BRAVE Program

Benefit - Risk Assessment Valuation & Evidence

Update on PPMD's
Patient Preference Research Program

Parent Project Muscular Dystrophy

JOIN THE FIGHT. END DUCHENNE.

What is patient preference information and why do we collect it?

Patient preference information is data that is systematically collected from patients and caregivers in order to understand how they think and feel about disease burden and impact, meaningful benefits, and potential risks of emerging treatments.

This information can inform:

- Regulators (FDA, EMA)
- Drug companies
- Researchers
- Healthcare professionals
- Payers (work in progress)
- Advocacy community (ourselves)

Stated Preference Methods

- Methods for collecting and analyzing data about what people think and feel
  - Special types of surveys that provide numbers to explain how important **‘good’** things are in comparison to **‘bad’** things.
  - How much **‘bad’** will people accept for the **‘good’**?

Gene Therapy Preference Study Update

Duchenne Gene Transfer Preference Study & Educational Initiative

Qualitative Interviews

Stated Preference Survey

Educational Initiative

Collaborator: RTI International (Holly Peay, PhD)

Stakeholder Advisory Board

Research Objective:
Explore preferences, risk tolerance and clinical trial decision making for emerging gene therapy technologies

Methods: Semi structured interviews, Threshold, BW Scaling

Qualitative (Interviews) Study

Qualitative Study (Interviews)

17 Parents, **6** Adults with Duchenne

Methods: Semi-structured interviews, Interviews were recorded, transcribed, coded, and analyzed using thematic analysis.

Anticipated benefits:

- Variable benefit based on time of initiation, with greater benefit at earlier stages of progression
- Potential impact on skeletal muscle, breathing, and heart function

Mode of administration:

- One-time IV administration

“Caveats” of gene therapy:

- Duration of benefits expected to be 8-10 years based on animal data But there is insufficient evidence to know for sure how long it would last. (uncertainty)
- Only one administration over the lifespan due to immune response
- Use causes ineligibility for most future clinical trials

Risks

- Main risk is massive immune response soon after gene therapy infusion
- Risk of death first described as 1 in 100; then described as 1 in 100,000

Qualitative Results – What we learned

Benefits

Respondents highly valued potential benefits to skeletal muscle, cardiac, and pulmonary function

- *Muscle*: **differently valued** for quality of life impacts **based on progression**
- *Cardiac/pulmonary*: greater relative importance with progression

Risks

More than half tolerant of 1% risk of death, with evidence of **increased risk tolerance in adults and at later stages**

Limitations (Caveats)

Most were concerned about limitations (possible one-time, time-limited benefit; loss of future trial eligibility)

- **Optimistic** about scientific advances
- Described a **'right time'** for use of gene therapy

Quantitative Gene Therapy Stated-Preference Study

Study aims 1 and 2

- **Aim 1:** What do participants **care most** and **least** about when **deciding** to join a gene therapy study

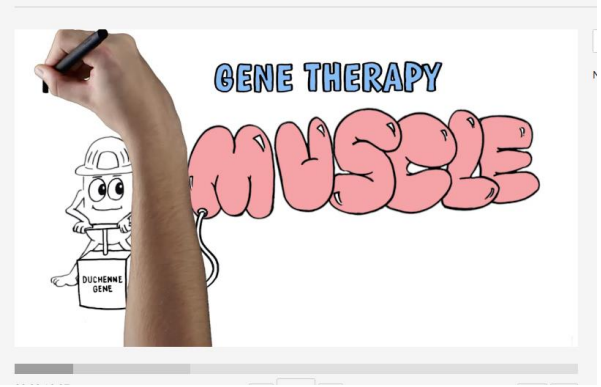
- **Aim 2:** How interested are participants in gene therapy clinical trial participation?

Eligible participants: Adults with Duchenne &
Duchenne parents/guardians (US only)

Method: Best-Worst scaling

Gene Therapy Story

- *We expect gene therapy to help people's muscles, lungs, and hearts work better for a longer amount of time.*
- *Gene therapy is not a cure for Duchenne.*
- *Very young children will probably have the most benefit, but gene therapy should be able to help almost everyone with Duchenne.*
- *Gene therapy may only be able to be used once in a person's entire life. This could change in the future with new research, but no one knows yet.*
- *Based on animal studies benefits could last for at least 10 years, but no one knows yet how long the benefits will last.*



Set up for experiment

Imagine {You are/Your child is} invited into an early phase clinical trial to determine whether gene therapy works, test the safety, and figure out how large a dose to give.

