168
Change from Baseline			
Mean (SD)	-5.36 (7.156)	-3.67 (3.606)	-5.07 (6.701)
LS Mean (SE) [1]	-5.28 (0.552)	-3.73 (0.542)	-5.02 (0.471)
95% CI [1]	-6.37, -4.19	-4.84, -2.62	-5.94, -4.09
Median	-4.93	-3.00	-4.00
Q1, Q3	-10.00, 0.00	-6.00, -1.00	-9.00, 0.00
Min, Max	-26.0, 19.0	-11.0, 3.0	-26.0, 19.0
n	139	29	168

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 21 - 24			
Mean (SD)	11.23 (8.008)	2.86 (3.202)	9.78 (8.048)
Median	10.00	2.15	8.00
Q1, Q3	5.00, 17.00	1.00, 4.00	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 13.0	0.0, 28.0
n	138	29	167
Change from Baseline			
Mean (SD)	-5.49 (6.679)	-3.92 (3.444)	-5.22 (6.259)
LS Mean (SE) [1]	-5.41 (0.530)	-3.96 (0.563)	-5.16 (0.451)
95% CI [1]	-6.46, -4.37	-5.12, -2.81	-6.05, -4.27
Median	-5.22	-4.00	-5.00
Q1, Q3	-10.00, 0.00	-6.00, -2.54	-9.00, -0.85
Min, Max	-26.0, 15.0	-11.0, 3.8	-26.0, 15.0
n	138	29	167
Week 25 - 28			
Mean (SD)	11.43 (8.585)	2.31 (2.445)	9.86 (8.594)
Median	10.00	1.64	7.26
Q1, Q3	4.00, 17.00	0.50, 3.62	2.00, 15.00
Min, Max	0.0, 28.0	0.0, 9.0	0.0, 28.0
n	135	28	163
Change from Baseline			
Mean (SD)	-5.36 (6.941)	-4.50 (2.633)	-5.21 (6.412)
LS Mean (SE) [1]	-5.24 (0.561)	-4.42 (0.405)	-5.09 (0.473)
95% CI [1]	-6.35, -4.13	-5.25, -3.58	-6.02, -4.15
Median	-5.00	-4.00	-5.00
Q1, Q3	-10.00, -1.00	-5.92, -3.00	-9.00, -1.00
Min, Max	-25.0, 14.0	-11.0, 0.0	-25.0, 14.0
n	135	28	163

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 29 - 32			
Mean (SD)	11.31 (8.217)	2.61 (3.460)	9.80 (8.286)
Median	10.00	2.00	8.00
Q1, Q3	4.00, 17.00	0.50, 3.06	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 16.0	0.0, 28.0
n	134	28	162
Change from Baseline			
Mean (SD)	-5.45 (7.287)	-4.19 (4.024)	-5.23 (6.841)
LS Mean (SE) [1]	-5.31 (0.567)	-4.15 (0.635)	-5.11 (0.486)
95% CI [1]	-6.43, -4.19	-5.45, -2.85	-6.07, -4.15
Median	-5.00	-4.50	-5.00
Q1, Q3	-9.00, -1.00	-7.00, -2.00	-9.00, -1.00
Min, Max	-26.0, 14.0	-12.0, 5.0	-26.0, 14.0
n	134	28	162
Week 33 - 36			
Mean (SD)	11.08 (8.204)	2.75 (2.524)	9.63 (8.162)
Median	10.00	2.00	7.00
Q1, Q3	4.15, 17.00	1.00, 4.41	3.00, 15.00
Min, Max	0.0, 28.0	0.0, 9.0	0.0, 28.0
n	133	28	161
Change from Baseline			
Mean (SD)	-5.66 (6.961)	-4.05 (3.445)	-5.38 (6.508)
LS Mean (SE) [1]	-5.53 (0.544)	-3.97 (0.476)	-5.26 (0.462)
95% CI [1]	-6.60, -4.45	-4.94, -2.99	-6.17, -4.35
Median	-5.00	-3.83	-5.00
Q1, Q3	-10.18, -1.00	-6.36, -2.00	-10.00, -1.00
Min, Max	-26.0, 15.0	-11.0, 3.8	-26.0, 15.0
n	133	28	161

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 37 - 40			
Mean (SD)	11.30 (8.027)	2.22 (2.270)	9.71 (8.121)
Median	10.19	1.26	7.40
Q1, Q3	5.00, 17.00	1.00, 4.00	3.00, 14.00
Min, Max	0.0, 28.0	0.0, 10.0	0.0, 28.0
n	132	28	160
Change from Baseline			
Mean (SD)	-5.35 (6.991)	-4.58 (3.474)	-5.22 (6.512)
LS Mean (SE) [1]	-5.19 (0.546)	-4.50 (0.439)	-5.08 (0.466)
95% CI [1]	-6.27, -4.11	-5.40, -3.59	-5.99, -4.16
Median	-5.00	-4.50	-5.00
Q1, Q3	-10.70, -1.00	-7.00, -2.00	-9.00, -1.00
Min, Max	-25.0, 22.0	-11.0, 2.5	-25.0, 22.0
n	132	28	160
Week 41 - 44			
Mean (SD)	11.11 (8.179)	2.93 (3.250)	9.67 (8.162)
Median	9.00	2.00	7.00
Q1, Q3	5.00, 17.00	0.50, 5.00	3.00, 14.00
Min, Max	0.0, 28.0	0.0, 14.0	0.0, 28.0
n	131	28	159
Change from Baseline			
Mean (SD)	-5.56 (7.093)	-3.87 (4.394)	-5.26 (6.716)
LS Mean (SE) [1]	-5.37 (0.560)	-3.61 (0.683)	-5.09 (0.482)
95% CI [1]	-6.47, -4.26	-5.03, -2.19	-6.04, -4.14
Median	-5.00	-4.93	-5.00
Q1, Q3	-11.00, -0.54	-7.00, -1.81	-9.00, -0.78
Min, Max	-23.0, 19.0	-11.0, 6.7	-23.0, 19.0
n	131	28	159

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-5
Monthly Acute Medication Days: Summary of Baseline, Post-baseline and Change from Baseline
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 45 - 48			
Mean (SD)	11.54 (7.972)	3.00 (3.112)	10.03 (8.037)
Median	10.00	2.04	8.15
Q1, Q3	5.38, 17.00	0.50, 4.50	3.00, 16.00
Min, Max	0.0, 28.0	0.0, 11.0	0.0, 28.0
n	130	28	158
Change from Baseline			
Mean (SD)	-5.10 (7.427)	-3.80 (3.350)	-4.87 (6.892)
LS Mean (SE) [1]	-4.92 (0.564)	-3.62 (0.580)	-4.73 (0.482)
95% CI [1]	-6.04, -3.80	-4.82, -2.43	-5.68, -3.77
Median	-5.00	-4.00	-4.67
Q1, Q3	-10.00, -1.00	-5.50, -1.50	-9.00, -1.00
Min, Max	-24.0, 18.0	-12.0, 2.2	-24.0, 18.0
n	130	28	158
Week 49 - 52			
Mean (SD)	11.38 (7.905)	2.83 (2.980)	9.86 (7.975)
Median	10.37	2.15	8.30
Q1, Q3	5.19, 16.59	0.50, 3.00	3.00, 15.56
Min, Max	0.0, 28.0	0.0, 12.0	0.0, 28.0
n	130	28	158
Change from Baseline			
Mean (SD)	-5.26 (7.425)	-3.97 (3.354)	-5.03 (6.890)
LS Mean (SE) [1]	-5.11 (0.565)	-3.86 (0.543)	-4.91 (0.482)
95% CI [1]	-6.22, -3.99	-4.98, -2.74	-5.86, -3.96
Median	-5.79	-4.00	-5.39
Q1, Q3	-9.74, -1.59	-6.00, -2.00	-8.81, -1.77
Min, Max	-26.0, 22.4	-10.0, 5.4	-26.0, 22.4
n	130	28	158

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

表10

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Baseline			
Mean (SD)	24.35 (13.194)	11.24 (7.386)	22.16 (13.331)
Median	21.99	9.86	20.15
Q1, Q3	13.98, 32.14	5.30, 13.62	12.43, 30.22
Min, Max	0.2, 71.5	1.9, 28.8	0.2, 71.5
n	145	29	174
Week 1 - 4			
Mean (SD)	14.11 (11.854)	5.35 (4.758)	12.66 (11.466)
Median	10.88	3.92	9.44
Q1, Q3	4.52, 22.32	1.73, 8.47	3.93, 19.23
Min, Max	0.0, 53.7	0.0, 15.9	0.0, 53.7
n	147	29	176
Change from Baseline			
Mean (SD)	-10.28 (11.940)	-5.89 (7.475)	-9.54 (11.416)
LS Mean (SE) [1]	-10.06 (0.829)	-5.83 (0.857)	-9.33 (0.710)
95% CI [1]	-11.70, -8.43	-7.58, -4.07	-10.74, -7.93
Median	-9.46	-5.10	-8.40
Q1, Q3	-17.29, -2.71	-8.98, -2.12	-14.85, -2.71
Min, Max	-48.3, 19.5	-21.0, 10.9	-48.3, 19.5
n	144	29	173

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 5 - 8			
Mean (SD)	13.70 (11.775)	4.69 (4.181)	12.29 (11.412)
Median	10.43	3.98	8.27
Q1, Q3	4.09, 20.00	0.74, 7.67	3.54, 17.52
Min, Max	0.0, 56.6	0.0, 17.4	0.0, 56.6
n	145	27	172
Change from Baseline			
Mean (SD)	-10.40 (11.659)	-6.75 (6.709)	-9.82 (11.080)
LS Mean (SE) [1]	-10.22 (0.823)	-6.32 (0.728)	-9.53 (0.702)
95% CI [1]	-11.85, -8.59	-7.82, -4.82	-10.91, -8.14
Median	-9.57	-6.17	-8.47
Q1, Q3	-16.56, -3.32	-9.67, -3.41	-15.61, -3.36
Min, Max	-44.1, 16.3	-25.9, 5.0	-44.1, 16.3
n	141	27	168
Week 9 - 12			
Mean (SD)	13.98 (12.204)	4.56 (3.496)	12.44 (11.772)
Median	10.43	3.91	8.88
Q1, Q3	4.88, 20.55	1.53, 6.53	3.78, 16.67
Min, Max	0.0, 55.9	0.0, 12.8	0.0, 55.9
n	143	28	171
Change from Baseline			
Mean (SD)	-9.93 (11.673)	-6.83 (7.015)	-9.41 (11.074)
LS Mean (SE) [1]	-9.77 (0.841)	-6.54 (0.635)	-9.18 (0.719)
95% CI [1]	-11.43, -8.11	-7.85, -5.23	-10.59, -7.76
Median	-8.14	-6.35	-7.51
Q1, Q3	-16.48, -3.64	-9.22, -2.80	-15.13, -3.26
Min, Max	-43.0, 22.7	-25.1, 4.4	-43.0, 22.7
n	139	28	167

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 13 - 16			
Mean (SD)	13.89 (12.107)	4.16 (4.044)	12.29 (11.748)
Median	10.61	3.77	7.68
Q1, Q3	4.44, 20.31	0.88, 5.33	3.55, 18.32
Min, Max	0.0, 46.9	0.0, 18.1	0.0, 46.9
n	137	27	164
Change from Baseline			
Mean (SD)	-10.53 (12.269)	-7.28 (7.360)	-9.98 (11.632)
LS Mean (SE) [1]	-9.98 (0.852)	-7.08 (0.747)	-9.42 (0.731)
95% CI [1]	-11.67, -8.30	-8.62, -5.54	-10.87, -7.98
Median	-10.20	-7.00	-9.32
Q1, Q3	-17.45, -2.40	-10.41, -2.10	-16.24, -2.25
Min, Max	-47.3, 18.9	-24.3, 4.8	-47.3, 18.9
n	133	27	160
Week 17 - 20			
Mean (SD)	13.74 (12.265)	3.98 (2.928)	12.06 (11.811)
Median	10.33	3.17	8.35
Q1, Q3	3.57, 21.31	1.99, 5.53	2.94, 18.16
Min, Max	0.0, 56.8	0.0, 10.7	0.0, 56.8
n	135	28	163
Change from Baseline			
Mean (SD)	-10.71 (12.375)	-7.40 (7.544)	-10.13 (11.723)
LS Mean (SE) [1]	-10.18 (0.882)	-7.17 (0.557)	-9.62 (0.753)
95% CI [1]	-11.93, -8.44	-8.32, -6.03	-11.11, -8.13
Median	-9.97	-6.61	-9.11
Q1, Q3	-17.31, -2.72	-9.94, -1.89	-16.81, -2.59
Min, Max	-54.9, 25.9	-24.5, 7.7	-54.9, 25.9
n	132	28	160

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 21 - 24			
Mean (SD)	12.79 (11.333)	3.18 (2.978)	11.21 (11.017)
Median	9.22	2.96	7.90
Q1, Q3	3.93, 19.89	0.92, 4.29	2.84, 16.31
Min, Max	0.0, 51.6	0.0, 11.4	0.0, 51.6
n	132	26	158
Change from Baseline			
Mean (SD)	-11.63 (11.858)	-8.03 (8.415)	-11.03 (11.410)
LS Mean (SE) [1]	-10.72 (0.834)	-7.84 (0.587)	-10.16 (0.719)
95% CI [1]	-12.37, -9.07	-9.05, -6.63	-11.58, -8.74
Median	-10.35	-7.07	-9.88
Q1, Q3	-18.22, -4.48	-10.95, -1.93	-17.45, -3.64
Min, Max	-52.2, 17.5	-24.8, 9.5	-52.2, 17.5
n	129	26	155
Week 25 - 28			
Mean (SD)	12.79 (11.743)	3.04 (3.118)	11.17 (11.385)
Median	8.83	2.18	7.29
Q1, Q3	3.57, 20.83	0.95, 3.78	2.43, 16.42
Min, Max	0.0, 50.0	0.0, 11.1	0.0, 50.0
n	130	26	156
Change from Baseline			
Mean (SD)	-11.49 (12.137)	-8.17 (7.244)	-10.93 (11.502)
LS Mean (SE) [1]	-10.89 (0.868)	-8.00 (0.586)	-10.33 (0.740)
95% CI [1]	-12.60, -9.17	-9.20, -6.79	-11.80, -8.87
Median	-10.78	-7.10	-9.88
Q1, Q3	-19.69, -3.98	-12.05, -3.63	-17.62, -3.87
Min, Max	-46.9, 17.4	-26.3, 8.7	-46.9, 17.4
n	127	26	153

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 29 - 32			
Mean (SD)	13.13 (11.960)	3.77 (4.261)	11.53 (11.573)
Median	9.39	2.04	7.90
Q1, Q3	3.30, 21.07	0.80, 5.52	2.22, 18.13
Min, Max	0.0, 52.0	0.0, 18.1	0.0, 52.0
n	131	27	158
Change from Baseline			
Mean (SD)	-11.42 (13.193)	-7.39 (8.376)	-10.72 (12.563)
LS Mean (SE) [1]	-10.72 (0.917)	-7.18 (0.848)	-10.07 (0.790)
95% CI [1]	-12.53, -8.91	-8.93, -5.43	-11.63, -8.51
Median	-10.79	-6.63	-10.07
Q1, Q3	-18.47, -3.75	-10.68, -2.01	-18.08, -3.50
Min, Max	-54.9, 23.4	-27.2, 9.8	-54.9, 23.4
n	129	27	156
Week 33 - 36			
Mean (SD)	13.15 (12.738)	3.04 (2.884)	11.44 (12.267)
Median	9.34	2.40	7.39
Q1, Q3	3.40, 18.65	0.41, 4.08	2.45, 16.94
Min, Max	0.0, 63.4	0.0, 10.9	0.0, 63.4
n	128	26	154
Change from Baseline			
Mean (SD)	-10.87 (13.409)	-8.17 (7.957)	-10.41 (12.663)
LS Mean (SE) [1]	-10.35 (0.962)	-7.97 (0.572)	-9.88 (0.823)
95% CI [1]	-12.25, -8.45	-9.15, -6.79	-11.50, -8.25
Median	-10.39	-7.74	-9.85
Q1, Q3	-19.78, -2.78	-10.41, -2.70	-17.84, -2.74
Min, Max	-54.9, 28.8	-26.4, 9.0	-54.9, 28.8
n	126	26	152

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 37 - 40			
Mean (SD)	13.13 (12.702)	3.00 (4.092)	11.35 (12.274)
Median	9.15	0.95	7.08
Q1, Q3	3.47, 20.12	0.14, 3.85	2.50, 15.54
Min, Max	0.0, 58.6	0.0, 15.8	0.0, 58.6
n	127	27	154
Change from Baseline			
Mean (SD)	-10.08 (12.995)	-8.17 (9.301)	-9.74 (12.410)
LS Mean (SE) [1]	-9.95 (0.979)	-7.93 (0.794)	-9.56 (0.847)
95% CI [1]	-11.88, -8.01	-9.57, -6.29	-11.23, -7.89
Median	-9.82	-7.31	-9.14
Q1, Q3	-17.50, -3.41	-12.74, -2.51	-16.72, -3.18
Min, Max	-46.1, 34.2	-27.8, 13.9	-46.1, 34.2
n	124	27	151
Week 41 - 44			
Mean (SD)	12.84 (11.480)	4.20 (6.278)	11.37 (11.240)
Median	9.37	2.30	7.76
Q1, Q3	3.89, 19.18	0.24, 5.81	2.74, 17.55
Min, Max	0.0, 52.2	0.0, 29.9	0.0, 52.2
n	127	26	153
Change from Baseline			
Mean (SD)	-11.01 (12.092)	-7.02 (10.675)	-10.33 (11.923)
LS Mean (SE) [1]	-10.58 (0.855)	-6.51 (1.238)	-9.87 (0.761)
95% CI [1]	-12.27, -8.89	-9.07, -3.96	-11.38, -8.37
Median	-9.58	-6.56	-9.38
Q1, Q3	-17.45, -3.55	-11.74, -3.20	-17.03, -3.36
Min, Max	-46.4, 25.0	-24.8, 28.1	-46.4, 28.1
n	125	26	151

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.1
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Performance of Daily Activities Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 45 - 48			
Mean (SD)	13.24 (12.472)	3.35 (4.933)	11.51 (12.104)
Median	9.29	1.43	7.77
Q1, Q3	3.20, 20.92	0.00, 4.24	2.24, 16.88
Min, Max	0.0, 56.6	0.0, 21.5	0.0, 56.6
n	123	26	149
Change from Baseline			
Mean (SD)	-9.84 (12.623)	-7.13 (8.803)	-9.36 (12.055)
LS Mean (SE) [1]	-9.83 (0.946)	-7.82 (1.000)	-9.40 (0.824)
95% CI [1]	-11.70, -7.96	-9.89, -5.75	-11.03, -7.78
Median	-9.38	-7.84	-8.78
Q1, Q3	-17.32, -2.63	-11.43, -2.59	-15.83, -2.59
Min, Max	-47.1, 24.9	-24.8, 19.6	-47.1, 24.9
n	121	26	147
Week 49 - 52			
Mean (SD)	12.96 (11.892)	4.21 (5.399)	11.41 (11.509)
Median	9.39	3.01	7.50
Q1, Q3	3.81, 21.03	0.86, 4.91	2.69, 17.83
Min, Max	0.0, 52.1	0.0, 25.3	0.0, 52.1
n	121	26	147
Change from Baseline			
Mean (SD)	-9.95 (12.425)	-6.28 (8.884)	-9.30 (11.925)
LS Mean (SE) [1]	-9.94 (0.903)	-6.83 (1.081)	-9.35 (0.791)
95% CI [1]	-11.72, -8.15	-9.06, -4.60	-10.92, -7.79
Median	-8.50	-6.05	-8.18
Q1, Q3	-17.55, -3.77	-10.41, -2.08	-16.57, -3.55
Min, Max	-49.8, 24.8	-22.7, 23.4	-49.8, 24.8
n	119	26	145

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

表11

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Baseline			
Mean (SD)	24.10 (13.003)	10.81 (6.829)	21.89 (13.151)
Median	22.88	9.11	19.49
Q1, Q3	15.19, 32.38	4.82, 15.21	11.07, 29.64
Min, Max	0.4, 66.8	2.7, 27.9	0.4, 66.8
n	145	29	174
Week 1 - 4			
Mean (SD)	13.71 (11.246)	5.42 (5.213)	12.34 (10.926)
Median	10.18	4.00	8.52
Q1, Q3	5.36, 21.00	1.92, 7.60	3.96, 18.33
Min, Max	0.4, 59.5	0.0, 20.4	0.0, 59.5
n	147	29	176
Change from Baseline			
Mean (SD)	-10.42 (11.901)	-5.40 (7.239)	-9.58 (11.394)
LS Mean (SE) [1]	-10.16 (0.802)	-5.45 (0.940)	-9.35 (0.689)
95% CI [1]	-11.75, -8.58	-7.37, -3.52	-10.71, -7.99
Median	-8.93	-5.21	-8.20
Q1, Q3	-17.82, -3.43	-9.11, -2.68	-16.81, -3.26
Min, Max	-48.0, 27.3	-17.7, 15.7	-48.0, 27.3
n	144	29	173

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 5 - 8			
Mean (SD)	13.58 (11.118)	5.07 (5.310)	12.24 (10.864)
Median	9.80	3.39	8.66
Q1, Q3	5.00, 18.89	0.93, 7.83	3.82, 17.56
Min, Max	0.2, 55.4	0.0, 22.7	0.0, 55.4
n	145	27	172
Change from Baseline			
Mean (SD)	-10.27 (11.640)	-6.11 (6.094)	-9.60 (11.032)
LS Mean (SE) [1]	-10.03 (0.791)	-5.70 (0.890)	-9.26 (0.679)
95% CI [1]	-11.60, -8.47	-7.53, -3.86	-10.60, -7.92
Median	-8.68	-5.57	-8.38
Q1, Q3	-17.16, -2.13	-9.29, -3.26	-15.80, -3.01
Min, Max	-44.4, 14.6	-23.2, 8.6	-44.4, 14.6
n	141	27	168
Week 9 - 12			
Mean (SD)	13.89 (11.833)	4.94 (4.381)	12.43 (11.448)
Median	10.56	3.75	9.23
Q1, Q3	5.23, 17.37	2.50, 7.84	3.93, 16.25
Min, Max	0.0, 58.9	0.0, 21.3	0.0, 58.9
n	143	28	171
Change from Baseline			
Mean (SD)	-9.83 (11.661)	-6.14 (5.970)	-9.21 (10.989)
LS Mean (SE) [1]	-9.70 (0.820)	-5.87 (0.740)	-8.99 (0.699)
95% CI [1]	-11.32, -8.08	-7.40, -4.35	-10.37, -7.61
Median	-8.93	-5.54	-7.96
Q1, Q3	-15.98, -3.10	-8.35, -2.34	-14.95, -3.07
Min, Max	-43.3, 26.8	-22.5, 4.6	-43.3, 26.8
n	139	28	167

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 13 - 16			
Mean (SD)	13.61 (11.277)	4.38 (4.277)	12.09 (10.991)
Median	10.80	3.46	9.64
Q1, Q3	4.82, 18.57	0.83, 5.80	3.54, 17.27
Min, Max	0.0, 49.8	0.0, 17.3	0.0, 49.8
n	137	27	164
Change from Baseline			
Mean (SD)	-10.39 (11.938)	-6.80 (6.163)	-9.78 (11.240)
LS Mean (SE) [1]	-10.00 (0.790)	-6.60 (0.739)	-9.36 (0.677)
95% CI [1]	-11.57, -8.44	-8.12, -5.08	-10.69, -8.02
Median	-9.66	-6.07	-8.61
Q1, Q3	-18.06, -3.05	-10.54, -2.14	-16.67, -2.23
Min, Max	-45.5, 16.8	-21.8, 2.0	-45.5, 16.8
n	133	27	160
Week 17 - 20			
Mean (SD)	13.59 (11.419)	4.28 (2.966)	11.99 (11.034)
Median	10.40	3.56	8.21
Q1, Q3	5.40, 20.56	1.96, 6.24	3.40, 16.07
Min, Max	0.0, 55.5	0.0, 10.8	0.0, 55.5
n	135	28	163
Change from Baseline			
Mean (SD)	-10.47 (12.452)	-6.80 (6.739)	-9.83 (11.723)
LS Mean (SE) [1]	-10.02 (0.840)	-6.58 (0.557)	-9.39 (0.716)
95% CI [1]	-11.68, -8.36	-7.72, -5.43	-10.80, -7.98
Median	-9.36	-4.98	-8.63
Q1, Q3	-17.95, -3.00	-10.18, -2.63	-16.28, -2.90
Min, Max	-52.7, 31.2	-22.7, 4.7	-52.7, 31.2
n	132	28	160

