Patient-Reported Outcomes in Adults With Focal-Onset Seizures Who Completed 12 Months of Adjunctive Brivaracetam in Earlier Treatment Lines: Post Hoc Analysis of Interim Real-World Data From BRITOBA

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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.
- Patient-reported outcomes (PROs) can be used to measure the impact of a medication on the daily life of patients, including aspects such as disease symptoms, treatment side effects, functional outcomes, and health-related quality of life (HRQoL).[6]
- Few observational, prospective, real-world studies of BRV have reported PROs.[7-9]
- 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 change in clinical condition, HRQoL, seizure severity, depressive symptoms, work productivity and activity impairment, and treatment satisfaction in adults with FOS as reported by patients after 12 months of adjunctive BRV therapy in earlier treatment lines.

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 antiseizure medication (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.

OUTCOMES AND MEASUREMENTS

- 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.
- This analysis included patients in the SS who completed ≥1 PRO assessment both at baseline and at 12 months.
- Outcomes included Patient's Global Impression of Change (PGIC), Patient-Weighted Quality of Life in Epilepsy Inventory-10-P (QOLIE-10-P), Treatment Satisfaction Questionnaire for Medication-9 (TSQM-9), Work Productivity and Activity Impairment Questionnaire: General Health (WPAI:GH), Seizure Severity Questionnaire (SSQ), Neurological Disorders Depression Inventory in Epilepsy (NDDI-E), and treatment-emergent adverse events (TEAEs).

Results

PATIENT DISPOSITION AND DEMOGRAPHICS

- At data cutoff of the second interim analysis (May 16, 2023), 139 of the 392 patients in the SS completed ≥1 PRO assessment at both baseline and 12 months.
- The most common reason for starting BRV was lack of efficacy of the current therapy (131 [94.2%]).

Baseline patient characteristics

Patients in the SS who completed ≥1 PRO assessment at both baseline and 12 months

	ALL PATIENTS (N=139)
Age, mean (SD), years	49.2 (18.54)
Male, n (%)	72 (51.8)
Time since epilepsy diagnosis, mean (SD), years	12.60 (12.83)[a]
Any baseline FOS, n (%)	138 (99.3)
Baseline FOS frequency per 28 days, median (Q1, Q3)[b]	2.00 (1.00, 4.00)[a]
Any baseline FBTCS, n (%)	54 (38.8)
Baseline FBTCS frequency per 28 days, median (Q1, Q3)[b]	0.67 (0.33, 1.00)[c]
Number of lifetime ASMs[d], mean (SD)	2.0 (0.77)
Number of concomitant ASMs at BRV initiation[e], mean (SD)	1.4 (0.53)
Number of concomitant ASMs[f], mean (SD)	1.5 (0.56)
Number of prior ASMs[g], mean (SD)	0.5 (0.65)

[a]n=138; [b]Based on the 3 months before baseline; [c]n=54; [d]Lifetime ASMs are a sum of the prior ASMs and concomitant ASMs at BRV initiation. An ASM is counted as a lifetime ASM if it was used for the treatment of seizures for ≥7 consecutive days (1 week) any time before BRV initiation (excluding benzodiazepines or other rescue medications used short term per physician discretion); [e]Concomitant ASMs at BRV initiation are ASMs ongoing and being taken on the same day as first BRV administration; [f]Concomitant ASMs are ASMs taken ≥1 day in common with BRV; [g]Prior ASMs are ASMs discontinued before the date of first BRV administration. ASM, antiseizure medication; FBTCS, focal to bilateral tonic-clonic seizures; FOS, focal-onset seizure; PRO, patient-reported outcome; Q1, first quartile; Q3, third quartile.

Overview

QUESTION

What effect does 12-month adjunctive brivaracetam (BRV) therapy in earlier treatment lines have on health-related quality of life, work productivity, or other patient-reported outcomes (PROs) 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 completed ≥1 PRO assessment at both baseline and 12 months: N=139.

