SUPPLEMENTARY MATERIAL

Effectiveness During 12-Month Adjunctive Brivaracetam Treatment in Patients with Focal-Onset Seizures in a Real-Life Setting: A Prospective, Observational Study in Europe

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Sample size calculation

A sample size of 430 patients was initially calculated to obtain 385 patients in the Full Analysis Set (all enrolled patients who received at least one dose of brivaracetam [BRV] and who did not receive BRV before entering this study), which allowed for approximately 10% of patients to be nonevaluable. A protocol amendment was applied to increase the sample size by 100 patients, to limit the influence of the inclusion of a very heterogeneous patient population with different baseline disease characteristics on the primary outcome analysis. This was a consequence of a longer than planned enrollment period to reach the targeted sample size.

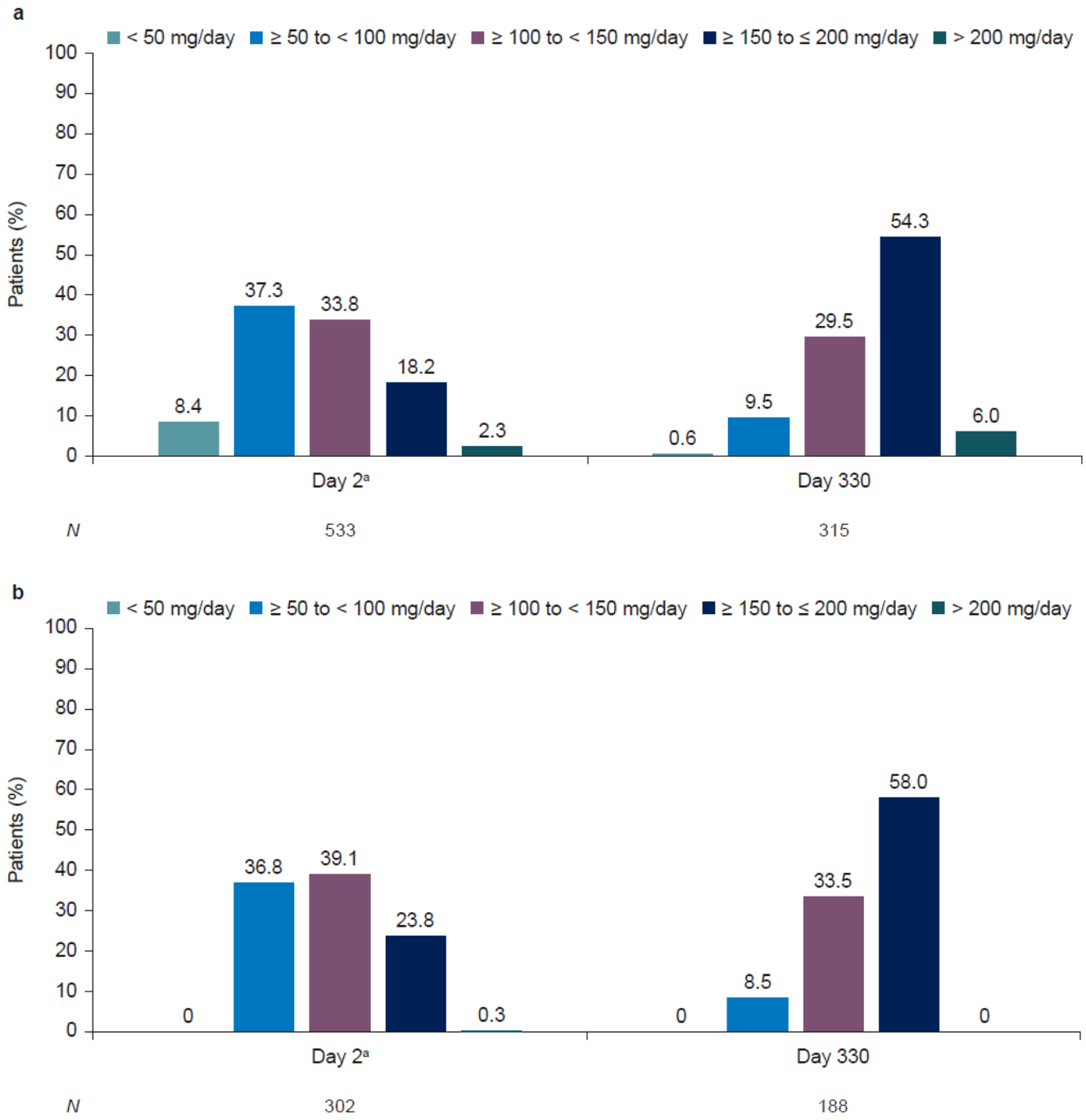


Fig. S1 BRV dosing by timepoint in **a** SS and **b** mFAS. Percentages were based on the number of patients taking BRV at each timepoint (*N*). *BRV* brivaracetam, *mFAS* Modified Full Analysis Set, *SS* Safety Set. [a]Day 2 was assessed because it was the first full day of dosing

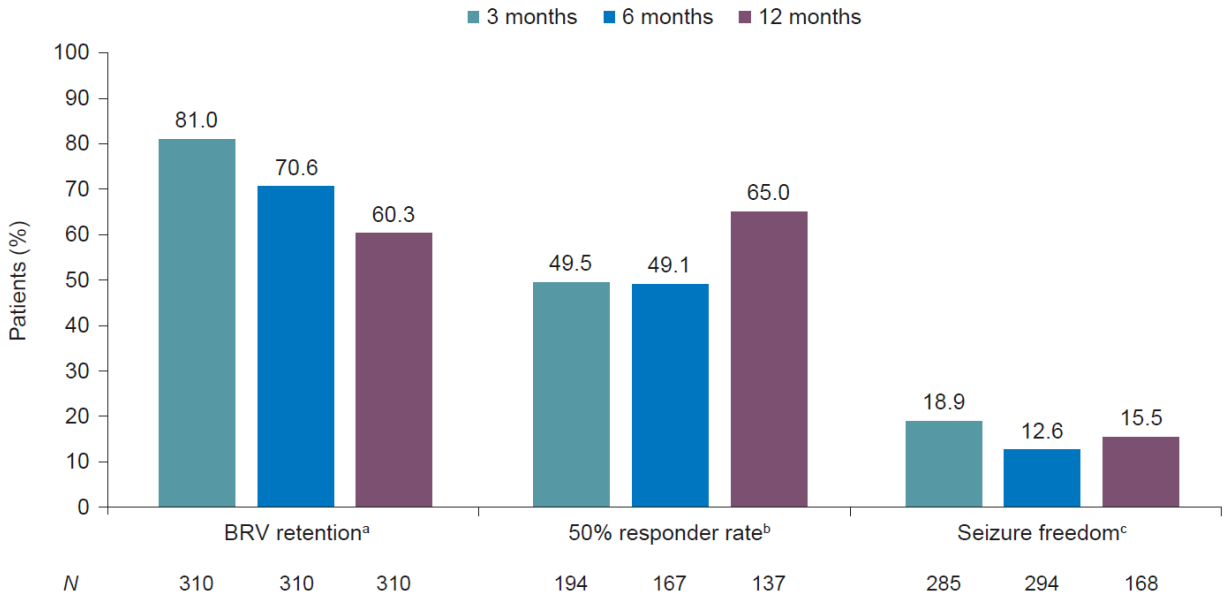


Fig. S2 Effectiveness outcomes at 3, 6, and 12 months for the overall study population (mFAS). For BRV retention, percentages were based on the number of patients with data in the mFAS. For 50% responder rate and seizure freedom, percentages were based on the number of patients with data at respective visits in the mFAS. *BRV* brivaracetam, *mFAS* Modified Full Analysis Set. [a]Patients who remained in the study and were on BRV treatment at least 3 months (≥ 90 days), at least 6 months (≥ 180 days), or at least 12 months (≥ 330 days) after first BRV administration were classified as having 3, 6, or 12 months of treatment retention, respectively. The 95% confidence interval was 76.1, 85.2 at 3 months, 65.2, 75.7 at 6 months, and 54.6, 65.8 at 12 months. [b]The proportion of patients with a ≥ 50% reduction from baseline in 28-day adjusted focal-onset seizure frequency. Patients for whom the baseline seizure frequency was 0 were excluded. [c]Seizure freedom was defined as having no date of first seizure recorded in the study on or before the target visit date (3 months = day 90, 6 months = day 180, 12 months = day 330), having not discontinued before the visit, and having available seizure data at the visit. Patients with a date of first seizure before the target visit date or patients who discontinued BRV or terminated the study before the target visit date were counted as not seizure-free. Patients with missing seizure data but who were still on the study were excluded from the analysis

