DOI: https://doi.org/10.54393/pjhs.v6i7.2771

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 07 (July 2025)

Original Article

OPEN ACCESS

Adjunctive Brivaracetam Therapy in Epilepsy: A Prospective Clinical Study

Abdul Hafeez Bughio[1*], Muslim Ali Lakhiar[1], Sajid Hussain Seelro[2], Noor Nabi Siyal[3], Neeta Maheshwary[4], Muhammad Iqbal Asif[5] and Muhammad Athar Khan[6]

[1]Department of Neurology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
[2]Department of Neurology, Bilawal Medical College, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
[3]Department of Neurology, Peoples University of Medical and Health Sciences, Nawabshah, Pakistan
[4]Ziauddin University, Karachi, Pakistan
[5]Department of Medicine, Karachi Medical and Dental College, Karachi, Pakistan
[6]Department of Community Medicine, Liaquat College of Medicine and Dentistry, Karachi, Pakistan

ARTICLE INFO

Keywords:
Adjunctive Brivaracetam, Epilepsy, Seizures, Anticonvulsants

How to Cite:
Bughio, A. H., Lakhiar, M. A., Hussain Seelro, S., Nabi Siyal, N., Maheshwary, N., Iqbal Asif, M., & Athar, M. (2025). Adjunctive Brivaracetam Therapy in Epilepsy: A Prospective Clinical Study: Adjunctive Brivaracetam Therapy in Epilepsy. Pakistan Journal of Health Sciences, 6(7), 126-131. https://doi.org/10.54393/pjhs.v6i7.2771

Corresponding Author:
Abdul Hafeez Bughio
Department of Neurology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
dyhafeez80@hotmail.com

Received Date: 14th January, 2025
Revision Date: 13th July, 2025
Acceptance Date: 18th July, 2025
Published Date: 31st July. 2025

ABSTRACT

Epilepsy is one of those primary illnesses that affect the brain, and the population is estimated to be around 50 million people. **Objective:** To evaluate the efficacy and safety of adjunctive Brivaracetam therapy in adult patients with epilepsy. **Methods:** This observational, non-interventional, single-center study assessed the use of adjunctive Brivaracetam (BRV) in patients aged ≥16 years over six months (October 2023–March 2024). Eligible participants had stable antiepileptic drug (AED) regimens for at least one month before BRV initiation. Demographic data, seizure type, frequency, and intensity were documented at baseline, 3 months, and 6 months. The primary endpoint was the change in seizure frequency. Secondary outcomes included ≥50% seizure reduction, seizure freedom, and adverse events. Data were analyzed using SPSS version 23.0. **Results:** A total of 168 patients (mean age: 25.1 ± 12.9 years) received adjunctive BRV therapy. Partial seizures and comorbid depression were the most common indications for BRV use. Mean seizure frequency decreased from 5.26 ± 0.29 at baseline to 2.41 ± 0.24 at 3 months. All patients achieved seizure freedom by 6 months. Reported adverse effects were generally mild: somnolence 12 (7%), headache 10 (6%), and dizziness 9 (5%). **Conclusions:** Adjunctive BRV therapy demonstrated significant efficacy in reducing seizure frequency and achieving seizure freedom, with a favourable safety profile. These findings support BRV as a promising treatment option for patients with epilepsy unresponsive to conventional AEDs.

INTRODUCTION

Epilepsy is one of those primary illnesses that affect the brain, and the population is estimated to be around 50 million people. Epilepsy is a neurological disorder that is marked by recurrent seizures, which in many ways affect the subject's quality of life, social standing, cognitive abilities, as well as physical wellbeing due to the possibility of the subject experiencing a fit at any given time [1]. It is important to state that the epilepsy disease burden is not evenly spread across the world; however, LMICs seem to be further burdened with this disease by factors such as limited health care access, high perinatal brain damage incidence, and neuro-infection [2]. In Pakistan, the treatment deficit for epilepsy has been reported to be over 70%, which is due to social factors, inadequate knowledge about epilepsy, and the availability of neurological services [3]. Despite the use of first-line Anti-epileptic drugs (AEDs)-carbamazepine, sodium valproate and lamotrigine, many patients are still poorly controlled or experience side effects that are not tolerable, warranting the introduction of Brivaracetam as an added third-generation AED [4].

