

Gene Therapy Clinical Trials in Rare Diseases: Considerations and Tools for Observing Delayed Adverse Events Transnationally

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Introduction

- There are roughly 7,000 rare diseases and the vast majority have no FDA-approved treatment. As 80% of rare diseases are genetic in origin, these are attractive targets for gene replacement or gene editing therapeutics.
- The low prevalence and wide geographic distribution of rare disease patients poses a unique challenge to trial enrollment. Cross-Border Enrollment, wherein a patient enrolls in a clinical trial located at a site outside their country of residence, is an effective solution to this dilemma. This solution, however, is at odds with the regulatory requirement for the long-term follow up (LTFU) of patients participating in gene therapy trials.
- It is neither realistic nor feasible to subject patients to several years of international travel required for safety surveillance in these studies. Remote data collection across geographical location would drastically reduce burden on participants and sites.

Methods: Study Design

- Post-marketing, prospective registry for pediatric rare disease gene therapy
- Single treatment site in Italy, cross-border enrollment of 50 international patients
- Following treatment, all patients return to home countries (Western Europe and Africa)
- Need for a multilingual technology platform to engage patients, caregivers, and healthcare providers and capture long-term safety and efficacy data



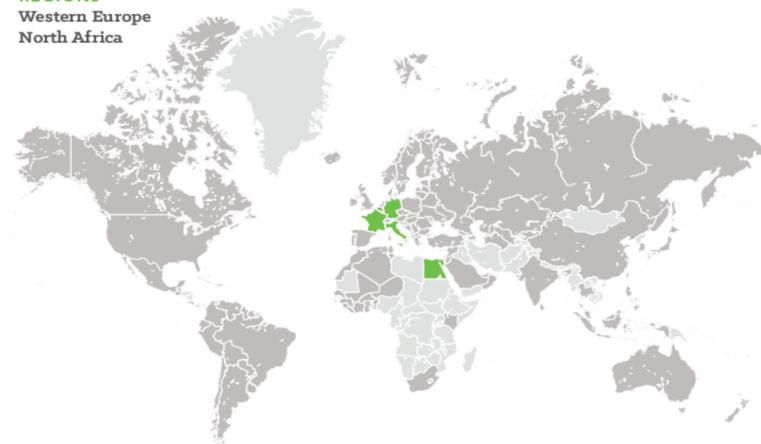
PRIMARY ENDPOINT
The primary objective of this study is to collect safety and efficacy data for patients treated with gene therapy.

INDICATION
Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID)

DRUG CLASS
Gene Therapy

STUDY PHASE
Phase IV

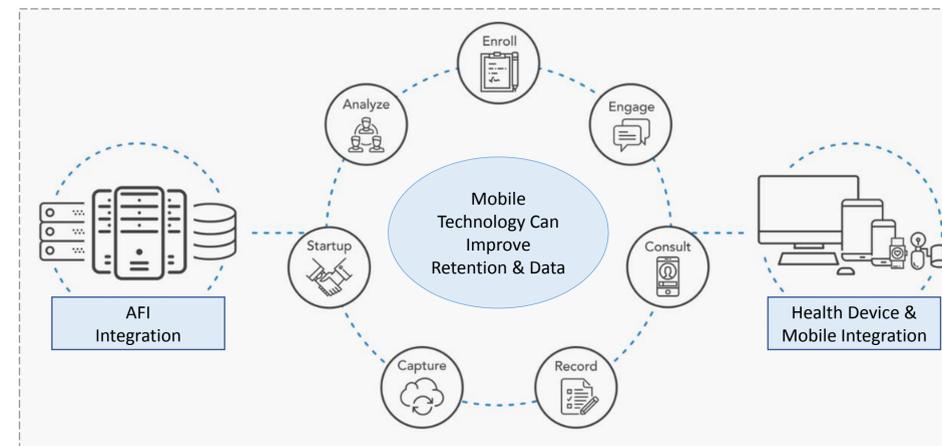
REGIONS
Western Europe
North Africa



Aims

- To accomplish this LTFU of patients over considerable distances, we are using a device-agnostic mobile phone platform developed to support remote data collection and enable virtual clinic visits.
- We are remotely collecting LTFU data from international pediatric patients and caregivers who are participating in a rare disease gene therapy 15-year registry (n=50) collecting safety and efficacy data, including adverse events (AEs), serious adverse events (SAEs), biometrics, and quality of life electronic Patient Reported Outcomes (ePROs).

Digital Platform Considerations



Attributes

- Ongoing, remote data collection across time and geographical location
- Support recruitment, engagement, and retention by reducing burden on participants and sites
- Multilingual technology capabilities
- Maintain robust safety oversight and regulatory compliance
- Flexible, global "bring your own device" (BYOD) platform
- Infrastructure to support ongoing technical evolution over 15-year study period
- Document and consent updates immediately delivered to patients
- Collects patient data from connected mobile health devices
- Embedded eCRF and ePRO interfaces
- Data integrity: platform's EDC export to CTMS or EMR, or link directly to third party EDC
- Data locks: Soft locks or hard locks at patient, cohort, or country level

Adverse Event Reporting

Event Reporter	Patient Adds Pictures	Physician Reviews
<p>Ankle Rash Today, 10:25 AM Adverse Symptom I woke up this morning and was feeling great...</p> <p>New Symptoms Yesterday Adverse Symptom Some interesting symptoms to report...</p> <p>Moderate Hypoglycemia March 15 Adverse Symptom Feeling okay today...</p>		<p>Symptom Recorded Your symptoms have successfully been recorded. Your physician will receive this symptom report and be in touch.</p> <p>Ok</p>

Results

- Primary outcomes data has been successfully captured.
- Excessive long-distance travel was reduced.
- Patients were able to complete follow-up assessments from their home countries without having to rely on traditional site visits.
- The digital platform was able to collect AEs and other healthcare utilization information in case report forms (CRFs), which triggered email alerts to the PI and care team at the treatment center in Italy.
- **To date, the registry's retention rate is 100%.**
- Patient's created and engaged their care team in a "Care Circle" before leaving the treatment center in Italy:

THE CARE CIRCLE – A GLOBAL PATIENT SUPPORT NETWORK

CAREGIVERS Care management, visit set up, and relationship development	PRINCIPAL INVESTIGATORS Telemedicine visits, clinical oversight, AE management, and assessment	FAMILY & FRIENDS Emotional support, motivation, and communication
SUPPORT & CRO Study management, concierge services, and study analytics		CLINICAL RESEARCH CENTERS & SITES Day-to-day patient management, clinical oversight, and engagement

Conclusions/Future Directions

- Digital platforms that support execution of virtual visits strengthen patient engagement, refines data collection, and boosts overall patient retention, enabling the FDA recommended LTFU of gene therapy trials (5-15 years)
- In the rare disease space, drug development is moving away from traditional approaches that rely on patients to travel long distances to clinical sites and toward a more patient-focused paradigm.
- Patients in this study will continue to use the technology to continue collection of outcomes data while also providing important safety data required by regulatory authorities.

Acknowledgments:

This presentation was funded solely by PRA Health Sciences. The authors gratefully acknowledge contributions by Ansel, D and Pruitt, B (PRAHS). The authors report no conflicts of interest for this work.