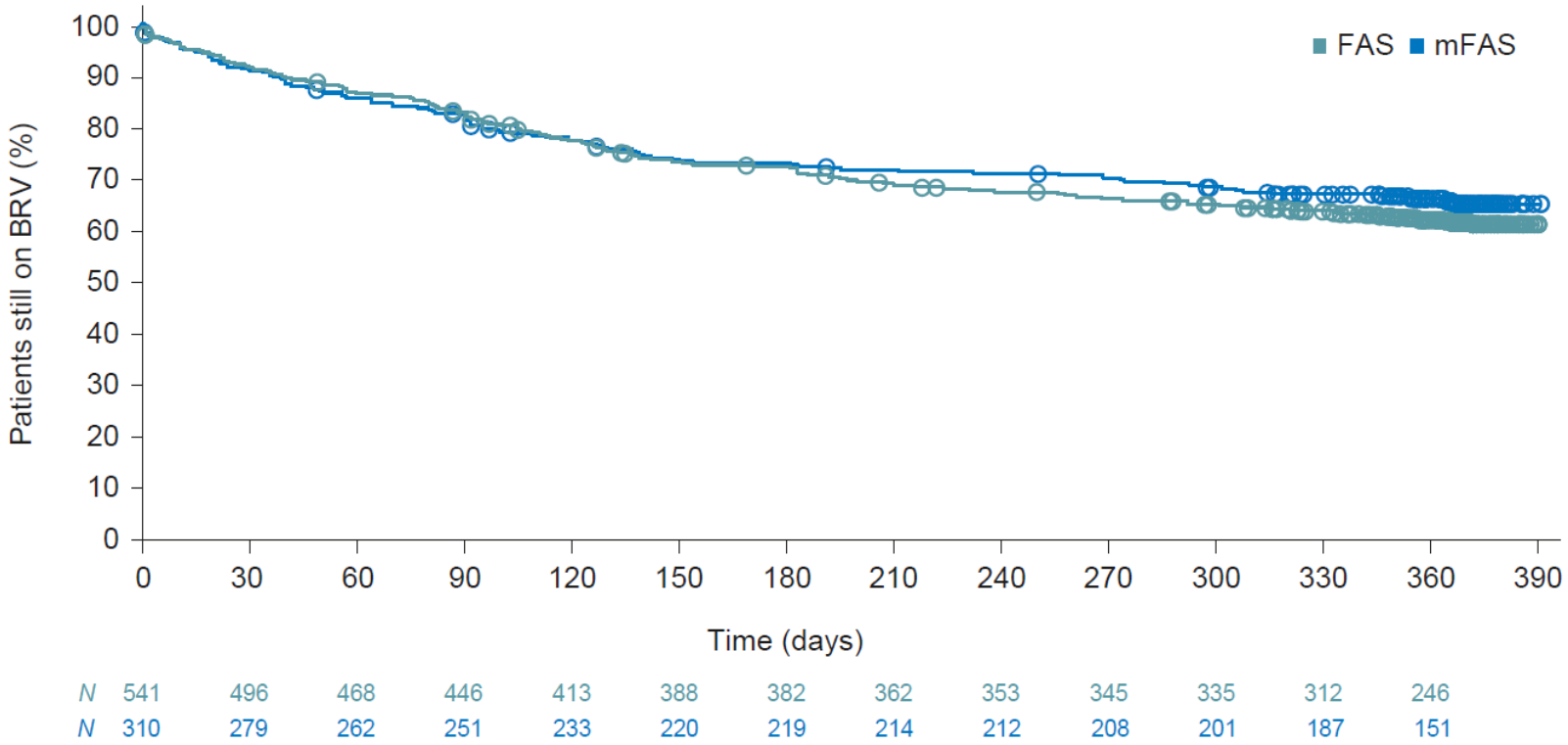


Fig. S3 Kaplan-Meier estimates for time to discontinuation of BRV or early study termination for the FAS and mFAS. Time to discontinuation of BRV or early study termination was calculated as: minimum of (date of last administration of BRV, date of study termination) – date of first BRV administration + 1. A patient was considered to have had an event if the patient discontinued from the study or if the patient was not prescribed BRV after exiting the study. All other patients were considered not to have had an event and were censored at the date of study termination. The numbers below the plot represent the number of patients at risk at the start of each 30-day period. The symbols represent censored patients. *BRV* brivaracetam, *FAS* Full Analysis Set, *mFAS* Modified Full Analysis Set

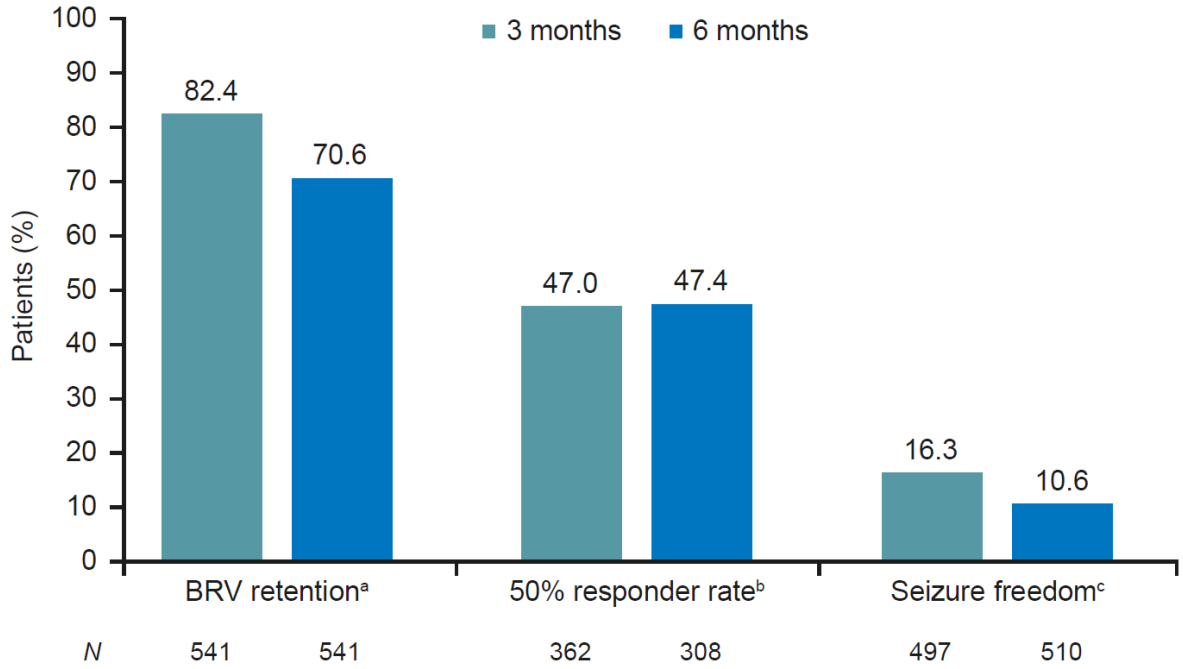


Fig. S4 Effectiveness outcomes at 3 and 6 months for the overall study population (FAS). For BRV retention, percentages were based on the number of patients with data in the FAS. For 50% responder rate and seizure freedom, percentages were based on the number of patients with data at respective visits in the FAS. *BRV* brivaracetam, *FAS* Full Analysis Set. [a]Patients who remained in the study and were on BRV treatment at least 3 months (≥ 90 days) or at least 6 months (≥ 180 days) after first BRV administration were classified as having 3 or 6 months of treatment retention, respectively. The 95% confidence interval was 79.0, 85.6 at 3 months and 66.6, 74.4 at 6 months. [b]The proportion of patients with a ≥ 50% reduction from baseline in 28-day adjusted focal-onset seizure frequency. Patients for whom the baseline seizure frequency was 0 were excluded. [c]Seizure freedom was defined as having no date of first seizure recorded in the study on or before the target visit date (3 months = day 90, 6 months = day 180), having not discontinued before the visit, and having available seizure data at the visit. Patients with a date of first seizure before the target visit date or patients who discontinued BRV or terminated the study before the target visit date were counted as not seizure-free. Patients with missing seizure data but who were still on the study were excluded from the analysis