Copyright © 2025. PJHS, Published by Crosslinks International Publishers LLC, USA
This work is licensed under a Creative Commons Attribution 4.0 International License.

DOI: https://doi.org/10.54393/pjhs.v6i7.2771

Anti-epileptic treatment is most commonly a lifelong process that involves administering AEDs to prevent seizures while limiting side effects in patients with epilepsy [5]. New AEDs have increased the availability of drugs for the treatment of epilepsy, and the situation when patients cannot tolerate conventional treatment or suffer from its side effects. Out of these, Brivaracetam, a drug that binds to the SV2A protein, has been found useful in treating focal seizures as an adjunct therapy to primary treatment in adults with epilepsy [6, 7]. Brivaracetam has been described to act through the SV2A protein as its binding partner in the synaptic vesicle and the course of synaptic transmitter release or recycling. This high selectivity of the drug to SV2A, as earlier pointed out, helps explain the drug's anticonvulsant efficacy, particularly in the focal seizures [8, 9]. As for its pharmacokinetics and anti-seizure mechanism, Brivaracetam has been discovered to be useful in patients with refractory focal seizures that are not effectively controlled with first-line AEDs [10]. Several papers and primary source articles were used for the literature review on randomized controlled trials and observational treatments with Brivaracetam (BRV) as an adjunct therapy for focal seizures. In a phase III study by Biton *et al.*, Brivaracetam was proved to be effective in treating patients with refractory focal epilepsy, with seizure frequency reduction rates of 50% of range from 34-38% [11]. In the 2-year, open-label extension study, Klein *et al.*, proved the long-term efficacy and safety with brivaracetam treatment, which includes the AE like dizziness, somnolence, and fatigue [12]. The BRIVAFIRST study is very beneficial in establishing the effectiveness of Brivaracetam (BRV) in actual focal epilepsy circumstances. That is 16.4% of the patients reported having no seizures at all within the 12 months, and 37.2% reported that at least their seizures were reduced by 50% from the baseline. These results provide evidence of BRV's ability to provide substantial seizure control to different patient groups and shed further light on the drug's role as a viable treatment in epilepsy [13]. An additional interventional study is an international, multicenter, non-interventional post-marketing individual patient data meta-analysis by The EXPERIENCE/EPD332 study, entailing epilepsy patients initiating the treatment with brivaracetam (BRV) in Spain, Germany, Australia, United States. This study included various clinical settings and patient categories. It was established that BRV was safe in the general clinical use and proved to be efficient as well [14]. Altogether, there is a growing epilepsy burden in Pakistan, and a large proportion of the population remains untreated; therefore, there is importance in the identification of well-tolerated AEDs for long-term management of epilepsy. However, there is little information on the efficacy and safety of brivaracetam with lamotrigine in the local population.

This study aims to evaluate the efficacy and safety of adjunctive brivaracetam therapy in adult patients with epilepsy.

