Poster P258

Brivaracetam adjunctive therapy in earlier treatment lines in adults with focal-onset seizures in Europe and Canada: second interim results of 12-month real-world data from BRITOBA

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Overview

QUESTION

What is the effectiveness of adjunctive brivaracetam (BRV) in earlier treatment lines in adults with focal-onset seizures evaluated for up to 12 months?

INVESTIGATION

Planned second interim analysis of BRITOBA (EP0103), a prospective, non-interventional, post-marketing study in Europe (France, Germany, Italy, and Spain) and Canada. Safety Set (SS): N=392.

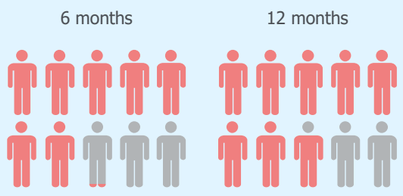
RESULTS (SS)

Effectiveness

Seizure freedom for ≥6 consecutive months[a]

40.9% (110/269)

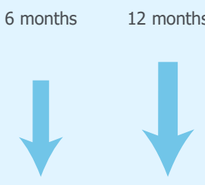
Proportion of patients with ≥50% reduction in focal-onset seizure frequency from baseline[b,c]



70.5% (194/275)

77.9% (152/195)

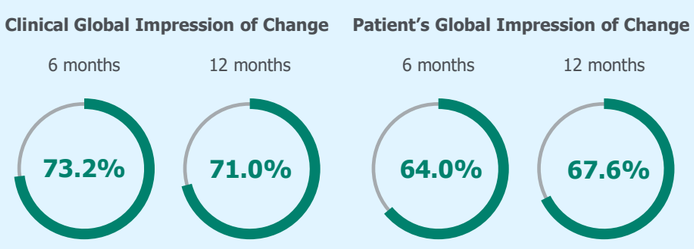
Median percentage reduction in focal-onset seizure frequency from baseline[b]



83.7% (n=275)

100% (n=195)

Patients showing any improvement in their clinical condition (minimally, much, or very much improved)

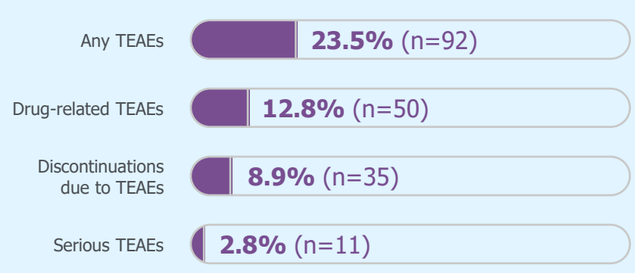


(197/269) (137/193) (137/214) (94/139)

[a]Patients with ≥6 consecutive months of seizure freedom, regardless of study completion; [b]The denominator was the number of patients who completed the respective time point with non-missing data; [c]All types of focal-onset seizures.

Tolerability

Treatment-emergent adverse events (N=392)



TEAE, treatment-emergent adverse event.

CONCLUSIONS

In this second interim analysis of BRITOBA, adjunctive BRV was effective in adults with focal-onset seizures in earlier treatment lines (median of 2 lifetime antiseizure medications, median BRV dose of 50 mg/day at baseline). Adjunctive BRV was well tolerated (12.8% of patients reported drug-related treatment-emergent adverse events [TEAEs] and 8.9% discontinued due to TEAEs) and no new safety signals were observed.

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Background

- Brivaracetam (BRV) is indicated for adjunctive therapy of focal-onset (partial-onset) seizures in patients ≥2 years of age in the European Union,[1] monotherapy and adjunctive therapy of focal-onset seizures in patients ≥1 month of age in the United States,[2] and adjunctive therapy of focal-onset seizures in patients ≥4 years of age (oral administration) and adult patients (oral and intravenous administration) in Canada.[3]
- Post-marketing data confirm BRV to be an effective and well-tolerated therapeutic option in difficult-to-treat populations with drug-resistant epilepsy.[4-7] Therefore, patients on earlier antiseizure medication (ASM) regimens might significantly benefit from combination with BRV.

