Poster #56

Real-World Trofinetide Treatment Patterns Among Individuals with Rett Syndrome: A Descriptive Analysis of Early Utilization Trends

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BACKGROUND

- Rett syndrome (RTT) is a rare neurodevelopmental disorder that has a significant impact on early childhood development, causing loss of acquired skills in speech, fine motor hand skills, and ambulation [1,2].
- Trofinetide (TROF), the first and only treatment for RTT, received US FDA approval in March 2023 [3].
- Understanding the early treatment patterns and dosing outcomes of TROF in real-world settings is needed to help inform clinical decision-making and advance RTT treatment and management.

OBJECTIVES

- To assess the clinical characteristics, early treatment utilization and dosing patterns among individuals with RTT who initiated TROF in real-world settings.

METHODS

Study Design and Data Source

- Retrospective analysis was performed utilizing tokenized linked data consisting of medical claims data from IQVIA's Anonymized Patient Level Database and TROF prescription (RX) data from a specialty pharmacy network.

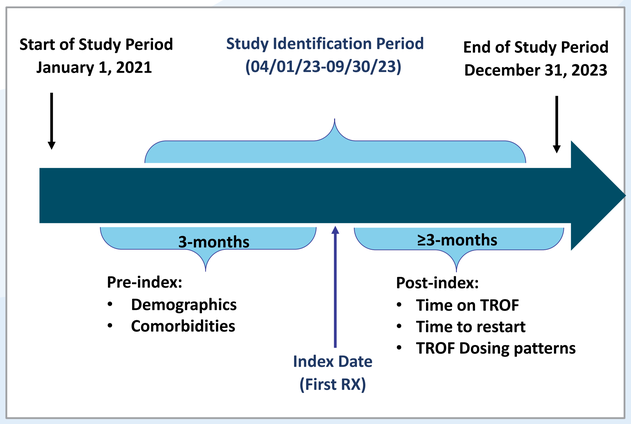
Study Population

- The study population, presented in Figures 1 & 2, comprised of individuals diagnosed with RTT (ICD-10 code F84.2) who received ≥1 RX of TROF between April 1, 2023, and September 30, 2023. The date of first RX fill was considered as the index date.
- To be eligible for inclusion, the individuals had to fulfill two additional criteria:
  - i. Have ≥2 RX fills, and
  - ii. Have ≥3-months of post-index follow-up.

Study Groups

- The eligible sample was further stratified into two groups for analysis based on treatment persistency status.
  - **Treatment Persistent Group:** identified as the proportion of individuals on continuous TROF treatment with an allowable treatment gap of ≤60 days.
  - **Treatment Non-Persistent Group:** identified as the proportion of individuals with no RX refill within the allowable treatment gap of ≤60 days.
    - **TROF Restart Group:** identified as the proportion of individuals in the non-persistent group who re-initiated TROF after a gap of >60 days.

Figure 1: Study Schema



Abbreviations: TROF, Trofinetide; RX, Prescription

Pre-index Demographics and Clinical Characteristics

- **Demographics:** age and gender were identified at index date.
- **Clinical Characteristics:** comorbidities (e.g., aspiration, convulsions, epilepsy, etc.) were measured during 3-months pre-index.

METHODS (CONTINUED)