METHODS

An observational study was conducted in a real-world clinical setting from October 2023 to March 2024. The study did not involve any experimental or investigational use of Brivaracetam (Brivera; Helix Pharma Pvt Ltd, Sindh, Pakistan). The study was conducted by the principles of the Declaration of Helsinki and received ethical approval from the research ethics committee, Liaquat University of Medical and Health Sciences (LUMHS/REC/168). Informed consent was obtained from the patients, and patients' confidentiality was strictly maintained. All patients received Brivaracetam solely as part of their routine medical care, with treatment decisions made independently by their respective physicians, without any influence from the study investigators. A total of 168 patients were included, based on consecutive patient availability during the study period. In line with real-world evidence methodologies, no formal sample size calculation was performed, as the study design did not involve randomization, controlled interventions, or experimental protocols. The objective was to document treatment patterns and clinical outcomes as they occurred naturally in practice. Patients aged 16 years or older with a confirmed diagnosis of epilepsy were included if they had been on a stable dose of other antiepileptic drugs (AEDs) for at least one month before initiating adjunctive Brivaracetam (BRV) and had completed at least one follow-up after BRV titration. Patients were excluded if they had incomplete medical records, discontinued BRV before the first follow-up, had a known allergy to BRV, or had severe comorbidities that could interfere with follow-up visits. Patient characteristics, including age, sex, epilepsy type and origin, baseline seizure frequency, comorbidities, and prior antiepileptic drug (AED) use, such as the number, type, and duration of AEDs, were obtained from clinical records. Information gathered at 3 and 6 months after the beginning of BRV comprised information on the frequency of seizures and any associated adverse consequences. Seizure reduction was defined as at least a 50% reduction of seizures from the baseline [15]. Seizure frequency was assessed based on clinical follow-up evaluations and patient-maintained seizure diaries, reviewed at each scheduled visit (baseline, 3 months, and 6 months). Seizure freedom was defined as the complete absence of seizures during the entire 6-month treatment period, as confirmed by patient/caregiver reports and medical record documentation [15]. Safety was supported by the low incidence of mild adverse events and the absence of

Copyright © 2025. PJHS, Published by Crosslinks International Publishers LLC, USA
This work is licensed under a Creative Commons Attribution 4.0 International License.

DOI: https://doi.org/10.54393/pjhs.v6i7.2771

serious drug-related complications. Brivaracetam (50–200 mg/day) was prescribed as adjunctive therapy, with dose adjustments based on clinical response and tolerability. It was administered alongside other antiepileptic drugs (AEDs), including lamotrigine, sodium valproate, carbamazepine, oxcarbazepine, phenobarbitone, and topiramate. Data were collected using a structured clinical assessment form adapted from a previously published phase III clinical trial on adjunctive brivaracetam therapy in adult Asian patients with focal-onset seizures [16]. Data were anonymized and stored securely, with access limited to authorized personnel only. Adverse drug reactions (ADRs) were monitored throughout the study. All reported adverse events were assessed for causality using the WHO-UMC causality assessment system [17]. Descriptive statistics were used to summarize the study variables. Categorical variables, such as gender, education level, seizure type, EEG findings, neuroimaging results, and antiepileptic drug combinations, were presented as frequencies and percentages. Continuous variables, including age, frequency of seizure and duration of epilepsy, were expressed as mean ± standard deviation (SD). Seizure frequency, measured at baseline, 3 months, and 6 months, was analyzed using non-parametric methods due to non-normal data distribution and lack of variance at the final time point. For repeated measurements of seizure frequency over time (Baseline, 3 Months, and 6 Months), the Friedman test was applied, as it is the non-parametric equivalent of repeated measures ANOVA. Pairwise comparisons between time points (Baseline vs. 3 Months, Baseline vs. 6 Months, 3 Months vs. 6 Months) were conducted using the Wilcoxon signed-rank test. A p-value<0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The study included 168 participants with a mean age of 25.1 ± 6.9 years (19- 65 years). Among the participants, 79 (47%) were male, and 89 (53%) were female. Education levels showed notable variation among the 95 participants who provided their educational background, with 15 (8.9%) being graduates, 22 (13.1%) having completed intermediate education, 36 (21.4%) completing matriculation, 48 (28.6%) with primary education, and 47 (28%) being uneducated. In terms of seizure types, 76 (45.2%) participants had focal onset seizures, 57 (33.9%) had focal onset with secondary generalization, 27 (16.1%) had generalized onset seizures, and 8 (4.8%) had unknown onset seizures. Brain imaging results were normal in 113 (67.3%) participants, while 12 (6.9%) had right MCA infarcts, 7 (4.2%) had mesial temporal sclerosis, 7 (4.2%) had CVST, 5 (2.9%) had encephalomalacia, and 24 (14.5%) had other abnormalities. EEG results showed normal findings in 115 (68.5%) participants and abnormal findings in 53 (31.5%). Sodium valproate was the most commonly used monotherapy, prescribed to 39 (23.2%)patients, followed by carbamazepine in 35 (20.8%) patients, oxcarbazepine in 29 (17.3%)patients, lamotrigine in 27 (16.1%) patients, phenobarbitone in 24 (14.3%) patients, and topiramate in 14 (8.3%)patients.