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 21 - 24			
Mean (SD)	12.96 (10.971)	3.29 (2.981)	11.37 (10.715)
Median	9.53	2.73	8.09
Q1, Q3	5.21, 18.72	1.04, 4.47	3.21, 15.00
Min, Max	0.0, 58.0	0.0, 11.7	0.0, 58.0
n	132	26	158
Change from Baseline			
Mean (SD)	-11.13 (11.747)	-7.66 (7.890)	-10.55 (11.247)
LS Mean (SE) [1]	-10.35 (0.809)	-7.50 (0.578)	-9.79 (0.702)
95% CI [1]	-11.95, -8.76	-8.69, -6.31	-11.18, -8.41
Median	-10.18	-6.14	-9.46
Q1, Q3	-18.86, -3.87	-12.43, -2.71	-17.71, -3.83
Min, Max	-50.1, 25.9	-26.6, 8.3	-50.1, 25.9
n	129	26	155
Week 25 - 28			
Mean (SD)	12.96 (10.944)	3.19 (3.108)	11.33 (10.705)
Median	9.91	2.16	8.23
Q1, Q3	4.60, 19.12	0.71, 4.82	2.84, 15.51
Min, Max	0.0, 51.8	0.0, 10.9	0.0, 51.8
n	130	26	156
Change from Baseline			
Mean (SD)	-11.07 (11.656)	-7.76 (6.612)	-10.51 (11.017)
LS Mean (SE) [1]	-10.54 (0.803)	-7.51 (0.586)	-9.99 (0.689)
95% CI [1]	-12.13, -8.96	-8.71, -6.30	-11.35, -8.63
Median	-9.63	-7.18	-9.03
Q1, Q3	-19.46, -5.40	-10.71, -4.63	-18.07, -5.00
Min, Max	-42.7, 19.6	-25.2, 6.2	-42.7, 19.6
n	127	26	153

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 29 - 32			
Mean (SD)	13.09 (11.223)	3.91 (4.383)	11.52 (10.932)
Median	10.18	1.67	8.93
Q1, Q3	4.11, 19.04	0.80, 6.07	3.04, 16.15
Min, Max	0.0, 50.0	0.0, 17.7	0.0, 50.0
n	131	27	158
Change from Baseline			
Mean (SD)	-11.07 (12.956)	-6.94 (7.860)	-10.36 (12.306)
LS Mean (SE) [1]	-10.55 (0.872)	-6.71 (0.871)	-9.85 (0.755)
95% CI [1]	-12.27, -8.82	-8.50, -4.91	-11.34, -8.36
Median	-9.70	-5.00	-8.67
Q1, Q3	-20.40, -3.39	-10.71, -2.14	-19.55, -2.75
Min, Max	-53.3, 23.2	-24.8, 6.6	-53.3, 23.2
n	129	27	156
Week 33 - 36			
Mean (SD)	13.12 (11.785)	3.18 (2.973)	11.44 (11.432)
Median	9.09	2.72	7.40
Q1, Q3	4.00, 19.00	0.93, 4.05	3.33, 15.71
Min, Max	0.0, 51.6	0.0, 11.2	0.0, 51.6
n	128	26	154
Change from Baseline			
Mean (SD)	-10.63 (12.814)	-7.77 (7.445)	-10.14 (12.094)
LS Mean (SE) [1]	-10.29 (0.885)	-7.63 (0.581)	-9.76 (0.762)
95% CI [1]	-12.04, -8.54	-8.83, -6.44	-11.26, -8.26
Median	-10.41	-7.00	-9.77
Q1, Q3	-19.37, -1.93	-10.71, -3.07	-18.02, -2.38
Min, Max	-53.3, 25.4	-27.9, 7.8	-53.3, 25.4
n	126	26	152

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 37 - 40			
Mean (SD)	13.10 (11.583)	2.95 (3.684)	11.32 (11.304)
Median	9.46	0.95	7.55
Q1, Q3	4.42, 20.00	0.19, 5.38	3.33, 15.00
Min, Max	0.0, 57.9	0.0, 12.8	0.0, 57.9
n	127	27	154
Change from Baseline			
Mean (SD)	-9.88 (12.797)	-7.89 (8.336)	-9.53 (12.121)
LS Mean (SE) [1]	-9.84 (0.902)	-7.77 (0.712)	-9.44 (0.784)
95% CI [1]	-11.63, -8.06	-9.24, -6.31	-10.98, -7.89
Median	-9.00	-6.25	-8.39
Q1, Q3	-18.08, -3.04	-11.07, -3.08	-15.71, -3.08
Min, Max	-44.5, 32.1	-27.5, 9.4	-44.5, 32.1
n	124	27	151
Week 41 - 44			
Mean (SD)	12.91 (10.580)	4.35 (6.459)	11.46 (10.492)
Median	10.56	2.26	8.39
Q1, Q3	4.69, 18.64	0.42, 5.36	3.33, 15.93
Min, Max	0.0, 53.6	0.0, 29.6	0.0, 53.6
n	127	26	153
Change from Baseline			
Mean (SD)	-10.55 (12.039)	-6.60 (10.062)	-9.87 (11.787)
LS Mean (SE) [1]	-10.23 (0.810)	-6.20 (1.264)	-9.51 (0.727)
95% CI [1]	-11.83, -8.62	-8.81, -3.60	-10.94, -8.07
Median	-9.27	-7.05	-8.52
Q1, Q3	-18.48, -3.10	-11.41, -3.57	-17.47, -3.10
Min, Max	-41.0, 22.5	-26.7, 26.2	-41.0, 26.2
n	125	26	151

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-7.2
AIM-D (Activity Impairment in Migraine - Diary): Summary of Baseline, Post-baseline and Change from Baseline in Monthly Physical Impairment Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 45 - 48			
Mean (SD)	13.31 (11.537)	3.54 (5.180)	11.60 (11.317)
Median	9.64	1.43	8.65
Q1, Q3	4.82, 17.60	0.00, 4.29	3.21, 16.25
Min, Max	0.0, 56.4	0.0, 21.6	0.0, 56.4
n	123	26	149
Change from Baseline			
Mean (SD)	-9.43 (12.828)	-6.71 (8.289)	-8.95 (12.170)
LS Mean (SE) [1]	-9.44 (0.912)	-7.56 (1.057)	-9.00 (0.799)
95% CI [1]	-11.24, -7.63	-9.74, -5.38	-10.57, -7.42
Median	-8.60	-6.50	-8.24
Q1, Q3	-17.99, -2.14	-10.54, -2.13	-16.13, -2.13
Min, Max	-44.6, 30.1	-26.4, 18.2	-44.6, 30.1
n	121	26	147
Week 49 - 52			
Mean (SD)	13.10 (11.461)	4.28 (5.485)	11.54 (11.159)
Median	9.78	2.59	7.80
Q1, Q3	4.81, 18.33	0.54, 5.38	3.39, 16.52
Min, Max	0.0, 60.4	0.0, 25.0	0.0, 60.4
n	121	26	147
Change from Baseline			
Mean (SD)	-9.35 (12.874)	-5.98 (8.333)	-8.74 (12.230)
LS Mean (SE) [1]	-9.43 (0.913)	-6.68 (1.102)	-8.87 (0.801)
95% CI [1]	-11.24, -7.63	-8.95, -4.41	-10.45, -7.29
Median	-8.44	-5.18	-8.08
Q1, Q3	-18.75, -1.15	-10.54, -2.95	-17.73, -1.75
Min, Max	-48.5, 28.2	-25.7, 21.6	-48.5, 28.2
n	119	26	145

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

表12

Table 14.2-16

MSQ (Migraine Specific Quality of Life Questionnaire): Summary of Baseline, Post-baseline and Change from Baseline in the Role Function Restrictive Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Baseline			
Mean (SD)	56.93 (17.551)	64.10 (14.887)	58.13 (17.305)
Median	60.00	65.71	60.00
Q1, Q3	45.71, 68.57	60.00, 77.14	48.57, 68.57
Min, Max	8.6, 94.3	20.0, 85.7	8.6, 94.3
n	150	30	180
Week 12			
Mean (SD)	74.42 (16.153)	80.57 (15.710)	75.44 (16.201)
Median	80.00	82.86	80.00
Q1, Q3	62.86, 85.71	80.00, 91.43	65.71, 85.71
Min, Max	25.7, 100.0	37.1, 100.0	25.7, 100.0
n	150	30	180
Change from Baseline			
Mean (SD)	17.49 (18.783)	16.48 (15.517)	17.32 (18.244)
LS Mean (SE) [1]	17.26 (1.224)	15.78 (2.562)	16.96 (1.106)
95% CI [1]	14.84, 19.68	10.53, 21.03	14.78, 19.15
Median	17.14	18.57	17.14
Q1, Q3	5.71, 31.43	5.71, 25.71	5.71, 31.43
Min, Max	-42.9, 65.7	-22.9, 51.4	-42.9, 65.7
n	150	30	180

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-16
MSQ (Migraine Specific Quality of Life Questionnaire): Summary of Baseline, Post-baseline and Change from Baseline in the Role Function Restrictive Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 24			
Mean (SD)	73.11 (17.474)	82.96 (14.718)	74.81 (17.394)
Median	77.14	82.86	77.14
Q1, Q3	60.00, 85.71	71.43, 97.14	62.86, 85.71
Min, Max	20.0, 100.0	54.3, 100.0	20.0, 100.0
n	139	29	168
Change from Baseline			
Mean (SD)	16.16 (17.628)	17.34 (17.645)	16.36 (17.584)
LS Mean (SE) [1]	15.65 (1.273)	17.11 (2.732)	15.87 (1.165)
95% CI [1]	13.14, 18.17	11.51, 22.71	13.57, 18.17
Median	17.14	14.29	14.29
Q1, Q3	5.71, 28.57	5.71, 28.57	5.71, 28.57
Min, Max	-22.9, 60.0	-22.9, 60.0	-22.9, 60.0
n	139	29	168
Week 36			
Mean (SD)	74.11 (18.093)	80.61 (19.493)	75.24 (18.447)
Median	77.14	82.86	80.00
Q1, Q3	60.00, 85.71	74.29, 95.71	62.86, 88.57
Min, Max	20.0, 100.0	5.7, 100.0	5.7, 100.0
n	133	28	161
Change from Baseline			
Mean (SD)	16.50 (18.803)	14.08 (20.690)	16.08 (19.099)
LS Mean (SE) [1]	16.06 (1.388)	14.10 (3.653)	15.68 (1.307)
95% CI [1]	13.31, 18.80	6.61, 21.60	13.10, 18.26
Median	14.29	17.14	14.29
Q1, Q3	5.71, 28.57	4.29, 25.71	5.71, 28.57
Min, Max	-34.3, 77.1	-54.3, 48.6	-54.3, 77.1
n	133	28	161

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-16
MSQ (Migraine Specific Quality of Life Questionnaire): Summary of Baseline, Post-baseline and Change from Baseline in the Role Function Restrictive Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 48			
Mean (SD)	73.22 (16.414)	87.96 (12.810)	75.81 (16.777)
Median	74.29	90.00	80.00
Q1, Q3	62.86, 85.71	80.00, 100.00	65.71, 88.57
Min, Max	20.0, 100.0	60.0, 100.0	20.0, 100.0
n	131	28	159
Change from Baseline			
Mean (SD)	15.38 (18.089)	21.43 (17.152)	16.44 (18.024)
LS Mean (SE) [1]	15.02 (1.274)	21.79 (2.461)	16.04 (1.190)
95% CI [1]	12.50, 17.54	16.74, 26.84	13.69, 18.39
Median	14.29	20.00	17.14
Q1, Q3	2.86, 25.71	8.57, 35.71	5.71, 28.57
Min, Max	-31.4, 77.1	-17.1, 60.0	-31.4, 77.1
n	131	28	159
Week 52			
Mean (SD)	74.09 (17.870)	84.59 (14.240)	75.95 (17.705)
Median	77.14	85.71	80.00
Q1, Q3	62.86, 85.71	71.43, 100.00	65.71, 88.57
Min, Max	20.0, 100.0	60.0, 100.0	20.0, 100.0
n	130	28	158
Change from Baseline			
Mean (SD)	16.37 (18.648)	18.06 (16.515)	16.67 (18.250)
LS Mean (SE) [1]	16.02 (1.378)	17.62 (2.735)	16.22 (1.242)
95% CI [1]	13.29, 18.74	12.00, 23.23	13.77, 18.67
Median	14.29	17.14	15.71
Q1, Q3	2.86, 28.57	5.71, 28.57	5.71, 28.57
Min, Max	-34.3, 60.0	-11.4, 60.0	-34.3, 60.0
n	130	28	158

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

Table 14.2-16

MSQ (Migraine Specific Quality of Life Questionnaire): Summary of Baseline, Post-baseline and Change from Baseline in the Role Function Restrictive Domain Score
Modified Intent-to-Treat Population

Visit Statistics	3101-303-002 CM Completers (N=150)	De Novo EM Participants (N=30)	Total (N=180)
Week 56 (Safety Follow-up)			
Mean (SD)	61.48 (18.438)	67.71 (17.374)	62.52 (18.365)
Median	60.00	68.57	62.86
Q1, Q3	51.43, 74.29	60.00, 82.86	51.43, 77.14
Min, Max	5.7, 100.0	28.6, 94.3	5.7, 100.0
n	149	30	179
Change from Baseline			
Mean (SD)	4.72 (18.599)	3.62 (17.531)	4.53 (18.381)
LS Mean (SE) [1]	4.44 (1.341)	2.88 (2.947)	4.16 (1.216)
95% CI [1]	1.79, 7.09	-3.15, 8.92	1.77, 6.56
Median	5.71	5.71	5.71
Q1, Q3	-5.71, 14.29	-11.43, 14.29	-5.71, 14.29
Min, Max	-42.9, 51.4	-31.4, 28.6	-42.9, 51.4
n	149	30	179

[1] LS Mean, SE and 95% CI derived from an MMRM with visit as a categorical fixed effect, baseline score, and a baseline-by-visit interaction as covariates.
For 3103-303-002 Completers, baseline is the baseline value in the lead-in study (3101-303-002).

表13

Table 14.3-1.1
Adverse Events: Overall Number (%) of Participants with Adverse Events
Safety Population

	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
All Treatment-Emergent Adverse Events (TEAE)	137 (88.4)	28 (90.3)	165 (88.7)
Treatment-Related TEAE	25 (16.1)	6 (19.4)	31 (16.7)
Treatment-Emergent Serious AE (TESAE)	7 (4.5)	0 (0.0)	7 (3.8)
Treatment-Related TESAE	0 (0.0)	0 (0.0)	0 (0.0)
TEAE Leading to Study Intervention Discontinuation	9 (5.8)	0 (0.0)	9 (4.8)
Deaths	0 (0.0)	0 (0.0)	0 (0.0)

表14

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Participants with at least one TEAE	137 (88.4)	28 (90.3)	165 (88.7)
血液およびリンパ系障害	4 (2.6)	0 (0.0)	4 (2.2)
貧血	1 (0.6)	0 (0.0)	1 (0.5)
鉄欠乏性貧血	1 (0.6)	0 (0.0)	1 (0.5)
リンパ節痛	1 (0.6)	0 (0.0)	1 (0.5)
リンパ節炎	1 (0.6)	0 (0.0)	1 (0.5)
リンパ節症	1 (0.6)	0 (0.0)	1 (0.5)
心臓障害	2 (1.3)	0 (0.0)	2 (1.1)
動悸	1 (0.6)	0 (0.0)	1 (0.5)
上室性期外収縮	1 (0.6)	0 (0.0)	1 (0.5)
耳および迷路障害	11 (7.1)	2 (6.5)	13 (7.0)
回転性めまい	6 (3.9)	1 (3.2)	7 (3.8)
耳鳴	2 (1.3)	1 (3.2)	3 (1.6)
耳痛	2 (1.3)	0 (0.0)	2 (1.1)
突発性難聴	2 (1.3)	0 (0.0)	2 (1.1)
内分泌障害	2 (1.3)	0 (0.0)	2 (1.1)
高プロラクチン血症	1 (0.6)	0 (0.0)	1 (0.5)
甲状腺機能亢進症	1 (0.6)	0 (0.0)	1 (0.5)
眼障害	15 (9.7)	4 (12.9)	19 (10.2)
ドライアイ	4 (2.6)	2 (6.5)	6 (3.2)
眼精疲労	3 (1.9)	1 (3.2)	4 (2.2)
アレルギー性結膜炎	4 (2.6)	0 (0.0)	4 (2.2)
眼瞼痙攣	1 (0.6)	0 (0.0)	1 (0.5)
霰粒腫	1 (0.6)	0 (0.0)	1 (0.5)
結膜充血	0 (0.0)	1 (3.2)	1 (0.5)
角膜びらん	1 (0.6)	0 (0.0)	1 (0.5)
眼の炎症	1 (0.6)	0 (0.0)	1 (0.5)
眼瞼下垂	1 (0.6)	0 (0.0)	1 (0.5)
仮性近視	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
網膜出血	1 (0.6)	0 (0.0)	1 (0.5)
強膜炎	0 (0.0)	1 (3.2)	1 (0.5)
胃腸障害	53 (34.2)	14 (45.2)	67 (36.0)
便秘	17 (11.0)	4 (12.9)	21 (11.3)
下痢	8 (5.2)	2 (6.5)	10 (5.4)
上腹部痛	6 (3.9)	2 (6.5)	8 (4.3)
悪心	7 (4.5)	1 (3.2)	8 (4.3)
齲歯	4 (2.6)	1 (3.2)	5 (2.7)
口内炎	3 (1.9)	2 (6.5)	5 (2.7)
腹部不快感	3 (1.9)	1 (3.2)	4 (2.2)
腹痛	4 (2.6)	0 (0.0)	4 (2.2)
胃食道逆流性疾患	4 (2.6)	0 (0.0)	4 (2.2)
歯痛	3 (1.9)	1 (3.2)	4 (2.2)
小腸炎	2 (1.3)	1 (3.2)	3 (1.6)
胃炎	3 (1.9)	0 (0.0)	3 (1.6)
痔核	3 (1.9)	0 (0.0)	3 (1.6)
消化不良	2 (1.3)	0 (0.0)	2 (1.1)
腹部膨満	0 (0.0)	1 (3.2)	1 (0.5)
下腹部痛	0 (0.0)	1 (3.2)	1 (0.5)
口唇のひび割れ	1 (0.6)	0 (0.0)	1 (0.5)
大腸炎	1 (0.6)	0 (0.0)	1 (0.5)
胃ポリープ	1 (0.6)	0 (0.0)	1 (0.5)
舌炎	0 (0.0)	1 (3.2)	1 (0.5)
裂孔ヘルニア	1 (0.6)	0 (0.0)	1 (0.5)
非感染性歯肉炎	1 (0.6)	0 (0.0)	1 (0.5)
がま腫	0 (0.0)	1 (3.2)	1 (0.5)
埋伏歯	1 (0.6)	0 (0.0)	1 (0.5)
嘔吐	1 (0.6)	0 (0.0)	1 (0.5)
一般・全身障害および投与部位の状態	65 (41.9)	2 (6.5)	67 (36.0)
発熱	52 (33.5)	2 (6.5)	54 (29.0)
倦怠感	9 (5.8)	1 (3.2)	10 (5.4)
疲労	3 (1.9)	0 (0.0)	3 (1.6)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
注射部位疼痛	3 (1.9)	0 (0.0)	3 (1.6)
非心臓性胸痛	3 (1.9)	0 (0.0)	3 (1.6)
ワクチン接種部位腫脹	3 (1.9)	0 (0.0)	3 (1.6)
末梢性浮腫	2 (1.3)	0 (0.0)	2 (1.1)
顔面浮腫	1 (0.6)	0 (0.0)	1 (0.5)
顔面痛	1 (0.6)	0 (0.0)	1 (0.5)
低体温	1 (0.6)	0 (0.0)	1 (0.5)
注射部位腫脹	1 (0.6)	0 (0.0)	1 (0.5)
疼痛	1 (0.6)	0 (0.0)	1 (0.5)
肝胆道系障害	1 (0.6)	0 (0.0)	1 (0.5)
胆石症	1 (0.6)	0 (0.0)	1 (0.5)
免疫系障害	1 (0.6)	0 (0.0)	1 (0.5)
季節性アレルギー	1 (0.6)	0 (0.0)	1 (0.5)
感染症および寄生虫症	47 (30.3)	20 (64.5)	67 (36.0)
上咽頭炎	18 (11.6)	12 (38.7)	30 (16.1)
膀胱炎	11 (7.1)	1 (3.2)	12 (6.5)
COVID-19	1 (0.6)	6 (19.4)	7 (3.8)
胃腸炎	7 (4.5)	0 (0.0)	7 (3.8)
口腔ヘルペス	5 (3.2)	1 (3.2)	6 (3.2)
歯周炎	4 (2.6)	0 (0.0)	4 (2.2)
歯肉炎	1 (0.6)	2 (6.5)	3 (1.6)
結膜炎	1 (0.6)	1 (3.2)	2 (1.1)
ウイルス性胃腸炎	2 (1.3)	0 (0.0)	2 (1.1)
咽頭炎	1 (0.6)	1 (3.2)	2 (1.1)
副鼻腔炎	2 (1.3)	0 (0.0)	2 (1.1)
扁桃炎	2 (1.3)	0 (0.0)	2 (1.1)
虫垂炎	1 (0.6)	0 (0.0)	1 (0.5)
コロナウイルス感染	0 (0.0)	1 (3.2)	1 (0.5)
毛包炎	1 (0.6)	0 (0.0)	1 (0.5)
ヘリコバクター感染	1 (0.6)	0 (0.0)	1 (0.5)
単純ヘルペス	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
麦粒腫	1 (0.6)	0 (0.0)	1 (0.5)
インフルエンザ	0 (0.0)	1 (3.2)	1 (0.5)
咽喉頭炎	1 (0.6)	0 (0.0)	1 (0.5)
外耳炎	1 (0.6)	0 (0.0)	1 (0.5)
歯髄炎	0 (0.0)	1 (3.2)	1 (0.5)
鼻炎	0 (0.0)	1 (3.2)	1 (0.5)
尿路感染	1 (0.6)	0 (0.0)	1 (0.5)
水痘	0 (0.0)	1 (3.2)	1 (0.5)
外陰部腟カンジダ症 [f]	1 (0.7)	0 (0.0)	1 (0.6)
傷害、中毒および処置合併症	13 (8.4)	2 (6.5)	15 (8.1)
動物咬傷	2 (1.3)	0 (0.0)	2 (1.1)
刺創	2 (1.3)	0 (0.0)	2 (1.1)
節足動物咬傷	1 (0.6)	0 (0.0)	1 (0.5)
節足動物刺傷	1 (0.6)	0 (0.0)	1 (0.5)
挫傷	1 (0.6)	0 (0.0)	1 (0.5)
上顎炎	1 (0.6)	0 (0.0)	1 (0.5)
転倒	1 (0.6)	0 (0.0)	1 (0.5)
足骨折	1 (0.6)	0 (0.0)	1 (0.5)
尾骨骨折	1 (0.6)	0 (0.0)	1 (0.5)
頭部損傷	1 (0.6)	0 (0.0)	1 (0.5)
免疫反応	1 (0.6)	0 (0.0)	1 (0.5)
処置による疼痛	1 (0.6)	0 (0.0)	1 (0.5)
熱傷	0 (0.0)	1 (3.2)	1 (0.5)
歯牙破折	0 (0.0)	1 (3.2)	1 (0.5)
臨床検査	20 (12.9)	4 (12.9)	24 (12.9)
アラニンアミノトランスフェラーゼ増加	11 (7.1)	3 (9.7)	14 (7.5)
アスパラギン酸アミノトランスフェラーゼ増加	8 (5.2)	2 (6.5)	10 (5.4)
体重減少	4 (2.6)	1 (3.2)	5 (2.7)
血中アルカリホスファターゼ増加	2 (1.3)	0 (0.0)	2 (1.1)
血中クレアチンホスホキナーゼ増加	1 (0.6)	0 (0.0)	1 (0.5)
血中尿素増加	1 (0.6)	0 (0.0)	1 (0.5)
心電図QT延長	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
尿潜血	1 (0.6)	0 (0.0)	1 (0.5)
尿量減少	1 (0.6)	0 (0.0)	1 (0.5)
尿中白血球陽性	1 (0.6)	0 (0.0)	1 (0.5)
代謝および栄養障害	9 (5.8)	3 (9.7)	12 (6.5)
食欲減退	5 (3.2)	2 (6.5)	7 (3.8)
脂質異常症	2 (1.3)	1 (3.2)	3 (1.6)
脱水	1 (0.6)	0 (0.0)	1 (0.5)
過食	1 (0.6)	0 (0.0)	1 (0.5)
筋骨格系および結合組織障害	29 (18.7)	5 (16.1)	34 (18.3)
関節痛	8 (5.2)	2 (6.5)	10 (5.4)
筋肉痛	10 (6.5)	0 (0.0)	10 (5.4)
背部痛	3 (1.9)	1 (3.2)	4 (2.2)
四肢痛	4 (2.6)	0 (0.0)	4 (2.2)
頚部脊柱管狭窄症	1 (0.6)	0 (0.0)	1 (0.5)
尾骨痛	0 (0.0)	1 (3.2)	1 (0.5)
線維筋痛	1 (0.6)	0 (0.0)	1 (0.5)
筋骨格系胸痛	0 (0.0)	1 (3.2)	1 (0.5)
結節性変形性関節症	1 (0.6)	0 (0.0)	1 (0.5)
脊椎すべり症	1 (0.6)	0 (0.0)	1 (0.5)
滑液嚢腫	1 (0.6)	0 (0.0)	1 (0.5)
全身性エリテマトーデス	1 (0.6)	0 (0.0)	1 (0.5)
顎関節症	1 (0.6)	0 (0.0)	1 (0.5)
腱炎	1 (0.6)	0 (0.0)	1 (0.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	0 (0.0)	1 (0.5)
子宮平滑筋腫[f]	1 (0.7)	0 (0.0)	1 (0.6)
神経系障害	20 (12.9)	3 (9.7)	23 (12.4)
頭痛	8 (5.2)	1 (3.2)	9 (4.8)
浮動性めまい	1 (0.6)	1 (3.2)	2 (1.1)
傾眠	2 (1.3)	0 (0.0)	2 (1.1)

