Poster # 57

Patient Characteristics and Trofinetide Utilization Patterns among Males Diagnosed with Rett Syndrome within the United States

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BACKGROUND

- Rett Syndrome (RTT) is a rare, severe, and progressive neurodevelopmental disorder that affects females due to its X-linked inheritance pattern. However, prevalence among male individuals may be on the rise, potentially due to better detection, with an estimated annual prevalence ranging from 0.08 to 0.10 per 10,000 between 2017 and 2019 [1,2].
- In March 2023, trofinetide (TROF) became the first and only FDA approved therapy for RTT among individuals aged ≥2 years from LAVENDER, LILAC, and DAFFODIL trials [3-5].
- While TROF is approved for use in both female and male RTT individuals [5], males were not included in the clinical trial program. Thus, there's a need to better understand TROF's use in male RTT individuals.

OBJECTIVES

To examine real-world demographic, clinical characteristics, and treatment patterns among males with RTT who initiated TROF vs. who did not initiate TROF.

METHODS

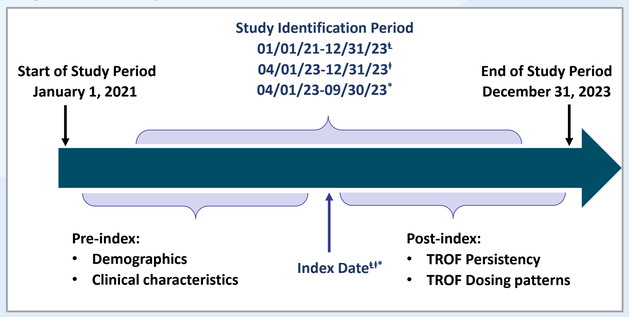
Study Design and Data Source

- A retrospective database analysis was conducted using linked data from IQVIA's Anonymized Patient Level Database and TROF prescription claims from a specialty pharmacy database.

Study Population

- The study population, presented in Figures 1 & 2, included males with ≥2 diagnostic (ICD-10-CM: F84.2) claims for RTT at least 30 days apart between January 1, 2021 to December 31, 2023 (study period).
- Individuals with a medical claim of cerebrovascular disease (ICD-10-CM: I60.xx–I69.xx) or brain trauma (ICD-10-CM: S06.xx) during the study period were excluded.
- The male RTT population was stratified into two groups based on TROF treatment status:
  - **TROF Group:** those who initiated TROF between April 1, 2023, to December 31, 2023.
    - ➢ index date was defined as the first TROF prescription (RX) fill date.
  - **No-TROF Group:** those who did not initiate TROF between April 1, 2023, to December 31, 2023.
    - ➢ index date was defined as the first diagnostic claim for RTT.
- Pre-index and Post-index period:
  - Pre-index period was defined as anytime before the respective index dates for both groups.
  - Post-index period (TROF group) was defined as anytime after TROF index.

Figure 1: Study Schema



Abbreviations: TROF, Trofinetide; [L]RTT diagnosis among No-TROF group; [I]First prescription fill date of TROF among TROF group; *Persistency analysis: First prescription fill date of TROF among TROF group

Pre-index Demographics and Clinical Characteristics

- **Demographics:** age and differential diagnosis.
- **Comorbidity Characteristics:** comorbidities (aspiration, epilepsy, convulsions, dysphagia, gastrostomy, vomiting etc.) were measured during anytime in the pre-index.

