

Paul Fagan¹, Kela Roberts^{1,3}, Roger Xu¹, Dominic Abrams^{1,2,3}
¹Massachusetts Institute of Technology, Sloan School of Management, Cambridge, MA, USA
²Boston Children's Hospital, Boston, MA, USA ³Harvard Medical School, Boston, MA, USA



Paul Fagan



Kela Roberts



Roger Xu

H-Lab 2019 Team:

Abstract

Boston Children's Hospital (BCH) is seeking to improve the standard of care given to, and overall clinical management of, individuals suffering from catecholaminergic polymorphic ventricular tachycardia (CPVT). Patients with CPVT often first present with episodes as children. Unless an exercise Stress Test is given to the patient at this time, it is unlikely that CPVT will be the initial diagnosis.¹ Sudden cardiac death can also be the first presentation of CPVT.¹ The BCH team has been researching and developing a possible genetic therapy to provide a better alternative to existing therapies. BCH has done pre-clinical work to develop a gene therapy candidate, AAV9-GFP-AIP, which has effectively suppressed ventricular arrhythmias induced in both mouse and human iPSC-CM models.¹ This can reduce the possibility of sudden cardiac death occurring even while the patient is utilizing existing therapies. As such, this gene therapy treatment has the potential to commercially address an unmet need in the CPVT patient population.

Background

Directed by Dr. Dominic J.R. Abrams, the Inherited Cardiac Arrhythmia Program (ICAP) in the Department of Cardiology at BCH provides personalized care to patients with a history of cardiac arrhythmias, congenital heart disease, and sudden cardiac arrest. In 2016, ICAP researchers pioneered a novel gene therapy for CPVT. Trials in rodents and other animal models provided promising results and the team is looking for the best way to align their research for commercialization. ICAP's leadership, with the H-Lab team, is evaluating the gene therapy's cost/benefit and market potential.

Objectives

- To develop a decision tree type analysis estimating the cost of treating different patient groups subject to CPVT with current therapies; and
- To develop a general cost/benefit framework analysis of treating CPVT patients with current treatment versus with the gene therapy in development by BCH; and
- To address barriers to commercialization/reaching patients

Methods

In accordance with the H-Lab Work Plan, the H-Lab team met with the BCH ICAP team to understand the scope of the project and to develop a pathway forward for commercialization. The H-Lab team concluded that there should be several key deliverables including a decision tree analysis and a cost/benefit framework for treating different patient groups afflicted with CPVT. Information from BCH, United States Food and Drug Administration, and the European Medicines Agency (EMA) were collected and analyzed; industry findings are as illustrated. Case studies from other approved gene therapies were summarized.

Acknowledgements and References

- Bezzarides VJ, Caballero A, Wang S, Ai Y, Hylind RJ, Lu F, Heims-Waldron DA, Chambers KD, Zhang D, Abrams DJ, Pu WT. Gene Therapy for Catecholaminergic Polymorphic Ventricular Tachycardia by Inhibition of Ca²⁺/Calmodulin-Dependent Kinase II. *Circulation*. 2019 Jul 30;140(5):405-419.
 - Watanabe H, Chopra N, Laver D, Hwang HS, Davies SS, Roach DE, Duff HJ, Roden DM, Wilde AA, Knollmann BC. Flecainide prevents catecholaminergic polymorphic ventricular tachycardia in mice and humans. *Nat Med*. 2009;15:380-383. doi: 10.1038/nm.1942.
 - Varian K, Tang WHW. Therapeutic Strategies Targeting Inherited Cardiomyopathies. *Curr Heart Fail Rep*. 2017; 14(4) pp.321-330.
- For full list of references with regards to our research, please contact us.

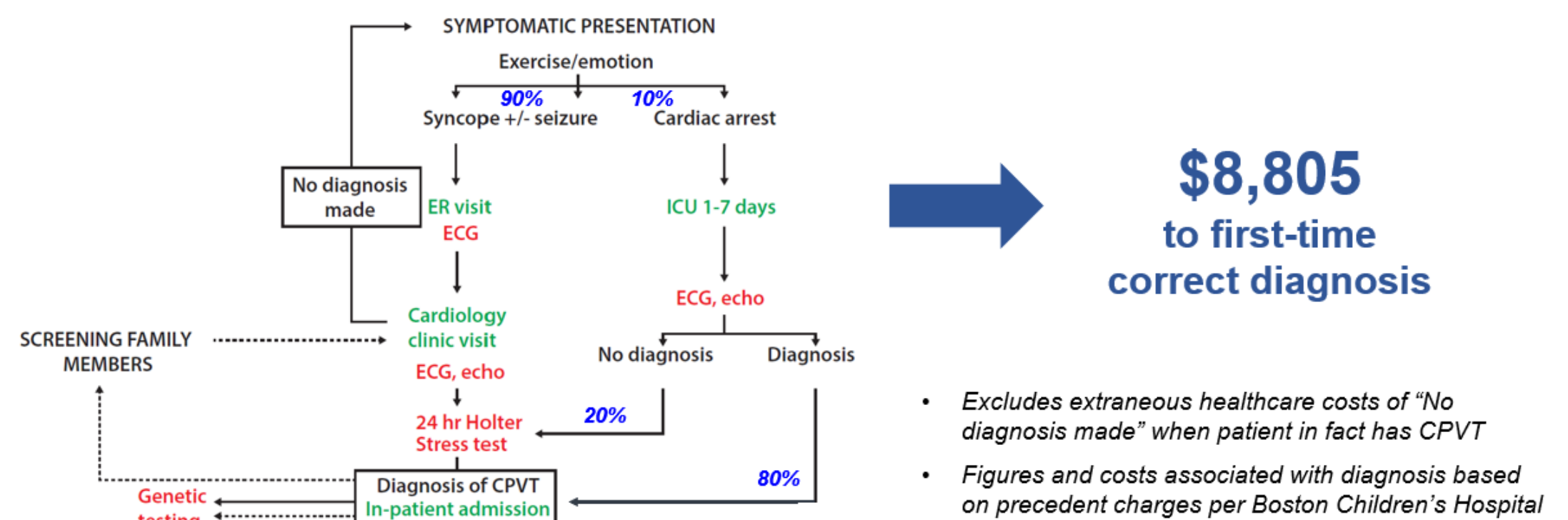
Donald Triner, MIT Sloan
Anne Quaadgras, PhD, MIT Sloan
Jónas Oddur Jónasson, PhD, MPhil, MSc.

