New Epilepsy Therapies in 2024 and Beyond

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DISCLOSURE

The presenter received speaker's or consultancy fees from Eisai, GRIN Therapeutics, Sintetica, SKL Life Science, Sun Pharma, Takeda, UCB Pharma and Xenon Pharmaceuticals, and royalties from Wiley, Elsevier, and Wolters Kluwers.

DISCLAIMER

Statements in this presentation about the properties of specific medications the presenter's interpretation of available evidence and do not represent the view of regulatory authorities. When prescribing, consult prescribing information in your country.

Outline

- Overview of antiseizure medications (ASMs) introduced in the last few years
- Current state of medical therapies for epilepsy
- The pipeline of emerging newer drugs and strategies applied in modern drug development
- A glimpsae into epileptogenesis and disease modification

ASMs Approved by the FDA in the Last 6 Years

ASM	FDA approval	Approved indication (seizure type)
Ganaxolone	2022	Seizures associated with CDKL5 deficiency disorder
Fenfluramine	2020	Seizures associated with DS and LGS
Cenobamate	2020	Focal seizures
Stiripentol	2018	Seizures associated with DS
Cannabidiol	2018	Seizures associated with DS, LGS and TSC
Everolimus	2018	Focal seizures associated with TSC

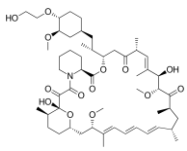
5 out of 6 ASMs approved since 2018 are treatments for rare (orphan) diseases (vs 2 of 37 ASMs approved before 2018)

CDKL5, cyclin-dependent kinase-like 5; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome: TSC, tuberous sclerosis complex

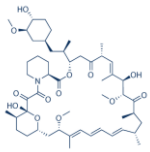
Everolimus

Streptomyces hygroscopicus

Rapa Nui



Rapamycin (sirolimus)



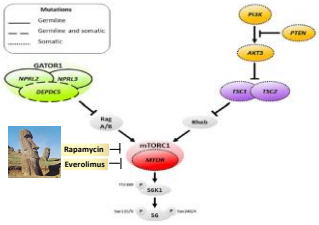
Everolimus

Mutations in mTOR Pathway Genes Are Involved in Many Epileptogenic Disorders

Epileptogenic mTORopathies

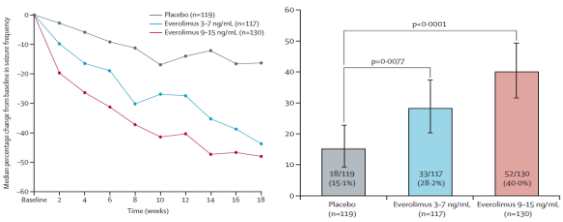
- **Tuberous sclerosis complex (TSC)**
- **Hemimegalencephaly (HME)**
- **Polyhydramnios, megalencephaly & symptomatic epilepsy (PMSE) syndrome**
- **Focal cortical dysplasias (FCDs) types I, IIa, IIb**
- **Gangliogliomas**
- **Dysembrioplastic neuroepithelial tumors (DNETs)**

A number of acquired epileptogenic insults (including brain injury) and seizures themselves can activate the PI3K/mTOR pathway



Marsan & Baulac, *Neuropathol Appl Neurobiol* 2018;44:6-17; Goldstein & Hauptman, *Frontiers Neurol* 2021;12:639319; Goldstein & Hauptman, *Frontiers Neuroanat0my* 2021;15:664695

A Randomized Trial of Everolimus in Focal Seizures Associated with Tuberous Sclerosis Complex (TSC)