Table 1: Demographic Characteristics of Participants (n=106)

Demographics Variables	n (%)
Age (Years)	
Mean ± SD	25.1 ± 6.9
Min, Max	19, 65
Gender	
Male	79 (47%)
Female	89 (53%)
Education (n=95)	
Graduate	15 (8.9%)
Intermediate	22 (13.1%)
Matric	36 (21.4%)
Primary	48 (28.6%)
Uneducated	47 (28%)
Duration of Epilepsy	
Mean ± SD	7.57 + 6.4
Min, Max	2 Months, 35 Years
Type of Seizures	
Focal Onset	76 (45.2%)
Focal Onset with Secondary Generalization	57 (33.9%)
Generalized Onset	27 (16.1%)
Unknown Onset	8 (4.8%)
Findings on Brain Imaging	
Normal	113 (67.3%)
Right MCA Infarct	12 (6.9%)
Mesial Temporal Sclerosis	7 (4.2%)
CVST	7 (4.2%)
Encephalomalacia	5 (2.9%)
Others (Encephalitis, Fungal Mass, Left MCA Infarct, Left Temporal Contusion, Leukoencephalopathy, Trauma)	24 (14.5%)
EEG Findings	
Normal	115 (68.5%)
Abnormal	53 (31.5%)

The most common reason for initiating adjunctive brivaracetam therapy was inadequate seizure control, reported in 75 (44.6%) of patients. Other prominent reasons included depression associated with prior antiepileptic drugs (AEDs) in 43 (25.6%) of cases and adverse drug reactions to previously administered AEDs in 42 (25.0%). A smaller proportion of patients 8 (4.8%), were switched to brivaracetam due to the use of an inappropriate drug as monotherapy (Figure 1).

Copyright © 2025. PJHS, Published by Crosslinks International Publishers LLC, USA
This work is licensed under a Creative Commons Attribution 4.0 International License.

DOI: https://doi.org/10.54393/pjhs.v6i7.2771

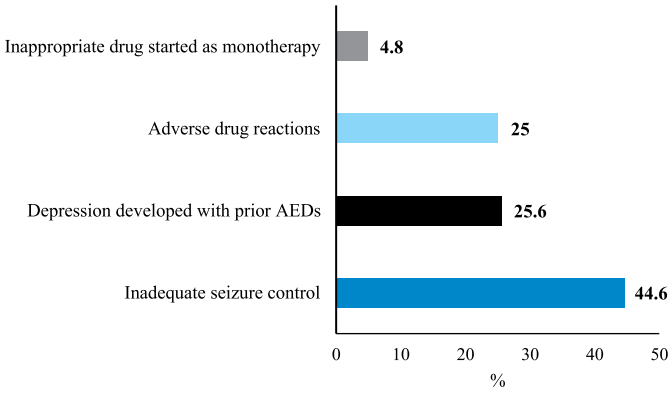

Figure 1: Reason to Start Adjunctive Brivaracetam (n=168)

Seizure frequency showed a significant reduction over time during adjunctive Brivaracetam therapy. The mean seizure frequency at baseline was 5.26 ± 0.29, which decreased to 2.41 ± 0.24 at 3 months and reached 0.00 at 6 months. At the 6-month mark, all participants were seizure-free, resulting in a seizure frequency of 0.00 with no variability (SEM=0). The overall comparison using the Friedman test indicated a statistically significant difference across the three time points ($p<0.001$). Post hoc pairwise comparisons using the Wilcoxon signed-rank test revealed that seizure frequency significantly decreased from baseline to 3 months ($p<0.001$), from baseline to 6 months ($p<0.001$), and from 3 months to 6 months ($p<0.001$), confirming a consistent and progressive reduction in seizure burden throughout the follow-up period (Table 2).

