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RESEARCH ARTICLE

Long-term individual retention with cenobamate in adults with focal seizures: Pooled data from the clinical development program

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Abstract

Objective: We determined retention on open-label cenobamate therapy in the clinical development program to assess the long-term efficacy and tolerability of adjunctive cenobamate in individuals with uncontrolled focal seizures.

Methods: Data from two randomized, controlled cenobamate studies and one open-label safety and pharmacokinetic study were pooled. Based on the percentage of participants remaining on treatment, retention rates were estimated using Kaplan-Meier survival analyses. We performed two additional analyses to assess factors contributing to retention, stratifying a robust data set (through 2 years) by cenobamate modal dose and frequently used concomitant anti-seizure medications. Cenobamate discontinuations and treatment-emergent adverse events were summarized.

Results: Data from 1844 participants were pooled: 149 from a single-dose randomized trial, 355 from a multi-dose randomized trial, and 1340 from an open-label safety and pharmacokinetic study. Most participants from randomized trials continued in open-label extensions, and pooled data represent >95% of participants exposed to cenobamate. Baseline characteristics and disease and treatment histories were similar across studies. Median duration of cenobamate exposure was 34 months, with a median modal dose of 200 mg/day. Kaplan-Meier estimates of cumulative cenobamate retention rates were 80% at 1 year and 72% at 2 years. Once participants reached the maintenance phase, retention rates were consistently high in participants receiving ≥100 mg/day cenobamate, and concomitant anti-seizure medications did not affect long-term retention. By 2 years, 535 (29%) had actually discontinued cenobamate; the most common reasons for discontinuation were adverse events (37.6%), withdrawal of consent (21.1%), and other (16.8%).

Significance: Treatment retention rates provide a proxy measure for long-term efficacy, safety, tolerability, and adherence. The consistently high retention rates

we found suggest that cenobamate may be an effective and well-tolerated new treatment option for people with drug-resistant focal seizures.

KEYWORDS
efficacy, epilepsy, open-label, retention rate, tolerability

1 | INTRODUCTION

Cenobamate is a new anti-seizure medication (ASM) available in the United States to treat adults with focal seizures. In Europe, cenobamate is indicated as an adjunctive treatment for adults with focal seizures whose seizures have not been adequately controlled despite treatment with at least two ASMs.[1,2] Cenobamate is believed to have a dual mechanism of action. Preclinical studies suggest that cenobamate acts as a positive allosteric modulator of γ-aminobutyric acid receptor A ($GABA_A$) and preferentially blocks the persistent sodium current.[3,4] These mechanisms of action are likely complementary and probably act by preventing seizure initiation and potentially limiting the spread of seizures.[5–9]

Two randomized controlled trials of adjunctive cenobamate in adults with uncontrolled focal seizures showed substantial seizure reductions in the maintenance phases of the studies; one study (randomized study 1; Table S1) reported seizure freedom (100% seizure reduction) in 28.3% of participants administered 200 mg/day cenobamate vs 8.8% of those taking placebo.[10] The other study (randomized study 2; Table S1) reported seizure freedom in 21.1% of participants taking 400 mg/day cenobamate vs 1% taking placebo.[11] Both trials had open-label extensions. A third study, an open-label safety study (Table S1) in adults with drug-resistant focal seizures, included a 12-week titration phase to 200 mg/day cenobamate. A dose-optimization/maintenance phase followed, during which participants could receive up to 400 mg/day cenobamate for 12 months or longer if clinical benefit continued.[12]

Retention rates of treatment with ASMs provide a composite measure of clinical efficacy, tolerability, safety, and adherence over a specified time frame.[13–17] Clinicians managing people with difficult-to-treat seizure disorders may find that long-term retention is a useful measure of ASM effectiveness. The use of retention data as an outcome measure is now recommended by the European Medicines Agency (EMA) as a global indicator of a drug's clinical effectiveness.[18] Data from retention studies may also provide much-needed benchmarks for interpreting and comparing the clinical efficacy of newly approved ASMs.[19] They also reassure that the results of controlled clinical trials may be generalizable for tolerability and sustained clinical benefit.[16] Here, we present pooled exposure, retention, and safety data from a large population that received open-label adjunctive cenobamate treatment in the clinical development program.

Key Points

- Cenobamate estimated retention rates were 80% at 1 year and 72% at 2 years
- After titration, retention remained high, with cenobamate doses ≥100 mg/day; concomitant anti-seizure medications did not impact retention
- Cenobamate discontinuation was most often due to adverse events, withdrawal of consent, or other reasons
- High long-term cenobamate retention suggests sustained clinical efficacy and tolerability

2 | METHODS

2.1 | Study design

Study design and inclusion/exclusion criteria for the two randomized controlled trials and the open-label safety study were published previously.[10–12] Key aspects of these study designs are summarized in Table S1. This post hoc analysis used a data cutoff of June 1, 2020.

