



Full Length Article

The FOP Connection Registry: Design of an international patient-sponsored registry for Fibrodysplasia Ossificans Progressiva[☆]



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ABSTRACT

The Fibrodysplasia Ossificans Progressiva (FOP) Connection Registry is an international, voluntary, observational study that directly captures demographic and disease information initially from patients with FOP (the patient portal) and in the near future from treating physicians (the physician portal) via a secure web-based tool. It was launched by the International FOP Association (IFOPA) with a guiding vision to develop and manage one unified, global, and coordinated Registry allowing the assembly of the most comprehensive data on FOP. This will ultimately facilitate greater access and sharing of patient data and enable better and faster development of therapies and tracking their long-term treatment effectiveness and safety. This report outlines the FOP Connection Registry's design and procedures for data collection and reporting, as well as the long-term sustainability of

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Registry. Patient-reported, aggregate data are summarized for the first 196 enrolled patients, representing participation from 42 countries and approximately 25% of the world's known FOP population. Fifty-seven percent of the current Registry participants are female with a mean age of 23.8 years (median = 21 years, range = 1, 76 years). Among the Registry participants who provided their FOP type, 51% reported FOP Classic (R206H), 41% reported FOP Type Unknown, and 8% reported FOP Variant. Patients reported 5.4 years (median = 3.0 years, range = 0, 45.8 years) as the mean age at which they noticed their first FOP symptoms and a mean age at final FOP diagnosis of 7.5 years (median = 5.0 years, range = 0.1, 48.4 years). Information on the patients' diagnostic journeys in arriving at a correct diagnosis of FOP is also presented. These early patient-reported data suggest that the IFOPA's vision of one, unified, global, and coordinated approach to the FOP Connection Registry is well underway to being realized. In addition, the positive response from the FOP patient community to the initial launch of the Registry's patient portal has created a solid foundation upon which to build the largest international registry for monitoring the clinical progression of FOP among patients.

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1. Introduction

Perhaps no other area of clinical research is benefiting more by the growth in popularity of patient registries than research in rare diseases. By assembling clinical information and patient reported outcomes from individuals with a rare disease in one Registry database, researchers can better understand the disease's clinical characteristics and progression. This advancement in knowledge contributes to the development of new drug treatments and improved clinical practices for patients with unmet medical needs. Leading advocacy groups have championed the idea that patient communities with well-implemented registries and active patient organizations have a higher likelihood of developing a treatment. The advocacy groups have also suggested that consistently collecting long-term follow-up data on patients facilitates the creation of standards of care and dramatically improves patient outcomes and life expectancy even in the absence of new therapies [1]. In addition to patient advocacy groups and physician researchers, registries are also being recognized by other critical stakeholders—including biopharmaceutical companies, regulators, and health policy makers—as unique sources of evidence to support life-cycle assessments of new medicinal products from basic research to marketing authorization and the evaluation of their effectiveness and safety in clinical practice [2].

1.1. About FOP and the International FOP Association

Fibrodysplasia Ossificans Progressiva (FOP) is an extremely rare and severely disabling genetic disease in which bone abnormally forms in soft tissues (i.e., heterotopic ossification, or HO), ultimately imprisoning affected individuals in a second skeleton. HO can form bridges of extra bone across the joints, progressively restricting movement and leading to eventual immobility. The disease is caused by point mutations in the gene encoding the ALK-2 (ACVR1) receptor, resulting in abnormal transduction of signals in the cells to form bone. Researchers estimate the disease incidence at 1 in 2 million, suggesting that there are approximately 3000 individuals living with FOP worldwide. Today, there are approximately 800 FOP cases known to the scientific and patient communities [3–5]. The International FOP Association (IFOPA) is a registered 501(c)(3) non-profit organization with a mission to fund research to find a cure for FOP while supporting, connecting, and advocating for individuals with FOP and their families, and raising awareness worldwide. Today, the IFOPA has members in over 50 countries.