French et al., The Lancet 2016; 388:2153-63

Everolimus vs Placebo: Adverse Events

	Placebo (n=119)		Everolimus 3-7 ng/mL (n=117)		Everolimus 9-15 ng/mL (n=130)	
	All grades	Grade 3 or 4	All grades	Grade 3 or 4	All grades	Grade 3 or 4
Any adverse event	92 (77%)	13 (11%)	108 (92%)	21 (18%)	123 (95%)	31 (24%)
Stomatitis*	11 (9%)	0	64 (55%)	4 (3%)	83 (64%)	5 (4%)
Diarrhoea	6 (5%)	0	20 (17%)	0	28 (22%)	0
Nasopharyngitis	19 (16%)	0	16 (14%)	0	21 (16%)	0
Upper respiratory tract infection	15 (13%)	1 (1%)	15 (13%)	0	20 (15%)	0
Pyrexia	6 (5%)	0	23 (20%)	0	18 (14%)	1 (1%)
Cough	4 (3%)	0	13 (11%)	0	13 (10%)	0
Rash	3 (3%)	0	7 (6%)	0	13 (10%)	0
Vomiting	11 (9%)	0	14 (12%)	0	13 (10%)	2 (2%)
Headache	6 (5%)	0	3 (3%)	0	11 (8%)	1 (1%)
Hypercholesterolaemia	3 (3%)	0	6 (5%)	0	9 (7%)	1 (1%)
Decreased appetite	7 (6%)	0	10 (9%)	1 (1%)	9 (7%)	1 (1%)
Acne	3 (3%)	0	3 (3%)	0	8 (6%)	0
Hypertriglyceridaemia	2 (2%)	0	6 (5%)	1 (1%)	8 (6%)	0
Pharyngitis	1 (1%)	0	6 (5%)	2 (2%)	8 (6%)	0
Ear infection	1 (1%)	0	2 (2%)	1 (1%)	7 (5%)	0
Epistaxis	1 (1%)	0	3 (3%)	0	7 (5%)	0
Influenza	4 (3%)	0	5 (4%)	1 (1%)	7 (5%)	0
Rhinorrhoea	1 (1%)	0	6 (5%)	0	4 (3%)	0

Data are n (%), unless otherwise specified. *Included all the related terms—mouth ulceration, aphthous ulcer, lip ulceration, tongue ulceration, mucosal inflammation, and gingival pain.

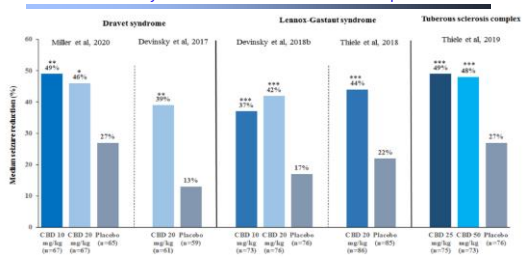
French et al., The Lancet 2016; 388:2153-63

Cannabidiol

Cannabis indica

Charlotte Figi (2013), the girl who changed the world https://www.charlottesweb.com/

Median Percent Seizure Reduction in Randomised Double-Blind Add-On Trials of Cannabidiol (CBD) in Dravet Syndrome, Lennox Gastaut Syndrome and Tuberous Sclerosis Complex



*P < 0·05; **P ≤ 0·01; ***P ≤ 0·001 (vs placebo)

Franco and Perucca, Neuropharmacology 2021; 185:108442

Randomised Double-Blind Add-On Trial of Cannabidiol (20 mg/kg) in Dravet Syndrome: Adverse Events

Adverse events occurring with a frequency >10% in either group

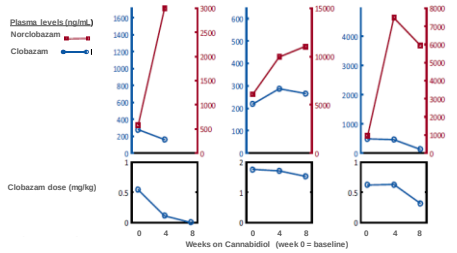
System Organ Class and Preferred Term	GW cannabidiol (n=61)	Placebo (n=59)
	No of patients (%)	
Diarrhoea	19 (31)	6 (10)
Vomiting	9 (15)	3 (5)
Fatigue	12 (20)	2 (3)
Pyrexia	9 (15)	5 (8)
Infections	7 (11)	5 (8)
Decreased appetite	17 (28)	3 (5)
Convulsion	7 (11)	3 (5)
Lethargy	8 (13)	3 (5)
Somnolence	22 (36)	6 (10)

