
azafaros
A Beacon For People Living
with Severe Rare Metabolic Disorders
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XIV FORESIGHT TRAINING COURSE - Fondazione Gianni Benzi

The health emergency: regulatory crash and future perspectives

The opportunity of decentralized Clinical Trials in rare diseases: the PRONTO study

PROspective Longitudinal Study of Neurological Disease TrajectOry in Children Living with Late-infantile or Juvenile Onset Of GM1 Or GM2 Gangliosidosis

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Study objectives

To produce well characterized natural history cohorts of patients with GM1 or GM2 Gangliosidoses to serve as control for new experimental therapy trials. The data will be used to compare with data from pivotal study with investigational drug.

Understanding how the disease progresses with a focus on neurological manifestations.

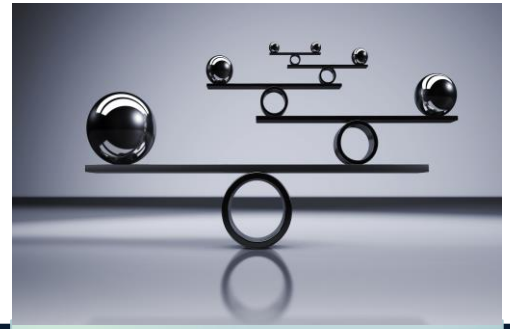
To develop a disease progression model able to identify clusters of disease progression and predict disease trajectory.

Overview Study Design

Study design

Natural history of neurological disease study

Prospective Longitudinal approach

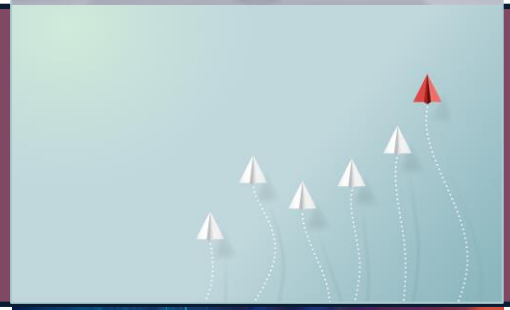


Study sites

US, Brazil, France, Italy, Germany and UK (18 sites)

Sample size

At least 75 patients



Duration

48 months

Indication

GM1 Gangliosidosis or GM2 Gangliosidosis (Tay-Sachs or Sandhoff disease)

