



Ulixacaltamide Demonstrates Broad Functional Improvement Across Individual Domains of Activities of Daily Living in Essential Tremor

ESSENTIAL3

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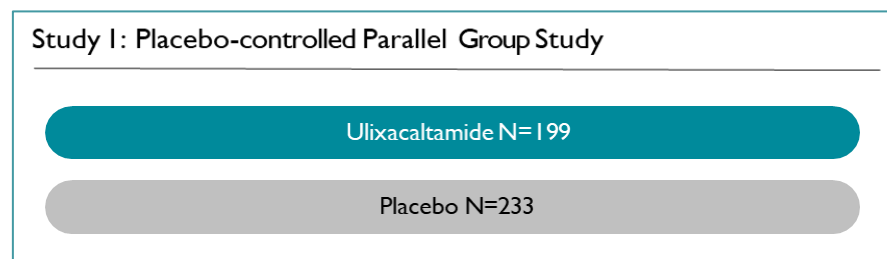
BACKGROUND

- Essential tremor (ET) is a chronic, progressive neurological disorder affecting approximately 7 million people in the U.S.
- Functional disability is reported in >85% of patients and burden is widespread across daily activities: up to 80% report needing to adjust how they complete routine tasks due to their ET symptoms, with the greatest challenges often involving writing, pouring, and drinking, and related impact to work and social engagement.
- Beyond functional limitations, ET carries substantial psychosocial burden and negative emotional impact (frustration, shame, worry, sadness, hopelessness); up to 77% of patients report their symptoms are not manageable with current treatment options.
- While composite measures of tremor-related activities of daily living (ADL) capture overall impairment, item-level analysis of therapeutic effects can characterize the extent of functional disability and further identify the relative magnitude of benefit across specific domains.
- Understanding the hierarchy of improvement across individual ADL domains can therefore enrich characterization of real-world treatment effects.

➤ **Here we report the breadth of functional improvement in adults with ET treated with ulixacaltamide in Study 1 of the Phase 3 ESSENTIAL3 program (NCT06087276).**

ESSENTIAL3 STUDY 1 DESIGN AND ADL ENDPOINTS

- Randomized, double-blind, placebo-controlled trial enrolling participants aged 18–85 years with ET (symptoms ≥3 years; if on ET medication(s), stable dose for ≥28 days prior to screening).
- Integrated, innovative, decentralized design:
 - Unified, single screening and eligibility review process, with study allocation blinded to investigators, participants, and study staff
 - ET diagnosis confirmed by standardized neuro exam adjudicated by Movement Disorder specialists on Eligibility Review Committee
 - Site staff blinded to protocol criteria for threshold of disability and mADL11 stability
 - Contemporaneous data entry with no visibility to endpoint transformation
- Participants randomized 1:1 to ulixacaltamide 60 mg QD (after 2-week titration) or placebo for 12 weeks.



Activities of Daily Living Endpoints

- The Essential Tremor Rating Assessment Scale – Activities of Daily Living (TETRAS-ADL) subscale was collected and used for exploratory analysis of efficacy.
- 12-item assessment of typical daily activities that are impacted by tremor, with the impact to each function rated on a 5-point Likert scale from 0 to 4. The full ADL subscale score is calculated as the sum of all 12 items and ranges from 0 to 48.

