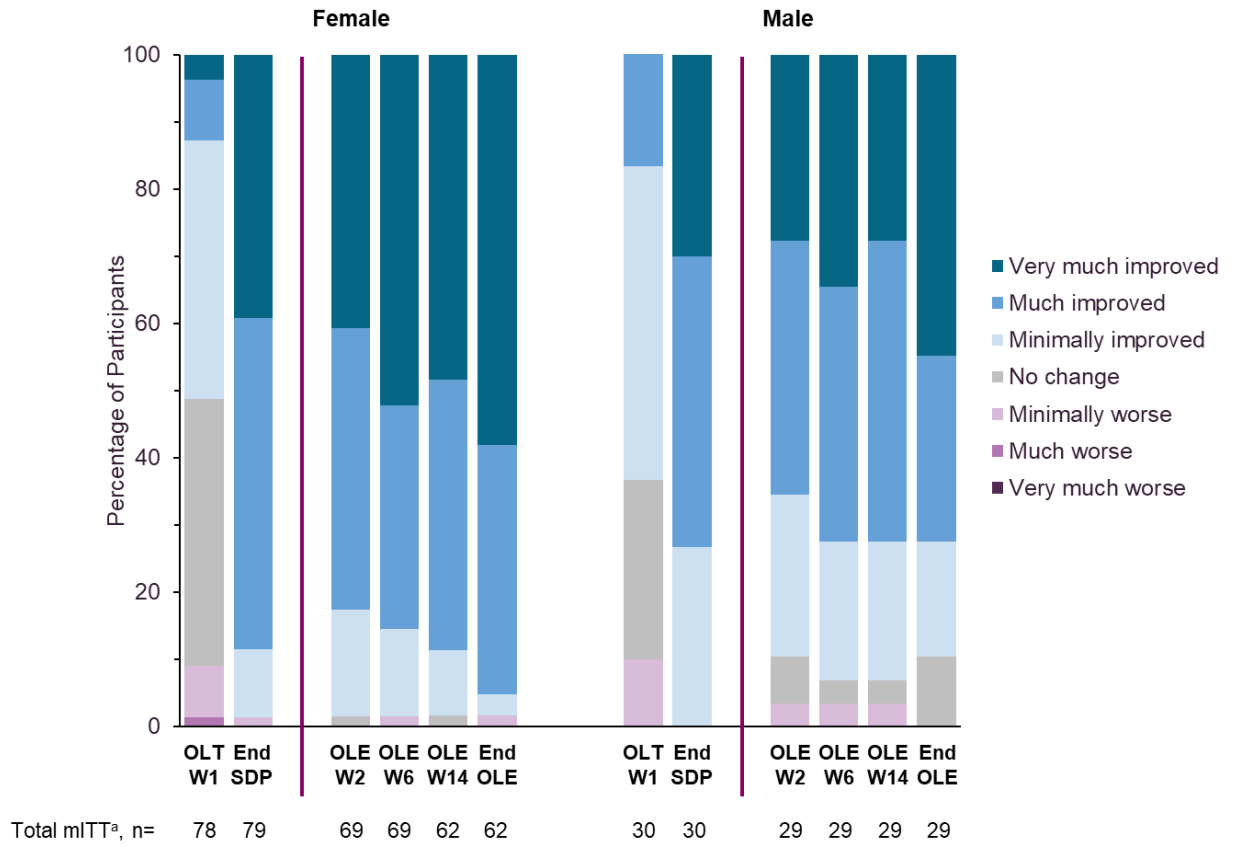