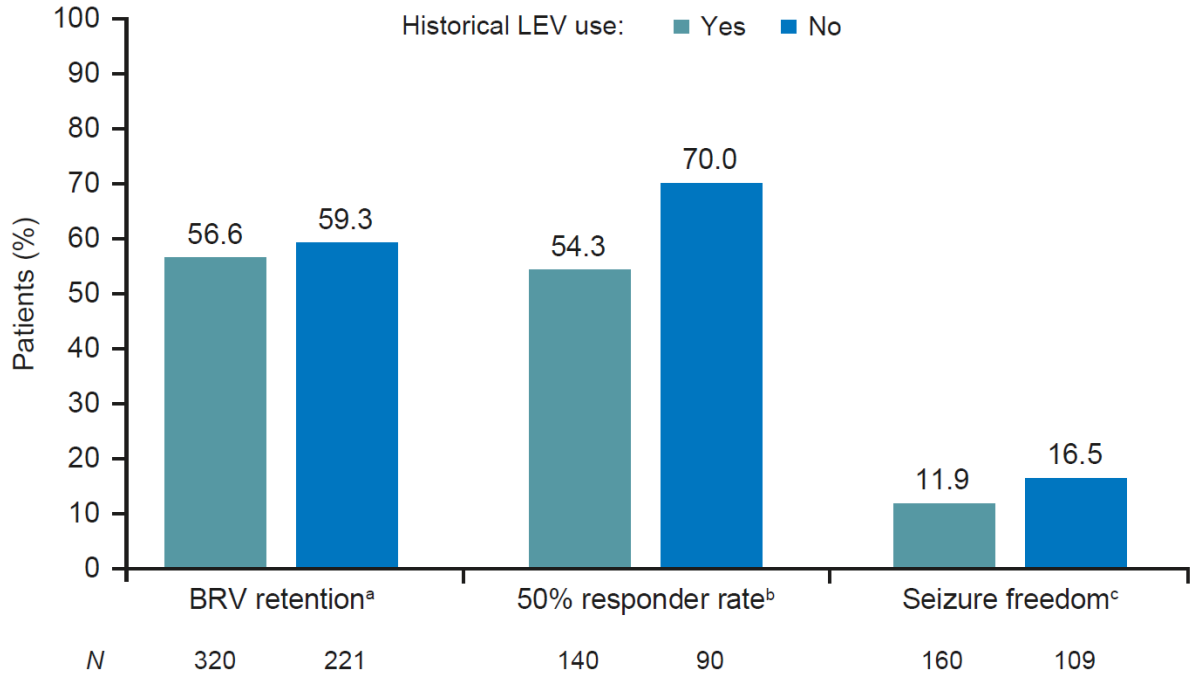


Fig. S5 Effectiveness outcomes at 12 months, by historical use of LEV (FAS). Historical LEV use was defined as LEV discontinued before visit 1 (baseline). For BRV retention, percentages were based on the number of patients with data in the FAS within the subgroup. For 50% responder rate and seizure freedom, percentages were based on the number of patients with data at the 12-month visit in the FAS within the subgroup. *BRV* brivaracetam, *FAS* Full Analysis Set, *LEV* levetiracetam. [a]Patients who remained in the study and were on BRV treatment at least 12 months (≥ 330 days) after first BRV administration were classified as having 12 months of treatment retention. The 95% confidence interval was 50.9, 62.1 for patients with historical LEV use and 52.5, 65.8 for patients without historical LEV use. [b]The proportion of patients with a ≥ 50% reduction from baseline in 28-day adjusted focal-onset seizure frequency. Patients with a baseline seizure frequency of 0 were excluded. This outcome was analyzed post hoc. [c]Seizure freedom was defined as having no date of first seizure recorded in the study on or before the target visit date (day 330), having not discontinued before the visit, and having available seizure data at the visit. Patients with a date of first seizure before the target visit date or patients who discontinued BRV or terminated the study before the target visit date were counted as not seizure-free. Patients with missing seizure data but who were still on the study were excluded from the analysis