RESULTS

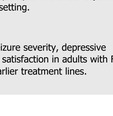
Global Impression of Change and HRQoL

PGIC

Patients reporting any improvement in clinical condition at 12 months

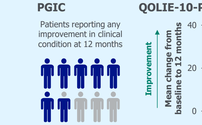
67.6% (94/139)

QOLIE-10-P

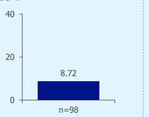


Treatment satisfaction (TSQM-9)

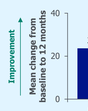
Work productivity and activity impairment (WPAI:GH)



Seizure severity (SSQ)



Neurological Disorders Depression (NDDI-E)



HRQoL, health-related quality of life; NDDI-E, Neurological Disorders Depression Inventory in Epilepsy; PGIC, Patient's Global Impression of Change; QOLIE-10-P, Patient-Weighted Quality of Life in Epilepsy Inventory-10-P; SSQ, Seizure Severity Questionnaire; TSQM-9, Treatment Satisfaction Questionnaire for Medication-9; WPAI:GH, Work Productivity and Activity Impairment Questionnaire: General Health.

CONCLUSIONS

In this post hoc interim analysis, patients who completed 12 months of adjunctive BRV therapy in earlier treatment lines (failure of ≤3 lifetime antiseizure medications) showed improvements in clinical condition, health-related quality of life, treatment satisfaction, perceived cognitive effects after seizures, and depressive symptoms, as assessed by PROs.

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The most commonly reported concomitant and prior ASMs

Patients in the SS who completed ≥1 PRO assessment at both baseline and 12 months

PATIENTS, n (%)	ALL PATIENTS (N=139)
The most common concomitant ASMs[a] (≥20% of patients)	
Lacosamide	44 (31.7)
Levetiracetam	37 (26.6)
Lamotrigine	33 (23.7)
The most common prior ASMs[b] (≥5% of patients)	
Levetiracetam	26 (18.7)
Carbamazepine	10 (7.2)
Valproate[c]	8 (5.8)

[a]Concomitant ASMs are ASMs taken ≥1 day in common with BRV; [b]Prior ASMs are ASMs discontinued before the date of first BRV administration; [c]Valproate includes valproate sodium, valproate semisodium, valproate bismuth, valproate magnesium, valpromide, ergenyl chrono, valproic acid, valproate, and 'valproate sodium; valproic acid'. ASM, antiseizure medication; PRO, patient-reported outcome.

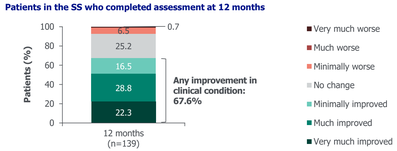
BRV DOSING

- The median BRV total daily dose was 100.0 mg/day at BRV initiation (n=139), 6 months (n=132), 9 months (n=131), and 12 months (n=136).
- The median BRV modal dose and the median last BRV dose assessed were both 100.0 mg/day (n=139).

HRQoL

PGIC

Patients in the SS who completed assessment at 12 months

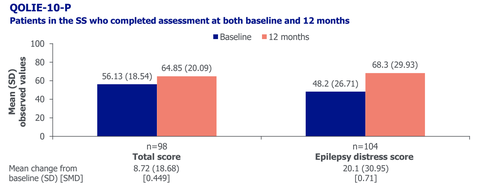


PGIC was completed at 12 months only and describes how the patient felt over the past 4 weeks vs before they entered the study. PGIC, Patient's Global Impression of Change.

- Most patients reported improved clinical condition at 12 months vs study entry.

QOLIE-10-P

Patients in the SS who completed assessment at both baseline and 12 months



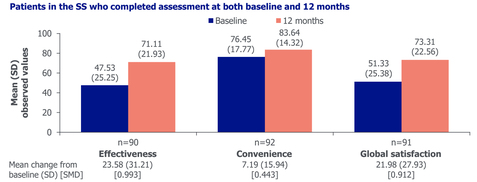
QOLIE-10-P total and distress scores range from 0-100 and 0-100, respectively, with higher scores reflecting better functioning and lower distress. The total score is calculated as the sum of the 10 items scores of the QOLIE-10-P divided by the number of answered items as long as there is no more than 1 missing response. Where >1 of the items scores is missing, the QOLIE-10-P score is missing. The SMD is the parameter that expresses the size of the intervention effect in the study relative to the variability observed in that study. QOLIE-10-P, Patient-Weighted Quality of Life in Epilepsy Inventory-10-P; SMD, standardized mean difference.

- HRQoL improved and distress in epilepsy was reduced at 12 months compared to baseline.

