Epilepsy & Behavior 69 (2017) 80–85

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Health-related quality of life in double-blind Phase III studies of brivaracetam as adjunctive therapy of focal seizures: A pooled, post-hoc analysis

Christian Brandt [a], Simon Borghs [b,*], Sami Elmoufti [c], Knut Mueller [d], Rebecca Townsend [e], Christine de la Loge [f,1]

[a] Department of General Epileptology, Bethel Epilepsy Centre, Mara Hospital, Maraweg 21, D-33617 Bielefeld, Germany
[b] UCB Pharma, 208 Bath Road, Slough, Berkshire SL1 3WE, UK
[c] UCB Pharma, 8010 Arco Corporate Drive, Raleigh, NC 27617, USA
[d] UCB Pharma, Alfred-Nobel-Strasse 10, 40789 Monheim, Germany
[e] UCB Pharma, 1950 Lake Park Drive South East, Smyrna, GA 30080, USA
[f] 57, rue de Lyon, 89200 Avallon, France

ARTICLE INFO

Article history:
Received 9 September 2016
Revised 22 November 2016
Accepted 22 November 2016
Available online 23 February 2017

Keywords:
Brivaracetam
Focal seizures
Adjunctive
QOLIE-31
Seizure Worry
Refractory epilepsy

ABSTRACT

Purpose: The effect of adjunctive brivaracetam on health-related quality of life (HRQoL) was assessed in a post-hoc analysis using pooled data from three randomized, double-blind, placebo-controlled Phase III studies in patients with refractory focal seizures (NCT00490035, NCT00464269, and NCT01261325).
Methods: The Patient-Weighted Quality of Life in Epilepsy Questionnaire (QOLIE-31-P) was completed at randomization, and weeks 4, 8 (in two of three studies), and 12 (end of the treatment period). Mean change from baseline to week 12 or early discontinuation, and percentage of patients with clinically meaningful improvement were reported for the placebo and brivaracetam 50, 100, and 200 mg/day groups.
Results: At baseline, mean QOLIE-31-P scores were similar between treatment groups. At week 12 or early discontinuation, mean (standard deviation) changes from baseline in QOLIE-31-P total score were 2.8 (12.7), 3.0 (14.0), 2.4 (14.0), and 3.0 (12.1) points for the placebo and brivaracetam 50, 100, and 200 mg/day groups, respectively, indicating HRQoL improved slightly over time during the treatment period, but was similar for placebo and brivaracetam groups. All subscale score changes were positive, indicating stable or improved HRQoL over time. The brivaracetam 100 and 200 mg/day groups showed the largest differences compared with placebo in Seizure Worry subscale scores (7.3 and 8.8 vs. 5.0 points). Approximately 40% of patients had improvements in QOLIE-31-P scores beyond the Minimal Important Change (MIC) thresholds. The subgroup of ≥50% focal seizure frequency responders had higher improvements for all treatment arms and all subscales than for those in the overall pooled population.
Conclusion: In this post-hoc analysis, adjunctive brivaracetam treatment was shown to be associated with stable or improving overall HRQoL over time, similar to placebo, with modest improvements in subscales sensitive to efficacy, and no deterioration in subscales sensitive to tolerability. These results reflect the known efficacy and tolerability profile of brivaracetam.
© 2016 Ellen Carey, UCB Brussels, Belgium. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Epilepsy significantly affects patients' health-related quality of life (HRQoL). Seizures and their frequency, seizure severity, comorbidities such as depression and anxiety, and stigma in relation to epilepsy are among the factors which can contribute to poor patient HRQoL. Side effects attributable to antiepileptic drug (AED) treatment can also impact patients' HRQoL [1–3]. Studies indicate that approximately 30% of patients with focal (partial-onset) seizures do not achieve seizure control on their current AED treatment [4–6] and hence require a new treatment. HRQoL is an important consideration in AED treatment choice and when assessing the effectiveness of AED treatment in clinical studies.

The objective of this post-hoc analysis was to assess the effect on HRQoL of approved doses of brivaracetam, as measured using the Patient-Weighted Quality of Life in Epilepsy Questionnaire (QOLIE-31-

* Corresponding author.
E-mail addresses: christian.brandt@mara.de (C. Brandt), simon.borghs@ucb.com (S. Borghs), sami.elmoufti@ucb.com (S. Elmoufti), knut.mueller@ucb.com (K. Mueller), rebecca.townsend@ucb.com (R. Townsend), cdelaloge@hotmail.fr (C. de la Loge).
[1] UCB Pharma employee at the time the studies were conducted.

http://dx.doi.org/10.1016/j.yebeh.2016.11.031
1525-5050/© 2016 Ellen Carey, UCB Brussels, Belgium. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

P) [7]. Brivaracetam is a selective, high-affinity synaptic vesicle protein 2A ligand [8], which has been shown to be efficacious and generally well tolerated as adjunctive treatment of refractory focal seizures in adults [9–11]. Brivaracetam is approved as adjunctive therapy for focal seizures in adults.

