Poster #5

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Real-World Demographic, Clinical Characteristics, and Treatment Patterns among Males Treated with Trofinetide for Rett Syndrome

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DISCLOSURES

KR and VY are employees of Anlitiks Inc., who received funding from Acadia Pharmaceuticals Inc. to conduct this study.
NR is an employee of Acadia Pharmaceuticals Inc.

REFERENCES

1. Amir RE, et al. Nat Genet. 1999;23(2):185–188. 2. Reichow B, et al. J Autism Dev Disord. 2015;45(10):3377–3383. 3. Schönewolf-Greulich B, et al. Clin Genet. 2019;95(3):403–408. 4. Neul JL, et al. *Nat Med* 2023;29(6):1468-1475. 5. Percy AK, et al. *Med.* 202.Sep 13;3(9):1178-1189.e3. 6. Percy AK, et al. *Med.* 2024 Oct 11;5(10):1275-1281.e2. 7. Percy AK, et al. *Med.* 2025 Jun 13;6(6):100608.

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INTRODUCTION

- Rett syndrome (RTT) is a rare neurodevelopmental disease primarily associated with loss-of-function mutations in the transcriptional regulator methyl-CpG binding protein-2 (MECP2) gene [1].
- RTT presents predominantly in female individuals, yet recent developments in genetic testing have added support to clinical observations that RTT can occur in males [2,3].
- Trofinetide (TROF) is approved for individuals with Rett syndrome (RTT) regardless of sex aged ≥2 years based on efficacy and safety established among individuals aged 5-20 years in pivotal Phase 3 LAVENDER trial, open-label extension trials (LILAC, LILAC-2) and among 2-4 years in the Daffodil trial [4-7].
- Since TROF is indicated as a treatment for RTT among all individuals, it is important to understand the demographic and patient characteristics among males with RTT who initiated TROF in the real-world setting.

OBJECTIVES

- To examine demographic and clinical characteristics among male individuals with RTT who initiated TROF versus those who did not initiate TROF.
- To examine time to non-persistence of TROF among male RTT individuals who initiated on TROF.

METHODS

Study Design & Data Source

- A retrospective cohort study was conducted using a tokenized linked medical and pharmacy databases from 01/01/2021 to 09/30/2024 (i.e., study period) (**Figure 1**):
  - Medical claims from IQVIA's Anonymized Patient Level Data
  - Pharmacy claims from a specialty pharmacy TROF prescription (RX) database

Study Population & Time Period Definitions

- Individuals with ≥1 medical claim of RTT (ICD-10 code: F84.2) were included.
- The eligible population was stratified into two groups based on TROF treatment status (i.e., treated or untreated) between 01/01/2023, through 03/31/2024 (i.e., identification period).
  - Treated: Individuals with ≥1 pharmacy claims for TROF during the identification period. Index date was the first TROF RX fill date.
  - Untreated: Individuals 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.
- Eligible individuals were further required to have ≥6-months of pre- and post-index continuous enrollment.
- Individuals with cerebrovascular disease or brain trauma anytime before RTT diagnosis were excluded.

Study Measures: Baseline/Pre-index Characteristics

- Baseline demographics (i.e., age) was identified at index date; patient clinical characteristics or comorbidities were evaluated 6 months prior to index date; physician specialty (e.g., child neurologist, clinical neurophysiologists etc.) closest to TROF index among treated and closest to RTT diagnosis among untreated were examined.
- Differential diagnosis (e.g., non-specific developmental delay (NSDD), autism spectrum disorder (ASD) etc.), were examined any time before TROF index among treated and anytime before RTT diagnosis among untreated were examined.
- Baseline comorbidities such as epilepsy, gastrostomy etc., were assessed during pre-index.