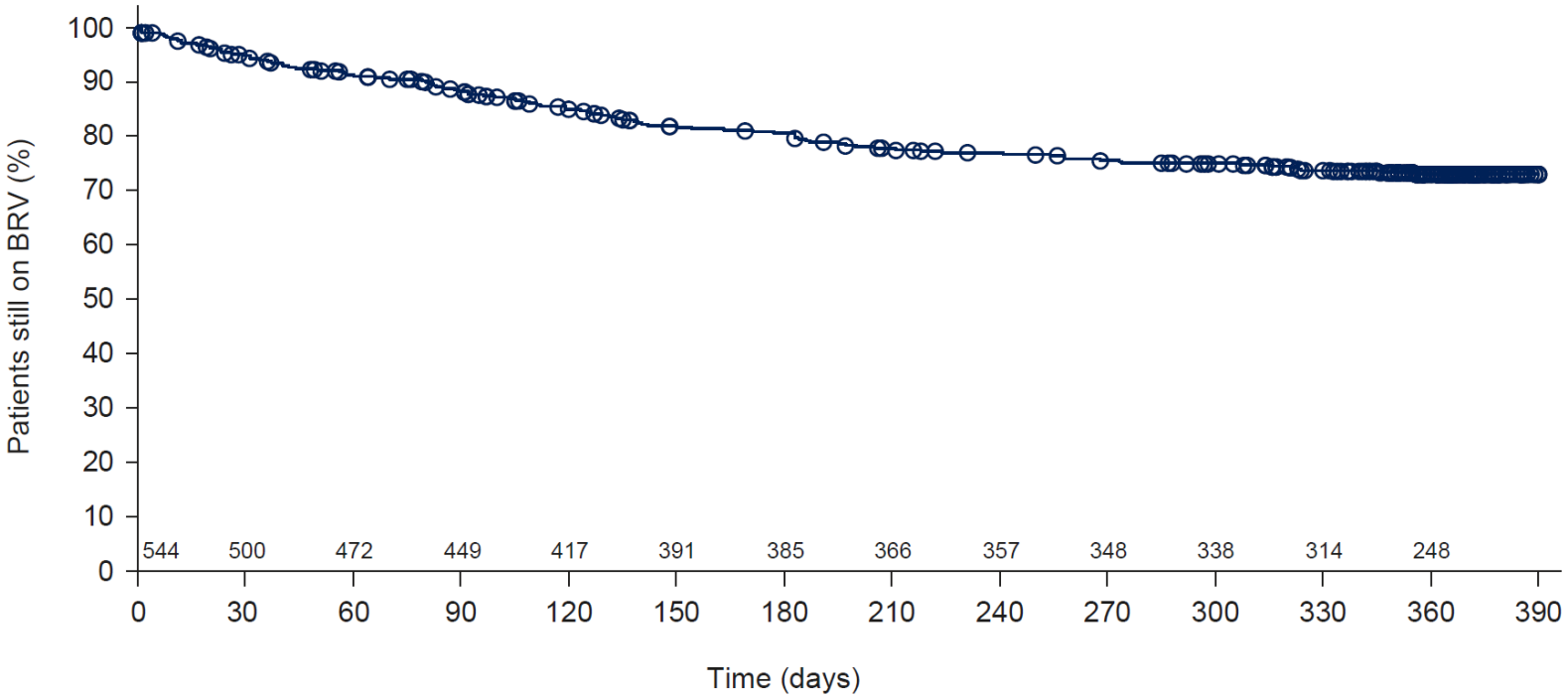
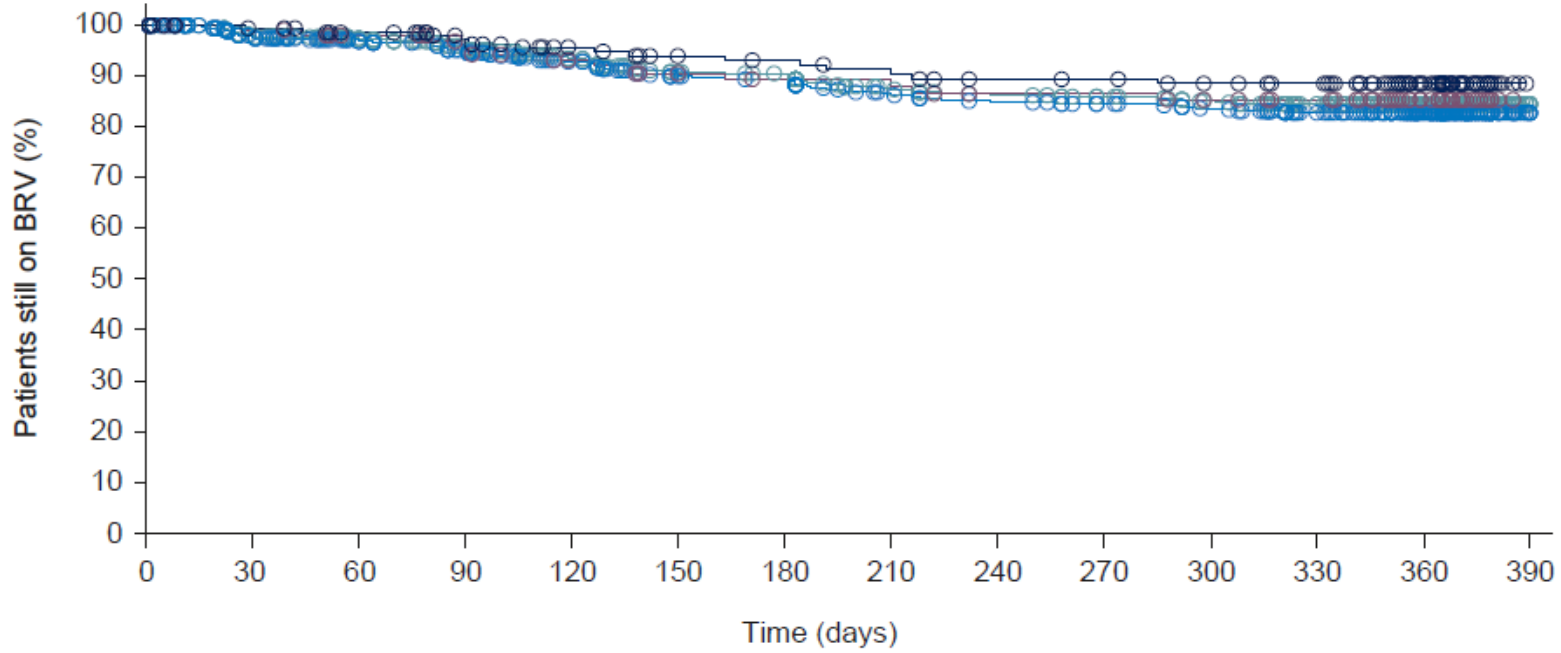


Fig. S6 Kaplan-Meier estimates for time to discontinuation of BRV due to drug-related TEAEs (SS). Time to discontinuation of BRV due to drug-related TEAEs was calculated as: date of last administration of BRV while in the study – date of first BRV administration + 1. Patients with a drug-related TEAE with action = "drug withdrawn" were classed as events. All other patients were censored. The median time to discontinuation could not be calculated since <50% discontinued due to drug-related TEAEs. The numbers inside the plot represent the number of patients at risk at the start of each 30-day period. The symbols represent censored patients. *BRV* brivaracetam, *SS* Safety Set, *TEAE* treatment-emergent adverse event

a


Patients still on BRV (%)
100
90
80
70
60
50
40
30
20
10
0
0
30
60
90
120
150
180
210
240
270
300
330
360
390
Time (days)

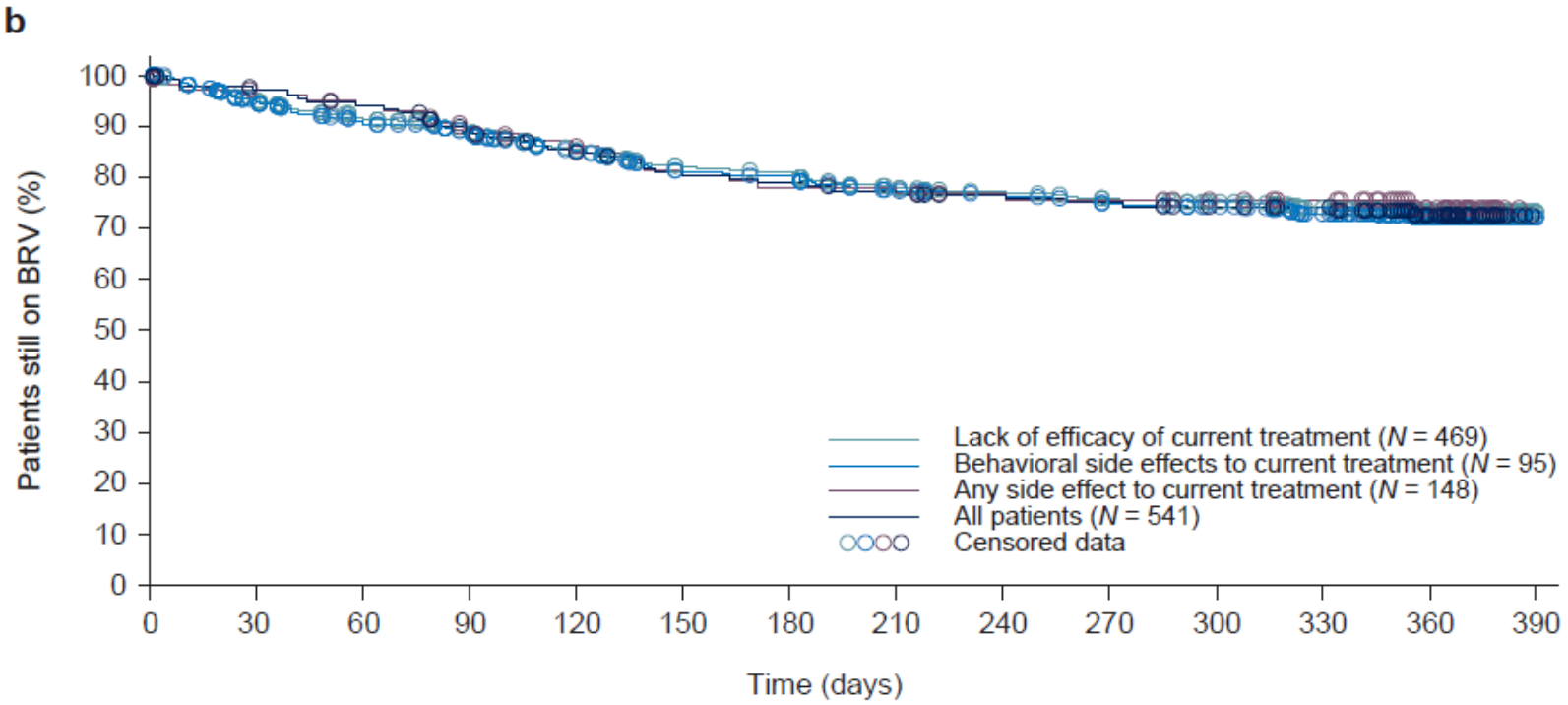
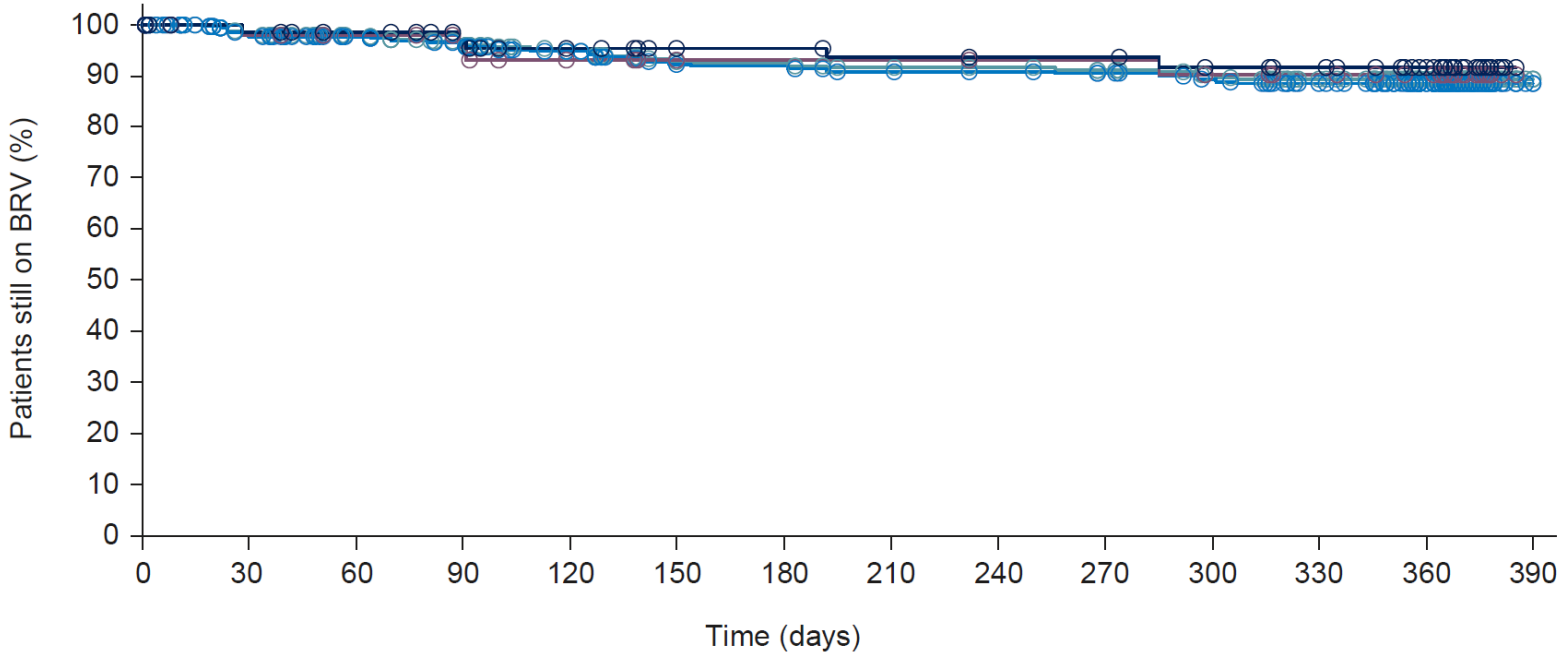