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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
自律神経失調	1 (0.6)	0 (0.0)	1 (0.5)
手根管症候群	1 (0.6)	0 (0.0)	1 (0.5)
顔面麻痺	1 (0.6)	0 (0.0)	1 (0.5)
味覚減退	1 (0.6)	0 (0.0)	1 (0.5)
嗅覚減退	1 (0.6)	0 (0.0)	1 (0.5)
肋間神経痛	1 (0.6)	0 (0.0)	1 (0.5)
意識消失	1 (0.6)	0 (0.0)	1 (0.5)
片頭痛	1 (0.6)	0 (0.0)	1 (0.5)
神経痛	1 (0.6)	0 (0.0)	1 (0.5)
睡眠不足	0 (0.0)	1 (3.2)	1 (0.5)
緊張性頭痛	1 (0.6)	0 (0.0)	1 (0.5)
精神障害	8 (5.2)	1 (3.2)	9 (4.8)
不眠症	2 (1.3)	1 (3.2)	3 (1.6)
うつ病	2 (1.3)	0 (0.0)	2 (1.1)
適応障害	1 (0.6)	0 (0.0)	1 (0.5)
抑うつ気分を伴う適応障害	1 (0.6)	0 (0.0)	1 (0.5)
不安	1 (0.6)	0 (0.0)	1 (0.5)
気分の落ち込み	1 (0.6)	0 (0.0)	1 (0.5)
自殺念慮	1 (0.6)	0 (0.0)	1 (0.5)
腎および尿路障害	1 (0.6)	1 (3.2)	2 (1.1)
緊張性膀胱	1 (0.6)	0 (0.0)	1 (0.5)
蛋白尿	0 (0.0)	1 (3.2)	1 (0.5)
生殖系および乳房障害	8 (5.2)	0 (0.0)	8 (4.3)
腺筋症 [f]	1 (0.7)	0 (0.0)	1 (0.6)
乳房石灰化	1 (0.6)	0 (0.0)	1 (0.5)
乳房障害	1 (0.6)	0 (0.0)	1 (0.5)
乳房腫瘤	1 (0.6)	0 (0.0)	1 (0.5)
子宮頚管ポリープ [f]	1 (0.7)	0 (0.0)	1 (0.6)
月経中間期出血 [f]	1 (0.7)	0 (0.0)	1 (0.6)
閉経期症状 [f]	1 (0.7)	0 (0.0)	1 (0.6)
月経前症候群 [f]	1 (0.7)	0 (0.0)	1 (0.6)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.2
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
呼吸器、胸郭および縦隔障害	14 (9.0)	3 (9.7)	17 (9.1)
口腔咽頭痛	5 (3.2)	1 (3.2)	6 (3.2)
咳嗽	2 (1.3)	1 (3.2)	3 (1.6)
過換気	2 (1.3)	0 (0.0)	2 (1.1)
喘息	1 (0.6)	0 (0.0)	1 (0.5)
咳喘息	1 (0.6)	0 (0.0)	1 (0.5)
鼻出血	1 (0.6)	0 (0.0)	1 (0.5)
鼻閉	0 (0.0)	1 (3.2)	1 (0.5)
痰貯留	1 (0.6)	0 (0.0)	1 (0.5)
上気道咳症候群	1 (0.6)	0 (0.0)	1 (0.5)
皮膚および皮下組織障害	18 (11.6)	3 (9.7)	21 (11.3)
湿疹	5 (3.2)	0 (0.0)	5 (2.7)
蕁麻疹	2 (1.3)	1 (3.2)	3 (1.6)
ざ瘡	1 (0.6)	1 (3.2)	2 (1.1)
接触皮膚炎	2 (1.3)	0 (0.0)	2 (1.1)
皮膚乾燥	1 (0.6)	1 (3.2)	2 (1.1)
そう痒症	2 (1.3)	0 (0.0)	2 (1.1)
皮脂欠乏症	1 (0.6)	0 (0.0)	1 (0.5)
アレルギー性皮膚炎	1 (0.6)	0 (0.0)	1 (0.5)
皮脂欠乏性湿疹	1 (0.6)	0 (0.0)	1 (0.5)
紅斑	1 (0.6)	0 (0.0)	1 (0.5)
ばら色粃糠疹	1 (0.6)	0 (0.0)	1 (0.5)
発疹	1 (0.6)	0 (0.0)	1 (0.5)
血管障害	4 (2.6)	0 (0.0)	4 (2.2)
高血圧	3 (1.9)	0 (0.0)	3 (1.6)
本態性高血圧症	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表15

Table 14.3-1.4
Treatment-Related Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Participants with at least one Treatment-related TEAE	25 (16.1)	6 (19.4)	31 (16.7)
胃腸障害	16 (10.3)	4 (12.9)	20 (10.8)
便秘	11 (7.1)	3 (9.7)	14 (7.5)
腹部不快感	2 (1.3)	1 (3.2)	3 (1.6)
悪心	2 (1.3)	1 (3.2)	3 (1.6)
上腹部痛	2 (1.3)	0 (0.0)	2 (1.1)
腹痛	1 (0.6)	0 (0.0)	1 (0.5)
一般・全身障害および投与部位の状態	2 (1.3)	0 (0.0)	2 (1.1)
倦怠感	2 (1.3)	0 (0.0)	2 (1.1)
臨床検査	8 (5.2)	2 (6.5)	10 (5.4)
アラニンアミノトランスフェラーゼ増加	7 (4.5)	1 (3.2)	8 (4.3)
アスパラギン酸アミノトランスフェラーゼ増加	6 (3.9)	0 (0.0)	6 (3.2)
体重減少	1 (0.6)	1 (3.2)	2 (1.1)
血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)	1 (0.5)
代謝および栄養障害	2 (1.3)	2 (6.5)	4 (2.2)
食欲減退	2 (1.3)	2 (6.5)	4 (2.2)
神経系障害	3 (1.9)	0 (0.0)	3 (1.6)
傾眠	2 (1.3)	0 (0.0)	2 (1.1)
味覚減退	1 (0.6)	0 (0.0)	1 (0.5)
嗅覚減退	1 (0.6)	0 (0.0)	1 (0.5)
皮膚および皮下組織障害	1 (0.6)	0 (0.0)	1 (0.5)
そう痒症	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.

表16

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Participants with at least one TEAE	137 (88.4)	28 (90.3)	165 (88.7)
Mild	107 (69.0)	25 (80.6)	132 (71.0)
Moderate	26 (16.8)	3 (9.7)	29 (15.6)
Severe	4 (2.6)	0 (0.0)	4 (2.2)
血液およびリンパ系障害	4 (2.6)	0 (0.0)	4 (2.2)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
貧血	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
動悸	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
上室性期外収縮	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	11 (7.1)	2 (6.5)	13 (7.0)
Mild	9 (5.8)	2 (6.5)	11 (5.9)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	6 (3.9)	1 (3.2)	7 (3.8)
Mild	4 (2.6)	1 (3.2)	5 (2.7)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	2 (1.3)	1 (3.2)	3 (1.6)
Mild	2 (1.3)	1 (3.2)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
耳痛	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
突発性難聴	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
高プロラクチン血症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能亢進症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	15 (9.7)	4 (12.9)	19 (10.2)
Mild	15 (9.7)	4 (12.9)	19 (10.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
ドライアイ	4 (2.6)	2 (6.5)	6 (3.2)
Mild	4 (2.6)	2 (6.5)	6 (3.2)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
眼精疲労	3 (1.9)	1 (3.2)	4 (2.2)
Mild	3 (1.9)	1 (3.2)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性結膜炎	4 (2.6)	0 (0.0)	4 (2.2)
Mild	4 (2.6)	0 (0.0)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼痙攣	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
角膜びらん	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
眼の炎症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼下垂	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
仮性近視	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
網膜出血	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	53 (34.2)	14 (45.2)	67 (36.0)
Mild	46 (29.7)	12 (38.7)	58 (31.2)
Moderate	7 (4.5)	2 (6.5)	9 (4.8)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
便秘	17 (11.0)	4 (12.9)	21 (11.3)
Mild	17 (11.0)	4 (12.9)	21 (11.3)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
下痢	8 (5.2)	2 (6.5)	10 (5.4)
Mild	8 (5.2)	2 (6.5)	10 (5.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
上腹部痛	6 (3.9)	2 (6.5)	8 (4.3)
Mild	5 (3.2)	2 (6.5)	7 (3.8)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
悪心	7 (4.5)	1 (3.2)	8 (4.3)
Mild	4 (2.6)	1 (3.2)	5 (2.7)
Moderate	3 (1.9)	0 (0.0)	3 (1.6)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	4 (2.6)	1 (3.2)	5 (2.7)
Mild	4 (2.6)	1 (3.2)	5 (2.7)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	3 (1.9)	2 (6.5)	5 (2.7)
Mild	2 (1.3)	2 (6.5)	4 (2.2)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	3 (1.9)	1 (3.2)	4 (2.2)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	1 (0.6)	1 (3.2)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
腹痛	4 (2.6)	0 (0.0)	4 (2.2)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	4 (2.6)	0 (0.0)	4 (2.2)
Mild	4 (2.6)	0 (0.0)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	3 (1.9)	1 (3.2)	4 (2.2)
Mild	3 (1.9)	1 (3.2)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	2 (1.3)	1 (3.2)	3 (1.6)
Mild	2 (1.3)	1 (3.2)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	3 (1.9)	0 (0.0)	3 (1.6)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
痔核	3 (1.9)	0 (0.0)	3 (1.6)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
下腹部痛	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (3.2)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
裂孔ヘルニア	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
非感染性歯肉炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
がま腫	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
埋伏歯	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
嘔吐	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	65 (41.9)	2 (6.5)	67 (36.0)
Mild	58 (37.4)	2 (6.5)	60 (32.3)
Moderate	7 (4.5)	0 (0.0)	7 (3.8)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
発熱	52 (33.5)	2 (6.5)	54 (29.0)
Mild	47 (30.3)	2 (6.5)	49 (26.3)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	5 (3.2)	0 (0.0)	5 (2.7)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	9 (5.8)	1 (3.2)	10 (5.4)
Mild	7 (4.5)	1 (3.2)	8 (4.3)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
疲労	3 (1.9)	0 (0.0)	3 (1.6)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
注射部位疼痛	3 (1.9)	0 (0.0)	3 (1.6)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	3 (1.9)	0 (0.0)	3 (1.6)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
ワクチン接種部位腫脹	3 (1.9)	0 (0.0)	3 (1.6)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
顔面浮腫	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
顔面痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
低体温	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
注射部位腫脹	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
疼痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	47 (30.3)	20 (64.5)	67 (36.0)
Mild	46 (29.7)	19 (61.3)	65 (34.9)
Moderate	1 (0.6)	1 (3.2)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
上咽頭炎	18 (11.6)	12 (38.7)	30 (16.1)
Mild	18 (11.6)	12 (38.7)	30 (16.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	11 (7.1)	1 (3.2)	12 (6.5)
Mild	11 (7.1)	1 (3.2)	12 (6.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
COVID-19	1 (0.6)	6 (19.4)	7 (3.8)
Mild	1 (0.6)	6 (19.4)	7 (3.8)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
胃腸炎	7 (4.5)	0 (0.0)	7 (3.8)
Mild	7 (4.5)	0 (0.0)	7 (3.8)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	5 (3.2)	1 (3.2)	6 (3.2)
Mild	5 (3.2)	1 (3.2)	6 (3.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	4 (2.6)	0 (0.0)	4 (2.2)
Mild	4 (2.6)	0 (0.0)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
歯肉炎	1 (0.6)	2 (6.5)	3 (1.6)
Mild	1 (0.6)	2 (6.5)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	1 (0.6)	1 (3.2)	2 (1.1)
Mild	1 (0.6)	1 (3.2)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.6)	1 (3.2)	2 (1.1)
Mild	1 (0.6)	1 (3.2)	2 (1.1)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
虫垂炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
コロナウイルス感染	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
単純ヘルペス	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
咽喉頭炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
外耳炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	1 (3.2)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
外陰部腟カンジダ症[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	1 (0.7)	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	13 (8.4)	2 (6.5)	15 (8.1)
Mild	11 (7.1)	2 (6.5)	13 (7.0)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
刺創	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
節足動物咬傷	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
節足動物刺傷	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
挫傷	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
上顎炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
転倒	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
足骨折	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
尾骨骨折	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
免疫反応	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	20 (12.9)	4 (12.9)	24 (12.9)
Mild	16 (10.3)	4 (12.9)	20 (10.8)
Moderate	3 (1.9)	0 (0.0)	3 (1.6)
Severe	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
アラニンアミノトランスフェラーゼ増加	11 (7.1)	3 (9.7)	14 (7.5)
Mild	7 (4.5)	3 (9.7)	10 (5.4)
Moderate	3 (1.9)	0 (0.0)	3 (1.6)
Severe	1 (0.6)	0 (0.0)	1 (0.5)
アスパラギン酸アミノトランスフェラーゼ増加	8 (5.2)	2 (6.5)	10 (5.4)
Mild	5 (3.2)	2 (6.5)	7 (3.8)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	1 (0.6)	0 (0.0)	1 (0.5)
体重減少	4 (2.6)	1 (3.2)	5 (2.7)
Mild	4 (2.6)	1 (3.2)	5 (2.7)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	2 (1.3)	0 (0.0)	2 (1.1)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
心電図QT延長	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
尿潜血	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
尿量減少	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	9 (5.8)	3 (9.7)	12 (6.5)
Mild	9 (5.8)	3 (9.7)	12 (6.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	5 (3.2)	2 (6.5)	7 (3.8)
Mild	5 (3.2)	2 (6.5)	7 (3.8)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
脂質異常症	2 (1.3)	1 (3.2)	3 (1.6)
Mild	2 (1.3)	1 (3.2)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
脱水	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
過食	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	29 (18.7)	5 (16.1)	34 (18.3)
Mild	26 (16.8)	5 (16.1)	31 (16.7)
Moderate	3 (1.9)	0 (0.0)	3 (1.6)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
関節痛	8 (5.2)	2 (6.5)	10 (5.4)
Mild	8 (5.2)	2 (6.5)	10 (5.4)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
筋肉痛	10 (6.5)	0 (0.0)	10 (5.4)
Mild	9 (5.8)	0 (0.0)	9 (4.8)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
背部痛	3 (1.9)	1 (3.2)	4 (2.2)
Mild	3 (1.9)	1 (3.2)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	4 (2.6)	0 (0.0)	4 (2.2)
Mild	4 (2.6)	0 (0.0)	4 (2.2)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
頚部脊柱管狭窄症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
尾骨痛	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
結節性変形性関節症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
滑液嚢腫	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
全身性エリテマトーデス	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
顎関節症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
腱炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.6)	0 (0.0)	1 (0.5)
子宮平滑筋腫[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.7)	0 (0.0)	1 (0.6)
神経系障害	20 (12.9)	3 (9.7)	23 (12.4)
Mild	14 (9.0)	3 (9.7)	17 (9.1)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	4 (2.6)	0 (0.0)	4 (2.2)
Severe	2 (1.3)	0 (0.0)	2 (1.1)
頭痛	8 (5.2)	1 (3.2)	9 (4.8)
Mild	6 (3.9)	1 (3.2)	7 (3.8)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (0.6)	1 (3.2)	2 (1.1)
Mild	1 (0.6)	1 (3.2)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
自律神経失調	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
顔面麻痺	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
味覚減退	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
嗅覚減退	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
肋間神経痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
意識消失	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	1 (0.6)	0 (0.0)	1 (0.5)
片頭痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
神経痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
睡眠不足	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	8 (5.2)	1 (3.2)	9 (4.8)
Mild	7 (4.5)	1 (3.2)	8 (4.3)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	2 (1.3)	1 (3.2)	3 (1.6)
Mild	2 (1.3)	1 (3.2)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	2 (1.3)	0 (0.0)	2 (1.1)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
適応障害	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分を伴う適応障害	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
不安	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
気分の落ち込み	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
自殺念慮	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害	1 (0.6)	1 (3.2)	2 (1.1)
Mild	1 (0.6)	1 (3.2)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
緊張性膀胱	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	8 (5.2)	0 (0.0)	8 (4.3)
Mild	6 (3.9)	0 (0.0)	6 (3.2)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
腺筋症[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.7)	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
乳房石灰化	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
乳房障害	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
乳房腫瘤	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
子宮頚管ポリープ[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	1 (0.7)	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
月経中間期出血[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	1 (0.7)	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
閉経期症状[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	1 (0.7)	0 (0.0)	1 (0.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群[f]	1 (0.7)	0 (0.0)	1 (0.6)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.7)	0 (0.0)	1 (0.6)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	14 (9.0)	3 (9.7)	17 (9.1)
Mild	12 (7.7)	3 (9.7)	15 (8.1)
Moderate	2 (1.3)	0 (0.0)	2 (1.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	5 (3.2)	1 (3.2)	6 (3.2)
Mild	5 (3.2)	1 (3.2)	6 (3.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	2 (1.3)	1 (3.2)	3 (1.6)
Mild	2 (1.3)	1 (3.2)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
過換気	2 (1.3)	0 (0.0)	2 (1.1)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
喘息	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
咳喘息	1 (0.6)	0 (0.0)	1 (0.5)
Mild	0 (0.0)	0 (0.0)	0 (0.0)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	0 (0.0)	1 (3.2)	1 (0.5)
Mild	0 (0.0)	1 (3.2)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
痰貯留	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	18 (11.6)	3 (9.7)	21 (11.3)
Mild	17 (11.0)	3 (9.7)	20 (10.8)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
湿疹	5 (3.2)	0 (0.0)	5 (2.7)
Mild	5 (3.2)	0 (0.0)	5 (2.7)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	2 (1.3)	1 (3.2)	3 (1.6)
Mild	2 (1.3)	1 (3.2)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
ざ瘡	1 (0.6)	1 (3.2)	2 (1.1)
Mild	1 (0.6)	1 (3.2)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
接触皮膚炎	2 (1.3)	0 (0.0)	2 (1.1)
Mild	2 (1.3)	0 (0.0)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	1 (0.6)	1 (3.2)	2 (1.1)
Mild	1 (0.6)	1 (3.2)	2 (1.1)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	2 (1.3)	0 (0.0)	2 (1.1)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	1 (0.6)	0 (0.0)	1 (0.5)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
皮脂欠乏症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
皮脂欠乏性湿疹	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
ばら色粃糠疹	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
発疹	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	4 (2.6)	0 (0.0)	4 (2.2)
Mild	4 (2.6)	0 (0.0)	4 (2.2)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.3
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term, and Severity
Safety Population

System Organ Class Preferred Term Severity	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
高血圧	3 (1.9)	0 (0.0)	3 (1.6)
Mild	3 (1.9)	0 (0.0)	3 (1.6)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)
本態性高血圧症	1 (0.6)	0 (0.0)	1 (0.5)
Mild	1 (0.6)	0 (0.0)	1 (0.5)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)
Severe	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表17

Table 14.3-2.1
Treatment-Emergent Serious Adverse Events: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Participants with at least one TESAE	7 (4.5)	0 (0.0)	7 (3.8)
耳および迷路障害	1 (0.6)	0 (0.0)	1 (0.5)
回転性めまい	1 (0.6)	0 (0.0)	1 (0.5)
肝胆道系障害	1 (0.6)	0 (0.0)	1 (0.5)
胆石症	1 (0.6)	0 (0.0)	1 (0.5)
感染症および寄生虫症	1 (0.6)	0 (0.0)	1 (0.5)
虫垂炎	1 (0.6)	0 (0.0)	1 (0.5)
臨床検査	1 (0.6)	0 (0.0)	1 (0.5)
アラニンアミノトランスフェラーゼ増加	1 (0.6)	0 (0.0)	1 (0.5)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.6)	0 (0.0)	1 (0.5)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	0 (0.0)	1 (0.5)
子宮平滑筋腫［f］	1 (0.7)	0 (0.0)	1 (0.6)
神経系障害	2 (1.3)	0 (0.0)	2 (1.1)
意識消失	1 (0.6)	0 (0.0)	1 (0.5)
片頭痛	1 (0.6)	0 (0.0)	1 (0.5)
精神障害	1 (0.6)	0 (0.0)	1 (0.5)
うつ病	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

表18

Table 14.3-2.3
Treatment-Emergent Adverse Events Leading to Study Intervention Discontinuation: Number (%) of Participants by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	3101-303-002 CM Completers (N=155) n (%)	De Novo EM Participants (N=31) n (%)	Total (N=186) n (%)
Participants with at least one TEAE leading to study intervention discontinuation	9 (5.8)	0 (0.0)	9 (4.8)
胃腸障害	3 (1.9)	0 (0.0)	3 (1.6)
腹部不快感	1 (0.6)	0 (0.0)	1 (0.5)
上腹部痛	1 (0.6)	0 (0.0)	1 (0.5)
悪心	1 (0.6)	0 (0.0)	1 (0.5)
肝胆道系障害	1 (0.6)	0 (0.0)	1 (0.5)
胆石症	1 (0.6)	0 (0.0)	1 (0.5)
臨床検査	4 (2.6)	0 (0.0)	4 (2.2)
アラニンアミノトランスフェラーゼ増加	4 (2.6)	0 (0.0)	4 (2.2)
アスパラギン酸アミノトランスフェラーゼ増加	3 (1.9)	0 (0.0)	3 (1.6)
血中アルカリホスファターゼ増加	1 (0.6)	0 (0.0)	1 (0.5)
筋骨格系および結合組織障害	1 (0.6)	0 (0.0)	1 (0.5)
全身性エリテマトーデス	1 (0.6)	0 (0.0)	1 (0.5)
神経系障害	1 (0.6)	0 (0.0)	1 (0.5)
顔面麻痺	1 (0.6)	0 (0.0)	1 (0.5)
皮膚および皮下組織障害	1 (0.6)	0 (0.0)	1 (0.5)
そう痒症	1 (0.6)	0 (0.0)	1 (0.5)

AE terms are coded using the dictionary: MedDRA27.0.

