Effectiveness and Tolerability of Brivaracetam in Adults With Epilepsy Etiology of Cerebral Neoplasm, Cerebrovascular Accident, or Cranial Trauma: Pooled Data Analyses From Two Real-World Studies

Poster P033

Hina Dave[1]
Michael R Sperling[2]
Brian Moseley[3]
Sami Elmoufti[3]
Allison Little[4]
Dimitrios Bourikas[5]
Bernhard J Steinhoff[6]

1. McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, USA
2. Thomas Jefferson University, Philadelphia, PA, USA
3. UCB Pharma, Morrisville, NC, USA
4. UCB Pharma, Smyrna, GA, USA
5. UCB Pharma, Alimos, Greece
6. Kork Epilepsy Center, Kehl-Kork and Medical Faculty, University of Freiburg, Freiburg, Germany

Overview

QUESTION

What is the real-world effectiveness and tolerability of brivaracetam (BRV) in adults with acquired structural epilepsy etiology of cerebral neoplasm, cerebrovascular accident, or cranial trauma?

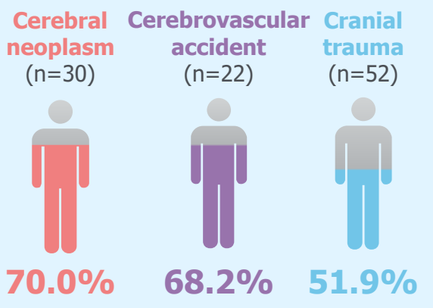
INVESTIGATION

Post hoc analysis of data pooled from two 12-month, prospective, non-interventional studies assessing BRV outcomes in patients with acquired structural epilepsy etiology of cerebral neoplasm (n=30), cerebrovascular (n=22), and cranial trauma (n=52), respectively.

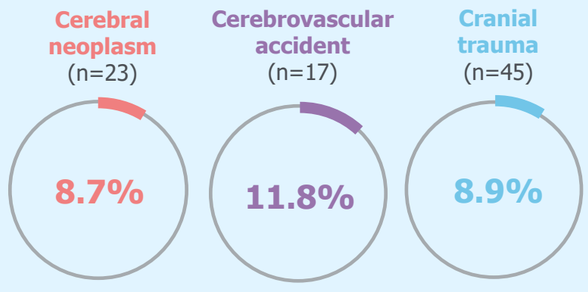
RESULTS

Effectiveness

BRV retention at 12 months

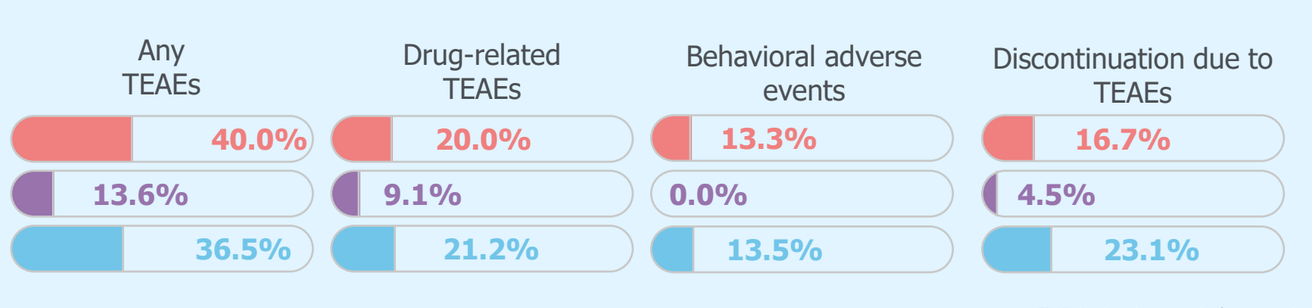


Continuous seizure freedom during 12-months from baseline



Tolerability

TEAEs during BRV treatment



TEAE, treatment-emergent adverse event.