ALT – alanine transaminase
AST – aspartate transaminase
CBD – cannabidiol
CLM - clobazam
ULN – upper limit of normal
VPA – valproate

- Elevations in transaminase enzymes (ALTs or ASTs >3x ULN) occurred in 12 CBD and 1 placebo patients
  - All were taking concomitant VPA
  - 3 patients withdrew from the CBD group and one in the placebo group
- Pooled analysis of studies (US package insert): elevations > 3x UNL occurred in 30% of patients on both VPA and CLB, in 21% of those on VPA without CLB, in 4% of those on CLB without VPA, and in 3% of patients on neither drug

Devinsky O, et al NEJM 2017;376:2011–2020

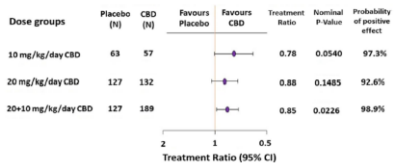
Effect of Cannabidiol on the Plasma Levels of Clobazam and Norclobazam in Three Representative Individuals



Geffrey et al, Epilepsia 2015;56:1246-1251

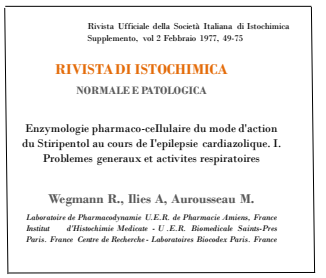
Incremental Effect of CBD in Reducing Seizure Frequency in Patients not Comedicated with Clobazam

(Pooled Analysis of Data from Controlled Trials in Dravet and Lennox-Gastaut Syndrome)



Bialer & Perucca, Epilepsia 2020;61:1082-1089.

Stiripentol



Rivista Ufficiale della Società Italiana di Istochimica
Supplemento, vol 2 Febbraio 1977, 49-75

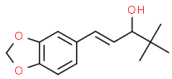
RIVISTA DI ISTOCHIMICA

NORMALE E PATOLOGICA

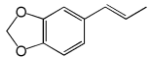
Enzymologie pharmaco-cellulaire du mode d'action du Stiripentol au cours de l'epilepsie cardiazolique. I. Problemes generaux et activites respiratoires

Wegmann R., Ilies A, Aurousseau M.

Laboratoire de Pharmacodynamie U.E.R. de Pharmacie Amiens, France Institut d'Histochimie Medicale - U .E.R. Biomedicale Saints-Pres Paris. France Centre de Recherche - Laboratoires Biocodex Paris. France



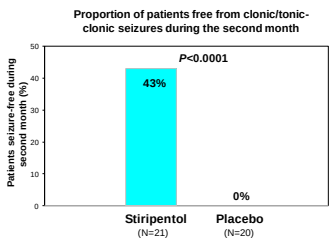
Stiripentol

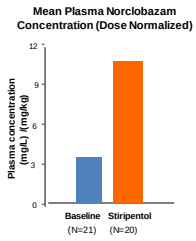


Isosafrole (LDH inhibitor)

Sassafras plant

Randomised Double-Blind Add-On Trial of Stiripentol in Patients with Dravet syndrome)





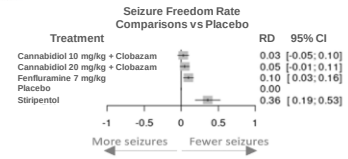
Chiron *et al. Lancet* 2000;**356**:1638–42

ORIGINAL ARTICLE

Epilepsia Open. 2024;9:689–703.