1.2. “One registry” philosophy

One obstacle to conducting research in extremely small and dispersed rare disease patient populations such as FOP is that creating meaningfully-sized cohorts of patients from which to collect data is extremely challenging. It is also common in rare disease research for multiple sponsoring organizations—patient advocacy groups, academic research institutions, and biopharmaceutical companies—to introduce

individual registry programs within a relatively short period of time, thereby creating a danger that patient data becomes fragmented across a number of proprietary databases. With escalating activities in FOP research, it became increasingly important for the FOP community to be well-organized to support clinical trials and to contribute to a solid foundation of data that documents the impact of FOP in a systematic way. This data would include disease natural history as reported by physicians and also the functional, emotional, and psychological impact of the disease as reported by patients, family members, and caregivers over time. To achieve these goals and to meet the needs of the large and diverse group of FOP health care delivery and drug development stakeholders, the IFOPA had a guiding vision: to develop and manage one unified, global, and coordinated approach to the FOP Connection Registry that will assemble the most comprehensive data on FOP, ultimately facilitating greater access and sharing of patient data, enabling better and faster development of therapies, and tracking long-term treatment effectiveness and safety.

2. Registry design

The FOP Connection Registry is an international, voluntary, observational study that directly captures demographic and disease information initially from patients with FOP and (in the near future) from treating physicians via a secure web-based tool (www.fopconnection.org). No experimental intervention is involved.

The objectives of the FOP Connection Registry are to:

- Organize the global FOP community for potential participation in clinical trials or other research studies;
- Enable FOP patients worldwide to report data on their own disease state in a shared forum, ultimately empowering both individual patients and the community as a whole;
- Improve the collective understanding of FOP natural history and its functional, emotional, and psychological impact over time;
- And when treatments are available, to advance the understanding of FOP treatment outcomes.

The FOP Connection Registry is comprised of two portals—a patient portal and a physician portal.

2.1. Patient portal

The initial design phase of the FOP Connection Registry, the patient portal, focused on individuals with FOP, their families, and their caregivers. Four principles guided its development. First, the IFOPA focused on information that can be better reported (or only reported) by the individual with FOP, rather than by the individual's physician. Second, the IFOPA focused on collecting the medical information that, over time, will foster the development of drug treatments for FOP. Third, the

IFOPA attempted to minimize the individual's burden to participate in the Registry by limiting data collection to the most important FOP disease information of clinical interest. Finally, the IFOPA assumed that the patient information that is gathered will help to identify groups of FOP patients who share common symptoms or experiences for more in-depth research.

The IFOPA launched the patient portal in July 2015. Patients and their families who were on the IFOPA's global membership list were the first to receive an invitation to participate via the Registry's web-based tool's secure email function. Information about the Registry and instructions on how to join were also communicated to the 17 FOP national organizations and their memberships. Finally, there is a prominent Registry link on the IFOPA's website (www.IFOPA.org) and Registry status updates, milestones, and aggregate data are communicated through IFOPA newsletters and social media posts. The IFOPA anticipates that patient enrollment will grow when the physician portal is launched and physicians begin to enroll FOP patients from their practices.

The FOP Connection Registry was originally introduced in English and later expanded in mid-2017 to include an additional five languages (French, German, Italian, Portuguese, and Spanish) in partnership with several national FOP associations. The patient portal allows FOP patients and caregivers to enter information about themselves and their experiences living with FOP directly into the web-based data collection tool. Because the patient portal is designed to accommodate participants across a broad spectrum of FOP severity, most of the data fields are optional, allowing participants a high degree of flexibility in how much information they contribute, which also minimizes participant burden.

During the registration process, potential Registry participants are asked to complete the following tasks:

- Provide contact information for themselves and any alternate contacts,
- Confirm their FOP diagnosis by submitting a copy of a clinical or laboratory report, or by providing the FOP organization to which they belong and a contact person at that organization,
- Provide the name of their local physician and hospital where they receive care, and indicate whether they would like to be informed of future FOP research opportunities,
- Create a unique username and private password,
- Review and provide electronic acceptance of the informed consent information.

The registration information is stored in an administrative database that is accessible by only the Registry Study Manager and designated Registry team members at the website vendor. After the Study Manager reviews and approves the registration information, participants may access the patient portal and enter baseline data using a web-based enrollment survey.

The enrollment survey captures patient demographic and diagnostic pathway information, as well as health resource utilization information and medical history data related to 10 signs and symptoms of FOP (Table 1). To assess the functional (performance of self-care and mobility activities), emotional, and psychological impact of FOP, patients are asked to complete patient reported outcome measures (PROs), including the FOP-Physical Functioning Questionnaire (FOP-PFQ) [6], the PROMIS Global Health Scale [7], and an IFOPA-developed Aids, Assistive Devices, and Adaptations questionnaire. Registry participants are encouraged to update their health resource utilization information and FOP signs and symptoms data, as well as the PROs at least two times per year, although this frequency is not mandated. Depending on the participant's age and/or mobility status, the Registry surveys may also be completed by a parent, legal guardian, or designated caregiver. Registry participants may withdraw their consent in the Registry at any time without prejudice and with no explanation needed. If a participant

Table 1

Patient-reported disease signs/symptoms and health resource utilization data captured in the FOP Connection Registry.