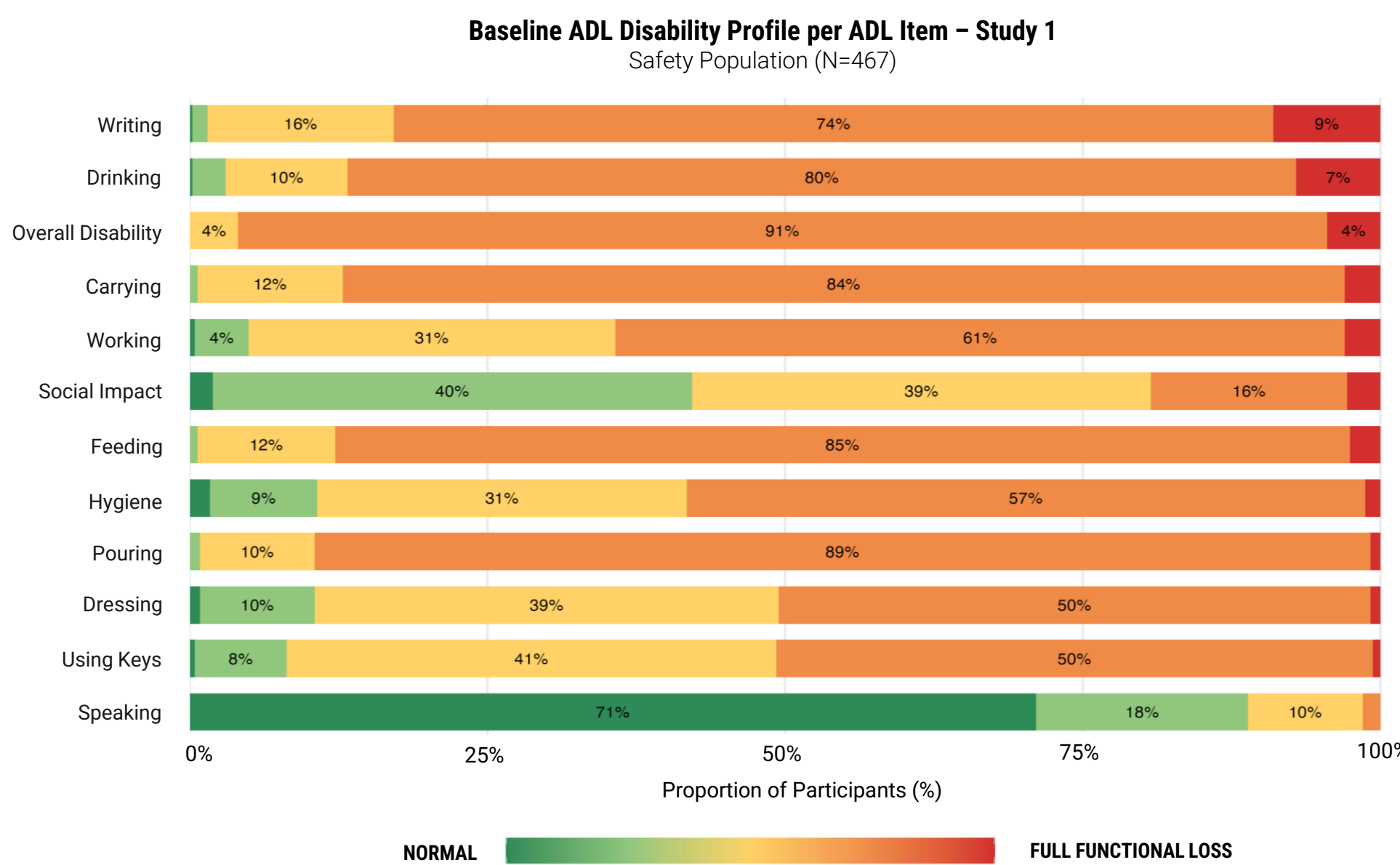
ESSENTIAL3 Study 1 Demographics and Baseline Characteristics (mITT)

	ULIXACALTAMIDE (N=199)	PLACEBO (N=233)
Age, Mean (SD)	67.9 (9.1)	68.9 (8.1)
Gender, Male/Female %	57.3% / 42.7%	56.7% / 43.3%
Race, White/Other %	98.5% / 1.5%	95.7% / 4.3%
Years since ET Onset, Mean (Median)	29.8 (26.0)	31.1 (27.0)
ET symptoms worsened over past 3 years, Yes %	188 (94.5%)	216 (92.7%)
Currently on ET Medication, Yes %	44.2%	48.1%
Currently on Propranolol, Yes %	35.7%	36.5%
Family History of ET, Yes/No/Unknown %	71.9% / 20.6% / 7.5%	72.1% / 19.7% / 8.2%
Presence of Intention Tremor, Yes %	65.3%	66.1%
TETRAS-ADL, Mean (SD)	30.7 (3.0)	30.6 (3.0)
Patient Global Impression – Severity, Mean (SD)	3.0 (0.7)	2.9 (0.7)
Clinician Global Impression – Severity, Mean (SD)	4.0 (0.6)	4.0 (0.6)