Objective

- The overall objective of BRITOBA (Brivaracetam Adjunctive Therapy in Early Treatment Line Combinations; EP0103) is to evaluate the effectiveness, tolerability, and quality of life (QoL) of adjunctive BRV in earlier treatment lines in adults with focal-onset seizures in a non-interventional setting.
- The current second interim analysis evaluated effectiveness, tolerability, and QoL for up to approximately 12 months.

Methods

STUDY DESIGN

- Planned second interim analysis of BRITOBA (EP0103), a prospective, non-interventional, post-marketing study of adjunctive BRV at 81 clinical/office-based sites in Europe (France, Germany, Italy, and Spain) and Canada.
- BRV was prescribed per standard practice. Patients were observed for up to approximately 12 months.
- Eligible patients were ≥18 years of age, with a history of focal-onset seizures (with/without focal to bilateral tonic-clonic seizures), no BRV treatment before study entry, ≥1 ASM at BRV initiation, and ≤3 lifetime ASMs (prior and concomitant at BRV initiation).
- Patients had the option of reporting seizure frequency and completing the questionnaires using the mobile application Helpilepsy™ instead of conventional paper collection.

OUTCOMES AND MEASUREMENTS

- Outcomes included seizure freedom for ≥6 consecutive months (primary endpoint), defined as seizure freedom for ≥6 consecutive months over 12 months of observation; ≥50% response in focal-onset seizures (≥50% reduction in all types of focal-onset seizures from baseline); Clinical Global Impression of Change (CGIC) and Patient's Global Impression of Change (PGIC); and treatment-emergent adverse events (TEAEs).
  - Interim QoL outcomes from BRITOBA are presented in poster 517.
- All Patients Documented (APD) Set: all patients included in the study with valid data consent and at least visit 1 (baseline) documented.
- Safety Set (SS): all patients in the APD Set who received ≥1 dose of BRV.
- Per-Protocol Set (PPS): all patients in the SS who were treated according to the approved Summary of Product Characteristics during their observation period, representing on-label use of BRV in Europe and Canada. Patients who violated ≥1 selection criterion were excluded.

Results

PATIENT DISPOSITION AND DEMOGRAPHICS

- At the time of the data snapshot (16 May 2023), 392 patients had received ≥1 dose of BRV (SS), of whom 319 were included in the PPS.
  - In the SS, 169 patients were enrolled in Germany (PPS: 151), 107 in Italy (PPS: 80), 84 in France (PPS: 60), 25 in Spain (PPS: 24), and 7 in Canada (PPS: 4).
- In the SS, 282 (71.9%) patients completed the 6-month visit (PPS: 232 [72.7%]), and 199 (50.8%) patients completed the 12-month/end-of-study visit (PPS: 163 [51.1%]) at the time of this interim analysis.

Demographics and baseline epilepsy characteristics

	SS (N=392)	PPS (N=319)
Patient demographics		
Age, mean (SD), years	44.9 (17.4)	46.0 (17.5)
Male, n (%)	204 (52.0)	171 (53.6)
Epilepsy characteristics		
Time since epilepsy diagnosis, mean (SD), years	13.1 (13.2)[a]	13.4 (13.6)[b]
Age at first diagnosis, mean (SD), years	31.8 (20.1)[a]	32.5 (20.7)[b]
Percentage of life with epilepsy, mean (SD), %	31.5 (28.6)[a]	31.7 (28.8)[b]
Any baseline focal-onset seizures, n (%)	381 (97.2)[c]	311 (97.5)[d]
Any baseline focal to bilateral tonic-clonic seizures, n (%)	143 (36.5)[e]	123 (38.6)[f]
Baseline seizure frequency per 28 days,[g] mean (SD)		
Focal-onset seizures	6.3 (21.7)[h]	6.9 (23.9)[i]
Focal to bilateral tonic-clonic seizures	1.3 (2.9)[j]	1.2 (2.6)[k]
Helpilepsy™ user, n (%)	134 (34.2)	96 (30.1)

[a]n=388; [b]n=315; [c]9 (2.3%) patients had missing data; [d]8 (2.5%) patients had missing data; [e]8 (2.0%) patients had missing data; [f]7 (2.2%) patients had missing data; [g]Based on the previous 3 months; [h]n=381; [i]n=311; [j]n=143; [k]n=123.

