SUPPORTING INFORMATION

TABLE S1

Baseline patient demographics and characteristics (3-month population)

	Lacosamide (n = 210)	Carbamazepine (n = 221)	Total (n = 431)
Age, mean (SD), years	39.0 (16.4)	37.8 (15.8)	38.4 (16.1)
<25 years, n (%)	52 (24.8)	58 (26.2)	110 (25.5)
25 to <45 years, n (%)	86 (41.0)	87 (39.4)	173 (40.1)
45 to <65 years, n (%)	52 (24.8)	63 (28.5)	115 (26.7)
≥65 years, n (%)	20 (9.5)	13 (5.9)	33 (7.7)
Male, n (%)	118 (56.2)	128 (57.9)	246 (57.1)
Weight, kg, mean (SD)	70.8 (16.0)	72.3 (15.7)	71.5 (15.8)
Body mass index, mean (SD), kg/m^2	24.4 (4.7)	24.9 (4.9)	24.7 (4.8)
<25, n (%)	123 (58.6)	124 (56.1)	247 (57.3)
25 to <30, n (%)	63 (30.0)	73 (33.0)	136 (31.6)
≥30, n (%)	24 (11.4)	24 (10.9)	48 (11.1)
Comorbid endocrine disorders, metabolism and nutrition disorders, social circumstances, vascular disorders reported by ≥2% of total patients[i]			
Hypertension, n (%)	31 (14.8)	41 (18.6)	72 (16.7)
Postmenopause, n (%)	12 (5.7)	11 (5.0)	23 (5.3)
Hypercholesterolemia, n (%)	7 (3.3)	11 (5.0)	18 (4.2)
Obesity, n (%)	3 (1.4)	10 (4.5)	13 (3.0)
Menopause, n (%)	3 (1.4)	10 (4.5)	13 (3.0)
Hypothyroidism, n (%)	3 (1.4)	8 (3.6)	11 (2.6)

Total cholesterol			
Patients with levels below upper limit of the reference range, n (%)[a]	135 (64.6)[c]	149 (67.4)	284 (66.0)[d]
Patients with levels above upper limit of the reference range, n (%)[b]	74 (35.4)[c]	72 (32.6)	146 (34.0)[d]
LDL-cholesterol			
Patients with levels below upper limit of the reference range, n (%)[e]	154 (73.7)[c]	176 (81.1)[g]	330 (77.5)[h]
Patients with levels above upper limit of the reference range, n (%)[f]	55 (26.3)[c]	41 (18.9)[g]	96 (22.5)[h]

Abbreviations: LDL, low-density lipoprotein; SD, standard deviation.

[a]Total cholesterol levels ≤200 mg/dL.

[b]Total cholesterol levels >200 mg/dL.

[c]n = 209.

[d]n = 430.

[e]LDL-cholesterol levels ≤130 mg/dL.

[f]LDL-cholesterol levels >130 mg/dL.

[g]n = 217.

[h]n = 426.

[i]Hepatobiliary disorders were also evaluated; however, no preferred term was reported by ≥2% Total patients.

TABLE S2

Percentage of patients on each dose level at 12 months and 3 months

	12-month population			3-month population		
Patients (%)	**LCM (n = 138)**	**CBZ (n = 133)**	**Total (n = 271)**	**LCM (n = 210)**	**CBZ (n = 221)**	**Total (n = 431)**
Dose level 1	93.5	91.7	92.6	72.9	73.8	73.3
Dose level 2	3.6	6.0	4.8	17.6	19.0	18.3
Dose level 3	2.9	2.3	2.6	9.5	7.2	8.4

Abbreviations: CBZ, carbamazepine; LCM, lacosamide.

Lacosamide: dose level 1: 200 mg/d; dose level 2: 400 mg/d; dose level 3: 600 mg/d; carbamazepine: dose level 1: 400 mg/d; dose level 2: 800 mg/d; dose level 3: 1200 mg/d.

