Poster 3.286

# Tolerability and Efficacy of Adjunctive Brivaracetam in Japanese and Chinese Patients With Focal Seizures: Phase 3, Open-Label Extension Trial

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## Background

- Brivaracetam (BRV) is an antiseizure medication (ASM) approved for the treatment of focal seizures in patients ≥1 month of age in the United States,[1] as adjunctive therapy of focal seizures in patients ≥2 years of age in the European Union,[2] and as monotherapy and adjunctive therapy for the treatment of focal seizures with or without secondary generalization in adult patients in Japan.[3,4]
- It is important that the efficacy, tolerability, and safety of ASMs are maintained over the long term, given that chronic treatment is required by many patients with epilepsy.

## Objective

- To evaluate the long-term safety, tolerability, and maintenance of efficacy of adjunctive BRV in Japanese and Chinese patients ≥16 years of age with focal seizures.

## Methods

### TRIAL DESIGN

- EP0085 (ClinicalTrials.gov: NCT03250377) was an open-label, long-term follow-up trial of adjunctive BRV 50-200 mg/day in Japanese and Chinese patients ≥16 years of age with focal seizures, conducted from August 2017 to December 2024.
- Interim results from this trial have been published[5]; here we present the final results.
- The trial population included patients who rolled over from two previous BRV trials (EP0083 [NCT03083665][6] and N01379 [NCT01339559][7]) and directly enrolled patients.
  - For patients who rolled over into EP0085, baseline was the baseline period of the core trial (EP0083 or N01358/NCT01261325 [the core trial of N01379]).
  - For direct enrollers, the baseline period for seizure outcomes was the 8 weeks before first BRV administration; for all other outcomes, the baseline period was trial days on or after the EP0085 screening visit and before the start of the evaluation period in EP0085.
- Rollover patients from N01379 were started at a dose of up to 200 mg/day BRV.
- Directly enrolled patients and rollover patients from EP0083 were started on BRV 100 mg/day (50 mg twice daily), maintained for ≥2 weeks unless unable to tolerate this treatment.
- The dose of BRV could subsequently be adjusted between 50 mg/day and 200 mg/day, according to seizure control and tolerability; dose decreases were not to exceed 50 mg/day.
- Chinese patients were only able to remain in EP0085 for 2 years (patients could continue in the trial until market approval in countries where market approval was requested, and for 2 years in countries where market approval was not requested or obtained, ie, China).

### ANALYSES

- The Safety Set (SS) included all enrolled patients who took ≥1 dose of BRV in EP0085.
- The Full Analysis Set (FAS) included all patients in the SS with ≥1 seizure record on the daily record card during the evaluation period (patients could have recorded 0 seizures).
- The primary safety outcome was the incidence of treatment-emergent adverse events (TEAEs).
- Efficacy outcomes included the median percentage reduction in focal seizure frequency per 28 days from baseline to the evaluation period, 50% responder rate (≥50% reduction in focal seizure frequency per 28 days from baseline), seizure freedom (from focal seizures and all epileptic seizures [focal, generalized, unclassified]) during the evaluation period, and the proportion of patients continuously seizure-free from focal seizures and all seizure types for ≥6 and ≥12 months during the evaluation period (in those exposed to BRV for ≥6 and ≥12 months, respectively).
- The proportion of patients not discontinuing BRV due to any reason, due to lack of efficacy, or due to TEAEs over time was estimated using the Kaplan-Meier method.

## Results

### PATIENT DISPOSITION AND BASELINE CHARACTERISTICS

- 207 patients enrolled, 135 (65.2%) completed the trial, and 72 (34.8%) discontinued; all 207 patients were included in both the SS and FAS.

**Patient disposition**

211 screened

Screening failures
Ineligibility 4 (1.9%)

**Started trial (SS/FAS) 207**
Japan 132
China 75

**Discontinued 72 (34.8%)**
Lack of efficacy 23 (11.1%)
Patient withdrawal 18 (8.7%)
Adverse event 10 (4.8%)
Protocol violation 3 (1.4%)
Lost to follow-up 1 (0.5%)
Other 17 (8.2%)

**Completed trial 135 (65.2%)**

## Overview

### QUESTION

What are the long-term safety, tolerability, and maintenance of efficacy of adjunctive brivaracetam (BRV) in Japanese and Chinese patients ≥16 years of age with focal seizures?

### INVESTIGATION

EP0085 (NCT03250377) was an open-label, long-term follow-up trial of adjunctive BRV 50-200 mg/day in Japanese and Chinese patients (N=207).