表19

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
Participants with at least one TEAE	73 (47.1)	61 (43.0)	62 (45.6)	62 (47.0)	20 (15.4)
血液およびリンパ系障害	2 (1.3)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)
貧血	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節痛	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
リンパ節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
心臓障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
耳および迷路障害	4 (2.6)	5 (3.5)	3 (2.2)	3 (2.3)	0 (0.0)
突発性難聴	2 (1.3)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
回転性めまい	2 (1.3)	2 (1.4)	1 (0.7)	1 (0.8)	0 (0.0)
耳痛	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	0 (0.0)	0 (0.0)	1 (0.7)	2 (1.5)	0 (0.0)
内分泌障害	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
高プロラクチン血症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能亢進症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
眼障害	5 (3.2)	4 (2.8)	3 (2.2)	3 (2.3)	1 (0.8)
アレルギー性結膜炎	2 (1.3)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)
ドライアイ	2 (1.3)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.8)
眼精疲労	1 (0.6)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
霰粒腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
N = number of participants in the Safety Population of the cohort.
N1 = number of participants in the Safety Population who had treatment duration greater than or equal to the start of the time interval.
n = number of participants out of N1 who had the first episode of the TEAE occurring during the time interval.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
眼瞼痙攣	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
角膜びらん	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
仮性近視	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
網膜出血	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
胃腸障害	22 (14.2)	18 (12.7)	12 (8.8)	11 (8.3)	4 (3.1)
便秘	9 (5.8)	6 (4.2)	2 (1.5)	0 (0.0)	0 (0.0)
悪心	5 (3.2)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
齲歯	3 (1.9)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
下痢	3 (1.9)	0 (0.0)	3 (2.2)	0 (0.0)	2 (1.5)
上腹部痛	2 (1.3)	2 (1.4)	0 (0.0)	2 (1.5)	0 (0.0)
胃炎	2 (1.3)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
腹部不快感	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)
小腸炎	1 (0.6)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	1 (0.6)	1 (0.7)	1 (0.7)	1 (0.8)	0 (0.0)
痔核	1 (0.6)	1 (0.7)	1 (0.7)	1 (0.8)	0 (0.0)
非感染性歯肉炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	1 (0.6)	1 (0.7)	0 (0.0)	2 (1.5)	1 (0.8)
歯痛	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)
腹痛	0 (0.0)	2 (1.4)	2 (1.5)	0 (0.0)	0 (0.0)
口唇のひび割れ	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
消化不良	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
裂孔ヘルニア	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
埋伏歯	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)

AE terms are coded using the dictionary: MedDRA27.0.
N = number of participants in the Safety Population of the cohort.
N1 = number of participants in the Safety Population who had treatment duration greater than or equal to the start of the time interval.
n = number of participants out of N1 who had the first episode of the TEAE occurring during the time interval.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	1 (0.8)
一般・全身障害および投与部位の状態	19 (12.3)	14 (9.9)	18 (13.2)	22 (16.7)	4 (3.1)
発熱	12 (7.7)	11 (7.7)	17 (12.5)	18 (13.6)	2 (1.5)
疲労	2 (1.3)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)
倦怠感	2 (1.3)	3 (2.1)	3 (2.2)	1 (0.8)	0 (0.0)
非心臓性胸痛	2 (1.3)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
顔面浮腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面痛	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低体温	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位疼痛	1 (0.6)	0 (0.0)	1 (0.7)	2 (1.5)	0 (0.0)
末梢性浮腫	1 (0.6)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
ワクチン接種部位腫脹	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	2 (1.5)
肝胆道系障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	19 (12.3)	20 (14.1)	14 (10.3)	8 (6.1)	3 (2.3)
上咽頭炎	8 (5.2)	6 (4.2)	2 (1.5)	3 (2.3)	0 (0.0)
膀胱炎	4 (2.6)	3 (2.1)	3 (2.2)	1 (0.8)	1 (0.8)
口腔ヘルペス	2 (1.3)	3 (2.1)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.6)	0 (0.0)	3 (2.2)	2 (1.5)	1 (0.8)

AE terms are coded using the dictionary: MedDRA27.0.
N = number of participants in the Safety Population of the cohort.
N1 = number of participants in the Safety Population who had treatment duration greater than or equal to the start of the time interval.
n = number of participants out of N1 who had the first episode of the TEAE occurring during the time interval.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
ウイルス性胃腸炎	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
単純ヘルペス	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.6)	2 (1.4)	1 (0.7)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
外陰部腟カンジダ症 [f]	1 (0.7)	1 (0.8)	1 (0.8)	1 (0.8)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
COVID-19	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
結膜炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
歯肉炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター感染	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
咽喉頭炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.8)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
副鼻腔炎	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	3 (1.9)	4 (2.8)	1 (0.7)	5 (3.8)	0 (0.0)
上顎炎	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尾骨骨折	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
挫傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)

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n = number of participants out of N1 who had the first episode of the TEAE occurring during the time interval.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
頭部損傷	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
免疫反応	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
刺創	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
臨床検査	8 (5.2)	5 (3.5)	3 (2.2)	3 (2.3)	4 (3.1)
アラニンアミノトランスフェラーゼ増加	6 (3.9)	3 (2.1)	0 (0.0)	2 (1.5)	1 (0.8)
アスパラギン酸アミノトランスフェラーゼ増加	4 (2.6)	2 (1.4)	0 (0.0)	2 (1.5)	1 (0.8)
血中アルカリホスファターゼ増加	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	1 (0.6)	1 (0.7)	1 (0.7)	1 (0.8)	0 (0.0)
血中尿素増加	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
尿潜血	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
尿量減少	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
代謝および栄養障害	2 (1.3)	1 (0.7)	3 (2.2)	0 (0.0)	3 (2.3)
食欲減退	2 (1.3)	1 (0.7)	1 (0.7)	0 (0.0)	1 (0.8)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
脂質異常症	0 (0.0)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)
過食	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)
筋骨格系および結合組織障害	5 (3.2)	8 (5.6)	6 (4.4)	11 (8.3)	2 (1.5)
関節痛	2 (1.3)	3 (2.1)	1 (0.7)	2 (1.5)	0 (0.0)
背部痛	1 (0.6)	1 (0.7)	0 (0.0)	1 (0.8)	0 (0.0)
筋肉痛	1 (0.6)	3 (2.1)	1 (0.7)	4 (3.0)	2 (1.5)

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Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
四肢痛	1 (0.6)	0 (0.0)	3 (2.2)	0 (0.0)	0 (0.0)
滑液嚢腫	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頚部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
結節性変形性関節症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
全身性エリテマトーデス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
顎関節症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
腱炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫 [f]	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	7 (4.5)	3 (2.1)	10 (7.4)	1 (0.8)	2 (1.5)
頭痛	2 (1.3)	0 (0.0)	5 (3.7)	1 (0.8)	2 (1.5)
傾眠	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自律神経失調	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
味覚減退	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
顔面麻痺	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
嗅覚減退	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
肋間神経痛	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)

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n = number of participants out of N1 who had the first episode of the TEAE occurring during the time interval.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
緊張性頭痛	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	4 (2.6)	2 (1.4)	2 (1.5)	1 (0.8)	0 (0.0)
不眠症	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
適応障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分の落ち込み	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分を伴う適応障害	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
不安	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	0 (0.0)	1 (0.7)	1 (0.7)	0 (0.0)	0 (0.0)
自殺念慮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
腎および尿路障害	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
緊張性膀胱	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
生殖系および乳房障害	4 (2.6)	0 (0.0)	3 (2.2)	1 (0.8)	0 (0.0)
腺筋症 [f]	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房障害	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経中間期出血 [f]	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群 [f]	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房石灰化	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
子宮頚管ポリープ [f]	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)
閉経期症状 [f]	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
呼吸器、胸郭および縦隔障害	5 (3.2)	3 (2.1)	4 (2.9)	2 (1.5)	0 (0.0)
過換気	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	1 (0.6)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)

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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

3101-303-002 CM Completers (N=155)

System Organ Class Preferred Term	<3 months (N1=155) n (%)	>=3 and <6 months (N1=142) n (%)	>=6 and <9 months (N1=136) n (%)	>=9 and <12 months (N1=132) n (%)	>=12 months (N1=130) n (%)
咳喘息	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.6)	2 (1.4)	1 (0.7)	1 (0.8)	0 (0.0)
喘息	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
痰貯留	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	6 (3.9)	6 (4.2)	4 (2.9)	4 (3.0)	0 (0.0)
接触皮膚炎	2 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	2 (1.3)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
ざ瘡	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	1 (0.6)	1 (0.7)	2 (1.5)	1 (0.8)	0 (0.0)
皮脂欠乏症	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
皮脂欠乏性湿疹	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
ばら色粃糠疹	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.8)	0 (0.0)
蕁麻疹	0 (0.0)	0 (0.0)	1 (0.7)	1 (0.8)	0 (0.0)
血管障害	0 (0.0)	2 (1.4)	2 (1.5)	0 (0.0)	0 (0.0)
本態性高血圧症	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
高血圧	0 (0.0)	2 (1.4)	1 (0.7)	0 (0.0)	0 (0.0)

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Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

De Novo EM Participants (N=31)

System Organ Class Preferred Term	<3 months (N1=31) n (%)	>=3 and <6 months (N1=29) n (%)	>=6 and <9 months (N1=28) n (%)	>=9 and <12 months (N1=28) n (%)	>=12 months (N1=28) n (%)
Participants with at least one TEAE	20 (64.5)	12 (41.4)	14 (50.0)	14 (50.0)	4 (14.3)
耳および迷路障害	1 (3.2)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
耳鳴	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	2 (6.5)	0 (0.0)	2 (7.1)	0 (0.0)	0 (0.0)
ドライアイ	2 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜充血	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼精疲労	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
胃腸障害	6 (19.4)	6 (20.7)	3 (10.7)	3 (10.7)	0 (0.0)
便秘	3 (9.7)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
下腹部痛	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
上腹部痛	0 (0.0)	0 (0.0)	2 (7.1)	1 (3.6)	0 (0.0)
齲歯	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
下痢	0 (0.0)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
がま腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
口内炎	0 (0.0)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)

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Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

De Novo EM Participants (N=31)

System Organ Class Preferred Term	<3 months (N1=31) n (%)	>=3 and <6 months (N1=29) n (%)	>=6 and <9 months (N1=28) n (%)	>=9 and <12 months (N1=28) n (%)	>=12 months (N1=28) n (%)
一般・全身障害および投与部位の状態	0 (0.0)	0 (0.0)	1 (3.6)	1 (3.6)	0 (0.0)
倦怠感	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
発熱	0 (0.0)	0 (0.0)	1 (3.6)	1 (3.6)	0 (0.0)
感染症および寄生虫症	7 (22.6)	5 (17.2)	7 (25.0)	10 (35.7)	1 (3.6)
上咽頭炎	4 (12.9)	2 (6.9)	3 (10.7)	7 (25.0)	1 (3.6)
歯肉炎	2 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
COVID-19	1 (3.2)	3 (10.3)	1 (3.6)	2 (7.1)	0 (0.0)
コロナウイルス感染	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
口腔ヘルペス	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
咽頭炎	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	0 (0.0)	1 (3.4)	0 (0.0)	1 (3.6)	0 (0.0)
熱傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)
歯牙破折	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	2 (6.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (7.1)
アラニンアミノトランスフェラーゼ増加	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	2 (7.1)
体重減少	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	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 (0.0)	0 (0.0)	0 (0.0)	2 (7.1)

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[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

De Novo EM Participants (N=31)

System Organ Class Preferred Term	<3 months (N1=31) n (%)	>=3 and <6 months (N1=29) n (%)	>=6 and <9 months (N1=28) n (%)	>=9 and <12 months (N1=28) n (%)	>=12 months (N1=28) n (%)
代謝および栄養障害	1 (3.2)	0 (0.0)	2 (7.1)	0 (0.0)	0 (0.0)
食欲減退	1 (3.2)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
脂質異常症	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	1 (3.2)	3 (10.3)	1 (3.6)	0 (0.0)	0 (0.0)
背部痛	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節痛	0 (0.0)	1 (3.4)	1 (3.6)	0 (0.0)	0 (0.0)
尾骨痛	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	3 (9.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠不足	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
不眠症	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
腎および尿路障害	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)
呼吸器、胸郭および縦隔障害	1 (3.2)	2 (6.9)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	1 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	0 (0.0)	1 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)

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n = number of participants out of N1 who had the first episode of the TEAE occurring during the time interval.
[m] = event specific to male; [f] = event specific to female; percentages for sex-specific TEAE are relative to the number of participants of the appropriate sex.

Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

De Novo EM Participants (N=31)

System Organ Class Preferred Term	<3 months (N1=31) n (%)	>=3 and <6 months (N1=29) n (%)	>=6 and <9 months (N1=28) n (%)	>=9 and <12 months (N1=28) n (%)	>=12 months (N1=28) n (%)
皮膚および皮下組織障害	0 (0.0)	0 (0.0)	3 (10.7)	0 (0.0)	0 (0.0)
ざ瘡	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)
蕁麻疹	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)

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Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

Total (N=186)

System Organ Class Preferred Term	<3 months (N1=186) n (%)	>=3 and <6 months (N1=171) n (%)	>=6 and <9 months (N1=164) n (%)	>=9 and <12 months (N1=160) n (%)	>=12 months (N1=158) n (%)
Participants with at least one TEAE	93 (50.0)	73 (42.7)	76 (46.3)	76 (47.5)	24 (15.2)
血液およびリンパ系障害	2 (1.1)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
貧血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鉄欠乏性貧血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
リンパ節炎	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
心臓障害	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.3)	0 (0.0)
動悸	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
上室性期外収縮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
耳および迷路障害	5 (2.7)	6 (3.5)	3 (1.8)	3 (1.9)	0 (0.0)
突発性難聴	2 (1.1)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
回転性めまい	2 (1.1)	3 (1.8)	1 (0.6)	1 (0.6)	0 (0.0)
耳鳴	1 (0.5)	0 (0.0)	1 (0.6)	2 (1.3)	0 (0.0)
耳痛	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
高プロラクチン血症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺機能亢進症	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
眼障害	7 (3.8)	4 (2.3)	5 (3.0)	3 (1.9)	1 (0.6)
ドライアイ	4 (2.2)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
アレルギー性結膜炎	2 (1.1)	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)
眼精疲労	1 (0.5)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)
霰粒腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

Total (N=186)

System Organ Class Preferred Term	<3 months (N1=186) n (%)	>=3 and <6 months (N1=171) n (%)	>=6 and <9 months (N1=164) n (%)	>=9 and <12 months (N1=160) n (%)	>=12 months (N1=158) n (%)
結膜充血	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼痙攣	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
角膜びらん	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
眼の炎症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
眼瞼下垂	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
仮性近視	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
網膜出血	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
強膜炎	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
胃腸障害	28 (15.1)	24 (14.0)	15 (9.1)	14 (8.8)	4 (2.5)
便秘	12 (6.5)	7 (4.1)	2 (1.2)	0 (0.0)	0 (0.0)
悪心	6 (3.2)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
齲歯	3 (1.6)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)
下痢	3 (1.6)	2 (1.2)	3 (1.8)	0 (0.0)	2 (1.3)
腹部不快感	2 (1.1)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
上腹部痛	2 (1.1)	2 (1.2)	2 (1.2)	3 (1.9)	0 (0.0)
小腸炎	2 (1.1)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
胃炎	2 (1.1)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
歯痛	2 (1.1)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
胃食道逆流性疾患	1 (0.5)	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)
痔核	1 (0.5)	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)
非感染性歯肉炎	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口内炎	1 (0.5)	3 (1.8)	0 (0.0)	2 (1.3)	1 (0.6)
腹部膨満	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
腹痛	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)
下腹部痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
口唇のひび割れ	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)

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Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

Total (N=186)

System Organ Class Preferred Term	<3 months (N1=186) n (%)	>=3 and <6 months (N1=171) n (%)	>=6 and <9 months (N1=164) n (%)	>=9 and <12 months (N1=160) n (%)	>=12 months (N1=158) n (%)
消化不良	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
舌炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
裂孔ヘルニア	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
がま腫	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
埋伏歯	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
嘔吐	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
一般・全身障害および投与部位の状態	19 (10.2)	14 (8.2)	19 (11.6)	23 (14.4)	4 (2.5)
発熱	12 (6.5)	11 (6.4)	18 (11.0)	19 (11.9)	2 (1.3)
疲労	2 (1.1)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
倦怠感	2 (1.1)	3 (1.8)	3 (1.8)	2 (1.3)	0 (0.0)
非心臓性胸痛	2 (1.1)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
顔面浮腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低体温	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位疼痛	1 (0.5)	0 (0.0)	1 (0.6)	2 (1.3)	0 (0.0)
末梢性浮腫	1 (0.5)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位腫脹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
疼痛	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
ワクチン接種部位腫脹	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	2 (1.3)
肝胆道系障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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Safety Population

Total (N=186)

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感染症および寄生虫症	26 (14.0)	25 (14.6)	21 (12.8)	18 (11.3)	4 (2.5)
上咽頭炎	12 (6.5)	8 (4.7)	5 (3.0)	10 (6.3)	1 (0.6)
膀胱炎	5 (2.7)	3 (1.8)	3 (1.8)	1 (0.6)	1 (0.6)
歯肉炎	2 (1.1)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	2 (1.1)	3 (1.8)	1 (0.6)	0 (0.0)	0 (0.0)
COVID-19	1 (0.5)	3 (1.8)	1 (0.6)	2 (1.3)	1 (0.6)
コロナウイルス感染	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	1 (0.5)	0 (0.0)	3 (1.8)	2 (1.3)	1 (0.6)
ウイルス性胃腸炎	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
単純ヘルペス	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	1 (0.5)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)
咽頭炎	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
鼻炎	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
外陰部腟カンジダ症 [f]	1 (0.6)	1 (0.6)	1 (0.7)	1 (0.7)	0 (0.0)
虫垂炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
結膜炎	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
毛包炎	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
ヘリコバクター感染	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
インフルエンザ	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
咽喉頭炎	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
外耳炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
歯髄炎	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
副鼻腔炎	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
水痘	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)

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Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

Total (N=186)

System Organ Class Preferred Term	<3 months (N1=186) n (%)	>=3 and <6 months (N1=171) n (%)	>=6 and <9 months (N1=164) n (%)	>=9 and <12 months (N1=160) n (%)	>=12 months (N1=158) n (%)
傷害、中毒および処置合併症	3 (1.6)	5 (2.9)	1 (0.6)	6 (3.8)	0 (0.0)
上顎炎	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尾骨骨折	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
節足動物刺傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
挫傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
足骨折	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
頭部損傷	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
免疫反応	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
刺創	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
歯牙破折	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	10 (5.4)	5 (2.9)	3 (1.8)	3 (1.9)	6 (3.8)
アラニンアミノトランスフェラーゼ増加	7 (3.8)	3 (1.8)	0 (0.0)	2 (1.3)	3 (1.9)
アスパラギン酸アミノトランスフェラーゼ増加	4 (2.2)	2 (1.2)	0 (0.0)	2 (1.3)	3 (1.9)
血中アルカリホスファターゼ増加	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重減少	2 (1.1)	1 (0.6)	1 (0.6)	1 (0.6)	0 (0.0)
血中クレアチンホスホキナーゼ増加	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
心電図QT延長	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
尿潜血	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
尿量減少	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)

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Table 14.3-1.5.A
Treatment-Emergent Adverse Events: Number (%) of Participants by System Organ Class, Preferred Term and AE Onset Time Intervals
Safety Population

Total (N=186)

System Organ Class Preferred Term	<3 months (N1=186) n (%)	>=3 and <6 months (N1=171) n (%)	>=6 and <9 months (N1=164) n (%)	>=9 and <12 months (N1=160) n (%)	>=12 months (N1=158) n (%)
代謝および栄養障害	3 (1.6)	1 (0.6)	5 (3.0)	0 (0.0)	3 (1.9)
食欲減退	3 (1.6)	1 (0.6)	2 (1.2)	0 (0.0)	1 (0.6)
脱水	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
脂質異常症	0 (0.0)	0 (0.0)	3 (1.8)	0 (0.0)	0 (0.0)
過食	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
筋骨格系および結合組織障害	6 (3.2)	11 (6.4)	7 (4.3)	11 (6.9)	2 (1.3)
関節痛	2 (1.1)	4 (2.3)	2 (1.2)	2 (1.3)	0 (0.0)
背部痛	2 (1.1)	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)
筋肉痛	1 (0.5)	3 (1.8)	1 (0.6)	4 (2.5)	2 (1.3)
四肢痛	1 (0.5)	0 (0.0)	3 (1.8)	0 (0.0)	0 (0.0)
滑液嚢腫	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頚部脊柱管狭窄症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
尾骨痛	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
線維筋痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
筋骨格系胸痛	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
結節性変形性関節症	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
全身性エリテマトーデス	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
顎関節症	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
腱炎	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮平滑筋腫 [f]	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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神経系障害	10 (5.4)	3 (1.8)	10 (6.1)	1 (0.6)	2 (1.3)
頭痛	3 (1.6)	0 (0.0)	5 (3.0)	1 (0.6)	2 (1.3)
傾眠	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自律神経失調	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
味覚減退	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
片頭痛	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠不足	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手根管症候群	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
顔面麻痺	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
嗅覚減退	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
肋間神経痛	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	4 (2.2)	2 (1.2)	3 (1.8)	1 (0.6)	0 (0.0)
不眠症	2 (1.1)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
適応障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気分の落ち込み	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分を伴う適応障害	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
不安	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
自殺念慮	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
腎および尿路障害	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	1 (0.6)
緊張性膀胱	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
蛋白尿	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)

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生殖系および乳房障害	4 (2.2)	0 (0.0)	3 (1.8)	1 (0.6)	0 (0.0)
腺筋症 [f]	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房障害	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経中間期出血 [f]	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
月経前症候群 [f]	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房石灰化	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
乳房腫瘤	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
子宮頚管ポリープ [f]	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)
閉経期症状 [f]	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
呼吸器、胸郭および縦隔障害	6 (3.2)	5 (2.9)	4 (2.4)	2 (1.3)	0 (0.0)
過換気	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咳嗽	1 (0.5)	1 (0.6)	1 (0.6)	0 (0.0)	0 (0.0)
咳喘息	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻閉	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.5)	3 (1.8)	1 (0.6)	1 (0.6)	0 (0.0)
喘息	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
鼻出血	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
痰貯留	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
上気道咳症候群	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	6 (3.2)	6 (3.5)	7 (4.3)	4 (2.5)	0 (0.0)
接触皮膚炎	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
そう痒症	2 (1.1)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
ざ瘡	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
湿疹	1 (0.5)	1 (0.6)	2 (1.2)	1 (0.6)	0 (0.0)
皮脂欠乏症	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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アレルギー性皮膚炎	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)	0 (0.0)
皮脂欠乏性湿疹	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
ばら色粃糠疹	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
蕁麻疹	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)
血管障害	0 (0.0)	2 (1.2)	2 (1.2)	0 (0.0)	0 (0.0)
本態性高血圧症	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
高血圧	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)

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3101-302-002 試験［参考資料］

治験の標題：
A Phase 3, Multicenter, Randomized, Open-Label Study to Evaluate the Long-Term Safety and Tolerability of Oral Atogepant for the Prevention of Migraine in Participants with Episodic Migraine

施設数 / 実施国名：
111 施設 / 米国

治験責任医師：
[redacted], MS, MD

公表文献（参考資料）：
なし

治験期間：
治験開始日（最初の被験者の初回来院日）：2018 年 10 月 8 日
治験終了日（最後の被験者の最終来院日）：2020 年 5 月 29 日

開発のフェーズ：
第 III 相

治験の種類：
多施設共同，無作為化，非盲検，52 週長期安全性，第 III 相試験

目的：
反復性片頭痛（EM）予防に対するアトゲパント水和物（以下「アトゲパント」）60 mg 1 日 1 回（以下「QD」）の 52 週の長期安全性及び忍容性を評価する。

