

Supplementary table 1: Study schedule

Procedure	Inclusion	Titration		Maintenance/Treatment				Vx
		V1	V2	V3	V4	V5	V6	
Visit	V0	V1	V2	V3	V4	V5	V6	Vx
Week	0	3	6	18	30	42	58	
Informed Consent	X							
Inclusion/Exclusion	X							
Medical and Psychiatric History	X							
Seizure history and classification	X	X	X	X	X	X	X	X
Concomitant Medication	X	X	X	X	X	X	X	X
AED dosage		X	X	X	X	X	X	X
EEG and MRI/CCT ¹	X							
Physical and neurological exam ²	X						X	
Brief neurological exam			X	X	X			X
Clinical Labs: Chemistry/Haematology	X		X		X		X	
PK Serum sample – drugs			X		X		X	
Seizure Diary review			X	X	X	X	X	X
Randomization	X							
Dispensing of subject diary	X		X	X	X	X		
Dispensing of trial medication	X		X	X	X	X		
Return of trial medication			X	X	X	X	X	
Tel. Contact		X						
AE Reporting		X	X	X	X	X	X	X
QOLIE-31 ³	X				X		X	
Toxicity scale ⁴	X				X		X	
EpiTrack ⁵	X				X		X	
Final information							X	
Post trial medication							X	

1 – If not done within the last 6 months prior screening

2 – Including vital signs (RR, pulse rate) and recording of body weight in kg

3 – Quality of life assessment (QOLIE-31)

4 – Portland neurotoxicity scale (PNS) questionnaire

5 – Standardized cognitive testing

Vx – additional, optional visit at the discretion of the investigator

Supplementary table 2: Retention rate at week 58 stratified by number of seizures at study entry (modified intent-to-treat population, n = 359)

Number of seizures at study entry	Patient number	Retention rate (95% CI), %			p value [§]
		Carbamazepine	Lamotrigine	Levetiracetam	
		(n=117)	(n=114)	(n=120)	
1*	151	32.7 (20.3–45.1)	51.1 (36.5–65.7)	60.8 (47.4–74.2)	0.013
2	91	53.8 (34.7–73.0)	59.5 (43.6–75.3)	50.0 (31.5–68.5)	0.75
3–5	71	72.2 (51.5–92.9)	66.7 (46.5–86.8)	78.1 (63.8–92.4)	0.66
>5	38	44.4 (21.5–67.4)	45.5 (16.0–74.9)	55.6 (23.1–88.0)	0.92

*Plus epileptiform electroencephalogram or lesion on cranial magnetic resonance or computed tomography imaging; [§] between all groups

Supplementary table 3: Treatment emergent adverse events reported by $\geq 5\%$ of patients in any treatment group (safety population, n = 360)

No. (%)	Overall (n=360)	CR-Carbamazepine (n=121)	Lamotrigine (n=117)	Levetiracetam (n=122)
Nervous system disorders				
Dizziness	86 (23.9)	29 (24.0)	26 (22.2)	31 (25.4)
Headache	54 (15.0)	20 (16.5)	18 (15.4)	16 (13.1)
General disorders				
Fatigue	89 (24.7)	41 (33.9)	19 (16.2)	29 (23.8)
Gait disturbance	22 (6.1)	10 (8.3)	5 (4.3)	7 (5.7)
Gastrointestinal disorders				
Nausea	38 (10.6)	14 (11.6)	15 (12.8)	9 (7.4)
Constipation	13 (3.6)	10 (8.3)	2 (1.7)	1 (0.8)
Diarrhea	18 (5.0)	7 (5.8)	6 (5.1)	5 (4.1)
Dry mouth	12 (3.3)	5 (4.1)	6 (5.1)	1 (0.8)
Skin and subcutaneous tissue disorders				
Pruritus	13 (3.6)	6 (5.0)	4 (3.4)	3 (2.5)
Investigations				
Gamma-glutamyltransferase increased	24 (6.7)	18 (14.9)	5 (4.3)	1 (0.8)
Renal and urinary disorders				
Renal failure	10 (2.8)	0	7 (6.0)	3 (2.5)
Psychiatric disorders				
Sleep disorder	13 (3.6)	2 (1.7)	8 (6.8)	3 (2.5)

Supplementary table 4: Adverse events reported by patients in any treatment group (safety population, n = 360)