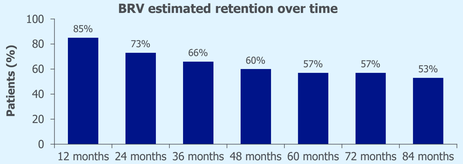
### RESULTS

**Duration of BRV exposure**

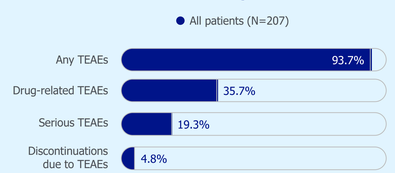
**Mean:** 984.7 days

**Median**: 710.0 days

**Estimated BRV retention (N=207)**




**Tolerability**




TEAE, treatment-emergent adverse event.

**Efficacy**

**Median percentage reduction from baseline in focal seizure frequency per 28 days**


Evaluation period (N=207)

**≥50% reduction from baseline in focal seizure frequency per 28 days**


Evaluation period (N=207)

### CONCLUSIONS

Long-term adjunctive BRV 50-200 mg/day was well tolerated and efficacious in Japanese and Chinese patients with focal seizures. No new safety signals were observed. Efficacy outcomes for seizure frequency and seizure freedom indicate the maintenance of BRV efficacy for ≥12 months from the first dose of BRV in this trial.

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**Baseline demographics and epilepsy characteristics**

| | ALL PATIENTS (N=207) |
|---|---|
| **Age, mean (SD), years** | 36.7 (14.1) |
| **Female, n (%)** | 107 (51.7) |
| **Ethnic subgroup, n (%)** | |
| **Japanese** | 131 (63.3) |
| **Chinese** | 75 (36.2) |
| **Other** | 1 (0.5) |
| **Age at onset of epilepsy, mean (SD), years** | 19.50 (15.26)[a] |
| **Duration of epilepsy, mean (SD), years** | 17.16 (13.10)[a] |
| **Baseline focal seizure frequency/28 days, median (Q1, Q3)** | 7.59 (4.39, 20.00) |
| **Seizure classification at any time before core trial entry,[b] n (%)** | |
| **Any focal seizures** *(partial onset)* | 207 (100.0) |
| **Focal preserved consciousness** *(simple partial)* | 104 (50.2) |
| **Focal impaired consciousness** *(complex partial)* | 174 (84.1) |
| **Focal to bilateral tonic-clonic** *(partial evolving to secondarily generalized)* | 110 (53.1) |
| **Any generalized seizures** | 6 (2.9) |
| **Tonic** | 3 (1.4) |
| **Tonic-clonic** | 4 (1.9) |
| **Unclassified epileptic seizures** | 2 (1.0) |
| **Number of previous ASMs,[c] n (%)** | |
| **0-1** | 78 (37.7) |
| **2-4** | 75 (36.2) |
| **≥5** | 54 (26.1) |

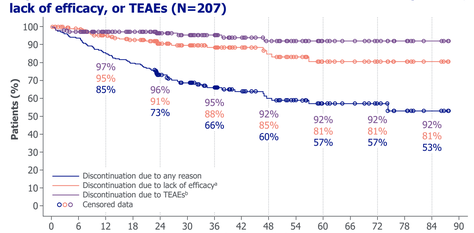
[a]n=206; [b]Patients could have had >1 response. Seizure types are listed per the ILAE 2025 classification[8] with the seizure types per the trial protocol (ILAE 1981)[9] provided in parentheses; [c]Previous ASMs are ASMs taken at any time and discontinued before entry into the previous double-blind trial for rollover patients or before entry into EP0085 for direct enrollers.
ASM, antiseizure medication; ILAE, International League Against Epilepsy; Q1, 25th percentile; Q3, 75th percentile.

### BRV EXPOSURE AND DOSING

- The total duration of BRV exposure was 558.1 patient-years.
- Mean duration of BRV exposure was 984.7 days (SD 633.9 days; median 710.0 days; range 5-2630 days), with a median modal dose of 200.0 mg/day (range 25.0-200.0 mg/day).

