CLEMENTIA PHARMACEUTICALS AND INTERNATIONAL FOP ASSOCIATION (IFOPA) COLLABORATE TO ADVANCE DRUG DEVELOPMENT

Stéphanie Hoffmann, VP General Manager Europe, Clementia Pharmaceuticals; Donna Grogan, MD, Chief Medical Officer, Clementia Pharmaceuticals; Betsy Bogard, Director of Global Research Development, International FOP Association (IFOPA); Chris Bedford-Gay, International President's Council Chairman, IFOPA

ABSTRACT

Fibrodysplasia ossificans progressiva (FOP) is an extremely rare genetic disease that causes disabling extra-skeletal bone formation (heterotopic ossification [HO]) in muscle and soft tissue and results in a progressive decline in mobility and loss of function. Currently, only palliative measures exist for FOP. Clementia, the International FOP Association (IFOPA), and the FOP community teamed up to develop and validate a disease-specific physical function (PF) questionnaire. Using the Patient Reported Outcomes Measurement Information System (PROMIS) physical function item bank, interviews with FOP patients, and interviews with FOP clinical experts, 28 questions were devised and incorporated into the questionnaire, which is called the Fibrodysplasia Ossificans Progressiva Physical Function Questionnaire (FOP-PFQ). Subsequently, a pediatric version of the FOP-PFQ was developed. The FOP-PFQ is now being used in several Clementia-sponsored clinical trials and in the IFOPA-sponsored FOP Connection Registry to better understand the association of progressive HO and loss of physical function in individuals with FOP. These data will provide valuable insight into a rare disease for which much remains unknown.

OBJECTIVE

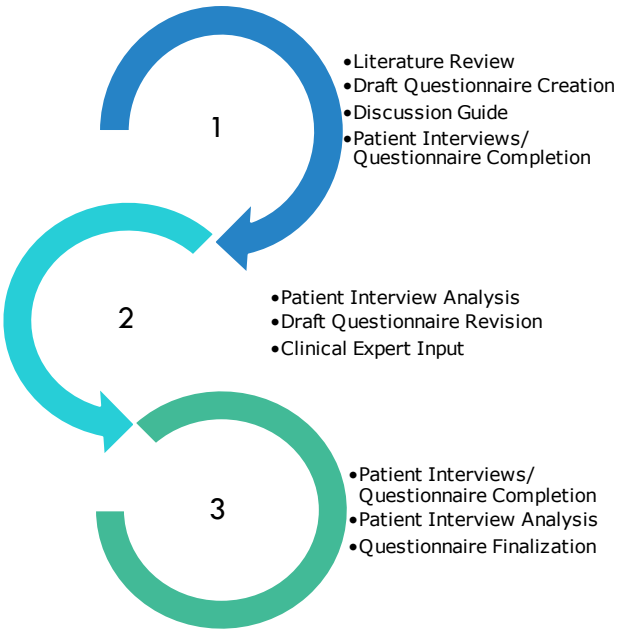
To develop and validate a disease-specific questionnaire in order to evaluate physical functioning in patients with FOP.

BACKGROUND

- Fibrodysplasia ossificans progressiva (FOP) is a rare and progressive genetic condition characterized by heterotopic ossification.
- FOP prevalence is 1:1,000,000 – 1:2,000,000.
- Heterotopic bone formation progressively restricts movement by locking joints, leading to cumulative loss of function, disability, and increased risk of early death.
- The median lifespan is 56 years old.
- Virtually all newborns with FOP have a hallmark toe malformation in which both big toes are shortened and bent inwards, resembling bunions.
- There were no disease-specific questionnaires to evaluate physical function in patients with FOP that could be used to assess potential treatments in clinical trials.

METHODS

Using the Patient Reported Outcomes Measurement Information System (PROMIS) physical function item bank, and following ethics committee approval, interviews with FOP patients and FOP clinical experts were conducted to prepare a draft questionnaire. This questionnaire underwent FDA-recommended psychometric evaluation that resulted in a 28-item questionnaire called the Fibrodysplasia Ossificans Progressiva Physical Function Questionnaire (FOP-PFQ). Subsequently, a pediatric version of the FOP-PFQ was developed. The IFOPA was instrumental in coordinating the patient interviews.



RESULTS

- Twenty-one (21) participants took part in initial FOP patient interviews at the IFOPA 25th Anniversary and FOP Family Gathering (Nov 2013) in Orlando, FL.
- Mean age was 30 years (range 16–54 years); 58% were female and 42% were male.
- Ten (10) additional participants took part in interviews to validate the content of the draft FOP-PFQ at a later stage.
- Mean age was 31 years (range 16–57 years); 50% were female and 50% were male.
- The final FOP-PFQ contains 28 items and covers mobility, upper extremity function, and transferring between various positions (e.g., lying in bed to standing).
- Pediatric versions were subsequently developed using a similar process.
- Versions are available in English, Spanish, Italian and French.

CONCLUSION

Clementia Pharmaceuticals has implemented clinical trials investigating palovarotene as a potential treatment for FOP. Given the need to demonstrate effectiveness, which is defined by regulatory agencies as how patients feel, function, or survive, Clementia, the IFOPA, and the FOP community are collaborating to develop and validate this disease-specific physical function questionnaire.

The FOP-PFQ is now being used in several Clementia-sponsored clinical trials to better understand the association of progressive HO and loss of physical function in individuals with FOP. These data will provide valuable insight into a rare disease for which much remains unknown. Additionally, Clementia and the IFOPA executed an innovative data-sharing agreement that allows the IFOPA to utilize these new questionnaires in its global FOP registry (FOP Connection Registry) and allows for the exchange of data between a Clementia-sponsored Natural History Study and the IFOPA-sponsored registry. The entire FOP community benefits, thereby making it an innovative collaboration.

The study was sponsored by Clementia Pharmaceuticals Inc. The International FOP Association (IFOPA) was instrumental in coordinating the patient interviews and supporting this questionnaire development. Drs. Fred Kaplan and Robert Pignolo from the Center for Research in FOP and Related Disorders (UPENN) were involved in the study design and in the analysis and interpretation of data. Evidera was deeply involved in study design and responsible for the collection, analysis and interpretation of data.