Fig. S7 Kaplan-Meier estimates for ***a*** time to discontinuation of BRV due to lack of efficacy, by reason for BRV initiation and ***b*** time to discontinuation of BRV due to drug-related TEAEs, by reason for BRV initiation (FAS). Note: time to discontinuation of BRV or early study termination was calculated as: minimum of (date of last administration of BRV, date of study termination) – date of first BRV administration + 1. A patient was considered to have had an event if the patient discontinued from the study or if the patient was not prescribed BRV after exiting the study. All other patients were considered not to have had an event and were censored at the date of study

termination. Time to discontinuation of BRV due to drug-related TEAEs was calculated as: date of last administration of BRV while in the study – date of first BRV administration + 1. Patients with a drug-related TEAE with action = “drug withdrawn” were classed as events. All other patients were censored. The symbols represent censored patients. The categorization of a side effect as a behavioral side effect was done by the treating physician without guidance from UCB. *BRV* brivaracetam, *FAS* Full Analysis Set, *TEAE* treatment-emergent adverse event

a


Patients still on BRV (%)
100
90
80
70
60
50
40
30
20
10
0
0
30
60
90
120
150
180
210
240
270
300
330
360
390
Time (days)

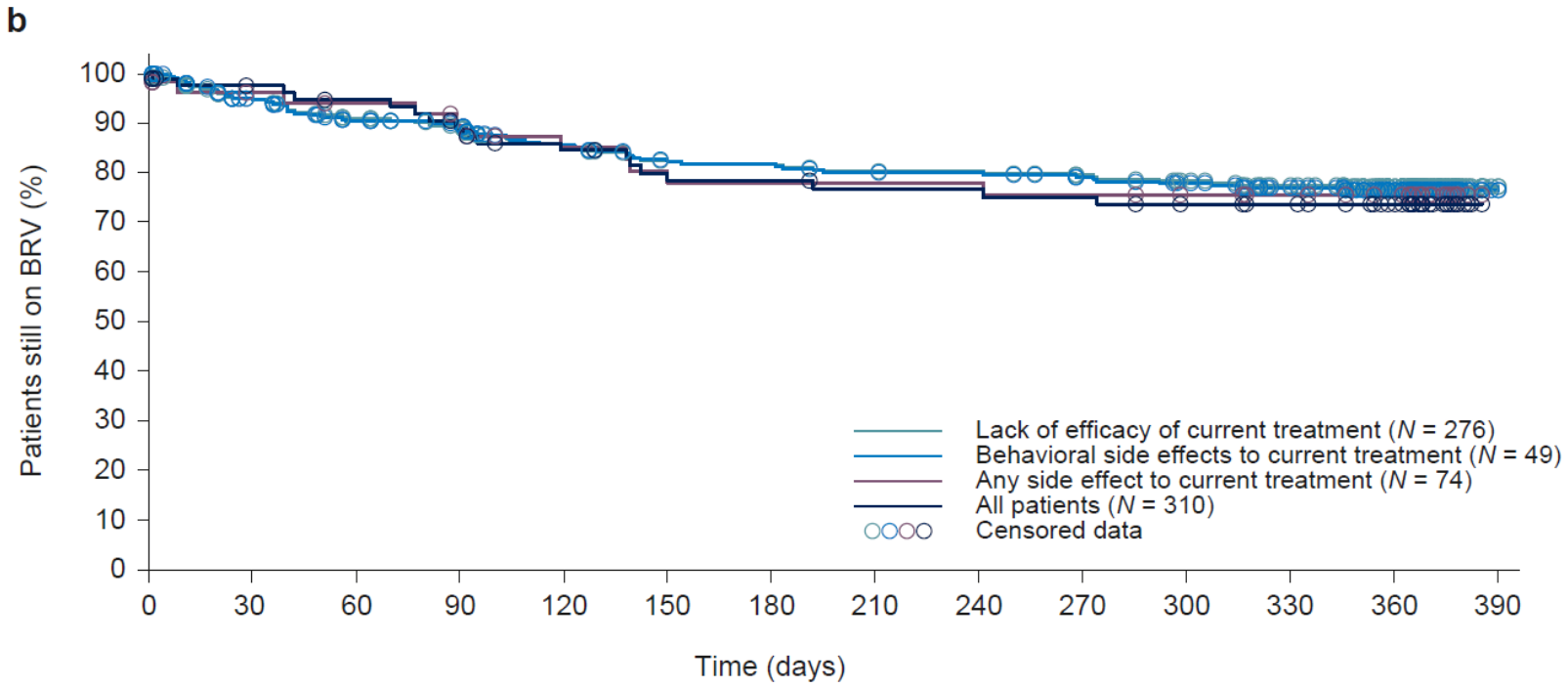


Fig. S8 Kaplan-Meier estimates for **a** time to discontinuation of BRV due to lack of efficacy, by reason for BRV initiation and **b** time to discontinuation of BRV due to drug-related TEAEs, by reason for BRV initiation (mFAS). Time to discontinuation of BRV or early study termination was calculated as: minimum of (date of last administration of BRV, date of study termination) – date of first BRV administration + 1. A patient was considered to have had an event if the patient discontinued from the study or if the patient was not prescribed BRV after exiting the study. All other patients were considered not to have had an event and were censored at the date of study termination. Time to discontinuation of BRV due to drug-related TEAEs was calculated as: date of last administration of BRV while in the study – date of first BRV administration + 1. Patients with a drug-related TEAE with action = "drug withdrawn" were classed as events. All other patients were censored. The symbols represent censored patients. The

categorization of a side effect as a behavioral side effect was done by the treating physician without guidance from UCB. *BRV* brivaracetam, *mFAS* Modified Full Analysis Set, *TEAE* treatment-emergent adverse event

