

Real-World Trofinetide Dosing for Rett Syndrome: The LOTUS Study

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BACKGROUND

• Rett syndrome (RTT) is a rare neurodevelopmental disorder characterized by a regression in early childhood, predominantly observed in speech, fine motor hand skills, and ambulation¹

• RTT is associated with a broad set of symptoms including deficits in communication, breathing, stereotypies, nighttime behaviors, vocalizations, facial expressions, mood, and seizures^{1,2}

• 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^{3,4}

• Trofinetide is recommended to be dosed twice a day following weight-banded dosing^{3,4}

• In LAVENDER, a phase 3, randomized, placebo-controlled study of trofinetide in girls and women with RTT, the trial participants started trofinetide at their full weight-banded dose; dose reductions to manage tolerability were allowed⁵

OBJECTIVES

• To characterize trofinetide dosing patterns in the real world with the 12-month follow-up of the LOTUS study

METHODS

LOTUS Study Design and Study Population

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

• 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

• Real-world dosing and gastrointestinal (GI) health were reported weekly for the first 3 months of the study and then monthly using a caregiver-reported questionnaire

• Participants reporting zero doses of trofinetide on the date of the questionnaire are excluded from that timepoint

• Dosing was reported by caregivers using a dropdown menu that used 5-mL ranges; the middle of the range was used in analyses

• The first 12 weeks of dosing for both groups are shown, as the doses and metrics of GI function converge before the end of the 12-week sampling period

• Due to ongoing enrollment, data were presented up to 9 months since the initiation of trofinetide

RESULTS

Demographics and Baseline Characteristics

• In total, 192 participants, with ages ranging from 2 to 60 years, were included (**Table 1**)

Table 1. Baseline Demographic and Clinical Characteristics

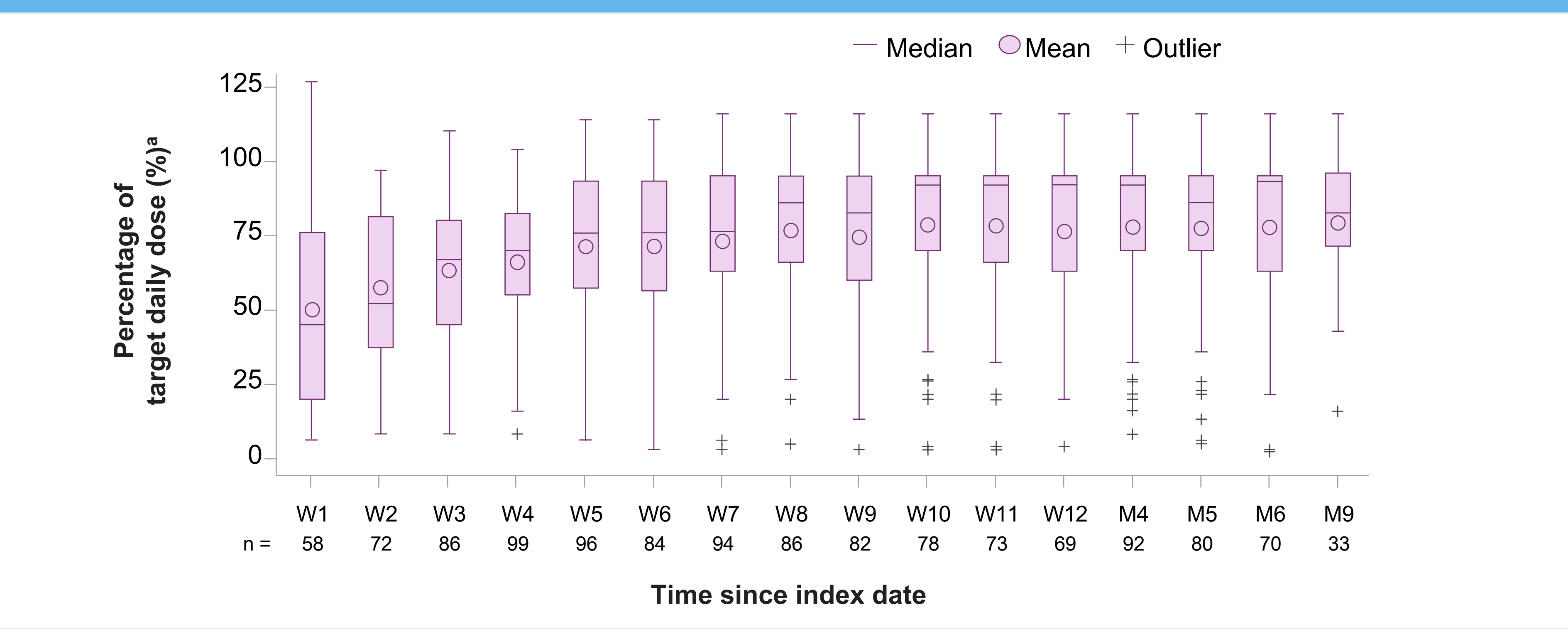
Characteristic	Total (N = 192)
RTT type, n (%) ^a	
Classic	101 (66.0)
Atypical	41 (26.8)
Does not meet diagnostic criteria for either	11 (7.2)
Sex, n (%)	
Male	8 (4.2)
Female	183 (95.8)
Median (IQR) age at time of RTT diagnosis, years ^b	3.0 (2.0–5.0)
Median (IQR) age at time of trofinetide initiation,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

