# Real-World Use of Trofinetide: A Survey of Tolerability From US Rett Syndrome Centers of Excellence

Erin Prange,[1] Shannon M. Standridge,[2] Constance Smith-Hicks,[3] Jennifer Martelle Tu,[4] Davut Pehlivan,[5] Steven Skinner,[6] Cary Fu,[7] Stephanie Kyle,[8] Alyssa Peckham[8]

[1]Children's Hospital of Philadelphia, Philadelphia, PA, USA; [2]University of Cincinnati School of Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; [3]Center for Synaptic Disorders, Rett and Related Disorders Clinic, Kennedy Krieger Institute, Baltimore, MD, USA; [4]University of California San Francisco Benioff Children's Hospital Oakland, CA, USA; [5]Baylor College of Medicine, Houston, TX, USA; [6]Greenwood Genetic Center, Greenwood, SC, USA; [7]Vanderbilt Kennedy Center, Vanderbilt University Medical Center, Nashville, TN, USA; [8]Acadia Pharmaceuticals Inc., San Diego, CA, USA

## BACKGROUND

- Rett syndrome (RTT) is a rare neurodevelopmental disorder characterized by loss of verbal communication with limited nonverbal skills, loss of fine and gross motor function, behavioral issues, seizures, hand stereotypies, and gastrointestinal problems[1,2]
- Trofinetide was approved by the US Food and Drug Administration in March 2023 for the treatment of RTT in adults and pediatric patients aged ≥2 years[3]
- Diarrhea was the most common adverse event and the leading cause of treatment discontinuation in clinical trials[4-6]; dose titration strategies are being used to improve tolerability in the real world

## OBJECTIVE

- To explore real-world experience with trofinetide dose titration and its impact on tolerability in the real world

## METHODS

### Study Design

- An electronic prescriber experience survey was designed to collect real-world trofinetide dosing strategies and their impact on tolerability
- The survey was sent in May 2024 to 33 prescribers at 18 US RTT centers of excellence (COEs) designated by the International Rett Syndrome Foundation

### Data Analysis

- All results were summarized with descriptive statistics

## RESULTS

### Study Participation

- Overall, 22 prescribers from 16 COEs completed the electronic survey
- The prescribers targeted for survey completion accounted for 38.1% of trofinetide prescriptions in the United States since approval (**Table 1**)

**Table 1. Electronic Survey Participation and Representation**

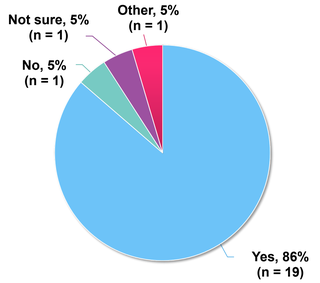
| | US trofinetide prescribers (N = 697)[a] | US trofinetide prescriptions (N = 1553)[a] |
|---|---|---|
| Non-COE providers, n (%) | 665 (95.4) | 962 (61.9) |
| COE providers, n (%) | 32 (4.6)[b] | 591 (38.1) |

[a]As of May 2024. [b]One eligible prescriber was associated with zero prescriptions
COE, center of excellence

### Trofinetide Dose Titration Impact on Tolerability

- In total, 86% (n = 19) of survey respondents indicated that titrating trofinetide improves tolerability in treatment-naïve patients (**Figure 1**)
- Specific tolerability improvements observed by respondents included decreased diarrhea severity (77%, n = 17), decreased trofinetide discontinuations (73%, n = 16), improved caregiver quality of life (64%, n = 14), and improved patient quality of life (59%, n = 13) (**Figure 2**)

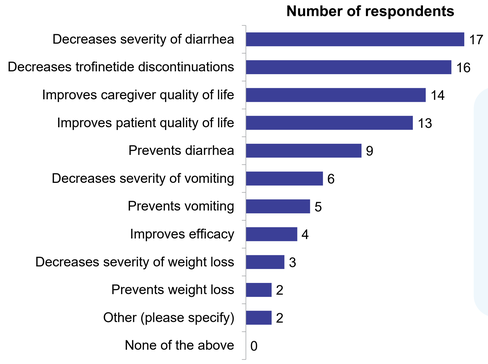
**Figure 1. Survey Respondents' Assessment of Impact of Trofinetide Dose Titration on Tolerability**




**Survey question:**
*As compared with your experience when starting trofinetide at labeled dose (ie, clinical trial setting or real-world setting), has titration helped improve overall tolerability of trofinetide? If no or not sure, please explain how in comment field below.*

**Responses:**
"No": *Some patients do not like the taste; another vomits even with 5 mL dose.*
**"Not sure"**: *I think there are patients that it doesn't matter for, patients it is critical for, and patients that don't tolerate no matter what we do.*
**"Other"**: *Did not participate in the trofinetide clinical trials and/or I have never started patients at the full weight-banded dose.*