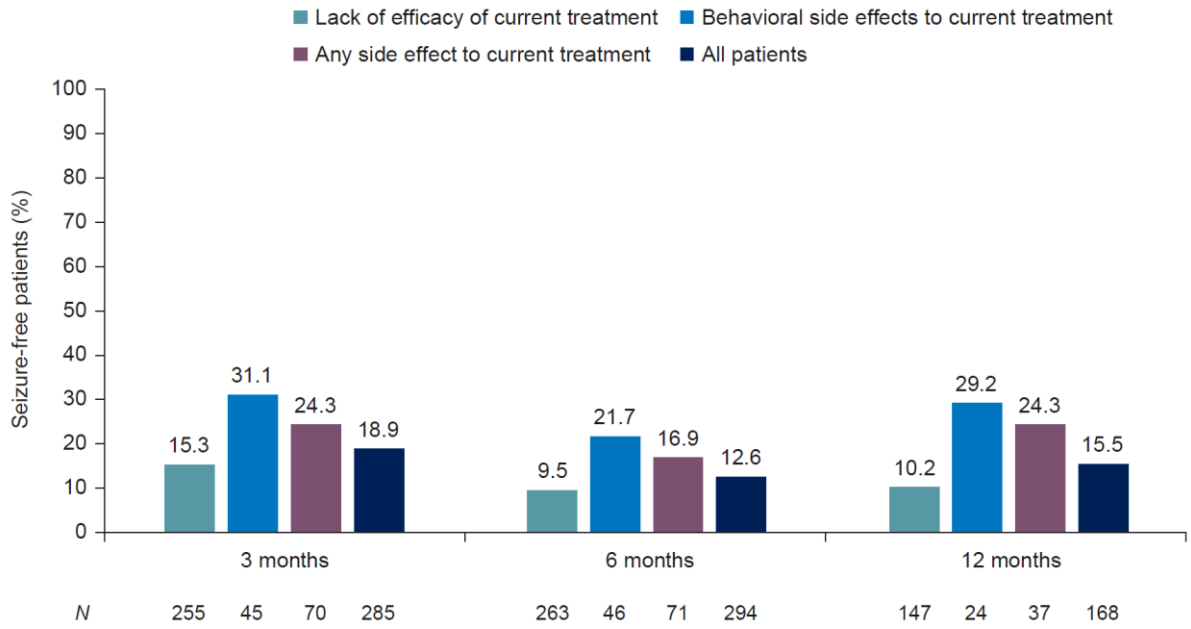


Fig. S9 Seizure freedom since BRV initiation at 3, 6, and 12 months, by reason for BRV initiation (mFAS). Seizure freedom was defined as having no date of first seizure recorded in the study on or before the target visit date (3 months = day 90, 6 months = day 180, 12 months = day 330), having not discontinued before the visit, and having available seizure data at the visit. Patients with a date of first seizure before the target visit date or patients who discontinued BRV or terminated the study before the target visit date were counted as not seizure-free. Patients with missing seizure data but who were still on the study were excluded from the analysis. Percentages were based on the number of patients with data at the respective visit. The categorization of a side effect as a behavioral side effect was done by the treating physician without guidance from UCB. *BRV* brivaracetam, *mFAS* Modified Full Analysis Set

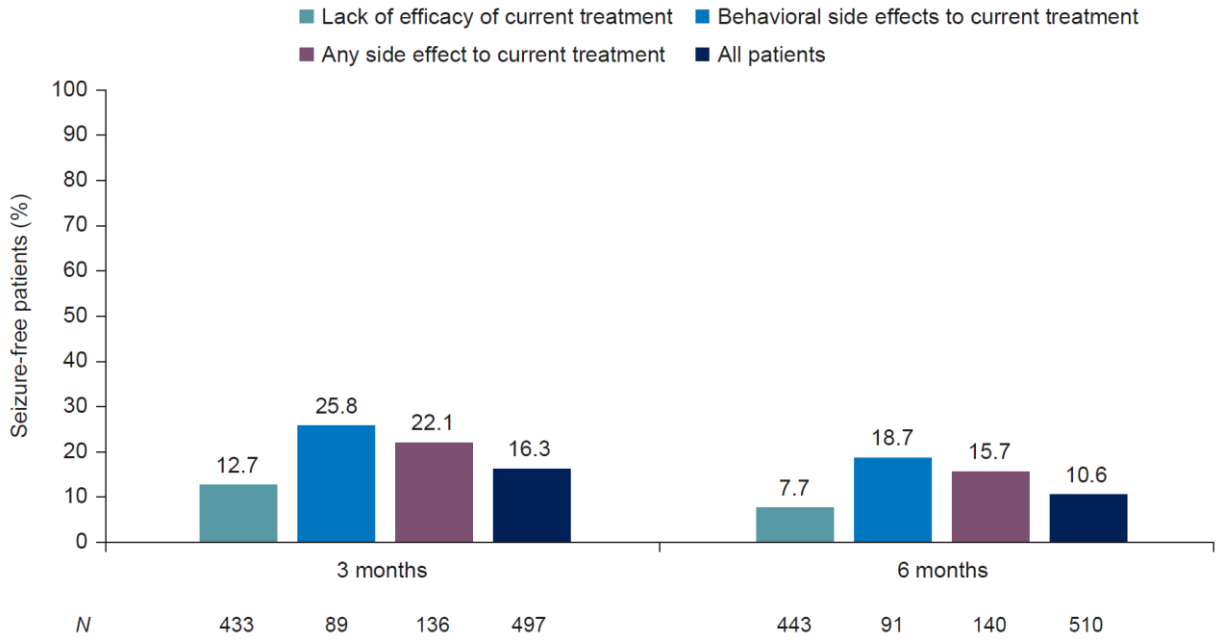


Fig. S10 Seizure freedom since BRV initiation at 3 and 6 months, by reason for BRV initiation (FAS). Seizure freedom was defined as having no date of first seizure recorded in the study on or before the target visit date (3 months = day 90, 6 months = day 180), having not discontinued before the visit, and having available seizure data at the visit. Patients with a date of first seizure before the target visit date or patients who discontinued BRV or terminated the study before the target visit date were counted as not seizure-free. Patients with missing seizure data but who were still on the study were excluded from the analysis. Percentages were based on the number of patients with data at the respective visit. The categorization of a side effect as a behavioral side effect was done by the treating physician without guidance from UCB. *BRV* brivaracetam, *FAS* Full Analysis Set

