Perceptions and attitudes towards gene replacement therapy in parents of children with cardiomyopathy

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INTRODUCTION

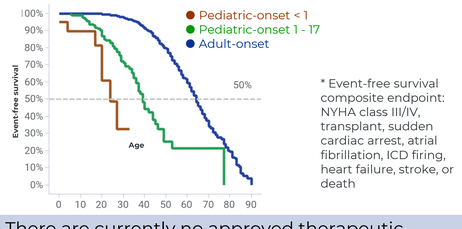
Pediatric cardiomyopathies are the leading cause of heart transplant and sudden cardiac arrest in children

- Approximately 50% of pediatric cardiomyopathy cases are hypertrophic cardiomyopathy (HCM) [1]
- Over 60% of HCM cases are due to known sarcomeric genetic mutations[2]
- ~20% of all HCM cases are due to *MYBPC3* gene mutations [2]

A natural history[3] study of >220 individuals under age 18 with *MYBPC3*-associated HCM showed that:

- Children are at greater risk for severe outcomes, particularly those with complex genotype
- Infants and children with more than one *MYBPC3* mutation develop markedly different disease with rapid progression and severe cardiac outcomes in first years of life

Time to event* since birth[4]



* Event-free survival composite endpoint: NYHA class III/IV, transplant, sudden cardiac arrest, atrial fibrillation, ICD firing, heart failure, stroke, or death

There are currently no approved therapeutic treatments for HCM in patients under age 18.

An investigational gene therapy is the subject of an ongoing clinical trial in adults with HCM due to *MYBPC3* variants and is available via expanded access on a case-by-case basis to pediatric patients.

Caregivers are critical stakeholders in the development of therapies for patients under 18. However, information on their awareness of gene therapy is limited.

- **50% of parents would enroll their child in a gene therapy trial for cardiomyopathy**
- **42% of parents uncertain about the decision to enroll; therefore, continued education is critical**
- **Only 20% of families recalled knowing their genetic mutation; AHA[5] guideline recommends universal genetic testing**
- **66% of parents assessed impact of cardiomyopathy to their child as moderate to severe**

METHODS

Sponsors developed a survey for caregivers of pediatric cardiomyopathy patients to quantify:

- perceived disease burden in affected children,
- motivators for complex treatment decisions,
- self-assessed understanding of gene therapy
- awareness / attitudes of AAV-based gene replacement therapy

Surveys were administered to caregivers by

- clinic staff where patients receive care using paper forms (primarily Amish population)
- patient advocacy group via email to their constituents

Survey collection was anonymous and responses were entered into a single database. Statistical analyses are descriptive in nature.

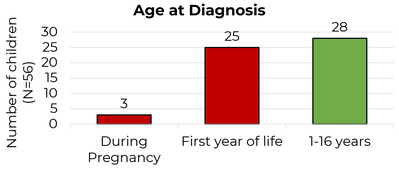
~ 2,100 caregivers of pediatric cardiomyopathy patients were contacted to participate

- Responses were collected from 52 individuals (7 via paper forms, 45 electronically) with 60 children with cardiomyopathy

AGE AT DIAGNOSIS

- 63% diagnosed after emergence of symptoms
- Only 20% recalled knowing their genetic mutation (*MYH7, MYBPC3, TTN* and *RBM20)*

Age at Diagnosis



RESULTS

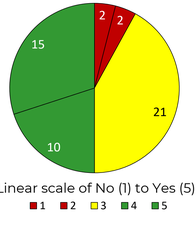
DISEASE BURDEN

- **66% assessed impact of cardiomyopathy to their child as moderate to severe**
- **Nearly 80% reported urgent access to treatments for their children as very important**
- **81% of children take medication for their condition**

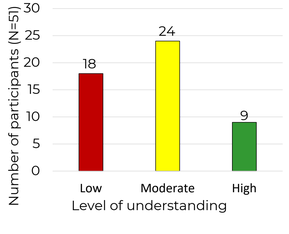
GENE THERAPY KNOWLEDGE / PARTICIPATION

- **Half of all respondents would enroll their child in a gene therapy trial, if made available**
- Most had heard of gene therapy online; but ranked their **children's physician as the preferred source for education, followed by advocacy groups**
- **Trust in the physician was ranked as the strongest factor in decision to enroll in any clinical trial**
- No association was observed between level of understanding & willingness to enroll their child in a gene therapy trial

Would you enroll your child in a trial for gene therapy? (N=50)

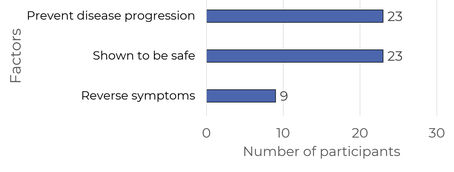


Self-assessed understanding of gene therapy (N=51)

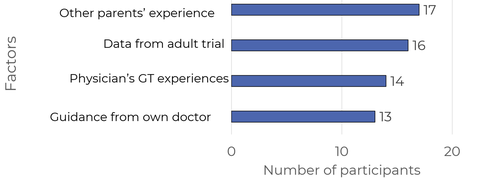


TOP DECISION MAKING FACTORS*

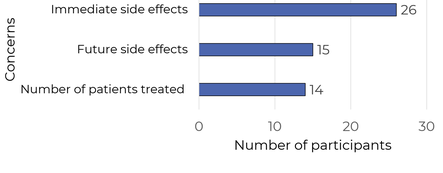
Top 3 factors ranked when choosing whether to enroll child(ren) in a gene therapy trial



Top 4 factors ranked as most useful in deciding to enroll child(ren) in a gene therapy (GT) trial



Top 3 concerns ranked for enrolling child(ren) in a gene therapy trial



*Some participants ranked more than 1 item as the most important factor / concern

CONCLUSION

Parents of children with cardiomyopathy recognize the disease severity and urgently want effective treatments to prevent disease progression and serious cardiac events, while focusing on safety of treatment options.

Enthusiasm for access to pediatric gene therapy trials is high. Education and recruitment will be most successful when physicians engage families in a culturally appropriate manner and provide:

- **connections to caregivers who have experience with gene therapy**
- **data from adult gene therapy trials**

Additional considerations included plain language explanations of trial safety monitoring and the availability of psychosocial support

Respondents are more likely to represent a more engaged subpopulation who is educated on new treatments. The broader population may have lower awareness of gene therapy and different concerns.

ACKNOWLEDGEMENTS

We are grateful for the participation of the parents and caregivers who completed this survey.

INFORMATION

For further information, please visit:

- DDC: https://www.ddcclinic.org/
- CCF: https://www.childrenscardiomyopathy.org/
- Tenaya: www.hcmstudies.com or email patient.advocacy@tenayathera.com

REFERENCES

[1]Lipshultz, et al., *NEJM* 2003
[2]Marston, et al., *Eur Heart J* 2021
[3]Brugada, et al., ESC 2025
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[5]Meisner, et al., HCMS 2024