被験者数（計画時と解析時）：
計画時：本試験は，新規被験者及び CGP–MD–01 試験完了者の 2 つのグループで構成された。約 700 例の被験者の無作為化を予定し，そのうち 200 例以上はアトゲパント 60 mg QD 群に無作為化された新規被験者とした。
解析時：合計 744 例の被験者を無作為化し，そのうち 546 例をアトゲパント 60 mg QD 群に，198 例を片頭痛予防の標準治療薬を投与する標準治療群に割り付けた。解析対象集団の概要を以下に示す：

集団	標準治療	アトゲパント 60 mg QD	合計
スクリーニング，N			1727
ITT 集団，N	198	546	744
安全性解析対象集団，N	196	543	739
mITT 集団，N		521	521

intent–to–treat（ITT）集団 = 無作為化されたすべての被験者。
安全性解析対象集団 = 治験薬（アトゲパント又は標準治療薬）を 1 回以上投与されたすべての被験者。
modified intent–to–treat（以下「mITT」）集団 = 安全性解析対象集団の被験者のうちアトゲパントを 1 回以上投与され，評価可能なベースライン期間の電子日誌（以下「eDiary」）データを有し，評価可能なベースライン後 4 週間の eDiary データを 1 つ以上有する被験者。
eDiary データは，標準治療群については収集しなかった。

新規被験者 637 例のうち，467 例がアトゲパント 60 mg QD 投与群に，170 例が標準治療群に無作為化された。CGP–MD–01 試験完了者 107 例のうち，79 例がアトゲパント 60 mg QD 群に，28 例が標準治療群に無作為化された。
設定根拠
目的は，ICH E1 の曝露要件に準拠するよう，300 例以上の被験者にアトゲパントを 6 ヵ月間投与し，100 例以上の被験者に 12 ヵ月間投与することであった。過去の試験[1,2]のデータに基づき，約 60%の被験者が 6 ヵ月間の投

与を完了し，65%が 12 ヵ月間の投与を完了すると推定した。したがって，本試験では，合計 700 例の被験者を 5：2 の比率でアトゲパント 60 mg QD 群と標準治療群に無作為化し，目標とする 6 ヵ月間及び 12 ヵ月間のアトゲパント投与被験者数を得ることとした。

診断と組入れ基準：

選択基準

すべての患者に適用される選択基準は以下のとおりである：

1. 本試験に関するあらゆる手順が開始される前に文書同意及び患者のプライバシーに関する情報（Written Authorization for Use and Release of Health and Research Study Information など）を得られた患者。
2. 標準治療を受ける意思のある患者（患者は，治験実施計画書で規定された片頭痛予防の標準治療薬を 1 種類以上処方される可能性がある）。
3. 試験期間を通して，治験実施計画書に規定された医学的に許容され，効果の高い避妊法を使用している患者。

新規患者のみに適用される選択基準は以下のとおりである：

4. スクリーニング（Visit 1）時に 18 歳以上 80 歳以下の男性患者又は女性患者。
5. 国際頭痛分類第 3 版（以下「ICHD–3」）に基づく診断と一致する前兆のある片頭痛又は前兆のない片頭痛を 1 年以上有する患者。
6. 片頭痛の発症年齢が 50 歳未満の患者。
7. 治験責任医師の判断による Visit 1 前 3 ヵ月間の平均月間片頭痛日数（以下「MMD」）が 4–14 日である患者。
8. eDiary で 28 日間のベースライン期間に片頭痛の日数が 4–14 日である患者。

CGP–MD–01 試験完了者のみに適用される選択基準は以下のとおりである：

9. CGP–MD–01 試験（Visit 8）を完了し，重大な治験実施計画書からの逸脱（治験実施計画書に規定された手順の不遵守など）がなく，治験責任医師の判断により許容できない安全性リスクを示唆する有害事象が認められなかった患者。

新規患者と CGP–MD–01 試験完了者の両方に適用される選択基準は以下のとおりである：

10. ベースライン期間 28 日間のうち 20 日間以上 eDiary への入力があり，治験質問票及び eDairy を読解し，入力することができると治験責任医師が判断した患者。

除外基準

新規患者のみに適用される除外基準は以下のとおりである：

1. 片頭痛を緊張型頭痛又はその他の頭痛と区別することが困難な患者。
2. 複視若しくは意識レベルの低下を伴う片頭痛，又は ICHD–3 に定義されている網膜片頭痛の既往歴を有する患者。
3. ICHD–3 に定義されている慢性片頭痛（CM），新規発症持続性連日性頭痛，三叉神経・自律神経性頭痛（群発頭痛など），又は有痛性脳神経ニューロパチーと現在診断されている患者。
4. 治験責任医師の判断で Visit 1 前 3 ヵ月間の平均月間頭痛日数が 15 日以上である患者。
5. eDiary で 28 日間のベースライン期間の頭痛日数が 15 日以上である患者。
6. オピオイド若しくはバルビツール酸系薬剤を 1 ヵ月あたり 2 日超，トリプタン系薬剤若しくはエルゴタミン製剤を 1 ヵ月あたり 10 日以上，又は単一成分の鎮痛薬（アスピリン，非ステロイド性抗炎症薬［NSAIDs］，アセトアミノフェンなど）を 1 ヵ月あたり 15 日以上，Visit 1 前の 3 ヵ月間に使用したと治験責任医師が判断した，若しくはベースライン期間に使用した患者。すべての患者に，スクリーニング前の 30 日間及びベースライン期間中，バルビツール酸系薬剤の使用は認められない。アトゲパント 60 mg QD 群に無作為化された患者には，試験期間中もバルビツール酸系薬剤の使用は認められない。

特に記載がない限り，すべての患者に適用される除外基準は以下のとおりである：

7. 併用禁止薬若しくは併用禁止療法の一覧（治験実施計画書で規定）に記載されている薬剤，食事（グレープフルーツジュースなど），又は非薬物療法が必要であり，それらを中止できなかった若しくは許容される別

の薬剤や治療法への切り替えができなかった患者。これには片頭痛予防への有効性が示されている併用薬（アミトリプチリン，トピラマート，プロプラノロールなど）も含まれる。

8. 妊娠している，本試験期間中に妊娠を計画している，又は現在授乳中の女性患者。妊娠可能な女性患者は，Visit 1 及び Visit 2 の尿妊娠検査が陰性であること。
9. スクリーニング（Visit 1）時に心電図（以下「ECG」）に臨床的に重大な異常を有すると治験責任医師により判断された患者。
10. 中央検査機関による ECG についての最終報告で Visit 1 に Fridericia 補正法を用いて心拍数で補正した QT 間隔が男性は 450 msec 超，女性は 470 msec 超の患者。
11. 臨床的に重大な心血管疾患又は脳血管疾患を有すると治験責任医師が判断した患者。これには以下の疾患を含むが，これらに限定されない。
    - 臨床的に重大な虚血性心疾患（不安定狭心症など）。
    - 臨床的に重大な心調律異常若しくは心伝導異常（心房細動，第 2 度又は第 3 度心ブロックなど）又はトルサードドポアントの危険因子（心不全，低カリウム血症，徐脈など）。
    - Visit 1 前 6 ヵ月以内の心筋梗塞，一過性脳虚血発作，又は脳卒中。
    - ニューヨーク心臓協会の心機能分類（NYHA 分類）で III 度又は IV 度と定義される心不全。
12. Visit 1 又は Visit 2 に座位収縮期血圧が 160 mm Hg 超又は座位拡張期血圧が 100 mm Hg 超の高血圧の患者。これらの上限を超えた場合，バイタルサインを一回のみ再測定可能とした。
13. Visit 1 の臨床検査値に臨床的に重大な異常が認められた患者。これには以下の臨床検査値を含むが，これらに限定されない。
    - アラニンアミノトランスフェラーゼ（以下「ALT」）値又はアスパラギン酸アミノトランスフェラーゼ（以下「AST」）値が基準値の上限（以下「ULN」）の 1 倍超。
    - 総ビリルビン値が ULN の 1 倍超（ジルベール症候群と診断された患者を除く）。
    - 血清アルブミン値が 2.8 g/dL 未満。
14. 臨床的に重大な血液疾患，内分泌疾患，肺疾患，腎疾患，肝疾患，消化管疾患，又は神経疾患を有する患者。
    - これらの疾患の既往歴を有するものの，Visit 1 前 1 年超，状態が安定しており，本試験への参加に支障をきたすおそれはないと治験責任医師が判断した患者は組入れ可能とした。
    - 腎不全による透析中の患者は除外することとした。
15. スクリーニング（Visit 1）前 6 ヵ月以内の急性肝炎の既往歴若しくは慢性肝疾患（非アルコール性脂肪性肝炎を含む）を有する，又は抗 A 型肝炎 IgM 抗体，B 型肝炎表面抗原，抗 C 型肝炎抗体，若しくは抗 E 型肝炎 IgM 抗体の検査で陽性であった患者。
16. 混合した精神状態，認知症，てんかん，又は片頭痛以外の重大な神経障害を有すると治験責任医師が判断した患者。
17. 現在の頭痛障害に重大な影響を及ぼす可能性がある他の疼痛疾患（線維筋痛，顔面痛など）を併発していると治験責任医師が判断した患者。
18. 臨床面接及びコロンビア自殺評価スケール（以下「C–SSRS」）の回答により自傷行為の重大なリスクが認められた患者，又は他害行為の重大なリスクがあると治験責任医師が判断した患者。過去 6 ヵ月以内に実行の意図を伴う自殺念慮（計画の有無は問わない）（C–SSRS でタイプ 4 又は 5）を報告した患者，又は Visit 1 若しくは Visit 2 の評価前 6 ヵ月以内に何らかの自殺行動を報告した患者は除外することとした。
19. スクリーニング（Visit 1）前 5 年間に悪性腫瘍の既往歴を有する患者（適切に治療された基底細胞癌，扁平上皮癌，又は子宮頚部上皮内癌は除く）。
20. 治験薬の吸収又は代謝に影響を及ぼす可能性のある消化管疾患（下痢症候群，炎症性腸疾患など）の既往歴を有する患者。肥満症に対する胃への処置（ラップバンドなど）を受けたものの，その処置を元に戻した患者は組入れ可能とした。
21. スクリーニング（Visit 1）時にレクリエーショナルドラッグ又は違法薬物の使用者であった患者，又は過去 1 年以内に薬物若しくはアルコールの乱用若しくは依存の既往歴を有する患者。

22. スクリーニング（Visit 1）時の尿中薬物検査が陽性であった患者（片頭痛のために処方されたオピオイド薬などの併用薬物で説明がつく場合は除く）。
23. 治験薬又は治験機器を用いた試験（市販の製剤又は機器を用いた試験も含む）に現在参加中，又は Visit 1 前 30 日以内に参加したことがある患者。
24. 以下の薬剤への曝露歴がある患者：
    a) 過去 6 ヵ月以内にカルシトニン遺伝子関連ペプチド（以下「CGRP」）経路を遮断する注射用モノクローナル抗体
    b) ubrogepant（3 回超投与）
    c) リメゲパント（3 回超投与）
25. CGRP 受容体拮抗薬に対する過敏症又は臨床的に重大な副作用の既往歴を有する患者。
26. 治験責任医師，治験スタッフ，治験依頼者のいずれかに雇用されている，又はその近親者（両親，配偶者，兄弟姉妹，又は子供）。
27. 患者を重大なリスクにさらす，試験結果を混乱させる，又は患者の本試験の参加で著しく支障をきたす可能性があると治験責任医師が判断した状態又は状況にあった患者。
28. 医学的又はその他の理由（試験手順や来院予約を遵守しない可能性がある，試験期間中に転居する予定があるなど）で本試験に不適格と治験責任医師が判断した患者。

治験方法：

3101–302–002 試験は，米国の 111 施設（111 施設で被験者のスクリーニングを行い，106 施設で 1 例以上の被験者を無作為に割り付けた）で実施された多施設共同，無作為化，非盲検，52 週長期安全性試験であった。被験者を 5：2 の比率でアトゲパント 60 mg QD 群（n = 546）又は標準治療群（n = 198）のいずれかに無作為に割り付けた。標準治療群に無作為化されたすべての被験者には，片頭痛の予防治療として安全かつ有効であると認められている経口薬が投与された。片頭痛予防薬の選択は，被験者と協議した上で治験責任医師の判断に基づいていた。選択された片頭痛予防薬に忍容性のない被験者，又はその薬剤の効果が十分でない被験者（治験責任医師の判断による）に対しては，治験責任医師は以下を選択することができた：

1. 片頭痛の予防に安全かつ有効であると認められている薬剤の中から代替薬を処方する。
2. 片頭痛の予防に安全かつ有効であると認められている薬剤にリストされていない代替片頭痛予防薬（リボフラビン，カルバマゼピン，ガバペンチンなど）を処方する。
3. 代替片頭痛予防薬を処方しない。

標準治療群の目的は，52 週間の比較安全性データを収集することであった。したがって，当初選択された片頭痛予防薬に忍容性のない被験者，又はその薬剤の効果が十分でない被験者（治験責任医師の判断による）は，治験責任医師が選択した上記の代替オプション（1，2，又は 3）に関わらず，試験を継続することができた。また，当初の片頭痛予防薬の試行後，代替薬（オプション 1 又は 2）を処方されたが，代替片頭痛予防薬に耐容性のない被験者，又はその薬剤の効果が十分でない被験者は，治験責任医師が選択した上記の代替オプション（1，2，又は 3）に関わらず，試験を継続することができた。更に，治験責任医師が代替予防薬を処方しないことを選択した被験者には，試験期間中いつでも代替薬（オプション 1 又は 2）を処方できる。このプロセスは，治験責任医師の判断で試験期間中必要に応じて繰り返すことができた。

本試験に参加できるのは，以下の 2 つの被験者グループであった：

- 新規被験者：アトゲパントへの曝露歴がなく，選択基準を満たし，除外基準に該当しない被験者。
- CGP–MD–01 試験完了者：重大な治験実施計画書の逸脱（治験実施計画書に規定された手順を遵守しないなど）なく CGP–MD–01 試験（Visit 8）を完了し，選択基準を満たし，除外基準に該当しない被験者。

  CGP–MD–01 試験の完了者は，CGP–MD–01 試験の完了から本長期安全性試験の開始まで，6 ヵ月以上の期間があった。そのため，試験に対する適格性を再度確認し，スクリーニング期間中にベースラインの片頭痛日数を再設定（28 日間のうち 20 日間以上 eDiary に入力）する必要があった（ただし，片頭痛日数は無作為化の選択基準 / 除外基準として使用しなかった）。

本試験は，4 週間のスクリーニング及びベースライン期間，52 週間の投与期間，4 週間の安全性追跡調査期間で構成された。被験者は，適格性が確認された Visit 2 で無作為に割り付けられた。無作為化来院（Visit 2）後の来

院は，52 週間の投与期間中，4 週間ごとであった。被験者は，無作為化来院から 4，8，12，16，20，24，28，32，36，40，44，48，及び 52 週後に，安全性評価のため治験実施医療機関に来院した。安全性追跡調査のための来院は，アトゲパント 60 mg QD の最後の投与から 4 週間後，標準治療群の場合は最後の来院から 4 週間後に実施することとした。

本試験の主な目的は，アトゲパントの長期投与の安全性と忍容性を評価することである。予定されている安全性評価には，有害事象，臨床検査値，ECG，バイタルサイン，身体所見，及び C–SSRS が含まれる。

安全性データ及び要約報告書をレビューし，安全性の問題及び傾向を特定し，新たなデータが予期せぬ臨床的に重大な有害事象を示した場合に試験の変更又は早期中止などを治験依頼者に提言するために，独立したデータ安全性モニタリング委員会（DSMB）を設置した。

判定手順を策定し，臨床判定委員会による治験薬投与終了後の ULN の 3 倍以上の ALT 及び / 又は AST 上昇の監視，モニタリング，及び判定のプロセスを規定した。本判定手順の目的は，ALT 及び / 又は AST 上昇とアトゲパントの因果関係を判定するための標準化したプロセスを提供することであった。

被験薬，用量，投与方法及びロット番号：

アトゲパント 60 mg QD，錠剤，経口投与，ロット番号：[redacted]，[redacted] 及び [redacted]

対照薬，用量，投与方法及びロット番号：

標準治療群に無作為化された被験者は，治験責任医師と協議した上で，片頭痛の予防に安全かつ有効であると認められた薬剤を投与された。治験依頼者は，片頭痛予防の標準治療薬を治験実施医療機関に提供しなかった。

許容される片頭痛予防の標準治療薬は以下のとおりである：

薬理学的分類	薬剤名
抗てんかん薬	バルプロ酸，バルプロ酸ナトリウム，divalproex sodium，トピラマート
三環系抗鬱薬	アミトリプチリン，ノルトリプチリン
β 遮断薬	メトプロロール，ビソプロロール，アテノロール，ナドロール，プロプラノロール，チモロール
カルシウム拮抗剤	フルナリジン
アンジオテンシン受容体拮抗薬（ARB）	カンデサルタン
アンジオテンシン変換酵素（ACE）阻害薬	リシノプリル
セロトニン・ノルアドレナリン再取り込み阻害薬（SNRI）	デスベンラファキシン，ベンラファキシン
その他（米国以外の国のみ）	治験実施国で承認された片頭痛予防薬（oxetrone，pizotifen など）

治療期間：60 週間（4 週間のスクリーニング / ベースライン期間［Visit 2 に無作為化］，52 週間の二重盲検期間，及び 4 週間の安全性追跡調査期間）

評価基準：

有効性：

本試験の主要目的はアトゲパント投与の長期安全性・忍容性を評価することであるため，有効性変数に「主要」，「副次」，又は「追加」という分類は行わなかった。

アトゲパント群の長期有効性を評価するための有効性評価項目は，以下のとおりであった。

- MMD のベースラインからの変化量
- 月間頭痛日数のベースラインからの変化量
- 急性期治療薬の月間使用日数のベースラインからの変化量
- MMD が 25%以上，50%以上，75%以上，及び 100%改善（減少）した被験者の割合

- 月間累積頭痛時間のベースラインからの変化量
- トリプタンの月間使用日数のベースラインからの変化量
- 中等度 / 重度の月間頭痛日数のベースラインからの変化量
- 重度の月間頭痛日数のベースラインからの変化量
- 12，24，36，48，52 及び 56 週時の片頭痛特有の生活の質に関する質問票第 2.1 版（以下「MSQ v2.1」）日常役割機能の制限（以下「RFR」）ドメインスコアのベースラインからの変化量
- 片頭痛による活動障害－ダイアリー（以下「AIM–D」］の日常活動機能ドメイン月間スコアのベースラインからの変化量
- AIM–D の身体障害ドメイン月間スコアのベースラインからの変化量

アトゲパント 60 mg QD 群に対するその他のヘルスアウトカム評価項目は以下のとおりである。

- AIM–D の月間合計スコアのベースラインからの変化量
- 片頭痛予防としての治験薬に「満足している」又は「非常に満足している」と報告した被験者の割合
- Headache Impact Test（以下「HIT–6」）合計スコアのベースラインからの変化量
- HIT–6 合計スコアがベースラインから 5 ポイント以上改善（減少）した被験者の割合
- 12，24，36，48 及び 52 週時に患者の全般的印象度－変化（PGIC）で「かなり改善した」又は「非常に改善した」と評価した被験者の割合
- 仕事の生産性及び活動障害に関する質問票：片頭痛第 2.0 版（WPAI: MIGRAINE）で評価した片頭痛による生産性損失のベースラインからの変化量
  - percent work time missed ドメイン
  - percent impairment while working ドメイン
  - percent overall impairment ドメイン
  - percent activity impairment ドメイン
- European Quality of Life – 5–Dimensional - 5 Level（以下「EQ–5D–5L」）の記述方式指標スコアのベースラインからの変化量
- EQ–5D–5L の視覚的評価尺度（VAS）スコアのベースラインからの変化量
- 12，24，36，48，及び 52 週時の Migraine Disability Assessment（以下「MIDAS」）合計スコアのベースラインからの変化量
- 12，24，36，48，及び 52 週時の MIDAS 欠勤スコア（質問 1，3，及び 5）のベースラインからの変化量
- 12，24，36，48，及び 52 週時の MIDAS 疾病就業スコア（質問 2 及び 4）のベースラインからの変化量
- 患者の全般的印象度－重症度（PGIS）スコアのベースラインからの変化量
- 12，24，36，48，52 及び 56 週時の MSQ v2.1 日常役割機能の妨げドメインスコアのベースラインからの変化量
- 12，24，36，48，52 及び 56 週時の MSQ v2.1 感情的機能ドメインスコアのベースラインからの変化量
- 月間活動レベルのベースラインからの変化量
- 月間活動制限のベースラインからの変化量

安全性：

有害事象，臨床検査値，バイタルサイン，ECG，C–SSRS

統計手法：

有効性：

すべての有効性解析は，mITT 集団を用いて実施した。mITT 集団は，治験薬を 1 回以上投与され，評価可能なベースライン期間の eDiary データを有し，評価可能なベースライン後 4 週間の eDiary データを 1 つ以上有する無作為化されたすべての被験者で構成された。標準治療群の被験者から有効性の測定結果を収集しなかったため，mITT 集団はアトゲパント 60 mg QD 群のみに対して定義した。

有効性の評価項目は，MMD のベースラインからの変化量，月間頭痛日数のベースラインからの変化量，MMD

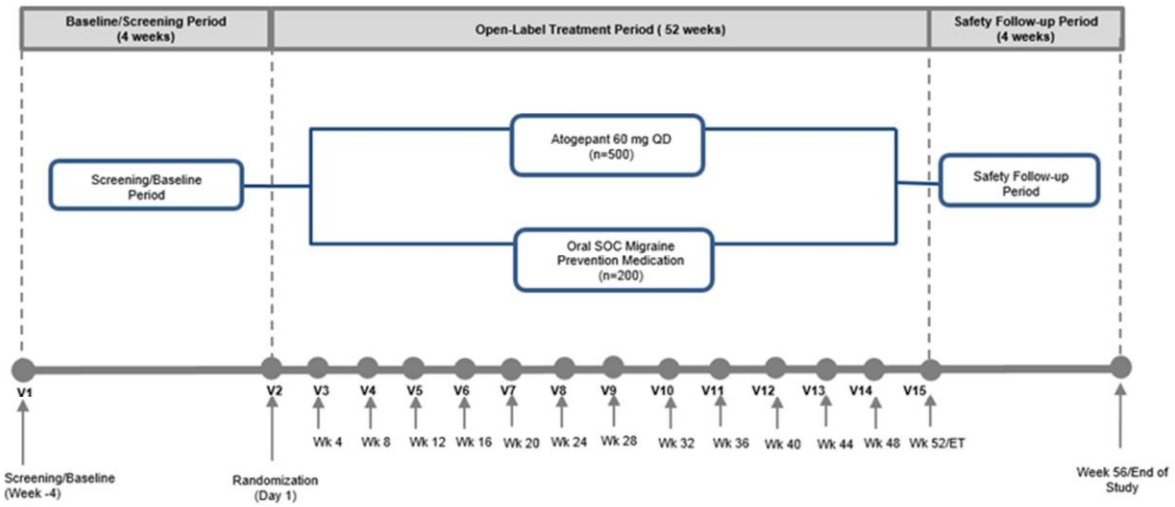
の 50%以上の減少などであった。解析の目的上，4 週間（28 日）を 1 ヵ月とみなした。各月間期間の MMD のベースラインからの変化量は，来院をカテゴリー変数の固定効果とし，ベースラインスコア及びベースラインと来院の交互作用を共変量として反復測定混合効果モデル（以下「MMRM」）を用いて解析した。月間頭痛日数のベースラインからの変化量は同様に解析した。各月間期間の 50%レスポンダーについて要約統計量を示した。50%レスポンダーは，MMD がベースラインから 50%以上減少した被験者と定義した。