Table 2: Comparisons of Seizure Frequency over Time and Across Time Points (Baseline, 3 Months, and 6 Months)

Time Point	Mean Seizures (Mean ± SEM)	p-Value**	Comparison	p-Value***
Baseline	5.26 ± 0.29	<0.001	Baseline vs. 3 Months	<0.001
3 Months	2.41 ± 0.24		Baseline vs. 6 Months	<0.001
6 Months	0*		3 Months vs. 6 Months	<0.001

*At 6 months, all participants were seizure-free. Seizure frequency was recorded as 0.00 with no variability (SEM=0); **Friedman Test; ***Wilcoxon signed-rank test

A progressive and clinically meaningful reduction in seizure frequency was observed over the 6 months of adjunctive Brivaracetam therapy. Compared to baseline, seizure frequency decreased by 54% at 3 months, indicating a substantial early treatment response. By 6 months, all participants were seizure-free, reflecting a complete 100% reduction in seizure frequency from baseline. This consistent downward trend underscores the effectiveness of Brivaracetam in sustained seizure control. The magnitude of reduction depicts the percentage change over time. The highest 50% responder rate defined as a ≥50% reduction in seizure frequency was observed with BRV combined with sodium valproate, significantly outperforming combinations with oxcarbazepine (15.1%), carbamazepine (14.6%), and lamotrigine (12%). However, the 100% responder rate (complete seizure freedom) was comparable across all combinations, suggesting that while initial response rates varied by adjunctive therapy, BRV was broadly effective in achieving seizure freedom irrespective of the background AED regimen (Figure 2).

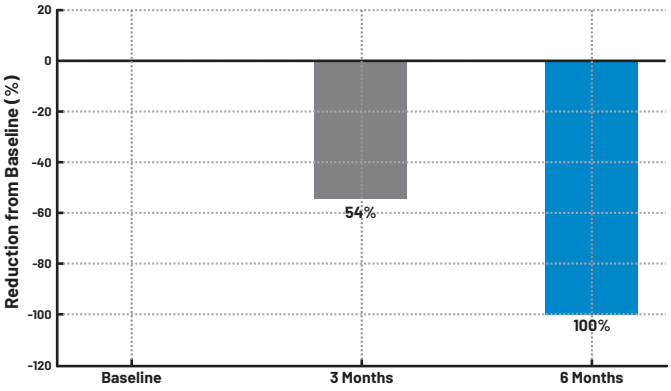

Figure 2: Percentage Reduction in Seizure Frequency at 3 and 6 Months Compared to Baseline during Adjunctive Brivaracetam Therapy

The most common treatment-emergent adverse events (TEAEs) observed in our study were somnolence 12 (7.1%), headache 10 (6.0%), 8 (4.8%), fatigue 5 (3.0%), and irritability 5 (3.0%). Less frequently reported TEAEs included insomnia and anxiety 3 (1.8%), and depression 2 (1.2%).

DISCUSSION

Brivaracetam (BRV) is approved in over 50 countries for treating focal-onset (also known as partial-onset) seizures, whether or not they evolve into secondary generalized seizures [14]. In our study Sodium valproate emerged as the most frequently prescribed monotherapy among patients, with carbamazepine following closely. Oxcarbazepine and lamotrigine were also common choices, while phenobarbitone and topiramate were prescribed less frequently. In a study conducted by Siddiqui *et al.*, in Pakistan, the greatest reductions in seizures were observed when BRV was combined with sodium valproate, followed closely by its combination with carbamazepine. BRV paired with oxcarbazepine and lamotrigine also led to notable reductions in seizures, while combinations with phenobarbitone and topiramate resulted in smaller reductions [18]. Current study demonstrated a marked improvement in seizure control over the 6-month treatment period. Initially, patients exhibited frequent seizures, which substantially decreased within the first 3 months of treatment, indicating a positive early response. By the end of the 6 months, all patients achieved seizure freedom, illustrating the sustained efficacy of the treatment in preventing seizures over time. This significant reduction suggests that the therapy not only addresses immediate seizure frequency but also supports long-term control, which is essential for improving patients' quality of life and stability. Previous analyses have demonstrated that

Copyright © 2025. PJHS, Published by Crosslinks International Publishers LLC, USA
This work is licensed under a Creative Commons Attribution 4.0 International License.