Dominic Abrams, MD, MRCP
Robyn Hylind, MS, CGC

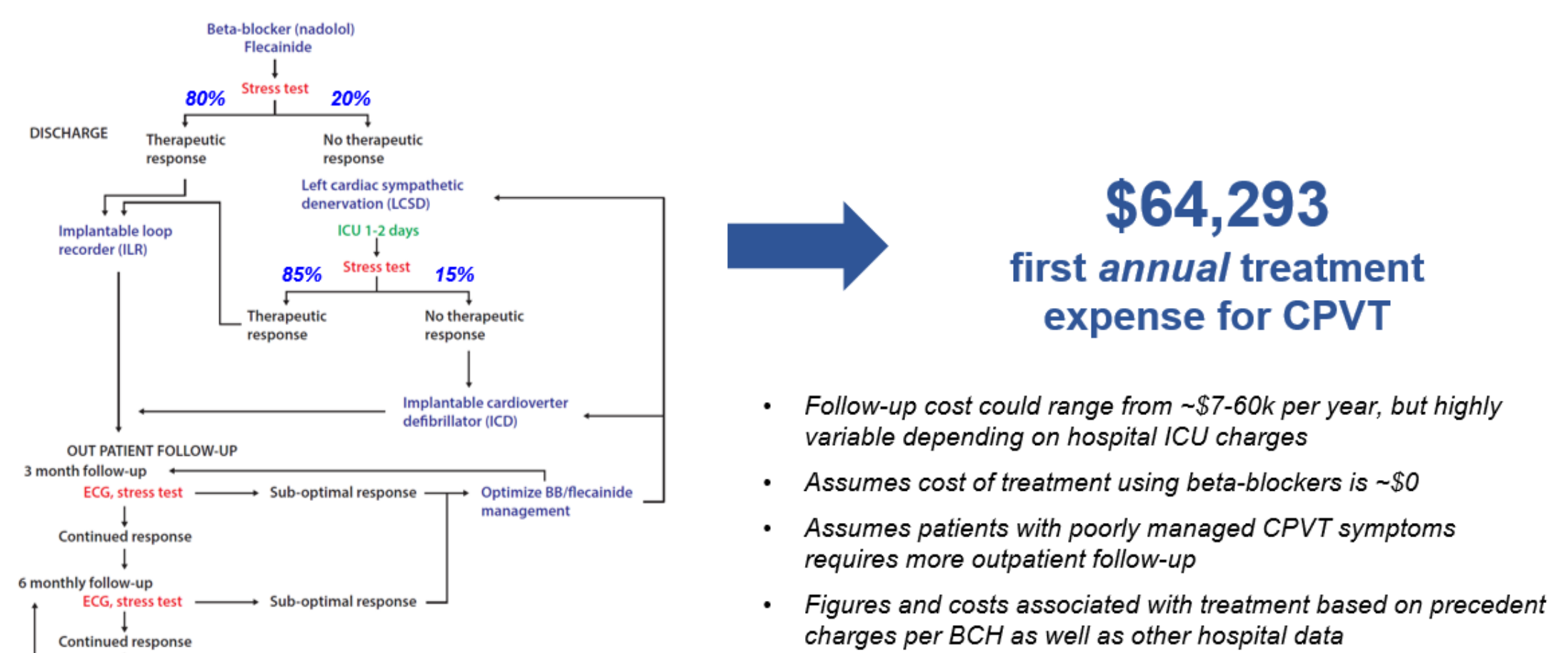
William Pu, MD
Vassilios J. Bezzarides, MD

Treatment Pathway and Costs

CPVT Diagnosis Pathway and Expected Cost



CPVT Treatment Pathway and Expected First-Annual Cost of Treatment



Based on precedent gene therapies price listings, cost will likely be in the mid-to-low \$100k's. **Our estimate for analysis is ~\$250k.**

Payer Perspectives

The lower the lifetime cost of any non-gene therapy treatment of a medical condition (e.g., CPVT), the increased amount of data and level of efficacy that is required for a payer to support the cost of any gene therapy for that medical condition.

In the case of CPVT, any gene therapy is going to need to address the root cause, not what is "thought" to be the root cause, with sufficient data and documented clinical outcomes in order for a payer to give reasonable consideration to providing coverage.

Payers are slowly incorporating QoL improvements in their assessment of which therapies to reimburse, but this is still an evolving criterion.

Conclusion and Recommendations

In assessing the cost/benefit of BCH's CPVT gene therapy versus existing treatment paradigm, we found a large price discrepancy. While this price gap from a financial perspective seems large, our discussion with payers has still signaled positive momentum in reimbursing expensive gene therapies as long as there is significant benefit to patients. As further clarity is obtained with regards to payment structure, and as HRQoL slowly becomes incorporated into coverage guidelines, we believe BCH's gene therapy for CPVT still has potential to reach market.

We recommend BCH take the following next steps:

- further elucidate biology behind CPVT
- identify a partner for development and commercialization
- keep a watchful eye on other gene therapy stories, particularly incorporation of HRQoL parameters