TABLE S3

Total cholesterol and LDL cholesterol at Baseline and 3 months and change from Baseline to 3 months (3-month population) in patients with baseline levels below or above the upper limit of the reference range

				Analysis of covariance model[b] Change in lipid levels from Baseline at 3 months		
Treatment	**n**	**Baseline, mean (SD)**	**3-month treatment[a], mean (SD)**	**n**	**LS mean (SE)**	***P*-value (treatment)**
Total cholesterol below upper limit of the reference range at Baseline[c]						
LCM, mg/dL	135	168.1 (24.4)	169.3 (28.2)	135	1.8 (1.9)	< .001
CBZ, mg/dL	149	161.0 (26.3)	179.4 (31.4)****	149	18.4 (1.8)	
Total cholesterol above upper limit of the reference range at Baseline[d]						
LCM, mg/dL	74	227.1 (21.7)	214.6 (30.2)****	74	−11.3 (4.0)	< .001
CBZ, mg/dL	72	227.3 (20.3)	248.1 (48.8)****	72	20.2 (4.0)	
LDL cholesterol below upper limit of the reference range at Baseline[e]						
LCM, mg/dL	154	96.1 (21.5)	96.8 (25.6)	154	1.1 (1.6)	< .001
CBZ, mg/dL	176	89.7 (23.9)	101.1 (30.2)****	176	11.2 (1.5)	
LDL cholesterol above upper limit of the reference range at Baseline[f]						
LCM, mg/dL	55	147.7 (14.9)	135.7 (21.8)****	55	−11.0 (3.1)	< .001
CBZ, mg/dL	41	151.5 (14.0)	168.2 (30.5)***	41	16.1 (3.7)	

Abbreviations: ANCOVA, analysis of covariance; CBZ, carbamazepine; LCM, lacosamide; LDL, low-density lipoprotein; LS, least squares; SD, standard deviation; SE, standard error.

[a]The 3-month lipid levels included lipid values collected at 90 days (plus a 30-day window) of treatment during the Treatment period.

[b]The ANCOVA model included treatment as a main effect and age, sex, body mass index, and Baseline lipid level as covariates.

[c]Total cholesterol levels ≤200 mg/dL.

[d]Total cholesterol levels >200 mg/dL.

[e]LDL-cholesterol levels ≤130 mg/dL.

[f]LDL-cholesterol levels >130 mg/dL.