n (%)	Overall (n=360)	Carbamazepine (n=121)	Lamotrigine (n=117)	Levetiracetam (n=122)
Blood and lymphatic system disorders	7 (1.9)	3 (2.5)	3 (2.6)	1 (0.8)
Anemia	3 (0.8)	1 (0.8)	2 (1.7)	0
Iron deficiency anemia	1 (0.3)	0	0	1 (0.8)
Lymphadenopathy	3 (0.8)	2 (1.7)	1 (0.9)	0
Cardiac disorders	22 (6.1)	5 (4.1)	7 (6.0)	10 (8.2)
Acute coronary syndrome	2 (0.6)	1 (0.8)	0	1 (0.8)
Acute myocardial infarction	1 (0.3)	0	0	1 (0.8)
Angina pectoris	5 (1.4)	2 (1.7)	1 (0.9)	2 (1.6)
Arrhythmia	1 (0.3)	1 (0.8)	0	0
Cardiac failure	2 (0.6)	0	0	2 (1.6)
Cardiac flutter	1 (0.3)	0	0	1 (0.8)
Cardiovascular disorder	1 (0.3)	1 (0.8)	0	0
Coronary artery disease	1 (0.3)	0	0	1 (0.8)
Coronary artery stenosis	2 (0.6)	0	1 (0.9)	1 (0.8)
Extrasystoles	2 (0.6)	0	2 (1.7)	0
Myocardial infarction	3 (0.8)	0	2 (1.7)	1 (0.8)
Palpitations	3 (0.8)	1 (0.8)	2 (1.7)	0
Ventricular hypokinesia	1 (0.3)	0	0	1 (0.8)
Congenital, familial and genetic disorders	2 (0.6)	1 (0.8)	1 (0.9)	0
Epidermolysis	1 (0.3)	0	1 (0.9)	0
Odontogenic cyst	1 (0.3)	1 (0.8)	0	0
Ear and labyrinth disorders	24 (6.7)	6 (5.0)	9 (7.7)	9 (7.4)
Cerumen impaction	1 (0.3)	0	1 (0.9)	0
Ear pain	1 (0.3)	0	1 (0.9)	0
Hearing impaired	1 (0.3)	1 (0.8)	0	0
Hypoacusis	3 (0.8)	0	1 (0.9)	2 (1.6)
Sudden hearing loss	1 (0.3)	0	1 (0.9)	0
Tinnitus	9 (2.5)	4 (3.3)	2 (1.7)	3 (2.5)
Vertigo	9 (2.5)	2 (1.7)	3 (2.6)	4 (3.3)
Eye disorders	31 (8.6)	10 (8.3)	11 (9.4)	10 (8.2)
Abnormal sensation in eye	1 (0.3)	1 (0.8)	0	0
Cataract	1 (0.3)	0	0	1 (0.8)
Conjunctival hemorrhage	1 (0.3)	0	0	1 (0.8)
Conjunctivitis	1 (0.3)	1 (0.8)	0	0
Diplopia	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Eye disorder	1 (0.3)	1 (0.8)	0	0
Eye haemorrhage	1 (0.3)	1 (0.8)	0	0
Eye irritation	1 (0.3)	0	1 (0.9)	0
Eye pain	1 (0.3)	1 (0.8)	0	0
Eye pruritus	2 (0.6)	1 (0.8)	1 (0.9)	0
Glaucoma	1 (0.3)	1 (0.8)	0	0
Lacrimation increased	1 (0.3)	0	1 (0.9)	0
Ocular hyperaemia	1 (0.3)	0	1 (0.9)	0
Photopsia	1 (0.3)	0	1 (0.9)	0

Saccadic eye movement	3 (0.8)	1 (0.8)	0	2 (1.6)
Scintillating scotoma	3 (0.8)	1 (0.8)	2 (1.7)	0
Vision blurred	7 (1.9)	2 (1.7)	4 (3.4)	1 (0.8)
Visual acuity reduced	2 (0.6)	1 (0.8)	0	1 (0.8)
Visual impairment	10 (2.8)	2 (1.7)	4 (3.4)	4 (3.3)
Vitreous detachment	1 (0.3)	0	0	1 (0.8)
Gastrointestinal disorders	140 (38.9)	54 (44.6)	47 (40.2)	39 (32.0)
Abdominal discomfort	3 (0.8)	2 (1.7)	1 (0.9)	0
Abdominal distension	2 (0.6)	0	0	2 (1.6)
Abdominal pain	9 (2.5)	5 (4.1)	2 (1.7)	2 (1.6)
Abdominal pain lower	1 (0.3)	0	0	1 (0.8)
Abdominal pain upper	12 (3.3)	5 (4.1)	4 (3.4)	3 (2.5)
Constipation	23 (6.4)	16 (13.2)	5 (4.3)	2 (1.6)
Diarrhea	39 (10.8)	16 (13.2)	14 (12.0)	9 (7.4)
Diverticulum	1 (0.3)	0	0	1 (0.8)
Diverticulum intestinal	1 (0.3)	0	0	1 (0.8)
Dry mouth	13 (3.6)	5 (4.1)	7 (6.0)	1 (0.8)
Dyspepsia	7 (1.9)	3 (2.5)	2 (1.7)	2 (1.6)
Dysphagia	3 (0.8)	0	1 (0.9)	2 (1.6)
Fecal incontinence	1 (0.3)	0	0	1 (0.8)
Feces discoloured	2 (0.6)	0	1 (0.9)	1 (0.8)
Feces hard	1 (0.3)	0	1 (0.9)	0
Flatulence	8 (2.2)	3 (2.5)	1 (0.9)	4 (3.3)
Frequent bowel movements	2 (0.6)	0	1 (0.9)	1 (0.8)
Gastric disorder	1 (0.3)	0	0	1 (0.8)
Gastritis	2 (0.6)	1 (0.8)	1 (0.9)	0
Gastrointestinal disorder	4 (1.1)	1 (0.8)	3 (2.6)	0
Gastrointestinal hemorrhage	1 (0.3)	1 (0.8)	0	0
Gastrointestinal motility disorder	1 (0.3)	0	0	1 (0.8)
Gastrointestinal pain	2 (0.6)	0	1 (0.9)	1 (0.8)
Hematochezia	1 (0.3)	0	1 (0.9)	0
Ileus	1 (0.3)	0	1 (0.9)	0
Intestinal ischemia	1 (0.3)	1 (0.8)	0	0
Intestinal polyp	1 (0.3)	0	0	1 (0.8)
Nausea	48 (13.3)	20 (16.5)	17 (14.5)	11 (9.0)
Pancreatitis acute	1 (0.3)	0	0	1 (0.8)
Stomatitis	1 (0.3)	1 (0.8)	0	0
Subileus	2 (0.6)	1 (0.8)	1 (0.9)	0
Swollen tongue	1 (0.3)	0	1 (0.9)	0
Tongue discolouration	1 (0.3)	1 (0.8)	0	0
Toothache	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Vomiting	19 (5.3)	7 (5.8)	7 (6.0)	5 (4.1)
General disorders and administration site conditions	150 (41.7)	60 (49.6)	42 (35.9)	48 (39.3)
Asthenia	6 (1.7)	1 (0.8)	3 (2.6)	2 (1.6)
Chest discomfort	3 (0.8)	2 (1.7)	0	1 (0.8)
Chest pain	4 (1.1)	2 (1.7)	2 (1.7)	0
Chills	1 (0.3)	0	1 (0.9)	0
Death	2 (0.6)	1 (0.8)	0	1 (0.8)
Device occlusion	1 (0.3)	1 (0.8)	0	0
Drug interaction	1 (0.3)	1 (0.8)	0	0
Edema peripheral	11 (3.1)	5 (4.1)	3 (2.6)	3 (2.5)
Facial pain	3 (0.8)	0	1 (0.9)	2 (1.6)
Fatigue	100 (27.8)	46 (38.0)	23 (19.7)	31 (25.4)