Heterotopic bone	Gastrointestinal	Cardiovascular
Flare-up symptoms	Nausea	Angina/chest pain
Joint mobility	Vomiting	Heart palpitations
Neurologic	Stomach	Swelling in
	aches/cramps	extremities
Neuropathic pain	Trouble	Urinary
	digesting food	
Abnormal movement disorders	Loss of appetite	Flank pain
Recurrent headaches	Severe	Abnormal urine
	constipation	
Seizures or convulsions	Severe diarrhea	Kidney stones
Spinal cord/brain injuries	Rectal bleeding	Incontinence
	or	
Weakness	Blood in the	Endocrine
	stool	
Learning difficulties	Difficulty	Menstrual cramps
	swallowing	(females)
Sleep	Heartburn	Excessive thirst
Poor sleep quality	Respiratory	Intolerance to
		heat/cold
Taking a long time to fall asleep	Allergies	Health resource
		utilization
Snoring	Shortness of	Doctor
	breath	visits/physical health
Excessive leg movements during	Wheezing	Doctor visits/mental
sleep		health
Waking up with shortness of	Cough	Dentist visits
breath or difficulty breathing		
Dermatologic	Spitting up	Hospital admissions,
	blood	reason(s) for
		admission
Skin rash	Pulmonary	
	infections/illness	
Skin ulcers/blisters	Auditory	
	Hearing loss	
	Tinnitus	
	Earaches/ear	
	drainage	

chooses to opt out, their data are no longer available for future analysis or reporting, but may not be retrievable from previously reported or published datasets as part of related research projects.

2.2. Physician portal

The physician portal, targeted for release in late 2017, will add to the patient portal data by allowing physicians to enter clinical data about patients under their care. Similar principles are guiding the development of the physician portal as the patient portal, focusing on clinical data that can be better reported by a physician rather than by the patient. The physician portal data elements parallel those in the patient portal and include clinical assessments by body system, heterotopic bone, medical events like hospitalizations, imaging, and FOP-related medications. The IFOPA anticipates that the first physician participants will be members of the Registry's Medical Advisory Board. Additional physicians will be referred by the medical advisors or by patients with FOP and their families.

2.3. Additional data sources

In the spirit of the IFOPA's "one registry" vision to promote greater access and sharing of FOP patient data, the FOP Connection Registry was also designed to facilitate the incorporation of data obtained from completed or ongoing academic or industry-sponsored clinical trials, as exemplified by the IFOPA's innovative data sharing agreement with Clementia Pharmaceuticals and their Natural History Study in FOP (NCT02322255). For Natural History Study subjects who are also enrolled in the Registry, the data elements common to both studies will be incorporated into the Registry database at specified times. The

IFOPA will explore similar data sharing agreements with other clinical trial sponsors as FOP research grows and evolves.

2.4. Participant eligibility

The FOP Connection Registry is open to any individual with a diagnosis of FOP (either by clinical assessment by a physician or genotype analysis) and has no exclusion criteria. The individual with FOP wishing to participate in FOP Connection Registry (or depending on the patient's age, a parent or legal guardian as appropriate) is asked to read the informed consent form and check a box stating they understand and agree to the terms to participate in the FOP Connection Registry. If permission to use protected health information is withdrawn, it is the IFOPA's responsibility to ensure that no further data will be collected from the patient and the patient will be removed from the study.

Each patient receives a unique alphanumeric identifier that is common in both portals to avoid duplicate enrollments, as well as to enable the linking of the patient data in the physician portal with the corresponding data in the patient portal. The key for the coded identifiers is accessible only by designated FOP Connection Registry team members for administrative purposes and no participant contact information or other personal identifiers are shared outside the IFOPA.

Before launching the FOP Connection Registry's patient portal to the FOP community, the IFOPA obtained appropriate ethics review and approval of the protocol and informed consent form from the Chesapeake Institutional Review Board, Columbia, MD, USA. Prior to the launch of the Registry's physician portal, the IFOPA will obtain the appropriate national and institutional ethics and legal reviews and approvals as required by local laws to allow physicians to enter clinical data about the patients under their care. The FOP Connection Registry is planned to be an ongoing effort with no protocol-defined treatment, schedule of assessments, or end date. It will continue to exist for as long as it is sustainable and useful to the FOP community.