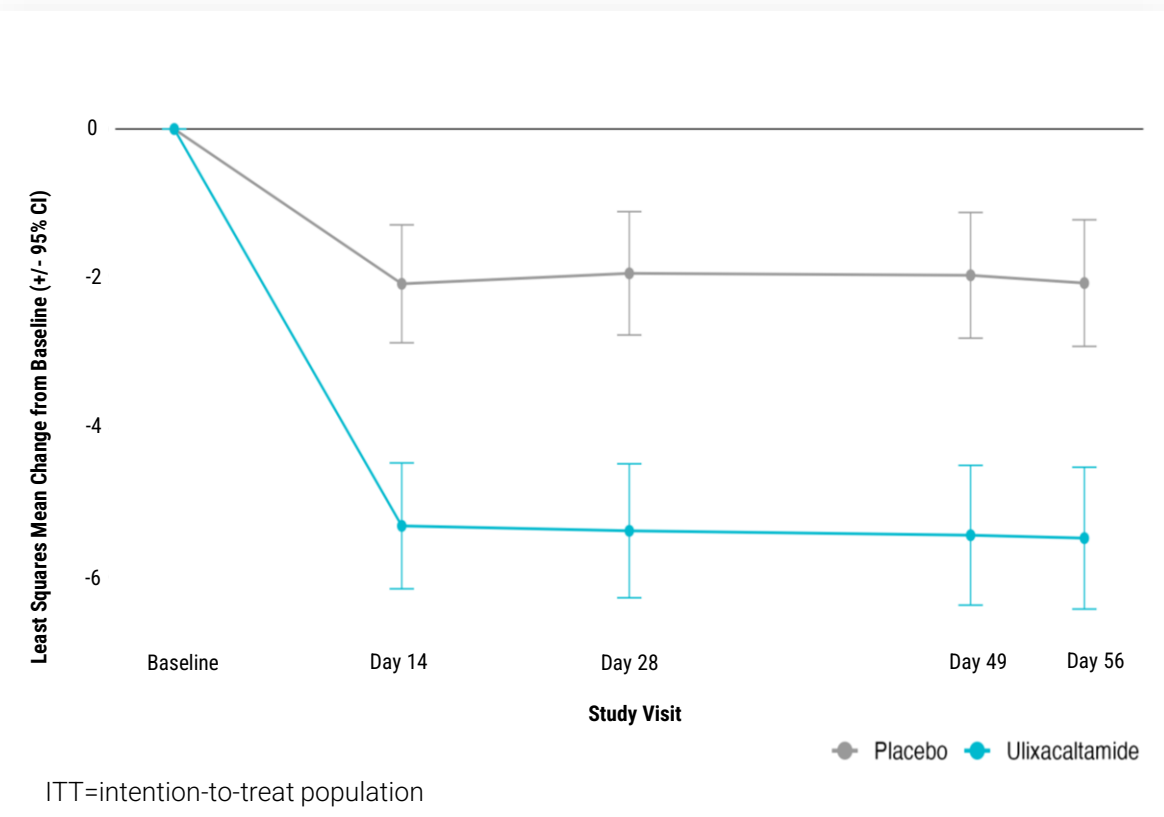
ULIXACALTAMIDE DEMONSTRATES CONSISTENT, CLINICALLY MEANINGFUL, MULTI-DOMAIN BENEFIT IN ACTIVITIES OF DAILY LIVING

- Ulixacaltamide demonstrated rapid onset and clinically meaningful benefit in ADL across all study visits
- Responder analyses at Day 56 favored ulixacaltamide across increasingly stringent ADL response thresholds.
- Improvement relative to placebo was observed across all 12 ADL domains at Day 56 or 84, indicating broad functional benefit; standardized effect sizes significant in favor of ulixacaltamide for all items.
- Separation from placebo was evident by Day 14 and sustained through Day 84 across all domains, including social impact.