安全性：

安全性解析対象集団は，治験薬（アトゲパント又は片頭痛予防の標準治療薬）を 1 回以上投与されたすべての被験者と定義した。すべての安全性解析は，アトゲパント 60 mg QD 群及び標準治療群について，計画した無作為化に従って割り付けた投与群とは関係なく，実際の投与に基づいて実施した。

臨床検査，バイタルサイン，ECG の各パラメータについて，初回投与前の欠損値ではない最後の安全性評価値を，その安全性パラメータのすべての解析のベースライン値として使用した。連続変数は，被験者数と平均値，標準偏差，中央値，最小値，及び最大値で要約した。カテゴリー変数は，被験者の人数と割合で要約した。

図 1. 試験デザインの概略（3101–302–002 試験）



ET = 早期中止，V = Visit，Wk = Week

Cross reference: 3101–302–002 final CSR Figure 9-1

試験結果

被験者の内訳

被験者の内訳を表 1 に示す。

744 例の被験者が無作為化され，52 週の非盲検投与期間を完了した被験者の割合は 68.4%であり，試験を中止した被験者の割合は 31.6%であった。非盲検投与期間で割合が高かった試験中止の主な理由は，被験者による同意撤回（14.0%），追跡不能（5.2%），治験実施計画書からの逸脱（5.1%），及び有害事象（4.8%）であった。

人口統計学的及び他のベースラインの特性

人口統計学的特性，ベースライン特性及び原疾患のベースライン特性をそれぞれ表 2，表 3 及び表 4 に示す。

安全性解析対象集団では，被験者の人口統計学的及び身体的なベースライン特性は，全体的にアトゲパント 60 mg QD 群及び標準治療群で同様であった。全体で年齢の平均値は 42.2 歳，88.1%が女性，75.9%が白人，84.7%がヒスパニック又はラテン系以外，体重の平均値は 83.91 kg，体格指数（以下「BMI」）の平均値は 30.55 kg/m^2（中央値は 29.2 kg/m^2）であった。全体で，被験者の 25%は 96.20 kg 以上であり，被験者の 25%は BMI が 34.94 kg/m^2 以上であった。全体で被験者の 26.5%が片頭痛予防の有効性が認められた薬剤を事前に使用していた。

全体で，被験者の 22.1%が前兆のある片頭痛，41.4%が前兆のない片頭痛，36.5%が前兆のない片頭痛及び前兆のある片頭痛の両方と診断された。片頭痛の平均罹病期間は 20.6 年であり，31.7%が過去に（有効性が認められた又は認められていない）片頭痛予防薬を使用していた。平均 MMD（スクリーニング前 3 ヵ月間のデータに基づく）は 7.3 日であり，平均月間頭痛日数（スクリーニング前 3 ヵ月間のデータに基づく）は 9.3 日であった。

曝露状況

曝露状況を表 5 に示す。

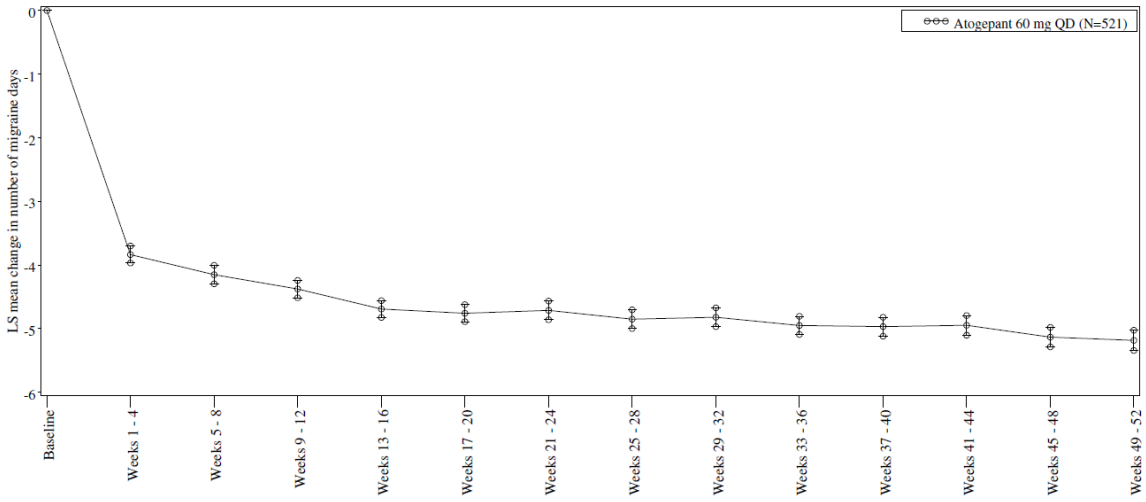
アトゲパント 60 mg QD 群では，試験期間中 180 日以上及び 360 日以上投与された被験者は，それぞれ 428 例（78.8%）及び 362 例（66.7%）であった。アトゲパントを投与された被験者の平均曝露日数は 291.6 日であった。アトゲパント 60 mg QD 群の曝露期間は 433.6 人年であった。

有効性の結果

有効性評価項目の結果を表 6–表 15 に示す。

臨床的に意義がある平均 MMD の減少が最初の 1 ヵ月間に認められ，1 年間の投与期間中持続した（図 2）。アトゲパントの投与によって，最初の 1 ヵ月間（1–4 週）の MMD の最小二乗平均値は 3.84 日減少した。52 週間の投与期間の残りの期間も改善が続き，最後の 1 ヵ月間（49–52 週）のベースラインからの変化量の最小二乗平均値の減少は 5.19 日であった。

図 2. MMD のベースラインからの変化量（MMRM）の最小二乗平均値（±SE）（3101–302–002 試験，投与期間，mITT 集団）



SE = 標準誤差
MMRM は，無構造の共分散行列を用いて，来院（月として導出される）をカテゴリー変数の固定効果とし，ベースラインスコア及びベースラインと来院の交互作用を共変量として含める。
Cross reference: 3101–302–002 final CSR Figure 14.2-1.1

49–52 週では，ベースラインからの MMD の 25%以上の減少が 90.7%（304 / 335 例），50%以上の減少が 84.2%（282 / 335 例），75%以上の減少が 69.9%（234 / 335 例），及び 100%の減少が 48.4%（162 / 335 例）で認められた。

アトゲパント 60 mg QD 群では，月間頭痛日数にも MMD と同様の経時的反応が認められた。月間頭痛日数のベースラインからの変化量の最小二乗平均値は，1–4 週に–4.00 日，49–52 週に–5.99 日であった。

アトゲパントの投与によって，月間累積頭痛時間も減少した。月間累積頭痛時間のベースラインからの変化量の最小二乗平均値は，1–4 週に–25.55 時間，49–52 週に–32.97 時間であった（3101-302-002 final CSR Table 14.2-5.1）。

アトゲパントの投与によって，急性期治療薬の月間使用日数及びトリプタン系薬剤の使用日数も減少した。急性期治療薬の月間使用日数のベースラインからの変化量の最小二乗平均値は，1–4 週に–4.04 日，49–52 週に–4.93 日であった。トリプタン系薬剤の月間使用日数のベースラインからの変化量の最小二乗平均値は，1–4 週に–1.26 日，49–52 週に–1.48 日であった（3101–302–002 final CSR Table 14.2-5.2）。

ヘルスアウトカムの評価（MSQ v2.1 の RFR ドメインスコア並びに AIM–D の日常活動機能及び身体障害ドメインスコア）の結果は，アトゲパント群で改善を示した。反応は最初の 1 ヵ月（1–4 週）に始まり，52 週間の投与期間の残りの期間も改善が持続した。MSQ v2.1 の RFR ドメ

インスコアのベースラインからの変化量の最小二乗平均値（標準誤差［以下「SE」］）は，12 週時に 30.02（0.944），52 週時に 34.70（0.997）であった。AIM–D の日常活動機能ドメイン平均月間スコアのベースラインからの変化量の最小二乗平均値（SE）は 1–4 週に–7.61（0.329），49–52 週に–10.17（0.370）であった。AIM–D の身体障害ドメイン平均月間スコアのベースラインからの変化量の最小二乗平均値（SE）は，1–4 週に–5.56（0.290），49–52 週に–7.20（0.357）であった。

安全性の結果

有害事象

有害事象の発現状況を以下に示す。

有害事象の発現割合は，アトゲパント 60 mg QD 群 67.0%（364 / 543 例），標準治療群 78.6%（154 / 196 例）であった。

いずれかの投与群で発現割合が 5%以上の有害事象は，上気道感染（アトゲパント 60 mg QD 群 10.3%［56 例］，標準治療群 12.2%［24 例］，以下同順），便秘（7.2%［39 例］，3.1%［6 例］），悪心（6.3%［34 例］，6.1%［12 例］），尿路感染（5.2%［28 例］，4.6%［9 例］），上咽頭炎（4.4%［24 例］，5.1%［10 例］），浮動性めまい（3.1%［17 例］，11.2%［22 例］），不安（2.9%［16 例］，5.6%［11 例］），疲労（2.6%［14 例］，6.1%［12 例］），及び体重増加（1.3%［7 例］，5.6%［11 例］）であった。

治験薬と関連ありの有害事象の発現割合は，アトゲパント 60 mg QD 群 18.0%（98 例），標準治療群 36.2%（71 例）であった。

いずれかの投与群で発現割合が 2%以上の治験薬と関連ありの有害事象は，便秘（アトゲパント 60 mg QD 群 4.8%［26 例］，標準治療群 1.5%［3 例］，以下同順），悪心（2.9%［16 例］，4.6%［9 例］），口内乾燥（0.4%［2 例］，3.1%［6 例］），下痢（0%，3.1%［6 例］），疲労（2.2%［12 例］，4.6%［9 例］），体重増加（0.4%［2 例］，2.6%［5 例］），浮動性めまい（1.1%［6 例］，7.7%［15 例］），傾眠（0.6%［3 例］，2.6%［5 例］），頭痛（0.2%［1 例］，2.0%［4 例］），錯感覚（0.2%［1 例］，4.6%［9 例］），鎮静（0%，2.0%［4 例］），不安（0.4%［2 例］，2.6%［5 例］），及び不眠症（0.2%［1 例］，3.1%［6 例］）であった。

アトゲパント 60 mg QD 群で報告された有害事象の大半は軽度（25.8%）又は中等度（34.4%）であった。高度の有害事象の発現割合は，アトゲパント 60 mg QD 群 6.8%（37 / 543 例），標準治療群 5.1%（10 / 196 例）であった。

いずれかの投与群で 2 例以上に発現した高度の有害事象は，非心臓性胸痛（アトゲパント 60 mg QD 群 0%，標準治療群 1.0%［2 例］，以下同順），アスパラギン酸アミノトランスフェラーゼ増加（0.4%［2 例］，0%），アラニンアミノトランスフェラーゼ増加（0.4%［2 例］，0.5%［1 例］），関節痛（0.4%［2 例］，0%），片頭痛（0.4%［2 例］，0%），及び不安（0.4%［2 例］，1.0%［2 例］）であった。

投与終了後の有害事象の発現割合は，アトゲパント 60 mg QD 群 7.7%（42 例），標準治療群 9.2%（18 例）であった（3101-302-002 final CSR Table 14.3-2.1.6）。

いずれかの投与群で 2 例以上に発現した投与終了後の有害事象は，悪心（アトゲパント 60 mg QD 群 0.4%［2 例］，標準治療群 0%，以下同順），尿路感染（0.2%［1 例］，1.0%［2 例］），上咽頭炎（0%，1.0%［2 例］），上気道感染（0%，1.5%［3 / 196 例］），片頭痛（0.9%［5 例］，0%），及び高血圧（0.4%［2 例］，0%）であった。

アトゲパントを投与した 2 例の被験者に死亡が認められ，これらの死亡（殺人の被害者及び β 溶血性レンサ球菌感染［中毒性ショック症候群］）は，治験責任医師によりアトゲパントと関連なしと判断された。

重篤な有害事象の発現割合は，アトゲパント 60 mg QD 群 4.4%（24 例），標準治療群 3.6%（7 例）であった。

重篤な有害事象は，回転性めまい（アトゲパント 60 mg QD 群 0.2%［1 例］，標準治療群 0%，以下同順），嘔吐（0.2%［1 例］，0%），非心臓性胸痛（0%，1.0%［2 例］），胆嚢炎（0.2%［1 例］，0%），β 溶血性レンサ球菌感染（0.2%［1 例］，0%），コロナウイルス感染（0.2%［1 例］，0%），肺炎（0.2%［1 例］，0%），敗血症（0.2%［1 例］，0%），関節脱臼（0.2%［1 例］，0%），過量投与（0.2%［1 例］，0%），肋骨骨折（0.2%［1 例］，0%），脱水（0.2%［1 例］，0%），電解質失調（0.2%［1 例］，0%），骨壊死（0%，0.5%［1 例］），結腸腺癌（0.2%［1 例］，0%），基底細胞癌（0.2%［1 例］，0%），悪性黒色腫（0.2%［1 例］，0%），遠隔転移を伴う神経内分泌癌（0.2%［1 例］，0%），子宮平滑筋腫（0.2%［1 / 479 例］，0%［0 / 172 例］），乳癌（0%，0.5%［1 例］），遠隔転移を伴う結腸癌（0%，0.5%［1 例］），頚髄神経根障害（0.2%［1 例］，0%），てんかん（0.2%［1 例］，0%），片頭痛（0.2%［1 例］，0%），片頭痛発作重積（0.2%［1 例］，0%），一過性全健忘（0.2%［1 例］，0%），医療機器機能不良（0%，0.5%［1 例］），不安（0.2%［1 例］，0%），自殺行為（0.2%［1 例］，0%），自殺企図（0.2%［1 例］，0%），自殺念慮（0%，0.5%［1 例］），卵巣嚢胞（0.2%［1 / 479 例］，0%［0 / 172 例］），子宮出血（0.2%［1 / 479 例］，0%［0 / 172 例］），急性呼吸窮迫症候群（0.2%［1 例］，0%），肺穿孔（0.2%［1 例］，0%），犯罪被害者（0.2%［1 例］，0%），及び殺人の被害者（0.2%［1 例］，0%）であった。

治験薬の投与中止に至った有害事象の発現割合は，アトゲパント 60 mg QD 群 5.7%（31 例），標準治療群 2.6%（5 例）であった。

アトゲパント 60 mg QD 群で 2 例以上に発現した治験薬の投与中止に至った有害事象は，悪心（アトゲパント 60 mg QD 群 0.6%［3 例］，標準治療群 0%，以下同順），疲労（0.4%［2 例］，0%），浮動性めまい（0.4%［2 例］，0.5%［1 例］），発疹（0.4%［2 例］，0%）であった。

試験期間中にアトゲパント 60 mg QD 群の 5 例及び標準治療群の 2 例が妊娠した。アトゲパント 60 mg QD 群の 1 例及び標準治療群の 1 例が健康な正期産児を出産し，標準治療群の 1 例が妊娠中絶した。アトゲパント群 60 mg QD の 1 例は正期産児を出産したが，正期産児に低血糖，低血中カリウム，及び新生児黄疸が認められた。新生児集中治療室に入院し，いずれも改善した。アトゲパント 60 mg QD 群の 3 例の妊娠については，情報が得られなかった。

特に注目すべき有害事象

非盲検投与期間中，アトゲパント 60 mg QD 群では 5 例（0.9%）が自殺念慮を報告し，そのうち 2 例が自殺行動（自殺企図）を伴ったが，いずれも治験責任医師により治験薬との関連なしと判断された。標準治療群では 5 例（2.6%）が自殺念慮を報告したが，自殺行動はなかった。非盲検投与期間中，アトゲパント 60 mg QD 群では 2 例にタイプ 5 の積極的な自殺念慮と自殺行動が認められ，標準治療群ではタイプ 4（実行する意思が多少あるが，具体的な計画はない）及びタイプ 5（具体的な計画及び実行する意思あり）の積極的な自殺念慮は認められなかった。いずれも重篤な有害事象として報告された。

安全性追跡調査期間中，アトゲパント 60 mg QD 群の 3 例（0.6%）及び標準治療群の 2 例（1.0%）が自殺念慮を報告し，アトゲパント 60 mg QD 群の 1 例（0.2%）及び標準治療群の 1 例（0.5%）が自殺行動を報告した。安全性追跡期間中にアトゲパント 60 mg QD 群の 1 例にタイプ 5 の自殺念慮及び自殺行動が認められ，標準治療群の 1 例にタイプ 4 の積極的自殺念慮及び自殺行動が認められた。いずれも重篤な有害事象として報告された。

潜在的な Hy's law 基準に該当した被験者は認められず，ALT 及び / 又は AST が ULN の 3 倍以上の上昇と総ビリルビンが ULN の 1.5 倍以上の上昇が同時に認められた被験者はいなかった。

ALT 又は AST が ULN の 3 倍以上の上昇は，アトゲパント 60 mg QD 群の 13 例（2.4%），標準治療群の 6 例（3.2%）に認められた。

ALT 又は AST が ULN の 3 倍以上の上昇が認められたアトゲパント群の 13 例のうち，独立した臨床判定委員会による盲検下での判定は，治験薬とおそらく関連なしが 11 例，治験薬と関連あるかもしれないが 2 例であった。被験者ごとの評価，臨床判定委員会による盲検下での判定，及び被験者全体のパターン及び / 又は傾向の評価に基づき，本試験では，アトゲパントに関連する肝臓への安全性上の問題は確認されなかった。標準治療群の 6 例については，規則に従い臨床判定委員会は因果関係を判定しなかった。

本試験で発現した有害事象を以下のとおり示す。

項目	全体集団
有害事象の要約	表 16（Table 14.3-2.1.1）
すべての有害事象	表 17（Table 14.3-2.1.2）
因果関係「関連あり」の有害事象	表 18（Table 14.3-2.1.5）
重症度別有害事象	表 19（Table 14.3-2.1.4）
重篤な有害事象	表 20（Table 14.3-2.2.1）
治験薬の投与中止に至った有害事象	表 21（Table 14.3-2.2.2）

臨床検査

その他の臨床検査値に臨床的に意義がある変化は認められなかった。被験者ごとの評価，臨床判定委員会による盲検下での判定，及び被験者全体のパターン及び / 又は傾向の評価に基づき，本試験では，アトゲパントに関連する肝臓への安全性の問題は確認されなかった。

バイタルサイン

本試験では，バイタルサインのパラメータの平均変化量及び臨床的に意義がある可能性のある（PCS）バイタルサイン値が認められた被験者の割合は，体重を除いて概して小さく，投与群間で同等であった。過体重集団（アトゲパント群のベースラインの平均 BMI が 30.54 kg/m^2）の平均体重は 1.42 kg 減少し，アトゲパント群の被験者の 24.1%で体重が 7%以上減少した。バイタルサインの結果に意義のある変化は認められなかった。

ECG

ECG の結果に意義のある変化は認められなかった。

結論

52 週間の投与期間でアトゲパント 60 mg QD が片頭痛予防として安全で忍容性も良好であることが裏付けられた。安全性に関する懸念は認められなかった。

MMD，月間頭痛日数，急性期治療薬の月間使用日数，トリプタン系薬剤の月間使用日数などの減少が示され，アトゲパント 60 mg QD の長期（52 週間）有効性が裏付けられた。ヘルスアウトカムの評価（MSQ v2.1 の RFR ドメインスコア，並びに AIM–D の日常活動機能及び身体障害ドメインスコア）の結果から，被験者の生活の質が改善したことが示された。

参考文献

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2. Rapoport A, Mauskop A, Diener HC, et al. Long-term migraine prevention with topiramate: open-label extension of pivotal trials. Headache. 2006;46(7):1151-60.

Allergan
Protocol 3101-302-002

Atogepant (AGN-241689)

Table 14.1-1.4
Participant Disposition
All Randomized Participants

Phase Disposition	Standard of Care (N=198) n (%)	Atogepant 60 mg QD (N=546) n (%)	Total (N=744) n (%)
Number of Participants Randomized	198 (100.0)	546 (100.0)	744 (100.0)
Number of Participants Treated	196 (99.0)	543 (99.5)	739 (99.3)
Open-Label Treatment Period			
Number of Participants Entered	198 (100.0)	546 (100.0)	744 (100.0)
Number of Participants Completed	136 (68.7)	373 (68.3)	509 (68.4)
Number of Participants Discontinued	62 (31.3)	173 (31.7)	235 (31.6)
Reason for Discontinuation			
Adverse Event	5 (2.5)	31 (5.7)	36 (4.8)
Lack of efficacy	2 (1.0)	5 (0.9)	7 (0.9)
Withdrawal by Subject	29 (14.6)	75 (13.7)	104 (14.0)
Lost to Follow-Up	16 (8.1)	23 (4.2)	39 (5.2)
Pregnancy	2 (1.0)	4 (0.7)	6 (0.8)
Protocol deviation	7 (3.5)	31 (5.7)	38 (5.1)
Non-compliance with study drug	1 (0.5)	3 (0.5)	4 (0.5)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (0.2)	1 (0.1)
Safety Follow-Up Period			
Number of Participants Entered	159 (80.3)	472 (86.4)	631 (84.8)
Number of Participants Completed	151 (76.3)	448 (82.1)	599 (80.5)
Number of Participants Discontinued	8 (4.0)	24 (4.4)	32 (4.3)
Reason for Discontinuation			
Adverse Event	0 (0.0)	1 (0.2)	1 (0.1)
Withdrawal by Subject	4 (2.0)	18 (3.3)	22 (3.0)
Lost to Follow-Up	4 (2.0)	1 (0.2)	5 (0.7)
Pregnancy	0 (0.0)	0 (0.0)	0 (0.0)
Protocol deviation	0 (0.0)	3 (0.5)	3 (0.4)
Study Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Site Terminated by Sponsor	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	1 (0.2)	1 (0.1)

N = Number of randomized participants.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

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Table 14.1-3.1.1
Demographics
Safety Population

Parameter	Standard of Care (N=196)	Atogepant 60 mg QD (N=543)	Total (N=739)
Age (years)			
Mean (SD)	41.1 (12.09)	42.5 (12.03)	42.2 (12.05)
Median	41.0	43.0	42.0
Q1, Q3	32.0, 49.0	34.0, 51.0	33.0, 50.0
Min, Max	19, 76	18, 78	18, 78
n	196	543	739
Age Group 1, n (%)			
< 20	1 (0.5)	7 (1.3)	8 (1.1)
20-29	40 (20.4)	80 (14.7)	120 (16.2)
30-39	48 (24.5)	142 (26.2)	190 (25.7)
40-49	61 (31.1)	156 (28.7)	217 (29.4)
50-59	30 (15.3)	110 (20.3)	140 (18.9)
60-69	14 (7.1)	41 (7.6)	55 (7.4)
>= 70	2 (1.0)	7 (1.3)	9 (1.2)
Age Group 2, n (%)			
< 40	89 (45.4)	229 (42.2)	318 (43.0)
40-64	101 (51.5)	296 (54.5)	397 (53.7)
>= 65	6 (3.1)	18 (3.3)	24 (3.2)
Age Group 3, n (%)			
< 75	195 (99.5)	539 (99.3)	734 (99.3)
>= 75	1 (0.5)	4 (0.7)	5 (0.7)
Sex, n (%)			
Male	24 (12.2)	64 (11.8)	88 (11.9)
Female	172 (87.8)	479 (88.2)	651 (88.1)

Age is relative to informed consent date.
[1] Participants who reported multiple races are only included in multiple category.
N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

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Allergan
Protocol 3101-302-002

Table 14.1-3.1.1
Demographics
Safety Population

Parameter	Standard of Care (N=196)	Atogepant 60 mg QD (N=543)	Total (N=739)
Race, n (%)			
White	145 (74.0)	416 (76.6)	561 (75.9)
Black or African American	38 (19.4)	100 (18.4)	138 (18.7)
Asian	5 (2.6)	12 (2.2)	17 (2.3)
American Indian Or Alaska Native	0 (0.0)	3 (0.6)	3 (0.4)
Native Hawaiian Or Other Pacific Islander	2 (1.0)	2 (0.4)	4 (0.5)
Multiple [1]	5 (2.6)	10 (1.8)	15 (2.0)
Missing	1 (0.5)	0 (0.0)	1 (0.1)
Race Group, n (%)			
White	145 (74.0)	416 (76.6)	561 (75.9)
All Other Races	50 (25.5)	127 (23.4)	177 (24.0)
Missing	1 (0.5)	0 (0.0)	1 (0.1)
Ethnicity, n (%)			
Hispanic or Latino	29 (14.8)	83 (15.3)	112 (15.2)
Not Hispanic or Latino	166 (84.7)	460 (84.7)	626 (84.7)
Missing	1 (0.5)	0 (0.0)	1 (0.1)

Age is relative to informed consent date.
[1] Participants who reported multiple races are only included in multiple category.
N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).

