Effectiveness and Tolerability of Adjunctive Brivaracetam in Adults With Focal-Onset Seizures on One Specific Antiseizure Medication: Post Hoc Analysis of Interim Real-World Data From BRITOBA

Edouard Hirsch[1]
Adrien Didelot[2]
Dimitrios Bourikas[3]
Sami Elmoufti[4]
Iryna Leunikava[5]
Bonita Réhel[6]

1. University Hospital of Strasbourg, Strasbourg, France
2. Hôpital Saint Joseph-Saint Luc, Lyon, France
3. UCB Pharma, Alimos, Greece
4. UCB Pharma, Morrisville, NC, USA
5. UCB Pharma, Monheim am Rhein, Germany
6. UCB Pharma, Oakville, ON, Canada

Background

- Brivaracetam (BRV) is indicated for the treatment of focal-onset seizures (FOS; partial-onset seizures) in patients ≥1 month of age in the United States,[1] adjunctive therapy of FOS in patients ≥2 years of age in the European Union,[2] adjunctive therapy of FOS in patients ≥4 years of age (oral administration) and adult patients (oral and intravenous administration) in Canada,[3] and the treatment of FOS in patients ≥15 years of age in Japan.[4,5] BRV is also approved in other countries.
- More than 50% of patients with epilepsy will require a change to their initial antiseizure medication (ASM) monotherapy, either substitution with an alternative monotherapy or addition of ASM(s), to further reduce seizure frequency or eliminate intolerable adverse events.[6]
- The overall objective of BRITOBA (Brivaracetam Adjunctive Therapy in Early Treatment Line Combinations; EP0103) is to evaluate effectiveness, tolerability, and quality of life under adjunctive BRV in earlier treatment lines in adults with FOS in an observational setting.

Objective

- The current analysis explored the effectiveness and tolerability of BRV in combination with 1 specific ASM in daily clinical practice.

Methods

STUDY DESIGN

- Post hoc analysis of the second interim data snapshot from BRITOBA (EP0103), a prospective, post-marketing, non-interventional study of adjunctive BRV at 62 clinical/office-based sites in Europe (France, Germany, Italy, and Spain) and Canada.
- BRV was prescribed according to standard clinical practice. Patients were observed for up to approximately 12 months.
- Eligible patients were ≥18 years of age, with a history of FOS (with/without focal to bilateral tonic-clonic seizures), no BRV treatment before study entry, ≥1 ASM at BRV initiation, and failure of ≤3 lifetime ASMs (prior and concomitant at BRV initiation).
- Patients had the option of completing questionnaires using the mobile application Helpilepsy™ instead of conventional paper collection.
- Safety Set (SS): all patients included in the study with valid data consent and at least visit 1 (baseline) documented who took ≥1 dose of BRV.

PATIENTS INCLUDED IN THE ANALYSIS

- Patients in the SS who were on a single specific ASM at BRV initiation (baseline) and who had the opportunity to complete ≥9 months of BRV at the time of this interim analysis.

SUBGROUPS

- All patients on 1 concomitant ASM at BRV initiation.
- Patients on the most common specific concomitant ASMs at BRV initiation (n≥25).

OUTCOMES AND MEASUREMENTS

- Outcomes included BRV retention, ≥50% response in FOS (≥50% reduction in all types of FOS from baseline), treatment-emergent adverse events (TEAEs), Clinical Global Impression of Change (CGIC), and Patient's Global Impression of Change (PGIC).

Results

PATIENT DISPOSITION AND DEMOGRAPHICS

- At data cutoff of the second interim analysis (May 16, 2023), 208 patients in the SS reported taking 1 concomitant ASM (any) at BRV initiation and had the opportunity to complete ≥9 months on BRV therapy ('total population').
  - 50 patients were on concomitant lacosamide (LCM), 50 on lamotrigine (LTG), 29 on carbamazepine (CBZ), and 28 on levetiracetam (LEV).
  - Because the total population is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months on BRV therapy, it is not the sum of the 4 concomitant ASM subgroups.

