Presenting author email address: pooja.nandi@koneksahealth.com
Poster no. 241

Cardiac biomarkers in Fabry disease

Pooja Nandi,[1] Robert Ellis,[2] Biliana O. Veleva-Rotse,[3] Jennifer Hiros,[3] Paul Howard[3]

[1]Product Management, Koneksa Health, New York, NY, USA; [2]Biomarker Exploration, Koneksa Health, New York, NY, USA; [3]Amicus Therapeutics, Inc., Princeton, NJ, USA

Presented at the 20th Annual WORLD*Symposium*™; San Diego, CA, USA; February 4–9, 2024.

See Supplement

Scan me
- Poster PDF
- Supplement

Introduction

- Cardiac involvement in Fabry disease (FD) progression remains poorly addressed by standard-of-care treatment and is a major cause of death.[1,2] New and accessible cardiac measures are needed to allow for accurate measuring and monitoring of cardiac disease. Such measures will facilitate the development cardiac progression, enabling timely intervention in patients living with FD.
- Digital tools that patients living with FD can use at home to provide high-frequency data collection may support novel therapy development, objectively capture the patient experience, inform appropriate treatment and management decisions, and detect elevated cardiac event risk.
- Here, we present a novel, composite measurement concept aligned to established guidance that utilizes innovative digital measures to improve the measurement of cardiac function in FD. Additionally, we outline the clinical association and concept development work that has been completed in designing with a view to build the proposed cardiac monitoring biomarker that meets industry standards.

Conclusions

- During the concept development work, there was agreement on the need for the development of a monitoring cardiac biomarker to support novel therapy development, care management situations, clinical conversations with patients living with FD, and remote monitoring.
- The development of a composite measurement concept that utilizes new and established digital measures to improve the measurement of cardiac function in FD is conceptually possible, based on the targeted literature search, feedback from patients living with FD, and clinical advisory boards. The strengths and limitations are outlined in the Supplement.
- The clinical association and concept development work completed to date aligns to the *Evidentiary Framework (V3)* and *Digital Health Technology Guidance (Figure S1)* for designing and building a novel measure.
- The composite measurement concept includes signs and symptoms that are most important to patients living with FD, as well as measures of relevance that can be staged in a progression model with clear group boundaries.
- The composite measurement concept outlined here may be used as the foundation for future analytical validation, usability, and clinical validation seeking to capture the progression of cardiac function in FD.

Background and methods

- FD is an X-linked, multisystemic, progressive lysosomal disorder caused by *GLA* variants resulting in α-galactosidase A deficiency.[3] Cardiac involvement is the leading cause of morbidity and mortality in FD.[1] Cardiac manifestations include arrhythmias, left ventricular hypertrophy (LVH), myocardial fibrosis, and strokes or transient ischemic attacks.[4]

Targeted literature search

- A PRISMA literature search was conducted across PubMed to identify cardiac and non-cardiac signs and symptoms related to FD, cardiac patient-reported outcomes (PROs), and other related outcome measures. The search was intended to inform the use of patient diaries in FD, current understanding of the FD progression model, and measures of interest.
- A measurement concept was developed based on the targeted literature search and feedback from both patient and clinical advisory boards.

Patient advisory board

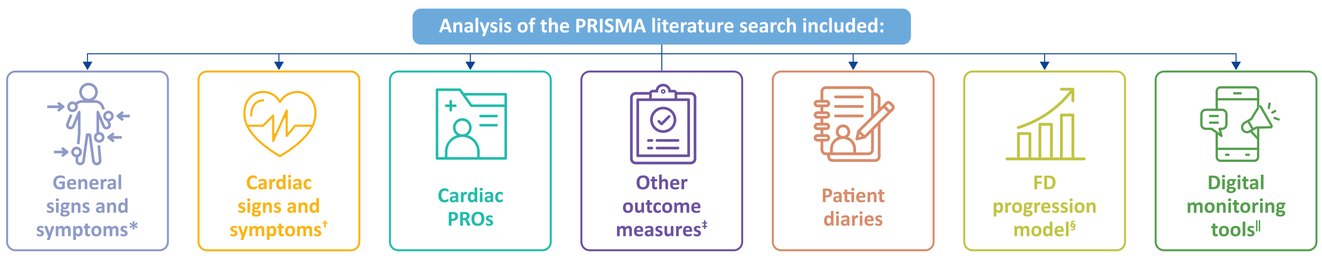
- Two remote sessions were conducted via Zoom with nine patients living with FD to qualitatively assess signs and symptoms of importance, determine willingness to use and tolerability of proposed sensors/wearable devices, completion of an at-home patient diary, and electronic PROs. A follow-up survey was completed by seven attendees. Patients living with FD were based in the USA, of mixed age (≥18) and gender, and had received a confirmed clinical diagnosis of FD.