CONCLUSIONS

In this descriptive analysis of pooled data from two real-world studies, BRV treatment was effective and generally well tolerated in patients with acquired structural epilepsy with etiology of cerebral neoplasm, cerebrovascular accident, or cranial trauma. However, further studies with greater patient numbers are needed to confirm these findings.

For a copy of the poster scan:
or visit:
UCBposters.com/EEC2024
Poster ID: **P033**

Background

- The 2017 ILAE classification of the epilepsies[1] and the 2017 ILAE operational classification of seizure types,[2] consider etiology to be an important component of classification. Six etiologic categories have been defined: genetic, structural, metabolic, infectious, immune, and unknown.
- Stroke, brain tumors, and traumatic brain injuries are frequently reported as main causes of acquired structural epilepsy.[3]
- Brivaracetam (BRV) is indicated for the treatment of focal-onset seizures in patients ≥1 month of age in the United States,[4] and as adjunctive therapy for the treatment of focal-onset seizures with or without secondary generalization in patients ≥2 years of age in the European Union.[5]
- Limited clinical data are available for BRV treatment in patients with acquired structural epilepsy etiologies.

Objective

- Given the high incidence of epilepsy in patients with cerebral neoplasm, cerebrovascular accident, and cranial trauma, and the lack of BRV data in these patient populations, an analysis was performed to assess the effectiveness and tolerability of adjunctive BRV in these specific patient populations in daily clinical practice.

Methods

STUDY DESIGN

- EP0077 (ClinicalTrials.gov: NCT02687711) and EP0088 were 12-month, prospective, non-interventional studies in patients initiating BRV in Europe and the United States, respectively.
- Patients received BRV as prescribed by their physician and were followed for up to 12 months from BRV initiation.

ANALYSIS

- Post hoc analysis of pooled data from EP0077 and EP0088 included patients (≥18 years of age) with focal-onset seizures, no prior BRV treatment, ≥1 lifetime antiseizure medication (ASM; stopped before BRV initiation and/or ongoing at BRV initiation), and at least 1 BRV dose during the study.
- Outcomes were assessed for all patients and for subgroups of patients with epilepsy etiology of cerebral neoplasm, cerebrovascular accident, or cranial trauma (patients with >1 etiology recorded were excluded from subgroup analyses).
  - BRV retention at 12 months: patients who remained in the study and were on BRV treatment for ≥12 months (≥330 days in EP0077, ≥309 days in EP0088) after BRV initiation.
  - Kaplan-Meier estimated time to discontinuation of BRV/early study termination due to any reason, due to lack of efficacy, or due to treatment-emergent adverse events (TEAEs).
  - Seizure freedom since BRV initiation for ≥12 months: patients who had post-baseline seizure data, no seizure recorded before study day 420, and did not discontinue BRV or terminate the study before that day (patients who discontinued BRV or terminated the study before day 420 were counted as data missing).
  - Incidence of TEAEs during the study.

Results

PATIENT DISPOSITION, DEMOGRAPHICS, AND BRV EXPOSURE

- Patients with cerebrovascular accident were older at the time of diagnosis compared with patients in the other etiology subgroups.
- In comparison with patients in other subgroups, patients with cranial trauma were more commonly male, had a numerically longer median epilepsy duration, and had a higher median number of lifetime ASMs (suggesting a more drug-resistant population).
- Before BRV initiation, 50.0-60.0% of patients in all subgroups had discontinued levetiracetam (LEV).

Baseline demographics and epilepsy characteristics (SS)

