THE FA GCC GLOBAL CLINICAL CONSORTIUM

JULY 2024 NEWSLETTER

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FARA Friedreich's Ataxia Research Alliance

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FA GCC Site Spotlight

Our June spotlight is an Q&A introduction to the Radboud UMC team located in Nijmegen, The Netherlands

Can you tell us about your background and your involvement in FA research?

Our Radboudumc expert center for rare and genetic movement disorders has a long history of clinical and research efforts into cerebellar ataxias. Over the years, we have installed dedicated, multidisciplinary clinics for specific ataxias, including FA, both for adult and pediatric patients. The prime focus of our research has traditionally been on other genetic ataxias, mainly SCA's and ataxia telangiectasia, but we see clear opportunities to expand our skills and expertise to FA-relevant topics. This aligns well with a strong wish of Dutch FA patients, who would very much like to see national FA research endeavors being set up and to have a Dutch FA hub in a wider network for collaborative studies and trials.

(Q&A continued on the next page...)

FA GCC management representatives visited the Radboud University Medical Center in March of 2024 and PI, Bart van de Warrenburg, gave the team a tour of their state-of-the-art genetic sequencing facility.

Left to right, **Radboud team in blue: Janneke Rigters-Schimmel - Research Coordinator**, Jaap Poelman - FA advocate, Cait Monette – FARA Director of Clinical Ops, **Dr. Bart van de Warrenburg – Principal Investigator, Roderick Maas – Research & FARA Grant Recipient, (back) Dr. Judith van Gaalen - Investigator**, (front) Myriam Rai - Director of Global Relations & Initiatives, Jennifer Farmer - Chief Executive Officer, and **Petra Maille-Wisse pediatric nurse practioner**

FA GCC Site Spotlight

Q&A with the Radboud UMC team located in The Netherlands (cont.)

What are some of the biggest challenges you face in your research/work related to rare diseases?

Given the enormous genetic heterogeneity of rare diseases, including ataxias, a single center – in particular for basic science studies - can only focus on a specific set of diseases to gain new, in-depth mechanistic knowledge. For clinical studies, the number of patients with a certain rare disease is always a challenge, and here collaboration with international partners, such as within EFACTS and now FA-GCC, is key. We also try to study more generic themes relevant across various ataxias, such as effects non-invasive cerebellar stimulation as a putative, generic treatment for ataxia symptoms. Funding for rare diseases is an obvious additional challenge, but relevant to keep mentioning.

What recent developments or breakthroughs have you been excited about in the field of Friedreich's Ataxia?

It is exciting to see the 'busy' therapy development pipeline for FA, in which one can clearly see that all mechanistic insights obtained over the past years is leading to the development of targeted treatments.

What message would you like to share with our other consortium members about the Radboud team joining the FA GCC?

The Radboud team is very happy and proud to join the FA GCC and is looking forward to the current and next collaborative projects. We aim to be an active and loyal member, and are keen to make our specific research expertise available to the FA community. In alignment with the mission of our hospital, we hope that this collaboration allows us to have a significant impact on the wellbeing of FA patients.

How can the broader community (researchers, clinicians, patients, advocates) contribute to advancing research and treatments for Friedreich's Ataxia?

Here, forming and acting as an actual multistakeholder community will really make a difference, as this will allow us to do better research, jointly draft the most relevant research questions, and generate more power as we lobby for funding to support FA research.

June FA GCC Site Visits

In early June FA GCC Management Team Representative, Jen Farmer, and FARA Co-Founder and President Ron Bartek, visited the University College London FA Global Clinical Consortium site.

They met with Professor Paola Giunti, Head of the **Ataxia Centre at UCL**, where a multi-disciplinary care clinic has been established along with numerous active FA research studies.

Additionally, they spoke with clinicians, researchers, and scientists at UCL including Suzanne Booth, clinical nurse specialist; Dr. Shpresa Pula, pediatric specialist; Dr. Nehzat Koohi, scientist and audiologist; Professor Jalesh Panicker, uro-neurologist; Professor Lisa Bunn, pediatric ataxia specialist and physiotherapist; and Dr. Rosella Abeti and Dr. Suran Nethisinghe, senior research fellows.