Participants who completed the double-blind phase of the two randomized controlled trials were eligible to continue to an open-label extension. This was the case for most sites participating in the trials. In the first trial, which evaluated 200 mg/day cenobamate vs placebo, individuals continuing to the open-label extension were transitioned to receive cenobamate 100 mg/day. Participants underwent upward titration of the dose by 50 mg/day every 2 weeks to 200 mg/day based on tolerability. Later, the maximum allowed dose was changed to 400 mg/day at the investigator's discretion. Participants could receive cenobamate without re-titration if a clinically meaningful response had been observed or if seizure control worsened during the transition to open-label. In the second trial, which evaluated 100, 200, or 400 mg/day cenobamate vs placebo,

individuals continuing to the open-label extension were transitioned to an initial target dose of 300 mg/day cenobamate. The investigator adjusted the cenobamate dose as clinically indicated, either down to a minimum of 50 mg/day or up to a maximum of 400 mg/day.

The open-label safety study had a 12-week titration phase to achieve an initial target dose of 200 mg/day. This was followed by a 12-month maintenance phase, which could be continued past the 12 months for participants benefiting from cenobamate.[12] During the maintenance phase, the cenobamate dose could be increased by 50 mg/day every other week to a maximum of 400 mg/day. In all the open-label studies, investigators could adjust therapy with other ASMs as clinically indicated (those taking concomitant phenytoin or phenobarbital in the open-label safety study were not permitted to add, remove, or adjust co-administered ASMs during titration), although monotherapy with cenobamate was not allowed.[12]

For this pooled analysis, safety outcomes through 2 years were summarized, including the incidence of treatment-emergent adverse events (TEAEs), serious adverse events, and discontinuations due to adverse events. All people included in this analysis received at least one dose of study medication.

Each study was conducted according to the International Council for Harmonisation guidelines. An institutional review board at each site approved the protocol.[10–12] All participants provided written, informed consent before entry.

2.2 | Statistical analyses

Baseline demographics, disease characteristics, exposure duration (defined as the date of the last dose minus date of the first dose of open-label treatment +1), reasons for discontinuation, and TEAEs were summarized with descriptive statistics for the pooled population.

Overall retention rates were estimated using Kaplan-Meier analyses and were derived from all participants who received open-label cenobamate, including those who enrolled in the first trial and for whom data through 8 years were available. To estimate retention rates stratified by modal dose (defined as the dose taken for the most days during the study) and by frequently used concomitant ASMs, data through 2 years of follow-up were used, representing the largest number of participants and, therefore, the most robust data set.

To compare retention rates between different ASMs, a search was conducted to identify OLE studies that were conducted with methodologies similar to those used in the cenobamate clinical study program (ie, adults with focal seizures) that reported retention rate data. Additional post-marketing estimated retention rates of commonly prescribed ASMs were evaluated based on published data from a single UK adult tertiary center for epilepsy. The published retention rate data were reviewed and qualitatively compared with the corresponding data for cenobamate.

3 | RESULTS

3.1 | Participant disposition and baseline demographics

Across the three studies, a total of 1844 participants received open-label cenobamate (Figure 1). The open-label phase was added as a protocol amendment to the first study. India did not approve the amendment, and thus 43 Indian participants did not have the option to participate in the open-label study. One hundred forty-nine participants from open-label phases of the first study, 355 from the second study and 1340 from the open-label safety study, were included in the analysis, representing over 95% of those exposed to cenobamate across the three studies.

The mean (SD) baseline age (39.5 [12.5] years) and sex (49.6% female) of the pooled population were similar to those in the individual studies (Table 1). Baseline demographics of the populations have been published previously.[10–12]

3.2 | History of epilepsy and exposure to ASMs

Epilepsy duration was similar across studies, with a mean (SD) of 23.1 (13.9) years for the pooled population (Table 1). Most participants (1482/1844, 80.4%) were taking two to three concomitant ASMs at the start of open-label treatment (mean 2.3 [0.8]). Seven hundred twenty-eight (39.5%) were taking two concomitant ASMs, and 754 (40.9%) were taking three. Table 1 also lists the individual concomitant ASMs used by 10% or more participants at the start of open-label cenobamate treatment. Approximately 80% received sodium channel blockers (including lamotrigine, carbamazepine, lacosamide, oxcarbazepine, eslicarbazepine acetate, and rufinamide).