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Table 14.1-3.1.3
Baseline Characteristics
Safety Population

Parameter	Standard of Care (N=196)	Atogepant 60 mg QD (N=543)	Total (N=739)
Weight (kg)			
Mean (SD)	83.49 (22.942)	84.06 (21.977)	83.91 (22.223)
Median	77.35	81.00	80.60
Q1, Q3	65.90, 97.35	68.50, 95.70	67.20, 96.20
Min, Max	46.7, 170.0	40.7, 176.8	40.7, 176.8
n	196	543	739
Height (cm)			
Mean (SD)	165.15 (8.711)	165.76 (8.895)	165.60 (8.845)
Median	163.75	165.10	165.10
Q1, Q3	159.75, 170.20	160.00, 171.40	160.00, 171.40
Min, Max	147.0, 195.6	140.0, 203.2	140.0, 203.2
n	196	543	739
BMI (kg/m^2)			
Mean (SD)	30.60 (8.028)	30.54 (7.440)	30.55 (7.595)
Median	28.22	29.34	29.20
Q1, Q3	24.65, 35.18	25.22, 34.90	24.95, 34.94
Min, Max	18.8, 60.3	17.5, 58.8	17.5, 60.3
n	196	543	739
Prior Exposure to a Migraine Prevention Medication with Proven Efficacy, n (%)			
Yes	46 (23.5)	150 (27.6)	196 (26.5)
No	150 (76.5)	393 (72.4)	543 (73.5)

N = Number of participants in the Safety Population.
n = Number of participants within a specific category.
Percentages are calculated as 100 x (n/N).
The prior exposure to a migraine prevention medication with proven efficacy (Yes/No) is from the prior and concomitant medications eCRF.

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Table 14.1-3.2.2
Number (%) of Participants with Migraine History
Safety Population

Parameter Category Statistics	Standard of Care (N=196)	Atogepant 60 mg QD (N=543)	Total (N=739)
Migraine Diagnosis, n1 (%)			
With Aura	47 (24.0)	116 (21.4)	163 (22.1)
Without Aura	83 (42.3)	223 (41.1)	306 (41.4)
Both	66 (33.7)	204 (37.6)	270 (36.5)
Migraine Disorder Duration in Years			
Mean (SD)	19.6 (12.41)	20.9 (12.38)	20.6 (12.39)
Median	17.5	19.0	19.0
Q1, Q3	10.0, 28.5	11.0, 28.0	10.8, 28.0
Min, Max	1, 60	1, 66	1, 66
n	196	543	739
Migraine Prevention Medication in the Past, n1 (%)			
Yes	55 (28.1)	179 (33.0)	234 (31.7)
No	141 (71.9)	364 (67.0)	505 (68.3)
Average Number of Migraine Days per Month in Last 3 Months			
Mean (SD)	7.2 (2.56)	7.3 (2.59)	7.3 (2.58)
Median	7.0	7.0	7.0
Q1, Q3	5.0, 9.0	5.0, 9.0	5.0, 9.0
Min, Max	4, 15	3, 14	3, 15
n	196	543	739
Average Number of Headache Days per Month in Last 3 Months			
Mean (SD)	9.4 (2.72)	9.2 (2.74)	9.3 (2.74)
Median	10.0	9.0	9.0
Q1, Q3	7.0, 12.0	7.0, 12.0	7.0, 12.0
Min, Max	4, 15	4, 17	4, 17
n	196	543	739

N = Number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).
n = Number of participants with non-missing values in the specific category.
[1] Current usual treatment for acute migraine.

Table 14.1-3.2.2
Number (%) of Participants with Migraine History
Safety Population

Parameter Category Statistics	Standard of Care (N=196)	Atogepant 60 mg QD (N=543)	Total (N=739)
Acute Medication Treatment [1], n1 (%)			
Yes	191 (97.4)	539 (99.3)	730 (98.8)
Triptan	71 (36.2)	215 (39.6)	286 (38.7)
Ergot or Ergot Combinations	0 (0.0)	0 (0.0)	0 (0.0)
NSAID	121 (61.7)	337 (62.1)	458 (62.0)
Opiate or Opiate Combination	1 (0.5)	15 (2.8)	16 (2.2)
Antiemetic Agent	5 (2.6)	31 (5.7)	36 (4.9)
Barbiturates	0 (0.0)	1 (0.2)	1 (0.1)
Other	123 (62.8)	326 (60.0)	449 (60.8)
No	5 (2.6)	4 (0.7)	9 (1.2)
Advice on Lifestyle Alterations, n1 (%)			
Yes	97 (49.5)	278 (51.2)	375 (50.7)
No	99 (50.5)	265 (48.8)	364 (49.3)

N = Number of participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).
n = Number of participants with non-missing values in the specific category.
[1] Current usual treatment for acute migraine.

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Allergan
Protocol 3101-302-002

Atogepant (AGN-241689)

Table 14.3-1.1
Treatment Duration
Safety Population

	Standard of Care (N=196)	Atogepant 60 mg QD (N=543)
Treatment Duration (Days), n1 (%)		
>= 1	196 (100.0)	543 (100.0)
>= 28	186 (94.9)	516 (95.0)
>= 56	174 (88.8)	495 (91.2)
>= 84	163 (83.2)	469 (86.4)
>= 90	160 (81.6)	459 (84.5)
>= 112	155 (79.1)	453 (83.4)
>= 140	150 (76.5)	441 (81.2)
>= 168	142 (72.4)	434 (79.9)
>= 180	140 (71.4)	428 (78.8)
>= 196	135 (68.9)	426 (78.5)
>= 224	129 (65.8)	413 (76.1)
>= 252	124 (63.3)	403 (74.2)
>= 270	123 (62.8)	397 (73.1)
>= 280	122 (62.2)	392 (72.2)
>= 360	115 (58.7)	362 (66.7)
Mean (SD)	278.9 (143.08)	291.6 (123.40)
Median	365.0	364.0
Q1, Q3	142.5, 392.0	231.0, 365.0
Min, Max	1, 406	1, 384
n	196	543
Participant-Years	149.6	433.6

Treatment Duration = last study treatment date - first study treatment date + 1.
Participant-Years = (total treatment duration in days)/365.25.
N = Number of Participants in the Safety Population.
n1 = Number of participants within a specific category.
Percentages are calculated as 100 x (n1/N).

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Allergan Atogepant (AGN-241689)
Protocol 3101-302-002 Page 1 of 13

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4		
Baseline	Mean	7.30
	SD	2.621
	SEM	0.116
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	513
Post-baseline	Mean	3.47
	SD	3.352
	SEM	0.148
	Median	3.00
	Q1, Q3	1.00, 5.00
	Min, Max	0.0, 25.0
	n	513
CFB	Mean	-3.84
	SD	3.316
	SEM	0.146
	Median	-4.00
	Q1, Q3	-6.00, -2.00
	Min, Max	-11.9, 12.4
	n	513
MMRM [1]	LS Mean (SE)	-3.84 (0.135)
	95% CI	-4.10, -3.57

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

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Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 5 - 8		
Baseline	Mean	7.31
	SD	2.621
	SEM	0.118
	Median	7.00
	Q1, Q3	5.38, 9.00
	Min, Max	0.0, 27.0
	n	490
Post-baseline	Mean	3.13
	SD	3.466
	SEM	0.157
	Median	2.07
	Q1, Q3	1.00, 4.67
	Min, Max	0.0, 28.0
	n	490
CFB	Mean	-4.18
	SD	3.569
	SEM	0.161
	Median	-4.27
	Q1, Q3	-6.46, -2.02
	Min, Max	-13.7, 14.0
	n	490
MMRM [1]	LS Mean (SE)	-4.15 (0.146)
	95% CI	-4.44, -3.87

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 9 - 12		
Baseline	Mean	7.29
	SD	2.617
	SEM	0.121
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	466
Post-baseline	Mean	2.85
	SD	3.251
	SEM	0.151
	Median	2.00
	Q1, Q3	0.00, 4.15
	Min, Max	0.0, 28.0
	n	466
CFB	Mean	-4.44
	SD	3.304
	SEM	0.153
	Median	-4.66
	Q1, Q3	-6.96, -2.74
	Min, Max	-16.3, 10.4
	n	466
MMRM [1]	LS Mean (SE)	-4.38 (0.136)
	95% CI	-4.65, -4.11

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

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Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 13 - 16		
Baseline	Mean	7.31
	SD	2.604
	SEM	0.124
	Median	7.00
	Q1, Q3	5.38, 9.00
	Min, Max	0.0, 27.0
	n	440
Post-baseline	Mean	2.52
	SD	3.140
	SEM	0.150
	Median	1.75
	Q1, Q3	0.00, 4.00
	Min, Max	0.0, 26.8
	n	440
CFB	Mean	-4.78
	SD	3.186
	SEM	0.152
	Median	-4.96
	Q1, Q3	-7.00, -3.00
	Min, Max	-13.0, 11.8
	n	440
MMRM [1]	LS Mean (SE)	-4.69 (0.133)
	95% CI	-4.95, -4.43

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 17 - 20		
Baseline	Mean	7.30
	SD	2.604
	SEM	0.127
	Median	7.00
	Q1, Q3	5.38, 9.00
	Min, Max	0.0, 27.0
	n	419
Post-baseline	Mean	2.33
	SD	3.007
	SEM	0.147
	Median	1.27
	Q1, Q3	0.00, 3.50
	Min, Max	0.0, 28.0
	n	419
CFB	Mean	-4.96
	SD	3.255
	SEM	0.159
	Median	-5.00
	Q1, Q3	-7.00, -3.00
	Min, Max	-15.2, 11.4
	n	419
MMRM [1]	LS Mean (SE)	-4.76 (0.134)
	95% CI	-5.02, -4.50

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 21 - 24		
Baseline	Mean	7.27
	SD	2.576
	SEM	0.126
	Median	7.00
	Q1, Q3	5.38, 9.00
	Min, Max	0.0, 27.0
	n	417
Post-baseline	Mean	2.37
	SD	3.205
	SEM	0.157
	Median	1.17
	Q1, Q3	0.00, 3.50
	Min, Max	0.0, 28.0
	n	417
CFB	Mean	-4.91
	SD	3.559
	SEM	0.174
	Median	-5.00
	Q1, Q3	-7.00, -3.00
	Min, Max	-14.0, 11.9
	n	417
MMRM [1]	LS Mean (SE)	-4.72 (0.147)
	95% CI	-5.00, -4.43

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 25 - 28		
Baseline	Mean	7.26
	SD	2.617
	SEM	0.131
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	398
Post-baseline	Mean	2.20
	SD	3.206
	SEM	0.161
	Median	1.04
	Q1, Q3	0.00, 3.65
	Min, Max	0.0, 28.0
	n	398
CFB	Mean	-5.06
	SD	3.543
	SEM	0.178
	Median	-5.11
	Q1, Q3	-7.30, -3.00
	Min, Max	-14.5, 12.7
	n	398
MMRM [1]	LS Mean (SE)	-4.85 (0.147)
	95% CI	-5.14, -4.56

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 29 - 32		
Baseline	Mean	7.27
	SD	2.625
	SEM	0.133
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	390
Post-baseline	Mean	2.12
	SD	3.058
	SEM	0.155
	Median	1.04
	Q1, Q3	0.00, 3.11
	Min, Max	0.0, 28.0
	n	390
CFB	Mean	-5.14
	SD	3.487
	SEM	0.177
	Median	-5.04
	Q1, Q3	-7.45, -3.19
	Min, Max	-16.3, 14.3
	n	390
MMRM [1]	LS Mean (SE)	-4.82 (0.147)
	95% CI	-5.11, -4.53

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 33 - 36		
Baseline	Mean	7.28
	SD	2.617
	SEM	0.134
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	379
Post-baseline	Mean	2.06
	SD	3.029
	SEM	0.156
	Median	1.04
	Q1, Q3	0.00, 3.00
	Min, Max	0.0, 28.0
	n	379
CFB	Mean	-5.22
	SD	3.335
	SEM	0.171
	Median	-5.19
	Q1, Q3	-7.26, -3.38
	Min, Max	-13.2, 12.6
	n	379
MMRM [1]	LS Mean (SE)	-4.95 (0.142)
	95% CI	-5.23, -4.67

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 37 - 40		
Baseline	Mean	7.25
	SD	2.632
	SEM	0.136
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	375
Post-baseline	Mean	2.08
	SD	3.078
	SEM	0.159
	Median	1.00
	Q1, Q3	0.00, 3.11
	Min, Max	0.0, 28.0
	n	375
CFB	Mean	-5.18
	SD	3.451
	SEM	0.178
	Median	-5.19
	Q1, Q3	-7.54, -3.23
	Min, Max	-14.0, 9.3
	n	375
MMRM [1]	LS Mean (SE)	-4.97 (0.148)
	95% CI	-5.26, -4.68

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 41 - 44		
Baseline	Mean	7.24
	SD	2.658
	SEM	0.140
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	363
Post-baseline	Mean	2.09
	SD	3.208
	SEM	0.168
	Median	1.04
	Q1, Q3	0.00, 3.00
	Min, Max	0.0, 28.0
	n	363
CFB	Mean	-5.15
	SD	3.552
	SEM	0.186
	Median	-5.19
	Q1, Q3	-7.30, -3.44
	Min, Max	-14.0, 11.1
	n	363
MMRM [1]	LS Mean (SE)	-4.95 (0.155)
	95% CI	-5.25, -4.65

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 45 - 48		
Baseline	Mean	7.29
	SD	2.678
	SEM	0.143
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	352
Post-baseline	Mean	1.91
	SD	3.220
	SEM	0.172
	Median	1.00
	Q1, Q3	0.00, 2.90
	Min, Max	0.0, 28.0
	n	352
CFB	Mean	-5.38
	SD	3.465
	SEM	0.185
	Median	-5.64
	Q1, Q3	-7.85, -4.00
	Min, Max	-14.9, 12.0
	n	352
MMRM [1]	LS Mean (SE)	-5.13 (0.154)
	95% CI	-5.44, -4.83

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Table 14.2-1.1
Change from Baseline in Number of Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52		
Baseline	Mean	7.28
	SD	2.704
	SEM	0.148
	Median	7.00
	Q1, Q3	5.19, 9.00
	Min, Max	0.0, 27.0
	n	335
Post-baseline	Mean	1.84
	SD	3.281
	SEM	0.179
	Median	1.00
	Q1, Q3	0.00, 2.43
	Min, Max	0.0, 28.0
	n	335
CFB	Mean	-5.44
	SD	3.587
	SEM	0.196
	Median	-5.73
	Q1, Q3	-7.84, -4.00
	Min, Max	-14.0, 14.4
	n	335
MMRM [1]	LS Mean (SE)	-5.19 (0.160)
	95% CI	-5.50, -4.87

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:20:24

Allergan
Protocol 3101-302-002

Atogepant (AGN-241689)

Table 14.2-4.4
Reduction of at Least 25% in Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4	Responders, n/N1(%)	400/513 (78.0)
	Non-responders, n/N1(%)	113/513 (22.0)
Weeks 5 - 8	Responders, n/N1(%)	400/490 (81.6)
	Non-responders, n/N1(%)	90/490 (18.4)
Weeks 9 - 12	Responders, n/N1(%)	390/466 (83.7)
	Non-responders, n/N1(%)	76/466 (16.3)
Weeks 13 - 16	Responders, n/N1(%)	384/440 (87.3)
	Non-responders, n/N1(%)	56/440 (12.7)
Weeks 17 - 20	Responders, n/N1(%)	369/419 (88.1)
	Non-responders, n/N1(%)	50/419 (11.9)
Weeks 21 - 24	Responders, n/N1(%)	361/417 (86.6)
	Non-responders, n/N1(%)	56/417 (13.4)
Weeks 25 - 28	Responders, n/N1(%)	347/398 (87.2)
	Non-responders, n/N1(%)	51/398 (12.8)
Weeks 29 - 32	Responders, n/N1(%)	340/390 (87.2)
	Non-responders, n/N1(%)	50/390 (12.8)
Weeks 33 - 36	Responders, n/N1(%)	338/379 (89.2)
	Non-responders, n/N1(%)	41/379 (10.8)
Weeks 37 - 40	Responders, n/N1(%)	328/375 (87.5)
	Non-responders, n/N1(%)	47/375 (12.5)
Weeks 41 - 44	Responders, n/N1(%)	322/363 (88.7)
	Non-responders, n/N1(%)	41/363 (11.3)
Weeks 45 - 48	Responders, n/N1(%)	319/352 (90.6)
	Non-responders, n/N1(%)	33/352 (9.4)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:24:41

Table 14.2-4.4
Reduction of at Least 25% in Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52	Responders, n/N1(%)	304/335 (90.7)
	Non-responders, n/N1(%)	31/335 (9.3)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:24:41

Allergan
Protocol 3101-302-002

Atogepant (AGN-241689)

Table 14.2-4.1
Reduction of at Least 50% in Monthly Migraine Days at each Month Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4	Responders, n/N1(%)	310/513 (60.4)
	Non-responders, n/N1(%)	203/513 (39.6)
Weeks 5 - 8	Responders, n/N1(%)	319/490 (65.1)
	Non-responders, n/N1(%)	171/490 (34.9)
Weeks 9 - 12	Responders, n/N1(%)	327/466 (70.2)
	Non-responders, n/N1(%)	139/466 (29.8)
Weeks 13 - 16	Responders, n/N1(%)	326/440 (74.1)
	Non-responders, n/N1(%)	114/440 (25.9)
Weeks 17 - 20	Responders, n/N1(%)	308/419 (73.5)
	Non-responders, n/N1(%)	111/419 (26.5)
Weeks 21 - 24	Responders, n/N1(%)	314/417 (75.3)
	Non-responders, n/N1(%)	103/417 (24.7)
Weeks 25 - 28	Responders, n/N1(%)	299/398 (75.1)
	Non-responders, n/N1(%)	99/398 (24.9)
Weeks 29 - 32	Responders, n/N1(%)	299/390 (76.7)
	Non-responders, n/N1(%)	91/390 (23.3)
Weeks 33 - 36	Responders, n/N1(%)	305/379 (80.5)
	Non-responders, n/N1(%)	74/379 (19.5)
Weeks 37 - 40	Responders, n/N1(%)	293/375 (78.1)
	Non-responders, n/N1(%)	82/375 (21.9)
Weeks 41 - 44	Responders, n/N1(%)	285/363 (78.5)
	Non-responders, n/N1(%)	78/363 (21.5)
Weeks 45 - 48	Responders, n/N1(%)	290/352 (82.4)
	Non-responders, n/N1(%)	62/352 (17.6)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

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Table 14.2-4.1
Reduction of at Least 50% in Monthly Migraine Days at each Month Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52	Responders, n/N1(%)	282/335 (84.2)
	Non-responders, n/N1(%)	53/335 (15.8)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:24:35

Allergan
Protocol 3101-302-002

Atogepant (AGN-241689)

Table 14.2-4.5
Reduction of at Least 75% in Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4	Responders, n/N1(%)	191/513 (37.2)
	Non-responders, n/N1(%)	322/513 (62.8)
Weeks 5 - 8	Responders, n/N1(%)	222/490 (45.3)
	Non-responders, n/N1(%)	268/490 (54.7)
Weeks 9 - 12	Responders, n/N1(%)	212/466 (45.5)
	Non-responders, n/N1(%)	254/466 (54.5)
Weeks 13 - 16	Responders, n/N1(%)	223/440 (50.7)
	Non-responders, n/N1(%)	217/440 (49.3)
Weeks 17 - 20	Responders, n/N1(%)	238/419 (56.8)
	Non-responders, n/N1(%)	181/419 (43.2)
Weeks 21 - 24	Responders, n/N1(%)	231/417 (55.4)
	Non-responders, n/N1(%)	186/417 (44.6)
Weeks 25 - 28	Responders, n/N1(%)	250/398 (62.8)
	Non-responders, n/N1(%)	148/398 (37.2)
Weeks 29 - 32	Responders, n/N1(%)	235/390 (60.3)
	Non-responders, n/N1(%)	155/390 (39.7)
Weeks 33 - 36	Responders, n/N1(%)	237/379 (62.5)
	Non-responders, n/N1(%)	142/379 (37.5)
Weeks 37 - 40	Responders, n/N1(%)	233/375 (62.1)
	Non-responders, n/N1(%)	142/375 (37.9)
Weeks 41 - 44	Responders, n/N1(%)	230/363 (63.4)
	Non-responders, n/N1(%)	133/363 (36.6)
Weeks 45 - 48	Responders, n/N1(%)	233/352 (66.2)
	Non-responders, n/N1(%)	119/352 (33.8)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:24:43

Table 14.2-4.5
Reduction of at Least 75% in Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52	Responders, n/N1(%)	234/335 (69.9)
	Non-responders, n/N1(%)	101/335 (30.1)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:24:43

Allergan
Protocol 3101-302-002

Atogepant (AGN-241689)

Table 14.2-4.6
Reduction of 100% in Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4	Responders, n/N1(%)	106/513 (20.7)
	Non-responders, n/N1(%)	407/513 (79.3)
Weeks 5 - 8	Responders, n/N1(%)	121/490 (24.7)
	Non-responders, n/N1(%)	369/490 (75.3)
Weeks 9 - 12	Responders, n/N1(%)	123/466 (26.4)
	Non-responders, n/N1(%)	343/466 (73.6)
Weeks 13 - 16	Responders, n/N1(%)	142/440 (32.3)
	Non-responders, n/N1(%)	298/440 (67.7)
Weeks 17 - 20	Responders, n/N1(%)	138/419 (32.9)
	Non-responders, n/N1(%)	281/419 (67.1)
Weeks 21 - 24	Responders, n/N1(%)	157/417 (37.6)
	Non-responders, n/N1(%)	260/417 (62.4)
Weeks 25 - 28	Responders, n/N1(%)	170/398 (42.7)
	Non-responders, n/N1(%)	228/398 (57.3)
Weeks 29 - 32	Responders, n/N1(%)	167/390 (42.8)
	Non-responders, n/N1(%)	223/390 (57.2)
Weeks 33 - 36	Responders, n/N1(%)	150/379 (39.6)
	Non-responders, n/N1(%)	229/379 (60.4)
Weeks 37 - 40	Responders, n/N1(%)	159/375 (42.4)
	Non-responders, n/N1(%)	216/375 (57.6)
Weeks 41 - 44	Responders, n/N1(%)	153/363 (42.1)
	Non-responders, n/N1(%)	210/363 (57.9)
Weeks 45 - 48	Responders, n/N1(%)	168/352 (47.7)
	Non-responders, n/N1(%)	184/352 (52.3)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:24:45

Table 14.2-4.6
Reduction of 100% in Monthly Migraine Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52	Responders, n/N1(%)	162/335 (48.4)
	Non-responders, n/N1(%)	173/335 (51.6)

N1 = Number of participants available for analysis at a specific time point in the mITT Population.
n = Number of participants within a specific category.