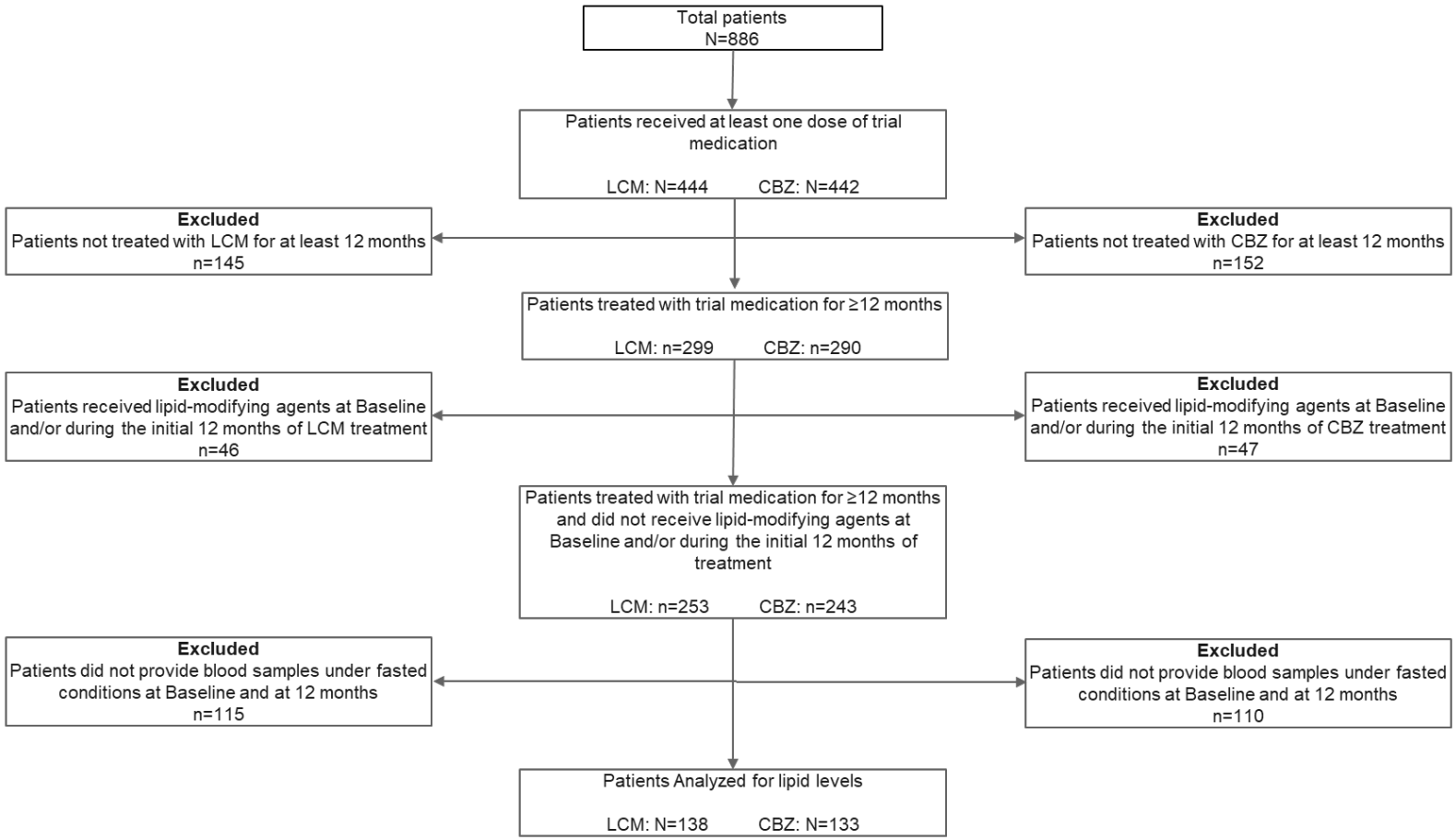
Within-treatment group comparison 3 months vs Baseline; paired *t* test