3.3 | Cenobamate exposure

At the data cutoff of June 2020, the mean (SD) cenobamate exposure duration was 33.7 (22.5) months (median 34 months, range [0.0–114.3]). In the open-label extensions of the individual randomized studies, the mean

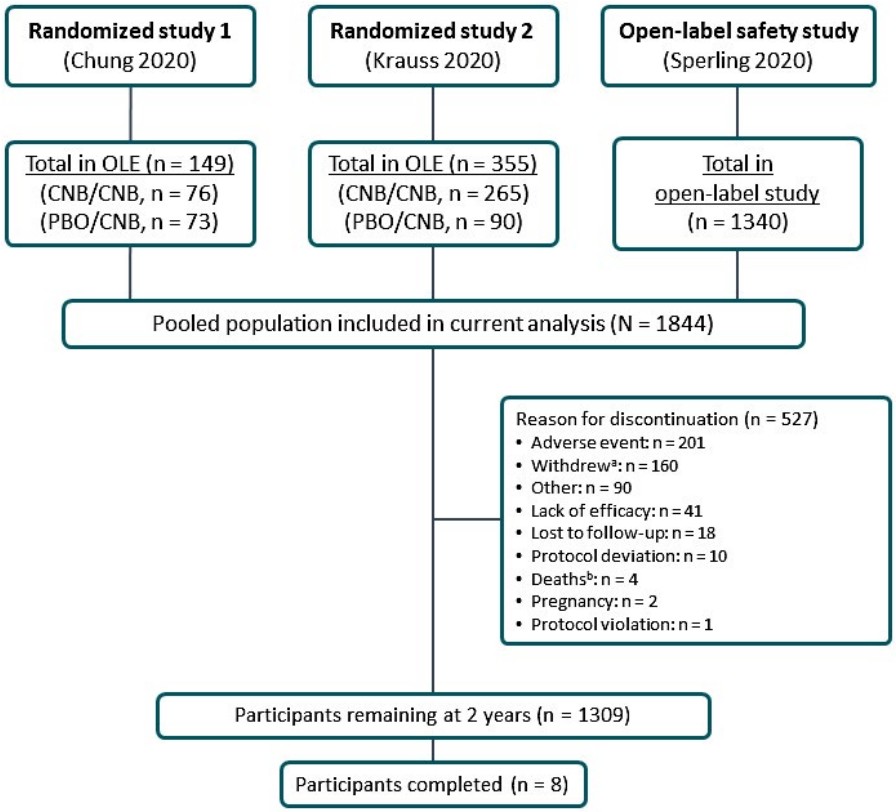

FIGURE 1 Participant disposition in cenobamate studies. CNB, cenobamate; OLE, open-label extension; PBO, placebo. [a]Withdrew, $n = 160$. Language describing withdrawal varied between the studies; combined total includes "withdrew consent for reasons other than adverse events" and "Withdrawal by participant." [b]13 participants in the pooled population experienced an adverse event with fatal outcome prior to the 2-year data cutoff. Nine of these were categorized under adverse event. None of the deaths were judged to be related to treatment

(SD) exposure duration was 58.6 (39.0) months (median 85.8 months [range, 0.3–104.8]) and 47.3 (26.0) months (median 64.9 months [range 1.1–79.8]). In the open-label safety study, the mean (SD) duration of exposure was 27.4 (13.7) months (median 33.4 months [range 0.03–114.3]). The median modal doses in the open-label segments of the randomized studies were 200 mg and 300 mg, and in the open-label study, the median modal dose was 200 mg. The median modal daily dose of cenobamate in the pooled population was 200 mg.

3.4 | Estimated cumulative retention rates

The estimated retention rates were 80% at 1 year and 72% at 2 years. These rates were consistent across the individual studies, ranging from 73% to 84% at 1 year and 67% to73% at 2 years. The probability of retention in those who continued participating was estimated to be 67% at 3 years and gradually decreasing to 57% through 8 years (Figure 2).

3.5 | Retention rate correlations with cenobamate doses and concomitant ASMs

When we stratified data through 2 years based on cenobamate modal dose (<100 mg/day, ≥100 to <200 mg/day, ≥200 to <300 mg/day, and ≥300 mg/day), estimates of retention ranged from 71% to 92% for participants who received cenobamate at doses ≥100 mg/day in the first year (Figure 3A). By comparison, retention rates for participants who received cenobamate at doses <100 mg/day fell to 19% in the first year. Participants in the <100 mg/day cohort included those who discontinued during the titration period. Among individuals who stopped cenobamate during the titration period, less than 10% reported ≥1 TEAE that started in the titration period and led to study drug discontinuation.

Estimates of retention rates stratified by the most commonly coadministered ASMs (used by 10% or more participants) appear similar (Figure 3B). The retention estimates at 1 year ranged from 77%–83% and at 2 years from 69%–75% across all subgroups of concomitant ASMs. This analysis suggests that the various ASMs administered concomitantly with cenobamate did not affect retention. Retention rate data for brivaracetam, lacosamide, and perampanel were obtained from published studies that employed methods comparable to those used for this analysis. Open-label extension studies of brivaracetam, lacosamide, and perampanel reported estimated retention rates from 62% to 80% at 1 year and 29% to 68% at 2 years.[20–23] This compares to our findings of an 80% estimated retention rate for cenobamate at 1 year and 72% at 2 years.