Feeling abnormal	4 (1.1)	1 (0.8)	1 (0.9)	2 (1.6)
Feeling cold	2 (0.6)	0	0	2 (1.6)
Feeling hot	1 (0.3)	0	0	1 (0.8)
Gait disturbance	26 (7.2)	12 (9.9)	5 (4.3)	9 (7.4)
General physical health deterioration	1 (0.3)	0	0	1 (0.8)
Hernia	1 (0.3)	0	1 (0.9)	
Irritability	5 (1.4)	2 (1.7)	0	3 (2.5)
Malaise	6 (1.7)	2 (1.7)	2 (1.7)	2 (1.6)
Pain	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Performance status decreased	2 (0.6)	0	1 (0.9)	1 (0.8)
Pyrexia	4 (1.1)	2 (1.7)	1 (0.9)	1 (0.8)
Sudden cardiac death	1 (0.3)	0	1 (0.9)	0
Temperature intolerance	1 (0.3)	0	0	1 (0.8)
Hepatobiliary disorders	4 (1.1)	3 (2.5)	1 (0.9)	0
Cholecystitis	1 (0.3)	1 (0.8)	0	0
Hepatic steatosis	1 (0.3)	0	1 (0.9)	0
Liver disorder	2 (0.6)	2 (1.7)	0	0
Immune system disorders	3 (0.8)	1 (0.8)	0	2 (1.6)
Drug hypersensitivity	1 (0.3)	0	0	1 (0.8)
Hypersensitivity	1 (0.3)	0	0	1 (0.8)
Seasonal allergy	1 (0.3)	1 (0.8)	0	0
Infections and infestations	93 (25.8)	30 (24.8)	31 (26.5)	32 (26.2)
Acute tonsillitis	1 (0.3)	1 (0.8)	0	0
Borrelia infection	1 (0.3)	0	0	1 (0.8)
Bronchitis	9 (2.5)	2 (1.7)	7 (6.0)	0
Bronchopneumonia	1 (0.3)	0	0	1 (0.8)
Cholecystitis infective	1 (0.3)	0	1 (0.9)	0
Cystitis	6 (1.7)	4 (3.3)	1 (0.9)	1 (0.8)
Erysipelas	1 (0.3)	1 (0.8)	0	0
Erythema migrans	1 (0.3)	0	0	1 (0.8)
Eye infection	2 (0.6)	1 (0.8)	0	1 (0.8)
Eyelid infection	1 (0.3)	0	1 (0.9)	0
Gastroenteritis	4 (1.1)	1 (0.8)	2 (1.7)	1 (0.8)
Gastroenteritis norovirus	1 (0.3)	0	1 (0.9)	0
Gastrointestinal infection	4 (1.1)	2 (1.7)	1 (0.9)	1 (0.8)
Herpes zoster	3 (0.8)	0	2 (1.7)	1 (0.8)
Infected dermal cyst	1 (0.3)	0	0	1 (0.8)
Infection	2 (0.6)	0	2 (1.7)	0
Infectious peritonitis	1 (0.3)	1 (0.8)	0	0
Influenza	1 (0.3)	1 (0.8)	0	0
Localized infection	1 (0.3)	1 (0.8)	0	0
Nasopharyngitis	41 (11.4)	13 (10.7)	8 (6.8)	20 (16.4)
Onychomycosis	1 (0.3)	0	0	1 (0.8)
Oral herpes	2 (0.6)	0	1 (0.9)	1 (0.8)
Pharyngitis	2 (0.6)	0	1 (0.9)	1 (0.8)
Pneumonia	5 (1.4)	3 (2.5)	1 (0.9)	1 (0.8)
Postoperative wound infection	1 (0.3)	0	1 (0.9)	0
Pyelonephritis	1 (0.3)	0	0	1 (0.8)
Rash pustular	1 (0.3)	0	0	1 (0.8)
Rhinitis	3 (0.8)	1 (0.8)	2 (1.7)	0
Sinusitis	2 (0.6)	1 (0.8)	1 (0.9)	0
Tooth infection	1 (0.3)	0	0	1 (0.8)
Tracheobronchitis	1 (0.3)	1 (0.8)	0	0
Urinary tract infection	13 (3.6)	6 (5.0)	3 (2.6)	4 (3.3)