Baseline patient characteristics

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy

CONCOMITANT ASM	LCM (n=50)	LTG (n=50)	CBZ (n=29)	LEV (n=28)	TOTAL[a] (N=208)
Age, years					
Mean (SD)	50.1 (15.99)	43.3 (17.10)	45.0 (16.95)	51.6 (17.47)	46.1 (17.30)
≥65, n (%)	10 (20.0)	7 (14.0)	3 (10.3)	7 (25.0)	33 (15.9)
Male, n (%)	24 (48.0)	26 (52.0)	20 (69.0)	17 (60.7)	118 (56.7)
Time since epilepsy diagnosis, mean (SD), years	9.65 (13.21)	11.45 (12.22)	20.19 (13.92)[b]	6.39 (7.86)	11.46 (12.50)[c]
Age at first diagnosis, mean (SD), years	40.49 (19.88)	31.85 (19.08)	24.34 (15.62)[b]	45.19 (21.74)	34.53 (20.10)[c]

[a]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups; [b]n=28; [c]n=206. ASM, antiseizure medication.

- Forty out of 50 (80.0%) patients on concomitant LCM, 33/50 (66.0%) on concomitant LTG, 20/29 (69.0%) on concomitant CBZ, 23/28 (82.1%) on concomitant LEV, and 155/208 (74.5%) in the total population completed ≥9 months at the time of the analysis (this means the patient did not discontinue before 9 months, defined as the patient's BRV start date + 9 months + 45-day window or 315 days).

Overview

QUESTION

What are the effectiveness and tolerability of brivaracetam (BRV) in combination with 1 specific antiseizure medication (ASM), in adults with focal-onset seizures?

INVESTIGATION

Post hoc analysis of the second interim data snapshot from BRITOBA (EP0103), a prospective, post-marketing, non-interventional study in Europe (France, Germany, Italy, and Spain) and Canada. Patients in the Safety Set who reported taking 1 concomitant ASM at BRV initiation and had the opportunity to complete ≥9 months on BRV therapy ('total population') at the time of the data snapshot: N=208.

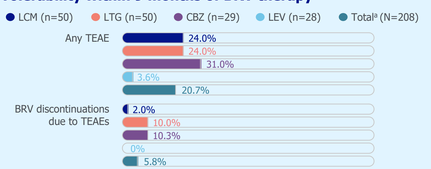
RESULTS

Effectiveness

BRV retention at 9 months

Percentage of patients with ≥50% reduction in FOS at 9 months

Tolerability within 9 months of BRV therapy



[a]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. ASM, antiseizure medication; BRV, brivaracetam; CBZ, carbamazepine; FOS, focal-onset seizure; LCM, lacosamide; LEV, levetiracetam; LTG, lamotrigine; TEAE, treatment-emergent adverse event.

CONCLUSIONS

BRV was effective and well tolerated in patients on 1 concomitant ASM, regardless of the ASM it was added to (carbamazepine [CBZ], lacosamide [LCM], levetiracetam [LEV], or lamotrigine [LTG]). After ≥9 months, BRV added to LCM or LEV offered numerically higher retention and fewer treatment-emergent adverse event–related discontinuations, and the percentage of patients achieving a ≥50% response was numerically higher in patients on concomitant CBZ or LEV.

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Presence and frequency of baseline FOS

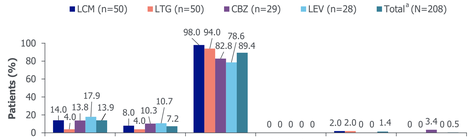
Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy

CONCOMITANT ASM	LCM (n=50)	LTG (n=50)	CBZ (n=29)	LEV (n=28)	TOTAL[a] (N=208)
Patients with FOS type at baseline[b,c], n (%)					
Any FOS	47 (94.0)	50 (100)	27 (93.1)	28 (100)	202 (97.1)
Any FBTCS	22 (44.0)	20 (40.0)	8 (27.6)	13 (46.4)	81 (38.9)
28-day baseline FOS frequency, median (Q1, Q3)					
FOS	2.33 (0.67, 4.00)[d]	1.33 (0.67, 3.33)	2.00 (1.00, 4.00)[e]	1.67 (0.33, 3.83)	1.50 (0.67, 3.33)[f]
FBTCS	0.33 (0.33, 0.67)[g]	0.50 (0.33, 0.67)[h]	0.33 (0.33, 1.50)[i]	0.67 (0.33, 0.67)[j]	0.33 (0.33, 0.67)[k]

[a]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups; [b]Two patients in the concomitant LCM subgroup, 2 patients in the concomitant CBZ subgroup, and 5 patients in the total population had missing information related to seizure type; [c]One patient in the concomitant LCM subgroup and 1 patient in the total population did not report FOS at baseline; [d]n=47; [e]n=27; [f]n=202; [g]n=22; [h]n=20; [i]n=8; [j]n=13; [k]n=81. ASM, antiseizure medication; FBTCS, focal to bilateral tonic-clonic seizure; FOS, focal-onset seizure; Q1, first quartile; Q3, third quartile.