3. Technology

Ensuring patient privacy is a primary responsibility and concern of the IFOPA. Steps were therefore taken to make sure individuals with FOP can provide their information in a secure setting. The FOP Connection Registry software is implemented using Digital Infuzion's Nof1 Health Research Platform based on the Microsoft Azure Infrastructure that is SSAE 16 SOC1 Type II compliant (the successor to SAS 70), ISO 27001, FISMA, and meets EU-U.S. Privacy Shield regulations. Digital Infuzion's Nof1 Software as a Service (SaaS) Registry Platform's infrastructure consists of 24 × 7 monitoring, advanced security logging, anti-virus protection, intrusion detection, encrypted communication, dedicated firewalls, and provided isolated networks.

4. Governance

To achieve the IFOPA's vision of one unified, global database of FOP patient data, a select group of FOP physician researchers and industry sponsors, along with the IFOPA, collaborated to develop clear and comprehensive guidelines on how to contribute, access, and share Registry data in support of often competing research priorities, while protecting the proprietary information of each researcher or company. As a first step to form the foundation for these guidelines, the IFOPA established an FOP Connection Registry governance charter that defines three governing bodies.

4.1. Patient Advisory Board

The Patient Advisory Board is a mixture of adults living with FOP and parents caring for young children with FOP representing a variety of regions around the world. The Patient Advisory Board provides patient perspective and input on development and use of the Registry's patient

portal. Topics on which the Patient Advisory Board may advise the IFOPA include: changes to the patient portal content, priorities for technology enhancements, use and sharing of data, community participation, and communicating about the Registry.

4.2. Medical Advisory Board

The Medical Advisory Board is an international group of physicians caring for patients with FOP and medical representatives from biopharmaceutical companies that are conducting FOP research. The Medical Advisory Board provides the clinical and scientific input on development and use of the Registry's physician portal, as well as on the FOP Connection Registry protocol. Similar to the Patient Advisory Board, topics on which the Medical Advisory Board may advise the IFOPA include changes to the physician portal content and priorities for technology enhancements. The Medical Advisory Board is also responsible for establishing a Publication Committee, which is accountable for developing and managing the Publication Guidelines for accessing and sharing aggregate Registry data, as well as for interpreting the results and making recommendations for further analyses.

4.3. FOP Connection Registry Executive Committee

The FOP Connection Registry Executive Committee is comprised of the IFOPA's Executive Director, the IFOPA's Director of Research Development and Partnerships, and the Chair of the IFOPA's Research Committee. The overall functions of the Executive Committee are to oversee, prioritize (specifically related to the IFOPA budget or staffing requirements), and coordinate the activities of the Patient and Medical Advisory Boards; to protect the integrity of the Registry and the collaborative spirit under which it is conducted; and to support the IFOPA's vision and research objectives for the FOP Connection Registry. In support of these functions, the Executive Committee is accountable for the Registry's 3–5 year plan, the governance charter, and the industry sponsorship guidelines.

4.4. Funding sources

As noted above, the IFOPA plans for the FOP Connection Registry to be an ongoing effort for as long as it is sustainable and provides useful information to the FOP patient community and research stakeholders. Depending on the scope and geographic distribution, a long-term registry program may require a substantial budget. Through their fundraising activities, the IFOPA was able to finance the development and launch of the FOP Connection Registry's patient portal. The physician portal, with its enhanced IT platform and infrastructure, the required national and institutional ethics and legal reviews, additional registry team support, and potential reimbursement to participating sites for their time working on the Registry, the IFOPA sought additional funding from industry through a three-year commitment, as outlined in the Registry's industry sponsorship guidelines, to facilitate the strategic planning and long-term implementation of the Registry.

Members of the Patient Advisory Board, Medical Advisory Board, and the Registry's Executive Committee all provided input to and approved the Registry's final governance charter.

5. Data quality control, analysis, and reporting

The IFOPA recognizes the importance of communicating Registry data and therefore encourages publication of such data in peer-reviewed scientific journals and at seminars or conferences. As a means to foster long-term participation among the FOP community, the IFOPA periodically publishes newsletters with Registry metrics, status updates, and summary statistics on the entire Registry population. To support these data communication efforts, the IFOPA has adopted several best practices for registry programs.