	ALL PATIENTS (N=720)	ACQUIRED STRUCTURAL EPILEPSY ETIOLOGY[a]		
		CEREBRAL NEOPLASM (n=30)	CEREBRO VASCULAR ACCIDENT (n=22)	CRANIAL TRAUMA (n=52)
Patient demographics				
Age, mean (SD), years	44.0 (14.2)	43.8 (14.7)	50.0 (17.8)	45.5 (13.2)
≥65 years, n (%)	60 (8.3)	3 (10.0)	5 (22.7)	4 (7.7)
Female, n (%)	380 (52.8)	17 (56.7)	10 (45.5)	16 (30.8)
Epilepsy characteristics				
Time since epilepsy diagnosis, median (Q1, Q3), years	21.4 (9.4, 32.4)[b]	10.6 (4.9, 18.4)	7.5 (2.7, 21.7)	22.9 (5.8, 32.8)
Age at diagnosis, median (Q1, Q3), years	17.7 (8.7, 31.1)[b]	28.9 (15.1, 44.8)	41.6 (7.9, 53.5)	22.4 (15.7, 32.7)
Number of ASMs				
Number of concomitant ASMs at BRV initiation, median (Q1, Q3)	2.0 (1.0, 3.0)	2.0 (1.0, 2.0)	2.0 (2.0, 3.0)	2.0 (1.0, 3.0)
Number of lifetime ASMs[c], median (Q1, Q3)	6.0 (3.0, 9.0)	4.0 (3.0, 6.0)	4.0 (3.0, 6.0)	5.5 (3.0, 7.0)
LEV stopped before BRV initiation, n (%)	387 (53.8)	18 (60.0)	11 (50.0)	29 (55.8)
BRV treatment duration[d], median (Q1, Q3), months	11.7 (4.1, 12.5)	12.2 (6.5, 12.9)	12.2 (3.9, 12.4)	11.2 (3.1, 12.4)

[a]5 patients who reported more than one acquired structural epilepsy etiology (cerebral neoplasm [CN], cerebrovascular accident [CVA], and cranial trauma [CT]) were excluded from the analysis (1 patient with etiology of CVA and CT; 1 patient with etiology of brain surgery, cerebral infection, CVA, and CT; 1 patient with etiology of CVA and CT; 1 patient with etiology of CN and CVA; and 1 patient with etiology of CVA and CT); [b]n=713; [c]ASMs stopped before BRV initiation and/or ASMs ongoing at BRV initiation; [d]BRV treatment duration during EP0077 and EP0088. ASM, antiseizure medication; Q1, 25th percentile; Q3, 75th percentile.

- Many patients with acquired structural epilepsy with etiology of cerebral neoplasm, cerebrovascular accident, or cranial trauma were likely drug-resistant as suggested by the number of lifetime ASMs before BRV initiation (median: ≥4.0 in any etiology subgroup).