Jen Farmer, and FARA's Kyle Bryant visited the Friedreich's Ataxia Global Clinical Consortium (FA GCC) site at **All India Institute of Medical Sciences (AIIMS)** in New Dehli, India.

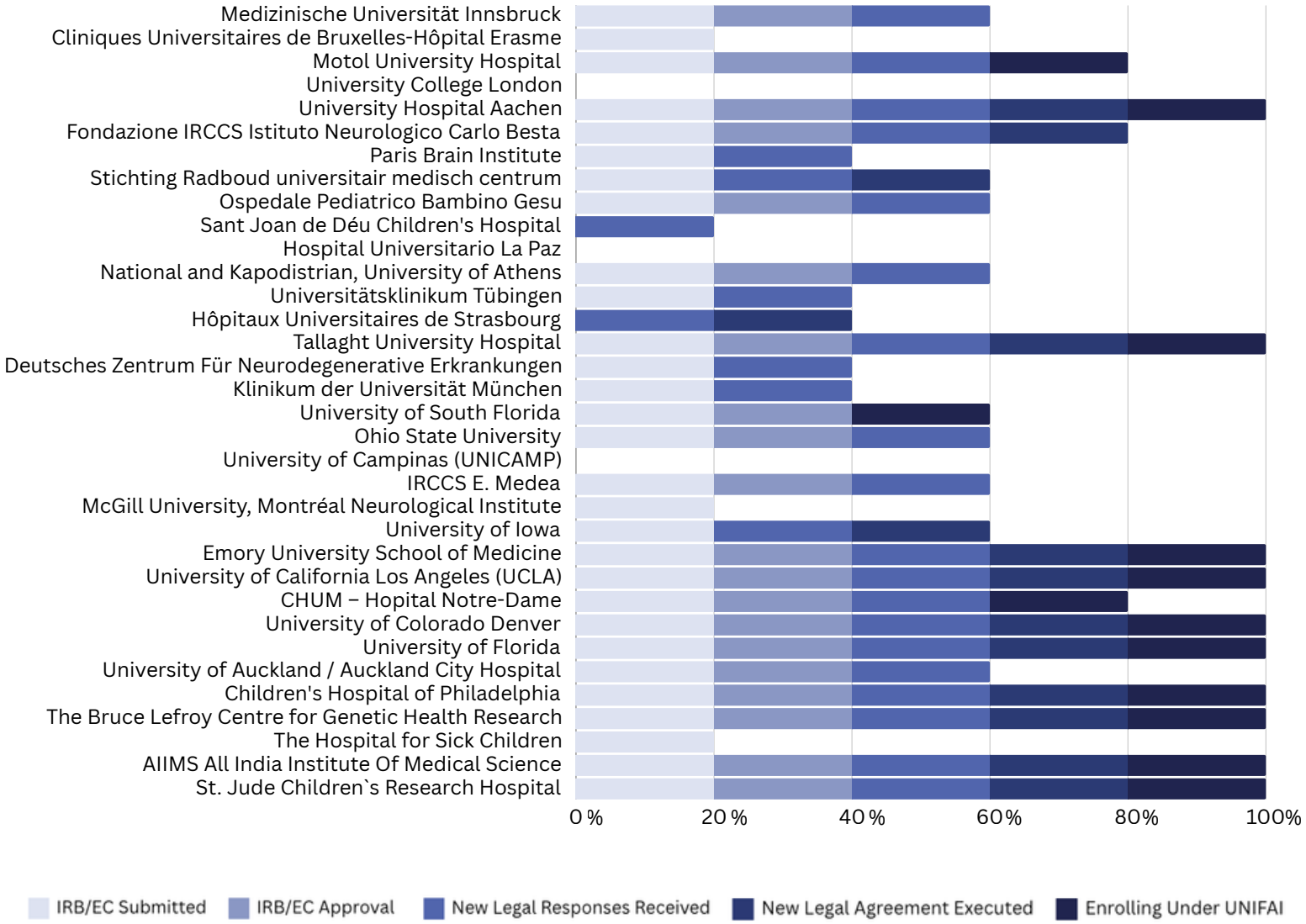
During this visit, they met with Dr. Achal Srivastava, the PI of the AIIMS FA GCC site. The Director of AIIMS, Dr. M Srinivas. We loved the site's plaque proudly displaying their FA GCC participation.

