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Long-term lacosamide retention—Real-world experience at a tertiary epilepsy center in Ireland

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ABSTRACT

Purpose: To estimate the rate of long-term lacosamide retention among a real-world group of patients at a tertiary epilepsy center in Ireland.
Methods: One-hundred adults first prescribed lacosamide for epilepsy between January 2010 and August 2014 at Cork University Hospital were randomly selected for a retrospective analysis of medical records covering two years of subsequent epilepsy clinic follow-up to ascertain whether lacosamide was continued or withdrawn.
Results: Of 100 patients, (51 males, mean age 40.8 years, 94 with drug-resistant epilepsy, 76 with focal epilepsy, 25 with intellectual disabilities, 34 with mental health disorders, and 42 with medical comorbidities), lacosamide was prescribed as an adjunct in 85. Lacosamide retention at 12 and 24 months was 76% and 71%, respectively. Twenty-five patients stopped lacosamide due to ineffective seizure control. Adverse-effects were responsible for lacosamide discontinuation in three patients and one patient stopped lacosamide pre-pregnancy.
Conclusion: The relatively high retention rate at two years suggests that lacosamide is generally well tolerated among people with a range of different epilepsy subtypes, intellectual disabilities, medical comorbidities, and mental health disorders, and can aid seizure control in adult patients with a range of difficult-to-treat epilepsies.

1. Introduction

The anti-epileptic drug (AED) lacosamide—a functionalized amino acid thought to selectively enhance slow inactivation of voltage-gated sodium channels [1,2]—was licensed in the European Union in 2008 as adjunctive therapy in the treatment of focal seizures with or without secondary generalization [3]. The efficacy and tolerability of lacosamide were demonstrated in double-blinded, placebo-controlled, multicenter, randomized trials [4–6]. Studies reporting post-marketing clinical experience with lacosamide [7–12] provide supplementary information based on cohorts that are more representative of circumstances encountered in day-to-day clinical practice. To date, no such evaluations from Ireland have been published and there is only limited real-world information reported for long-term adjunctive lacosamide use in people with intellectual disabilities, mental health disorders, multiple medical comorbidities, genetic generalized epilepsies or those prescribed lacosamide as monotherapy. This study aimed to add to real-world data on lacosamide use among a naturalistic cohort of patients at a tertiary epilepsy center in Ireland, by estimating the rate of long-term lacosamide retention as a marker of drug efficacy and tolerability.

2. Methods

All adult patients under the care of a single consultant epileptologist/neurologist at Cork University Hospital who were prescribed lacosamide for seizure control were identified through a search of an electronic patient database in August 2016. Patients first prescribed lacosamide between January 2010 and August 2014 were allocated an electronically generated random number, then arranged in ascending order of random numbers, and the first 100 patients were included in the study. A retrospective analysis of electronic and paper-based medical records was conducted for each patient to establish demographic details and whether lacosamide prescription continued over two years of serial routine outpatient clinic follow-up. If lacosamide was subsequently withdrawn, the stop date and reasons for discontinuation were recorded.

This study was conducted in full compliance with local and national Health Service Executive standards and guidelines regarding research ethics and informed patient consent.

Abbreviations: AED, anti-epileptic drug; CBZ, carbamazepine; CLB, clobazam; CLN, clonazepam; DZP, diazepam; EMU, epilepsy monitoring unit; ESL, eslicarbazepine; GGE, genetic generalised epilepsy; GBP, gabapentin; GTCS, generalised tonic clonic seizure; LCM, lacosamide; LEV, levetiracetam; LRE, localization-related epilepsy; LTG, lamotrigine; NTZ, nitrazepam; OXC, oxcarbazepine; PB, phenobarbital; PHT, phenytoin; PRM, primidone; RFN, rufinamide; SGE, symptomatic generalized epilepsy; TPM, topiramate; VNS, vagus nerve stimulator; VPA, sodium valproate; ZNS, zonisamide.

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Table 1
Clinical features of 100 epilepsy patients treated with lacosamide.
Mental health disorders were alcohol misuse (n = 5), autism (1), depression/anxiety (20), eating disorder (2), obsessive compulsive disorder (1), and psychosis (5). Medical comorbidities (multiple in some patients) were asthma (n = 6), atrial fibrillation (1), benign prostatic hyperplasia (2), cerebrovascular disease (2), diabetes mellitus type I (1), diabetes mellitus type II (1), diverticulitis (1), duodenal ulcer (1), end-stage kidney disease (1), folate deficiency (1), gastro-esophageal reflux disease (1), glaucoma (1), hepatitis C virus (1), hereditary spastic paraplegia (1), hyperlipidemia (15), hypertension (7), hypothyroidism (2), iron deficiency anemia (1), irritable bowel syndrome (2), ischemic heart disease (3), left ventricular failure (1), migraine (3), mitral regurgitation (1), multiple sclerosis (2), neurofibromatosis type I (1), obstructive sleep apnea (1), osteoarthritis (1), osteoporosis (2), polycystic ovarian syndrome (1), pulmonary stenosis (1), Raynaud's syndrome (2), renal abscess (1), renal calculi (1), septo-optic dysplasia (1), systemic lupus erythematosus (1), tuberous sclerosis complex (1), ulcerative colitis (1), urolithiasis (1), uterine fibroids (1), and visual impairment (4).