TREATMENT SATISFACTION

TSQM-9

Patients in the SS who completed assessment at both baseline and 12 months



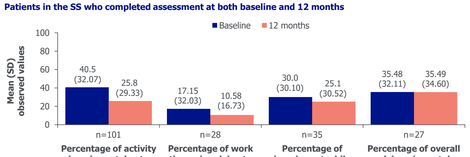
TSQM-9 domain scores were transformed into values ranging from 0-100, with a higher score reflecting better satisfaction. A score can be computed for a domain only if no more than 1 item is missing from that domain. The SMD is the parameter that expresses the size of the intervention effect in the study relative to the variability observed in that study. SMD, standardized mean difference; TSQM-9, Treatment Satisfaction Questionnaire for Medication-9.

- Overall, patients showed increased global satisfaction with the therapy regime at 12 months vs baseline.

WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT

WPAI:GH

Patients in the SS who completed assessment at both baseline and 12 months



The SMD is the parameter that expresses the size of the intervention effect in the study relative to the variability observed in that study. [a]The lower n numbers are likely due to patients who were not employed/working at the time they completed the questionnaire. SMD, standardized mean difference; WPAI:GH, Work Productivity and Activity Impairment Questionnaire: General Health.

- Activity impairment due to health problem and work time missed due to health problem were reduced at 12 months compared to baseline.

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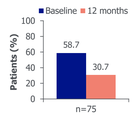
SEIZURE SEVERITY

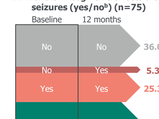
SSQ

Patients in the SS who completed assessment at both baseline and 12 months

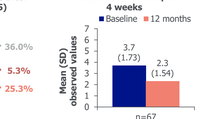
Question 5: Cognitive effects after seizures[a]



Question 5: Shift from baseline to 12 months in cognitive effects after seizures (yes/no[b]) (n=75)



Question 8: Severity (intensity) of seizures overall in past 4 weeks



The score for SSQ question 8 ranges from 1-7, with a higher score reflecting greater severity. Arrow thickness in the central figure is proportional to the percentage of patients. [a]The proportion of patients responding 'yes' is described; [b]Yes/no for cognitive effects. SSQ, Seizure Severity Questionnaire.

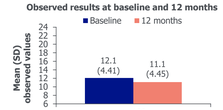
- Seizure severity and the percentage of patients with perceived cognitive effects after seizures were numerically reduced at 12 months vs baseline.

NEUROLOGICAL DISORDERS DEPRESSION

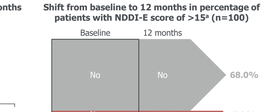
NDDI-E

Patients in the SS who completed assessment at both baseline and 12 months

Observed results at baseline and 12 months



Shift from baseline to 12 months in percentage of patients with NDDI-E score of >15[a] (n=100)



The NDDI-E score ranges from 6-24, with a higher score reflecting greater depressive behavior. An NDDI-E score of >15 is suggestive of a possible major depressive disorder. The SMD is the parameter that expresses the size of the intervention effect in the study relative to the variability observed in that study. Arrow thickness in the right-hand figure is proportional to the percentage of patients. [a]'Yes' means an NDDI-E score of >15; 'no' means a score of ≤15. NDDI-E, Neurological Disorders Depression Inventory in Epilepsy; SMD, standardized mean difference.

- There was a trend toward lower severity in depressive symptoms and a smaller percentage of patients with possible major depressive disorder at 12 months compared to baseline (more patients shifted from 'yes' for NDDI-E score of >15 at baseline to 'no' at 12 months than from 'no' at baseline to 'yes' at 12 months).

TOLERABILITY

TEAEs

Patients in the SS who completed ≥1 PRO assessment at both baseline and 12 months

PATIENTS, n (%)	ALL PATIENTS (N=139)
Any TEAE	23 (16.5)
Serious TEAEs	3 (2.2)
Drug-related TEAEs	10 (7.2)
Deaths (AEs leading to death)	0

AE, adverse event; PRO, patient-reported outcome; TEAE, treatment-emergent adverse event.

Limitations

- This was a post hoc analysis of the second interim data snapshot from the non-interventional BRITOBA study. Because this was an unplanned analysis, there is a potential for bias.
- Caution should be applied when interpreting these PROs.
  - At the time of this interim analysis, only one-third of patients in the SS completed ≥1 PRO assessment at both baseline and 12 months.
  - There were missing data for some questionnaire outcomes.

Conclusions

- In this post hoc analysis of the second interim data snapshot, patients who completed 12 months of adjunctive BRV therapy in earlier treatment lines (failure of ≤3 lifetime ASMs) showed improvements in clinical condition, HRQoL, treatment satisfaction, perceived cognitive effects after seizures, and depressive symptoms, as assessed by PROs.

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