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Allergan Atogepant (AGN-241689)
Protocol 3101-302-002 Page 1 of 13

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4		
Baseline	Mean	8.42
	SD	2.962
	SEM	0.131
	Median	8.00
	Q1, Q3	6.22, 10.08
	Min, Max	1.0, 27.0
	n	513
Post-baseline	Mean	4.40
	SD	3.748
	SEM	0.165
	Median	4.00
	Q1, Q3	2.00, 6.22
	Min, Max	0.0, 26.0
	n	513
CFB	Mean	-4.01
	SD	3.690
	SEM	0.163
	Median	-4.22
	Q1, Q3	-6.05, -1.89
	Min, Max	-14.3, 16.0
	n	513
MMRM [1]	LS Mean (SE)	-4.00 (0.150)
	95% CI	-4.30, -3.71

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 5 - 8		
Baseline	Mean	8.42
	SD	2.960
	SEM	0.134
	Median	8.00
	Q1, Q3	6.22, 10.08
	Min, Max	1.0, 27.0
	n	490
Post-baseline	Mean	3.97
	SD	3.755
	SEM	0.170
	Median	3.00
	Q1, Q3	1.08, 6.00
	Min, Max	0.0, 28.0
	n	490
CFB	Mean	-4.45
	SD	3.822
	SEM	0.173
	Median	-4.60
	Q1, Q3	-7.00, -2.26
	Min, Max	-16.9, 14.0
	n	490
MMRM [1]	LS Mean (SE)	-4.40 (0.155)
	95% CI	-4.71, -4.10

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 9 - 12		
Baseline	Mean	8.35
	SD	2.881
	SEM	0.133
	Median	8.00
	Q1, Q3	6.09, 10.00
	Min, Max	1.0, 27.0
	n	466
Post-baseline	Mean	3.51
	SD	3.524
	SEM	0.163
	Median	3.00
	Q1, Q3	1.00, 5.09
	Min, Max	0.0, 28.0
	n	466
CFB	Mean	-4.84
	SD	3.701
	SEM	0.171
	Median	-5.00
	Q1, Q3	-7.00, -2.54
	Min, Max	-17.4, 8.1
	n	466
MMRM [1]	LS Mean (SE)	-4.80 (0.148)
	95% CI	-5.09, -4.51

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 13 - 16		
Baseline	Mean	8.39
	SD	2.849
	SEM	0.136
	Median	8.00
	Q1, Q3	6.22, 10.00
	Min, Max	1.3, 27.0
	n	440
Post-baseline	Mean	3.19
	SD	3.398
	SEM	0.162
	Median	2.15
	Q1, Q3	0.50, 5.00
	Min, Max	0.0, 26.8
	n	440
CFB	Mean	-5.20
	SD	3.450
	SEM	0.164
	Median	-5.10
	Q1, Q3	-7.32, -3.00
	Min, Max	-19.5, 11.8
	n	440
MMRM [1]	LS Mean (SE)	-5.12 (0.143)
	95% CI	-5.40, -4.84

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 17 - 20		
Baseline	Mean	8.39
	SD	2.876
	SEM	0.140
	Median	8.00
	Q1, Q3	6.22, 10.00
	Min, Max	1.3, 27.0
	n	419
Post-baseline	Mean	2.84
	SD	3.322
	SEM	0.162
	Median	2.00
	Q1, Q3	0.00, 4.15
	Min, Max	0.0, 28.0
	n	419
CFB	Mean	-5.54
	SD	3.565
	SEM	0.174
	Median	-5.60
	Q1, Q3	-8.00, -3.36
	Min, Max	-19.5, 13.0
	n	419
MMRM [1]	LS Mean (SE)	-5.35 (0.146)
	95% CI	-5.64, -5.06

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 21 - 24		
Baseline	Mean	8.34
	SD	2.842
	SEM	0.139
	Median	8.00
	Q1, Q3	6.22, 10.00
	Min, Max	1.3, 27.0
	n	417
Post-baseline	Mean	2.87
	SD	3.466
	SEM	0.170
	Median	2.00
	Q1, Q3	0.00, 4.00
	Min, Max	0.0, 28.0
	n	417
CFB	Mean	-5.47
	SD	3.827
	SEM	0.187
	Median	-5.93
	Q1, Q3	-8.00, -3.71
	Min, Max	-19.5, 11.8
	n	417
MMRM [1]	LS Mean (SE)	-5.30 (0.157)
	95% CI	-5.61, -4.99

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 25 - 28		
Baseline	Mean	8.35
	SD	2.892
	SEM	0.145
	Median	8.00
	Q1, Q3	6.22, 10.00
	Min, Max	1.3, 27.0
	n	398
Post-baseline	Mean	2.74
	SD	3.593
	SEM	0.180
	Median	1.22
	Q1, Q3	0.00, 4.15
	Min, Max	0.0, 28.0
	n	398
CFB	Mean	-5.61
	SD	3.919
	SEM	0.196
	Median	-6.00
	Q1, Q3	-8.00, -3.42
	Min, Max	-19.5, 15.7
	n	398
MMRM [1]	LS Mean (SE)	-5.42 (0.163)
	95% CI	-5.74, -5.09

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 29 - 32		
Baseline	Mean	8.32
	SD	2.885
	SEM	0.146
	Median	8.00
	Q1, Q3	6.22, 10.00
	Min, Max	1.3, 27.0
	n	390
Post-baseline	Mean	2.62
	SD	3.414
	SEM	0.173
	Median	1.40
	Q1, Q3	0.00, 4.00
	Min, Max	0.0, 28.0
	n	390
CFB	Mean	-5.70
	SD	3.841
	SEM	0.195
	Median	-5.93
	Q1, Q3	-8.00, -3.69
	Min, Max	-19.5, 16.0
	n	390
MMRM [1]	LS Mean (SE)	-5.41 (0.161)
	95% CI	-5.72, -5.09

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 33 - 36		
Baseline	Mean	8.33
	SD	2.903
	SEM	0.149
	Median	8.00
	Q1, Q3	6.00, 10.00
	Min, Max	1.3, 27.0
	n	379
Post-baseline	Mean	2.47
	SD	3.315
	SEM	0.170
	Median	1.22
	Q1, Q3	0.00, 3.23
	Min, Max	0.0, 28.0
	n	379
CFB	Mean	-5.86
	SD	3.718
	SEM	0.191
	Median	-6.00
	Q1, Q3	-8.00, -4.00
	Min, Max	-19.5, 9.0
	n	379
MMRM [1]	LS Mean (SE)	-5.62 (0.155)
	95% CI	-5.92, -5.32

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 37 - 40		
Baseline	Mean	8.33
	SD	2.920
	SEM	0.151
	Median	8.00
	Q1, Q3	6.00, 10.00
	Min, Max	1.3, 27.0
	n	375
Post-baseline	Mean	2.45
	SD	3.284
	SEM	0.170
	Median	1.08
	Q1, Q3	0.00, 3.82
	Min, Max	0.0, 28.0
	n	375
CFB	Mean	-5.88
	SD	3.730
	SEM	0.193
	Median	-6.00
	Q1, Q3	-8.26, -4.00
	Min, Max	-19.5, 7.5
	n	375
MMRM [1]	LS Mean (SE)	-5.69 (0.156)
	95% CI	-6.00, -5.38

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 41 - 44		
Baseline	Mean	8.29
	SD	2.917
	SEM	0.153
	Median	8.00
	Q1, Q3	6.00, 10.00
	Min, Max	1.3, 27.0
	n	363
Post-baseline	Mean	2.45
	SD	3.450
	SEM	0.181
	Median	1.12
	Q1, Q3	0.00, 3.50
	Min, Max	0.0, 28.0
	n	363
CFB	Mean	-5.84
	SD	3.909
	SEM	0.205
	Median	-6.00
	Q1, Q3	-8.17, -3.80
	Min, Max	-19.5, 11.0
	n	363
MMRM [1]	LS Mean (SE)	-5.66 (0.166)
	95% CI	-5.99, -5.34

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 45 - 48		
Baseline	Mean	8.35
	SD	2.953
	SEM	0.157
	Median	8.00
	Q1, Q3	6.00, 10.00
	Min, Max	1.3, 27.0
	n	352
Post-baseline	Mean	2.23
	SD	3.427
	SEM	0.183
	Median	1.04
	Q1, Q3	0.00, 3.11
	Min, Max	0.0, 28.0
	n	352
CFB	Mean	-6.12
	SD	3.870
	SEM	0.206
	Median	-6.22
	Q1, Q3	-8.37, -4.00
	Min, Max	-19.5, 12.0
	n	352
MMRM [1]	LS Mean (SE)	-5.90 (0.164)
	95% CI	-6.22, -5.58

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Table 14.2-2.1
Change from Baseline in Number of Monthly Headache Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52		
Baseline	Mean	8.33
	SD	2.966
	SEM	0.162
	Median	8.00
	Q1, Q3	6.00, 10.00
	Min, Max	1.3, 27.0
	n	335
Post-baseline	Mean	2.13
	SD	3.540
	SEM	0.193
	Median	1.04
	Q1, Q3	0.00, 3.00
	Min, Max	0.0, 28.0
	n	335
CFB	Mean	-6.20
	SD	3.911
	SEM	0.214
	Median	-6.60
	Q1, Q3	-8.73, -4.15
	Min, Max	-19.5, 11.3
	n	335
MMRM [1]	LS Mean (SE)	-5.99 (0.171)
	95% CI	-6.33, -5.66

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:21:46

Allergan Atogepant (AGN-241689)
Protocol 3101-302-002 Page 1 of 13

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 1 - 4		
Baseline	Mean	6.63
	SD	3.256
	SEM	0.144
	Median	6.36
	Q1, Q3	4.48, 8.62
	Min, Max	0.0, 19.0
	n	513
Post-baseline	Mean	2.60
	SD	3.005
	SEM	0.133
	Median	1.75
	Q1, Q3	0.00, 4.00
	Min, Max	0.0, 19.7
	n	513
CFB	Mean	-4.03
	SD	3.403
	SEM	0.150
	Median	-4.02
	Q1, Q3	-6.00, -2.00
	Min, Max	-14.6, 17.6
	n	513
MMRM [1]	LS Mean (SE)	-4.04 (0.121)
	95% CI	-4.28, -3.81

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 5 - 8		
Baseline	Mean	6.62
	SD	3.239
	SEM	0.146
	Median	6.36
	Q1, Q3	4.48, 8.62
	Min, Max	0.0, 19.0
	n	490
Post-baseline	Mean	2.49
	SD	3.060
	SEM	0.138
	Median	1.30
	Q1, Q3	0.00, 4.00
	Min, Max	0.0, 25.0
	n	490
CFB	Mean	-4.12
	SD	3.579
	SEM	0.162
	Median	-4.00
	Q1, Q3	-6.22, -2.00
	Min, Max	-14.5, 17.3
	n	490
MMRM [1]	LS Mean (SE)	-4.11 (0.129)
	95% CI	-4.37, -3.86

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 9 - 12		
Baseline	Mean	6.55
	SD	3.207
	SEM	0.149
	Median	6.36
	Q1, Q3	4.31, 8.62
	Min, Max	0.0, 18.7
	n	466
Post-baseline	Mean	2.39
	SD	2.896
	SEM	0.134
	Median	1.10
	Q1, Q3	0.00, 4.00
	Min, Max	0.0, 16.5
	n	466
CFB	Mean	-4.16
	SD	3.557
	SEM	0.165
	Median	-4.31
	Q1, Q3	-6.46, -1.85
	Min, Max	-16.3, 10.9
	n	466
MMRM [1]	LS Mean (SE)	-4.18 (0.124)
	95% CI	-4.42, -3.94

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 13 - 16		
Baseline	Mean	6.55
	SD	3.193
	SEM	0.152
	Median	6.46
	Q1, Q3	4.25, 8.62
	Min, Max	0.0, 18.7
	n	440
Post-baseline	Mean	2.09
	SD	2.580
	SEM	0.123
	Median	1.08
	Q1, Q3	0.00, 3.36
	Min, Max	0.0, 16.2
	n	440
CFB	Mean	-4.46
	SD	3.368
	SEM	0.161
	Median	-4.48
	Q1, Q3	-6.98, -2.07
	Min, Max	-17.0, 12.4
	n	440
MMRM [1]	LS Mean (SE)	-4.46 (0.114)
	95% CI	-4.68, -4.23

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 17 - 20		
Baseline	Mean	6.64
	SD	3.183
	SEM	0.155
	Median	6.72
	Q1, Q3	4.31, 8.96
	Min, Max	0.0, 18.7
	n	419
Post-baseline	Mean	1.92
	SD	2.683
	SEM	0.131
	Median	1.00
	Q1, Q3	0.00, 3.00
	Min, Max	0.0, 19.7
	n	419
CFB	Mean	-4.72
	SD	3.433
	SEM	0.168
	Median	-4.95
	Q1, Q3	-7.00, -2.55
	Min, Max	-17.0, 17.6
	n	419
MMRM [1]	LS Mean (SE)	-4.56 (0.120)
	95% CI	-4.80, -4.33

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

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Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 21 - 24		
Baseline	Mean	6.63
	SD	3.135
	SEM	0.154
	Median	6.72
	Q1, Q3	4.31, 8.62
	Min, Max	0.0, 18.7
	n	417
Post-baseline	Mean	2.01
	SD	2.653
	SEM	0.130
	Median	1.04
	Q1, Q3	0.00, 3.11
	Min, Max	0.0, 16.6
	n	417
CFB	Mean	-4.62
	SD	3.481
	SEM	0.170
	Median	-4.85
	Q1, Q3	-7.00, -2.50
	Min, Max	-17.0, 10.0
	n	417
MMRM [1]	LS Mean (SE)	-4.49 (0.121)
	95% CI	-4.72, -4.25

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 25 - 28		
Baseline	Mean	6.65
	SD	3.172
	SEM	0.159
	Median	6.72
	Q1, Q3	4.31, 8.96
	Min, Max	0.0, 18.7
	n	398
Post-baseline	Mean	1.90
	SD	2.782
	SEM	0.139
	Median	1.00
	Q1, Q3	0.00, 3.00
	Min, Max	0.0, 21.0
	n	398
CFB	Mean	-4.75
	SD	3.687
	SEM	0.185
	Median	-5.00
	Q1, Q3	-7.00, -2.77
	Min, Max	-17.0, 18.9
	n	398
MMRM [1]	LS Mean (SE)	-4.59 (0.129)
	95% CI	-4.84, -4.34

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

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Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 29 - 32		
Baseline	Mean	6.68
	SD	3.158
	SEM	0.160
	Median	6.72
	Q1, Q3	4.48, 8.96
	Min, Max	0.0, 18.7
	n	390
Post-baseline	Mean	1.84
	SD	2.639
	SEM	0.134
	Median	1.00
	Q1, Q3	0.00, 3.00
	Min, Max	0.0, 18.0
	n	390
CFB	Mean	-4.84
	SD	3.442
	SEM	0.174
	Median	-5.00
	Q1, Q3	-7.00, -2.72
	Min, Max	-17.5, 8.0
	n	390
MMRM [1]	LS Mean (SE)	-4.54 (0.130)
	95% CI	-4.79, -4.28

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 33 - 36		
Baseline	Mean	6.68
	SD	3.204
	SEM	0.165
	Median	6.72
	Q1, Q3	4.31, 9.00
	Min, Max	0.0, 18.7
	n	379
Post-baseline	Mean	1.75
	SD	2.541
	SEM	0.131
	Median	1.00
	Q1, Q3	0.00, 2.43
	Min, Max	0.0, 16.0
	n	379
CFB	Mean	-4.93
	SD	3.417
	SEM	0.176
	Median	-5.00
	Q1, Q3	-7.00, -2.85
	Min, Max	-17.0, 6.4
	n	379
MMRM [1]	LS Mean (SE)	-4.66 (0.125)
	95% CI	-4.90, -4.41

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 37 - 40		
Baseline	Mean	6.67
	SD	3.199
	SEM	0.165
	Median	6.72
	Q1, Q3	4.31, 9.00
	Min, Max	0.0, 18.7
	n	375
Post-baseline	Mean	1.75
	SD	2.519
	SEM	0.130
	Median	1.00
	Q1, Q3	0.00, 2.55
	Min, Max	0.0, 16.0
	n	375
CFB	Mean	-4.92
	SD	3.481
	SEM	0.180
	Median	-5.00
	Q1, Q3	-7.26, -3.00
	Min, Max	-17.0, 6.0
	n	375
MMRM [1]	LS Mean (SE)	-4.68 (0.125)
	95% CI	-4.93, -4.44

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 41 - 44		
Baseline	Mean	6.68
	SD	3.206
	SEM	0.168
	Median	6.72
	Q1, Q3	4.31, 9.00
	Min, Max	0.0, 18.7
	n	363
Post-baseline	Mean	1.69
	SD	2.620
	SEM	0.138
	Median	1.00
	Q1, Q3	0.00, 2.33
	Min, Max	0.0, 18.0
	n	363
CFB	Mean	-4.99
	SD	3.504
	SEM	0.184
	Median	-5.00
	Q1, Q3	-7.03, -2.78
	Min, Max	-17.0, 5.3
	n	363
MMRM [1]	LS Mean (SE)	-4.71 (0.132)
	95% CI	-4.97, -4.46

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 45 - 48		
Baseline	Mean	6.75
	SD	3.196
	SEM	0.170
	Median	7.00
	Q1, Q3	4.31, 9.00
	Min, Max	0.0, 18.7
	n	352
Post-baseline	Mean	1.51
	SD	2.455
	SEM	0.131
	Median	0.00
	Q1, Q3	0.00, 2.07
	Min, Max	0.0, 15.0
	n	352
CFB	Mean	-5.24
	SD	3.509
	SEM	0.187
	Median	-5.00
	Q1, Q3	-7.57, -3.00
	Min, Max	-17.0, 8.0
	n	352
MMRM [1]	LS Mean (SE)	-4.90 (0.125)
	95% CI	-5.15, -4.66

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Table 14.2-3.1
Change from Baseline in Number of Monthly Acute Medication Use Days at each Monthly Period
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Weeks 49 - 52		
Baseline	Mean	6.76
	SD	3.183
	SEM	0.174
	Median	6.72
	Q1, Q3	4.48, 9.00
	Min, Max	0.0, 18.7
	n	335
Post-baseline	Mean	1.50
	SD	2.727
	SEM	0.149
	Median	0.00
	Q1, Q3	0.00, 2.00
	Min, Max	0.0, 21.6
	n	335
CFB	Mean	-5.26
	SD	3.571
	SEM	0.195
	Median	-5.28
	Q1, Q3	-7.92, -3.00
	Min, Max	-17.0, 11.1
	n	335
MMRM [1]	LS Mean (SE)	-4.93 (0.137)
	95% CI	-5.20, -4.66

[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:23:10

Allergan Atogepant (AGN-241689)
Protocol 3101-302-002

Table 14.2-6.1
Change from Baseline in the MSQ v2.1 Role Function Restrictive Domain Score at Weeks 12, 24, 36, 48, 52, and 56
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Week 12		
Baseline	Mean	48.09
	SD	20.289
	SEM	0.912
	Median	51.43
	Q1, Q3	34.29, 60.00
	Min, Max	0.0, 100.0
	n	495
Post-baseline	Mean	78.16
	SD	21.852
	SEM	0.982
	Median	80.00
	Q1, Q3	62.86, 100.00
	Min, Max	0.0, 100.0
	n	495
CFB	Mean	30.07
	SD	25.499
	SEM	1.146
	Median	25.71
	Q1, Q3	11.43, 45.71
	Min, Max	-34.3, 100.0
	n	495
MMRM [1]	LS Mean (SE)	30.02 (0.944)
	95% CI	28.16, 31.87

MSQ v2.1 = Migraine Specific Quality of Life Questionnaire, version 2.1.
[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:26:38

Table 14.2-6.1
Change from Baseline in the MSQ v2.1 Role Function Restrictive Domain Score at Weeks 12, 24, 36, 48, 52, and 56
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Week 24		
Baseline	Mean	47.88
	SD	20.572
	SEM	0.985
	Median	51.43
	Q1, Q3	34.29, 60.00
	Min, Max	0.0, 100.0
	n	436
Post-baseline	Mean	79.99
	SD	21.980
	SEM	1.053
	Median	82.86
	Q1, Q3	68.57, 100.00
	Min, Max	0.0, 100.0
	n	436
CFB	Mean	32.10
	SD	25.694
	SEM	1.231
	Median	30.00
	Q1, Q3	14.29, 48.57
	Min, Max	-42.9, 100.0
	n	436
MMRM [1]	LS Mean (SE)	30.79 (1.000)
	95% CI	28.83, 32.76

MSQ v2.1 = Migraine Specific Quality of Life Questionnaire, version 2.1.
[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:26:38

Table 14.2-6.1
Change from Baseline in the MSQ v2.1 Role Function Restrictive Domain Score at Weeks 12, 24, 36, 48, 52, and 56
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Week 36		
Baseline	Mean	47.98
	SD	20.544
	SEM	1.022
	Median	51.43
	Q1, Q3	34.29, 60.00
	Min, Max	0.0, 100.0
	n	404
Post-baseline	Mean	81.78
	SD	21.502
	SEM	1.070
	Median	85.71
	Q1, Q3	74.29, 100.00
	Min, Max	0.0, 100.0
	n	404
CFB	Mean	33.80
	SD	26.302
	SEM	1.309
	Median	31.43
	Q1, Q3	17.14, 51.43
	Min, Max	-42.9, 100.0
	n	404
MMRM [1]	LS Mean (SE)	32.34 (1.015)
	95% CI	30.35, 34.34

MSQ v2.1 = Migraine Specific Quality of Life Questionnaire, version 2.1.
[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:26:38

Table 14.2-6.1
Change from Baseline in the MSQ v2.1 Role Function Restrictive Domain Score at Weeks 12, 24, 36, 48, 52, and 56
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Week 48		
Baseline	Mean	48.23
	SD	20.509
	SEM	1.056
	Median	51.43
	Q1, Q3	37.14, 60.00
	Min, Max	0.0, 97.1
	n	377
Post-baseline	Mean	84.17
	SD	20.799
	SEM	1.071
	Median	91.43
	Q1, Q3	80.00, 100.00
	Min, Max	0.0, 100.0
	n	377
CFB	Mean	35.94
	SD	25.232
	SEM	1.300
	Median	37.14
	Q1, Q3	20.00, 51.43
	Min, Max	-31.4, 100.0
	n	377
MMRM [1]	LS Mean (SE)	34.32 (0.984)
	95% CI	32.38, 36.25

MSQ v2.1 = Migraine Specific Quality of Life Questionnaire, version 2.1.
[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:26:38

Table 14.2-6.1
Change from Baseline in the MSQ v2.1 Role Function Restrictive Domain Score at Weeks 12, 24, 36, 48, 52, and 56
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Week 52		
Baseline	Mean	48.16
	SD	20.425
	SEM	1.072
	Median	51.43
	Q1, Q3	37.14, 60.00
	Min, Max	0.0, 97.1
	n	363
Post-baseline	Mean	84.61
	SD	20.457
	SEM	1.074
	Median	91.43
	Q1, Q3	77.14, 100.00
	Min, Max	0.0, 100.0
	n	363
CFB	Mean	36.45
	SD	25.368
	SEM	1.332
	Median	37.14
	Q1, Q3	20.00, 54.29
	Min, Max	-34.3, 100.0
	n	363
MMRM [1]	LS Mean (SE)	34.70 (0.997)
	95% CI	32.74, 36.66

MSQ v2.1 = Migraine Specific Quality of Life Questionnaire, version 2.1.
[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:26:38

Table 14.2-6.1
Change from Baseline in the MSQ v2.1 Role Function Restrictive Domain Score at Weeks 12, 24, 36, 48, 52, and 56
Modified Intent-to-Treat Population

Derived Visit Parameter	Statistics	Atogepant 60 mg QD (N=521)
Week 56		
Baseline	Mean	47.82
	SD	20.524
	SEM	1.111
	Median	51.43
	Q1, Q3	37.14, 60.00
	Min, Max	0.0, 100.0
	n	341
Post-baseline	Mean	68.02
	SD	25.222
	SEM	1.366
	Median	68.57
	Q1, Q3	57.14, 85.71
	Min, Max	0.0, 100.0
	n	341
CFB	Mean	20.20
	SD	28.329
	SEM	1.534
	Median	20.00
	Q1, Q3	0.00, 40.00
	Min, Max	-60.0, 100.0
	n	341

MSQ v2.1 = Migraine Specific Quality of Life Questionnaire, version 2.1.
[1] MMRM = mixed-effects model for repeated measures for change from baseline. The model includes visit as a fixed effect, the baseline value as a covariate, and baseline by visit as an interaction term, with an unstructured covariance matrix.
n = Number of participants with evaluable value at both baseline and a specific time point in the mITT Population. CFB = change from baseline, SD = Standard Deviation, SEM = Standard Error of the Mean, Min=minimum, Max = maximum. LS = Least Squares, SE = standard error of the least squares, CI = Confidence Interval.

Program: [redacted] FINAL 20[redacted]-[redacted]-[redacted] 10:26:38