METHODS

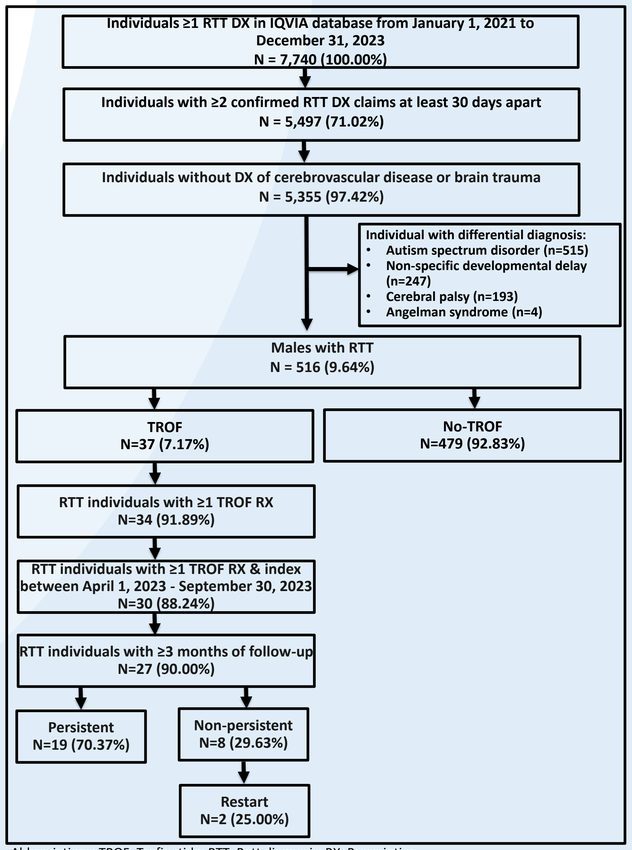
Post-index Outcomes

- **Treatment Persistent vs. Non-persistent:** evaluated among individuals in the TROF group that initiated it between April 1, 2023 to September 30, 2023, and met two additional criteria: having ≥2 TROF RX and at least three months of follow-up.
  - **Treatment Persistent:** identified as the proportion of individuals on continuous TROF treatment with an allowable treatment gap of ≤60 days.
  - **Treatment Non-Persistent:** identified as the proportion of individuals with no RX refill within the allowable treatment gap of ≤60 days.
- **TROF Dosing Patterns Among Persistent vs. Non-persistent:**
  - Mean dose BID (mL) from first RX to fifth RX.
  - Mean % of target dose (i.e., actual dose/target dose in mg/kg*100) at first 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 (%).

Figure 2: Study Population Selection



Abbreviations: TROF, Trofinetide; RTT, Rett diagnosis; RX, Prescription
Note: The attrition percentages reflect the relative change at each stage to previous step

RESULTS

Demographics and Clinical Characteristics

- Demographics and comorbidity characteristics are reported in Tables 1, 2 & Figure 2.
- Of the 5,497 with confirmed RTT diagnosis, 10% (n=516) were males. Of the 516 males, 37 (7%) initiated TROF while 479 (93%) did not initiate TROF.
- Mean age was higher at RTT diagnosis among TROF group (21.9±23.4) vs. No-TROF group (17.2±13.9); mean age at TROF index was 23.3±23.6.
- TROF group vs. No-TROF group also had approximately 2-3 times higher rates of respiratory failure, dysphagia, and epilepsy, among others.

RESULTS

Table 1: Demographics and Differential Diagnosis among Male Rett Individuals

Characteristics	Overall (N=516)	No-TROF Group (N=479)	TROF Group (N = 37)
Age at RTT diagnosis			
Mean (SD)	17.41 (14.57)	17.20 (13.91)	21.95 (23.49)
Median (IQR)	14 (16)	14 (16)	15 (20)
Age at TROF initiation			
Mean (SD)	-	-	23.30 (23.68)
Median (IQR)	-	-	17 (19)
Differential diagnosis, n (%)			
Autism spectrum disorder	189 (36.63%)	177 (37.50%)	12 (32.43%)
NSDD	165 (31.98%)	146 (30.93%)	19 (51.53%)
Cerebral palsy	129 (25.00%)	114 (24.15%)	15 (40.54%)
Angelman syndrome	3 (0.58%)	3 (0.64%)	0 (0.00%)

Abbreviations: IQR, Interquartile range; NSDD, Non-specific developmental delay; SD, Standard deviation; TROF, Trofinetide; RTT, Rett diagnosis

Demographics and Clinical Characteristics

- TROF group vs. no-TROF group had higher percentage of concomitant NSDD (52% vs. 31%) and cerebral palsy (40% vs. 24%). However, autism spectrum disorder was lower among TROF group vs. no-TROF group (32% vs. 37%).

Table 2: Rates of Comorbidities among Male Rett Individuals

Characteristics	Overall (N=516)	No-TROF Group (N=479)	TROF Group (N = 37)
Gastrointestinal disorders, n (%)			
Constipation	167 (32.36%)	151 (31.52%)	16 (43.24%)
Diarrhea	48 (9.30%)	46 (9.60%)	2 (5.41%)
Dysphagia	147 (28.49%)	130 (27.14%)	17 (45.95%)
Gallbladder dysfunction	13 (2.52%)	11 (2.30%)	2 (5.41%)
Gastroparesis	15 (2.91%)	11 (2.30%)	4 (10.81%)
Gastrostomy	138 (26.74%)	118 (24.63%)	20 (54.05%)
GERD	107 (20.74%)	91 (19.00%)	16 (43.24%)
Vomiting	102 (19.77%)	86 (17.95%)	16 (43.24%)
Growth abnormalities/ND, n (%)			
Growth abnormalities	37 (7.17%)	33 (6.89%)	4 (10.81%)
Nutritional deficiency and failure to thrive	101 (19.57%)	90 (18.79%)	11 (29.73%)
Infections/ Viruses, n (%)			
COVID-19	66 (12.79%)	59 (12.32%)	7 (18.92%)
Fever	162 (31.40%)	147 (30.69%)	15 (40.54%)
Influenza	44 (8.53%)	41 (8.56%)	3 (8.11%)
LRTI	122 (23.64%)	108 (22.55%)	14 (37.84%)
RSV	2 (0.39%)	0 (0.00%)	2 (5.41%)
URTI	176 (34.11%)	164 (34.24%)	12 (32.43%)
UTI	46 (8.91%)	39 (8.14%)	7 (18.92%)
Musculoskeletal disorders, n (%)			
K & SD	25 (4.84%)	20 (4.18%)	5 (13.51%)
Scoliosis	85 (16.47%)	73 (15.24%)	12 (32.43%)
Neurodevelopmental disorders, n (%)			
BDD symptoms	163 (31.59%)	153 (31.94%)	10 (27.03%)
Development progress delayed	63 (12.21%)	54 (11.27%)	9 (24.32%)
Loss of AC skills	118 (22.87%)	108 (22.55%)	10 (27.03%)
Loss of acquired motor skills	58 (11.24%)	51 (10.65%)	7 (18.92%)
Microcephaly	47 (9.11%)	40 (8.35%)	7 (18.92%)
Movement disorders	22 (4.26%)	19 (3.97%)	3 (8.11%)
Prominent hand apraxia/dyspraxia	37 (7.17%)	32 (6.68%)	5 (13.51%)
Sleep dysfunction	110 (21.32%)	106 (22.13%)	4 (10.81%)
Stereotypic, RHM	6 (1.16%)	5 (1.04%)	1 (2.70%)
Wasting, dystonia, bradykinesia	17 (3.29%)	14 (2.92%)	3 (8.11%)
Weakness/paralysis	96 (18.60%)	86 (17.95%)	10 (27.03%)
Neurological disorders, n (%)			
Convulsions	160 (31.01%)	141 (29.44%)	19 (51.35%)
Epilepsy	226 (43.80%)	200 (41.75%)	26 (70.27%)
Respiratory disorders, n (%)			
Aspiration	81 (15.70%)	72 (15.03%)	9 (24.32%)
Asthma	94 (18.22%)	84 (17.54%)	10 (27.03%)
Atelectasis	34 (6.59%)	31 (6.47%)	3 (8.11%)
Breathing irregularities*	114 (22.09%)	99 (20.67%)	15 (40.54%)
COPD	21 (4.07%)	18 (3.76%)	3 (8.11%)
Cough	166 (32.17%)	152 (31.73%)	14 (37.84%)
Respiratory failure	122 (23.64%)	103 (21.50%)	19 (51.35%)

