Poster # 3.49

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Demographic and Clinical Characteristics among Adult Individuals Treated or Untreated with Trofinetide For Rett Syndrome

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DISCLOSURES

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INTRODUCTION

- Trofinetide (TROF) is the only FDA-approved therapy for Rett syndrome (RTT).[1] Efficacy and safety of TROF was established among individuals aged 5-20 years in the 12-week placebo- controlled Phase 3 LAVENDER trial, and long-term outcomes was established in the 40-week LILAC-1 and 32-month LILAC-2 open-label extension trials.[2-4] Additionally, the Phase 2/3 open-label DAFFODIL trial examined the safety and tolerability of TROF in children (ages 2–4 years).[5]
- Since TROF is indicated as a treatment for RTT among all individuals ≥2 years, it is vital to understand the demographic characteristics, clinical characteristics, and real-world treatment outcomes (i.e., persistency) among TROF treated individuals who are >20 years of age.

OBJECTIVES

- To examine differences in demographics and clinical characteristics among RTT individuals >20 years of age who are treated with TROF compared to those who are not treated with TROF.
- To examine treatment persistency among individuals aged >20 years who are treated with TROF.

METHODS

Study Design & Data Source

- A retrospective cohort study using medical claims from IQVIA's Anonymized Patient Level Data linked with pharmacy claims from a specialty pharmacy database from January 01, 2021, to September 30, 2024 (i.e., study period) was conducted (Figure 1).

Study Population & Time Period Definitions

- Individuals with ≥1 medical claim diagnosis of RTT (ICD-10 code: F84.2) or ≥1 prescription (RX) claim for TROF (NDC: 63090-660-01, 63090-0660-01) during the study period were included.
- The eligible population was stratified into two groups based on TROF treatment status (i.e., treated or untreated) between April 1, 2023, through March 31, 2024 (i.e., identification period).
  - Treated Group: Individuals >20 years with ≥1 RX claim for TROF during the identification period:
    - Index date: first TROF RX claim date during the identification period.
      - The treated individuals were further stratified into two sub-groups based on persistency status.
        - Persistent Sub-group: proportion of individuals on continuous TROF treatment with an allowable treatment gap of ≤90 days.
        - Non-persistent Sub-group: proportion of individuals with no TROF RX refill claim within the allowable treatment gap of ≤90 days.
  - Untreated group: Individuals >20 years who did not initiate TROF during the identification period:
    - Index date: an assigned index date using a risk set sampling approach that is set to the elapsed time (in days) from RTT diagnosis to TROF initiation of every 1 treated individual to 5 untreated (1:5 ratio) individuals. This approach creates comparable person-time between groups and avoids immortal time bias.

Matching

- The treated and untreated (risk set sampled) groups were also age, sex and index date matched using 1:1 Mahalanobis distance matching (without replacement).

Baseline Characteristics and Clinical Comorbidities

- Baseline study measures were evaluated among both the unmatched and matched cohorts.
- Demographics (e.g., age) at index as well as differential diagnosis (e.g., autism spectrum disorder) and baseline comorbidities (i.e., epilepsy, gastrostomy, scoliosis etc.) were assessed during pre-index.
- Additionally, physician specialty type (e.g., neurologists) closest to TROF index and closest to RTT diagnosis were examined among treated and untreated groups, respectively.

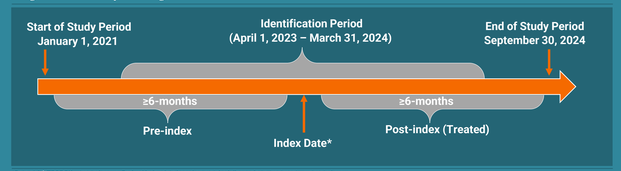
Post-index Outcomes among Treated Group

- Time on treatment (persistent vs. non-persistent sub-groups) was calculated using the following equation: Δ [(end of days' supply date after last RX fill - first RX fill date +1)/30].