Assessments

8 remote (Home) visits and 6 on-site visits

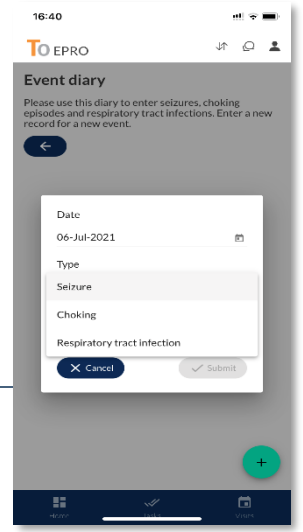
Decentralized study

How did we design PRONTO? Patient and Families first

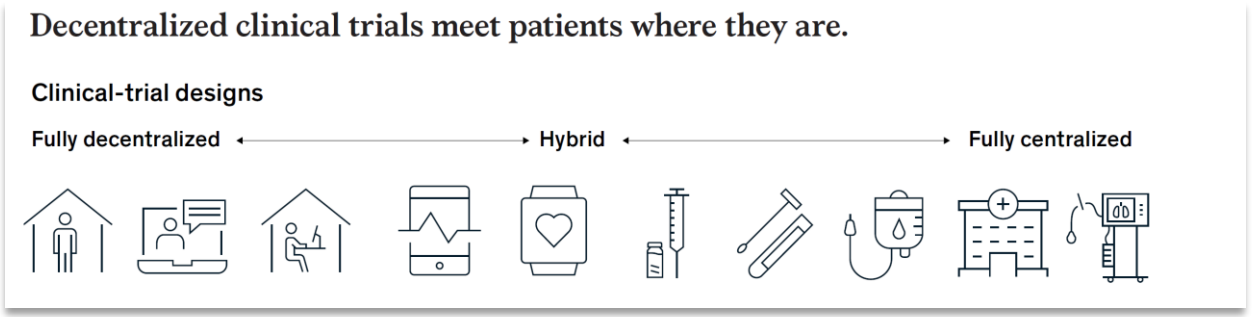
PRONTO Innovative technologies

- Virtual visits

- Web based e-PRO questonnaires

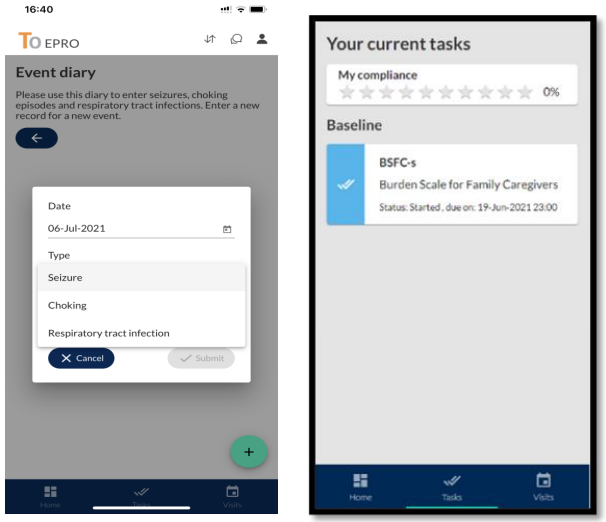


- Passive and continuous monitoring of vital signs, gait/balance



Trial OnLine Application for PRO questionnaires and eDiary

Available any time via phone, tablet or computer and can be completed at home by parents.



Electronic Data Capture system

Clinical assessments outcomes need to be recorded in the electronic Case Report Forms (eCRF) on Trial Online EDC.

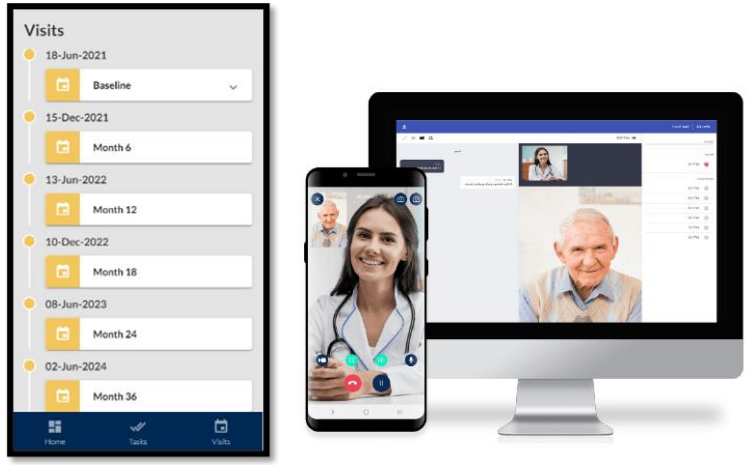
Users will be trained on this database.

Replior
May 2021

Several home visits via secured videoconference

Secured system for discussion between Patients/Parents and Investigators.

Parents will also be part of the video call.



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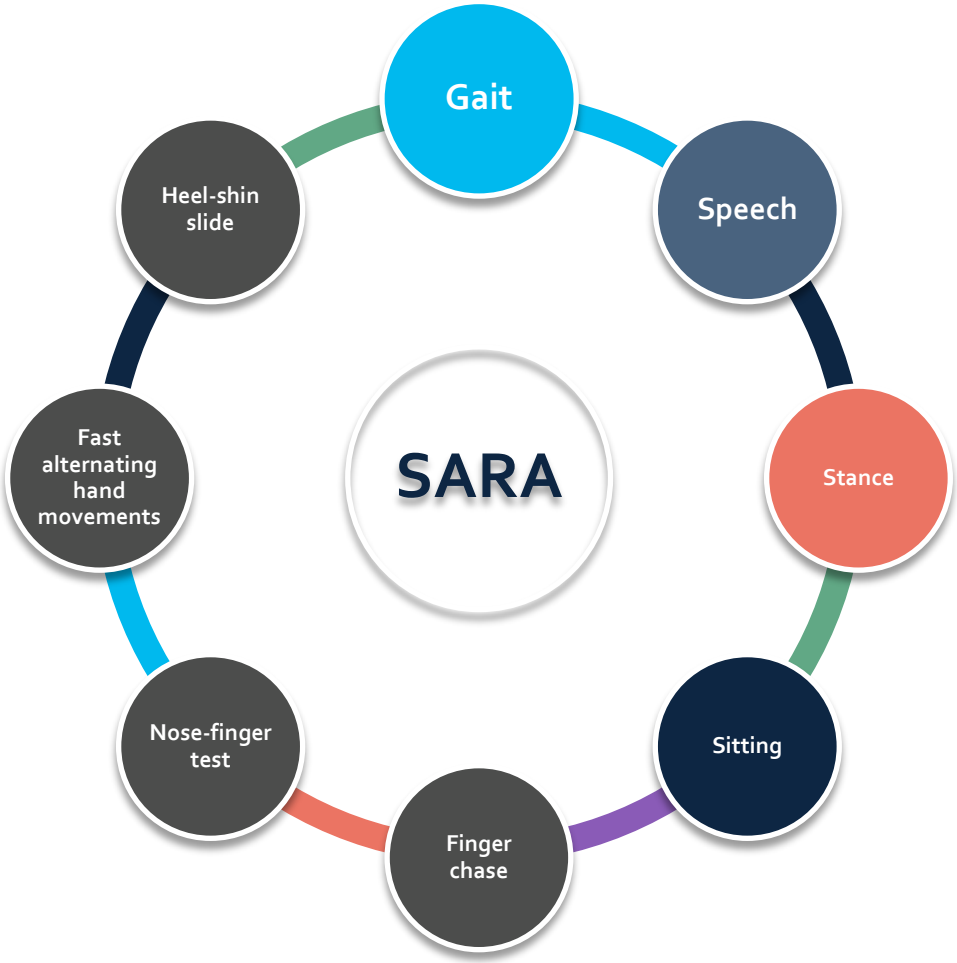
Inclusion criteria