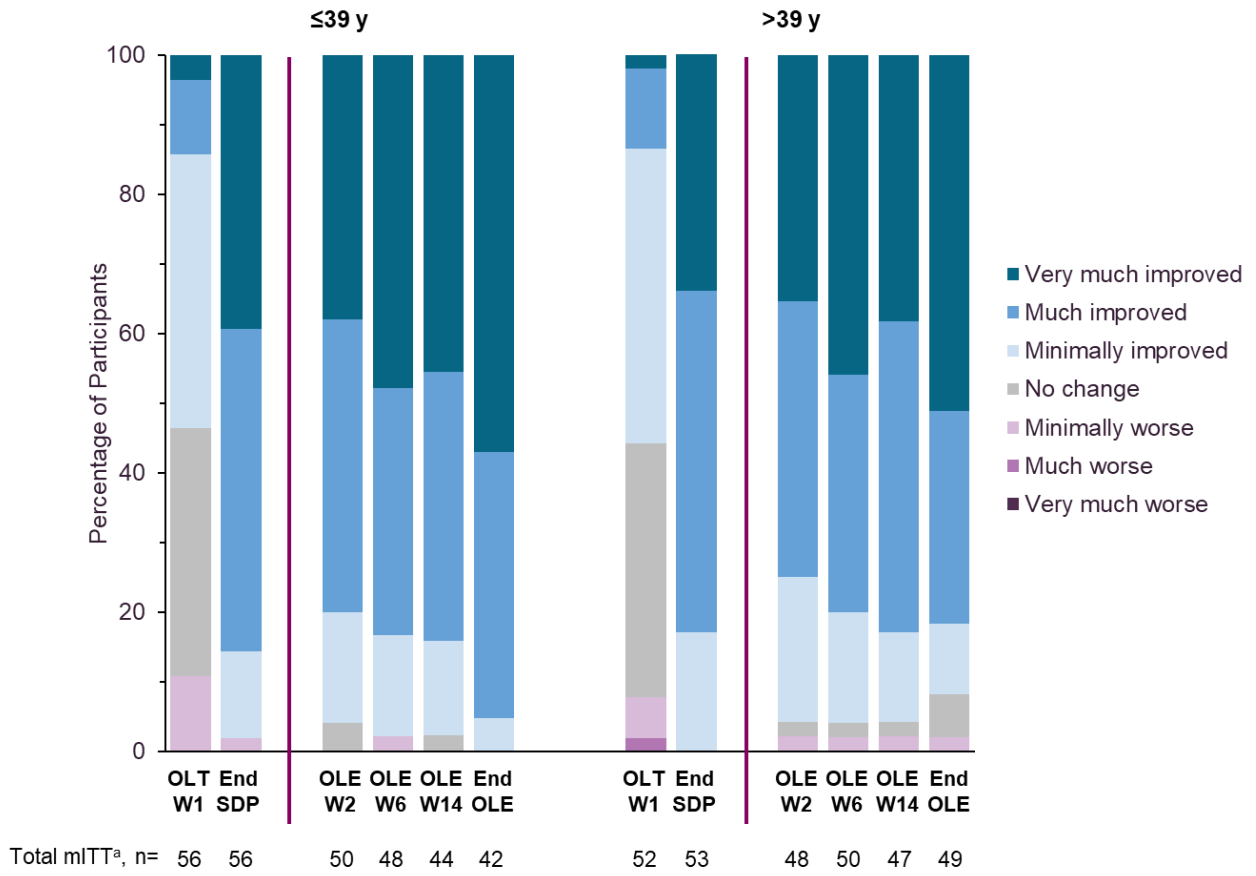