TABLE 1 Baseline demographics and concomitant ASMs (pooled population)

	Participants from randomized study 1[10] ($n = 149$)	Participants from randomized study 2[11] ($n = 355$)	Participants from open-label safety study[12] ($n = 1340$)	Pooled ($N = 1844$)
Age, mean (SD), years	37.6 (10.9)	39.6 (11.7)	39.7 (12.8)	39.5 (12.5)
Female, *n* (%)	77 (51.7)	170 (47.9)	667 (49.8)	914 (49.6)
BMI, kg/m^2, mean (SD)	26.3 (5.2)	26.4 (6.2)	26.9 (6.0)	26.8 (6.0)
Race, *n* (%)				
White	99 (66.4)	306 (86.2)	1064 (79.4)	1469 (79.7)
Black or African American	5 (3.4)	9 (2.5)	47 (3.5)	61 (3.3)
Asian	37 (24.8)	32 (9.0)	73 (5.4)	142 (7.7)
Other[a]	3 (2.0)	8 (2.3)	156 (11.6)	172 (9.3)
Duration of epilepsy, mean (SD)	23.0 (12.1)	24.3 (13.5)	22.8 (14.3)[b]	23.1 (13.9)[c]
Number of ASMs,[d] *n* (%)				
0	1 (0.7)	0 (0.0)	4 (0.3)	5 (0.3)
1	12 (8.1)	51 (4.4)	242 (18.1)	305 (16.5)
2	71 (47.7)	144 (40.6)	513 (38.3)	728 (39.5)
3	62 (41.6)	151 (42.5)	541 (40.4)	754 (40.9)
>3	3 (2.0)	9 (2.5)	40 (3.0)	52 (2.8)
Number of ASMs, mean (SD)	2.4 (0.69)	2.3 (0.75)	2.3 (0.80)	2.3 (0.79)
Most common concomitant ASMs[e] (≥10% of participants), *n* (%)				
Levetiracetam	65 (43.6)	155 (43.7)	485 (36.2)	705 (38.2)
Lamotrigine	51 (34.2)	119 (33.5)	412 (30.7)	582 (31.6)
Valproate	38 (25.5)	87 (24.5)	357 (26.6)	482 (26.1)
Carbamazepine	39 (26.2)	98 (27.6)	323 (24.1)	460 (24.9)
Lacosamide	27 (18.1)	62 (17.5)	297 (22.2)	386 (20.9)
Topiramate	35 (23.5)	63 (17.7)	146 (10.9)	244 (13.2)
Oxcarbazepine	27 (18.1)	49 (13.8)	149 (11.1)	225 (12.2)
Clobazam	9 (6.0)	34 (9.6)	160 (11.9)	203 (11.0)

Abbreviations: ASM, anti-seizure medication, OLE, open-label extension; SD, standard deviation.

[a] American Indian, Alaska Native, or unknown.

[b] Of a total of 1336 participants.

[c] Of a total of 1840 participants.

[d] ASMs used at the beginning of OL cenobamate dosing in each study.

[e] Participants may be counted more than once as they may have been taking >1 ASM.

