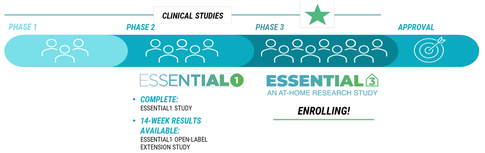
Characteristics of Adult Essential Tremor Patients Seeking Participation in a Decentralized US Clinical Trial: Pre-Screener Findings from the Essential3 Program Evaluating Efficacy and Safety of Ulixacaltamide

Richard Able[1], Ryan Walsh[1], Monique Giroux[1], Megan Sniecinksi[1], Taylor Crush[1], Alex La Croix[1], Claudio Santos[1], Steve Petrou[1], Marcio Souza[1], Aparna Wagle Shukla[2], Peter LeWitt[3]
on behalf of the Essential3 Study Team and the Tremor Research Group

[1]Praxis Precision Medicines, Boston, MA, USA; [2]Department of Neurology, University of Florida, Gainesville, FL; [3]Department of Neurology, Wayne State University School of Medicine, Detroit, MI

Background

- Essential tremor (ET) is characterized by involuntary progressive tremor especially in the hands and upper limbs, with patients experiencing significant disruption to their daily activities, often alongside multiple comorbid conditions.
- Existing treatment options are limited, with high discontinuation rates due to poor tolerability and modest efficacy.
- Ulixacaltamide is a novel, selective T-type calcium channel blocker in clinical development for ET treatment.
- Phase 2 studies showed improvement across TETRAS Activities of Daily Living (ADL) measures and Patient Global Impression, alongside favorable tolerability.
- Here, we characterize ET experience and unmet need in patients seeking participation in the Essential3 Phase 3 Program, an ongoing, innovative, decentralized multi-study combining in-home and telehealth visits to assess efficacy and safety of ulixacaltamide in adults with ET.



Essential3: Innovative, Multi-Study Design

- Two simultaneous, 12-week, decentralized, pivotal studies combine in-home and telehealth visits to assess efficacy of ulixacaltamide (60 mg) vs. placebo, and maintenance and durability of effect in responders following randomized withdrawal (RW). Participants have the option to undergo a long-term safety study up to ~1 year.
- Preliminary eligibility to participate in Essential3 was assessed via an online pre-screener capturing demographics, symptoms, and other clinical features. Assessment of qualifiers was based on (though not limited to): receiving an ET diagnosis; bilateral arm/hand tremor; symptoms >3 years; sufficient self-reported action tremor severity with higher likelihood of meeting inclusion criteria.
- Participants who passed the online pre-screener were invited to complete a secondary phone screening survey capturing additional clinical features, management and treatment details.
- Data are presented for over 175,000 pre-screener responders, of which over 27,000 referrals met pre-qualifying eligibility criteria.

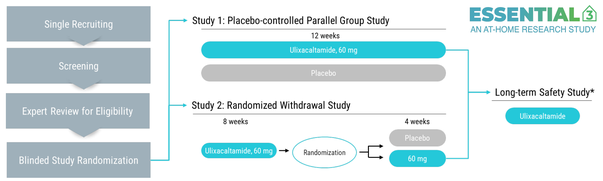


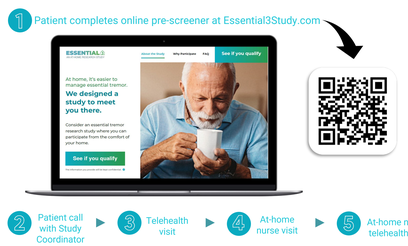
Figure 1. Essential3 Schema. *clinicaltrials.gov: NCT06087276*

*The full list of study eligibility criteria is available on clinicaltrials.gov: NCT06087276)

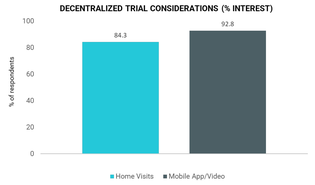
High Interest in Decentralized Design Among Pre-screener Responders

ESSENTIAL3: A RESEARCH STUDY PATIENTS CAN PARTICIPATE IN FROM HOME

- Home health visits with a study nurse
- Telehealth visits with study physician
- An assigned study nurse to guide patient through study participation
- Digital app for completion of questionnaires



~85% of pre-screener responders report willingness to allow home study visits, with >90% willing to use a mobile app and video calls if deemed eligible to participate



ET: Underdiagnosed, with Widespread Impact on Daily Living

Of those with an ET diagnosis, approximately half indicated being diagnosed/treated for ET by a neurologist, with most diagnosed in the last 10 years

70 years
Median age at survey completion

52%
Of participants had familial history of ET

52%
Diagnosed/treated by a neurologist

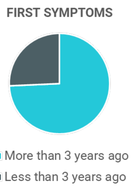
68%
Diagnosed in the last 10 years

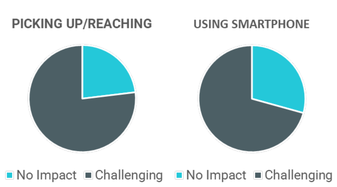
90%
Reported challenges in completing daily tasks

Most responders have been living with their ET symptoms for >3 years.

While the majority reported difficulty completing daily tasks, up to a 1/3 indicated no impact.

Almost 3/4
First noticed symptoms more than 3 years ago





ET: High Treatment and Comorbidity Burden

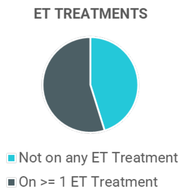
Most have not received interventions such as ultrasound/surgery, Cala Trio™, or Botox®

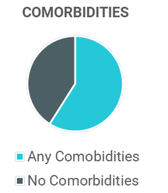
2%
Previously had ultrasound or surgery such as DBS or thalamotomy

6%
Currently use Cala Trio™ device

4%
Had a Botulinum Toxin (Botox®) injection in the last 6 months

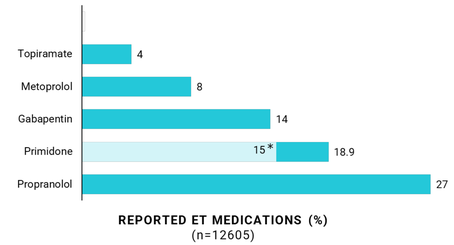
Nearly half are not receiving treatment for their ET





More than half reported comorbidities

Almost a third are currently on propranolol for their ET



Percentages reflect reported current or past ET medications trialed. *Denotes percentage of responders currently on primidone

Conclusions

- **Essential3, the Phase 3 program for ulixacaltamide, comprises two simultaneous Phase 3 studies including a 12-week, parallel design study and 12-week randomized withdrawal study for stable responders.**
- **Data are presented for over 175,000 pre-screener responders, of which over 27,000 referrals met pre-qualifying eligibility criteria for the Essential3 program. Topline results expected in 3Q2025.**
- **Consistent with the Praxis Essential Tremor Patient Research (Poster 5-011), findings from the largest ET survey to date show that patients seeking participation in a clinical trial report ET as a high-burden, inadequately managed disorder impacting several activities of daily living.**
- **Findings also suggest a degree of normalization of ET impact (likely necessitating ongoing patient and physician education) and emphasize the urgent need for innovation in developing effective, well-tolerated treatments.**

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@PraxisMedicines
Praxismedicines.com
Praxis Precision Medicines
clinicaltrials@praxismedicines.com

Connect with us Booth #2113

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