Feasibility of a neurobehavioral assessment battery in a clinical trial investigating therapies for Down Syndrome Regression Disorder

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BACKGROUND

- Down Syndrome Regression Disorder (DSRD) is a rare but debilitating condition in adolescents and young adults, marked by mutism, catatonia, and loss of daily living skills[1,2].
- We evaluated the feasibility of a cognitive battery within a sample of individuals with DSRD.

METHODS

- In this Phase 2 open-label clinical trial for individuals with possible or probable DSRD ages 8-30 years, participants are randomized to one of three treatment arms: lorazepam, intravenous immunoglobulin (IVIG), or tofacitinib (Xeljanz, Pfizer).

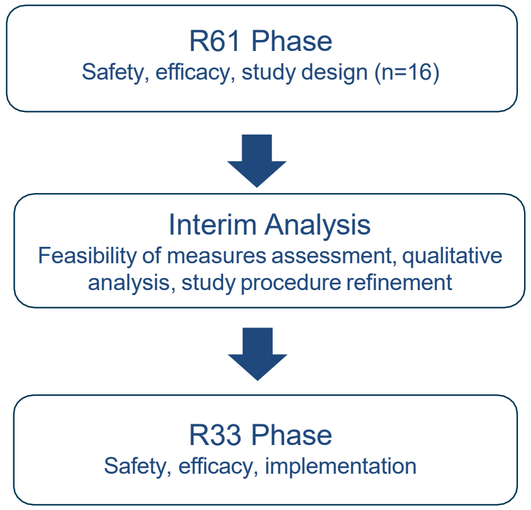


Figure 1. Study design approach allows for intentional assessment of study procedures at a defined time point.

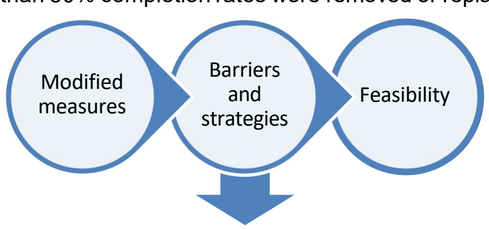
- Neurobehavioral assessment measures were administered at Baseline and 12 Weeks.
- Strategies to enhance feasibility included:
  - Phenotype-informed manual.
  - Standardized training.
  - Behavioral supports.
- Feasibility = participant completion rate + scalability.

RESULTS

Measure	Domain	Completion Rate	R33 Battery
Cambridge Neuropsychological Test Automated Battery (CANTAB) *Paired Associates Learning (PAL)* *Reaction Time Interval (RTI)* *Spatial Span (SS)*	Episodic Memory Processing Speed Spatial processing	18.75%	No
Down Syndrome Mental Status Exam (DSMSE)	Current Mental Status	100%	Yes
Developmental Neuropsychological Assessment, 2nd Edition: Visuomotor Precision (NEPSY-II: VP) *Car* *Motorcycle*	Visuomotor Control	65.6%	Yes
NIH Toolbox Picture Vocabulary Tool (PVT)	Receptive Language	78.1%	Yes
Kaufman Brief Intelligence Test-2 Revised (KBIT-II Revised)	Overall Developmental Status	59.6%	Yes
Timed 25-Foot Walk	Gait and Motor Function	100%	Yes
SALT Story Elicitation Task	Expressive Language	31.3%	No
Study Physician Reports *Neuropsychiatric Inventory (NPI)* *Bush-Francis Catatonia Rating Scale (BFCRS)*	Psychiatric Symptoms Catatonia Symptoms	100%	Yes
Caregiver Reports *Vineland Adaptive Behavior Scales-3 (VABS-3)* *Behavior Rating Inventory of Executive Function-2 (BRIEF-2)* *Developmental Behavioral Checklist-2 (DBC-2)** *Social Responsiveness Scale-2 (SRS-2)*	Adaptive Behavior Executive Function Behavior Social Interaction	100%*	Yes
Fitbit Inspire 3 Model	Sleep Habits	31.3%	No

Table 1. Neurobehavioral assessment battery for initial phase *DBC-2 had a completion rate of 96.2% due to one survey not completed at Baseline. Tests with less than 50% completion rates were removed or replaced during the R33 phase.

DSRD symptoms impacted completion rates. Behavioral strategies improved engagement, while specific modifications preserved data integrity.



DISCUSSION

Implementation of neurobehavioral assessments in individuals with DSRD to ensure high data integrity requires specific considerations such as:

- Behavioral strategies to address challenging behaviors, and to increase engagement.
- Fidelity and consistency of administration.
- Modifications for a unique neurodevelopmental profile.
- DSRD symptom severity may limit engagement despite modifications.
- A defined approach to determine a consensus on potential scoring challenges.
- Evaluation of measurement feasibility at pre-defined time points.
- Regular meetings to ensure consistent data collection and multi-site implementation.
- Evaluating trends in therapies associated with improvements in cognitive metrics in data analysis.

SUMMARY

- R61 enrollment (n=16) is complete; R33 enrollment is ongoing.
- Most measures met feasibility standards with modification.
- CANTAB, Fitbit, and the story elicitation task were removed from the battery.
- Detailed documentation of changes is essential to ensure reproducibility and data quality.

ACKNOWLEDGEMENTS

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