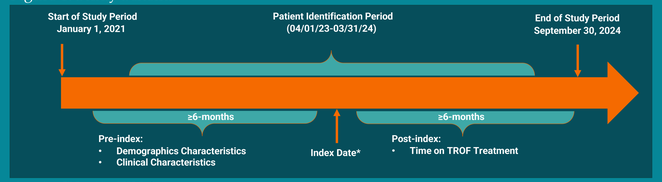
Study Measures: Clinical Outcomes

- Among the treated group, time on TROF treatment (TOT) was evaluated from index date to last RX claim date plus 90-day gap, or last follow-up date, or study end date, whichever came first was examined.

Statistical Methods

- Categorical variables such as physician specialty or comorbidities were reported as frequencies and percentages (%); continuous variables such as age was reported as mean, standard deviation (SD).
- Time on treatment was expressed using Kaplan Meier curves in months.

Figure 1: Study Schema

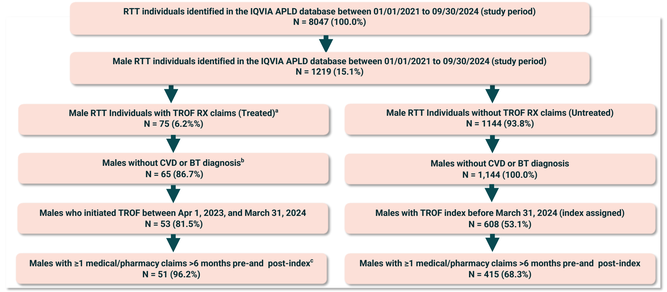


Abbreviations: **RX**, Prescription; **TROF**, Trofinetide
Date of 1st TROF RX – treated group; Derived index date based on matched diagnosis-to-treatment – untreated group

RESULTS

Study Population: Of 8,047 RTT individuals identified, 15.1% (n=1219) were males. Of those 1219 males with RTT, 6.2% (n=75) were treated with TROF and 93.8% were untreated. After the inclusion and exclusion criteria a total of 466 males formed the final study sample of which 10.9% (n=51) were treated in the treated group and 89.1% (n=415) formed the untreated group (**Figure 2**).

Figure 2: Attrition Table



Abbreviations: APLD, Anonymized Patient Level Data; **BT**, Brain Trauma; **CVD**, Cerebrovascular Disease; **RTT**, Rett Syndrome; **TROF**, Trofinetide.
Note: The percentages were calculated based on previous step.[a]1,467 female individuals ;[b] individuals had CVD or BT prior to RTT dx; [c]2 individuals had ≤6 months of continuous enrollment pre- or post-index.

Baseline/Pre-index Characteristics

Pre-index characteristics are reported in **Table 1**:

- The age for the treated males was a mean (SD) age of 18.8 (18.3) vs 17.7 (13.2) years compared to untreated males, respectively.
- Majority of individuals in both groups were managed by child neurologists (64.7% vs 12.7%; p=<0.001), followed by nurse practitioners (9.8% vs 5.1%; p=0.19); however, lower for pediatricians (5.9% vs 23.6%; p=<0.001), among treated vs untreated, respectively.

Table 1. Baseline Characteristics among TROF Treated vs Untreated Groups

Characteristics	Treated Group (n = 51)	Untreated Group (n = 415)	p-value
Age at Index (years), mean ± SD	18.8 ± 18.3	17.7 ± 13.2	0.91
Age Categories at TROF, n (%)			
2-4	12 (23.5%)	36 (8.7%)	<0.05
5-10	11 (21.6%)	111 (26.8%)	0.53
11-17	7 (13.7%)	102 (24.6%)	0.12
18-29	12 (23.5%)	99 (23.9%)	0.99
30-39	2 (3.9%)	35 (8.4%)	0.41
40-49	2 (3.9%)	15 (3.6%)	0.99
≥50	5 (9.8%)	17 (4.1%)	0.14
Physician Specialty Type, n (%)			
Unknown	0 (0.0%)	123 (29.6%)	<0.05
Known*	51 (100.0%)	292 (70.4%)	
Child Neurologists	33 (64.7%)	37 (12.7%)	<0.05
Nurse practitioners	5 (9.8%)	15 (5.1%)	0.19
Pediatricians	3 (5.9%)	69 (23.6%)	<0.05
Neurologists	3 (5.9%)	10 (3.4%)	0.42
Clinical Neurophysiologists	3 (5.9%)	7 (1.7%)	0.10

Abbreviations: SD, Standard deviation; * Percentages were estimated among the known physician specialty; other specialty includes child and adolescent physiatry, medical genetics, neurodevelopmental disabilities (psychiatry & neurology), neuromuscular medicine among treated with 1 each; among untreated - other specialty included behavioral health & social services (n=30), internal medicine (n=13), audiology (n=13), family medicine (n=10).

