

Assessing Experiences With Trofinetide for Rett Syndrome: Interviews With Caregivers of Patients in LAVENDER, LILAC, and LILAC-2 Studies

Kathie M. Bishop,¹ Amy M. Barrett,² Oyebimpe Olayinka-Amao,² Susan Martin,² Dilesh Doshi,¹ James M. Youakim¹

¹Acadia Pharmaceuticals Inc., San Diego, CA, USA; ²RTI Health Solutions, Research Triangle Park, NC, USA

BACKGROUND

- Rett syndrome (RTT) is a rare neurodevelopmental disorder characterized by a broad set of core symptoms including loss of verbal communication with limited nonverbal skills, loss of fine and gross motor function (including purposeful hand use), behavioral issues, seizures, hand stereotypies, and gastrointestinal problems^{1,2}
- Trofinetide, a synthetic analog of glycine-proline-glutamate, was approved by the US Food and Drug Administration (FDA) in March 2023 for the treatment of RTT in adults and pediatric patients aged ≥2 years³
 - In LAVENDER (NCT04181723), a 12-week, randomized, placebo-controlled, phase 3 study of trofinetide in RTT, significant differences were demonstrated between trofinetide and placebo in caregiver- and clinician-assessed efficacy endpoints relevant to RTT with an acceptable safety profile⁴
 - Treatment with trofinetide continued to improve symptoms of RTT in LILAC (NCT04279314) and LILAC-2 (NCT04776746), 40-week and 32-month open-label extension studies, respectively^{5,6}
- FDA guidance has emphasized the importance of understanding the patient's experience and seeking the patient voice during the drug development process⁷

OBJECTIVE

- To explore the experience of study participants with RTT treated with trofinetide in LAVENDER, LILAC, and LILAC-2 through the conduct of individual interviews with primary caregivers

METHODS

Study Population

- All caregivers (aged ≥18 years) of participants who completed the LAVENDER, LILAC, and LILAC-2 studies were eligible to participate in optional qualitative interviews that occurred at LILAC-2 treatment end or study exit
- Written consent was obtained from all participating caregivers, and caregivers were compensated for participation

Interview Methods

- Interviews lasted approximately 60 minutes and were conducted via telephone; interviews were audio-recorded and transcribed
- Each interview followed the methods and procedures outlined in the institutional review board–approved qualitative interview procedure guide and focused on observations of treatment benefit and meaningfulness of these benefits

Data Analysis

- Interview data were assigned thematic codes using a coding framework developed a priori and adapted to incorporate emerging themes
- A thematic data analysis approach was used to identify the key themes across interviews

RESULTS

Participant and Caregiver Characteristics

- Overall, 61 of 77 participants enrolled in LILAC-2 completed the study
- A total of 27 caregivers of 26 participants from 12 clinical trial sites took part in the exit interviews (**Table 1**)

Effects of RTT Reported by Caregivers

- The most frequently reported effects of RTT by caregivers were lack of verbal communication (92.3%), inability to use hands due to repetitive hand movements (57.7%), inability to walk (57.7%), and seizures (53.8%) (**Table 2**)
- Caregivers reported that the effects of RTT with the most impact on the lives of their children with RTT were the inability to communicate (53.8%), impaired use of hands (15.4%), and seizures (7.7%)

Table 2. Effects of RTT reported by ≥15% of caregivers

Effects of RTT reported by ≥15% of caregivers, n (%)	Caregivers (N = 26)
No verbal communication	24 (92.3)
Unable to use hands due to repetitive hand movements	15 (57.7)
Unable to walk	15 (57.7)
Seizures	14 (53.8)
Unable to perform self-care (eg, feeding, brushing teeth, getting dressed)	12 (46.1)
Breathing problems (breath holding or hyperventilating)	9 (34.6)
Mood disturbance (eg, frustrated, anxious, angry, irritable)	8 (30.8)
Constipation	7 (26.9)
Scoliosis	7 (26.9)
Difficulty swallowing	7 (26.9)
Requires feeding tube	7 (26.9)
Limited ability to use hands	6 (23.1)
Unable to crawl	6 (23.1)
Impaired social function	6 (23.1)
Unable to walk unassisted	4 (15.4)
Unable to toilet independently	4 (15.4)

