Real-World Benefits and Tolerability of Trofinetide for the Treatment of Rett Syndrome: Interim Analysis of the LOTUS Study

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Background

- RTT is a rare neurodevelopmental disorder characterized by a regression in early childhood, predominantly observed in speech, fine motor hand skills, and ambulation[1]

- Trofinetide is approved for the treatment of RTT in patients aged ≥2 years in the US, and patients aged ≥2 years weighing ≥9 kg in Canada[2,3]
  - The efficacy and safety of trofinetide were established in LAVENDER and maintained over LILAC and LILAC-2, open-label extension studies of LAVENDER[4-6]

- Clinicians and families are interested in real-world outcomes of trofinetide treatment, including RTT-symptom improvement, diarrhea characterization in the real world, impact on older patients, and effects on QoL

Study Design and Assessments

- LOTUS is an ongoing, phase 4, observational, real-world, prospective, online study involving caregivers of patients prescribed trofinetide under routine clinical care

- LOTUS study assessments include:
  - BIQ: Behavioral improvements
  - QI-Disability questionnaire: QoL improvements
  - GI Health questionnaire: GI health improvements

- Due to ongoing enrollment, data were presented up to 9 months

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Demographics and Baseline Characteristics

Characteristics	Total (N = 192)
RTT type, n (%)[a]	
Classic	101 (66.0)
Atypical	41 (26.8)
Does not meet diagnostic criteria for either	11 (7.2)
Sex, n (%)[b]	
Male	8 (4.2)
Female	183 (95.8)
Median (IQR) age at time of RTT diagnosis, years[c]	3.0 (2.0–5.0)
Median (IQR) age at time of trofinetide initiation, years[d,e]	15.0 (7.0–24.0)

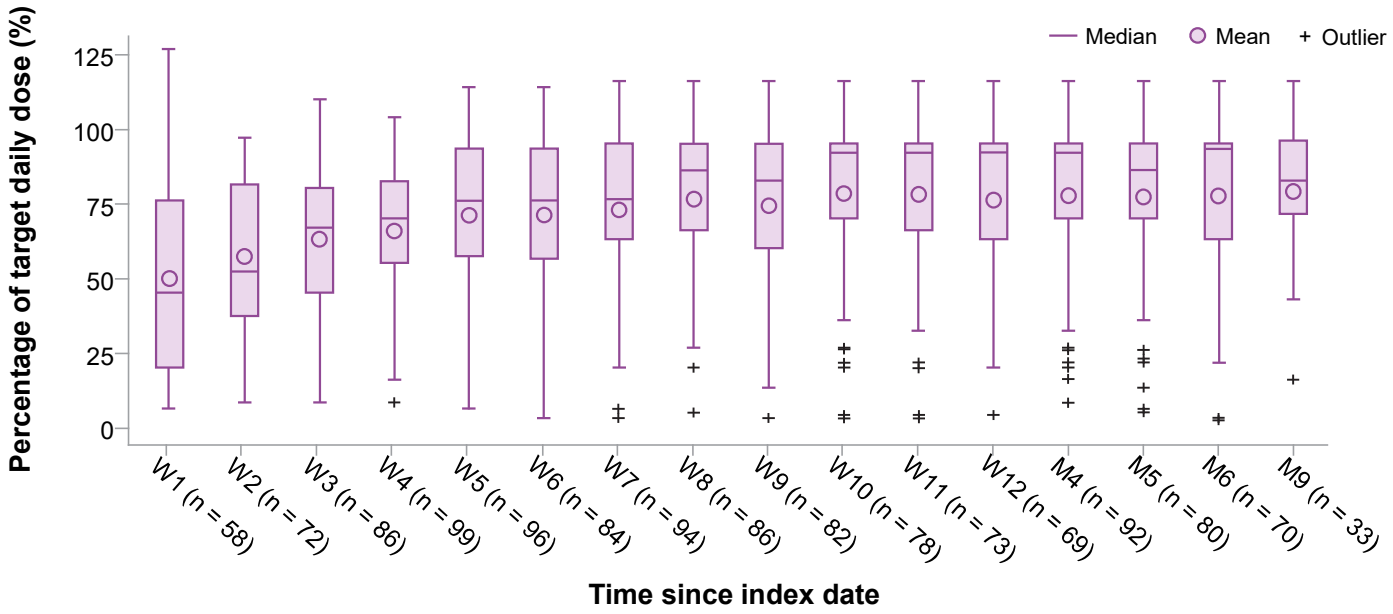
[a]n = 153. [b]n = 191. [c]n = 141. [d]n = 135. [e]Trofinetide initiation is the day of trofinetide shipment

- In total, 192 patients, with ages ranging from 2–60 years, were included

BIQ, Behavioral Improvement Questionnaire; GI, gastrointestinal; IQR, interquartile range; QI, Quality-of-Life Inventory; QoL, quality of life; RTT, Rett syndrome.

