Assessment of the Impact of Fibrodysplasia Ossificans Progressiva on Quality of Life for Patients and their Families Using an International Burden of Illness Survey

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Background

- Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare genetic disorder.[1]
- Individuals with FOP experience progressive heterotopic ossification (HO) within soft and connective tissues, resulting in cumulative loss of joint function[2] and independence.[3,4]
- The impact of HO and loss of joint function on quality of life (QoL) has not been quantified.

Objective

To determine the impact of loss of joint function on QoL for individuals with FOP and their family members using an international burden of illness (BoI) survey.

Methods

- An international, cross-sectional online survey (NCT04665323) was co-created with advisors from the FOP community.
- The survey was available online between 18th January and 30th April 2021 across 15 countries in 11 languages.
- Participants were recruited through the International FOP Association and national/regional FOP organisations.
- Individuals with FOP, their primary caregivers, non-primary caregivers and siblings (≥18 years) were eligible to participate.
  - The survey was completed by proxy for individuals with FOP aged <13 years.
- The planned survey enrolment was 300 patients/proxies and 100 family members.
- The impact of FOP on QoL was assessed using validated questionnaires including the EuroQoL health-related QoL questionnaire (EQ-5D-5L) and the Zarit Burden Interview (ZBI), and tailored questions **(Table 1)**.
- Descriptive analyses were performed for each population and by age group, Patient-Reported Mobility Assessment (PRMA) level, and body regions affected (data not shown).
- Linear regression analysis evaluated the relationship between patients' degree of joint impairment (PRMA total score) and EQ-5D-5L index score, adjusted for geographic region.

Results

- 405 individuals with FOP and their family members responded to the survey **(Figure 1; Figure 2)**.
- Participant demographics and patient clinical FOP characteristics are presented in **Table 2**.
- The overall mean (standard deviation [SD]) EQ-5D-5L index score for patients ≥13 years was 0.24 (0.36) compared with 0.85 (0.21) for all family members.
- For patients ≥13 years, EQ-5D-5L index scores decreased as PRMA Level increased **(Figure 3)**.
- There was a significant negative association between PRMA total score and EQ-5D-5L index score for patients ($p<0.0001$).
  - There was no significant association between the family members' EQ-5D-5L index score and the PRMA total score of the patient they cared for ($p=0.6737$).
- 45.1% of primary caregivers had a ZBI total score between 21–40, classified as a 'mild to moderate' impact of caring for an individual with FOP (ZBI total score <21 'little or absent': 39.9%; 41–60 'moderate to severe': 13.7%; 61–88 'severe': 1.3%).[5]

CONCLUSIONS

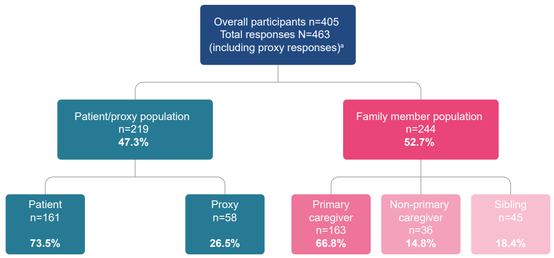
- Loss of joint function caused by HO has a significant, detrimental impact on QoL for individuals with FOP, as measured by the EQ-5D-5L index.
- Caring for an individual with FOP also has a mild to moderate impact on primary caregivers, as measured by ZBI total score.
- Data from this BoI survey will improve understanding of the impact of FOP on QoL for patients and their family members, which is important for identifying unmet needs, evaluating new healthcare interventions and optimising patient care.

Table 1. QoL and physical functioning assessments

Assessment	Definition	Patient/proxy population[a]	Family member population	
			Primary caregiver	Non-primary caregiver or sibling
Impact of FOP on QoL				
EuroQoL health-related quality of life questionnaire for adults (EQ-5D-5L)	• Measure of health-related QoL across five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression[6] • Index score ranges from <0 (worst health) to 1 (full health)	✓[b]	✓	✓
Patient-Reported Outcome Measure Information System (PROMIS)[c]	• For adults: Global Physical Health and Global Mental Health assessed, scores range from 4 (worse health) to 20 (better health)[7] • For children: a total score was calculated, ranging from 7 (worse health) to 35 (better health)	✓[d]	✓	✓
Emotional and social impact related to FOP	• 28 questions, developed to evaluate emotional impact (stress, worries/concern) or the impact on personal daily activities and relationships using a 5-point scale; high scores represent greater emotional impact		✓	✓
Zarit Burden Interview (ZBI)	• 22-item questionnaire[8] on the factors most frequently mentioned by caregivers as impacting their professional, health and/or social wellbeing • Total score out of 88; >60 considered to be severe		✓	
Physical functioning associated with FOP				
Patient-Reported Mobility Assessment (PRMA)	• Mobility at 15 anatomical locations (across 12 joints and 3 body regions) • Each joint/region rated on a 3-point scale: 0=not limited at all; 1=moderately limited; 2=extremely limited • Total score, 0–30; higher scores indicating more severe limitations in mobility/function • PRMA Levels: Level 1, total score 0–6; Level 2, total score 7–12; Level 3, total score 13–18; and Level 4, total score ≥19	✓		

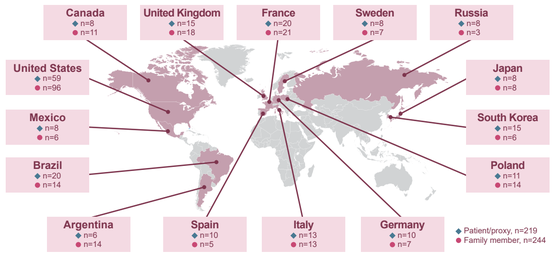
[a]Surveys were completed by a proxy for children <13 years of age; the survey was also completed by proxy for patients ≥13 years if they required additional assistance; [b]EQ-5D-5L was completed by patients ≥13 years; [c]Not available for participants from Poland as the questionnaire was not available in Polish; [d]For patients aged ≥5 years there were two pediatric forms available: one self-completed form designed for patients aged 8–14 years completed by participants aged 13–14 years and a proxy-completed form for patients aged <15 years used for participants aged 5–12 years.