^an = 129. ^bn = 119. ^cn = 121. ^dTrofinetide initiation is the day of trofinetide shipment
IQR, interquartile range; RTT, Rett syndrome

Trofinetide Dosing

- Most participants (59.6–93.1%) took trofinetide twice a day, while others took it either 1 time per day (0–4.7%), 3 times per day (1.9–6.9%), or 4 times per day (0–1.3%)
- The median dose reported at week 1 was 45.0% of the target weight-banded label dose; by week 12, the median dose was 92.0% of target (**Figure 1**)
 - There was wide variability in dosing at week 1 (interquartile range [IQR], 20.0–76.0% of labeled daily dose), suggesting a variety of dosing approaches used when initiating trofinetide in real-world clinical practice

Figure 1. Percentage of Target Daily Dose



^aPercentage of target daily dose was calculated as [actual daily dose] / [target daily dose based on patient's weight at shipment transaction] × 100
M, month; W, week

Trofinetide Dosing and Stool Type

- Despite different initial trofinetide dosing strategies, the mean trofinetide doses over time converged for the participants who received <75% versus ≥75% of trofinetide target dose as the first recorded dose (**Figure 2**)
- The incidence of diarrhea was lower in participants who received <75% versus ≥75% of target dose as first recorded dose at early weeks of treatment, yet most participants did not experience diarrhea regardless of dose (**Figure 3**)
- The frequency of diarrhea was similar between participants who received <75% versus ≥75% of target dose as first recorded dose, but the <75% group had fewer clothing changes compared with the ≥75% group over the first 12 weeks of treatment (**Figure 4**)

Figure 2. Trofinetide Dosing Reported by Caregivers of Participants Who Received ≥75% (A) and <75% (B) of Target Dose as First Recorded Dose