Comparative efficacy and safety of stiripentol, cannabidiol and fenfluramine as first-line add-on therapies for seizures in Dravet syndrome: A network meta-analysis

Renzo Guerrini[1,2] | Catherine Chiron[3,4] | Delphine Vandame[3] | Warren Linley[6] | Toby Toward[7]



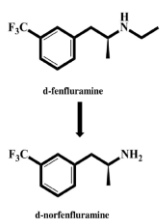
'The study found that stiripentol and fenfluramine were similarly effective in reducing seizures and both were more effective than cannabidiol. Stiripentol was the best drug for stopping seizures completely based on the available clinical trial data'

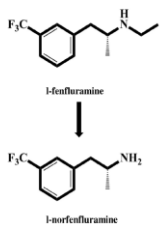
Amphetamine

Ephedra sinica

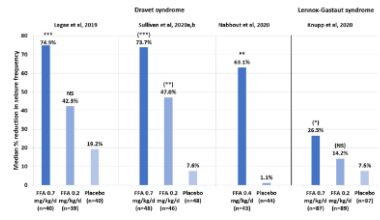
Ephedrine

Fenfluramine





Responder Rates in Randomised Double-Blind Add-On Trials of Fenfluramine (FFA) in Patients with Dravet Syndrome and Lennox Gastaut Syndrome



† P < 0.02; * P < 0.01; ** P < 0.001 (vs. placebo); *** P < 0.0001 (vs placebo).

Odi et al, Pharmacol Ther 2021; 226:107866

Fenfluramine: Most Common Adverse Events

	Dose Group			Combined Placebo Group[2]
	Study 1		Study 2	
	0.2 mg/kg/day	0.7 mg/kg/day	0.4 mg/kg/day[1]	
	N=39 %	N=40 %	N=43 %	N=84 %
Decreased appetite	23	38	49	8
Somnolence, sedation, lethargy	26	25	23	11
Abnormal echocardiogram[3]	18	23	9	6
Diarrhea	31	15	23	6
Constipation	3	10	7	0
Fatigue, malaise, asthenia	15	10	30	5
Ataxia, balance disorder, gait disturbance	10	10	7	1
Abnormal behavior	0	8	9	0
Blood pressure increased	13	8	0	5
Drooling, salivary hypersecretion	13	8	2	0
Hypotonia	0	8	0	0
Upper respiratory tract infection	21	5	7	10
Vomiting	10	5	5	8
Weight decreased	13	5	7	1

(1) Not an intermediate dose, because patients in Study 2 were comedicated with stiripentol + clobazam, which increases plasma fenfluramine levels
(2) Consisted of trace and mild nasal congestion, and trace aortic regurgitation, which are considered physiologic.

Modified from U.S. Prescribing Information data

FULL PRESCRIBING INFORMATION

WARNING: VALVULAR HEART DISEASE and PULMONARY ARTERIAL HYPERTENSION

There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension *[see Warnings and Precautions (5.1, 5.2)]*.

Echocardiogram assessments are required before, during, and after treatment with FINTEPLA. The benefits versus the risks of initiating or continuing FINTEPLA must be considered, based on echocardiogram findings *[see Dosage and Administration (2.1, 2.4) and Warnings and Precautions (5.1, 5.2)]*.

Because of the risks of valvular heart disease and pulmonary arterial hypertension, FINTEPLA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the FINTEPLA REMS *[see Warnings and Precautions (5.3)]*.

Pharmacology & Therapeutics 226 (2021) 107866

Contents lists available at ScienceDirect

Pharmacology & Therapeutics

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

Fenfluramine repurposing from weight loss to epilepsy: What we do and do not know

Reem Odi [a], Roberto William Invernizzi [b], Tamar Gallily [c], Meir Bialer [a,d,*,1], Emilio Perucca [e,1]

[a] Institute of Drug Research, School of Pharmacy, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel
[b] Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Milano, Italy
[c] Yissum Technology Transfer Company of the Hebrew University of Jerusalem, Jerusalem, Israel
[d] David R. Bloom Center for Pharmacy, The Hebrew University of Jerusalem, Jerusalem, Israel
[e] Division of Clinical and Experimental Pharmacology, Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy