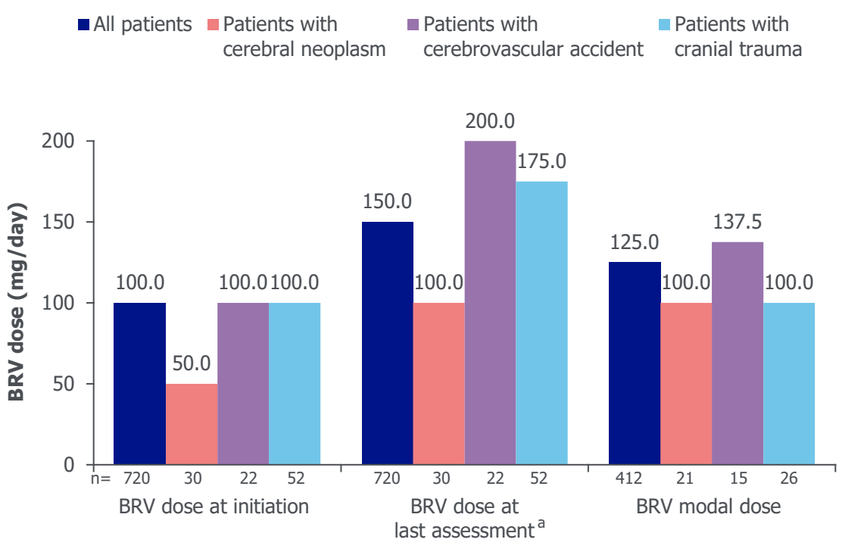
Reason for BRV initiation

	ALL PATIENTS (N=720)	ACQUIRED STRUCTURAL EPILEPSY ETIOLOGY[a]		
		CEREBRAL NEOPLASM (n=30)	CEREBRO VASCULAR ACCIDENT (n=22)	CRANIAL TRAUMA (n=52)
Lack of efficacy of current treatment	595 (82.6)	24 (80.0)	18 (81.8)	36 (69.2)
Behavioral side effects with current ASM	143 (19.9)	6 (20.0)	5 (22.7)	12 (23.1)
Other intolerance to current ASM	112 (15.6)	6 (20.0)	4 (18.2)	7 (13.5)
Administer therapeutic dose without titration	36 (5.0)	3 (10.0)	2 (9.1)	1 (1.9)
Other	20 (2.8)	0	0	2 (3.8)
Missing	5 (0.7)	0	0	2 (3.8)

ASM, antiseizure medication.

- Lack of efficacy of current treatment was the most common reason for BRV initiation (≥69% of patients) in all etiology subgroups.
- Approximately 40% of the patients in all etiology subgroups started BRV treatment due to tolerability challenges (behavioral side effects and other intolerance) with current ASMs.

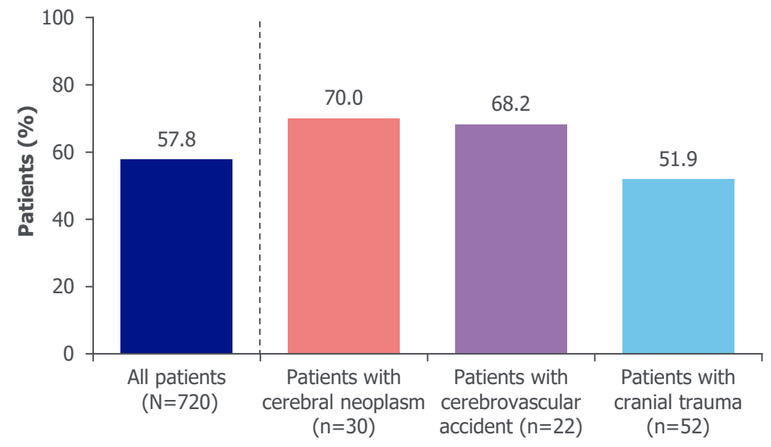
BRV dosing



[a]Median BRV dose at last assessment was assessed in 12-month completers.

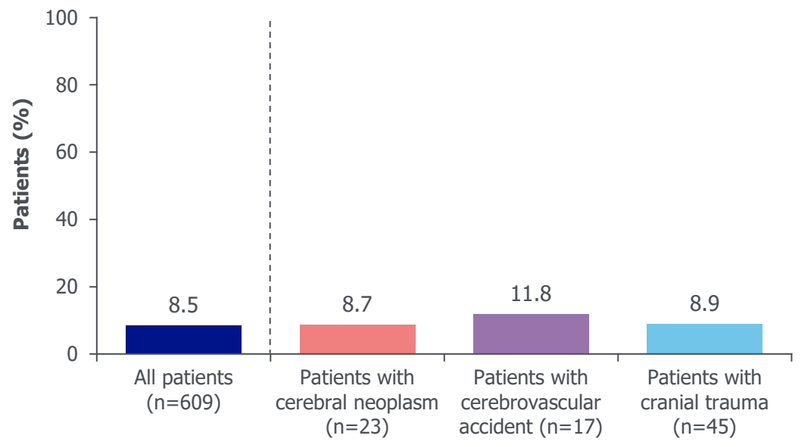
EFFECTIVENESS

BRV retention at 12 months[a]