DOI: https://doi.org/10.54393/pjhs.v6i7.2771

brivaracetam (BRV), administered at doses of 50–200 mg per day, is effective in patients concurrently taking carbamazepine, lamotrigine, or topiramate [19, 20]. Inoue *et al.* found that adjunctive BRV was effective in patients taking concurrent valproate (VPA), carbamazepine (CBZ), or lamotrigine (LTG), the most commonly prescribed antiepileptic drugs (ASMs) in their study, aligning with standard clinical practice [16]. These findings are in line with the Ryvlin study, which also demonstrated BRV's efficacy and tolerability across different types and numbers of concomitant ASMs [21]. Adverse events (AEs) are a significant contributor to treatment failure with antiepileptic drugs (ASMs), often leading to early discontinuation, poor adherence, and preventing patients from reaching optimal therapeutic doses [22]. The most common treatment-emergent adverse events (TEAEs) observed in our study were somnolence 12 (7.1%), headache 10 (6.0%), dizziness 8 (4.8%), fatigue 5 (3.0%), and irritability 5 (3.0%). Less frequently reported TEAEs included insomnia and anxiety 3 (1.8%), and depression 2 (1.2%). Current findings align with several pivotal studies that have established the safety and tolerability of adjunctive brivaracetam therapy. Biton *et al.*, and Ryvlin *et al.*, reported low rates of adverse drug reactions (ADRs), with somnolence, headache, and dizziness being the most common, which is consistent with our findings, reinforcing its suitability for sustained use in epilepsy management due to generally well-tolerated side effects, as also noted in larger meta-analyses on BRV's tolerability [11, 21]. A systematic review and network meta-analysis on short-term tolerability found that brivaracetam (BRV) is associated with a lower risk of intolerable AEs and has a low rate of treatment withdrawal due to AEs [23]. Additional reviews indicate that BRV may be one of the most well-tolerated third-generation ASMs for focal seizures in adults [24, 25]. Despite the strengths of our methodology and findings, several limitations must be acknowledged. First, its single-center, observational design without a control group limits the ability to establish causal relationships and generalize findings to broader populations. Second, the relatively small sample size and short follow-up duration (6 months) may not fully capture long-term efficacy and safety outcomes. Third, reliance on patient-reported seizure diaries may introduce recall bias [26, 27].

CONCLUSIONS

It was concluded that this study adds to the evidence supporting adjunctive BRV therapy's efficacy and safety for epilepsy management, underscoring its potential as an alternative for patients with inadequate response to other AEDs.

Authors Contribution

Conceptualization: AHB
Methodology: AHB, MAL, SHS, NNS, NM, MIS, MAK
Formal analysis: ANB, MIA, MAK
Writing review and editing: ANB, SHS, NNS, NM, MIS, MAK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] World Health Organization. Epilepsy [Internet]. 2024 Feb.
[2] Bankole ND, Dokponou YC, De Koning R, Dalle DU, Kesici Ö, Egu C *et al.* Epilepsy Care and Outcome in Low-and Middle-Income Countries: A Scoping Review. Journal of Neurosciences in Rural Practice. 2024 Feb; 15(1): 8. doi: 10.25259/JNRP_527_2023.
[3] International League Against Epilepsy. Conquering the Treatment Gap: Pakistan Starts Small, Stays Flexible, and Never Gives Up. Epigraph [Internet]. 2020 Winter; 22(1).
[4] Matias MR. Development of New Antiepileptic Drug Candidates: A Set of Lamotrigine-Related Compounds (Doctoral Dissertation, Universidade da Beira Interior (Portugal)). 2018.
[5] Epilepsy Society. Anti-seizure medication (ASM) [Internet]. 2020 Feb.
[6] Khilari M, Nair PP, Jha BK. Brivaracetam: How Well Does It Fare as an Anti-Epileptic? A Review. Neurology India. 2021 Mar; 69(2): 284-93. doi: 10.4103/0028-3886.314584.
[7] Chen Y, Li W, Lu C, Gao X, Song H, Zhang Y *et al.* Efficacy, Tolerability and Safety of Add-on Third-Generation Antiseizure Medications in Treating Focal Seizures Worldwide: A Network Meta-Analysis of Randomised, Placebo-Controlled Trials. E-Clinical Medicine. 2024 Apr; 70. doi: 10.1016/j.eclinm.2024.102513.
[8] Feyissa AM. Brivaracetam in the Treatment of Epilepsy: A Review of Clinical Trial Data. Neuropsychiatric Disease and Treatment. 2019 Sep: 2587-600. doi: 10.2147/NDT.S143548.
[9] Okada M, Fukuyama K, Shiroyama T, Ueda Y. Brivaracetam Prevents Astroglial L-Glutamate Release Associated with Hemichannel Through Modulation of Synaptic Vesicle Protein. Biomedicine and Pharmacotherapy. 2021 Jun; 138: 111462. doi: 10.1016/j.biopha.2021.111462.