As a general rule of thumb, patient registries are not strictly compliant with Good Clinical Practice (GCP) guidelines, and patient-reported data are not source-verified or queried. Patient registration forms are reviewed prior to enrollment to ensure individuals have an FOP diagnosis. All patient surveys are submitted via the web-based portal with minimal electronic edit checks on selected data entries. Data are analyzed primarily using descriptive statistics to support disease education efforts and selected research projects. Since prospective endpoints have not been defined, a formal FOP Connection Registry Statistical Analysis Plan has not been developed.

Access to aggregate Registry data is managed by a data request process as defined in the Registry's publication guidelines. With oversight from the Medical Advisory Board's Publication Committee, physicians and researchers can query the Registry database to obtain aggregate data output for individual research purposes or for possible publication in a scientific journal. In order to protect patient privacy and possible proprietary information that was submitted to the Registry, individual physicians and researchers do not have direct access to the Registry database. Rather, the IFOPA employs a consultant statistician who works with the requestor to refine the data request, create the analysis datasets, produce the statistical output (tables, figures, graphs, etc.), and assist with the interpretation of the results. The Publication Committee is also responsible for defining the schedule and content of scientific publications and presentations, identifying target journals and medical meetings, and determining authorship. In making determinations of authorship, the criteria set forth by the International Committee of Medical Journal Editors (Uniform Requirements for Manuscripts Submitted to Biomedical Journals) serves as a guide.

6. FOP Connection Registry: early data

The data presented below were derived from the first 196 enrolled patients, representing approximately 25% of the world's known FOP population. The initial examination of Registry data includes important patient information from the enrollment (baseline) survey and includes patient demographics (gender, age, and genotype) and information on the patients' diagnostic pathways. Variables are summarized using descriptive statistics, including mean, median, and minimum and maximum values. Because data are not available for all variables for every patient, the number of observations is designated when appropriate.

Registry participants represent 42 countries of origin (Table 2).

Data in Table 3 indicate that 57% of the current Registry participants are female with a mean age of 23.8 years (median = 21 years, range = 1, 76 years). Forty-two percent of the Registry participants are children (age 17 years and younger), which highlights the active participation by parents and caregivers of individuals with FOP in this research initiative. Among the Registry participants who provided their FOP type, 51% reported FOP Classic (R206H), 41% reported FOP Type Unknown, and 8% reported FOP Variant.

Table 2
Countries represented by the patients enrolled in the FOP Connection Registry.

Argentina	Ethiopia	Paraguay
Australia	France	Poland
Austria	Germany	Republic of Macedonia
Belarus	Greece	Romania
Belgium	India	Russian Federation
Bolivia	Iran	Serbia
Brazil	Israel	Spain
Canada	Italy	Sweden
Chile	Jordan	Uganda
China	Malta	United Arab Emirates
Colombia	Mexico	United Kingdom
Croatia	Morocco	United States of America
Denmark	Netherlands	Uruguay
Estonia	New Zealand	Venezuela

Table 3
Patient-reported demographics.

Total enrolled	Statistic	Value
	<i>N</i>	196
Gender	<i>n</i> (%)	
Male		84 (43)
Female		112 (57)
Current age (years)	Mean ± SD	23.8 ± 16.3
	Median	21
	Range	1, 76
FOP type	<i>n</i> (%)	
FOP classic (R206H)		65 (51)
FOP type unknown		53 (41)
FOP variant		10 (8)

Tables 4 and 5 provide information on the patients' diagnostic journeys in arriving at a correct diagnosis of FOP. In Table 4, patients reported 5.4 years (median = 3.0 years, range = 0, 45.8 years) as the mean age at which they noticed their first FOP symptoms. Patient-reported mean age at final FOP diagnosis was 7.5 years (median = 5.0 years, range = 0.1, 48.4 years). Registry participants were also asked to think back to the first time that they experienced symptoms of FOP (prior to a confirmed FOP diagnosis) and provide the specialty of the physician from whom they sought medical care. Among the top answers, the physicians' specialties included pediatrician (44%), general practitioner/internist (17%), orthopedist (16%), and an emergency room physician (11%). Registry participants were also asked to provide the specialty of the physician from whom they finally received a correct FOP diagnosis. Participants reported geneticist (26%), other (18%), orthopedist (16%), pediatrician (16%), and rheumatologist (11%). Participants who reported "other" (a free text field in the survey) indicated a combination of physician specialties, that they did not know the physician specialty, or provided the specific name of the physician who made the final correct FOP diagnosis (Table 5). These data suggest that educational efforts to increase awareness of FOP will need to be targeted to a variety of medical specialties.