2. Methods

2.1. Pooled studies

Six double-blind Phase II and III studies were conducted with adjunctive brivaracetam. Studies with similar study designs were selected for pooling. Three studies were excluded due to lack of QOLIE-31-P as a variable in one, presence of an up-titration period and shorter (10-week) treatment period in another, and the flexible-dose design of the third. The current analysis used pooled data from three randomized, double-blind, placebo-controlled, fixed-dose Phase III studies of adjunctive brivaracetam in adults with refractory focal seizures, all reported previously: NCT00490035 [11]; NCT00464269 [9]; NCT01261325 [10]. Briefly, each study comprised an 8-week prospective baseline period and a 12-week treatment period without titration, followed by either a down-titration period (1–4 weeks) or entry into long-term follow-up studies (NCT00175916, NCT00150800, or NCT01339559). After the baseline period, patients were randomized to placebo or brivaracetam 5, 20, 50, 100, or 200 mg/day, according to study, administered in two equally divided doses. Details of the study designs and inclusion criteria are available in the original papers [9–11] and in Table 1.

Data were pooled from patients who were randomized to placebo (all studies) or the approved brivaracetam doses of 50, 100, and 200 mg/day (doses were different in each study).

2.2. Assessments

The QOLIE-31-P was a secondary or exploratory efficacy variable in all the original studies. It was completed at randomization, at weeks 4, 8 (in studies NCT00490035 and NCT00464269 only), and 12 of the treatment period, or at early discontinuation.

The QOLIE-31-P was adapted from an earlier epilepsy-specific HRQoL measure, the QOLIE-31. Both measures consist of 30 items making up 7 subscales (Emotional Well-being, Daily Activities/Social Functioning, Energy/Fatigue, Cognitive Functioning, Seizure Worry, Medication Effects, Overall Quality of Life), a health status item, and an item on the relative importance of each subscale. The QOLIE-31-P also includes 7 items assessing the degree of 'distress' reported by the patient related to each subscale topic (distress scores). The total score is a weighted sum of the subscale scores [12]. Total score and subscale scores range from 0 to 100, with higher scores representing better HRQoL. Distress scores also range from 0 to 100, with higher scores indicating higher distress.

2.3. Statistical analysis

This analysis was conducted post-hoc on pooled data from three different brivaracetam studies. As in the original studies, the intent-to-treat (ITT) population was defined as all randomized patients who received at least one dose of study medication.

Mean baseline scores, and mean change from baseline to week 12 (or early discontinuation), are reported using the last observation carried forward method. Mean change from baseline was compared between each brivaracetam dose and placebo using analysis of covariance (ANCOVA), controlling for baseline score. As this analysis was exploratory and p-values were not controlled for multiple testing, the p-values were nominal and are presented for illustrative purposes.

Percentages of patients with clinically meaningful improvements in QOLIE-31-P scores were determined using Minimal Important Change (MIC) thresholds defined in the literature [13]. The MIC threshold is

Table 1
Summary of studies included.

Study	NCT number	Study design				Key inclusion criteria			Baseline characteristics	
		Baseline period (weeks)	Treatment period (weeks)	Timing of QOLIE-31-P measurements[a]	BRV dosages (mg/day)	Age at randomization (years)	Baseline focal seizures	Concomitant AEDs	Regions [14]	Time period of recording prior AEDs
N01252 [11]	NCT00490035	8	12	Randomization, weeks 4, 8, 12[b]	20, **50**, **100**	16–70	≥2 per month for 3 months prior to screening ≥8 during baseline period	1–2	Western Europe, Eastern Europe, Asia	For 5 years prior to baseline period
N01253 [9]	NCT00464269	8	12	Randomization, weeks 4, 8, 12[b]	5, 20, **50**	16–70	≥2 per month for 3 months prior to screening ≥8 during baseline period	1–2	North and Latin America, Australia	For 5 years prior to baseline period
N01358 [10]	NCT01261325	8	12	Randomization, week 12[b]	**100**, **200**	16–80	≥2 per month for 3 months prior to baseline period ≥8 during baseline period, with ≥2 per 4-week interval	1–2	North and Latin America, Western and Eastern Europe, Asia	At any time prior to baseline period

BRV dosages reported in the current analysis and retained as the efficacy doses are given in bold text.
AED, antiepileptic drug; BRV, brivaracetam; QOLIE-31-P, Patient-Weighted Quality of Life in Epilepsy Questionnaire.
[a] QOLIE-31-P was also measured at the early discontinuation visit in patients who discontinued treatment.
[b] Week 12 = end of the treatment period.

Download English Version:

https://daneshyari.com/en/article/5628404

Download Persian Version:

https://daneshyari.com/article/5628404

Daneshyari.com