Cenobamate: Approved Indications

FDA U.S. FOOD & DRUG ADMINISTRATION

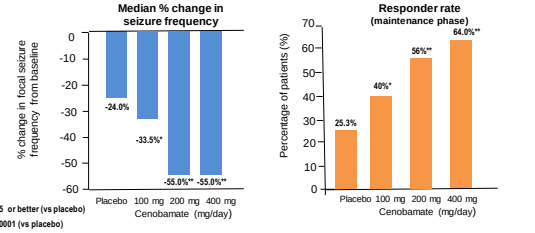
- Treatment of partial-onset seizures in adult patients

EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH

- Adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least 2 anti-epileptic medicinal products

Available as oral tablets

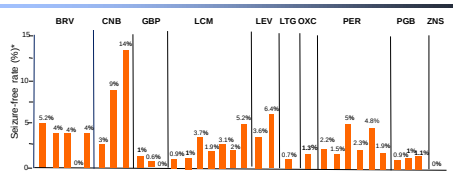
Efficacy Data from Cenobamate's Pivotal Placebo-Controlled Trial in Patients with Focal Seizures (12-Week Maintenance, n=437)



*p<0.05 or better (vs placebo)
**p<0.0001 (vs placebo)

Krauss et al. Lancet Neurol. 2020;19(1):38-48.

How Many Patients with Drug Resistant Focal Epilepsy Became Seizure-Free and Completed the Treatment Period in Placebo-Controlled Trials of Second-Generation ASMs?



BRV, brivaracetam; CNB, cenobamate, GBP, gabapentin; LCM, lacosamide, LEV, levetiracetam; LTG, lamotrigine, OXC, oxcarbazepine, PER, perampanel, PGB, pregabalin, ZNS, zonisamide

*ITT analysis (outcomes refer to effective doses only in trials with ≥12wk maintenance period)

Ben Menachem et al, Epilepsia 2007;48:1308-17; Gazzola et al. Epilepsia 2007;48:1303-7; Halasz et al, Epilepsia 2008;50:443-53; Chung et al, Epilepsia 2010;51:958-67; French et al, Neurology 2012;79:598-96; Krauss et al, Neurology 2012;78:1408-15; French et al, Epilepsia 2013;54:117-25; Biton et al, Epilepsia 2014;55:57-66; Ryvlin et al, Epilepsia 2014:55:47-56 ; Klein et al, Epilepsia 2015:56:1890-8.; Krauss et al, Lancet Neurol. 2020;19:38-48.

Incidence of Adverse Events* at Each Cenobamate Dose in the Pivotal Placebo-controlled Trial in Focal Epilepsy

	Placebo (n=108)	Cenobamate (mg/day) 100 (n=108)	200 (n=110)	400 (n=111)
Somnolence	9 (8%)	20 (19%)	23 (21%)	43 (37%)
Dizziness	15 (14%)	19 (18%)	22 (20%)	37 (33%)
Headache	6 (6%)	11 (10%)	12 (11%)	12 (11%)
Balance disorder	0	3 (3%)	2 (2%)	10 (9%)
Nystagmus	1 (<1%)	3 (3%)	4 (4%)	7 (6%)
Ataxia	1 (<1%)	2 (2%)	4 (4%)	7 (6%)
Dysarthria	0	2 (2%)	3 (3%)	7 (6%)
Fatigue	9 (8%)	13 (12%)	19 (17%)	27 (24%)
Gait disturbance	3 (3%)	1 (<1%)	6 (6%)	9 (8%)
Diplopia	2 (2%)	8 (7%)	11 (10%)	17 (15%)
Constipation	1 (<1%)	2 (2%)	3 (3%)	10 (9%)
Nausea	1 (<1%)	7 (7%)	1 (<1%)	10 (9%)
Vomiting	0	2 (2%)	3 (3%)	6 (5%)
Fall	6 (6%)	2 (2%)	4 (4%)	4 (4%)
Upper respiratory tract infection	6 (6%)	3 (3%)	4 (4%)	3 (3%)
Back pain	3 (3%)	4 (4%)	1 (<1%)	6 (5%)
Vertigo	3 (3%)	1 (<1%)	3 (3%)	6 (5%)
Decreased appetite	1 (<1%)	3 (3%)	1 (<1%)	6 (5%)