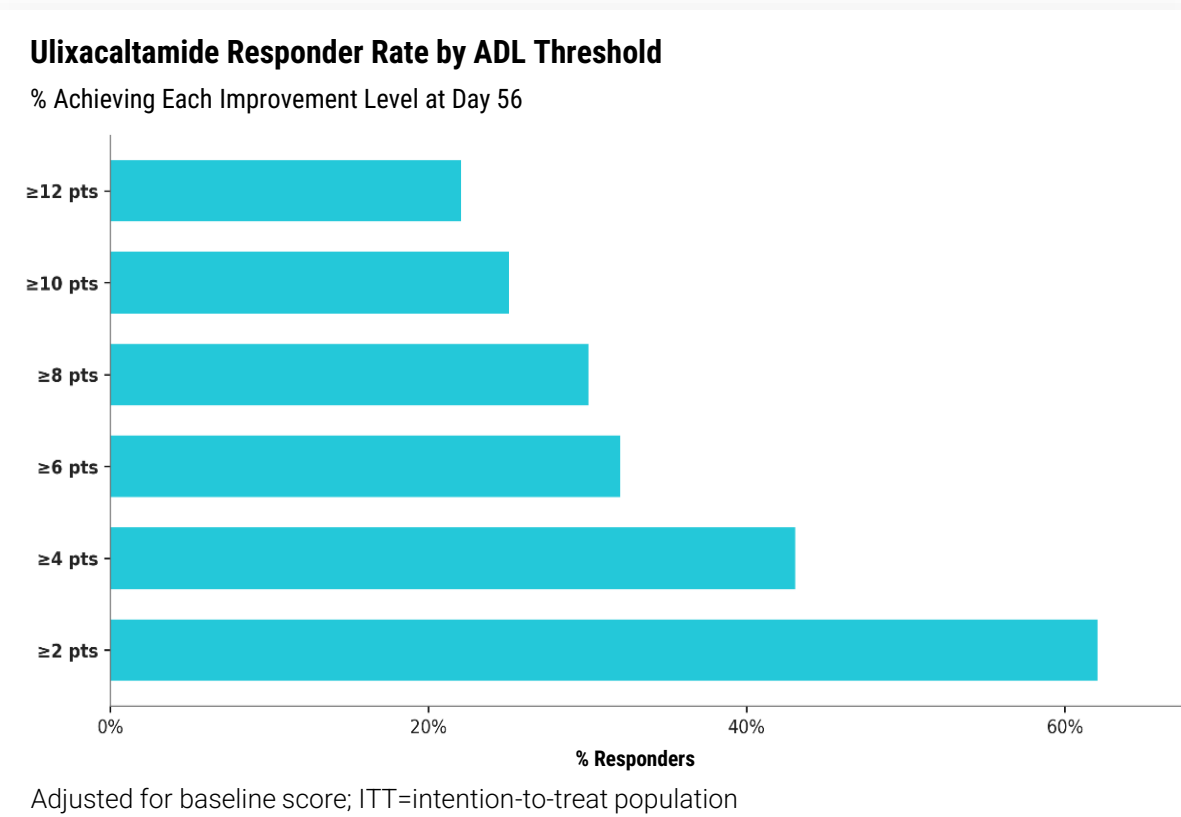
TETRAS-ADL Item Level Profile Demonstrating Functional Disability at Baseline (ITT)



Rapid Onset and Durable Clinically Meaningful Effect Observed in ADL (ITT)