Vestibular neuronitis	1 (0.3)	0	1 (0.9)	0
Viral infection	1 (0.3)	0	1 (0.9)	0
Injury, poisoning and procedural complications	38 (10.6)	11 (9.1)	16 (13.7)	11 (9.0)
Alcohol poisoning	1 (0.3)	0	1 (0.9)	0
Arthropod bite	1 (0.3)	1 (0.8)	0	0
Contusion	5 (1.4)	1 (0.8)	2 (1.7)	2 (1.6)
Excoriation	1 (0.3)	0	1 (0.9)	0
Fall	12 (3.3)	5 (4.1)	6 (5.1)	1 (0.8)
Hand fracture	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Head injury	1 (0.3)	0	1 (0.9)	0
Humerus fracture	1 (0.3)	0	1 (0.9)	0
Joint dislocation	1 (0.3)	0	1 (0.9)	0
Laceration	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Ligament sprain	4 (1.1)	1 (0.8)	0	3 (2.5)
Meniscus lesion	1 (0.3)	0	0	1 (0.8)
Muscle strain	4 (1.1)	1 (0.8)	1 (0.9)	2 (1.6)
Periorbital hematoma	1 (0.3)	1 (0.8)	0	0
Procedural pain	1 (0.3)	1 (0.8)	0	0
Radius fracture	2 (0.6)	0	2 (1.7)	0
Rib fracture	1 (0.3)	1 (0.8)	0	0
Spinal column injury	1 (0.3)	0	1 (0.9)	0
Tendon rupture	1 (0.3)	0	0	1 (0.8)
Thermal burn	1 (0.3)	0	0	1 (0.8)
Thoracic vertebral fracture	1 (0.3)	0	1 (0.9)	0
Wrist fracture	1 (0.3)	1 (0.8)	0	0
Investigations	75 (20.8)	34 (28.1)	20 (17.1)	21 (17.2)
Aspartate aminotransferase increased	1 (0.3)	1 (0.8)	0	0
Biopsy skin	1 (0.3)	1 (0.8)	0	0
Blood alkaline phosphatase abnormal	1 (0.3)	1 (0.8)	0	0
Blood alkaline phosphatase increased	2 (0.6)	2 (1.7)	0	0
Blood cholesterol increased	3 (0.8)	2 (1.7)	1 (0.9)	0
Blood creatinine increased	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Blood glucose fluctuation	1 (0.3)	0	1 (0.9)	0
Blood glucose increased	2 (0.6)	0	1 (0.9)	1 (0.8)
Blood potassium decreased	3 (0.8)	2 (1.7)	1 (0.9)	0
Blood potassium increased	1 (0.3)	1 (0.8)	0	0
Blood pressure increased	2 (0.6)	1 (0.8)	1 (0.9)	0
Blood sodium decreased	9 (2.5)	6 (5.0)	1 (0.9)	2 (1.6)
Blood sodium increased	1 (0.3)	0	0	1 (0.8)
Blood triglycerides increased	4 (1.1)	1 (0.8)	2 (1.7)	1 (0.8)
Blood urea increased	1 (0.3)	1 (0.8)	0	0
Cardiac murmur	1 (0.3)	0	1 (0.9)	0
Catheterisation cardiac	2 (0.6)	0	1 (0.9)	1 (0.8)
Endoscopy gastrointestinal	1 (0.3)	0	1 (0.9)	0
Endoscopy large bowel	1 (0.3)	0	0	1 (0.8)
Gamma-glutamyltransferase increased	27 (7.5)	18 (14.9)	5 (4.3)	4 (3.3)
Glomerular filtration rate decreased	1 (0.3)	0	0	1 (0.8)
Hepatic enzyme increased	1 (0.3)	1 (0.8)	0	0
Liver function test abnormal	6 (1.7)	4 (3.3)	2 (1.7)	0
Neurological examination abnormal	1 (0.3)	0	1 (0.9)	0