1. Neul JL, et al. *Ann Neurol*. 2010;68:944–950. 2. DAYBUE (trofinetide) [package insert]. San Diego, CA: Acadia Pharmaceuticals; 2024. 3. DAYBUE Canadian Product Monograph. Ontario, 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):1178-89 e3. 6. Percy AK, et al. *Med*. 2024;5(10):1275-81 e2.

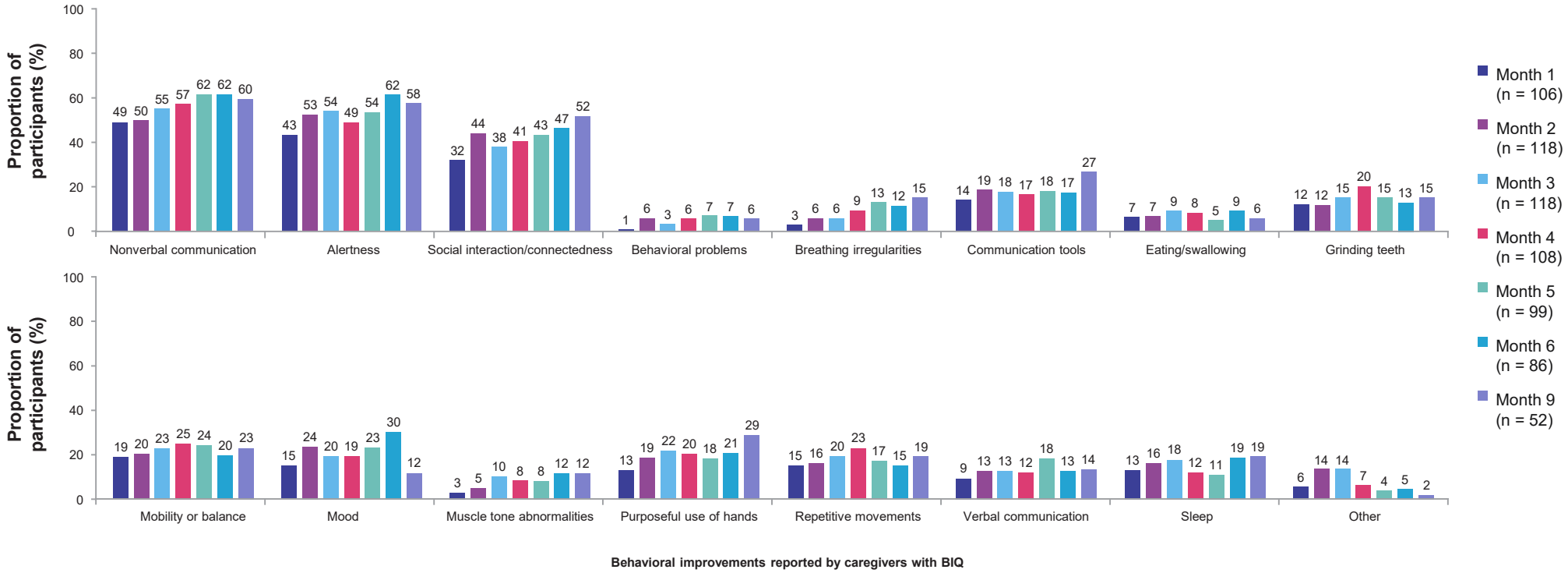
Trofinetide Dosing Reported by Caregivers



- Most patients (59.6–93.1%) took trofinetide twice daily
- The median dose reported at week 1 was 45.0% of the target weight-banded label dose; by week 9 onwards, the median dose was at least 80.0% of target
- There was wide variability in dosing at week 1 (IQR, 20.0–76.0% of labeled daily dose), suggesting a variety of dosing approaches used when initiating trofinetide in real-world clinical practice

IQR, interquartile range; M, month; W, week

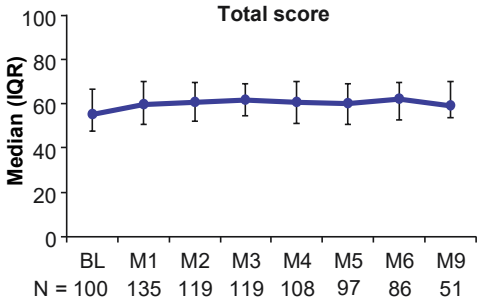
Behavioral Improvements Reported by Caregivers With BIQ