Jen and Kyle also had the opportunity to meet with many other researchers and clinicians including FARA-funded researcher, Dr. Shweta Sahni, to discuss how the FA GCC site at AIIMs functions. Find the link to learn more below

Learn more about Dr. Sahni's research here

Site Transition Status

current as of 7/1/24



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New FARA Website / FA GCC Page

The NEW curefa.org website is live, and we're excited for you to explore all it has to offer. The site was redesigned to make it easier to navigate and interact with information on Friedreich's ataxia (FA), FARA-funded research, and community happenings. It also includes new accessibility features to make the content more user-friendly.

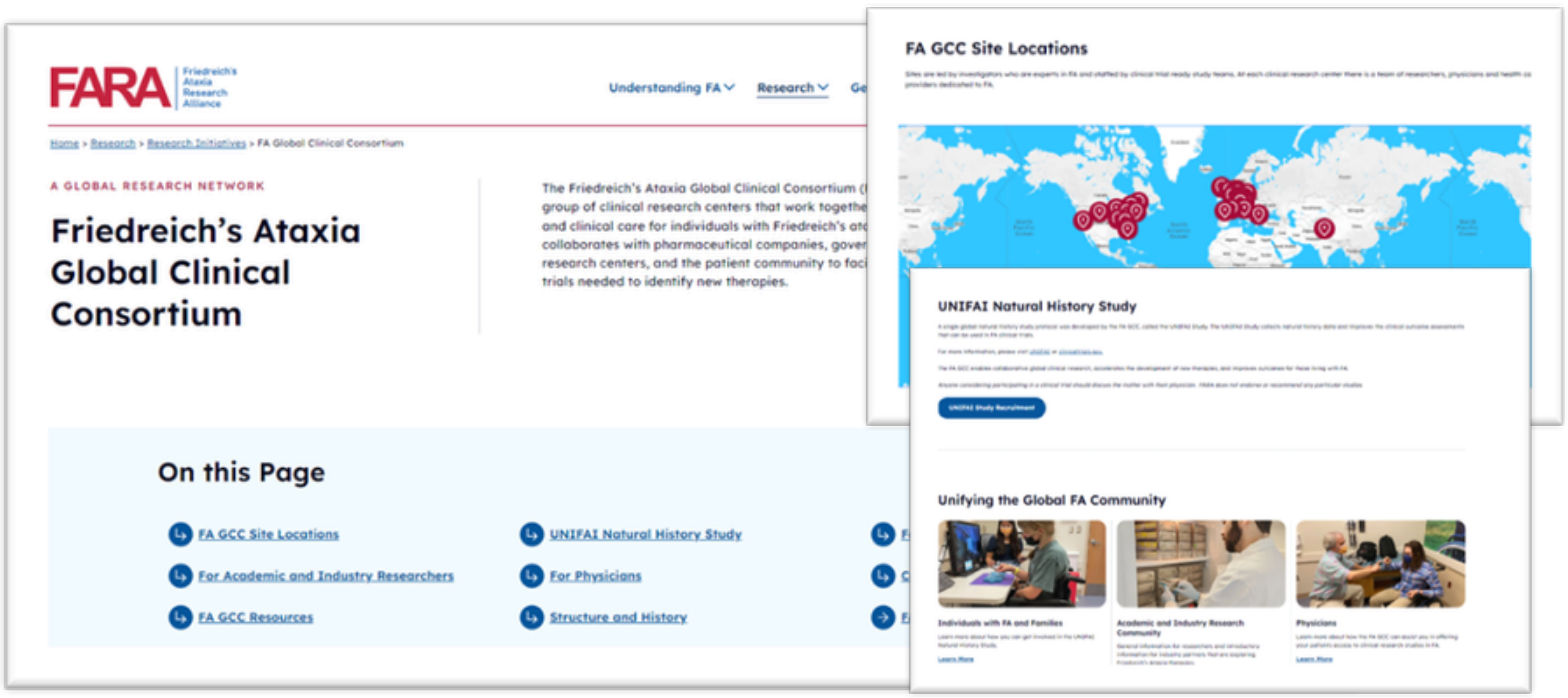
The FA GCC now has a dedicated page — check out the new website today at https://www.curefa.org/research/initiatives/fa-global-clinical-consortium/