Nuclear magnetic resonance imaging	1 (0.3)	0	0	1 (0.8)
Renal function test abnormal	1 (0.3)	0	1 (0.9)	0
Transaminases increased	1 (0.3)	1 (0.8)	0	0
Weight decreased	5 (1.4)	0	1 (0.9)	4 (3.3)
Weight increased	12 (3.3)	3 (2.5)	4 (3.4)	5 (4.1)
White blood cell count decreased	1 (0.3)	1 (0.8)	0	0
White blood cell count increased	1 (0.3)	0	0	1 (0.8)
Metabolism and nutrition disorders	43 (11.9)	21 (17.4)	14 (12.0)	8 (6.6)
Decreased appetite	11 (3.1)	4 (3.3)	4 (3.4)	3 (2.5)
Dehydration	1 (0.3)	0	1 (0.9)	0
Diabetes mellitus	2 (0.6)	0	2 (1.7)	0
Diabetes mellitus inadequate control	1 (0.3)	0	0	1 (0.8)
Fluid retention	1 (0.3)	1 (0.8)	0	0
Gout	2 (0.6)	1 (0.8)	1 (0.9)	0
Hypercholesterolemia	12 (3.3)	4 (3.3)	5 (4.3)	3 (2.5)
Hyperglycemia	2 (0.6)	2 (1.7)	0	0
Hyperlipidemia	5 (1.4)	5 (4.1)	0	0
Hypertriglyceridemia	7 (1.9)	4 (3.3)	2 (1.7)	1 (0.8)
Hyperuricemia	2 (0.6)	0	0	2 (1.6)
Hypochloremia	1 (0.3)	0	1 (0.9)	0
Hypoglycemia	1 (0.3)	1 (0.8)	0	0
Hypokalemia	1 (0.3)	1 (0.8)	0	0
Hyponatremia	1 (0.3)	1 (0.8)	0	0
Increased appetite	1 (0.3)	1 (0.8)	0	0
Musculoskeletal and connective tissue disorders	82 (22.8)	21 (17.4)	31 (26.5)	30 (24.6)
Arthralgia	23 (6.4)	6 (5.0)	10 (8.5)	7 (5.7)
Arthritis	2 (0.6)	0	1 (0.9)	1 (0.8)
Arthropathy	1 (0.3)	0	0	1 (0.8)
Back pain	20 (5.6)	4 (3.3)	7 (6.0)	9 (7.4)
Bursitis	1 (0.3)	0	1 (0.9)	0
Exostosis	1 (0.3)	0	0	1 (0.8)
Flank pain	1 (0.3)	0	1 (0.9)	0
Groin pain	1 (0.3)	0	1 (0.9)	0
Intervertebral disc protrusion	1 (0.3)	0	1 (0.9)	0
Joint range of motion decreased	1 (0.3)	0	0	1 (0.8)
Joint swelling	2 (0.6)	0	0	2 (1.6)
Limb discomfort	1 (0.3)	0	0	1 (0.8)
Muscle spasms	8 (2.2)	1 (0.8)	2 (1.7)	5 (4.1)
Muscle swelling	1 (0.3)	0	0	1 (0.8)
Muscle tightness	3 (0.8)	2 (1.7)	1 (0.9)	0
Muscle twitching	2 (0.6)	1 (0.8)	0	1 (0.8)
Muscular weakness	2 (0.6)	0	1 (0.9)	1 (0.8)
Musculoskeletal discomfort	1 (0.3)	1 (0.8)	0	0
Musculoskeletal pain	5 (1.4)	0	2 (1.7)	3 (2.5)
Musculoskeletal stiffness	1 (0.3)	0	1 (0.9)	0
Myalgia	13 (3.6)	3 (2.5)	8 (6.8)	2 (1.6)
Neck pain	3 (0.8)	1 (0.8)	0	2 (1.6)
Osteoarthritis	6 (1.7)	3 (2.5)	3 (2.6)	0