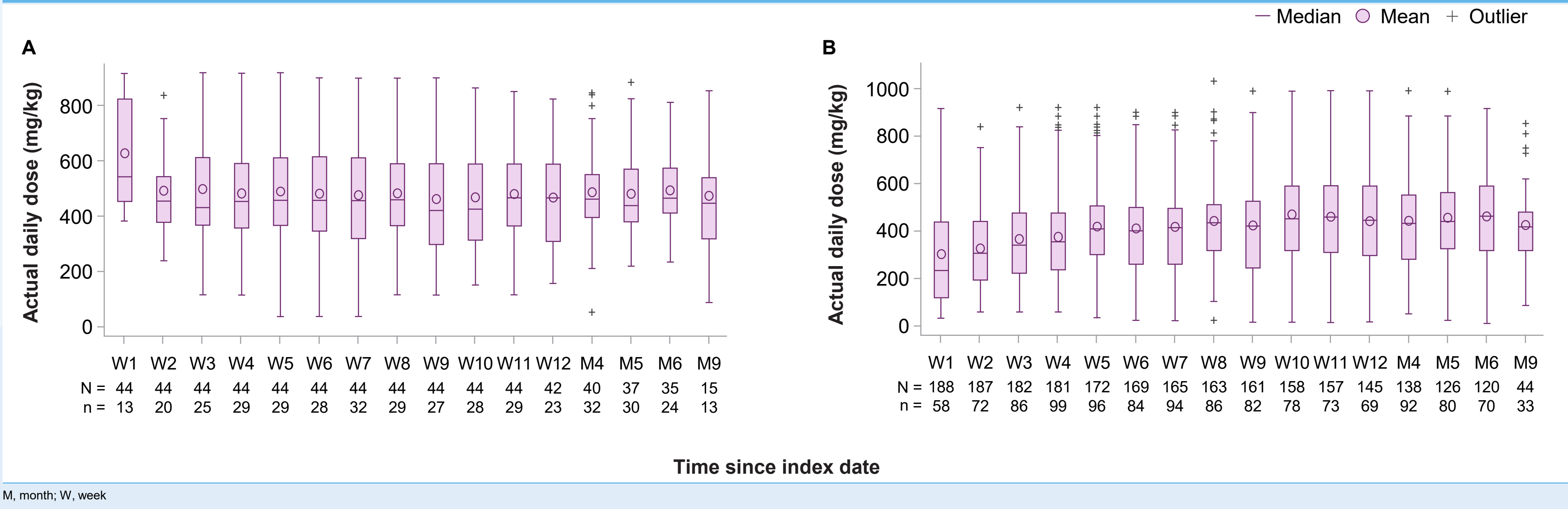
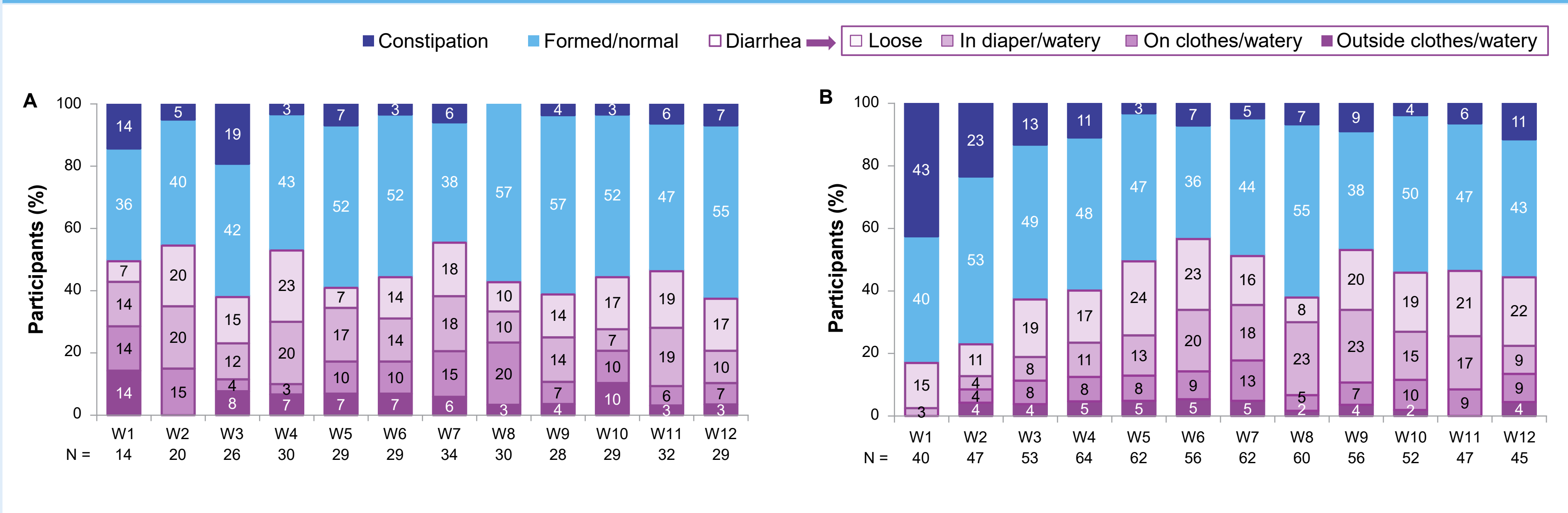