New FA GCC Page features:

- FA GCC Site Locations
- UNIFAI Natural History Study
- FA GCC:
  - For Individuals with FA and Families
  - For Academic and Industry Researchers
  - For Physicians
- Core Objectives
- FA GCC Research Resources
- Structure and History
- FA GCC Publications

We welcome your feedback if there is any additional information you would like to see added to the FA GCC Page.

New Website Preview



PHARMA NEWS

Biogen has initiated their (free) FA sponsored testing program. Sponsored by Biogen, this program provides no-cost genetic testing for Friedreich ataxia (FA).
Candidates for this testing program are patients in the United States and Puerto Rico with a suspected or clinical diagnosis of FA and are 16 years of age or older.
Learn More

Biogen initiated an open-label study evaluating the safety, tolerability, and pharmacokinetics (PK) of omaveloxolone following single dose administration in pediatric patients with FA. As of July 1, 2024, the first cohort of the study has completed enrollment and begun dosing of participants aged 12 to 15 years old.
Learn More

Larimar Therapeutics Selected by FDA to Participate in START Pilot Program for Nomlabofusp in Friedreich's Ataxia. START is a new milestone-driven program designed to accelerate development of novel therapies intended to address an unmet medical need for rare diseases.
Learn More

Larimar Therapeutics Announces FDA has Removed Partial Clinical Hold for Nomlabofusp Program in Friedreich's Ataxia. Food and Drug Administration (FDA) removed partial clinical hold following review of Phase 2 dose exploration study data.
Learn More

Astellas Shares that US FDA Cleared their IND with Fast Track Designation for Phase 1 Trial of their Investigational Gene Therapy for the Treatment of Cardiomyopathy in FA. In this study, ASP2016 is being tested in humans for the first time. The people taking part are adults with Friedreich Ataxia who have heart problems.
Learn More

PHARMA NEWS CONT.

LEXEO Therapeutics Announces Positive Interim Phase 1/2 Clinical Data of LX2006 for the Treatment of Friedreich Ataxia Cardiomyopathy. Lexeo Therapeutics reported the interim clinical results of their SUNRISE-FA Phase 1/2 clinical trial for the treatment of Friedreich ataxia cardiomyopathy (NCT05445323) and the Weill Cornell Medicine investigator-initiated Phase 1A trial (NCT05302271) (from 8 participants with > 6-months of follow-up)
Learn More

Lexeo Therapeutics Announces License Agreement to Accelerate Development of LX2006 for the Treatment of Friedreich Ataxia Cardiomyopathy. Lexeo Therapeutics gains intellectual property rights including current and future clinical data from ongoing Weill Cornell Medicine investigator-initiated trial of gene therapy candidate AAVrh.10hFXN (LX2006) to support regulatory discussions.
Learn More

Lexeo Therapeutics Granted FDA Fast Track Designation for LX2006, an AAV-Based Gene Therapy Candidate for the Treatment of Friedreich's Ataxia Cardiomyopathy. LX2006 is designed to deliver a functional frataxin gene to promote frataxin protein expression and restore mitochondrial function in myocardial cells.
Learn More

Stealth BioTherapeutics Presented Data of Novel Compound, SBT-589, in Friedreich's Ataxia Cardiac Models at the Welcome Trust Mitochondrial Medicine Conference. SBT-589 is a promising novel molecule that acts on mitochondrial pathways essential for cellular health and energy production that are impaired in FA cardiomyopathy.
Learn More

Design Therapeutics Outlines Progress Across GeneTAC™ Platform. New Drug Product for Friedreich Ataxia (FA) DT-216P2 with Favorable Nonclinical Pharmacokinetic and Injection Site Safety Profile; Complete GLP Studies by Year-end 2024 to Start Patient Trials in 2025.
Learn More

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UNIFAI Study - Frequently Asked Questions (FAQ)s

Q: Are translations of the study questionnaires into participants' local language available?