***$P < .001$.

****$P < .0001$.

FIGURE S1

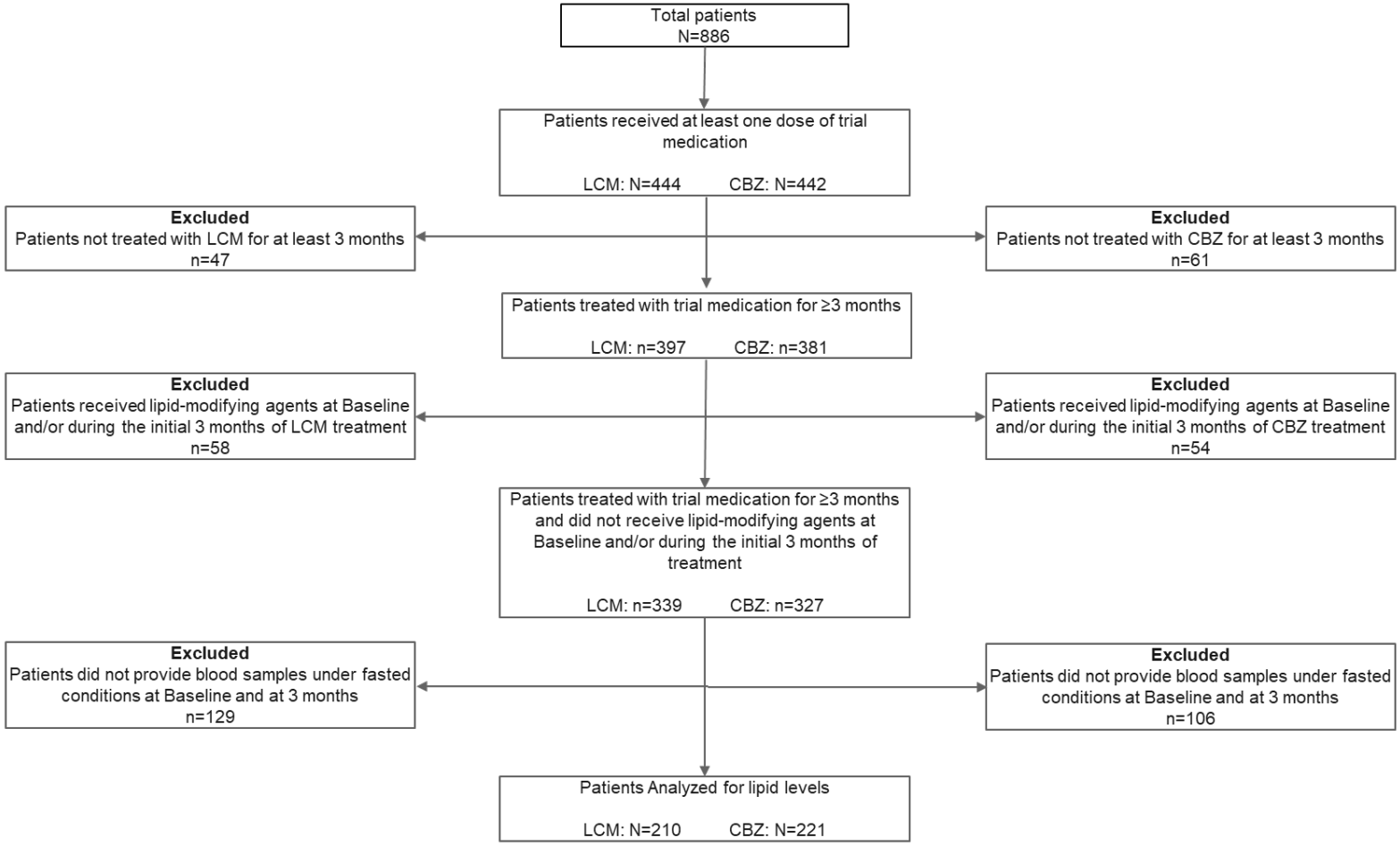
Patients included in the 12-month lipid analysis (Safety Set)



CBZ, carbamazepine; LCM, lacosamide.

FIGURE S2

Patients included in the 3-month lipid analysis (Safety Set)



CBZ, carbamazepine; LCM, lacosamide.

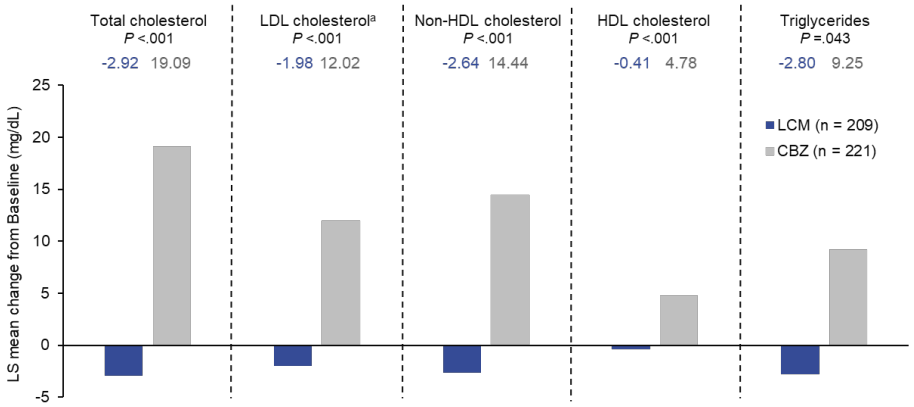
Supporting information: changes in lipids levels at 3 months

At 3 months, mean lipid levels at Baseline were generally similar between patients randomized to LCM and CBZ (Figure S1). Three-month LCM monotherapy did not increase the mean levels of TC, LDL-C, non-HDL-C, HDL-C, and TGs. Increases in the mean levels of TC, LDL-C, non-HDL-C, and TGs were observed after 3-month CBZ monotherapy.