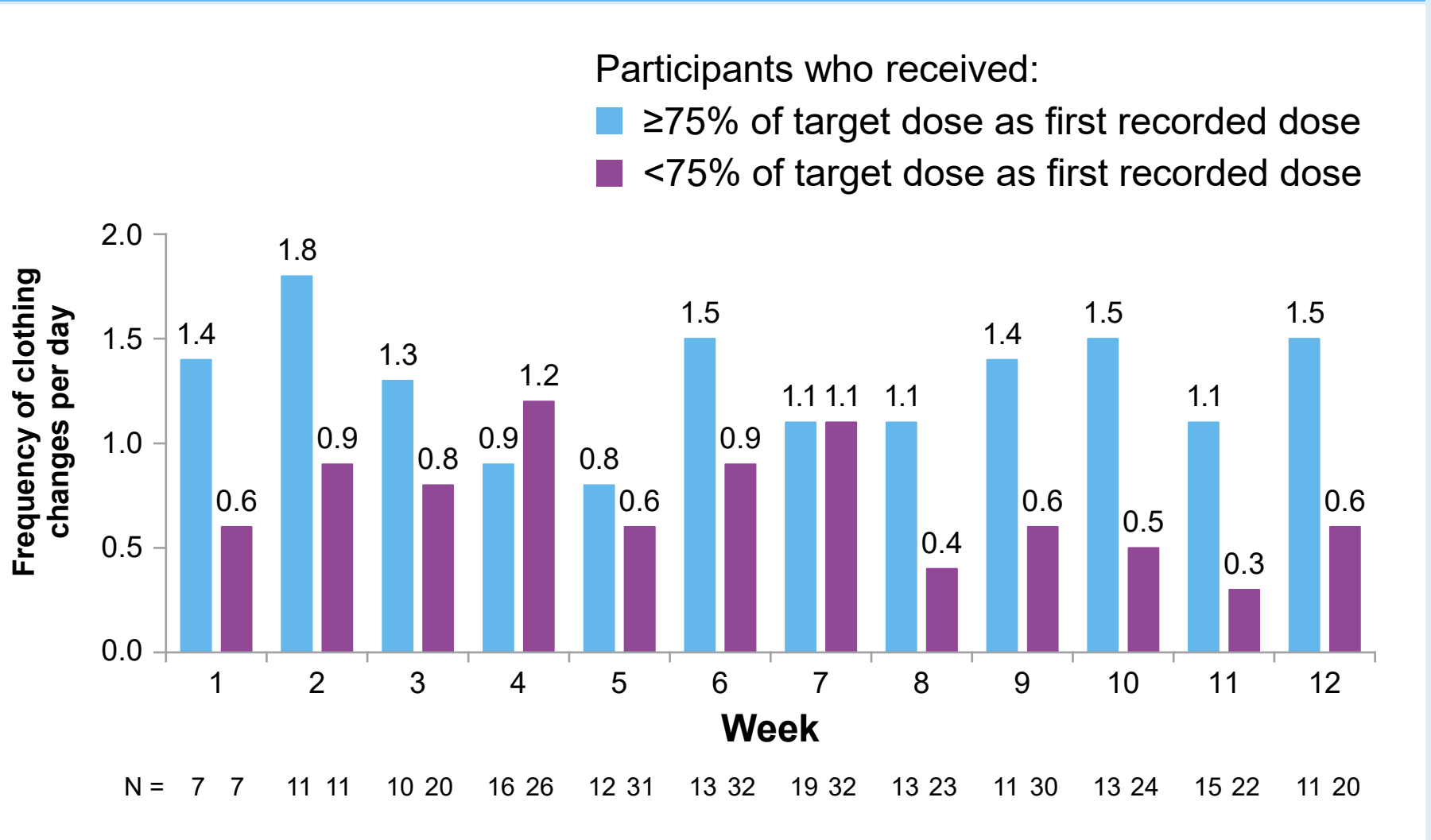