Pain in extremity	18 (5.0)	3 (2.5)	7 (6.0)	8 (6.6)
Sensation of heaviness	1 (0.3)	0	1 (0.9)	0
Systemic lupus erythematosus	1 (0.3)	1 (0.8)	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	9 (2.5)	3 (2.5)	5 (4.3)	1 (0.8)
Anaplastic astrocytoma	1 (0.3)	0	1 (0.9)	0
Basal cell carcinoma	1 (0.3)	0	1 (0.9)	0
Brain neoplasm	1 (0.3)	0	1 (0.9)	0
Eyelid tumor	1 (0.3)	0	1 (0.9)	0
Lymphoma	1 (0.3)	0	0	1 (0.8)
Malignant melanoma	1 (0.3)	1 (0.8)	0	0
Meningioma	1 (0.3)	0	1 (0.9)	0
Metastatic bronchial carcinoma	1 (0.3)	1 (0.8)	0	0
Neoplasm skin	1 (0.3)	0	1 (0.9)	0
Renal cancer	1 (0.3)	1 (0.8)	0	0
Nervous system disorders	226 (62.8)	72 (59.5)	77 (65.8)	77 (63.1)
Acquired epileptic aphasia	2 (0.6)	2 (1.7)	0	0
Akathisia	1 (0.3)	0	0	1 (0.8)
Aphasia	4 (1.1)	2 (1.7)	1 (0.9)	1 (0.8)
Ataxia	2 (0.6)	0	1 (0.9)	1 (0.8)
Aura	3 (0.8)	1 (0.8)	2 (1.7)	0
Balance disorder	13 (3.6)	5 (4.1)	5 (4.3)	3 (2.5)
Carotid artery occlusion	1 (0.3)	0	1 (0.9)	0
Carpal tunnel syndrome	2 (0.6)	0	2 (1.7)	0
Cerebellar syndrome	1 (0.3)	0	0	1 (0.8)
Cerebral infarction	1 (0.3)	0	0	1 (0.8)
Cerebrovascular accident	2 (0.6)	0	1 (0.9)	1 (0.8)
Cervicobrachial syndrome	1 (0.3)	0	1 (0.9)	0
Clumsiness	1 (0.3)	1 (0.8)	0	0
Cognitive disorder	3 (0.8)	2 (1.7)	1 (0.9)	0
Complex partial seizures	9 (2.5)	5 (4.1)	3 (2.6)	1 (0.8)
Convulsion	25 (6.9)	8 (6.6)	12 (10.3)	5 (4.1)
Coordination abnormal	1 (0.3)	0	1 (0.9)	0
Crying	1 (0.3)	0	0	1 (0.8)
Cubital tunnel syndrome	1 (0.3)	0	0	1 (0.8)
Dementia	2 (0.6)	2 (1.7)	0	0
Disturbance in attention	11 (3.1)	3 (2.5)	5 (4.3)	3 (2.5)
Dizziness	105 (29.2)	33 (27.3)	36 (30.8)	36 (29.5)
Dizziness postural	4 (1.1)	0	2 (1.7)	2 (1.6)
Dysarthria	1 (0.3)	1 (0.8)	0	0
Dysgeusia	1 (0.3)	0	1 (0.9)	0
Dysstasia	3 (0.8)	2 (1.7)	1 (0.9)	0
Epilepsy	48 (13.3)	11 (9.1)	15 (12.8)	22 (18.0)
Epileptic aura	3 (0.8)	1 (0.8)	0	2 (1.6)
Grand mal convulsion	14 (3.9)	2 (1.7)	10 (8.5)	2 (1.6)
Hemorrhage intracranial	1 (0.3)	0	1 (0.9)	0
Head discomfort	1 (0.3)	0	1 (0.9)	0
Headache	89 (24.7)	29 (24.0)	29 (24.8)	31 (25.4)
Hemiparesis	1 (0.3)	1 (0.8)	0	0
Hypersomnia	2 (0.6)	1 (0.8)	0	1 (0.8)
Hypertonia	5 (1.4)	1 (0.8)	3 (2.6)	1 (0.8)
Hypoesthesia	3 (0.8)	0	2 (1.7)	1 (0.8)
Hypokinesia	1 (0.3)	1 (0.8)	0	0
Intention tremor	1 (0.3)	1 (0.8)	0	0
Ischemic cerebral infarction	1 (0.3)	0	1 (0.9)	0

Lethargy	1 (0.3)	0	1 (0.9)	0
Loss of consciousness	2 (0.6)	1 (0.8)	0	1 (0.8)
Memory impairment	18 (5.0)	7 (5.8)	6 (5.1)	5 (4.1)
Mental impairment	1 (0.3)	1 (0.8)	0	0
Migraine	3 (0.8)	0	1 (0.9)	2 (1.6)
Monoplegia	1 (0.3)	0	0	1 (0.8)
Muscle spasticity	2 (0.6)	1 (0.8)	1 (0.9)	0
Myoclonic epilepsy	2 (0.6)	0	1 (0.9)	1 (0.8)
Neurological decompensation	1 (0.3)	0	0	1 (0.8)
Nystagmus	1 (0.3)	0	1 (0.9)	0
Orthostatic intolerance	1 (0.3)	0	1 (0.9)	0
Paraesthesia	9 (2.5)	3 (2.5)	3 (2.6)	3 (2.5)
Paralysis	1 (0.3)	0	0	1 (0.8)
Parkinson's disease	1 (0.3)	0	1 (0.9)	0
Parkinsonism	1 (0.3)	1 (0.8)	0	0
Parosmia	1 (0.3)	0	1 (0.9)	0
Partial seizures	17 (4.7)	5 (4.1)	10 (8.5)	2 (1.6)
Petit mal epilepsy	1 (0.3)	1 (0.8)	0	0
Poor quality sleep	1 (0.3)	0	0	1 (0.8)
Postictal paralysis	1 (0.3)	1 (0.8)	0	0
Presyncope	3 (0.8)	0	2 (1.7)	1 (0.8)
Sciatica	2 (0.6)	0	1 (0.9)	1 (0.8)
Simple partial seizures	1 (0.3)	0	1 (0.9)	0
Speech disorder	2 (0.6)	1 (0.8)	0	1 (0.8)
Status epilepticus	2 (0.6)	0	0	2 (1.6)
Syncope	5 (1.4)	2 (1.7)	1 (0.9)	2 (1.6)
Tongue biting	2 (0.6)	0	1 (0.9)	1 (0.8)
Transient ischemic attack	4 (1.1)	0	2 (1.7)	2 (1.6)
Tremor	17 (4.7)	5 (4.1)	6 (5.1)	6 (4.9)
Vocal cord paralysis	2 (0.6)	1 (0.8)	1 (0.9)	0
Psychiatric disorders	85 (23.6)	25 (20.7)	31 (26.5)	29 (23.8)
Aggression	4 (1.1)	1 (0.8)	1 (0.9)	2 (1.6)
Agitation	11 (3.1)	3 (2.5)	3 (2.6)	5 (4.1)
Agoraphobia	1 (0.3)	0	1 (0.9)	0
Anxiety	8 (2.2)	3 (2.5)	5 (4.3)	0
Apathy	8 (2.2)	3 (2.5)	2 (1.7)	3 (2.5)
Bradyphrenia	2 (0.6)	1 (0.8)	1 (0.9)	0
Bruxism	1 (0.3)	0	0	1 (0.8)
Completed suicide	1 (0.3)	0	0	1 (0.8)
Confusional state	10 (2.8)	5 (4.1)	2 (1.7)	3 (2.5)
Delirium	1 (0.3)	0	0	1 (0.8)
Depressed mood	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Depression	15 (4.2)	6 (5.0)	4 (3.4)	5 (4.1)
Disorientation	4 (1.1)	1 (0.8)	2 (1.7)	1 (0.8)
Hallucination	1 (0.3)	0	1 (0.9)	0
Impatience	1 (0.3)	0	0	1 (0.8)
Indifference	1 (0.3)	1 (0.8)	0	0
Initial insomnia	7 (1.9)	2 (1.7)	3 (2.6)	2 (1.6)
Insomnia	8 (2.2)	2 (1.7)	3 (2.6)	3 (2.5)
Nervousness	5 (1.4)	0	3 (2.6)	2 (1.6)
Nightmare	2 (0.6)	0	1 (0.9)	1 (0.8)
Panic attack	2 (0.6)	0	1 (0.9)	1 (0.8)
Parasomnia	1 (0.3)	0	0	1 (0.8)
Personality change	1 (0.3)	0	0	1 (0.8)
Psychomotor retardation	2 (0.6)	2 (1.7)	0	0