Lifetime and concomitant ASMs

	SS (N=392)	PPS (N=319)
Number of lifetime ASMs[a]		
Mean (SD)	2.0 (0.9)	1.9 (0.9)
Median (Q1, Q3)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)
Number of concomitant ASMs at BRV initiation[b]		
Mean (SD)	1.5 (0.8)	1.4 (0.6)
Median (Q1, Q3)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)
1, n (%)	239 (61.0)	198 (62.1)
2, n (%)	132 (33.7)	107 (33.5)
≥3, n (%)	21 (5.4)	14 (4.4)
Number of concomitant ASMs[c]		
Mean (SD)	1.5 (0.9)	1.5 (0.7)
Median (Q1, Q3)	1.0 (1.0, 2.0)	1.0 (1.0, 2.0)

[a]Sum of prior ASMs and concomitant ASMs at BRV initiation; if used for the treatment of seizures for ≥7 consecutive days any time before BRV initiation (excluding benzodiazepines or other rescue medications used short term per physician discretion); [b]ASMs ongoing and being taken on the same day as first BRV administration; [c]ASMs taken ≥1 day in common with BRV. ASM, antiseizure medication; Q1, first quartile; Q3, third quartile.

- In patients with 1 concomitant ASM at BRV initiation, the most common concomitant ASMs were lamotrigine (SS: 15.8%; PPS: 15.4%) and lacosamide (SS: 12.8%; PPS: 12.5%).

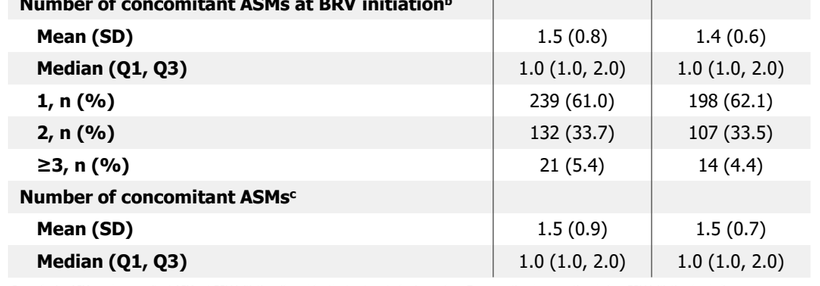
BRV DOSING

BRV exposure and dosing

	SS (N=392)	PPS (N=319)
Duration of BRV exposure, median (range), days	351.0 (1-630)	351.0 (1-630)
BRV daily dose at baseline (visit 1)		
Mean (SD), mg/day	81.8 (49.5)	86.2 (43.1)
Median (range), mg/day	50.0 (20-300)	100.0 (25-200)
BRV daily dose at month 12 (visit 5)	n=195	n=160
Mean (SD), mg/day	124.2 (65.1)	118.8 (46.4)
Median (range), mg/day	100.0 (50-500)	100.0 (50-200)