Abbreviations: AC, Acquired communication; BBD, Behavioral disorders and disturbance; CCI, Charlson Comorbidity Index; COPD, Chronic Obstructive Pulmonary Disease; COVID19, Coronavirus Disease 2019; GERD, Gastrointestinal Reflex disorder; IQR, Interquartile Range; K&SD, Kyphosis and other spinal deformities; LRTI, Lower Respiratory Tract Infection; N, Number; ND, Nutritional disorders; RSV, Respiratory syncytial virus; SD, Standard Deviation; TROF, Trofinetide; URTI, Upper Respiratory Tract Infection; UTI, Urinary Tract Infection; *Abnormal breathing

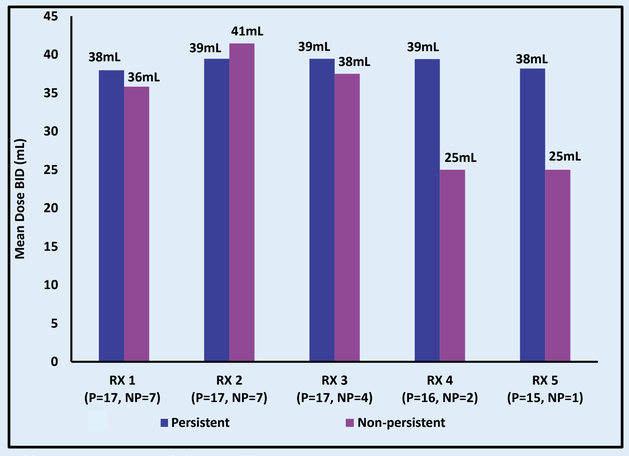
TROF Treatment Persistency

- Among the 73% (n=27) on TROF that were eligible for the persistency analysis, approximately 70% (n=19) were persistent.
- Among the non-persistent (n=8) individuals, 25% (n=2) restarted TROF treatment within a median of 71 days.

TROF Dosing Patterns

- Mean first RX dose (BID) among persistent and non-persistent was 38 mL vs. 36 mL, respectively [Figure 3].
- Mean % of target dose at first RX among persistent and non-persistent was 94.30% vs. 81.20%.

Figure 3: TROF Dosing Patterns among Persistent vs. Non-persistent for First Five RXs



Abbreviations: BID, Twice daily; mL, Milliliters; P, Persistent; NP, Non-persistent; RX, Prescription
Note: Three individuals were excluded from the dosing analysis due to having age other than those observed in pharmacy data

CONCLUSIONS

- In this first real-world analysis of males with RTT, those who initiated TROF were older, have approximately 3 times higher rates of pre-index epilepsy, respiratory failure, dysphagia, LRTI, and vomiting, among others.
- Of the males who initiated TROF, 2 out of 3 were persistent for more than 3 months, suggesting that males may experience similar TROF persistency as females.
- Majority of males with RTT did not initiate TROF. Thus, education about TROF's benefit in males may be warranted. Additionally, further research is needed to understand long-term treatment patterns.

LIMITATIONS

- As with any real-world studies this study has the same limitations of under coding and miscoding.
- Although the use of linked claims and pharmacy data provide insights into persistence, they do not capture actual medication intake and therefore may not accurately reflect the actual persistence.
- The findings of this descriptive analysis should be interpreted with caution as they are not intended to establish causal association.

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