Table S1 Baseline demographic and epilepsy characteristics (mFAS)

	mFAS (*N* = 310)
Age, mean (SD), years	44.9 (14.6)
Female, *n* (%)	165 (53.2)
Time since first diagnosis, mean (SD)[a], years	22.7 (15.5)
Age at time of first diagnosis, mean (SD)[a], years	22.2 (18.0)
Percentage of life with epilepsy, mean (SD)[a], %	51.8 (31.6)
Seizure profile[b], *n* (%)	
Focal-onset seizures (*partial-onset seizures*)	309 (99.7)
Focal aware seizures (*simple partial-onset seizures*)	114 (36.8)
Focal impaired awareness seizures (*complex partial-onset seizures*)	230 (74.2)
Focal to bilateral tonic-clonic seizures (*partial-onset seizures evolving to secondarily generalized*)	215 (69.4)
Baseline seizure frequency	
Any baseline focal-onset seizures, *n* (%)[c]	252 (88.7)
Any baseline focal to bilateral tonic-clonic seizures, *n* (%)[d]	97 (34.0)
28-day baseline focal-onset seizure frequency[c,e]	
Median (Q1, Q3)	2.7 (0.7, 7.0)
Mean (SD)	9.8 (23.1)
28-day baseline focal to bilateral tonic-clonic seizure frequency[d,e]	
Median (Q1, Q3)	0.0 (0.0, 0.7)
Mean (SD)	0.8 (2.2)

	mFAS **(*N* = 310)**
VNS use at study entry, *n* (%)[f]	23 (7.7)
Historical LEV use, *n* (%)	169 (54.5)
LEV use at study entry, *n* (%)	89 (28.7)
Discontinued LEV use post study entry, *n* (%)[g]	73 (82.0)
Number of ASMs at study entry[h], mean (SD)	2.3 (1.0)
0, *n* (%)	0
1, *n* (%)	70 (22.6)
2, *n* (%)	131 (42.3)
3, *n* (%)	74 (23.9)
>3, *n* (%)	35 (11.3)
Number of lifetime ASMs[i], mean (SD)	6.5 (4.0)
0–3, *n* (%)	82 (26.5)
4–6, *n* (%)	94 (30.3)
≥ 7, *n* (%)	134 (43.2)

ASM antiseizure medication, *BRV* brivaracetam, *LEV* levetiracetam, *mFAS* Modified Full Analysis Set, *Q1* first quartile, *Q3* third quartile, *SD* standard deviation, *VNS* vagus nerve stimulation

[a]*n* = 308

[b]Seizure profile includes all seizure types experienced in the patient's life so far; seizure types are listed per the International League Against Epilepsy 2017 classification [1], with the 1981 classification [2] in parentheses. A patient may have had multiple seizure classifications

[c]*n* = 284

[d]*n* = 285

[e]28-day adjusted baseline seizure frequency was calculated as the number of seizures recorded during the 3 months before first BRV administration divided by 3

[f]Percentage of patients with or without VNS use at study entry was based on a total of 298 patients reporting data

[g]Percentage was based on the number of patients with LEV use at study entry = "Yes"

[h]ASMs at study entry were defined as those being taken on the same day as first BRV administration, including VNS and LEV use if applicable

[i]Lifetime ASMs were a sum of historical ASMs (those discontinued before the date of first BRV administration) and ASMs at study entry (including VNS and LEV counted only once).

Table S2 Overview of TEAEs (mFAS)

***n* (%)**	**mFAS (*N* = 310)**
Any TEAEs (including drug ineffective and seizure)	104 (33.5)
Serious TEAEs	35 (11.3)
Discontinuations of BRV due to TEAEs	69 (22.3)
Drug-related TEAEs	89 (28.7)
Reported as related	67 (21.6)
Unavailable relationship, imputed (considered) as related	51 (16.5)
Serious drug-related TEAEs	22 (7.1)
Reported as related	14 (4.5)
Unavailable relationship, imputed (considered) as related	11 (3.5)
Discontinuations of BRV due to drug-related TEAEs	65 (21.0)
All deaths (AEs leading to death)	1 (0.3)
Drug-related TEAEs leading to death	1 (0.3)

Drug-related TEAEs included both AEs reported as related by the treating physician and AEs with unavailable relationship to BRV (all AEs where the relationship to BRV was unavailable per UCB clinical trial reporting convention). The same AE may have been reported on multiple occasions, with different causality. Therefore, the "reported as related" and "unavailable relationship, imputed (considered) as related" rows do not sum to the drug-related TEAEs.

AE adverse event, *BRV* brivaracetam, *mFAS* Modified Full Analysis Set, *TEAE* treatment-emergent adverse event.

Table S3 Baseline demographic and epilepsy characteristics, by reason for BRV initiation (SS and mFAS)

	SS			**mFAS**		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
Age, mean (SD), years	43.5 (14.0)	43.9 (15.3)	44.2 (14.5)	45.3 (14.5)	45.7 (16.1)	45.3 (15.3)
Female, *n* (%)	249 (52.8)	53 (55.8)	86 (58.1)	149 (54.0)	31 (63.3)	47 (63.5)
Time since first diagnosis, mean (SD), years	23.3 (15.1)[a]	22.4 (16.4)[b]	22.2 (15.6)[c]	23.0 (15.6)[d]	24.5 (17.3)[e]	23.0 (16.4)[f]
Age at time of first diagnosis, mean (SD), years	20.2 (16.6)[a]	21.5 (19.0)[b]	22.0 (17.9)[c]	22.2 (17.5)[d]	21.1 (20.7)[e]	22.3 (19.1)[f]
Percentage of life with epilepsy, mean (SD), %	54.7 (31.0)[a]	52.8 (33.7)[b]	51.7 (32.4)[c]	51.9 (31.2)[d]	55.7 (34.4)[e]	52.3 (33.3)[f]

	SS			mFAS		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
Seizure profile[g], *n* (%)						
Focal-onset seizures (*partial-onset seizures*)	470 (99.6)	95 (100)	148 (100)	275 (99.6)	49 (100)	74 (100)
Focal aware seizures (*simple partial-onset seizures*)	196 (41.5)	43 (45.3)	67 (45.3)	99 (35.9)	21 (42.9)	32 (43.2)
Focal impaired awareness seizures (*complex partial-onset seizures*)	359 (76.1)	79 (83.2)	122 (82.4)	204 (73.9)	40 (81.6)	59 (79.7)

	SS			mFAS		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
Focal to bilateral tonic-clonic seizures (*partial-onset seizures evolving to secondarily generalized*)	311 (65.9)	64 (67.4)	96 (64.9)	192 (69.6)	28 (57.1)	46 (62.2)
Baseline seizure frequency						
Any baseline focal-onset seizures, *n* (%)	411 (94.9)[h]	69 (76.7)[i]	109 (78.4)[j]	238 (93.7)[k]	30 (68.2)[m]	49 (73.1)[n]

	SS			mFAS		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
Any baseline focal to bilateral tonic-clonic seizures, *n* (%)	148 (34.1)[h]	22 (24.4)[i]	40 (28.8)[j]	92 (36.1)[l]	6 (13.6)[m]	18 (26.9)[n]
28-day focal-onset seizure frequency, median (Q1, Q3)[o]	4.0 (1.3, 14.0)[h]	1.7 (0.3, 8.7)[i]	2.7 (0.3, 11.0)[j]	3.0 (1.0, 8.0)[k]	1.2 (0.0, 6.5)[m]	1.3 (0.0, 8.0)[n]
28-day focal to bilateral tonic-clonic seizure frequency, median (Q1, Q3)[o]	0.0 (0.0, 0.7)[h]	0.0 (0.0, 0.0)[i]	0.0 (0.0, 0.3)[j]	0.0 (0.0, 0.7)[l]	0.0 (0.0, 0.0)[m]	0.0 (0.0, 0.3)[n]

	SS			mFAS		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
VNS use at study entry, *n* (%)	53 (11.5)[p]	6 (6.6)[q]	16 (11.1)[r]	21 (8.0)[s]	1 (2.2)[t]	6 (8.6)[u]
Historical LEV use, *n* (%)	284 (60.2)	56 (58.9)	86 (58.1)	153 (55.4)	30 (61.2)	45 (60.8)
LEV use at study entry, *n* (%)	116 (24.6)	43 (45.3)	58 (39.2)	72 (26.1)	22 (44.9)	29 (39.2)
Discontinued LEV use post study entry, *n* (%)[v]	116 (100)	43 (100)	58 (100)	72 (100)	22 (100)	29 (100)
Number of ASMs at study entry[w], mean (SD)	2.4 (1.2)	2.4 (1.1)	2.4 (1.4)	2.3 (1.0)	2.2 (0.9)	2.3 (1.0)