*adverse events reported in ≥5% of patients in any group

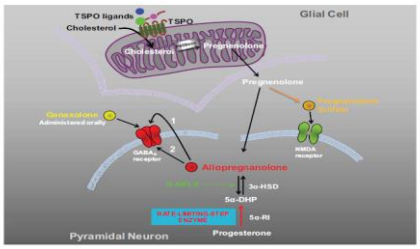
Adapted and modified from Krauss et al. Lancet Neurol. 2020;19(1):38-48.

Cenobamate – Recommended titration scheme

	Cenobamate dose /mg/day
Week 1-2	12.5
Week 3-4	25
Week 5-6	50
Week 7-8	100
Week 9-10	150
Week 11-12	200
Week 13-14	250
Week 15-16	300
Week 17-18	350
Week 19-20	400

There were no cases of DRESS when this titration scheme was applied in a Phase III trial that enrolled 1339 patients

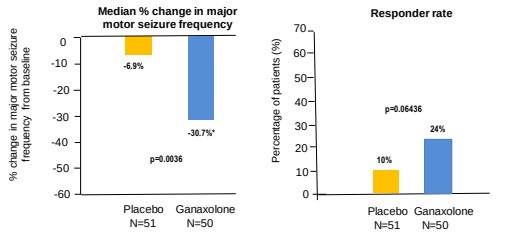
Modes of Action of Ganaxolone and Other Neurosteroids



TSPO, translocate protein (18kDa); 5α-DHP, 5α-dihydroprogesterone; 5α-RI, 5α-reductase type I; 3α-HSD, 3α-hydroxysteroid dehydrogenase; 5-NFLX, 5-norfluoxetine.

Pinna et al, Frontiers Pharmacol 2014; 4:166

Efficacy Data from the Ganaxolone Placebo-Controlled Trial in Patients with CKDL5 Deficiency Disorder



Pestana Knight et al. Lancet Neurol. 2022;121:417-27

Incidence of Adverse Events in the Placebo-controlled Trial of Ganaxolone in Patients with CDKL5 Deficiency Disorder

	Ganaxolone	Placebo
Somnolence	18 (36%)	8 (16%)
Pyrexia	9 (18%)	4 (8%)
Seizure	7 (14%)	9 (18%)
Vomiting	5 (10%)	10 (20%)
Upper respiratory tract infection	5 (10%)	3 (6%)
Constipation	3 (6%)	3 (6%)
Salivary hypersecretion	3 (6%)	1 (2%)
Sedation	3 (6%)	2 (4%)

Pestana Knight et al. Lancet Neurol. 2022;121:417-27

Advancing the Medical Treatment of Epilepsy: What Have We Achieved, and What is Next?

- Over 20 new antiseizure medicines (ASMs) have been developed - we learnt how to use them at best, including a more rational approach to combination therapy
- Thanks to better tolerated medicines, the burden of side effects has been reduced. However…
- Available medicines suppress the symptoms, but they have no impact on the underlyng disease
- About one third of patients remain drug resistant – the same as in 1970

Epilepsy Treatment for the Future: What Do We Need?

