The Critical Role of Patients In Advancing Gene Therapy Treatments for Rare Diseases

Wednesday, March 9, 2022, 11 a.m. – 12 p.m. ET

Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)
U.S. Food and Drug Administration (FDA)
Virtual Meeting Considerations

- The webinar will be recorded and available online after the event.
- Closed captioning is available in Zoom.
- Use the Q&A box to submit questions throughout the webinar.
- Use the chat box to share general comments and report technical difficulties.
RegenMedEd Webinar Series

- OTAT’s webinar series about regenerative medicine.

- Goals of the webinar series:
  - Discuss foundational information about regenerative medicine therapies, including gene therapy and cell therapy
  - Explore opportunities to engage with FDA and advance regenerative medicine research and drug development
  - Hear from FDA, patients, advocates, researchers, and other important stakeholders about their experiences
Rare Diseases and Gene Therapy

- 80 percent of rare diseases are caused by a single-gene defect.
- FDA has approved two gene therapies for single-gene disorders.
- More than 900 investigational new drug (IND) applications for ongoing gene and cell therapy clinical trials.
- Patient participation in clinical research is critical.
Featured Panelists

Debbie Drell
Director of Membership
National Organization for Rare Disorders (NORD)

Brian O’Mahony
Chief Executive
Irish Haemophilia Society

Julienne Vaillancourt, RPh, MPH
Rare Disease Liaison, FDA CBER
Captain, U.S. Public Health Service Commissioned Corps
MY PERSONAL JOURNEY

Conflict of Interest Disclosure

I have nothing to disclose except my love for my sister.
Your Diagnosis Journey

- 1 in 13 people are undiagnosed
- It takes 5 years or longer to receive a correct diagnosis
- Patients have to see multiple doctors
- Learn about diagnosis, genetic testing, and ways to support your best life
Share Your Story

- Write it for yourself
- Share it with someone you trust
- Consider sharing it with local media
- Share it with your rare disease organization
- Share it with NORD
- Share it with the world!

The Rare Learning Center

Toolkit #7 - Learn how to write an effective speech and powerful story while understanding how to deliver it to make an impact.

- How to Write an Effective Speech PDF
- How to Write a Patient Story
- How to Write an Effective Speech PPT
- Descargar pdf en español
Learn About Research

- What is research, and why participate?
- Natural History Studies vs Clinical Trials
- Is there a study or registry for your disease?
- Should you get involved?
- Do you have doubts about research? Talk to others:
  - Your family
  - Your medical team (doctor/nurses)
  - Other patients
  - A nonprofit
  - Research coordinators
THANK YOU!

FOR PARTICIPATING IN RARE DISEASE DAY®
Personal Experience of Haemophilia Gene Therapy

Brian O’Mahony

Chief Executive of the Irish Haemophilia Society,
Past President of WFH and EHC
Disclosures

- Advisory Board: BioMarin
- Honoraria: Freeline
Treatment History: Severe Haemophilia B

- Childhood: No treatment, many bleeds into joints, muscles, nosebleeds
- Age 14–17: Plasma
- Age 18–41: PCC or plasma-derived factor concentrate
- Age 41–58: Recombinant FIX
- Age 58–59: Recombinant FIX clinical trial
- Age 59–62: Extended half-life FIX
- Age 62: FIX gene therapy
Gene Therapy: My Expectations & Hopes

• **Duration of expression**: At least 10 years
• **Factor Expression**: Hoped for 20%–60%
• **Chronic Pain**: Hoped for less pain in damaged joints and reduced subclinical bleeding
• **Mental Health**: Freedom from burden of regular intravenous infusions and reduced time dealing with my personal haemophilia
• **ABR**: 0 or close to 0 (previously down to 0–1)
• **Factor Use**: Required only for surgery or major trauma
• **Activity Level**: Hoped to increase my physical activity level/fitness

Had to be prepared for a range of possible outcomes
Gene Therapy: My Concerns

- Transaminitis being missed, resulting in loss of expression
- Transaminitis requiring medium- to long-term steroid use
- Risk of cancer from insertional mutagenesis
- Risk of loss of expression achieved