Statistical Methods

- Categorical variables such as gender and physician specialty were reported as frequencies and %, continuous variables such as age was reported as mean, standard deviation (SD).
- Time (i.e., months) on treatment was defined as date of last available TROF RX claim + end of days supply or end of follow-up or end of study period, whichever occurred first. Additionally, Kaplan Meier curves were presented for time on treatment for the persistent and non-persistent sub-groups.

Figure 1. Study Design



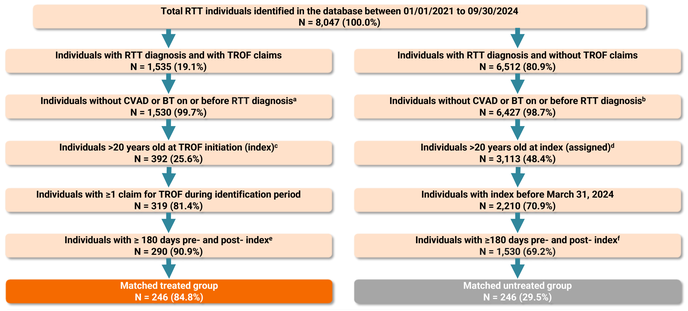
*Date of 1st TROF RX – treated group; Derived index date based on matched diagnosis-to-treatment – untreated group

RESULTS

Study Population

- Overall, 25.6% (n=392) of the 1,530 eligible treated individuals and 48.4% (n=3,113) of the 6,427 eligible untreated individuals were >20 years of age (Figure 2).
- Approximately,15.9% (n=290) treated and 84.1% (n=1,530) untreated individuals constituted the total eligible unmatched sample (n=1,820) >20 years of age. After matching, final sample had 246 individuals in both treated and untreated groups (Figure 2).

Figure 2: Attrition Table



Abbreviations: BT, Brain Trauma; **CVAD**, Cerebrovascular Disease; **RTT**, Rett Syndrome; **TROF**, Trofinetide.
Note: The percentages were calculated based on pervious step; Post-index period includes index.
*& individuals had CVAD or BT; #85 individuals had CVAD or BT; ^1,138 individuals were ≥20 years old; ¶3,314 individuals were ≥20 years old; *113 and 16 individuals had <180 days enrollment pre- and post-index (respectively); ¶592 and 288 individuals had <180 days enrollment pre- and post-index (respectively).

Baseline Characteristics and Clinical Comorbidities

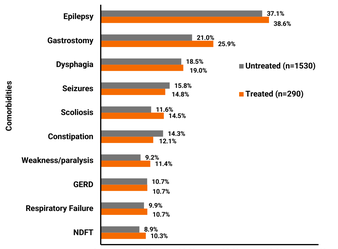
- After matching, both treated and untreated groups had similar mean age and gender distribution (Table 1).
- The treated group, however, had higher rates of baseline comorbidities such as epilepsy, gastrostomy, dysphagia, scoliosis, and paralysis compared to untreated group even after matching (Figures 3 and 4).

Table 1. Baseline Characteristics among Treated vs. Untreated Groups in Unmatched and Matched Cohorts

Characteristics	Unmatched		Matched	
	Treated (n = 290)	Untreated (n = 1,530)	Treated (n = 246)	Untreated (n = 246)
Age at Index (years), mean ± SD	30.9 ± 9.9	33.5 ± 10.0	30.4 ± 9.4	30.3 ± 8.5
Gender, n (%)				
Male	16 (5.5%)	103 (6.7%)	12 (4.9%)	12 (4.9%)
Female	274 (94.5%)	1,427 (93.3%)	234 (95.1%)	234 (95.1%)
Differential Diagnosis, n (%)				
Cerebral palsy	60 (20.7%)	88 (2.8%)	59 (24.0%)	11 (0.4%)
NSDD	32 (11.0%)	24 (0.8%)	30 (12.2%)	6 (0.2%)
ASD	28 (9.7%)	45 (1.4%)	27 (11.0%)	3 (0.1%)
Physician Specialty Type, n (%)				
Unknown	0 (0.0%)	791 (51.7%)	0 (0.0%)	127 (51.6%)
Known*	290 (100%)	739 (48.3%)	290 (100%)	119 (48.4%)
Child Neurologists	94 (32.4%)	99 (13.4%)	86 (35.0%)	16 (13.4%)
Pediatrician	24 (8.3%)	33 (4.5%)	21 (8.5%)	6 (5.0%)
Neurologists	62 (21.4%)	97 (13.1%)	54 (22.0%)	15 (12.6%)
Clinical Neurophysiologists	24 (8.3%)	30 (4.1%)	17 (6.9%)	8 (6.7%)
Family Medicine	26 (9.0%)	104 (14.1%)	20 (8.1%)	12 (10.1%)