Copyright © 2025. PJHS, Published by Crosslinks International Publishers LLC, USA
This work is licensed under a Creative Commons Attribution 4.0 International License.

DOI: https://doi.org/10.54393/pjhs.v6i7.2771

[10] Nicolas JM, Hannestad J, Holden D, Kervyn S, Nabulsi N, Tytgat D *et al.* Brivaracetam, A Selective High-Affinity Synaptic Vesicle Protein 2A (SV 2A) Ligand with Preclinical Evidence of High Brain Permeability and Fast Onset of Action. Epilepsia. 2016 Feb; 57(2): 201-9. doi: 10.1111/epi.13267.

[11] Biton V, Berkovic SF, Abou-Khalil B, Sperling MR, Johnson ME, Lu S. Brivaracetam as Adjunctive Treatment for Uncontrolled Partial Epilepsy in Adults: A Phase III Randomized, Double-Blind, Placebo-Controlled Trial. Epilepsia. 2014 Jan; 55(1): 57-66. doi: 10.1111/epi.12433.

[12] Klein P, Aboumatar S, Brandt C, Dong F, Krauss GL, Mizne S *et al.* Long-Term Efficacy and Safety from an Open-Label Extension of Adjunctive Cenobamate In Patients with Uncontrolled Focal Seizures. Neurology. 2022 Sep; 99(10): e989-98. doi: 10.1212/WNL.0000000000200792.

[13] Lattanzi S, Canafoglia L, Canevini MP, Casciato S, Chiesa V, Dainese F *et al.* Adjunctive Brivaracetam in Focal Epilepsy: Real-World Evidence from the Brivaracetam Add-on First Italian Network Study (BRIVAFIRST). Central Nervous System Drugs. 2021 Dec; 35(12): 1289-301.

[14] Szaflarski JP, Besson H, D'Souza W, Faught E, Klein P, Reuber M *et al.* Effectiveness and Tolerability of Brivaracetam in Patients with Epilepsy Stratified by Comorbidities and Etiology in the Real World: 12-Month Subgroup Data from the International Experience Pooled Analysis. Journal of Neurology. 2024 Jun; 271(6): 3169-85. doi: 10.1007/s00415-024-12253-z.

[15] Lattanzi S, Ascoli M, Canafoglia L, Paola Canevini M, Casciato S, Cerulli Irelli E *et al.* Sustained Seizure Freedom with Adjunctive Brivaracetam in Patients with Focal Onset Seizures. Epilepsia. 2022 May; 63(5): e42-50. doi: 10.1111/epi.17223.

[16] Inoue Y, Tiamkao S, Zhou D, Cabral-Lim L, Lim KS, Lim SH *et al.* Efficacy, Safety, and Tolerability of Adjunctive Brivaracetam in Adult Asian Patients with Uncontrolled Focal-Onset Seizures: A Phase III Randomized, Double-Blind, Placebo-Controlled Trial. Epilepsia Open. 2024 Jun; 9(3): 1007-20. doi: 10.1002/epi4.12929.