Clinical advisory board

- Two sessions were conducted via Zoom with eight expert healthcare professionals (HCPs) that treat FD to obtain feedback for a cardiac monitoring biomarker and the proposed composite measurement concept, and to share patient feedback collected to date.

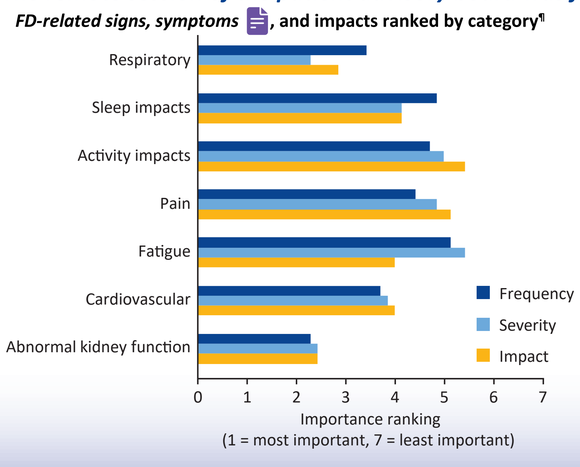
Results

Analysis of the PRISMA literature search across a range of categories highlighted a lack of specific digital monitoring tools

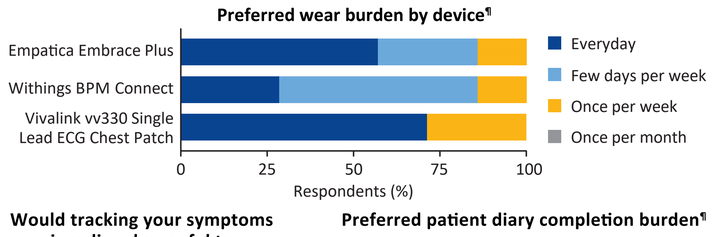


The remote session of the patient advisory board was followed up with a survey

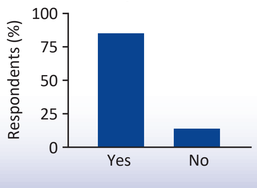
FD-related signs, symptoms, and impacts ranked by category¶



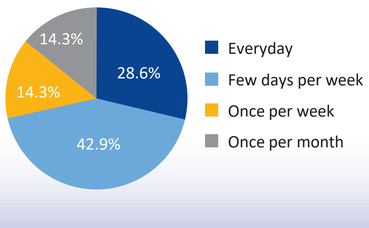
Preferred wear burden by device¶



Would tracking your symptoms in a diary be useful to you as a patient?¶



Preferred patient diary completion burden¶



Clinical advisory board

- Noted a lack of existing specific tools for diagnosis, monitoring and prognosis for FD.
- All indicators of *LVH as known group boundaries* were raised as important, as well as disease onset and progression differences with *age and gender.*
- Noted the impact of FD on cognition (anxiety, depression, etc), function and sleep.
- Expressed the importance of using cardiac outcome measures, specifically the Kansas City Cardiomyopathy Questionnaire (KCCQ), to assess cardiac status and provide context to objective measures.

Patient advisory board

- Noted that pain, gastrointestinal issues and fatigue were the top three symptoms of importance, but cardiac-related symptoms were also ranked as important.
- Would like to know when cardiac events are occurring.
- Expressed concern about not knowing how cardiac signs and symptoms impact their daily life, and fear of cardiac-related sudden death.
- Affected by fatigue and wanted to know whether their cardiac status had a role in that on a daily basis.

Patients are willing to wear a wrist device to collect signs and objective measures of impacts (1–3 days per week)

