Poster #1.541

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An Evaluation of Real-World Effectiveness and Safety of Trofinetide in Patients With Rett Syndrome: A Retrospective Chart Review

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DISCLOSURES

CS-H serves on the Acadia Pharmaceuticals Inc. advisory board and receives research support from the Kennedy Krieger Institute, which has an institutional agreement with Acadia Pharmaceuticals Inc. **SS** was a site PI for Acadia Pharmaceuticals Inc.; is a consultant with Acadia Pharmaceuticals Inc., and serves as a member of a data safety monitoring board for clinical trials conducted by Taysha Gene Therapies. **AA** has received funding for clinical trials from Acadia Pharmaceuticals Inc. Anavex, Neurogene, Taysha Pharmaceuticals, and UCB Therapeutics; and serves on the Sanofi advisory board. **CF** has received funding for clinical trials from Zogenix Pharmaceuticals and consultancy fees from Acadia Pharmaceuticals Inc. **AB** is a consultant to Acadia Pharmaceuticals Inc. **PH** has no disclosures. **DP** is supported by the Doris Duke Charitable Foundation (#2023-0235) and NINDS-1K23 NS125126-01A1 and is a consultant to Ionis Pharmaceuticals, M2DS Therapeutics, and Acadia Pharmaceuticals Inc. **RB** is an employee and stakeholder in Acadia Pharmaceuticals Inc.

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INTRODUCTION

- Rett syndrome (RTT) is a rare neurodevelopmental disease associated with developmental regression and difficulties with verbal communication, motor skills, and hand use[1]
- Patients with RTT experience several comorbidities due to the disease, including seizures, scoliosis, issues with sleep, and behavioral and gastrointestinal issues[2,3]
- Trofinetide is approved for the treatment of RTT in patients aged ≥2 years in the United States and patients aged ≥2 years weighing ≥9 kg in Canada[4,5]
- While trofinetide clinical trials have demonstrated the efficacy and safety of trofinetide in patients with RTT,[6-9] real-world data are essential to understand its impact in routine clinical practice

OBJECTIVE

- To assess the real-world effectiveness and safety of trofinetide in patients with RTT following its commercial availability in the United States in April 2023 using a retrospective chart review

CONCLUSIONS

The results of this chart review provide valuable insight into the real-world use of trofinetide in patients with RTT, including its effectiveness and safety

- Patients with severe RTT symptoms at baseline experienced improvements in the symptoms of the disease that may help reduce caregiver burden

The results of the chart review follow similar trends to the results of the trofinetide clinical program and the real-world LOTUS study[6-9,11]

- This chart review study complements the LOTUS study, which includes caregiver-reported assessments, by providing clinician-reported assessments

Further research is needed to confirm these trends in larger diverse populations

METHODS

Study Design

- This multi-site, non-interventional, observational, retrospective chart review study included patients with RTT aged ≥2 years across 6 clinical sites in the United States
- Patients were grouped based on time of initiation of trofinetide: Group A initiated trofinetide after commercial availability and Group B initiated trofinetide during clinical trials
  - Here we present interim results from the first 51 patients in Group A, who had completed status in the study database as of July 25, 2025
  - This presentation is focused on patients in Group A, due to small sample size of Group B and prior exposure to trofinetide

Study Assessments

- Data was extracted from electronic health records and included demographics, clinical characteristics, and safety outcomes
- Changes in the symptoms of RTT were assessed from baseline to 3, 6, 12, and >12 months post-initiation of commercial trofinetide
  - Data from >12-month post-initiation will be presented when the full dataset is available
- RTT symptom domains used in this study were derived from the Rett Syndrome Behaviour Questionnaire subdomains (general mood, breathing problems, hand behaviors, repetitive face movements, body rocking and expressionless face, nighttime behaviors, fear/anxiety, and walking/standing)[10] with some modifications to gather more detailed information
  - The RSBQ **hand behaviors** subdomain was divided into **hand behaviors** and **fine motor skills**; the **nighttime behaviors** subdomain was divided into **nighttime behaviors** and **sleep**
  - Three additional domains, **communication**, **connectedness**, and **alertness/awareness**, were added
  - Behavioral symptoms deemed clinically significant and recorded in the electronic health records that cannot be categorized in these domains were placed in the other behavioral symptoms domain
  - Other non-behavioral symptoms were captured in the additional symptoms domain
- Safety endpoints included the incidence of adverse events (AEs)
- Descriptive statistics were used to analyze the data

RESULTS

Demographics, Baseline Characteristics, and Patient Disposition

- Group A was comprised of 41 female patients with RTT, with a median (interquartile range [IQR]) age of 7.7 (4.5–17.4) years (Table 1)
  - All patients had a history of a pathogenic variant in the transcriptional regulator methyl-CpG binding protein-2 *(MECP2)* gene
  - In total, 14 (34.1%) patients in Group A discontinued trofinetide and 17 (41.5%) had ≥1 dose interruption