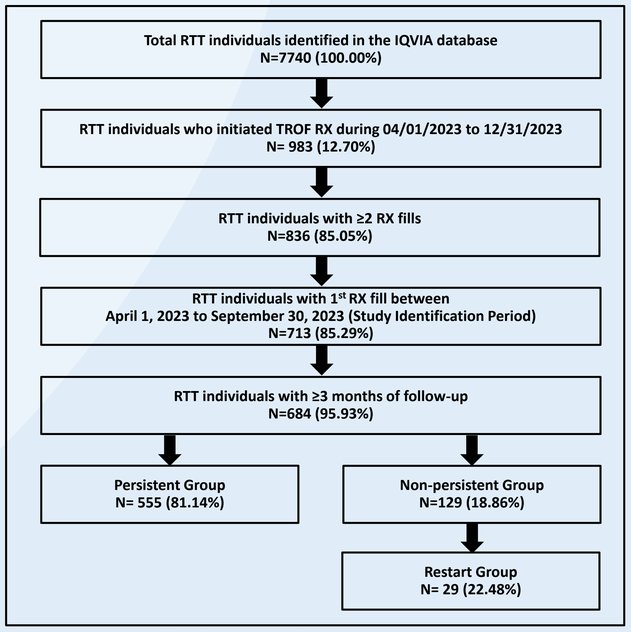
Post-index Outcomes

- **Dosing and Treatment Patterns in Persistent and Non-persistent Groups:**
  - Median Number of RX Fills
  - Mean First RX Dose and Mean Last RX Dose
    - expressed in milliliters (mL) twice daily (BID).
  - Mean Time (in days) on Treatment
    - defined as the time from first RX fill to last RX fill plus days of supply.
- **Dosing and Treatment Patterns in Restart Group:**
  - Mean Last RX Dose: among the non-persistent group (at the time of non-persistence).
  - Mean RX Restart Dose
    - expressed in milliliters (mL) twice daily (BID).
  - Mean Time (in days) to Restart
    - defined as time from non-persistence (i.e., the end of days' supply for last RX fill date) to first restart RX.

Statistical Methods:

- Continuous Variables: expressed as means and standard deviations (SD), median and interquartile range (IQR).
- Categorical Variables: expressed as counts (n) and percentages (%).
- Time on Treatment: expressed as mean (SD) in days among both the persistent and non-persistent groups.
- Time to Restart: expressed as mean (SD) in days in the non-persistent group.

Figure 2: Study Population Selection



Abbreviations: TROF, Trofinetide; RTT, Rett syndrome; RX, Prescription

RESULTS

Pre-index Demographic and Clinical Characteristics:

Pre-index characteristics are reported in Tables 1, 2 & Figure 3.

- A total of 983 RTT individuals initiated TROF treatment; with 836 (85.29%) having ≥2 RXs.
- Of the 684 eligible individuals, 555 (81.14%) were in the persistent group and 129 (18.86%) were in the non-persistent group.
- Persistent group was younger, with a mean (SD) age of 14 (11) years compared to 19 (15) years in the non-persistent group.
- Pre-index comorbidity rates (e.g., aspiration, convulsions, dysphagia and vomiting) were higher among persistent group compared to non-persistent group.

RESULTS

Table 1: Demographic Characteristics among TROF Individuals

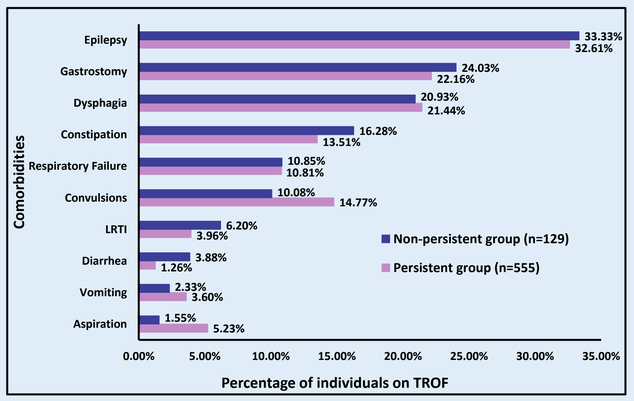
Characteristics	Eligible RTT Individuals on TROF N=684		Restart Among Non-persistent (n=29, 22.48%)
	Persistent Group (n=555, 81.14%)	Non-persistent Group (n=129, 18.86%)	
Age			
Mean (SD)	14.30 (10.68)	18.68 (14.88)	16.24 (9.85)
Median (IQR)	12 (13)	14 (14)	13 (13)
Gender, n (%)			
Male	19 (3.42%)	8 (6.20%)	2 (6.89%)
Female	536 (96.58%)	121 (93.79%)	27 (93.10%)
Pediatric, n (%)			
2-4	83 (14.95%)	13 (10.08%)	3 (10.34%)
5-10	162 (29.19%)	24 (18.60%)	4 (13.79%)
11-17	140 (25.23%)	42 (32.56%)	13 (44.83%)
Adult, n (%)			
18-29	130 (23.42%)	31 (24.03%)	5 (17.24%)
30-39	24 (4.32%)	8 (6.20%)	4 (13.79%)
40-49	8 (1.44%)	5 (3.88%)	0 (0.00%)
≥ 50	8 (1.44%)	6 (4.65%)	0 (0.00%)
Region, n (%)			
South	192 (34.59%)	50 (38.76%)	9 (31.03%)
West	93 (16.76%)	23 (17.83%)	6 (20.69%)
Midwest	163 (29.37%)	34 (26.36%)	11 (37.93%)
Northeast	83 (14.95%)	18 (13.95%)	2 (6.90%)
Unknown	24 (4.32%)	4 (3.10%)	1 (3.45%)