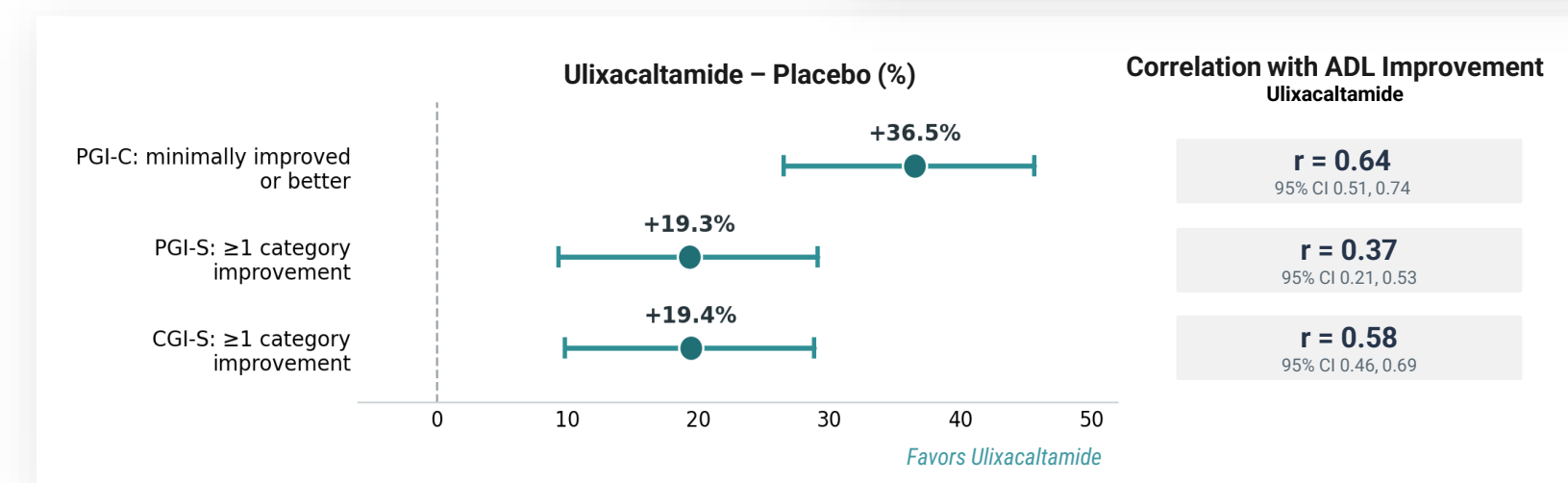
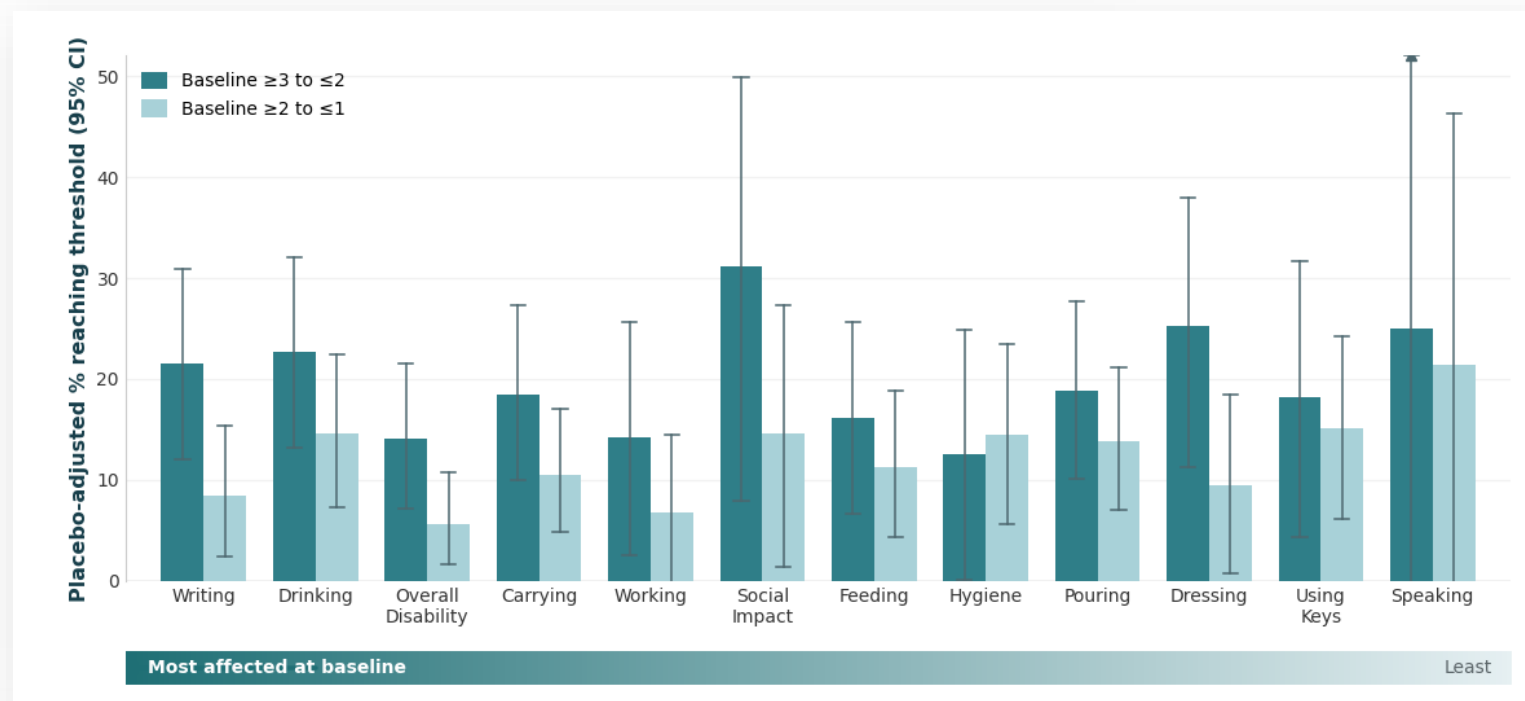
Responder Analysis – Benefit Maintained in ADL at Day 56 Across Increasing Response Thresholds (ITT)