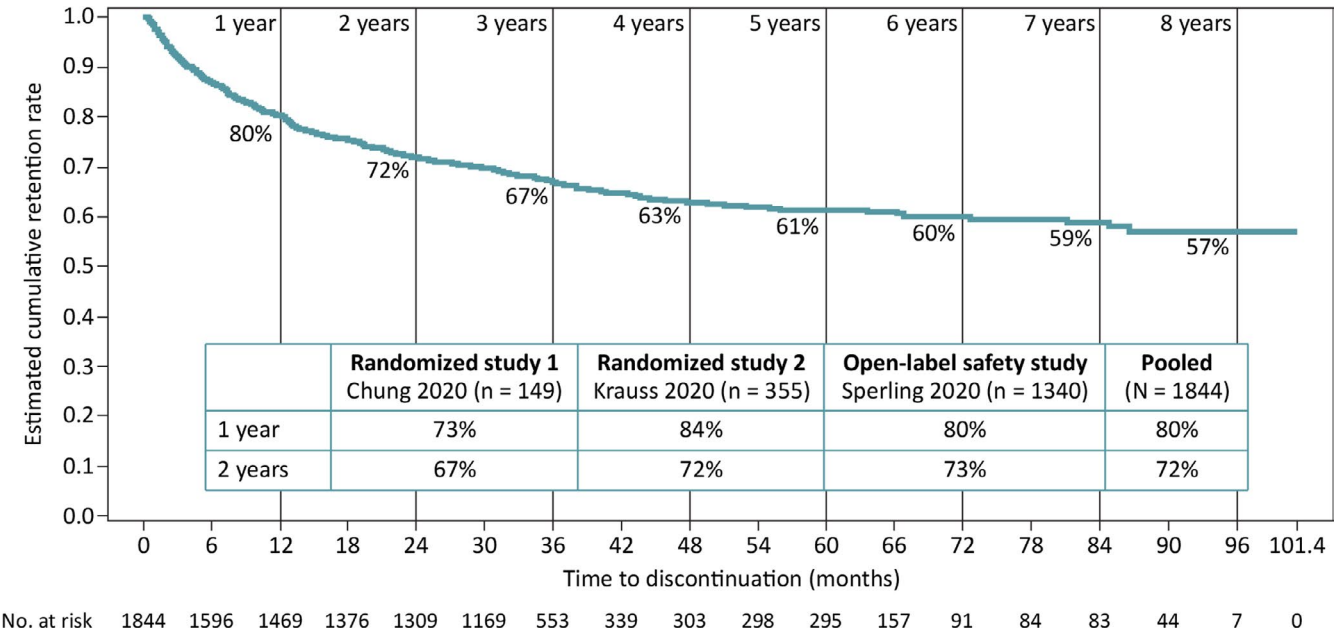

FIGURE 2 Kaplan-Meier estimates of time to discontinuation of open-label cenobamate for the pooled population. Table overlay shows the retention results from individual cenobamate studies as well as pooled data at 1 and 2 years

3.6 | Safety and discontinuations

We evaluated safety and discontinuation data in all 1844 participants receiving open-label cenobamate. A total of 1468 of 1844 individuals (80%) were still participating at the end of year 1 and 1309 (71%) by the end of 2 years (Table S2). At the end of year 2, a total of 535 of 1844 participants (29%) had discontinued cenobamate. The most common reasons for discontinuation were adverse events (201, 37.6%), withdrawal of consent for reasons other than adverse events (113, 21.1%), and other unspecified reasons (90, 16.8%) (Table S2).

The most common TEAEs across all three studies were central nervous system related (Table 2). Most TEAEs were mild or moderate in severity (75.8%). The most common treatment-related adverse events (TRAEs) were somnolence (26.8%), dizziness (24.9%), fatigue (15.3%), headache (7.8%), and balance disorder (5.5%). In individuals who experienced serious TEAEs, seizures were the most common and occurred in 1.7% of the pooled population. The most common TEAEs (≥5%) that led to study discontinuations were dizziness (10.4%), somnolence (7%), fatigue (5%), headache (5%), rash (5%), and seizures (5%). A total of 13 participants died before the 2-year cutoff for these analyses. None of the deaths were considered to be treatment related. Three died of sudden unexplained death in epilepsy (SUDEP), three of accident/trauma, two of sepsis, and one of suicide, status epilepticus, cardiac arrest, laryngospasm, and sudden death (not classified as SUDEP). The incidence of SUDEP among participants in this study is consistent with other similar design and scale studies.[20,23]

4 | DISCUSSION

Randomized clinical trials are the gold standard for demonstrating safety and efficacy of new drugs. Open-label studies, however, provide additional evidence for how a new drug will perform in everyday clinical use over more extended periods.[13,17,24] Retention rates reflect a balance between efficacy and tolerability and can be a good proxy indicator of the effectiveness and safety of new ASMs in real-world use.[13–17] The clinical relevance of retention data contributed to the decision of the EMA to require long-term follow-up (1-year minimum) and retention on therapy as evidence of clinical effectiveness.[18]

Our analyses demonstrate high rates of retention on cenobamate during the clinical development program. An estimated 80% remained on treatment at the end of 1 year and 72% at 2 years. Participants discontinued cenobamate most often due to adverse events, the nature of which are habitually seen with this class of medication. In the pooled population following 24 months of treatment, 29% withdrew from the studies (Table S2). Lack of efficacy was cited as the reason for discontinuation in only 7.7% of participants. In the combined studies, however, efficacy was not monitored in the majority of participants and it is possible that a proportion of participant-initiated discontinuations were due to perceived lack of efficacy.