Epilepsy description (n)	Drug resistant	Intellectual disability	Mental health disorder	Medical comorbidity	VNS	Post-epilepsy surgery	Awaiting epilepsy surgery	Awaiting EMU
GGE (7)	7	1	2	5	1	0	0	0
Lesional extra-temporal LRE (17)	17	5	6	8	3	0	0	0
Lesional temporal LRE (23)	23	4	7	10	1	9	3	2
LRE unclassified (21)	17	3	10	11	3	0	0	6
Non-lesional extra-temporal LRE (9)	9	–	3	–	1	0	2	0
Non-lesional temporal LRE (6)	6	1	1	1	1	1	1	0
SGE (11)	10	10	3	5	6	0	0	0
Unclassified (6)	5	1	2	2	0	0	0	1
TOTAL	94	25	34	42	16	10	6	9

EMU, epilepsy monitoring unit; *GGE*, genetic generalized epilepsy; *LRE*, localization-related epilepsy (focal epilepsy); *SGE*, symptomatic generalized epilepsy; *VNS*, vagus nerve stimulator.

3. Results

Three-hundred and nine patients were identified from the initial patient database interrogation and 137 met the inclusion criteria. Of the 100 randomly selected patients in the study, 51 were male and the mean age was 40.8 years (median 40, mode 32, range 18–84). The mean number of epilepsy out-patient clinic follow-up appointments during the two-year period following lacosamide initiation was 5 per patient (median 5, mode 4, range 3–12).

Seventy-six patients had focal epilepsy—lesional temporal lobe epilepsy, lesional extra-temporal epilepsy, and unclassified types of focal/localization-related epilepsy (LRE) were the most common subgroups (Table 1). Twenty-five patients had an intellectual disability. Thirty-four patients had a mental health disorder, with depression/anxiety, psychosis, and alcohol misuse the most prevalent. Forty-two patients had at least one medical comorbidity, of which the most common diagnoses were hyperlipidaemia, hypertension, asthma, migraine, and ischaemic heart disease.

Ninety-four patients were considered to have drug-resistant epilepsy, in that they experienced ongoing seizures despite trials of two or more tolerated, appropriately chosen and used AEDs. Seizures in all patients failed to adequately improve with at least one other AED prior to starting lacosamide (Fig. 1), with a mean number of failed AEDs (excluding lacosamide) per person of 4.9 (median 4, mode 4, range 1–14). Sixteen patients had vagus nerve stimulator (VNS) implants, ten

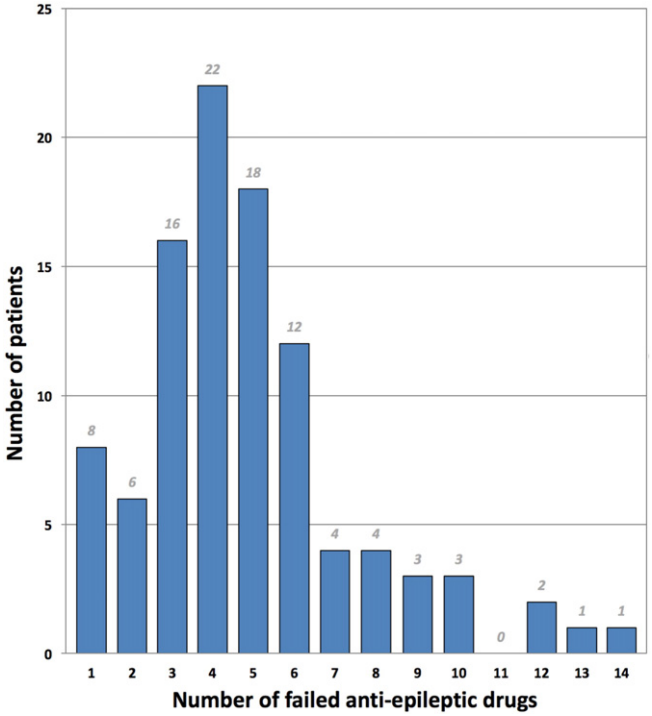

Fig. 1. Number of failed AEDs (excluding lacosamide) for 100 patients.

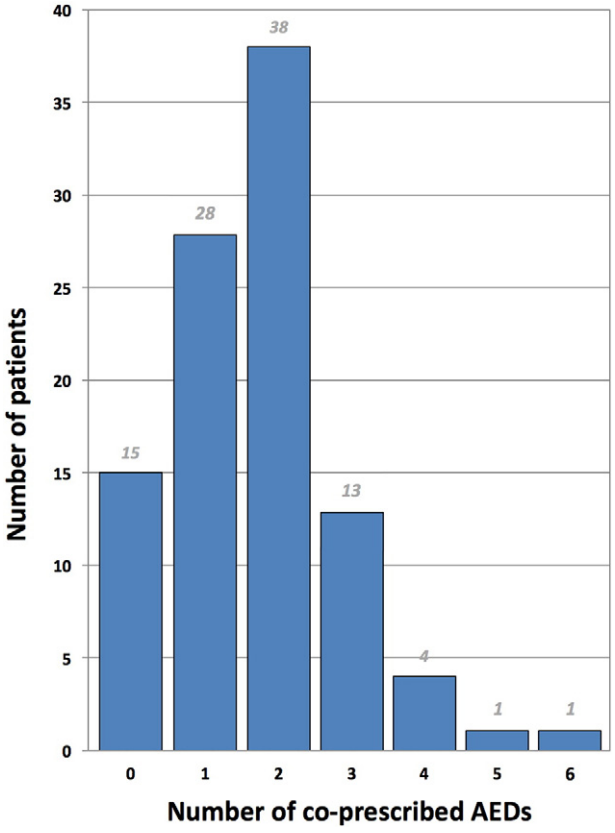

Fig. 2. Number of co-prescribed AEDs for 100 patients taking lacosamide. Fifteen patients received lacosamide monotherapy.