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Real-World Benefits and Tolerability of Trofinetide for the Treatment of Male Patients With Rett Syndrome: Interim Results of the LOTUS Study

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DISCLOSURES

AB is a consultant to Acadia Pharmaceuticals Inc. **LR, AP, LC,** and **RB** are employees and stakeholders in Acadia Pharmaceuticals Inc.

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INTRODUCTION

- Rett syndrome (RTT) is a rare neurodevelopmental disease primarily associated with loss-of-function mutations in the transcriptional regulator methyl-CpG binding protein-2 (*MECP2*) gene[1]
- RTT presents predominantly in female individuals, yet recent developments in genetic testing have added support to clinical observations that RTT can occur in males[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, regardless of sex[4,5]
- The benefits and tolerability of trofinetide in male patients with RTT have not been studied

OBJECTIVE

- To characterize real-world benefits and tolerability of trofinetide in male patients with RTT enrolled in LOTUS

METHODS

LOTUS Study Design and Population

- LOTUS is an ongoing, phase 4, observational, real-world, prospective, online study involving caregivers of patients prescribed trofinetide under routine clinical care[6]
- LOTUS participation lasts for ≥12 months from trofinetide initiation, with the option to extend participation for an additional 12 months
- Caregivers of any patients who were prescribed trofinetide under routine care are eligible for this study; there are no exclusion criteria

Relevant Study Assessments

- The Behavioral Improvement Questionnaire (BIQ) is a novel measure that has been adapted from the Rett Syndrome Behaviour Questionnaire, the top caregiver concerns from the US Natural History Study, and the RTT community list of symptoms in the Voice of the Patient Report [7-9]; it consists of questions soliciting a "yes" or "no" response from caregivers as to whether they observed new and/or maintained improvements following treatment with trofinetide compared with the period before starting trofinetide
  - A "yes" answer resulted in the opportunity to identify all areas of improvement from a checklist that included alertness, behavioral problems, breathing irregularities, communication tools, eating/swallowing, grinding teeth, mobility or balance, mood, muscle tone abnormalities, non-verbal communication, purposeful use of hands, repetitive movements, sleep, social interaction/connectedness, verbal communication, and other domains
  - The BIQ was assessed monthly for 6 months and every 3 months thereafter
- The Gastrointestinal (GI) Health Questionnaire was designed to assess GI health including dosing timing and amount, incidence of diarrhea, and the type of stool formation over the past 3 days, among others
  - Weekly assessments were conducted for the first 12 weeks of the study, followed by once a month for the next 3 months, then quarterly afterwards
- Data are reported to 12 months since the initiation of trofinetide

RESULTS

Demographics and Baseline Characteristics

- In total, 7 caregivers of male patients with RTT participated in this follow-up, representing patients with ages ranging from 2–33 years (Table 1)

Table 1. Patient Characteristics and Medical History

Characteristic	LOTUS males (n = 7)
RTT type	
Classic	2 (28.6)
Atypical	1 (14.3)
Unknown	4 (57.1)
Ethnicity	
Non-Hispanic	7 (100.0)
Median (IQR) age at time of RTT diagnosis, years (n = 3)	7 (1—25)
Median (IQR) age at time of trofinetide initiation, years[a]	8 (3—19)

Data are n (%) unless stated otherwise.
[a]Trofinetide initiation is the day of trofinetide shipment.
IQR, interquartile range; **RTT**, Rett syndrome.

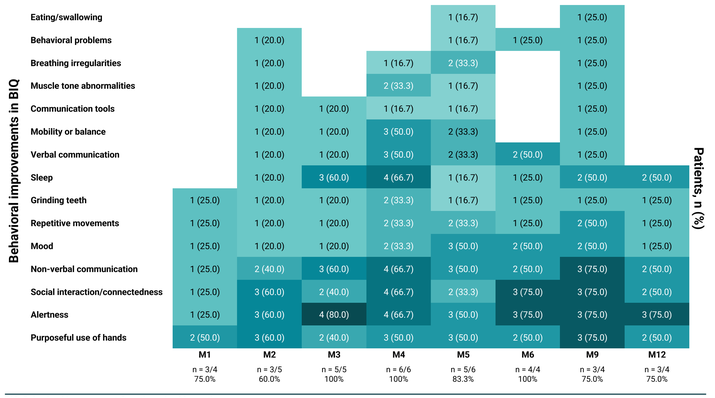
Trofinetide Dosing

- The median trofinetide dose at week 1 was 38.9% of the target dose and increased to over 89.2% by week 12
  - There was variability in dosing from months 4—12, reflecting dose discontinuations and reductions for the management of diarrhea

Behavioral Improvements

- The behavioral improvements repeatedly reported by caregivers on the BIQ from months 1—12 included alertness, mood, purposeful use of hands, repetitive movements, grinding teeth, non-verbal communication, and social interaction/connectedness (Figure 1)

Figure 1. Behavioral Improvements Reported by Caregivers With BIQ

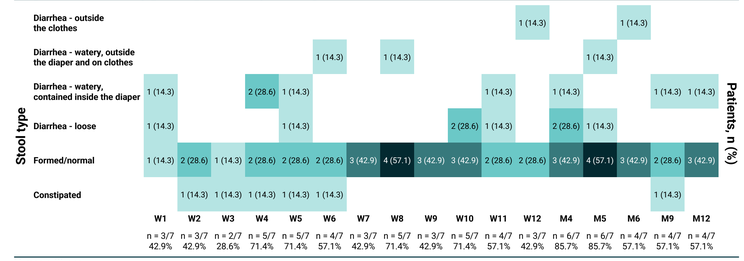


BIQ, Behavioral Improvement Questionnaire; **M**, month.

GI Health After Initiation of Trofinetide

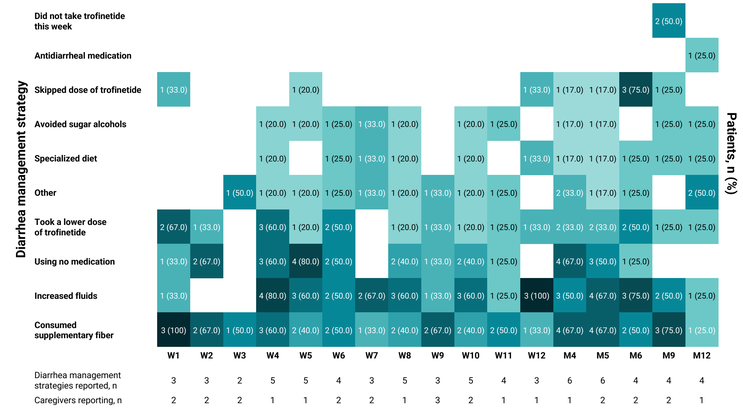
- Most caregivers reported formed/normal stools throughout the follow-up; most reports of diarrhea were contained inside the patients' diaper (Figure 2)
- The most common diarrhea management strategies reported by caregivers were increased fluid intake, trofinetide dose reductions, and temporary trofinetide discontinuation (Figure 3)

Figure 2. Stool Type Reported by Caregivers



M, month; **W**, week.

Figure 3. Diarrhea Management Strategies Reported by Caregivers



M, month; **W**, week.

Safety

- Adverse events were reported for 3 (42.9%) patients and consisted of pneumonia, sapovirus, and weight loss (n = 1 for each, 33.3%)

CONCLUSIONS

The results of the 7 males with RTT included in this interim analysis suggest that treating male and female patients with trofinetide patients looks similar in real-world clinical practice

The real-world benefits and tolerability of trofinetide in males follow similar trends with the predominantly female general population of LOTUS