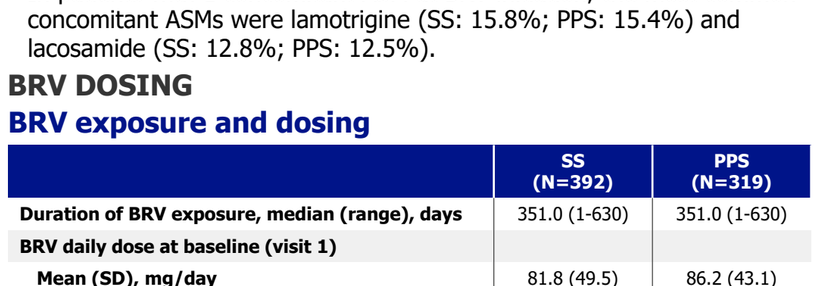
EFFECTIVENESS

≥6-month consecutive seizure freedom during 12 months



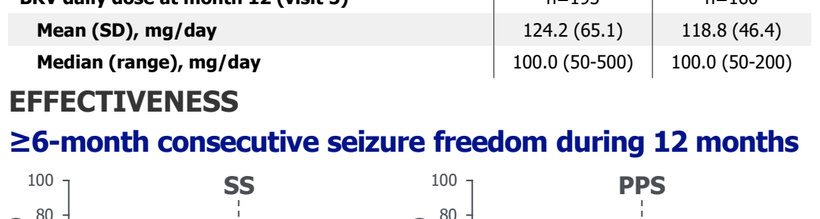
[a]Patients with ≥6 consecutive months of seizure freedom, regardless of study completion; visit dates of the 2 consecutive visits must be ≥6 months (≥180 days) apart; [b]Patients who completed 12 months in the study; the denominator was the number of patients who completed the respective 2 consecutive visits with non-missing data; visit dates of the 2 consecutive visits must be ≥6 months (≥180 days) apart. Any missing seizure counts between visits were not considered as seizure freedom.

≥50% response in focal-onset seizure frequency (all types)



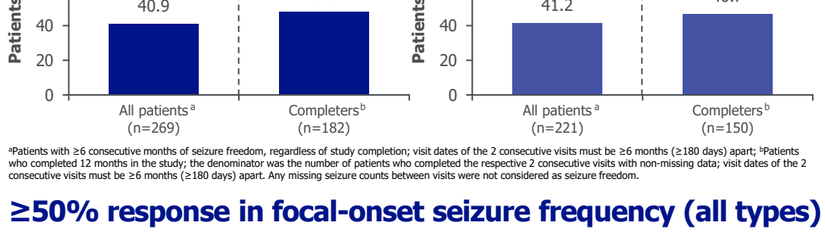
The denominator was the number of patients who completed the respective time point with non-missing data.

Median percentage reduction in focal-onset seizure frequency

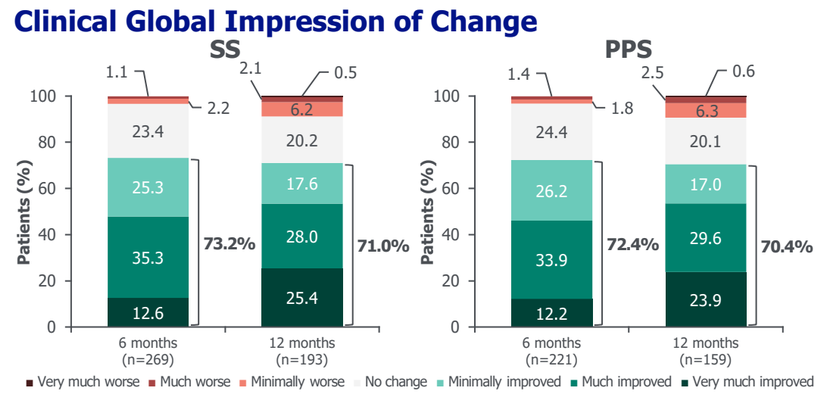


The denominator was the number of patients who completed the respective time point with non-missing data. Numbers in parentheses are: Q1, Q3. Q1, first quartile; Q3, third quartile.

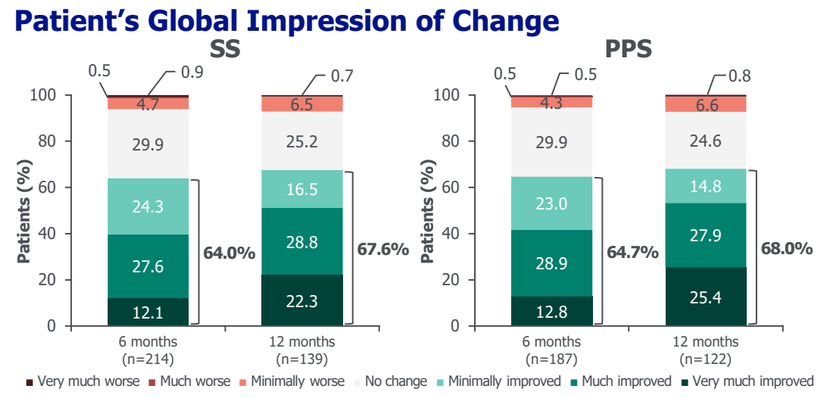
Discontinuation of BRV due to lack of efficacy