**Figure S1**—Change in PGIC ratings in subgroups by sex (A), age (B), baseline treatment (C), and LXB dosing regimen (D).

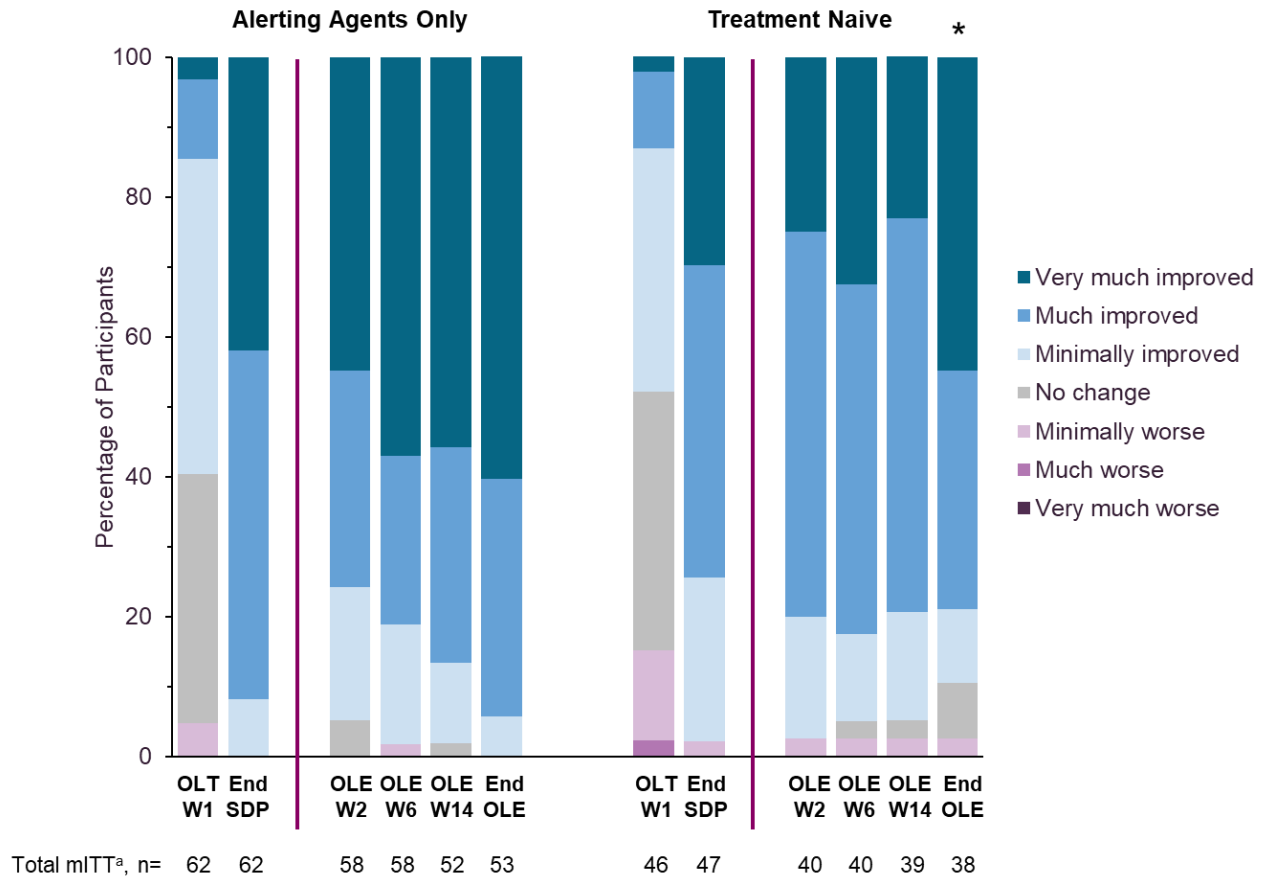
**A. Sex**



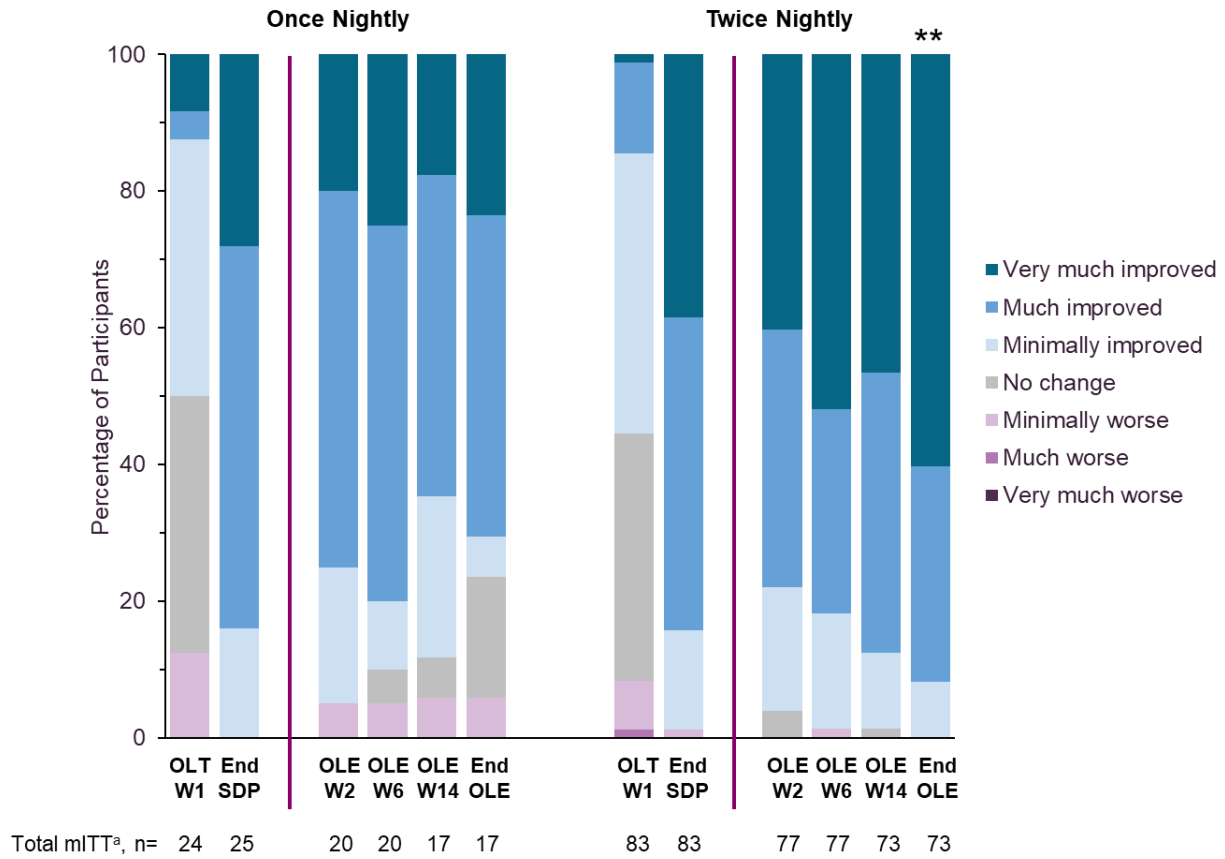
**B. Age**



### C. Baseline Treatment



## D. LXB Dosing Regimen



LXB, low-sodium oxybate; mITT, modified intent-to-treat; OLE, open-label extension period; OLT, open-label titration and optimization period; PGIC, Patient Global Impression of Change; SDP, stable-dose period; W, week.

<sup>a</sup>mITT population excludes participants taking high-sodium oxybate at baseline (n=6). Due to no adjustments for multiplicity, *P* values are nominal. Statistical tests are for the proportions who improved to any extent (minimally, much, or very much improved).

\**P*<0.05 vs alerting agents only; \*\**P*<0.001 vs once nightly.

**Table S1**—TEAEs newly reported<sup>a,b</sup> during OLE.

TEAE, n (%)	Alerting Agents Only (n=60)	Treatment Naive (n=41)	Total (N=106)
Any TEAE (new to a participant) <sup>a</sup>	31 (51.7)	15 (36.6)	48 (45.3)
TEAEs in $\geq 2$ participants			
Nasopharyngitis	3 (5.0)	3 (7.3)	7 (6.6)
Upper respiratory tract infection	3 (5.0)	2 (4.9)	5 (4.7)