### ESTIMATED BRV RETENTION

**Kaplan-Meier–estimated time to BRV discontinuation due to any reason, lack of efficacy, or TEAEs (N=207)**




| TIME (MONTHS) | 0 | 12 | 24 | 36 | 48 | 60 | 72 | 84 |
|---|---|---|---|---|---|---|---|---|
| Number of patients at risk | 207 | 176 | 102 | 72 | 48 | 26 | 16 | 4 |
| Cumulative number of events | | | | | | | | |
| Discontinuation of BRV due to any reason | 0 | 31 | 55 | 64 | 69 | 71 | 71 | 72 |
| Discontinuation of BRV due to lack of efficacy | 0 | 10 | 17 | 19 | 21 | 23 | 23 | 23 |
| Discontinuation of BRV due to TEAEs | 0 | 6 | 7 | 8 | 10 | 10 | 10 | 10 |

One month was defined as 30 days. [a]Patients who discontinued for reasons other than lack of efficacy were censored; [b]Patients who discontinued for reasons other than TEAEs were censored. TEAE, treatment-emergent adverse event.

- Estimated BRV retention at 1, 2, 3, 4, 5, 6, and 7 years was 85%, 73%, 66%, 60%, 57%, 57%, and 53%, respectively.
- The Kaplan-Meier–estimated proportion of patients discontinuing due to TEAEs was low over 8 years of treatment (≤8%).

### SAFETY AND TOLERABILITY

**Overall incidence of TEAEs**

| PATIENTS, n (%) | ALL PATIENTS (N=207) |
|---|---|
| **Any TEAEs** | 194 (93.7) |
| **Drug-related TEAEs** | 74 (35.7) |
| **Serious TEAEs[a]** | 40 (19.3) |
| **Discontinuation due to TEAEs** | 10 (4.8) |
| **TEAEs[b] occurring in ≥15% of all patients** | |
| **Coronavirus infection** | 57 (27.5) |
| **Nasopharyngitis** | 50 (24.2) |
| **Dizziness** | 37 (17.9) |
| **Pyrexia** | 37 (17.9) |
| **Headache** | 34 (16.4) |
| **Drug-related TEAEs[b] occurring in ≥5 patients** | |
| **Somnolence** | 21 (10.1) |
| **Dizziness** | 11 (5.3) |
| **Irritability** | 6 (2.9) |
| **TEAEs leading to discontinuation[b] occurring in ≥2 patients** | |
| **Irritability** | 3 (1.4) |
| **Seizure** | 2 (1.0) |
| **Somnolence** | 2 (1.0) |

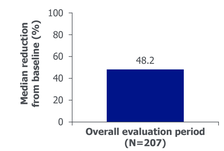
[a]TEAEs were classified as serious if they met ≥1 of the following criteria: death, life-threatening, significant or persistent disability or incapacity, congenital anomaly or birth defect (including that occurring in a fetus), important medical event that may jeopardize the patient and may require medical or surgical intervention to prevent one of the other serious TEAEs, or initial inpatient hospitalization or prolongation of hospitalization (except for hospitalizations for reasons not associated with the occurrence of an adverse event); [b]Preferred Term (Medical Dictionary for Regulatory Activities version 18.1). TEAE, treatment-emergent adverse event.

- Most TEAEs were mild (112 [54.1%]) or moderate (70 [33.8%]) in intensity.

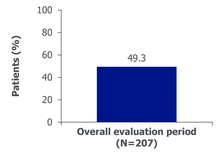
### EFFICACY

- Median focal seizure frequency per 28 days decreased from 7.59 (interquartile range: 4.39, 20.00) during baseline to 4.17 (1.61, 10.46) during the evaluation period.

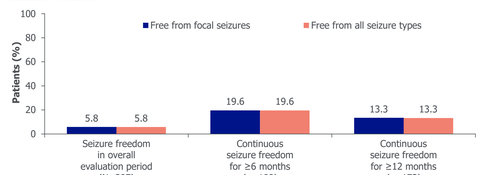
**Reduction in focal seizure frequency**




**50% responder rate in focal seizures**




**Seizure freedom**




## Conclusions

- Long-term adjunctive BRV 50-200 mg/day was well tolerated and efficacious in Japanese and Chinese patients with focal seizures.
- No new safety signals were observed.
- Efficacy outcomes for seizure frequency and seizure freedom indicate the maintenance of BRV efficacy for ≥12 months from the first dose of BRV in this trial.
- Estimated BRV retention at 1, 3, and 5 years was 85%, 66%, and 57%, respectively (176, 72, and 26 patients at risk at each time point, respectively); patients in China were only able to remain in the trial for 2 years.
- Over 8 years of treatment, the estimated proportion of patients discontinuing due to TEAEs was low (≤8%).

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