- More efficacious treatments for drug resistant patients
- Predictors of responses to individual drugs - would allow avoidance of the current trial-and-error approach
- Safer treatments for certain patient groups (e.g., females with generalized epilepsies)
- Treatments targeting the underlying disease, rather than merely symptomatic drugs

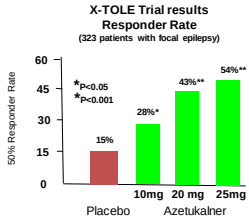
The Unrelenting Search for Newer ASMs: Some Compounds Currenty in Clinical Development

- ACT709478
- AMT-260
- Azetukalner
- Basimglurant (NOE-101)
- Beprodone (VLB 01)
- Bexicaserin (LP352)
- BHV-7000
- BHV-7010
- Blarcamesine (Anavex 2-73)
- Cannabidivarin
- Carisbamate (YKP509)
- Darigabat (CVL 865)
- 2-Deoxy-glucose
- ENX-101
- ETX 155
- Huperzyne (SPN-817)
- JNJ-40411813
- LPCN 2101
- LRP-661
- Naluzotan
- NBI 921352 (XEN 901)
- NRP2495
- NRTX-001
- Omaveloxolone (RTA408)
- OV329
- PRAX-562
- PRAX-628
- Radiprodil
- Sec-butyl-propylacetamide
- Soticlestat (TAK 935)
- STK-001
- Vatiquinone (EPI-743)
- Vixotrigine (CNV1014802)
- XEN 946 (ezogabine)

*List excludes compounds approved for other indications and being tested as potential ASMs

Compounds Acting on 'Established' Targets: Azetukalner as an Example

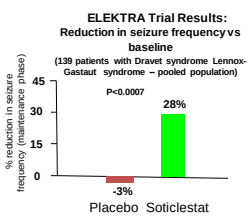
- Activator of $K_{V7.2/7.3}$ potassium channels
- Improved selectivity and improved pharmacokinetics compared with ezogabine. Putatively devoid of the pigmentation-related adverse effects of ezogabine



French et al, JAMA Neurol. 2023 ;80:145-1154

Compounds Acting on Novel Targets: Soticlestat as an Example

- Selective inhibitor of cholesterol-24-hydroxylase (CYP46A1)
- 24S-hydroxy-cholesterol is a positive allosteric modulator of NMDA receptors in the brain and may have other pro-epileptogenic actions
- Soticlestat is being developed for Dravet syndome and Lennox-Gastaut syndrome



https://www.takeda.com/newsroom/newsreleases/ (accessed February 10, 2022)

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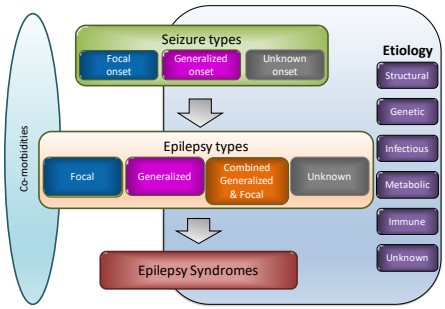
OSAKA, Japan and CAMBRIDGE, Massachusetts, June 17, 2024

Takeda Announces Phase 3 Topline Results for Soticlestat (TAK-935) in Patients with Dravet Syndrome and Lennox-Gastaut Syndrome

- *KYLINE Study in Dravet syndrome narrowly missed its primary endpoint … (P=0.06), though it showed … significant effects in multiple key secondary efficacy endpoints*
- *SKYWAY Study in Lennox-Gastaut syndrome missed its primary endpoint*
- *Takeda will move forward to discuss the totality of the data with regulatory authorities*

https://www.takeda.com/newsroom/newsreleases/2024/soticlestat-drevat-syndrom-phase3-results/ (accessed June 20, 2024)

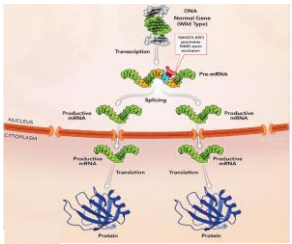
The Holy Grail of Epileptology: Preventing (or Modifying) Epileptogenesis



Scheffer et al, Epilepsia 2017;58:512-521

Addressing the Haploinsufficiency of Dravet Syndrome by Upregulating the Function of the Healthy Allele

- STK-001 is an antisense oligonucleotide that binds to SCN1A preRMNA from the healthy allele and promotes the exclusion of premature stop codons
- The resulting effect is prevention of Nonsense-Mediated mRNA Decay (NMDA) and increased production of functional protein
- i.c.v. STK-001 is undergoing clinical trials in patients with Dravet syndrome
- Preliminary results suggest a positive effect on seizure frequency



https://www.stoketherapeutics.com/wp-content/uploads/explainer_TANGO_final.pdf Perucca et al, CNS Drugs 2023 37:781-795.