A: All core/required questionnaires will be available to participant's translated into 10 local languages (English, Italian, French, Greek, Czech, Spanish, Dutch, German, Portuguese, and Hindi). **The electronic versions will be launched in Medrio EDC Fall of 2024.** Until then, they are only available in English electronically or translated on the paper versions.

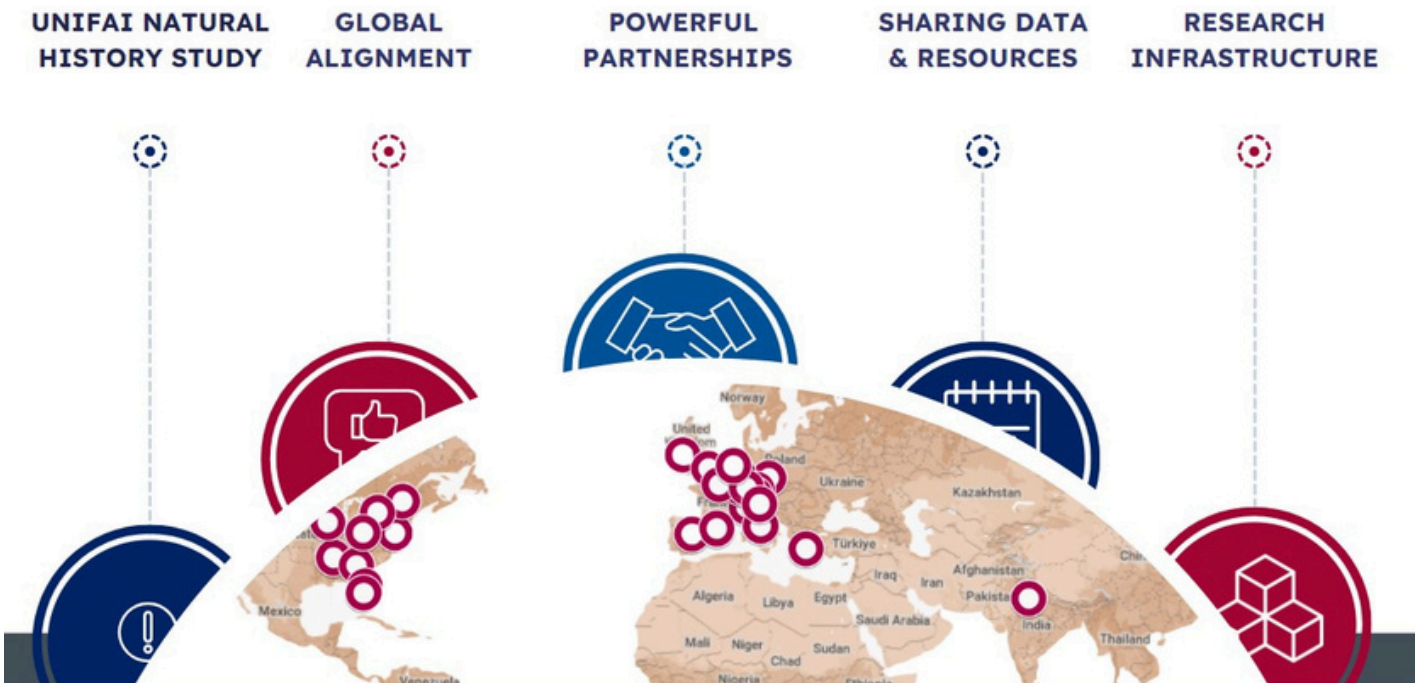
Q: What is the status of the historic data migration into Medrio EDC?

A: The data is being migrated in Phases as described below.

FACOMS Phase I (Demographics, mFARS, FDS, 9hpt, t25ftw) data migration is complete.
FACOMS Phase II will begin migrating next week (diagnosis of FA, visit status, medication and medical history).
EFACTS Phase I (SARA, INAS, Demographics, 9hpt, t25ftw) data migration is scheduled to start in September pending all signatures on the EFACTS consortium agreement addendum.
EFACTS Phase II migration will follow Phase I.