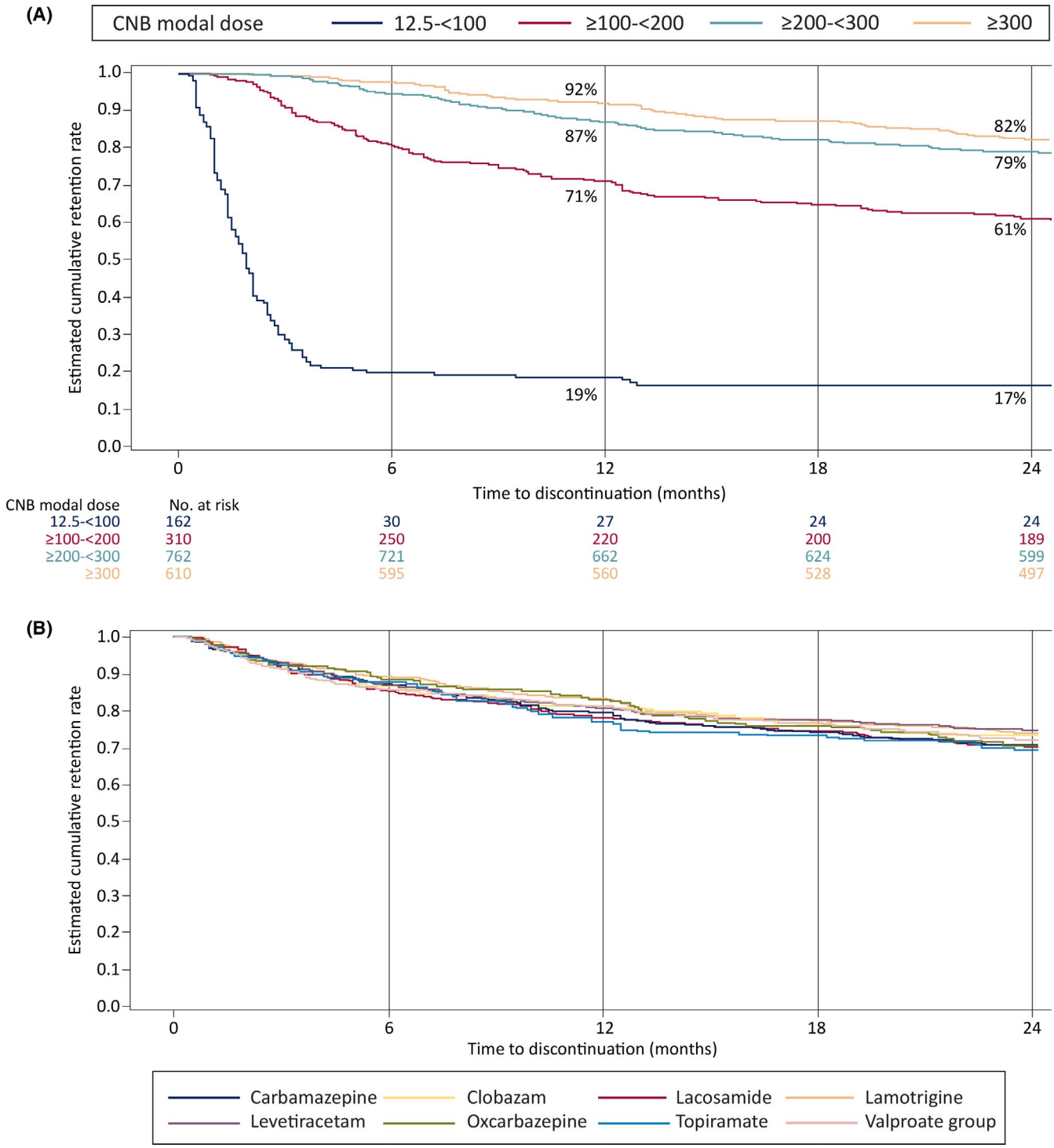

FIGURE 3 Kaplan-Meier estimates of cenobamate retention rates in the pooled population stratified by: (A) modal dose of cenobamate at 2 years and (B) most frequently used concomitant ASMs (10% or more of participants). ASMs, anti-seizure medications; CNB, cenobamate

Comparing participant retention rates between ASM clinical trials can be challenging. Reasons include lack of head-to-head comparison studies and the broad time range over which they have been performed (over the last several decades). Several caveats also apply, including differences in populations, differences in follow-up length, varying numbers and identities of concomitant ASMs, and different titration rules. Despite these factors, retention rates on cenobamate appear to be comparable to or better than rates reported for ASMs in pre-marketing open-label extension studies conducted as part of respective clinical development programs.[20–23,25–27] Often, when

TABLE 2 Summary of treatment-emergent adverse events (TEAEs; pooled population)

n (%)	Cenobamate (*N* = 1844)
Participants with ≥1 TEAEs (by severity)	1609 (87.3)
Mild	610 (33.1)
Moderate	788 (42.7)
Severe	211 (11.4)
TEAEs	
Somnolence	519 (28.1)
Dizziness	509 (27.6)
Fatigue	310 (16.8)
Headache	273 (14.8)
Diplopia	156 (8.5)
Viral upper respiratory tract infection	149 (8.1)
Upper respiratory tract infection	144 (7.8)
Nausea	137 (7.4)
Balance disorder	115 (6.2)
Gait disturbance	105 (5.7)
Fall	96 (5.2)
Seizure	94 (5.1)
Participants with ≥1 treatment-related TEAE	1349 (73.2)
Participants with ≥1 serious TEAE	250 (13.6)

Note: TEAEs were adverse events with onset after the start of study medication in the open-label extensions or in the open-label study, up to analysis cutoff date, or onset before study medication and worsened after starting study medication, up to analysis cutoff date.