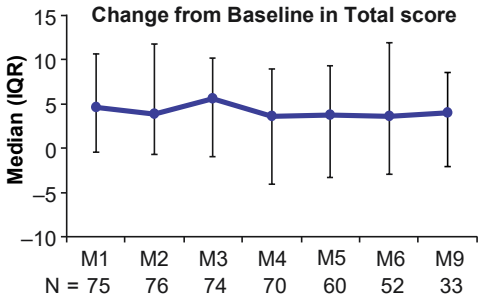


- Overall, 69–81% of caregivers reported behavioral improvements on the BIQ during months 1–9
  - Caregivers reported behavioral improvements in 59–77% of adult patients (≥18 years, n = 26–46) and 76–85% of pediatric patients (<18 years, n = 26–73)
- The greatest and most consistently reported improvements were nonverbal communication (49–62%), alertness (43–62%), and social interaction/connectedness (32–52%)
  - Same rank order of improvements were observed in adult and pediatric subgroups

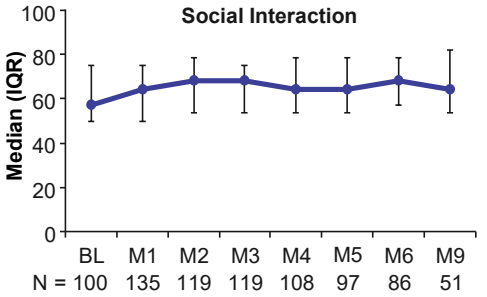
BIQ, Behavioral Improvement Questionnaire.

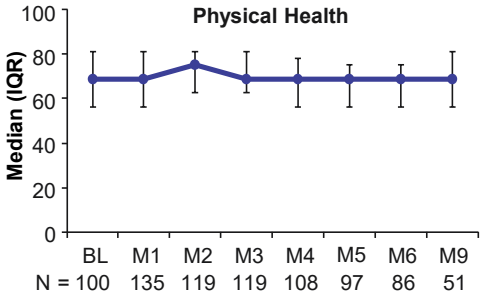
QoL Improvements Reported by Caregivers With QI-Disability Questionnaire

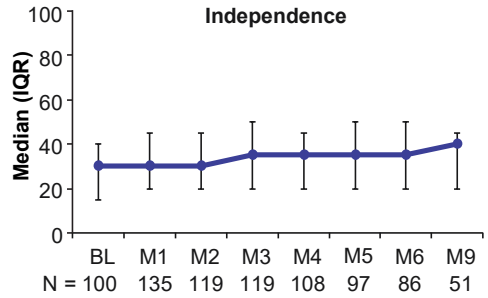


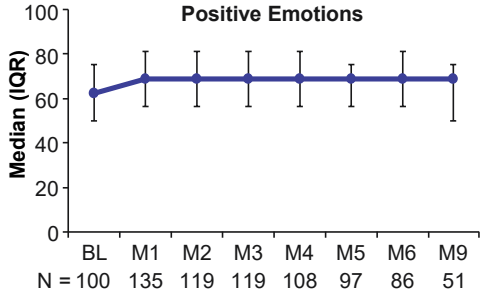


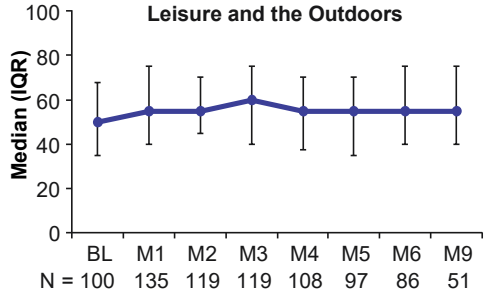
- QI-Disability questionnaire total score and change from baseline in total score indicate improvements in QoL
- Similar trends were observed for the social interaction, physical health, independence, positive emotions, leisure and the outdoors, and negative emotions individual domains scores