Q: Is there a central location to find other related resources?

A: Yes – UNIFAI resources can be found by clicking on the "UNIFAI" tab, then the "View Study Documents" link in Medrio. These resources currently include the UNIFAI Study Database Manual and a list of the site contacts for other UNIFAI sites. Please reach out to fagcc-info@curefa.org if you need updates made to the contact information for your site.



Selected Recent Publications

CALL for VOLUNTEERS

If your site has a junior investigator or fellow interested in providing a short editorial of a "recent publication" for the next quarterly newsletter, please reach out to fagcc-info@curefa.org.

O'Brien EM, Neiswinter N, Lin KY, Lynch D, Baldwin K, Profeta V, Flynn JM, Muhly WT. Perioperative management and outcomes for posterior spinal fusion in patients with Friedreich ataxia: A single-center, retrospective study. Paediatr Anaesth. 2024 Jul;34(7):654-661. doi: 10.1111/pan.14896. Epub 2024 Apr 24. PMID: 38655751.

Seabury J, Varma A, Weinstein J, Rosero SJ, Engebrecht C, Khosa S, Zizzi C, Wagner ES, Alexandrou D, Cohen BL, Dilek N, Heatwole JM, Lynch DR, Park CC, Wells M, Subramony SH, Heatwole CR. Friedreich Ataxia Caregiver-Reported Health Index: Development of a Novel, Disease-Specific Caregiver-Reported Outcome Measure. Neurol Clin Pract. 2024 Jun;14(3):e200303. doi: 10.1212/CPJ.0000000000200300. Epub 2024 May 10. PMID: 38751829; PMCID: PMC11092940.

Boesch S, Indelicato E. Approval of omaveloxolone for Friedreich ataxia. Nat Rev Neurol. 2024 Jun;20(6):313-314. doi: 10.1038/s41582-024-00957-9. PMID: 38570703.

Stovickova L, Hansikova H, Hanzalova J, Musova Z, Semjonov V, Stovicek P, Hadzic H, Novotna L, Simcik M, Strnad P, Serbina A, Karamazovova S, Schwabova Paulasova J, Vyhnalek M, Krsek P, Zumrova A. Exploring mitochondrial biomarkers for Friedreich's ataxia: a multifaceted approach. J Neurol. 2024 Jun;271(6):3439-3454. doi: 10.1007/s00415-024-12223-5. Epub 2024 Mar 23. PMID: 38520521; PMCID: PMC11136723.

Traschütz A, Fleszar Z, Hengel H, Klockgether T, Erdlenbruch F, Falkenburger BH, Klopstock T, Öztop-Çakmak Ö, Pedroso JL, Santorelli FM, Schöls L; RFC1 Study Group, PREPARE Consortium; Synofzik M. FARS-ADL across Ataxias: Construct Validity, Sensitivity to Change, and Minimal Important Change. Mov Disord. 2024 Jun;39(6):965-974. doi: 10.1002/mds.29788. Epub 2024 Mar 20. PMID: 38509638.

Recent Publications (cont.)

Casey HL, Shah VV, Muzyka D, McNames J, El-Gohary M, Sowalsky K, Safarpour D, Carlson-Kuhta P, Schmahmann JD, Rosenthal LS, Perlman S, Rummey C, Horak FB, Gomez CM. Standing Balance Conditions and Digital Sway Measures for Clinical Trials of Friedreich's Ataxia. Mov Disord. 2024 Jun;39(6):996-1005. doi: 10.1002/mds.29777. Epub 2024 Mar 12. PMID: 38469957.

Németh AH, Antoniades CA, Dukart J, Minnerop M, Rentz C, Schuman BJ, van de Warrenburg B, Willemse I, Bertini E, Gupta AS, de Mello Monteiro CB, Almoajil H, Quinn L, Perlman SB, Horak F, Ilg W, Traschütz A, Vogel AP, Dawes H; AGI Digital-Motor Biomarkers Working Group. Using Smartphone Sensors for Ataxia Trials: Consensus Guidance by the Ataxia Global Initiative Working Group on Digital-Motor Biomarkers. Cerebellum. 2024 Jun;23(3):912-923. doi: 10.1007/s12311-023-01608-3. Epub 2023 Nov 28. PMID: 38015365; PMCID: PMC11102363.