Abbreviation: TEAEs, treatment-emergent adverse events.

individuals do well in the clinical trials, they do as well or better in the post-marketing period. Figure 4 presents retention rate data from multiple long term-follow-up studies performed at a tertiary care center in the UK (National Hospital for Neurology and Neurosurgery at the Queen Square and Chalfont Centre sites). These studies were performed following market approval of other ASMs (gabapentin, lacosamide, lamotrigine, levetiracetam, perampanel, pregabalin, topiramate, and zonisamide) with up to 4 years of follow-up.[14,19,28–31]

Cenobamate retention rates compare favorably to rates reported for ASMs in post-marketing studies. In reviewing retention rates reported in ASM studies from a historical context, retention rates trended higher over the years, possibly due to improved effectiveness and tolerability as novel drugs are developed.

A strength of our study is the pooled study population followed, allowing further evaluation of reasons that may affect retention, including modal dose and concomitant medication use. By stratifying the analyses according to the modal dose administered, we found high retention rates across the assigned doses of cenobamate (100, 200, and 400 mg). Higher doses were associated with greater retention rates, and participants taking low doses of cenobamate (<100 mg/day) were less likely to remain. All three regulatory trials included titrations to cenobamate doses ≥100 mg/day. Participants in the <100 mg/day cohort included those who discontinued during the titration period; lower retention rates among those taking cenobamate <100 mg/day could potentially be attributed to insufficient treatment response and/or poor drug tolerance during the titration or maintenance phase. In one study of retention rates for brivaracetam, participants who received subtherapeutic doses (<50 mg/day) were excluded from the analysis to avoid incurring a bias toward a shorter overall retention duration.[24] We included the lower dose of cenobamate in our analysis to show that those taking 100 mg/day or more of cenobamate, up to 400 mg/day, had high retention rates, suggesting favorable tolerability and effective seizure control at recommended doses. Although the onset of the most common AEs occurred most frequently during the titration phase, the AEs were mainly mild or moderate in severity. The slower titration strategy used in the open-label safety study and the flexible dosing of concomitant medications during cenobamate titration reduced the severity of AEs.[32]

The present analysis was not designed to evaluate drug interactions, but we stratified the retention analyses by the most frequently used ASMs to assess how other drugs might influence whether participants would remain on cenobamate. The drugs most commonly used by the participants represent various classes of ASMs, including sodium channel blockers, benzodiazepines, GABA modulators, and levetiracetam (synaptic vesicle protein 2A receptor ligand). Retention curves stratified by ASMs were essentially superimposable, suggesting that the effectiveness and tolerability of cenobamate is maintained regardless of which ASMs were used concomitantly. Lowering the doses of concomitant ASMs has been found to improve tolerability problems such as dizziness or sedation and may also increase retention rates. Prescribing information includes recommendations for managing ASM dosing based on specific pharmacokinetic and metabolic interactions with cenobamate.[33]

Retention was estimated from the start of the open-label dosing rather than from the beginning of active therapy, and this is a limitation. Omission of the double-blind phases of trials as a starting point can overestimate the actual retention rate, since participants discontinuing the study before the open-label extension were excluded from our estimate.[24] This is not expected to impact the actual retention rate estimate of cenobamate substantially for two reasons. First, the number of participants randomized to cenobamate in the double-blind phases of the two randomized trials represented less than one-fourth of the total pooled analysis population. Second, the numbers of