Molecular Therapy
Opinion

Eliminating Panglossian thinking in development of AAV therapeutics

Radoslaw Kaczmarek,1 Glenn F. Pierce,2 Declan Noone,3 Brian O’Mahony,4 David Page,2 and Mark W. Skinner6
https://doi.org/10.1016/j.mther.2021.10.025

The US Food and Drug Administration (FDA) held a 3-day meeting (September 2-3, 2021) of the Cellular, Tissue and Gene Therapies Advisory Committee to consider toxicities, risks of adeno-associated virus (AAV), and the implications of these findings on the long-term clinical implications of AAV therapeutics. While it is hypothesized to be related to transgene overexpression and not capsid toxicity, this has not been well established.

Oncogenicity has so far been only a theoretical risk in humans, but preclinical studies continue to show that it is possible (https://investors.boynton.com/2021-09-06-U-S-FDA-Phased-a-Clinical-Hold-on-BMN-307-Phe-Patient-Phase-1-2-Gene-Therapy-Study-in-Adults-with-PKU-Based-on-Interim-Preclinical-Study-Findings). Contrary to the stubborn misconception, AAV vectors do integrate at a rate resulting in tens of millions of integrations with the currently used vector doses. AAV integration can trigger host-to-host
My Rationale

- **Before gene therapy**
  - Treatment with EHL FIX
  - Prophylaxis every 10 days
  - Venous access not great
  - ABR: 0–1
  - Knee replacement (2018)
  - Preexisting joint damage with degree of chronic pain

- **Rationale**
  - Hoped for factor expression between 20% and 60%
  - Decrease in chronic pain in joints
  - No requirement for constant IV infusions
  - Degree of mental freedom
  - Wanted to try life without severe haemophilia
  - Eligible for 1 trial
  - My age at time of infusion
  - I wanted to lead
Photos, Brian O’Mahony
Hospital Recovery
My Outcomes to Date

- Good factor expression (circa 50%)
  - I had hoped for 20% to 60%
- Some variability in FIX expression after year 1
  - Remained close to or within low normal range
- No requirement for steroids
- Chronic pain decreased in target joints
  - GT and time since surgery
- ABR 0 after 24 months
- Treatment required only for a biopsy, steroid injection (to 100%)
- No treatment required, despite 2 traumas
My Outcomes to Date

• Schedule of visits in first 3 months was challenging but not unexpected
• No treatment-related adverse events apart from iron deficiency (weekly blood draws)
• Fitter and healthier due to GT, lifestyle, and decrease in constant travel
• No treatment remorse
My Outcomes to Date

- Definite degree of mental freedom: having to plan treatments around activities/travel
- Freedom from regular intravenous infusions; freed up some hard drive space in my brain
- Veins recovered
- No loss of “identity”
- “Freedom” from haemophilia less for me, given my roles with IHS/EHC/WFH
CBER Perspective on the Critical Role of Patients in Advancing Gene Therapy Treatments for Rare Diseases

CAPT Julienne Vaillancourt, RPh, MPH
Rare Disease Liaison
Center for Biologics Evaluation and Research
Office of the Director
CBER is one of several centers at FDA
CBER is committed to facilitating and advancing the development and timely approval of safe and effective biologics to improve the lives of children and adults with rare diseases.
CBER Collaborates with Rare Disease Partners Across FDA to Support Many Activities

- Patient Engagement
- Training for Reviewers
- Stakeholder Outreach
- Review
- Cross-Cutting Issues
- Guidance Development
- FDA Rare Disease Day
- Special Projects
CBER Collaborates with External Stakeholders to Advance Development of Products for Rare Diseases

Accelerating Medicines Partnership® Bespoke Gene Therapy Consortium (AMP® BGTC)
Streamlining Adeno-Associated Virus (AAV) manufacturing and regulatory frameworks to increase accessibility of gene therapies for rare diseases

This public-private partnership between NIH, the Foundation for NIH, FDA/CBER and several public and private organizations was launched in October 2021.

