Behavioral Outcomes of Treatment With Cannabidiol Oral Solution in Individuals With Seizures Associated With Tuberous Sclerosis Complex and Epilepsy: Study Design of an Ongoing Phase 4 Trial (EpiCom)

For a more complete description, please visit https://clinicaltrials.gov/study/NCT05864846

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Background

- There are limited treatments for tuberous sclerosis complex (TSC)-associated neuropsychiatric disorders (TAND), which affect ~90% of individuals with TSC.[1]
- Neuropsychiatric outcomes in individuals with TSC are difficult to measure with the available tools because of limited validation, acceptance, and relevance.[1]
- Cannabidiol (CBD; Epidiolex®/Epidyolex®) treatment reduced the frequency of seizures associated with TSC and improved patients' overall clinical condition in clinical trials.[2]
- Although anecdotal reports suggest positive effect of CBD on behavior, prospective clinical studies are needed.

The EpiCom trial

(Clinical Trial Number: NCT05864846)

EpiCom is a multicenter, open-label, phase 4 study to evaluate behavioral outcomes following treatment with add-on CBD in individuals with TSC-associated seizures

Designed in collaboration with patient advisory groups and health care professionals (HCPs)

Decentralized design provides flexibility of virtual or in-person visits reducing burden on participants and caregivers

Enrollment commenced
Q2 2023

Expected patient numbers
~75

Enrolling Sites

USA · UK · Canada · Netherlands · Poland

Co-Creation Strategy

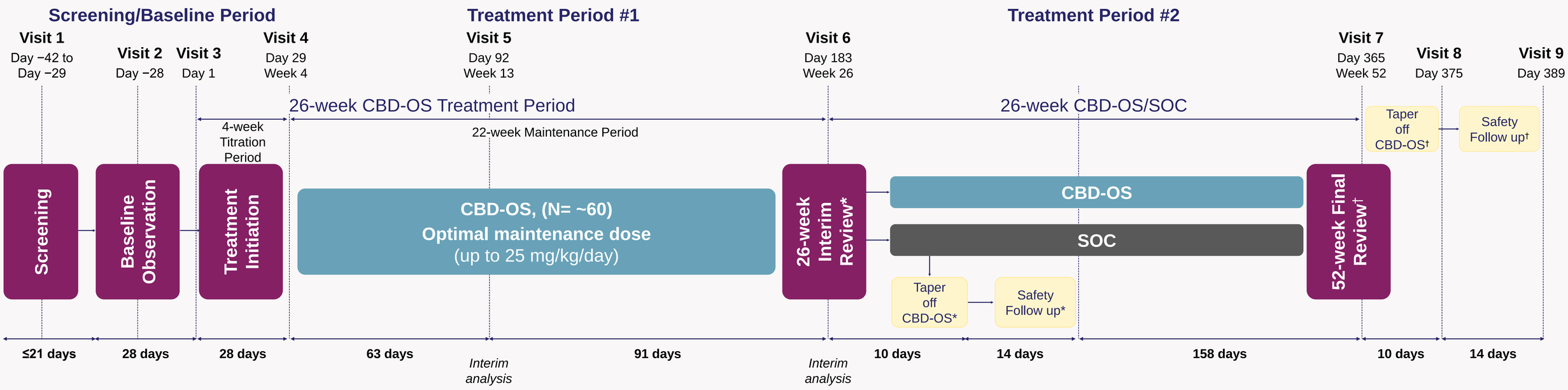
Identify, understand, and engage the TSC community of HCPs, patients, and their caregivers

Co-create the Advisory Board
- Discuss TAND outcomes of interest, study design, study population, and measurement tools

Patient Advisory Board · **HCP** Advisory Board

Integration of feedback from both groups into study design
- Joint patient–HCP steering committee established to advise throughout the study period

Trial Design



*Participants who decide to discontinue CBD-OS after the 26-week interim review visit but remain on study will form the SOC treatment arm. These participants will taper off CBD-OS and complete a safety follow-up.
†Participants who decide to discontinue CBD-OS after the 52-week interim review visit will taper off CBD-OS and complete a safety follow-up. For participants who wish to remain on CBD-OS after the study, the 52-week final review visit is the last study visit.
CBD-OS, cannabidiol oral solution; SOC, standard of care.