STOKE THERAPEUTICS

Stoke Therapeutics Announces Landmark New Data That Support the Potential for STK-001 to be the First Disease-Modifying Medicine for the Treatment of Patients with Dravet Syndrome

March 25, 2024

– Phase 1/2a End of Study Data: 70mg doses demonstrated substantial and sustained reductions in convulsive seizure frequency on top of the best available anti-seizure medicines; Median reductions of 85% (n=10) at 3 months and 74% (n=9) at 6 months after last dose –

– Open Label Extension Studies: Durable reductions in seizures and clinically meaningful improvements in multiple measures of cognition and behavior were maintained over 12 months with continued dosing at 30mg and 45mg –

– STK-001 generally well-tolerated –

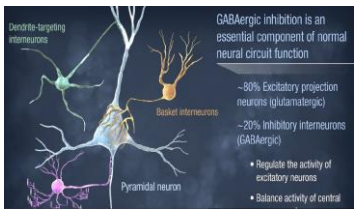
– Company to meet with regulatory agencies to discuss registrational study design with initial doses of 70mg followed by continued dosing at 45mg –

– Webcast and conference call for analysts and investors at 4:30 p.m. Eastern Time today –

Median % Reduction from Baseline in Convulsive Seizure Frequency	70mg (1 dose, n=8)	70mg (2 or 3 doses, n=11)
At 3 Months After Last Dose	43% (n=8)	85% (n=10[†])
At 6 Months After Last Dose	57% (n=7[†])	74% (n=9[†])

Enhancing GABAergic Inihibition in the Epileptic Focus through Direct Implantation of GABAergic Interneurons

- NRTX-1001 is a cryopreserved product comprising GABAergic, post-mitotic interneurons of a specific lineage derived from human pluripotent stem cells
- The interneurons are designed for implantation into the epileptogenic tissue to permit release of GABA and suppression of seizure activity
- Preminary results from clinical trials in patients with unilateral mesial temporal lobe epilepsy are encouraging



Perucca et al, CNS Drugs 2023;37:781-795.

https://www.neuronatherapeutics.com/

The Unrelenting Search for Newer ASMs: Some Compounds under Clinical Investigation for Potential Repurposing in Epilepsy

- Alprazolam
- Aspirin
- Ataluren
- Biperiden
- Empaglifozin
- Clemizole (EPX-100)
- Ibuprofen
- Ivermectin
- Ketamine
- Lorcaserin
- Memantine
- Methylpredinsolone
- Nifedine
- Onabotulinumtoxin A
- Pentoxifylline
- Rapamycin
- Rozanolixizumab
- Satralizumab
- THC combined with CBD
- Tocilizumab
- Triple therapy (esomeprazole, amoxicillin, chlaritromycin)

Perucca et al. Lancet Neurol 2023; 22:723-34 (updated)

JAMA Neurol. doi:10.1001/jamaneurol.2024.1714
Published online June 17, 2024.

JAMA Neurology | Original Investigation

Angiotensin Receptor Blockers for Hypertension and Risk of Epilepsy

Xuerong Wen, PhD, MS; Marianne N. Otoo, MPharm; Jie Tang, MD; Todd Brothers, PharmD; Kristina E. Ward, PharmD; Nicole Asal, PharmD; Kimford J. Meador, MD

CONCLUSIONS AND RELEVANCE This cohort study found that ARBs, mainly losartan, were associated with a lower incidence of epilepsy compared with other antihypertensive agents in hypertensive patients with no preexisting stroke or cardiovascular disease. Further studies, such as randomized clinical trials, are warranted to confirm the comparative antiepileptogenic properties of antihypertensive medications.