On applying the ANCOVA model for change in lipid levels from Baseline to 3 months a numerical difference was observed between LCM and CBZ for change in TC, LDL-C, non-HDL-C, HDL-C ($P < .001$ for each) and TGs ($P = .043$) levels.

FIGURE S3

Least squares mean change in lipids levels from Baseline at 3 months (ANCOVA), lipid levels at Baseline and 3 months (3-month population)



	Total cholesterol		LDL cholesterol[a]		Non-HDL cholesterol		HDL cholesterol		Triglycerides	
	LCM	CBZ	LCM	CBZ	LCM	CBZ	LCM	CBZ	LCM	CBZ
Baseline, mean (SD), mg/dL	189.0 (36.7)	182.6 (39.6)	109.7 (30.3)	101.4 (33.0)	131.2 (36.3)	124.0 (38.9)	57.8 (14.7)	58.6 (16.1)	108.3 (68.3)	113.4 (85.0)
3 months, mean (SD), mg/dL	185.4 (36.1)	201.7 (49.7)	107.1 (30.0)	113.7 (40.0)	128.0 (35.8)	138.7 (49.8)	57.4 (15.0)	63.0 (18.8)	106.4 (64.9)	122.2 (90.9)

The ANCOVA model included treatment as a main effect and age, sex, body mass index, and Baseline lipid level as covariates. [a]n = 217 for CBZ.

Table includes within treatment group comparison 3-month vs Baseline, paired *t* test; *P* values were based on means of observed values (unadjusted): LCM: Total cholesterol $P > .05$; LDL cholesterol $P > .05$; non-HDL-cholesterol $P > .05$; HDL cholesterol $P > .05$; triglycerides $P > .05$.

CBZ: Total cholesterol $P < .0001$; LDL cholesterol $P < .0001$; non-HDL-cholesterol $P < .0001$; HDL cholesterol $P < .0001$; triglycerides $P > .05$.

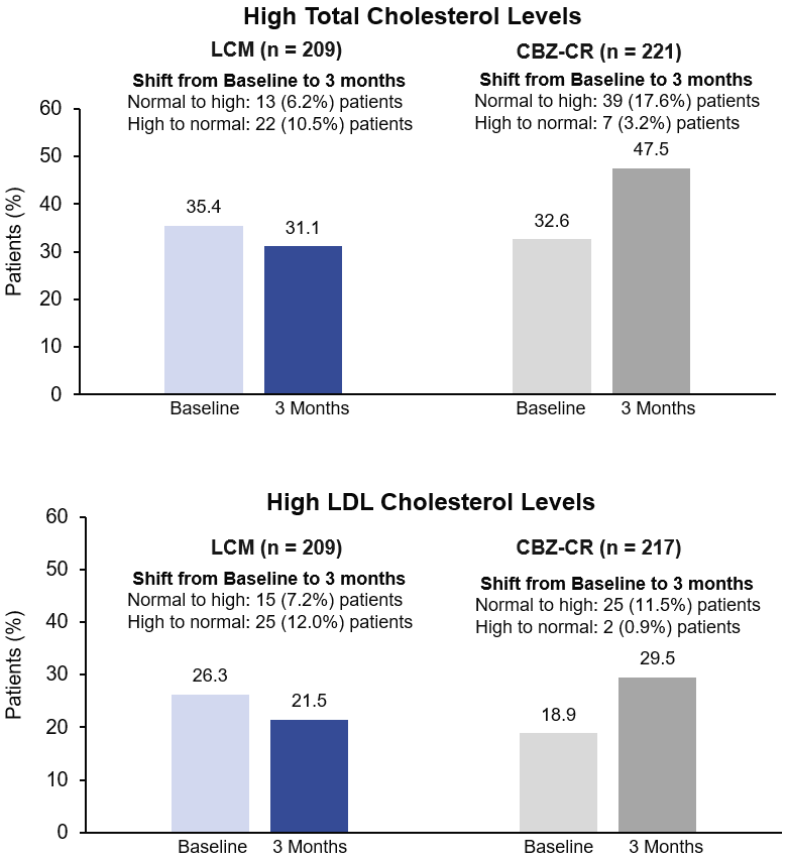
ANCOVA, analysis of covariance; CBZ, carbamazepine; HDL, high-density lipoprotein; LCM, lacosamide; LDL, low-density lipoprotein; LS, least squares; SD, standard deviation