Key Criteria

Inclusion

- **Confirmed diagnosis of TSC** with history of associated seizures
- **Moderate/severe behavioral challenges** (eg, aggression, impulsivity, temper tantrum, self-injury, and hyperactivity), with a most problematic behavior score of ≥6 on the TAND-SQ at baseline
- Aged **1–65 years**
- On **≥1 antiseizure medication**
- **Naive to CBD** or has been off CBD for ≥3 months before screening

Exclusion

- Any medical condition that could affect the study outcomes
- Felbamate initiation within the year before screening
- Recreational or medicinal cannabis use within the 3 months before screening
- Significant hepatic impairment and any history of suicidal behavior or ideation of type 4 or 5 as evaluated with the Columbia-Suicide Severity Rating Scale

Endpoints

Study objective: To investigate the **behavioral and other co-occurring outcomes** after initiation of treatment with add-on CBD in patients with TSC who experience seizures

- **Behavioral and neuropsychiatric outcomes:**
  Change from baseline in TAND-SQ, the most problematic behavior NRS score, ABC, ABCL/CBCL, and ASR at weeks 13, 26, and 52
- **Nonseizure outcomes, including executive function and sleep:**
  PROMIS at weeks 26 and 52; BRIEF, CSHQ, or PSQI at week 26
- **QOL and family functioning:**
  PedsQL and PedsQL FIM at week 26
- **Symptom severity and seizure outcomes:**
  Treatment responder rates, change in seizure frequency, seizure-free days, CareGI-S/PGI-S, and retention at weeks 4, 13, 26, and 52 following initiation of treatment
- **Safety and tolerability of CBD:**
  Incidence and severity of adverse events (AEs), discontinuations due to AEs, inpatient hospitalizations, and abnormal clinical laboratory parameters

Tools	Assessments	Ages (years)	Time
ABC	Irritability, social withdrawal, stereotypic behavior, hyperactive noncompliance, and inappropriate speech	All ages	10–15 min
TAND-SQ	TAND-related domains (ie, neuropsychiatric, cognitive, and behavioral symptoms)	All ages[a]	20–30 min
ABCL/CBCL	Caregiver-reported internalizing behaviors (eg, depression and anxiety), externalizing behaviors (eg, aggression), stress, obsessive-compulsive behaviors, and 'sluggish cognitive tempo'	1.5–5, 6–18 / ≥18	15–20 min
ASR[b]	Participant-reported version of the ABCL	≥18	15–20 min
PROMIS	Emotional distress (anger/irritability, anxiety), cognition, positive affect, and sleep disturbance	All ages	5 min
BRIEF	Caregiver-reported ability to control impulses, move freely between situations, modulate responses, anticipate future events, and monitor how an individual's behavior impacts others	Various ages	10–15 min
CSHQ	Caregiver-reported sleep habits, including bedtime habits, sleep behaviors, waking through the night, and morning wake-up	4–12	10 min
PSQI[b]	Overall sleep quality	≥18	10 min
PedsQL	Caregiver-reported assessment of QOL across physical, emotional, and social functioning as well as functioning in school	<18	5 min
PedsQL FIM	Caregiver-reported assessment of the impact of the child's chronic condition on family functioning	<18	10 min
CareGI-S/PGI-S/CGI-S	Caregiver/patient and clinician impression of overall severity of symptoms	All ages	5 min

[a]Under validation. [b]Completion is optional in this study.
ABC, Aberrant Behavior Checklist; ABCL, Adult Behavior Checklist; ASR, Adult Self-Report; BRIEF, Behavior Rating Inventory of Executive Function; CareGI-S, Caregiver Global Impression of Severity; CBCL, Child Behavior Checklist; CGI-S, Clinician Global Impression of Severity; CSHQ, Children's Sleep Habits Questionnaire; NRS, numerical rating scale; PedsQL, Pediatric Quality of Life Inventory; PedsQL FIM, Pediatric Quality of Life Survey Family Impact Module; PGI-S, Patient Global Impression of Severity; PROMIS, Patient-Reported Outcomes Measurement Information System; PSQI, Pittsburgh Sleep Quality Index; QOL, quality of life; TAND-SQ, Tuberous Sclerosis Complex-Associated Neuropsychiatric Disorders Self-report, Quantified Checklist.

References: **1.** Vanclooster S, et al. *J Neurodevelop Disord.* 2022;14:13. **2.** Hess E, et al. *Epilepsia.* 2016;57:1617-1624.

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Epidiolex® is approved in the US for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex in patients ≥1 years of age. Epidiolex® is not approved for any treatment in Canada.

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