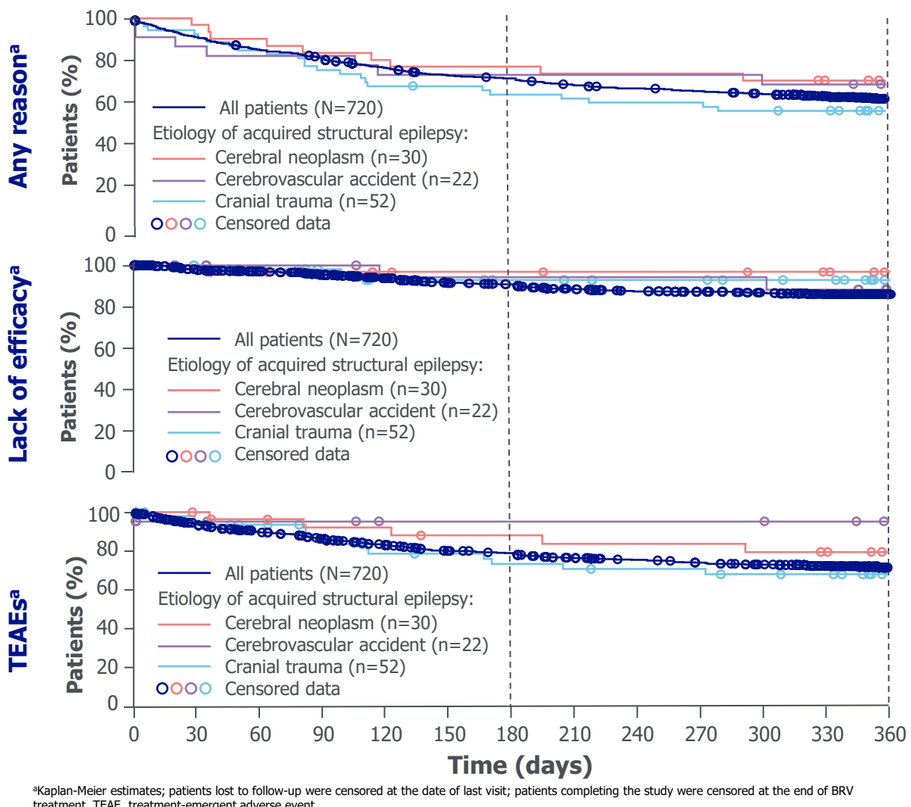
[a]Patients who remained in the study and were on BRV treatment for ≥12 months (≥330 days in EP0077, ≥309 days in EP0088) after BRV initiation.

Continuous seizure freedom during 12-months from baseline[a]



[a]Patients were considered seizure-free since BRV initiation for ≥12 months if they had post-baseline seizure data, no seizure recorded before study day 420, and did not discontinue BRV or terminate study before that day (patients who discontinued BRV or terminated the study before that day were counted as data missing).

Time to BRV discontinuation or study termination due to:

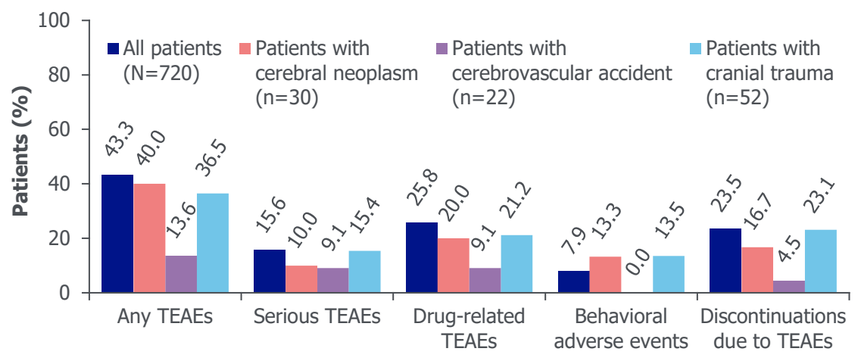


[a]Kaplan-Meier estimates; patients lost to follow-up were censored at the date of last visit; patients completing the study were censored at the end of BRV treatment. TEAE, treatment-emergent adverse event.

- There were no major differences between etiology subgroups in the discontinuation rate due to lack of efficacy.
- Patients with cerebrovascular accident were less likely to discontinue due to TEAEs than patients with cerebral neoplasm and patients with cranial trauma.

TOLERABILITY

TEAEs during the BRV treatment period



- Patients with epilepsy etiology of cerebrovascular accident had numerically lower incidences of TEAEs, drug-related TEAEs and discontinuations due to TEAEs compared to patients in the other etiology subgroups.
- Although approximately 40% of patients initiated BRV treatment due to behavioral side effects and other intolerance, 4.5-23.1% of patients discontinued BRV due to TEAEs in all etiology subgroups.
- No deaths (adverse events leading to deaths) occurred in patients with etiology of cerebral neoplasm, cerebrovascular accident, or cranial trauma.