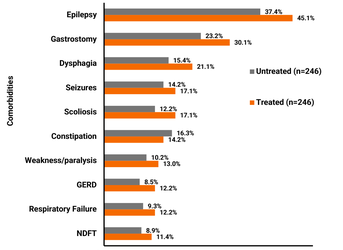
Abbreviations: ASD, Autism spectrum disorder; **NSDD,** Non-specific developmental delay; **SD,** Standard deviation
* The percentages were calculated based on the available information regarding physician specialties among unmatched untreated (n=739) and matched untreated (119) groups.

Figure 3: Top 10 Baseline Comorbidities in Unmatched Cohort



Abbreviations: GERD, Gastrointestinal reflux disease; **NDFT,** Nutritional deficiency and failure to thrive

Figure 4. Top 10 Baseline Comorbidities in Matched Cohort

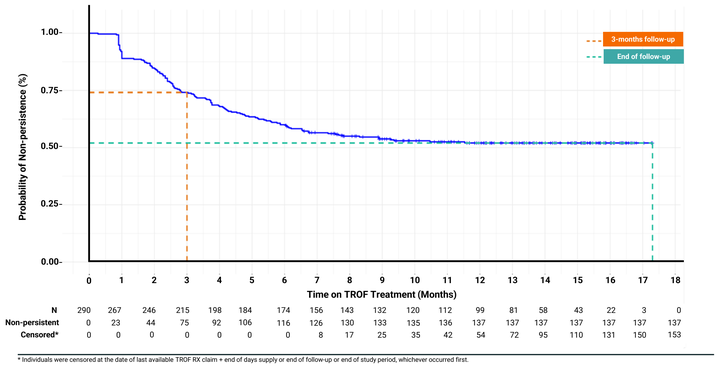


Abbreviations: GERD, Gastrointestinal reflux disease; **NDFT,** Nutritional deficiency and failure to thrive

Post-index Outcomes among Treated Group

- Of the individuals in the treated groups (n=290), 52.8% (n=153) were persistent and 47.2% (n=137) were non-persistent.
- Median (IQR) time on TROF among persistent vs. non-persistent sub-groups was 13.8 (4.8-17.8) months and 2.6 (0.3-11.5) months, respectively.
- Kaplan Meier analysis showed that approximately 75% of TROF individuals persisted on treatment for more than 3 months, and over half (>50%) continued treatment through the end of study follow-up (6.0-18.2 months) (Figure 5).

Figure 5. Time on Treatment among Treated Group



* Individuals were censored at the date of last available TROF RX claim + end of days supply or end of follow-up or end of study period, whichever occurred first.

CONCLUSIONS

Individuals over 20 years who are either treated or untreated with TROF in real-world settings also have similar baseline comorbidity characteristics (e.g., epilepsy, seizures, gastrostomy, etc.) as those observed in the TROF clinical trial program.[2]

Approximately 16% of eligible RTT individuals over 20 years of age initiate TROF treatment while 84% remained untreated.

A majority who initiated TROF remained persistent for ≥6 months of follow-up; median treatment duration among persistent individuals was approximately 14 months that is suggestive of real-world treatment effectiveness and acceptable tolerability.

These results suggest that TROF may be an appropriate treatment option and may be prescribed with confidence among RTT individuals over 20 years of age.

This analysis also shows that the first three months of TROF treatment may be crucial in ensuring persistency. Relationship between TROF dosing/titration and persistency are being examined to assist clinical decision-making.