Long-term Efficacy and Safety From an Open-Label Extension of Adjunctive Cenobamate in Patients With Uncontrolled Focal Seizures

Pavel Klein, MD, Sami Aboumatar, MD, Christian Brandt, MD, et al.

Cite as: Neurology® 2022;99:e989-e998. doi:10.1212/WNL.0000000000200792

Correspondence
Dr. Klein
kleinp@epilepsydc.com

Study Question
What is the long-term efficacy and tolerability of adjunctive cenobamate in adults with uncontrolled focal seizures?

What Is Known and What This Paper Adds
Two placebo-controlled double-blind studies demonstrated significant reductions in seizure frequency and high responder rates in cenobamate-treated adults with uncontrolled focal seizures during 6- and 12-week maintenance phases. This study provides Class IV evidence that oral cenobamate 50–400 mg/d is effective as an adjunctive treatment for the long-term management of patients with uncontrolled focal seizures previously treated with 1–3 antiseizure medications (ASMs).

Methods
Patients (aged 18–70 years) with uncontrolled focal seizures who were taking 1–3 ASMs and completed an 18-week double-blind randomized clinical trial (n = 360) could enter the open-label extension (OLE), where they underwent a 2-week blinded conversion to cenobamate (target dose, 300 mg/d; min/max, 50/400 mg/d). Seizure frequency was recorded in patient seizure diaries. Efficacy assessments included median percent change in focal seizure frequency over baseline (double-blind study) assessed over consecutive 6-month intervals and responder rates assessed at consecutive 12-month intervals. Safety assessments included treatment-emergent adverse events (TEAEs). The safety population was defined as all patients who entered the OLE and had taken at least 1 dose of cenobamate. Efficacy analyses used the OLE modified intent-to-treat (mITT) population, defined as all patients who took at least 1 dose of cenobamate and had any seizure data recorded in the OLE. The data cutoff was July 1, 2019.

Results and Study Limitations
The safety population included 355 patients (265 originally on cenobamate and 90 originally on placebo), and the mITT population included 354 patients. The median (range) duration of exposure was 53.9 (1.1–68.7) months. Retention rates at 12, 24, 36, and 48 months were 83%, 71%, 65%, and 62%, respectively. The median percent reduction in seizure frequency during the first 6 months of the OLE for all cenobamate OLE patients was 65.4% (interquartile range [IQR] 52.0%) and increased up to 76.1% (IQR 44.8%) at months 43–48. Reductions were similar among patients originally treated with cenobamate or placebo in the double-blind study. Among observed OLE mITT patients, 16.4% (36/220) achieved 100% and 39.1% (86/220) achieved ≥90% seizure reduction during months >36–48. Among the initial OLE mITT population, 10.2% (36/354) achieved 100% and 24.3% (86/354) achieved ≥90% seizure reduction during months >36–48. TEAEs included dizziness, somnolence, fatigue, and headache. Thirty-one patients (8.7%) had at least 1 TEAE, leading to discontinuation. Limitations of this OLE study include the uncontrolled study design. Potential confounders included the use of concomitant ASMs and allowance of dose adjustments. Results should be considered in the context of the reduced sample over time.

Registration, Study Funding, and Competing Interests
This study is registered on ClinicalTrials.gov (NCT01866111) and was funded by SK Life Science, Inc. (Paramus, NJ). The authors report additional competing interests. Go to Neurology.org/N for full disclosures.
Long-term Efficacy and Safety From an Open-Label Extension of Adjunctive Cenobamate in Patients With Uncontrolled Focal Seizures
Pavel Klein, Sami Aboumatar, Christian Brandt, et al.
Neurology 2022;99:e989-e998 Published Online before print June 15, 2022
DOI 10.1212/WNL.0000000000200792

This information is current as of June 15, 2022

| Updated Information & Services | including high resolution figures, can be found at: [http://n.neurology.org/content/99/10/e989.full](http://n.neurology.org/content/99/10/e989.full) |
| References | This article cites 22 articles, 2 of which you can access for free at: [http://n.neurology.org/content/99/10/e989.full#ref-list-1](http://n.neurology.org/content/99/10/e989.full#ref-list-1) |
| Subspecialty Collections | This article, along with others on similar topics, appears in the following collection(s):
  - All Clinical trials [http://n.neurology.org/cgi/collection/all_clinical_trials](http://n.neurology.org/cgi/collection/all_clinical_trials)
  - Antiepileptic drugs [http://n.neurology.org/cgi/collection/antiepileptic_drugs](http://n.neurology.org/cgi/collection/antiepileptic_drugs)
  - Class IV [http://n.neurology.org/cgi/collection/class_iv](http://n.neurology.org/cgi/collection/class_iv)
  - Partial seizures [http://n.neurology.org/cgi/collection/partial_seizures](http://n.neurology.org/cgi/collection/partial_seizures) |
| Permissions & Licensing | Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: [http://www.neurology.org/about/about_the_journal#permissions](http://www.neurology.org/about/about_the_journal#permissions) |
| Reprints | Information about ordering reprints can be found online: [http://n.neurology.org/subscribers/advertise](http://n.neurology.org/subscribers/advertise) |

*Neurology* ® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.