Drugs - Real World Outcomes

Efficacy and safety of long-term treatment with stiripentol in children and adults with drug-resistant epilepsies: a retrospective cohort study of 196 patients

Stiripentol in drug-resistant epilepsies

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Supplementary Table 1. Data collection template.

ID
recordid
gender
date of birth
date at seizure onset
epilepsy type
aetiology
epilepsy syndrome
focal onset Y/N
focal motor Y/N
focal non-motor Y/N
focal to bilateral tonic clonic Y/N
generalised tonic clonic Y/N
generalised spasms Y/N
generalised onset absence Y/N
generalised onset myoclonic
generalised onset atonic
spasm frequency before STP
generalised tonic clonic szs frequency before STP
absence frequency before STP
myoclonic szs frequency before STP
atonic szs frequency before STP
focal szs frequency before STP
focal to bilateral szs frequency before STP
generalised szs frequency before STP
Date at STP introduction
Max dose
Date when max dose was reached
Treatment with ACTH before STP (Y/N)
Treatment with CBZ before STP (Y/N)
Treatment with CLB before STP (Y/N)

Treatment with CLZ before STP (Y/N)
Treatment with ETX before STP (Y/N)
Treatment with FBM before STP (Y/N)
Treatment with hydrocortisone before STP (Y/N)
Treatment with LCS before STP (Y/N)
Treatment with LEV before STP (Y/N)
Treatment with LCS before STP (Y/N)
Treatment with LZP before STP (Y/N)
Treatment with NZP before STP (Y/N)
Treatment with OXC before STP (Y/N)
Treatment with PB before STP (Y/N)
Treatment with PER before STP (Y/N)
Treatment with PREG before STP (Y/N)
Treatment with PHT before STP (Y/N)
Treatment with RUF before STP (Y/N)
Treatment with TPM before STP (Y/N)
Treatment with VGB before STP (Y/N)
Treatment with VPA before STP (Y/N)
Treatment with ZNS before STP (Y/N)
Add-on drug to STP 1
Dose add-on drug to STP 1
Add-on drug to STP 2
Dose add-on drug to STP 2
Add-on drug to STP 3
Dose add-on drug to STP 3
Add-on drug to STP 4
Dose add-on drug to STP 4
spasm frequency on STP
generalised tonic clonic szs frequency on STP
absence frequency on STP
myoclonic szs frequency on STP
atonic szs frequency on STP

focal szs frequency on STP
focal to bilateral szs frequency on STP
generalised szs frequency on STP
Efficacy
outcome
Date at first FU after STP introduction
Relapse Y/N
Date at relapse
STP withdrawal
Date at STP withdrawal
Reason for withdrawal
Other info
Add-on treatment after STP introduction
Date at add-on treatment after STP introduction
Adverse events on STP Y/N
Type of adverse events: dermatological
Type of adverse events: haematological
Type of adverse events: neurological
Type of adverse events: hepatic
Type of adverse events: genitourinary
Type of adverse events: gastroenterological
Other adverse events
Date at last follow-up
Reduction concurrent treatment
Number of add-on treatments at last FU
Responder Y/N
Seizure freedom Y/N

Supplementary Table 2. List of patients exposed to stiripentol with genetic aetiologies other than Dravet syndrome.

Genetic abnormality	Age (years)	Responders (Y/N)	Relapse (Y/N, time in months after STP initiation)	Type of epilepsy	Type of seizures	Concomitant antiseizure medications	Comorbidities	Observation period (months)
SHANK3 c.4020_4021 del (frameshift); *de novo*	7	Y	Y, 4	generalised	Tonic-clonic (during sleep), atonic, myoclonic	VPA, ETM, CLB	Autism spectrum disorder	24
KMT2A c.3460C>T (missense) *de novo*	12	Y	Y, 8	generalised	Atypical absences, myoclonic	VPA, CLB	Moderate intellectual disability	11
HCN1 c.459G>C (missense); *de novo*	3	Y	Y, 7	focal	Tonic (during sleep), focal-onset	VPA, CLB	Autism spectrum disorder	50
STARD7 chr2:g.96862805AAAAT[(n)]/AAATG[(n)]; *de novo*	34	Y	N	generalised	Tonic-clonic	LMT, CLB	Intellectual disability, cortical tremor	103
PPP2R3A c. 2945G>T (VOUS); *de novo*	8	Y	Y, 25	generalised	Tonic (mainly during sleep)	PHT, CLB	Major malformations (dextrocardia, diaphragmatic hernia, radio-	46

							ulnar synostosis)	
KCNT1 c.1066C>T (missense); *de novo*	1	N	-	focal	Focal-onset with focal to bilateral tonic-clonic	CLB, PB	Spastic tetraparesis, severe intellectual disability, microcephaly	104
FAT4 c.1687G>T (missense) mat; c.8224A>G (missense) pat	4	Y	Y, 12	combined	Tonic	VPA, CLB	Severe intellectual disability, macrocephaly, dysmorphic features	35
CACNA1A c.6706-6716del mat; c.1917-3C>G (frameshift) pat	5	Y	Y, 2	generalised	Atypical absences	VPA, CLB	Mild intellectual disability	3
SYNGAP1 c.3061C>T (nonsense); *de novo*	3	Y	Y, 5	generalised	Atypical absences	VPA, CLB	Autism spectrum disorder	6
KCNT1 c.2782 C>T (missense); mat	14	Y	Y, 6	focal	Focal-onset (during sleep)	CLB	Mild intellectual disability	20
CDKL5 c.473G>C (missense); *de novo*	1	N	-	combined	Tonic, myoclonic, epileptic spasms	VPA, CLB	Dystonic-dyskinetic tetraparesis,	43