Hypertension	3 (5.0)	1 (2.4)	4 (3.8)
Vomiting	4 (6.7)	0	4 (3.8)
Anxiety	3 (5.0)	0	3 (2.8)
Diarrhea	3 (5.0)	0	3 (2.8)
Sinusitis	1 (1.7)	2 (4.9)	3 (2.8)
Fatigue	2 (3.3)	0	3 (2.8)
Night sweats	1 (1.7)	1 (2.4)	3 (2.8)
Pain in extremity	2 (3.3)	0	3 (2.8)
Abdominal pain upper	1 (1.7)	1 (2.4)	2 (1.9)
Alopecia	1 (1.7)	1 (2.4)	2 (1.9)
Arthropod bite	2 (3.3)	0	2 (1.9)
Bronchitis	1 (1.7)	1 (2.4)	2 (1.9)
Enuresis	2 (3.3)	0	2 (1.9)
Hemorrhoids	1 (1.7)	1 (2.4)	2 (1.9)
Insomnia	2 (3.3)	0	2 (1.9)
Libido decreased	0	2 (4.9)	2 (1.9)
Muscle spasms	2 (3.3)	0	2 (1.9)
Myalgia	2 (3.3)	0	2 (1.9)
Pharyngitis	1 (1.7)	1 (2.4)	2 (1.9)
Rash	1 (1.7)	1 (2.4)	2 (1.9)
Urinary tract infection	0	2 (4.9)	2 (1.9)
Any TEAE (new to OLE) <sup>b</sup>	18 (30.0)	9 (22.0)	29 (27.4)
TEAEs in $\geq 2$ participants			
Hypertension	3 (5.0)	1 (2.4)	4 (3.8)
Alopecia	1 (1.7)	1 (2.4)	2 (1.9)
Hemorrhoids	1 (1.7)	1 (2.4)	2 (1.9)
Libido decreased	0	2 (4.9)	2 (1.9)

OLE, open-label extension period; TEAE, treatment-emergent adverse event.

<sup>a</sup>TEAE that was not reported by that same participant in the main study.

<sup>b</sup>TEAE that was not reported by any participants in the main study.