The following is a list of things that may be important if you were deciding whether to enroll in the trial. We will ask your opinion about things that you would care about ***the most*** *and* ***the least*** *about if you were making a decision about whether to join a trial.*

When we talk about ***data*** *in this table, we mean data collected from animal studies before the trial. We do not yet have data from humans with Duchenne. Collecting that data is the goal of the clinical trial.*

Best-Worst Scaling Experiment

Clinical Trial Attributes Presented

Chance of improved muscle function
Chance of improved heart function
Chance of improved lung function

Benefit lasts 10 years
Trial uses placebo group
Lowest dose may be too low for benefit
Not eligible for future trials
No later use of gene therapies or gene editing (CRISPR)

Two muscle biopsies
Chance of long hospitalization
Chance of death

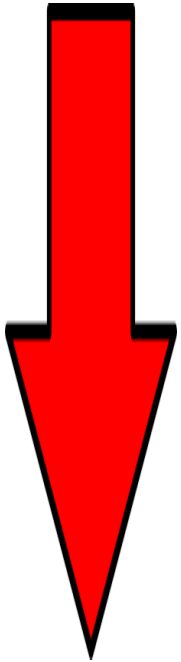
Which would you **care about the most** when deciding whether to join the trial?
Which would you **care about the least**?

I care about this the most		I care about this the least
○	Chance of improved muscle function	○
●	Not eligible for future trials	○
○	Chance of death (low risk)	○
○	Chance of long hospitalization	○
○	Chance of improved lung function	●

Participants answered 11 lists like this with different combinations

Results of Experiment (pooled results)