Psychotic disorder	1 (0.3)	0	1 (0.9)	0
Psychotic disorder due to a general medical condition	1 (0.3)	0	1 (0.9)	0
Restlessness	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Sleep disorder	18 (5.0)	5 (4.1)	9 (7.7)	4 (3.3)
Suicidal ideation	1 (0.3)	0	1 (0.9)	0
Renal and urinary disorders	33 (9.2)	6 (5.0)	11 (9.4)	16 (13.1)
Bladder disorder	1 (0.3)	0	0	1 (0.8)
Bladder pain	1 (0.3)	0	0	1 (0.8)
Micturition disorder	1 (0.3)	1 (0.8)	0	0
Micturition urgency	1 (0.3)	0	1 (0.9)	0
Nocturia	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Pollakiuria	1 (0.3)	1 (0.8)	0	0
Polyuria	2 (0.6)	2 (1.7)	0	0
Renal failure	18 (5.0)	0	8 (6.8)	10 (8.2)
Renal failure acute	2 (0.6)	0	1 (0.9)	1 (0.8)
Renal pain	2 (0.6)	1 (0.8)	0	1 (0.8)
Urinary retention	1 (0.3)	0	0	1 (0.8)
Reproductive system and breast disorders	11 (3.1)	3 (2.5)	3 (2.6)	5 (4.1)
Benign prostatic hyperplasia	5 (1.4)	0	2 (1.7)	3 (2.5)
Breast enlargement	1 (0.3)	1 (0.8)	0	0
Breast pain	1 (0.3)	0	0	1 (0.8)
Ejaculation disorder	1 (0.3)	1 (0.8)	0	0
Erectile dysfunction	3 (0.8)	2 (1.7)	0	1 (0.8)
Prostatitis	1 (0.3)	0	1 (0.9)	0
Respiratory, thoracic and mediastinal disorders	58 (16.1)	19 (15.7)	21 (17.9)	18 (14.8)
Asthma	2 (0.6)	0	1 (0.9)	1 (0.8)
Bronchitis chronic	1 (0.3)	1 (0.8)	0	0
Chronic obstructive pulmonary disease	1 (0.3)	0	1 (0.9)	0
Cough	26 (7.2)	9 (7.4)	8 (6.8)	9 (7.4)
Dysphonia	4 (1.1)	0	2 (1.7)	2 (1.6)
Dyspnea	8 (2.2)	2 (1.7)	4 (3.4)	2 (1.6)
Dyspnea exertional	3 (0.8)	1 (0.8)	0	2 (1.6)
Epistaxis	11 (3.1)	4 (3.3)	5 (4.3)	2 (1.6)
Hemoptysis	1 (0.3)	1 (0.8)	0	0
Hiccups	1 (0.3)	1 (0.8)	0	0
Lung disorder	1 (0.3)	0	0	1 (0.8)
Nasal dryness	1 (0.3)	1 (0.8)	0	0
Oropharyngeal pain	6 (1.7)	2 (1.7)	2 (1.7)	2 (1.6)
Productive cough	1 (0.3)	1 (0.8)	0	0
Pulmonary embolism	2 (0.6)	1 (0.8)	1 (0.9)	0
Sleep apnea syndrome	2 (0.6)	1 (0.8)	1 (0.9)	0
Vocal cord inflammation	1 (0.3)	0	0	1 (0.8)
Skin and subcutaneous tissue disorders	82 (22.8)	37 (30.6)	19 (16.2)	26 (21.3)
Acne	1 (0.3)	0	0	1 (0.8)
Actinic keratosis	1 (0.3)	1 (0.8)	0	0
Alopecia	8 (2.2)	3 (2.5)	3 (2.6)	2 (1.6)
Dermatitis allergic	5 (1.4)	4 (3.3)	0	1 (0.8)
Dermatitis atopic	1 (0.3)	1 (0.8)	0	0
Drug eruption	3 (0.8)	3 (2.5)	0	0