							severe intellectual disability, microcephaly	
SCL35A3 c.73C>T (missense); c.899_900delTTinsA (frameshift)	4	N	-	generalised	Tonic, epileptic spasms	VPA, CLZ	Dystonic-dyskinetics tetraparesis, severe intellectual disability, microcephaly, dysmorphic features, arthrogryposis	72
Ring 14	7	Y	Y,11	combined	Focal-onset, tonic	VPA, CLZ	Moderate intellectual disability, renal agenesis	26
CDKL5 c.119C>T (missense); *de novo*	0.4	Y	Y, 4	combined	Focal-onset, tonic, epileptic spasms	CLB	Dystonic-dyskinetic tetraparesis, severe intellectual disability, microcephaly	8

CACNA1A c.4067 C>T (missense); *de novo*	7	N	-	focal	Focal-onset, with focal to bilateral tonic-clonic	VPA, CLB	Tetraparesis, severe intellectual disability, macrocephaly	17
Del 5q12.3	3	Y	N	combined	Atypical absences, tonic-clonic, focal-onset	VPA, CLB	Moderate intellectual disability, behaviour disorder, sleep apnoea	43
Ring 20	9	N	-	combined	Tonic (during sleep), focal to bilateral tonic-clonic	VPA, CLZ, ZNS	Moderate intellectual disability, behaviour disorders	59
PIEZO1 c.3000C>A (missense) pat; c.5727A>C (missense) mat	4	Y	Y, 23	focal	Focal-onset with focal to bilateral tonic-clonic	VPA, CLB	Moderate intellectual disability	40
HCN1 c.2829A>G (missense); *de novo*	1	Y	Y, 10	combined	Tonic, epileptic spasms, focal-onset, tonic-clonic	VPA; CLB; PB	Spastic tetraparesis, severe intellectual disability, microcephaly	23

CDKL5 Del exon 1; *de novo*	3	N	-	combined	Tonic, epileptic spasms, focal-onset, tonic-clonic	VPA, CLB	Dystonic-dyskinetic tetraparesis, severe intellectual disability, microcephaly	14
Dup Xq28	2	N	-	generalised	Atonic	VPA, CLB	Intellectual disability	17
FOXG1 c.555G>A (missense); *de novo*	10	Y	N	combined	Myoclonic absences	VPA, ETM, CLB	Moderate intellectual disability, microcephaly	3
SCN8A c.5614C>T (missense), *de novo*	1	N	-	generalised	Tonic	VPA, CLB	Tetraparesis, severe intellectual disability, tremor and cortical myoclonus, microcephaly	42
PCDH19 c.2697dupA (frameshift), *de novo*	2	Y	Y, 1	combined	Focal-onset with focal to bilateral tonic-clonic, tonic	CLB	Autism spectrum disorder	30

GGA2 c.208 A>G (missense), *de novo* *TENM1* c.2972C>T (missense), mat *NDST2* c.1328 A>G (missense) *de novo* (VOUS)	0.8	Y	N	generalised	Tonic-clonic (mainly during fever)	CLB	Hyperactivity	17
Del19p13.2	10	Y	Y,5	generalised	Myoclonic, atypical absences, tonic-clonic	VPA, CLB	Moderate intellectual disability, severe behaviour disorder, microcephaly	14
Del16p13.3-13.2	11	Y	N	focal	Focal-onset motor	VPA, CLB	Moderate intellectual disability, severe oromotor dyspraxia, macrocephaly and hypotonia, dysmorphic features	5
NPRL3	8	N	-	focal	Focal-onset	CBZ, CLB	None	26

c.980C>T (missense) mat								
SLC35A3 c.73C>T (missense); c.899_900delTTinsA (frameshift)	2	Y	N	generalised	Tonic, epileptic spasms	VPA	Apostural tetraparesis, severe intellectual disability, microcephaly, dysmorphic features, arthrogryposis	72
SYNGAP1 c.3112del *de novo*	4	Y	N	generalised	Myoclonic absences	VPA, CLB	Severe intellectual disability	10
Ring 20	5	Y	N	focal	Focal-onset	VPA, CLB, CBZ	ADHD	17
SMC1A c.3103 C>T (non-sense); *de novo*	1	Y	N	combined	Focal-onset, tonic	CLB	Intellectual disability	2

Abbreviations: ADHD=attention deficit hyperactivity disorder, CBZ=carbamazepine, CLB=clobazam, CLZ=clonazepam, ETM=ethosuximide, LMT=lamotrigine, PB=phenobarbital, VPA=valproic acid, ZNS=zonisamide