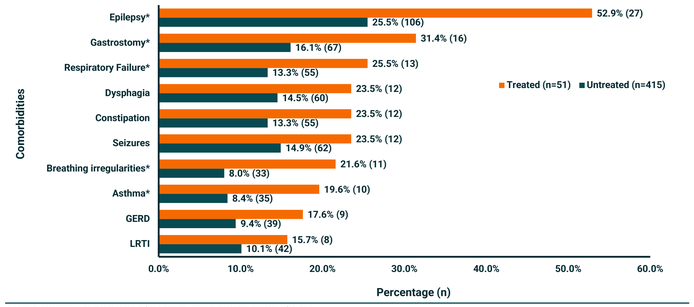
Baseline Characteristics

- Treated male individuals had a higher rates of epilepsy (52.9% vs 25.5%; p=<0.001), gastrostomy (31.4% vs16.1%; p=0.01), and respiratory failure (25.5% vs 13.3%; p=0.03) vs untreated.
- Similar patterns were observed for other comorbidities, including dysphagia (23.5% vs 14.5%; p=0.14) and constipation (23.5% vs 13.3%; p=0.08) for treated vs untreated male RTT individuals (**Figure 3**).

Clinical Outcomes

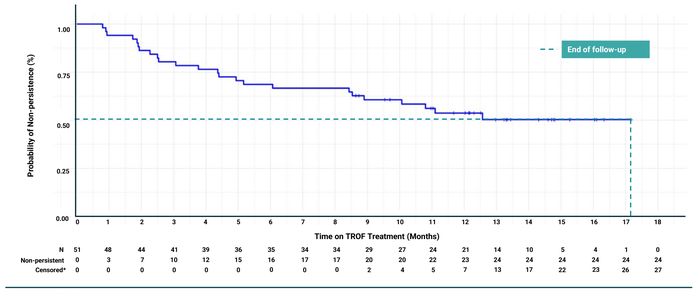
- Kaplan Meier analysis showed that approximately 80% of treated individuals were on TROF treatment for more than 3 months; 70% stayed on TROF for ≥ 6 months, respectively.
- Over half (>50%) continued TROF treatment through the end of study follow-up (~6.0-17.2 months) (**Figure 4**).

Figure 3: Baseline Comorbidities



Abbreviations: GERD, Gastroesophageal reflux disorder; **LRTI,** Lower respiratory tract infection
* Significantly different with a p-value <0.05
Note: Only the top 10 comorbidities studied were presented for clarity. Comorbidities were evaluated 6-months pre-index (i.e., within 6-months prior to first TROF initiation among treated group and within 6-months prior to the assigned index date among the untreated group.

Figure 4: Time on TROF Treatment



Abbreviations: TROF, Trofinetide
* Individuals were followed until the last available RX claim date, end of follow-up or end of study period which ever comes first.

CONCLUSIONS

In this real-world analysis, TROF was used among males with RTT, although a substantial proportion (9 in 10) remained untreated; highlighting an ongoing opportunity to educate and treat among this RTT sub-population.

Provider specialty patterns suggest treated patients are frequently managed within pediatric neurology.

The most common baseline comorbidities among male individuals with RTT treated versus untreated with TROF were epilepsy, gastrostomy, and dysphagia.

Among males who initiated TROF, approximately 8 in 10 remained on treatment beyond 3 months; and 7 in 10 individuals remained on treatment beyond 6 months, respectively.

More than half continued on TROF treatment for >17 months, suggesting a high persistency of TROF in the real-world setting.