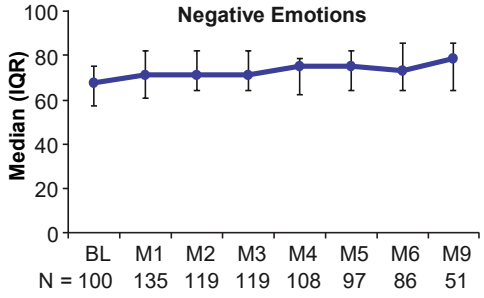






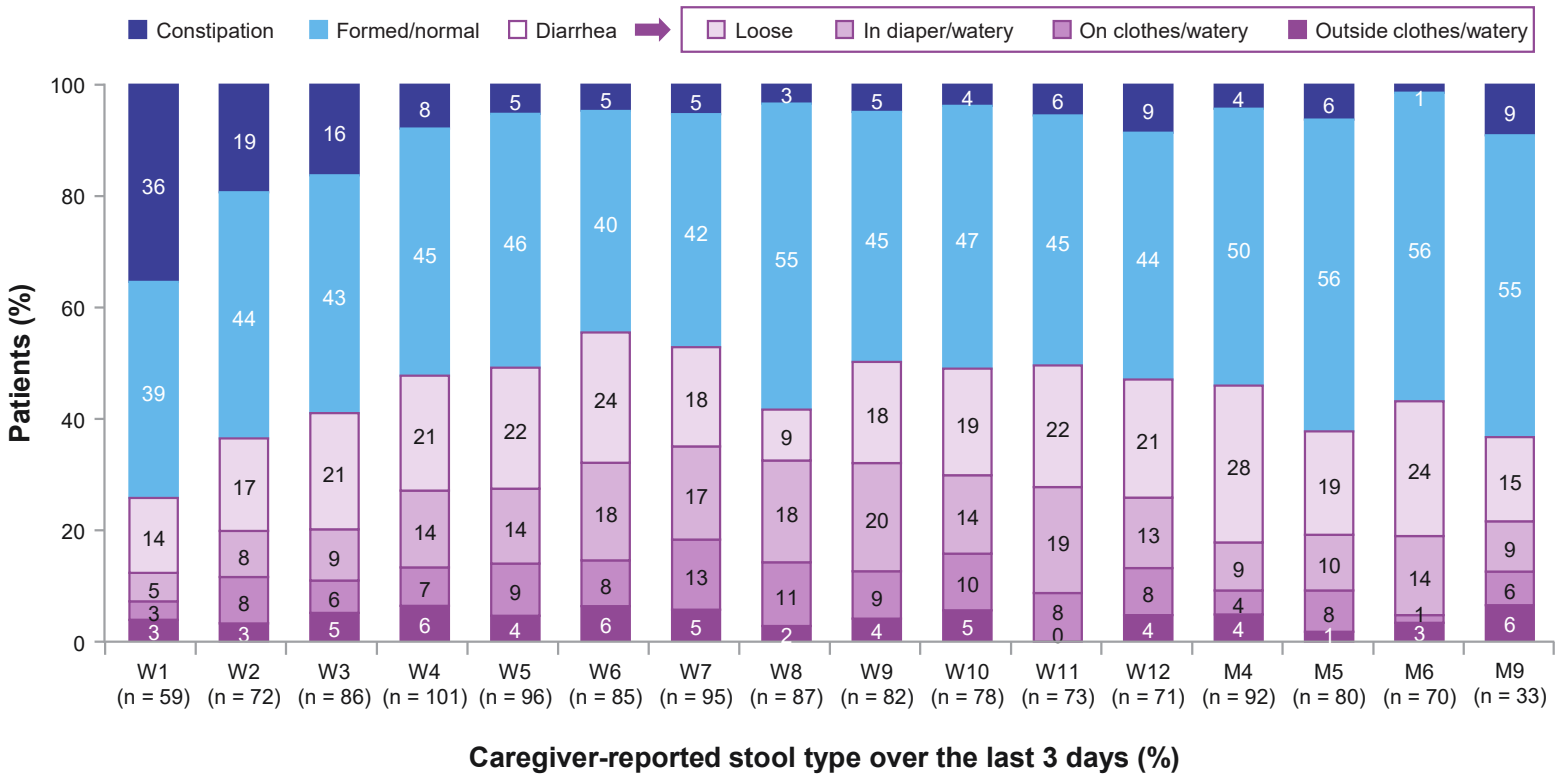






BL, baseline; IQR, interquartile range; M, month; QI, Quality-of-Life Inventory; QoL, quality of life.

GI Health Reported by Caregivers With GI Health Questionnaire



- Patients were most likely to void normal stools from weeks 1–12 (39–55%) and months 4–9 (50–56%)
- The incidence of diarrhea varied from weeks 1–12 (25–55%) and months 4–9 (36–46%), with the highest incidence of diarrhea reported at week 6 by 55% of caregivers
- Most reports of diarrhea were contained inside the patient's diaper
- Vomiting was uncommon throughout this follow-up (<7% at any time point)

GI, gastrointestinal; M, month; W, week.

Conclusions

- Caregivers of more than 87% of patients reported behavioral improvements of RTT symptoms at all time points, starting at the first time point
  - Nonverbal communication, alertness, and social interaction/connectedness were the most frequently reported improvements
- Consistent with behavioral improvements, caregivers reported improvements in QoL of patients starting at the first time point
- Diarrhea and formed/normal stool were both common, with diarrhea most commonly categorized as “loose” or “watery, contained inside the diaper”
- The results of this 12-month follow-up are limited by caregiver reports, the number of patients who have reached later time points, missing data, and the online nature of this study; further analysis will occur as more patients are enrolled in the study

GI, gastrointestinal; M, month; W, week.