[17] World Health Organization. The use of the WHO-UMC System for Standardised Case Causality Assessment. Uppsala: The Uppsala Monitoring Centre. 2005 Jul; 1.

[18] Siddiqui F, Soomro BA, Rehman EU, Numan A, Bano S, Salam JU *et al.* A Prospective, Observational, Multicentre Study to Evaluate the Efficacy of Brivaracetam as Adjuvant Therapy for Epilepsy: The Bravo Study. Drugs in Context. 2024 Jul; 13. doi: 10.7573/dic.2024-3-2.

[19] Benbadis S, Klein P, Schiemann J, Diaz A, Elmoufti S, Whitesides J. Efficacy, Safety, and Tolerability of Brivaracetam with Concomitant Lamotrigine or Concomitant Topiramate in Pooled Phase III Randomized, Double-Blind Trials: A Post-Hoc Analysis. Epilepsy and Behavior. 2018 Mar; 80: 129-34. doi: 10.1016/j.yebeh.2017.12.024.

[20] Brodie MJ, Fakhoury T, McDonough B, Colson AO, Stockis A, Elmoufti S *et al.* Brivaracetam-Induced Elevation of Carbamazepine Epoxide Levels: A Post-Hoc Analysis from the Clinical Development Program. Epilepsy Research. 2018 Sep; 145: 55-62. doi: 10.1016/j.eplepsyres.2018.06.002.

[21] Ryvlin P, Dimova S, Elmoufti S, Floricel F, Laloyaux C, Nondonfaz X *et al.* Tolerability and Efficacy of Adjunctive Brivaracetam in Adults with Focal Seizures by Concomitant Antiseizure Medication Use: Pooled Results from Three Phase 3 Trials. Epilepsia. 2022 Aug; 63(8): 2024-36. doi: 10.1111/epi.17304.

[22] Perucca E and Meador KJ. Adverse Effects of Antiepileptic Drugs. Acta Neurologica Scandinavica. 2005 Dec; 112: 30-5. doi: 10.1111/j.1600-0404.2005.00506.x.

[23] Zaccara G, Giovannelli F, Giorgi FS, Franco V, Gasparini S, Benedetto U. Tolerability of New Antiepileptic Drugs: A Network Meta-Analysis. European Journal of Clinical Pharmacology. 2017 Jul; 73(7): 811-7. doi: 10.1007/s00228-017-2245-z.

[24] Trinka E, Tsong W, Toupin S, Patten A, Wilson K, Isojarvi J *et al.* A Systematic Review and Indirect Treatment Comparison of Perampanel Versus Brivaracetam as Adjunctive Therapy in Patients with Focal-Onset Seizures with or Without Secondary Generalization. Epilepsy Research. 2020 Oct; 166: 106403. doi: 10.1016/j.eplepsyres.2020.106403.

[25] Lattanzi S, Trinka E, Zaccara G, Striano P, Russo E, Del Giovane C *et al.* Third-Generation Antiseizure Medications for Adjunctive Treatment of Focal-Onset Seizures in Adults: A Systematic Review and Network Meta-Analysis. Drugs. 2022 Feb; 82(2): 199-218. doi: 10.1007/s40265-021-01661-4.

[26] Yanes R, Briard JN, Nguyen TD, Sultanem M, Nguyen DK, Gibbs S *et al.* Prospective Post-Marketing Observational Study of Brivaracetam in People with Focal Epilepsy. Canadian Journal of Neurological Sciences. 2023 Dec:1-5. doi: 10.1017/cjn.2023.328.

[27] Fisher RS, Blum DE, DiVentura B, Vannest J, Hixson JD, Moss R *et al.* Seizure Diaries for Clinical Research and Practice: Limitations and Future Prospects. Epilepsy and Behavior. 2012 Jul; 24(3): 304-10. doi: 10.1016/j.yebeh.2012.04.128.

Copyright © 2025. PJHS, Published by Crosslinks International Publishers LLC, USA
This work is licensed under a Creative Commons Attribution 4.0 International License.