Dry skin	3 (0.8)	0	0	3 (2.5)
Dyshidrosis	1 (0.3)	0	0	1 (0.8)
Eczema	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Eczema asteatotic	1 (0.3)	1 (0.8)	0	0
Eczema nummular	1 (0.3)	1 (0.8)	0	0
Erythema	7 (1.9)	3 (2.5)	0	4 (3.3)
Hyperhidrosis	6 (1.7)	5 (4.1)	1 (0.9)	0
Lichen planus	1 (0.3)	1 (0.8)	0	0
Night sweats	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Onychoclasia	2 (0.6)	1 (0.8)	1 (0.9)	0
Pruritus	24 (6.7)	10 (8.3)	9 (7.7)	5 (4.1)
Pruritus generalized	1 (0.3)	1 (0.8)	0	0
Purpura	1 (0.3)	1 (0.8)	0	0
Rash	15 (4.2)	6 (5.0)	2 (1.7)	7 (5.7)
Rash generalized	3 (0.8)	0	2 (1.7)	1 (0.8)
Rash papular	1 (0.3)	0	1 (0.9)	0
Rash pruritic	3 (0.8)	1 (0.8)	1 (0.9)	1 (0.8)
Rosacea	1 (0.3)	0	0	1 (0.8)
Seborrhoeic dermatitis	1 (0.3)	1 (0.8)	0	0
Skin disorder	1 (0.3)	0	0	1 (0.8)
Skin exfoliation	1 (0.3)	0	1 (0.9)	0
Skin lesion	1 (0.3)	0	0	1 (0.8)
Skin ulcer	1 (0.3)	0	0	1 (0.8)
Xeroderma	1 (0.3)	1 (0.8)	0	0
Social circumstances	1 (0.3)	0	1 (0.9)	0
Treatment non-compliance	1 (0.3)	0	1 (0.9)	0
Surgical and medical procedures	27 (7.5)	9 (7.4)	11 (9.4)	7 (5.7)
Abscess management	1 (0.3)	1 (0.8)	0	0
Ankle arthroplasty	1 (0.3)	0	0	1 (0.8)
Arthroscopic surgery	1 (0.3)	1 (0.8)	0	0
Cardiac pacemaker replacement	1 (0.3)	1 (0.8)	0	0
Carotid endarterectomy	1 (0.3)	0	1 (0.9)	0
Cataract operation	6 (1.7)	1 (0.8)	3 (2.6)	2 (1.6)
Colostomy	1 (0.3)	0	0	1 (0.8)
Coronary arterial stent insertion	1 (0.3)	0	1 (0.9)	0
Ear operation	1 (0.3)	1 (0.8)	0	0
Eye laser surgery	1 (0.3)	1 (0.8)	0	0
Glaucoma surgery	1 (0.3)	1 (0.8)	0	0
Hip surgery	1 (0.3)	0	1 (0.9)	0
Influenza immunization	1 (0.3)	0	1 (0.9)	0
Meniscus operation	1 (0.3)	0	0	1 (0.8)
Nephrectomy	1 (0.3)	1 (0.8)	0	0
Radiotherapy to brain	1 (0.3)	0	1 (0.9)	0
Skin neoplasm excision	1 (0.3)	0	0	1 (0.8)
Spinal fusion surgery	1 (0.3)	1 (0.8)	0	0
Toe operation	1 (0.3)	0	1 (0.9)	0
Tooth extraction	3 (0.8)	1 (0.8)	2 (1.7)	0
Wart excision	1 (0.3)	0	0	1 (0.8)
Vascular disorders	20 (5.6)	5 (4.1)	7 (6.0)	8 (6.6)
Blood pressure fluctuation	1 (0.3)	0	1 (0.9)	0
Deep vein thrombosis	1 (0.3)	0	0	1 (0.8)
Hematoma	5 (1.4)	1 (0.8)	1 (0.9)	3 (2.5)
Hot flush	1 (0.3)	0	1 (0.9)	0
Hypertension	7 (1.9)	3 (2.5)	2 (1.7)	2 (1.6)
Hypertensive crisis	2 (0.6)	1 (0.8)	0	1 (0.8)

Hypotension	2 (0.6)	0	2 (1.7)	0
Peripheral coldness	1 (0.3)	0	1 (0.9)	0
Thrombosis	1 (0.3)	0	0	1 (0.8)
Varicose vein	1 (0.3)	0	1 (0.9)	0
Venous insufficiency	1 (0.3)	0	1 (0.9)	0

Supplementary table 5: Adverse events most frequently leading to discontinuation in $\geq 2\%$ of patients in any treatment group (safety population)

n (%)	Overall (n=360)	Carbamazepine (n=121)	Lamotrigine (n=117)	Levetiracetam (n=122)
Nervous system disorders				
Dizziness	7 (1.9)	3 (2.5)	2 (1.7)	2 (1.6)
Epilepsy	4 (1.1)	1 (0.8)	0	3 (2.5)
General disorders				
Fatigue	11 (3.1)	3 (2.5)	5 (4.3)	3 (2.5)
Renal and urinary disorders				
Renal failure	4 (1.1)	0	1 (0.9)	3 (2.5)
Skin and subcutaneous tissue disorders				
Dermatitis allergic	5 (1.4)	4 (3.3)	0	1 (0.8)
Drug eruption	3 (0.8)	3 (2.5)	0	0