- Age 2-20 years old at baseline
- Genetically confirmed GM1 gangliosidosis or Tay-Sachs or Sandhoff disease
- Achieved 12-month developmental milestones at normal developmental time points as per Principal Investigator's judgement
- Onset of neurological symptoms on or after the patient's first birthday
- Abnormal gait and/or speech disturbance, defined based on SARA Gait score and/or SARA Speech score at baseline

Scale for Assessment and Rating of Ataxia (SARA)

- Ataxic symptoms are the key neurological manifestation of GM1 and GM2 Gangliosidoses with late infantile and juvenile onset.
- SARA is an 8-domain clinical rating scale, chosen as a qualified tool to measure Ataxia :
  - Gait and speech seem to be affected early in the disease course = primary endpoints
  - Other items = exploratory endpoints
- Investigators trained/certified by web-based learning platform (DZNE) from University of Bonn
- Remote visits - SARA^{Home} :
  - Virtual visits tool for real time rating by the PI
  - Procedural Guidelines for Patients/Parents developed



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Exploratory Outcome Measures

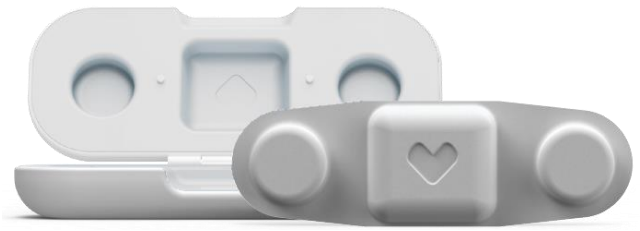
Caregiver/patient-reported outcomes

- Change in the overall composite score of the Vineland Adaptive Behavioral Scale (VABS).
- Change in BSFC-s score for each of the 10 items and the overall score.
- Change in presence/absence of seizures, choking episodes, respiratory tract infections and frequency of seizures.

Passive physiological Monitoring

- Changes in physiological data measured with the wearable sensors (physIQ)
  - Data collection with a **patch** in real time (vital signs and movements) without any specific tasks to be done by patients

VivaLNK Patch



Vineland Adaptive Behavioral Scale

VABS, 3rd edition

Communication	Receptive Expressive Written
Daily Living skills	Personal Domestic Community
Socialization	Interpersonal relationship Play and leisure Coping skills
Motor skills	Fine Motor Gross Motor
Maladaptive Behavior	Internalizing Externalizing Critical items

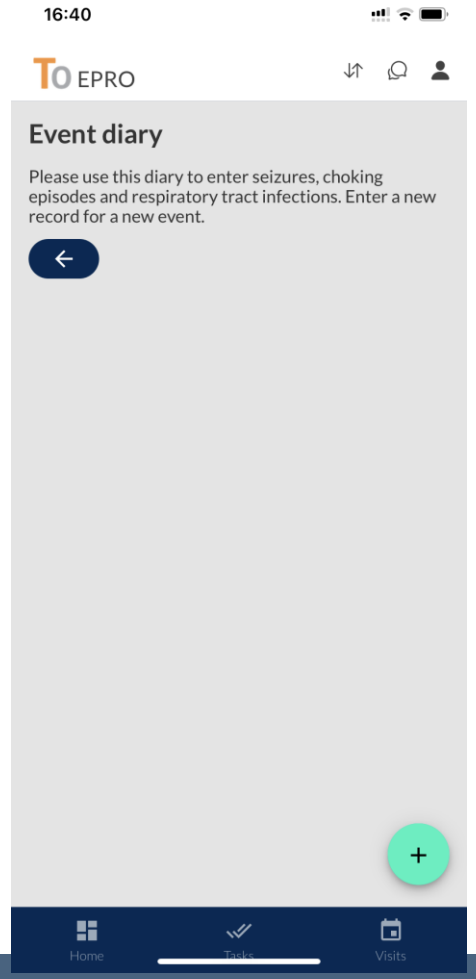
- Vineland questionnaire is an extensive questionnaire.
- **Caregivers/Parents input.**
- It will require ~45 min to complete.
- Parent/Patient centricity as it covers all domain of interest (motor skill) with impact on daily life.
- Score will be compared with healthy age matchedchildren.
- Very important data to identify clinical relevance of the signal detected with the clinical scales.