	SS			mFAS		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
0, *n* (%)	2 (0.4)	0	0	0	0	0
1, *n* (%)	96 (20.3)	20 (21.1)	31 (20.9)	63 (22.8)	9 (18.4)	12 (16.2)
2, *n* (%)	171 (36.2)	38 (40.0)	64 (43.2)	117 (42.4)	25 (51.0)	41 (55.4)
3, *n* (%)	132 (28.0)	22 (23.2)	31 (20.9)	65 (23.6)	11 (22.4)	15 (20.3)
>3, *n* (%)	71 (15.0)	15 (15.8)	22 (14.9)	31 (11.2)	4 (8.2)	6 (8.1)
Number of lifetime ASMs[x], mean (SD)	7.6 (4.7)	6.4 (3.9)	6.5 (3.8)	6.7 (4.1)	6.1 (3.3)	6.3 (3.1)
0–3, *n* (%)	98 (20.8)	27 (28.4)	38 (25.7)	68 (24.6)	13 (26.5)	17 (23.0)
4–6, *n* (%)	120 (25.4)	27 (28.4)	46 (31.1)	84 (30.4)	16 (32.7)	26 (35.1)

	SS			mFAS		
	Lack of efficacy of current treatment (*N* = 472)	**Behavioral side effects to current treatment (*N* = 95)**	**Any side effect to current treatment (*N* = 148)**	**Lack of efficacy of current treatment (*N* = 276)**	**Behavioral side effects to current treatment (*N* = 49)**	**Any side effect to current treatment (*N* = 74)**
≥ 7, *n* (%)	254 (53.8)	41 (43.2)	64 (43.2)	124 (44.9)	20 (40.8)	31 (41.9)

The categorization of a side effect as a behavioral side effect was done by the treating physician without guidance from UCB

ASM antiseizure medication, *BRV* brivaracetam, *LEV* levetiracetam, *mFAS* Modified Full Analysis Set, *Q1* first quartile, *Q3* third quartile, *SD* standard deviation, *SS* Safety Set, *VNS* vagus nerve stimulation

[a]*n* = 467

[b]*n* = 94

[c]*n* = 147

[d]*n* = 275

[e]*n* = 48

[f]*n* = 73

[g]Seizure profile includes all seizure types experienced in the patient's life so far; seizure types are listed per the International League Against Epilepsy 2017 classification [1], with the 1981 classification [2] in parentheses. A patient may have had multiple seizure classifications

[h]*n* = 433

[i]*n* = 90

[j]*n* = 139

[k]*n* = 254

[l]*n* = 255

[m]*n* = 44

[n]*n* = 67

[o]28-day adjusted baseline seizure frequency was calculated as the number of seizures recorded during the 3 months before first BRV administration divided by 3

[p]*n* = 460

[q]*n* = 91

[r]*n* = 144

[s]*n* = 264

[t]*n* = 45

[u]*n* = 70

[v]Percentage was based on the number of patients with LEV use at study entry = "Yes"

[w]ASMs at study entry were defined as those being taken on the same day as first BRV administration, including VNS and LEV use if applicable

[x]Lifetime ASMs were a sum of historical ASMs (those discontinued before the date of first BRV administration) and ASMs at study entry (including VNS and LEV counted only once).

Table S4 Overview of TEAEs by reason for BRV initiation (SS)

	Reason for BRV initiation		
	Lack of efficacy of current treatment (*N* = 472) ***n* (%)**	**Behavioral side effects to current treatment (*N* = 95)** ***n* (%)**	**Any side effect to current treatment (*N* = 148)** ***n* (%)**
Any TEAEs (including drug ineffective[a] and seizure[b])	198 (41.9)	34 (35.8)	58 (39.2)
Discontinuations of BRV due to TEAEs	125 (26.5)	25 (26.3)	43 (29.1)
Drug-related TEAEs	174 (36.9)	30 (31.6)	50 (33.8)
Discontinuations of BRV due to drug-related TEAEs	119 (25.2)	23 (24.2)	38 (25.7)
Reported as related	89 (18.9)	18 (18.9)	30 (20.3)
Unavailable relationship, imputed (considered) as related	75 (15.9)	15 (15.8)	25 (16.9)
Drug-related TEAEs leading to permanent discontinuation of BRV in ≥ 2% of patients in any subgroup (MedDRA v23.0 Preferred Term)			
Drug ineffective	52 (11.0)	9 (9.5)	13 (8.8)
Seizure	25 (5.3)	6 (6.3)	10 (6.8)
Behavior disorder	15 (3.2)	4 (4.2)	6 (4.1)

	Reason for BRV initiation		
	Lack of efficacy of current treatment (*N* = 472) *n* (%)	**Behavioral side effects to current treatment (*N* = 95) *n* (%)**	**Any side effect to current treatment (*N* = 148) *n* (%)**
AE	15 (3.2)	1 (1.1)	4 (2.7)
Fatigue	14 (3.0)	3 (3.2)	5 (3.4)
Dizziness	11 (2.3)	4 (4.2)	5 (3.4)
Drug intolerance	11 (2.3)	3 (3.2)	6 (4.1)
Irritability	11 (2.3)	1 (1.1)	3 (2.0)
Aggression	9 (1.9)	3 (3.2)	4 (2.7)
Depressed mood	9 (1.9)	2 (2.1)	3 (2.0)
Nausea	6 (1.3)	2 (2.1)	2 (1.4)
Headache	5 (1.1)	3 (3.2)	3 (2.0)

Drug-related TEAEs included both AEs reported as related by the treating physician and AEs with unavailable relationship to BRV (all AEs where the relationship to BRV was unavailable per UCB clinical trial reporting convention). The same AE may have been reported on multiple occasions, with different causality. Therefore, the "reported as related" and "unavailable relationship, imputed (considered) as related" rows do not sum to the drug-related TEAEs. The categorization of a side effect as a behavioral side effect was done by the treating physician without guidance from UCB

AE adverse event, *BRV* brivaracetam, *MedDRA* Medical Dictionary for Regulatory Activities, *SS* Safety Set, *TEAE* treatment-emergent adverse event

[a]Lack of efficacy of current treatment subgroup: 59 patients (12.5%), behavioral side effects to current treatment subgroup: nine patients (9.5%), any side effect to current treatment subgroup: 13 patients (8.8%)

[b]Lack of efficacy of current treatment subgroup: 36 patients (7.6%), behavioral side effects to current treatment subgroup: six patients (6.3%), any side effect to current treatment subgroup: 11 patients (7.4%).

Institutional Review Board/Independent Ethics Committee appendix

Central Independent Ethics Committees: Freiburger Ethik Kommission, Freiburg im Breisgau, Germany; Medical Research Council of Hungary (ETT), National Scientific and Ethical Committee (TUKEB), Budapest, Hungary; Fondazione IRCCS Istituto Neurologico Carlo Besta Ethics Committee, Milan, Italy; Medical Research Ethics Committee/Ethics Committee and Scientific Board of Epilepsy Centrum, Heeze, Netherlands; Universitair Medisch Centrum Groningen Ethics Committee, Groningen, Netherlands; Hospital General Universitario Gregorio Marañón, Comité Ético de Investigación Clínica, Madrid, Spain; Xunta de Galicia - CAEIG (Comité Autonómico de Ética de la Investigación de Galicia), A Coruña, Spain; West of Scotland Research Ethics Committee 3, West Glasgow Ambulatory Care Hospital, Glasgow, United Kingdom.

Local Independent Ethics Committees: Tallaght University Hospital/St James's Hospital Joint Research Ethics Committee, Tallaght University Hospital, Dublin, Ireland; Clinical Research Ethics Committee of the Cork Teaching Hospitals, Cork, Ireland; Comitato Etico per la Sperimentazione Clinica delle Province di Verona e Rovigo, Verona, Italy; Comitato Etico Interaziendale Milano Area 1, Milan, Italy; Comitato Etico Regionale per la Sperimentazione, Clinica della Regione Toscana, Florence, Italy; Regional Komité for Medisinsk og Helsefaglig Forskningsetikk Vest-Norge (REK vest), Universitetet i Bergen, Bergen, Norway.

Participating physician appendix

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