Natural History Of MEtachromatic Leukodystrophy (HOME) Study

Conducted by NORD and supported by CBER
HOME Study (https://rarediseases.org/mid-home-study)

Developed by IBM with CBER support.
Innovative data collection tool for patient-centered research.
Current use: HOME study

Discover the Features of SHAPE
Share your health journey, SHAPE future therapies

Developed by IBM with CBER support.
Innovative data collection tool for patient-centered research.
Current use: HOME study
Patients Can Help Advance Development of Gene Therapies for Rare Diseases in Many Ways

- Patient Listening Session
- Clinical Trial
- Public Meeting Speaker or Panelist
- Natural History Study
- Patient Registry
- FDA Review Division Meeting
- Special Government Employee (SGE)
Clinical Trials Support Medical Product Approval

• The sponsor of a clinical trial to be conducted in the United States must submit an Investigational New Drug (IND) application for FDA review.

• The IND contains the study protocol, information about the product, data from animal studies to support the clinical study, and more.

• If the proposed clinical study is allowed to proceed after initial FDA review, subsequent clinical studies may be conducted and reviewed by FDA under the same IND.

• Eventually the sponsor may submit a Biologics License Application (BLA) that includes clinical trial data to support the product’s safety and effectiveness in the intended population, along with many other types of data for FDA review and possible marketing approval.
“FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects…”

21 CFR 312.22 (a)
Gene Therapy Clinical Trial Participation

• Volunteering to participate, or not, is a **big decision**
  - Ask questions and discuss concerns
  - Learn and understand to make the best decision for you/your loved one

• Participating in a gene therapy clinical trial for a rare disease is
  - A contribution to the knowledge base about use of the investigational gene therapy product to treat your rare disease
  - A gift of your time and more
Where to Learn More

- FDA's “For Patients” webpage
  - Gateway for information on engaging with FDA, clinical trials, approvals, and more.
  - [https://www.fda.gov/patients](https://www.fda.gov/patients)

- ClinicalTrials.gov
  - Public database for clinical trials conducted around the world.
  - “For Patients and Families” – helpful links on how to search for a trial, glossary, and more.
  - [http://ClinicalTrials.gov](http://ClinicalTrials.gov)

- MedlinePlus provides related trusted information from NIH
  - [https://medlineplus.gov/](https://medlineplus.gov/)

- NIH/NCATS Genetic and Rare Disease Information Center (GARD)
  - Current, reliable, and easy-to-understand information about rare or genetic diseases in English or Spanish; also links to organizations, specialists, and more for each disease, if available.
  - [https://rarediseases.info.nih.gov/](https://rarediseases.info.nih.gov/)

- NIH/NCATS Toolkit for Patient-Focused Therapy Development
  - [https://ncats.nih.gov/toolkit](https://ncats.nih.gov/toolkit)

- Rare Disease Patient Advocacy Organizations
  - Example of a recent collaborative effort involving several organizations (EveryLife Foundation, BIO, National Health Council, PhRMA): Guide to Patient Involvement in Rare Disease Therapy Development
  - [https://everylifefoundation.org/pfdd-compendium/](https://everylifefoundation.org/pfdd-compendium/)
How to Contact Me

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Thank you
Panel Discussion

Please type your questions into the Q&A box.
Stay Connected and Engaged

Helpful Resources:

- Visit CBER’s website: [www.fda.gov/vaccines-blood-biologics](http://www.fda.gov/vaccines-blood-biologics)
- Sign up for our newsletter, “What’s New @ CBER”: [www.public.govdelivery.com/accounts/USFDA/subscribers/new](http://www.public.govdelivery.com/accounts/USFDA/subscribers/new)
- Follow us on Twitter: [@FDACBER](https://twitter.com/FDACBER)

#RegenMedEd
Thank you!

Webinar materials will be available in a few weeks on FDA.gov.

Stay tuned for OTAT’s Annual Patient Engagement & Regenerative Medicine Workshop in May!