Of the first 196 enrolled patients from whom these data were derived, 81 (41%) have submitted follow-up surveys to date. Follow-up data will be important for future analyses to describe the natural history of FOP and its functional, emotional, and psychological impact on patients over time. The IFOPA is continually evaluating methods to optimize patient engagement and to encourage timely completion of the Registry surveys.

7. Discussion

These initial patient-reported data suggest that the IFOPA's vision of one, unified, global, and coordinated approach to the FOP Connection Registry is well underway to being realized. The FOP patient community's response to the initial launch of the Registry's patient portal has created a solid foundation upon which to build the largest,

Table 4
Patient-reported ages at first FOP symptoms and final FOP diagnosis.

Total enrolled	Statistic	Value
	<i>N</i>	196
Age at first FOP symptoms (years)	<i>n</i> (%)	121 (62)
	Mean ± SD	5.4 ± 6.4
	Median	3.0
	Range	0 ^a , 45.8
Age at final FOP diagnosis (years)	<i>n</i> (%)	121 (62)
	Mean ± SD	7.5 ± 7.7
	Median	5.0
	Range	0.1, 48.4

^a Several participants reported their birth dates as the dates their FOP symptoms were first noted.

Table 5
Patient-reported diagnostic journey: physician specialties.

Total enrolled: N = 196	Physician specialty: from whom patients sought medical care at first FOP symptoms	Physician specialty: from whom patients received their correct FOP diagnosis
Statistic: n(%) (Responses ≥ 10%)	Pediatrician 54 (44)	Geneticist 32 (26)
	General practitioner/internist 21 (17)	Other 22 (18)
	Orthopedist 20 (16)	Orthopedist 20 (16)
	Emergency room physician 13 (11)	Pediatrician 20 (16)
		Rheumatologist 14 (11)

international registry for monitoring the clinical progression of FOP among patients worldwide. The Registry's patient-focused design and methodology have enabled patients from early childhood to late adulthood to participate equally, covering a broad spectrum of FOP severity. Consistent with the desired global reach of the Registry and its research objectives, patients from 42 countries on six continents are represented and contributing their unique FOP stories. Registry data have been presented in posters at two international scientific meetings, as well as used to answer several specific queries posed by FOP researchers in support of their research projects. In addition, the IFOPA has presented snapshots of Registry data in its newsletters to promote the Registry and to foster long-term community participation. As the FOP Connection Registry expands in available languages and scope to include the physician portal, the IFOPA anticipates that even more patients will enroll in the Registry and that a more comprehensive picture of the natural history of FOP will emerge to support the global FOP patient and research communities. Future publications will explore in more detail the clinical characteristics of FOP as reported by both patients and physicians.

7.1. Future directions

With all of the potential benefits of patient registries for rare diseases, there are a number of challenges that must be managed over time as research evolves and the number of stakeholders expands. Long-term participation by both patients and physicians must be continually nurtured by delivering innovative tools, informative data, research support, and other incentives (both monetary and non-monetary) that participants value. For example, the planned development of a mobile application that allows individuals with FOP to track

their flare-up episodes in “real time” has been enthusiastically supported by patients, physicians, and researchers alike and may be one way to increase participation. Another challenge, especially in rare diseases like FOP, is the competition for study subjects within a very small and widely dispersed patient population. Over a relatively short period of time as drug development expands, both patients and physician investigators may be approached to participate in multiple observational studies and well-controlled clinical trials from different sponsoring organizations. This inevitability makes the IFOPA's vision of one unified and shared FOP Connection Registry to improve the collective understanding of FOP and to help organize the FOP patient community for potential participation in clinical trials even more necessary. Together, these challenges require that the FOP Connection Registry's study documentation and processes must be flexible enough to accommodate this fluid research environment, but still adhere to registry “best practices” at the same time.

Overall, the future direction of registries in rare diseases is very bright. The power of Registry data is clear not only to patients, physicians, and researchers, but to regulatory authorities and reimbursement agencies. The IFOPA's plan to adapt the FOP Connection Registry over time as FOP research evolves—from supporting basic research to supplementing clinical trial results for regulatory review and providing a platform for potential post-marketing commitments—will serve many, diverse health care delivery and drug development stakeholders, enabling the IFOPA to deliver on its goal to enable better and faster development of successful therapies for FOP.

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