RTT, Rett syndrome

Table 1. Caregiver and clinical trial participant characteristics

Characteristic	Total
Caregivers (n = 27)^a	
Sex, n (%)	
Female	24 (88.9)
Male	3 (11.1)
Study participants with RTT (n = 26)	
Mean (SD) age, years	12.3 (4.7)
Mean (SD) age at diagnosis, years	2.7 (1.3)
Mean (SD) time since diagnosis, years	9.6 (4.7)

^aBoth parents of 1 study participant took part in an interview simultaneously. For all frequency counts and analyses, information from this interview was handled as 1 caregiver report
RTT, Rett syndrome; SD, standard deviation

- The following quotations highlight caregiver descriptions of effects of RTT
 - *She's nonverbal; she doesn't have any discernible words.*
 - *She lost the ability to finger feed, lost the ability to use her hands, to play with toys, drink from a cup, or hold anything.*
 - *She never walked completely.*
 - *She began having 10 to 15 seizures every day.*

Observed Improvements With Trofinetide Reported by Caregivers

- The most frequently reported improvements in RTT in the trofinetide studies were engagement with others (42.3%), hand use (38.5%), and eye gaze (30.8%) (**Table 3**)
 - Some participants acquired new words (19.2%) or new sounds (23.1%) (**Table 3**)
- Caregivers reported that the most important observed improvement in the effects of RTT were in areas related to communication (eg, eye gaze, attention/focus/concentration, Tobii eye tracker use, and ability to make sounds)

Table 3. Observed improvements with trofinetide reported by ≥15% of caregivers in LILAC

Area/type of improvement with trofinetide reported by ≥15% of caregivers, n (%)	Caregivers (N = 26)
Engagement with others	11 (42.3)
Hand use	10 (38.5)
Eye gaze	8 (30.8)
Attention/focus/concentration	7 (26.9)
Tobii eye tracker use	7 (26.9)
Ability to make sounds	6 (23.1)
Happier mood or disposition	6 (23.1)
Ability to walk	5 (19.2)
Alertness	5 (19.2)
New words	5 (19.2)
Seizures	4 (15.4)
Aware of environment	4 (15.4)
Repetitive hand movements	4 (15.4)

RTT, Rett syndrome

- The following quotations highlight caregiver descriptions of meaningful improvements observed in participants of LAVENDER, LILAC, and LILAC-2
 - *The biggest thing we noticed was better hand use.*
 - *She's totally alert and interested and involved. Like our family parties, that's where my family is like, "Wow, she's really engaged in everything."*
 - *I would say that the biggest things we saw were maybe an improvement in her eye gaze. She really became pretty accurate with her Tobii.*
 - *Her verbalization definitely improved, and she started saying more things.*

- *I would say just being able to concentrate and not be as upset during activities.... The concentration has made it easier to learn the different material that we've given her.*
- *We were at a restaurant after our drug study appointment, and she reached across the table and grabbed a French fry off of our plate and put it toward her mouth.*
- *It was her engagement level with the world outside of her—to me and to friends in school; [it] just blossomed, and it was like a light was turned on.*

Satisfaction With Benefits Observed With Trofinetide Reported by Caregivers

- Overall, 53.8% of caregivers reported a change in their daily lives as a result of treatment-related improvements experienced by their child
 - Areas of improvement included the family being happier, increased ability to attend family and social gatherings as a family, and the ability to interact with their child and have their child respond to them and others
- Among the 25 caregivers who reported their satisfaction with trofinetide, 24 were very satisfied or satisfied
- The following quotations illustrate the caregivers' satisfaction with trofinetide
 - *It's just improved her whole self, and it's improved our lives, by being able to communicate better with her and understand her more. And of course, not having any seizures.*
 - *She knows that she can get her answers out quicker and that she's answering accurately, and I think she's finally getting more reciprocation from peers that they're waiting for her responses. You see people around her are able to communicate with her more effectively.*
 - *All the improvements that we saw definitely made us feel good, and I know it made her feel good. We were so proud of her.*
 - *I feel like this medication has helped her on her screaming spells and her crying spells.*

CONCLUSIONS

- The results of these qualitative interviews provide insight into the range and meaningfulness of improvements in RTT that participants of LAVENDER, LILAC, and LILAC-2 experienced with trofinetide
 - Caregivers reported sustained and meaningful improvements with trofinetide treatment, with positive impact on their child's engagement with others, hand use, eye gaze, attention/focus, ability to make sounds, and mood
 - Caregivers also reported that their lives were improved by being able to interact with their child and have their child respond to them and others
- Future directions include integrating the results of these caregiver exit interviews with clinical trial outcomes

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DISCLOSURES

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