Peverill RE, Lin KY, Fogel MA, Cheung MMH, Moir WS, Corben LA, Cahoon G, Delatycki MB. Insights into the effects of Friedreich ataxia on the left ventricle using T1 mapping and late gadolinium enhancement. PLoS One. 2024 May 30;19(5):e0303969. doi: 10.1371/journal.pone.0303969. PMID: 38814901; PMCID: PMC11139319.

Rummey C, Perlman S, Subramony SH, Farmer J, Lynch DR. Evaluating mFARS in pediatric Friedreich's ataxia: Insights from the FACHILD study. Ann Clin Transl Neurol. 2024 May;11(5):1290-1300. doi: 10.1002/acn3.52057. Epub 2024 Mar 31. PMID: 38556905; PMCID: PMC11093230.

HMA/EMA workshop on Patient Registries

Read the full 2024 June - Report - Multistakeholder workshop on Patient Registries (europa.eu) here.

Major takeaways -

Objective 1: Discuss the EMA qualification procedure for patient registries with the aim to clarify the benefits, identify current limitations, and propose measures to optimise the process.

- Clarify the concept of qualification of patient registries.
- **Suggested action** – Explore possible mechanisms to increase awareness about and facilitate engagement with qualified registries. E.g., include a field to show the qualification status of registries in the HMA/EMA catalogues, including links to the qualification opinion.

Objective 2: Establish the value and enable the use of patient registries for regulatory decision-making by considering contexts of use for which registry data are 'fit for purpose' and examining tools to support data discoverability and assessment.

- Better integration of registry data in regulatory assessment and decision-making
- Establish a channel for informal dialogues with EMA/regulators to discuss questions related to registries
- Promote active dialogues (industry, registries, regulators, HTA and patients) on study concepts and protocols.
- **Suggested action** – promotion of existing tools to improve data quality . E.g., HMA/EMA Data Quality Framework and its draft Chapter on RWD sources once publicly available, the HMA-EMA Catalogues of real-world data sources and studies, the Guideline on Registry-based studies, the Good Pharmacovigilance Practice Module VIII on post-authorisation safety studies, and the Scientific guidance on post-authorisation efficacy studies.

Grant/Funding Opportunities

FARA research grants
General Research Grants, Postdoctoral Fellowships, and Research Awards –LOI deadline is August 15, 2024.
See FARA grant program priorities **here**.

National Ataxia Foundation funding opportunities
LOI submissions will be accepted beginning June 28, 2024. LOIs must be received by September 6, 2024.

Addressing Rare Diseases Topical PCORI Funding Announcement
This Topical PCORI Funding Announcement seeks to fund high-quality patient-centered comparative clinical effectiveness research projects that focus on rare diseases.

Innovation Grants to Nurture Initial Translational Efforts (IGNITE)
Development and Validation of Model Systems to Facilitate Neurotherapeutic Discovery (R61/R33 Clinical Trial Not Allowed)

FDA Rare Neurodegenerative Disease Grant Program
FDA launched the FDA Rare Neurodegenerative Disease Grant Program, which awards grants and contracts to public and private entities to cover costs of research and development of interventions intended to prevent, diagnose, mitigate, treat, or cure ALS and other rare neurodegenerative diseases in adults and children.

LifeArc funding opportunities
The LifeArc Philanthropic Fund provides grants and funding to academic researchers working to advance new treatments and diagnostics for rare diseases.

ARPA-H funding opportunities
ARPA-H opened its first Agency-wide Open BAA, seeking funding proposals for research aiming to improve health outcomes across patient populations, communities, diseases, and health conditions. The BAA calls for proposals to outline breakthrough research and technological advancements.
Opportunity to pursue novel ideas that are not currently covered by a program. Rolling submissions for 1 year.
Revolutionary ideas required.

Grant opportunities from CIRM can be found **here.**

Various MRC Funding Opportunities

Upcoming Meetings

September 24
FA GCC Quarterly Meeting
8am ET | 2pm CET

November 12
2024 in-person meeting
at ICAR London
11am –1pm GMT