Abbreviations: CCI, Charlson comorbidity index; IQR, Interquartile range; SD, Standard deviation

Post-index Outcomes:

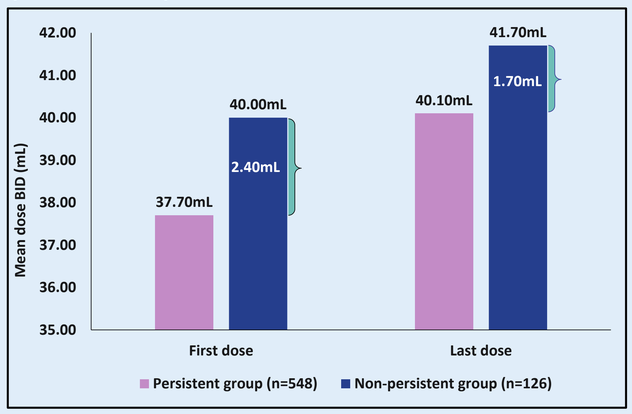
- Mean (SD) time on TROF was 182 (51) days and 74 (34) days in the persistent and non-persistent groups, respectively.
- Mean first dose (BID) was 37.70 mL vs. 40.00 mL, respectively among the persistent and non-persistent groups [Figure 4]. Compared to first dose, mean second dose (BID) was higher in both groups (persistent: 40.20 mL vs. non-persistent: 41.90 mL).
- The persistent group had a median of 6 doses (mean last dose (BID) was 40.10 mL). However, the non-persistent group had a median of only 2 doses (mean last dose (BID) was 41.70 mL) [Figure 4].
- Among individuals who restarted TROF, mean (SD) time to restart was 84 (18) days; mean restart dose (BID) was approximately 4 mL lower compared to the dose at the time they became non-persistent (35.50 mL vs. 39.40 mL, respectively) [Figure 5].

Figure 3: Rates of Top 10 Pre-index Comorbidities in Persistent vs. Non-Persistent Groups



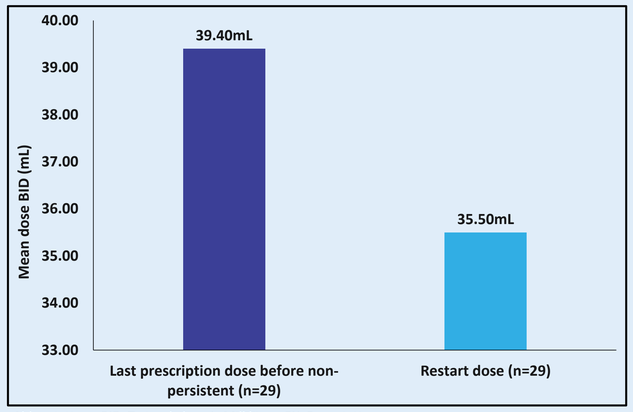
Abbreviations: LRTI, Lower respiratory tract infection; TROF, Trofinetide

Figure 4: TROF Dosing Patterns in Persistent vs. Non-persistent Groups



Abbreviations: BID, Twice daily; mL, Millilitres
Note: Ten individuals were excluded from the dosing analysis due to having ages other than those observed in pharmacy data

Figure 5: TROF Dosing Patterns in Restart Group



Abbreviations: BID, Twice daily; mL, Millilitres; RX, Prescription
Note: Ten individuals were excluded from the dosing analysis due to having ages other than those observed in pharmacy data

CONCLUSIONS

- Over 80% of RTT individuals initiating TROF remained persistent for at least 6 months; they were younger, more likely female, had a lower initial TROF dose and had higher rates of pre-index aspiration, convulsions, and vomiting compared to non-persistent individuals.
- Mean BID dose increased over time in both persistent and non-persistent groups suggesting that physicians may be adopting titration approaches for RTT treatment and management.
- Nearly 25% of the RTT individuals who were non-persistent restarted TROF at a lower dose within 90 days.
- Our findings underscore the need for deeper investigation into factors influencing TROF persistence and non-persistence.

LIMITATIONS

- This research used prescription (RX) shipment data and days between shipments as a proxy for RX filling behaviour and dose calculations.
- Given the potential for dose titration among individuals, future studies should examine data using greater than 60-day treatment gap, which may suggest that persistency rates could be higher.

REFERENCES

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2. DAYBUE (TROF) [package insert]. San Diego, CA: Acadia Pharmaceuticals; 2024
3. A First for Rett: FDA Approves Trofinetide for Treatment of Rett Syndrome! International Rett Syndrome Foundation

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