Most common TEAEs[a]

PREFERRED TERM[b], n (%)	ALL PATIENTS (N=720)	ACQUIRED STRUCTURAL EPILEPSY ETIOLOGY[a]		
		CEREBRAL NEOPLASM (n=30)	CEREBRO VASCULAR ACCIDENT (n=22)	CRANIAL TRAUMA (n=52)
TEAEs in ≥5% of patients in any etiology subgroup				
Drug ineffective	61 (8.5)	1 (3.3)	1 (4.5)	3 (5.8)
Seizure	60 (8.3)	1 (3.3)	1 (4.5)	5 (9.6)
Fatigue	42 (5.8)	0	0	4 (7.7)
Dizziness	40 (5.6)	4 (13.3)	0	2 (3.8)
Headache	24 (3.3)	1 (3.3)	0	3 (5.8)
Behavior disorder	19 (2.6)	2 (6.7)	0	1 (1.9)
Adverse event	18 (2.5)	3 (10.0)	0	3 (5.8)
Aggression	18 (2.5)	1 (3.3)	0	4 (7.7)
Nausea	16 (2.2)	2 (6.7)	0	3 (5.8)
Malaise	7 (1.0)	2 (6.7)	0	1 (1.9)
Agitation	6 (0.8)	2 (6.7)	0	1 (1.9)

[a]During the BRV treatment period; [b]Medical Dictionary for Regulatory Activities (MedDRA) v23.0. TEAE, treatment-emergent adverse event.

Limitations

- Post hoc analysis of pooled data from two prospective, non-interventional studies.
- No placebo or active comparator group.
- Lack of statistical analysis due to low number of patients in each of the subgroups.

Conclusions

- BRV treatment was effective and generally well tolerated in patients with acquired structural epilepsy with etiology of cerebral neoplasm, cerebrovascular accident, and cranial trauma.
- Effectiveness and tolerability of BRV were similar in each etiology subgroup and in all patients.
- These results add to the limited data on BRV outcomes in patients with acquired epilepsy of different etiologies.
- Given the lower number of patients included in this analysis, further studies with greater patient numbers are needed to confirm these findings.

References

1. Scheffer IE, et al. *Epilepsia* 2017;58(4):512-521.
2. Fisher RS, et al. *Epilepsia* 2017;58(4):522-530.
3. Annegers JF, et al. *Epilepsia* 1995;36(4):327-333.
4. Briviact® (brivaracetam) US Prescribing Information. UCB Inc. 2023. https://www.briviact.com/briviact-PI.pdf Accessed July 22, 2024.
5. Briviact® (brivaracetam) EU Summary of Product Characteristics. UCB Pharma SA. 2024. https://www.ema.europa.eu/en/documents/product-information/briviact-epar-product-information_en.pdf Accessed July 22, 2024.
6. Nickels KC, et al. *Nat Rev Neurol* 2016;12(8):465-476.

UCB Pharma-sponsored. UCB Pharma was involved in the design of the study, the collection, analysis, and interpretation of data, and review of the poster. The authors thank the patients and their caregivers in addition to the investigators and their teams who contributed to the EP0077 and EP0088 studies. The authors acknowledge Tom Grant, PhD (UCB Pharma, Slough, UK) for managing the development of the poster, and Emma Budd, PhD (Evidence Scientific Solutions, Horsham, UK) for writing assistance, which was funded by UCB Pharma. Author contributions: B Moseley, S Elmoufti, A Little, and D Bourikas designed the study. S Elmoufti analysed the data. All authors interpreted the data, critically reviewed the poster and approved the final version for presentation.

15th European Epilepsy Congress Rome, Italy | 7—11 September 2024

Previously presented at American Epilepsy Society, 77th Annual Meeting Orlando, FL, USA |1-5 December 2023