Clinical Global Impression of Change

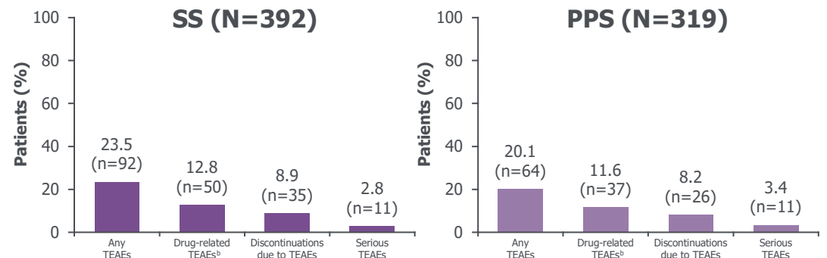


Patient's Global Impression of Change



TOLERABILITY

Incidence of TEAEs[a]



[a]Defined as adverse events occurring on or after the date of first BRV administration up to 4 weeks (28 days) after BRV discontinuation; [b]Patients with a response of 'related' for the question of 'related to study medication' on the adverse events electronic case report form; missing relatedness was excluded. TEAE, treatment-emergent adverse event.

- In the SS, 9 patients (2.3%; PPS: 6 [1.9%]) had drug-related behavioural TEAEs.
- No deaths were reported during the study.

Most common TEAEs[a] and drug-related TEAEs[b]

	SS (N=392)	PPS (N=319)
TEAEs reported by ≥2% of patients, n (%)[c]		
Fatigue	18 (4.6)	9 (2.8)
Anxiety	11 (2.8)	7 (2.2)
Seizure	9 (2.3)	7 (2.2)
Coronavirus infection	8 (2.0)	6 (1.9)
Somnolence	8 (2.0)	4 (1.3)
Drug-related TEAEs[b] reported by ≥2% of patients, n (%)[c]		
Fatigue	12 (3.1)	8 (2.5)

[a]Defined as adverse events occurring on or after the date of first BRV administration up to 4 weeks (28 days) after BRV discontinuation; [b]Patients with a response of 'related' for the question of 'related to study medication' on the adverse events electronic case report form; missing relatedness was excluded; [c]Medical Dictionary for Regulatory Activities Version 18.1 Preferred Term. TEAE, treatment-emergent adverse event.

Limitations

- Second interim analysis of the non-interventional BRITOBA study.
- Caution should be applied when interpreting outcomes.
  - 50.8% of patients in the SS and 51.1% in the PPS completed the 12-month visit at the cut-off date.
  - Due to missing data for some outcomes, the results shown are for observed cases.

Conclusions

- In this second interim analysis of BRITOBA, a 12-month, prospective, non-interventional study in Europe and Canada, adjunctive BRV was effective in adults with focal-onset seizures in earlier treatment lines (median 2 lifetime ASMs, median BRV dose of 50 mg/day at baseline).
- In the SS:
  - 40.9% of patients were seizure-free for ≥6 consecutive months during 12-month observation period.
  - 77.9% of patients were ≥50% responders in focal-onset seizure frequency at 12 months.
  - At 12 months, 67.6% of patients reported improvement of their clinical condition (PGIC) and 71.0% of physicians reported improvement in their patients' clinical condition (CGIC).
- Adjunctive BRV was well tolerated (12.8% of patients experienced drug-related TEAEs as reported by the treating physicians and 8.9% discontinued BRV treatment due to TEAEs; SS), and no new safety signals were observed.

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