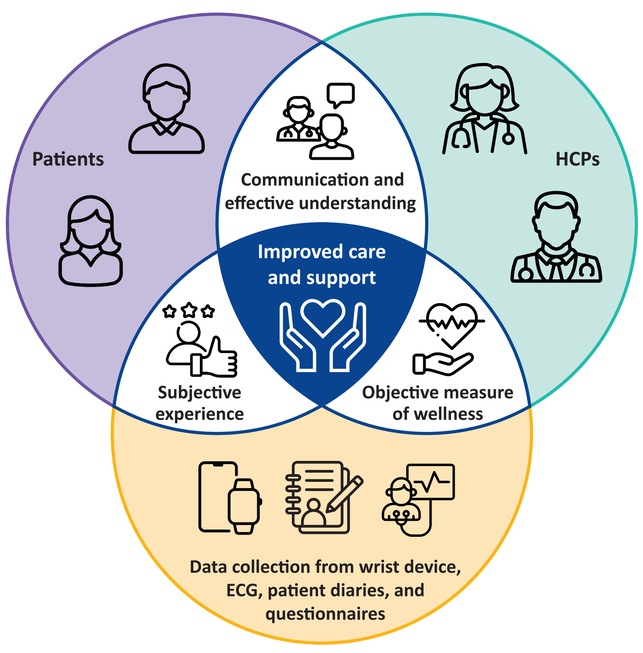
Patients are willing to spend up to 15 minutes per day completing a patient diary

Patients are willing to wear ECG devices (eg Preventice[6] or Vivalink[7]) for 15 minutes each day on 3-weekly cycles to collect cardiac measures

Patients are willing to spend up to 15 minutes a few times a week completing questionnaires, ideally without overlap, eg KCCQ, EQ-5D-5L

*Pain, gastrointestinal problems, temperature intolerance, and fatigue as the most severe and impactful symptoms in FD. Though cardiac events and hypertension are less frequently reported, they also rank highly in terms of severity and impact on daily life;[5] †Proximal cardiac measures of interest, HRV, and hypertension; ‡Fatigue and functional status; §LVH boundary, gender-based differences, risk prediction model capable of predicting a 5-year risk of adverse cardiac outcome for patients living with FD utilizing LVH mass, QRS duration, and other measures; ‖None specific to FD; ¶Patient advisory board – follow-up survey results (n=7). BP, blood pressure; BPM, Blood Pressure Monitor; ECG, electrocardiogram; EQ-5D-5L, EuroQol 5 Dimensions 5 Level; HRV, heart rate variability.

Combining views and input from multiple sources leads to a holistic care approach, with physicians better understanding patient experiences and patients increasing their health literacy



The composite measurement concept was developed to include impacts on HRV, ECG, BP, and quality of life as measures of interest within the cardiac domain

Instrument/device	Measure	Concept
Empatica Embrace Plus	HRV	Cardiac
Vivalink vv330 Single Lead ECG Chest Patch	ECG	
Withings BPM Connect	BP	
KCCQ	Impacts	
Clinic	ECG	
Functional Assessment of Chronic Illness Therapy – Fatigue (V4)	Multiple	Fatigue
Empatica Embrace Plus	Activity level, walking, sleep	Functional change
EQ-5D-5L	Impacts	
Patient diary	Impression of change during day/night time	
Clinic	Lab values	Renal

References

1. Waldek S *et al. Genet Med* 2009;11:790–6.
2. Baig S *et al. Europace* 2018;20:f153–61.
3. Bokhari SRA *et al. Fabry Disease.* Treasure Island (FL): StatPearls Publishing 2022.
4. Pieroni M *et al. J Am Coll Cardiol* 2021;77:922–36.
5. Hamed A *et al. Orphanet J Rare Dis* 2021;16:285.
6. Boston Scientific. BodyGuardian™ MINI Remote Cardiac Monitor for patients. Available at: https://www.preventicesolutions.com/patients/body-guardian-mini (accessed January 2024).
7. VivaLink. Ambulatory continuous cardiac monitoring. Available at: https://www.vivalink.com/ambulatory-cardiac-monitoring (accessed January 2024).

Acknowledgments and disclosures

The authors would like to thank the following patients who participated in the patient advisory board: Nathaniel Goldman, Cindy Westhoff, Robin Richardson, Jerry Walter, Isabella Nebel, Paul Rakoski, Amanda Luchento, Jack Johnson, and Kacie Anderson-Stacey.

The authors would like to thank the following HCPs who participated in the clinical advisory board: Antonia Camporeale, MD; Geu-Ru Hong, MD, PhD; Caroline Kistorp, MD, PhD; Johanna Kuusisto, MD; Marty Maron, MD; Mehdi Namdar, MD; Iacopo Olivotto, MD, PhD; and Rick Steeds, MD.

This study was supported by Amicus Therapeutics, Inc.

Editorial assistance was provided by Lucy Wust, MSc, at Cogent (an AMICULUM® agency), funded by Amicus Therapeutics, Inc.

The presenter, Pooja Nandi, is an employee and shareholder of Koneksa Health.