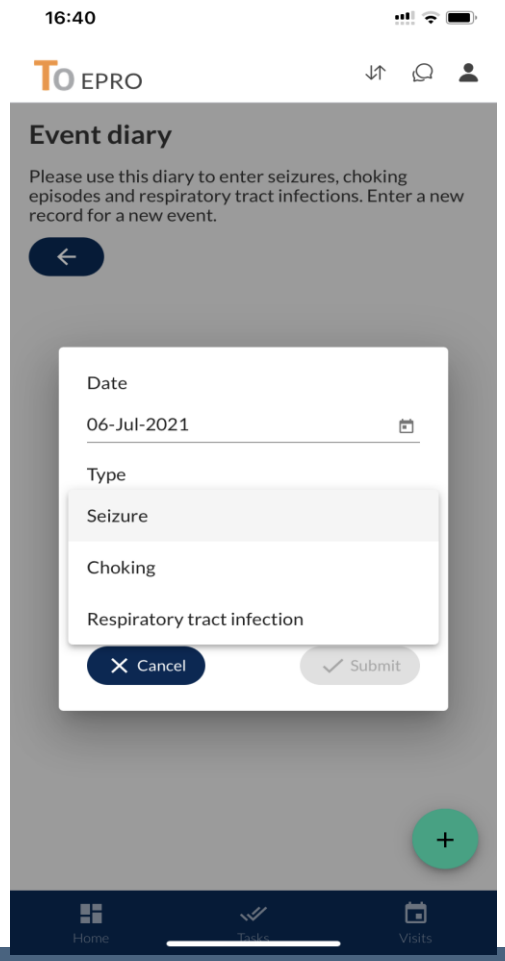
Collection of important diseases related events

In an electronic diary with Trial On-line Application

The following events will be collected :

- Date of seizure
- Date of choking episode
- Date of respiratory tract infection
- Reporting will be done by parent/caregiver





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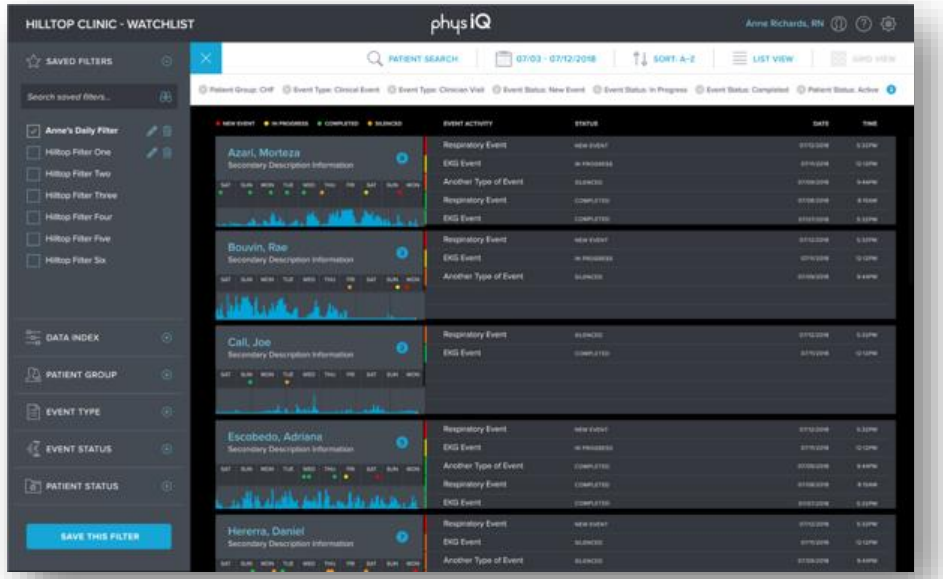
Data collection and analytics

data are streamed continuously from the wearable VivaLNK biosensors…

…cloud platform then applies FDA-cleared analytics…



- Gait
- Walking, Step, Stride
- Trunk movement regularity and asymmetry
- Frequency of sway
- Side-to side symmetry

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