Table 1. Baseline Demographic and Clinical Characteristics

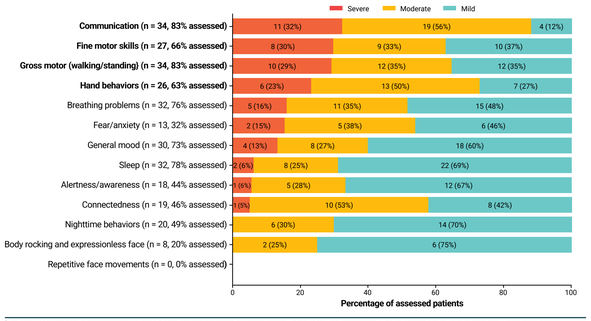
Characteristic	Group A (N = 41)
Median (IQR) age of trofinetide initiation, years	7.7 (4.5–17.4)
Median (IQR) age at time of RTT diagnosis, years	2.0 (1.8–4.1)
RTT type	
Classic	37 (92.5)
Atypical	3 (7.5)
Unknown	1 (2.4)
Ethnicity	
White	35 (85.4)
American Indian or Alaskan Native	1 (2.4)
Other	1 (2.4)
Unknown	4 (9.8)

Data are n (%) unless stated otherwise.
IQR, interquartile range; **RTT**, Rett syndrome.

Baseline RTT Symptom Severity Across Domains

- The most commonly reported severe RTT symptoms at baseline in Group A included issues with communication, gross motor skills (walking/standing), fine motor skills, hand behaviors, and breathing problems (Figure 1)

Figure 1. Baseline RTT Symptom Severity Across Domains[a]



[a]Patients without domain assessments or in which no issues were noted are not shown. "Other behavioral symptoms" (including teeth grinding, fatigue, head banging, afternoon screaming, and aggressive behavior) and "additional non-behavioral symptoms" (such as seizures and gastrointestinal symptoms) are not shown because they represent a diverse group of presentations in relatively few patients, making categorical analysis difficult to interpret. These will be examined further when the full dataset is available.
RTT, Rett syndrome.

Safety

- AEs were reported for 37 (90.2%) patients in Group A (Table 2)
  - The most commonly reported AEs in Group A were diarrhea (75.6%) and vomiting (34.1%) (Table 2)
- There were 2 patients with serious AEs: 1 patient with 4 events (3 status epilepticus events and 1 pneumonia; all unrelated to treatment), and 1 patient with 1 event (pneumonia; related to treatment)
  - Both patients recovered from all events

Table 2. Incidence of Adverse Events

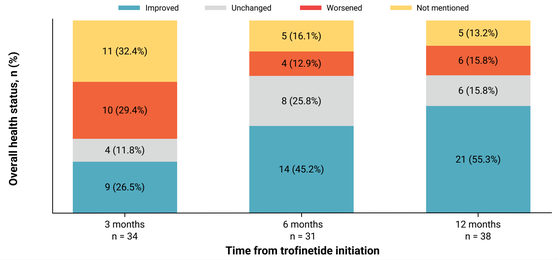
Group A (N =41)	AEs in ≥5.0% of patients	AEs possibly/probably related	AEs that led to dose interruption	AEs that led to discontinuation
Any	37 (90.2)			
Diarrhea	31 (75.6)	11 (26.8)	9 (22.0)	5 (12.2)
Vomiting	14 (34.1)	7 (17.1)	5 (12.2)	4 (9.8)
Seizure[a]	6 (14.6)	1 (2.4)	2 (4.9)	-
Constipation	5 (12.2)	2 (4.9)	-	1 (2.4)
Decreased appetite	4 (9.8)	3 (7.3)	2 (4.9)	-
Pneumonia	3 (7.3)	-	-	1 (2.4)
Urinary tract infection	3 (7.3)	-	-	-
Behavior disorder	2 (4.9)	-	1 (2.4)	1 (2.4)
Fatigue	2 (4.9)	2 (4.9)	-	1 (2.4)
Irritability	2 (4.9)	2 (4.9)	1 (2.4)	1 (2.4)
Respiratory tract infection	2 (4.9)	1 (2.4)	-	1 (2.4)
Sleep disorder	2 (4.9)	1 (2.4)	-	-
Weight decreased	2 (4.9)	1 (2.4)	-	1 (2.4)

Data are n (%) unless stated otherwise. *Twenty-four patients were noted to have epilepsy or seizures at baseline.
AE, adverse event.

Overall Health Status Compared With Baseline

- Patients in Group A experienced overall health improvements from months 3–12 of trofinetide treatment (Figure 2)

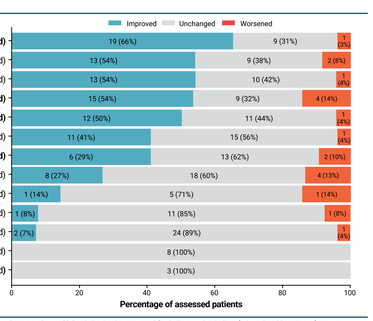
Figure 2. Overall Health Status Compared With Baseline



Change in Symptoms of RTT From Baseline to Month 12 of Trofinetide Treatment

- Improvements in the symptoms of RTT were consistently reported in the subdomains of communication, gross motor skills, alertness/awareness, connectedness, and fine motor skills (Figure 3)

Figure 3. Change in Symptoms of RTT From Baseline to Month 12 of Trofinetide Treatment[a]



[a]Patients without domain assessments or in which no issues were noted are not shown. "Other behavioral symptoms" (including teeth grinding, fatigue, head banging, afternoon screaming, and aggressive behavior) and "additional non-behavioral symptoms" (such as seizures and gastrointestinal symptoms) are not shown because they represent a diverse group of presentations in relatively few patients, making categorical analysis difficult to interpret. These will be examined further when the full dataset is available.
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