Supporting information: patients with TC and LDL-C levels above the upper limit of the reference range at Baseline and 3 months

In patients on LCM monotherapy, the proportion with TC or LDL-C levels above the upper limit of the reference range was similar at Baseline and at 3 months (Figure S4). In patients on CBZ monotherapy, the proportion with TC or LDL-C levels above the upper limit of the reference range was higher at 3 months compared with Baseline.

FIGURE S4

Proportion of patients with total cholesterol and/or LDL cholesterol levels above the upper limit of the reference range at Baseline and 3 months (3-month population)



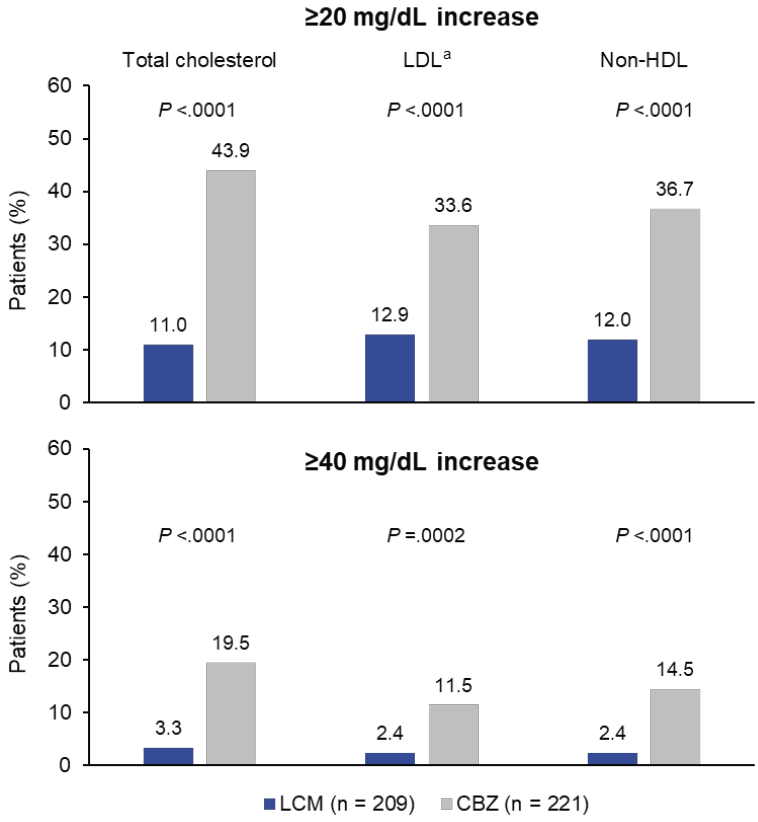
Reference ranges for total cholesterol: normal was 130-200 mg/dL, high was >200 mg/dL; Reference ranges for LDL cholesterol: under 18 years of age, normal was 0-110 mg/dL, high was >110 mg/dL; age 18 years and older, normal was 0-130 mg/dL, high was >130 mg/dL. CBZ, carbamazepine; LCM, lacosamide; LDL, low-density lipoprotein

Supporting information: proportion of patients with specified increase in lipid level between Baseline and 3 months

For TC, LDL-C, and non-HDL-C, the proportion of patients with a ≥20 or ≥40 mg/dL increase between Baseline and 3 months was higher in patients on CBZ than in those on LCM monotherapy (Figure S5).

FIGURE S5

Proportion of patients with a ≥20 or ≥40 mg/dL increase in total cholesterol, LDL cholesterol, and non-HDL cholesterol levels from Baseline at 3 months (3-month population)



P-values are from the Fisher's exact test; [a]n = 217 for CBZ.

CBZ, carbamazepine; HDL, high-density lipoprotein; LCM, lacosamide; LDL, low-density lipoprotein; TC, total cholesterol.