Reason(s) for initiating BRV

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy



A patient may report multiple reasons for initiating BRV. [a]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. ASM, antiseizure medication.

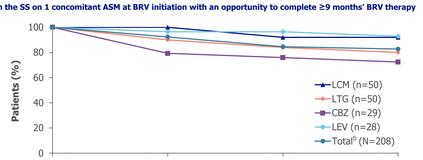
BRV DOSING

- The median BRV modal dose up to approximately month 9 was 100.0 mg/day in all concomitant ASM subgroups and in the total population.

EFFECTIVENESS

BRV retention[a]

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy

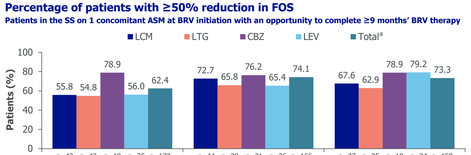


	BRV initiation	3 months	6 months	9 months
LCM, %	100	100	92.0	92.0
LTG, %	100	90.0	84.0	80.0
CBZ, %	100	79.3	75.9	72.4
LEV, %	100	96.4	96.4	92.9
Total[b], %	100	92.3	84.6	82.7

[a]The denominator is the sum of the number of patients who have dropped out before the corresponding visit and the number of patients who did not drop out before the corresponding visit and have stayed in the study for ≥80 days, ≥170 days, and ≥260 days since first BRV administration for the visit at 3, 6, and 9 months, respectively; [b]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. Plotted values are shown below the figure. ASM, antiseizure medication.

Percentage of patients with ≥50% reduction in FOS

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy



Percentages are based on the denominator for the number of patients who completed the respective time point with non-missing data. [a]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. ASM, antiseizure medication; FOS, focal-onset seizure.

TOLERABILITY

TEAE incidence within 9 months of BRV therapy

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy

[a]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. AE, adverse event; ASM, antiseizure medication; TEAE, treatment-emergent adverse event.

QUALITY OF LIFE

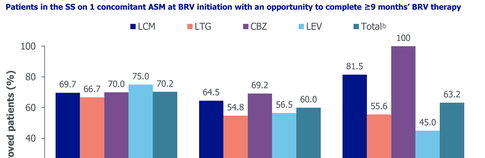
CGIC – improved patients[a]

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy

CGIC describes the clinician's assessment of the patient's condition over the past 4 weeks compared with baseline (as assessed by the treating physician) according to 7 categories (very much improved, much improved, minimally improved, no change, minimally worse, much worse, and very much worse). [a]Includes very much improved, much improved, and minimally improved; [b]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. ASM, antiseizure medication; CGIC, Clinical Global Impression of Change.

PGIC – improved patients[a]

Patients in the SS on 1 concomitant ASM at BRV initiation with an opportunity to complete ≥9 months' BRV therapy



PGIC describes how the patient felt over the past 4 weeks compared with before they entered the study, according to 7 categories (very much improved, much improved, minimally improved, no change, minimally worse, much worse, and very much worse). [a]Includes very much improved, much improved, and minimally improved; [b]The 'total' group is all patients on 1 concomitant ASM (any) at BRV initiation with an opportunity for ≥9 months' BRV therapy and therefore, it is not the sum of the 4 concomitant ASM subgroups. ASM, antiseizure medication; PGIC, Patient's Global Impression of Change.

Limitations

- This was a post hoc analysis of the second interim data snapshot from the non-interventional BRITOBA study. As an unplanned analysis, there is a potential for bias.
- Outcomes in the concomitant ASM subgroups should be interpreted with caution due to small patient numbers and differences in baseline patient characteristics between the subgroups.

Conclusions

- The main reason for BRV initiation (>78%) was lack of efficacy of current treatment, irrespective of which ASM BRV was added to (CBZ, LCM, LEV, or LTG).
- BRV was effective and well tolerated in patients on 1 concomitant ASM regardless of the ASM it was added to, including LEV.
- After ≥9 months,
  - BRV added to LCM or LEV offered numerically higher retention and fewer TEAE-related discontinuations;
  - The percentage of patients achieving a ≥50% response was numerically higher in patients on concomitant CBZ or LEV;
  - BRV added to LCM, LEV, or CBZ offered a numerically greater CGIC improvement, while a numerically greater PGIC improvement was observed in patients on concomitant CBZ or LCM.
- The results presented here are compelling. Future studies and additional data would be beneficial in exploring these conclusions.

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Phone: +1-844-599-CARE (2273)
Email: UCBCares@ucb.com

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