Figure 1. Study populations



[a]Family members who acted as proxies and completed the survey on behalf of patients <13 years could also participate themselves as family members and were included in both the patient/proxy and family member populations.

Figure 2. Study populations by country



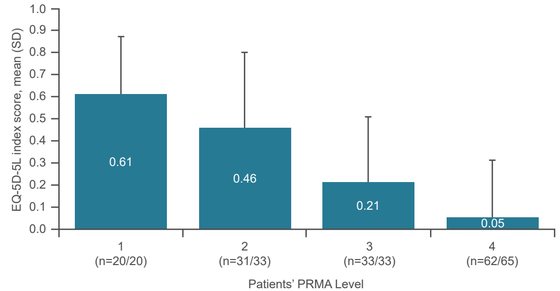
One patient's sibling lived in Australia.

Table 2. Baseline demographics and patient clinical characteristics

	Patient/proxy population n=219	Family member population n=244		
		Primary caregiver n=163	Non-primary caregiver n=36	Sibling n=45
Age, years, median (95% CI)	24.0 (21.0–27.0)	47.0 (43.0–51.0)	55.0 (51.0–60.0)	33.0 (29.0–36.0)
Gender, n (%)[a]				
Male	57 (35.4)	20 (12.7)	30 (85.7)	20 (44.4)
Female	102 (63.4)	135 (85.4)	5 (14.3)	25 (55.6)
Non-binary	2 (1.2)	1 (0.6)	0	0
Not defined[b]	NR	2 (1.3)	0	0
FOP diagnosis confirmed by genotyping, n (%)	170 (87.2)	N/A		
PRMA Level [total score], n (%)				
Level 1 (0–6)	47 (24.1)	N/A		
Level 2 (7–12)	43 (22.1)			
Level 3 (13–18)	39 (20.0)			
Level 4 (≥19)	66 (33.8)			

[a]Patients' gender was not collected in questionnaires completed by proxies; [b]In the case of Russia, gender could be 'Male', 'Female', or 'Not defined'.

Figure 3. Impact of functional impairment (PRMA Level) on QoL (EQ-5D-5L index) in patients with FOP (≥13 years)



Patient population (≥13 years) n=161, there were 10 missing PRMA values for these patients. PRMA is a measure of range of motion across 12 joints and 3 body regions; scores range from 0–30 with higher scores indicating more severe limitations in mobility and function. PRMA Level 1: total score 0–6; Level 2: 7–12; Level 3: 13–18; Level 4: ≥19. EQ-5D-5L is a tool used to measure health-related QoL; the index ranges from <0 (worst health) to 1 (full health).

Abbreviations CI: confidence interval; EQ-5D-5L: health-related QoL questionnaire; FOP: fibrodysplasia ossificans progressiva; HO: heterotopic ossification; N/A: not applicable; NR: not reported; PRMA: Patient-Reported Mobility Assessment; PROMIS: Patient-Reported Outcome Measure Information System; QoL: quality of life; SD: standard deviation; ZBI: Zarit Burden Interview.

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Author contributions Substantial contributions to study conception/design, or acquisition/analysis/interpretation of data: MAM, KST, MD, KC, ASG, JW, FSK; Drafting of the publication, or revising it critically for important intellectual content: MAM, KST, MD, KC, ASG, JW, FSK; Final approval of the publication: MAM, KST, MD, KC, ASG, JW, FSK.

Disclosures MAM: Research investigator: Clementia/Ipsen, Regeneron; Non-paid consultant: BioCryst, Blueprint Medicines, Daiichi Sankyo, Incyte, Keros; Advisory board (all voluntary): IFOPA Registry Medical Advisory Board, Incyte, International Clinical Council on FOP; non-restricted educational fund from Excel and Catalyst sponsored by Ipsen; KST: Research funding from Clementia/Ipsen and Regeneron; MD: Member of the Rare Bone Disease Alliance Steering Committee and the Global Genes RARE Global Advocacy Leadership Council; KC: Employee of Ipsen; ASG: Employee of Atlanstat, contractor for Ipsen; JW: Employee of Ipsen at the time of the study; FSK: Research investigator: Clementia/Ipsen, Regeneron; Advisory Board: IFOPA Registry Medical Advisory Board; Founder and Immediate Past-President of the International Clinical Council (ICC) on FOP; Chair of the Publications Committee of the ICC on FOP.
In April 2019, Ipsen acquired Clementia Pharmaceuticals.

Acknowledgements The authors thank the FOP study team, which includes Adam Sherman, IFOPA, and the following FOP community advisors, who all contributed to the design of this study: Amanda Cali, US; Anna Belyaeva, Russia; Julie Collins, Australia; Suzanne Hollywood, US; Antoine Lagoutte, France; Moira Liljesthröm, Argentina; Karen Munro, Canada; Lucy Pratt, UK; Nancy Sando, US. We thank Marin Wallace, Canada and Roger zum Felde, Germany for their contributions to this project prior to their passing. The survey was carried out by Engage Health.

Medical writing support The authors thank Saoirse Moriarty, BSc, of Costello Medical, Cambridge, UK for providing medical writing support, and the Costello Medical Design Team, for design support, which was sponsored by Ipsen in accordance with Good Publication Practice guidelines.