CONVERGENT EVIDENCE OF MEANINGFUL BENEFIT: GLOBAL MEASURES FAVORED ULIXACALTAMIDE AND IMPROVED ALONGSIDE ADL FUNCTION

- Across all individual ADL items, a higher proportion of ulixacaltamide-treated participants who started with more significant disability (baseline score ≥3) improved by ≥1 level vs placebo, with consistent shifts among those with baseline ≥2 to near-normal level of functioning.
- All item levels showed consistent, clinically meaningful improvement, supporting a broad, item-level treatment effect rather than benefit concentrated or isolated to specific movements or tasks.
- The relatively modest correlation observed between global impression measures (PGI-C, PGI-S, CGI-S) and the ADL indicates that these endpoints capture distinct, complementary dimensions of treatment response. Because these endpoints are not strongly correlated, the convergent improvement with ulixacaltamide represents independent lines of evidence that reinforce a multidimensional treatment effect on both functioning and overall patient/clinician-perceived benefit.

Placebo-adjusted Proportion of Participants Improving Across ADL Items at Varying Degrees of Baseline Functional Impairment



Proportion of Responders, as Measured By Independent Patient- and Clinician-rated Global Impression Endpoints, Consistently Favored Ulixacaltamide at Day 56 (all $p < 0.05$)

Observed Day 56 data. Fisher exact tests. Spearman r relates the fraction of initially affected activities improved to global improvement in ulixacaltamide recipients. Correlation CIs use 1,000 bootstrap samples. All tests two-sided and nominal. CGI-S=Clinical Global Impression of Severity; PGI-C=Patient Global Impression of Change; PGI-S=Patient Global Impression of Severity

CONCLUSIONS

- ESSENTIAL3 Study 1 item-level analysis reveals broad functional improvement with ulixacaltamide across all ADL domains affected by ET.
- Independent patient- and clinician-rated global measures consistently favored ulixacaltamide and improved alongside ADL function.
- Findings demonstrate that clinically meaningful treatment benefits extend beyond upper-extremity motor tasks, complementing primary composite measure findings, and providing granular insight into the full breadth of potential therapeutic benefit.
- The NDA for ulixacaltamide is under FDA review, with a PDUFA target action date of January 29, 2027.

REFERENCES

- Louis & Ottman 2014 *Tremor Other Hyperkinet Mov (N Y)*
- Elble 2013 *Curr Neurol Neurosci Rep*
- Putzke et al 2006 *J Neurol Neurosurg Psychiatry*
- Louis et al 2001 *Movement Disorders*
- Chandran & Pal 2013 *Parkinsonism Relat Disord*
- Vetterick et al 2022 *Adv Ther*
- Elble et al 2012 *Mov Disord*
- Able et al AAN 2025a
- Able et al AAN 2025b
- Farmer et al AAN 2026
- Brillman et al AAN 2026
- Shtilbans et al AAN 2026

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