Figure 3. Stool Type Reported by Caregivers of Participants Who Received ≥75% (A) and <75% (B) of Target Dose as First Recorded Dose



W, week

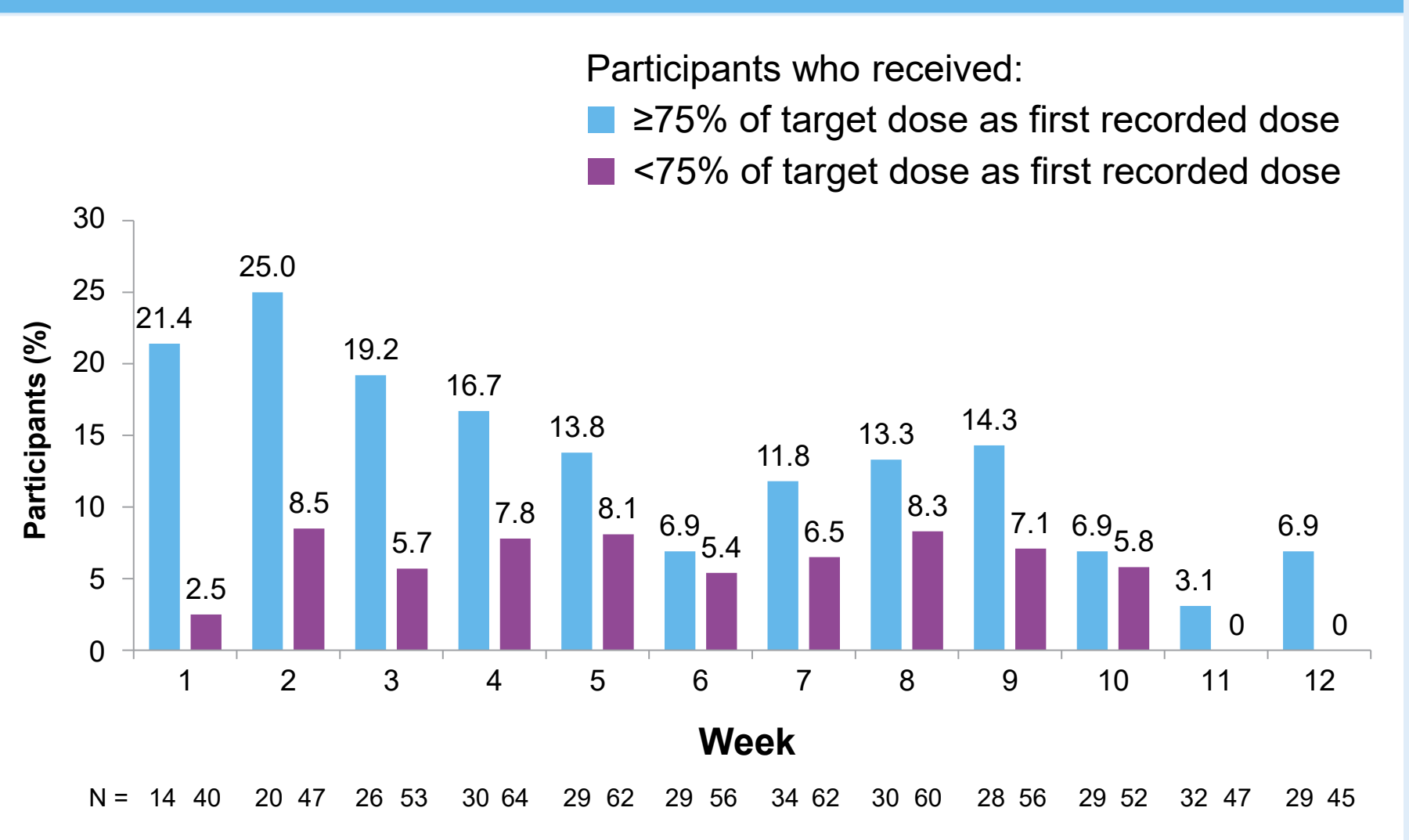
Figure 4. Frequency of Clothing Changes Required Due to Diarrhea Reported by Caregivers



Trofinetide Dosing and Vomiting

- The proportion of participants who experienced vomiting was lower in participants who received <75% versus ≥75% of target dose as first recorded dose over the first 12 weeks of treatment (**Figure 5**)

Figure 5. Frequency of Vomiting Reported by Caregivers



CONCLUSIONS

- Based on this 12-month interim analysis, most participants of LOTUS initiated trofinetide at a lower dose than suggested in the label but increased their dose close to target dose by week 12 of treatment

- Trofinetide dose titration did not influence the overall prevalence of diarrhea and vomiting but might improve user experience by reducing their incidence in early weeks

- The lower number of clothing changes in the titrating group suggests that families may find it easier to navigate a slower onset of diarrhea

- The results of this 12-month follow-up are limited by caregiver-reported observations, participant enrollment, and the online nature of this study; further analysis will occur as more participants are enrolled in the study

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DISCLOSURES

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