**Figure 2. Trofinetide Tolerability Improvements With Dose Titration Reported by Survey Respondents**



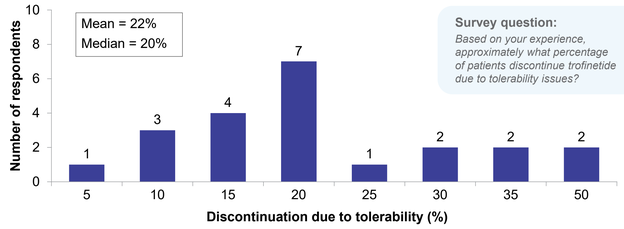

**Survey question:**
*Since you indicated that trofinetide titration has improved tolerability, please select specific tolerability improvements from the list provided based on your experience.*

**Reponses:**
**"Other"** responses: *Easier to find maximum tolerated dose; allows trofinetide improvements without the need for Imodium.*

### Trofinetide Tolerability-Related Discontinuation

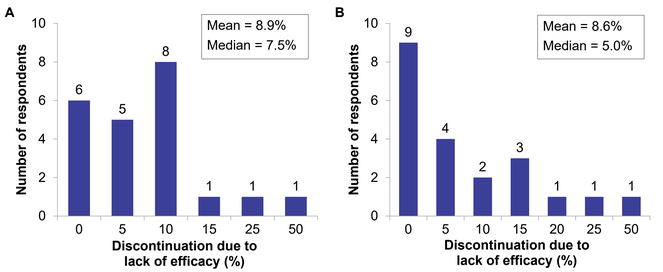
- Survey respondents indicated that approximately 20% of patients may still discontinue trofinetide due to tolerability issues (**Figure 3**)
- Trofinetide discontinuation due to lack of efficacy was estimated to be much lower at approximately 5–8% (**Figure 4**)

**Figure 3. Trofinetide Discontinuation Due to Tolerability Issues**




**Survey question:**
*Based on your experience, approximately what percentage of patients discontinue trofinetide due to tolerability issues?*

**Figure 4. Trofinetide Discontinuation Due to Lack of Efficacy: (A) Discontinuation Due to Lack of Efficacy in Patients Who Achieve Full Weight-Banded Dose; (B) Discontinuation Due to Lack of Efficacy in Patients on Sub Weight-Banded Doses**




**Survey questions:**
*Have you or do you currently have any patients on a full weight-banded dose? If yes, based on your experience, approximately what percentage of patients on full weight-banded dose discontinue due to lack of efficacy? Have you or do you currently have any patients on a sub weight-banded dose? If yes, based on your experience, approximately what percentage of patients on sub weight-banded dose discontinue due to lack of efficacy?*

## CONCLUSIONS

- Prescribers believe trofinetide titration helps with overall tolerability, specifically to decrease diarrhea severity and treatment discontinuations while improving patient and caregiver quality of life
- Tolerability issues may persist in some patients, which can lead to discontinuation
- Prescribers believe discontinuation due to lack of efficacy remains low

### REFERENCES

1. Neul JL, et al. *Ann Neurol.* 2010;68(6):944–950.
2. Motil KJ, et al. *J Pediatr Gastroenterol Nutr.* 2012;55(3):292–298.
3. DAYBUE (trofinetide) [package insert]. San Diego, CA: Acadia Pharmaceuticals; 2024.
4. Neul JL, et al. *Nat Med.* 2023;29(6):1468–1475.
5. Percy AK, et al. *Med.* 2024;5(9):1178–1189.e3.
6. Percy AK, et al. *Med.* 2024;5(10):1275–1281.e2.

### ACKNOWLEDGMENTS

The study was supported by Acadia Pharmaceuticals Inc. (San Diego, CA, USA). Medical writing support was provided by Juan Sanchez-Cortes, PhD, of Evidence Scientific Solutions, Inc., and funded by Acadia Pharmaceuticals Inc.

### DISCLOSURES

**EP** is a consultant to Acadia Pharmaceuticals Inc. **SMS** is a consultant to Acadia Pharmaceuticals Inc. **CS-H** serves on the Acadia Advisory Board and receives research support from the Kennedy Krieger Institute, which has an institutional agreement with Acadia. **JMT** is a consultant to Acadia Pharmaceuticals Inc. **DP** is supported by the Doris Duke Charitable Foundation (#2023-0235) and NINDS 1K23 NS125126-01A1 and is a consultant to Ionis Pharmaceuticals. **SS** is a consultant to Acadia Pharmaceuticals Inc. **CF** is a consultant to Acadia Pharmaceuticals Inc. **SK** and **AP** are employees and stakeholders in Acadia Pharmaceuticals Inc.

Presented at the NAPNAP National Conference on Pediatric Health Care, March 10–13, 2025, Chicago, IL, USA

ACADIA®