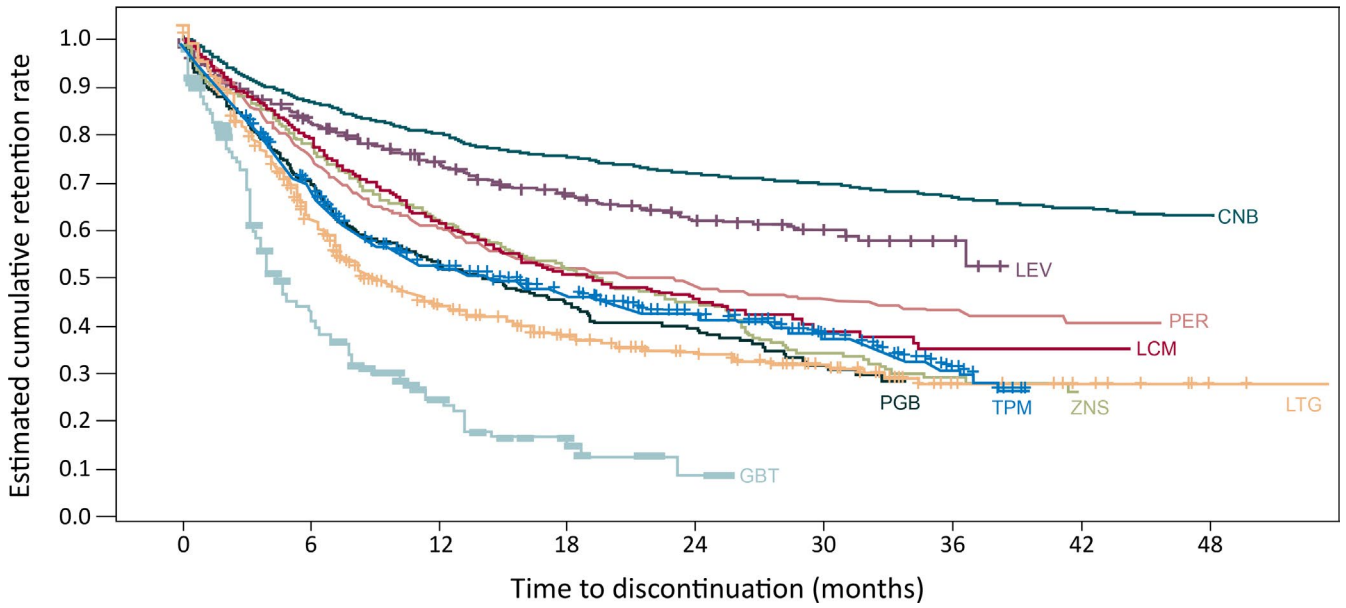

FIGURE 4 Cenobamate retention estimates based on Kaplan-Meier survival analysis compared with historical retention estimates of commonly prescribed anti-seizure medications (ASMs). Retention estimates of cenobamate (CNB) from pooled pre-marketing study data ($N = 1844$) compared with retention estimates from post-marketing studies conducted in the UK (National Hospital for Neurology and Neurosurgery at Queen Square and Chalfont Centre sites) of participants taking levetiracetam (LEV; $n = 811$),[14] perampanel (PER; $n = 376$),[30] lacosamide (LCM; $n = 376$),[19] lamotrigine (LTG; $n = 424$),[29] topiramate (TPM; $n = 393$),[29] zonisamide (ZNS; $n = 417$),[28] pregabalin (PGB; $n = 402$),[31] and gabapentin (GBT; $n = 158$).[29] Adapted from Novy J, et al. *Epilepsy Res*. 2013;106(1–2):250–6.[19] Used with permission

participants discontinuing from active cenobamate in the double-blind phases were relatively low (9.45%–17.6%).[10,11] A general problem with retention data is that participants may remain on the study drug because it is available at no cost, and product approval and labeling can delay continued access. Efficacy was tracked in only one of the three extension studies, so retention rate is a used as a proxy indicator for cenobamate effectiveness. Discontinuation due to withdrawal of consent or other reasons may indicate a lack of efficacy. These and other factors not unique to our study (such as improved access to care or physician incentives to keep participants on the study) can artificially enhance retention rates vs those observed in actual clinical practice.[16] Finally, interpreting any incremental effectiveness implied by retention rates observed with other ASMs should be done cautiously, given differences in methodologies, population, concomitant medications, and times when studies were conducted.

5 | CONCLUSIONS

The consistently high retention rates in the cenobamate open-label studies provide real-world, practical evidence of long-term effectiveness and tolerability, suggesting that it may be an effective and well-tolerated new treatment option for drug-resistant focal epilepsy.

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CONFLICT OF INTEREST

JWS reports personal fees as a speaker or consultant from Arvelle, Eisai, GW Pharmaceuticals, UCB Pharma, and Zogenix. WER is a consultant/advisor for SK Life Science, Inc.; a speaker for Eisai, Greenwich Biosciences (GW Pharmaceuticals), SK Life Science, Inc., Sunovion, and UCB

Pharma; and receives research support from Greenwich Biosciences, Marinus, Medtronic, Neurelis, Ovid, SK Life Science, Inc., Takeda, UCB Pharma, and Upsher-Smith. JJH is a consultant/advisor for Cerevel Pharmaceuticals, Marinus, Intuitap, and Takeda; and a board member (stock owner) for CortiCare. BJS is a consultant/advisor for Arvelle Therapeutics, B. Braun Melsungen, Desitin, Eisai, GW Pharmaceuticals, UCB Pharma, and Zogenix; and receives research support from Eisai, GW Pharmaceuticals, SK Life Science, Inc., and UCB Pharma. VB receives research support from SK Life Science, Inc. MT is a consultant/advisor for Angelini-Arvelle Therapeutics, BIAL, Eisai, GW Pharmaceuticals, and UCB Pharma. The authors confirm that they have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

PREVIOUS PRESENTATION

Portions of this work were presented at the Association of British Neurologists Annual Meeting, May 13–15, 2020, Bournemouth, UK: Sander JW, et al. "Long-term cenobamate retention in people with focal onset seizures: pooled data from open-label studies."

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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