Cared about most

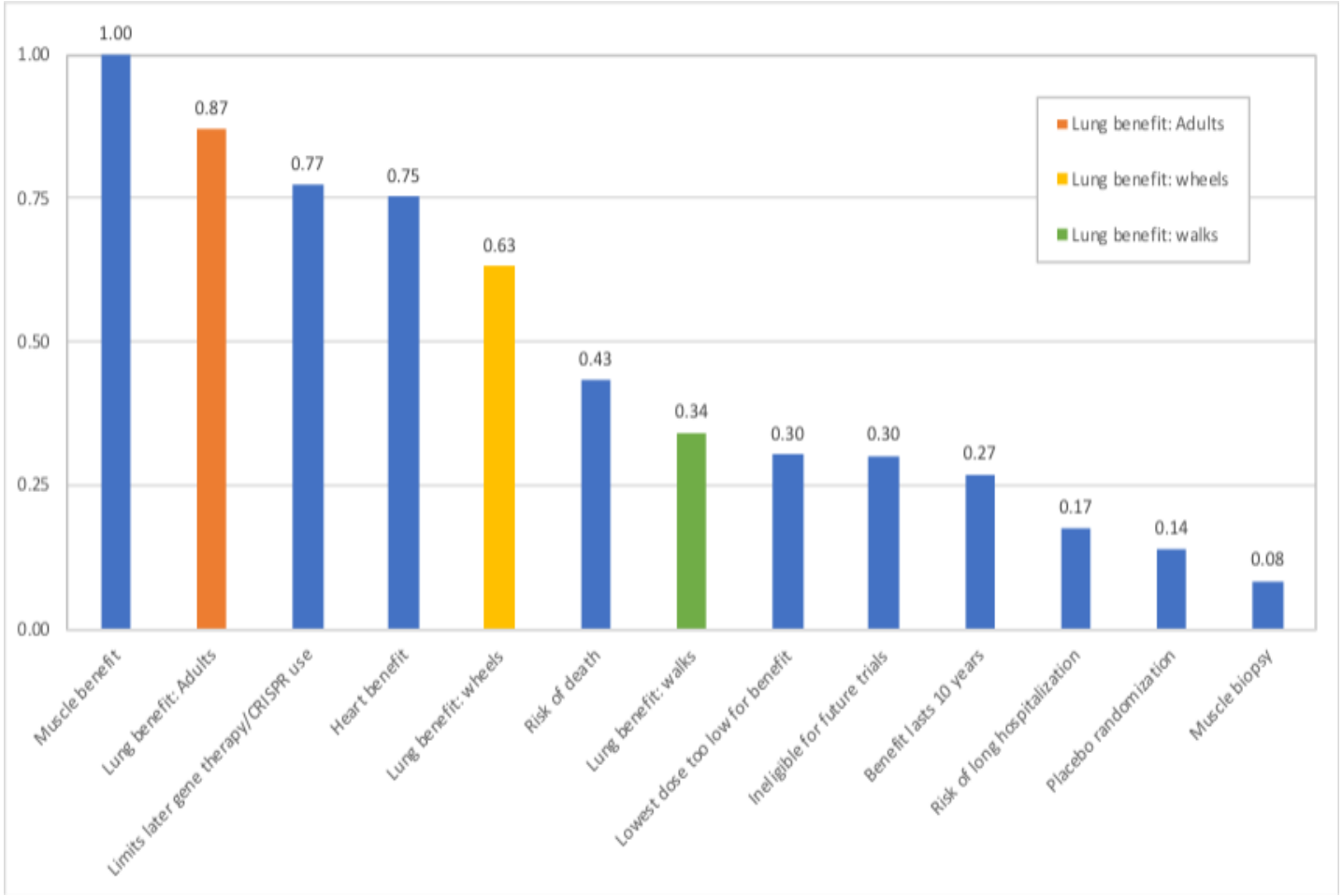


Cared about least

Order attribute importance
Chance of improved muscle function
Chance of improved heart function
Limits later use of gene therapies or CRISPR
Chance of improved lung function
Chance of death (low risk)
Not eligible for future trials
Lowest dose may be too low for benefit
Benefit lasts about 10 years
Chance of long hospitalization
Chance of being in placebo group
Two muscle biopsies required

N=
243 caregivers
34 adults

Priority Differences – Lung Benefit



Adults

Non ambulatory

Ambulatory

We learned what's important to clinical trial decision making, but do people want to be able to make the decision?

1. What if there was a 3-hour information and screening visit at your regular neuromuscular clinic? The screening requires a physical exam and a blood draw.

How likely is it that you would go to this screening visit, if the visit was required to be considered for trial participation?

- Very likely
- Somewhat likely
- Not very likely
- Not at all likely

2. What if you had to drive 8 hours to the trial site and spend two nights so you could attend a full-day information and screening visit? The screening would require a physical exam, muscle function testing, and a blood draw. Assume that your expenses would be covered.

How likely is it that you would go to this screening visit, if the visit was required to be considered for trial participation?

- Very likely
- Somewhat likely
- Not very likely
- Not at all likely

Scenario 1 (3 hour screening visit)

Parents

Category	(%)	Response Count
Very likely	84.6	208
Somewhat likely	13	32
Not very likely	2	5
Not at all likely	0.4	1

Adults with Duchenne

Category	**(%)**	**Response Count**
Very likely	73.3	22
Somewhat likely	26.7	8
Not very likely	--	0
Not at all likely	--	0

The vast majority were very likely to screen

Scenario 2 (8 hour drive, 2 nights)

Parents

Response	%	Count
Very likely	69.5	171
Somewhat likely	20.3	50
Not very likely	6.9	17
Not at all likely	3.3	8

Adults with Duchenne

Response	%	Count
Very likely	43.3	13
Somewhat likely	30	9
Not very likely	20	6
Not at all likely	6.7	2

Most were somewhat or very likely to screen

Best-Worst Experiment – What we learned

- Possible benefits are driving decision making more than possible risks

- While benefits are important motivators for clinical trial participation, we see importance of maintaining later access to therapies
  -We see this in the gene therapy/CRISPR item and also the low dose item

- Procedural/protocol items that we have previously found to be important (biopsies and chance for placebo randomization) were the least important to clinical trial decision making for gene therapy

But do people actually want to join these trials?

- The majority are very or somewhat likely to attend a screening visit,
  even if it requires a long drive, 2 night stay, blood draws

Thank you SAB and sponsors

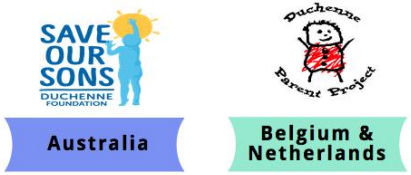
Stakeholder Advisory Board
Colin Rensch – Adult
Amy Martin - Caregiver
Katherine Beaverson – Pfizer
Sharon Hesterlee – Pfizer
Annie Ganot – Solid
Carl Morris – Solid
Dr. Eddie Smith – Duke

PPMD Team
Annie Kennedy
Pat Furlong
Abby Bronson

Upcoming opportunity to participate in a new study

Treatment Preferences for Duchenne: A global study (2018)

Treatment Preferences for Duchenne: A global study (2018)



Collaborator: The Ohio State University
(Dr. John Bridges and Nonie Crossnohere)

Aims:

- Conduct a multi-country study to **quantify treatment preferences in DMD**
- Explore global **research and advocacy unmet needs**
- Develop a survey instrument that can be **replicated internationally**
- Facilitate the **dissemination and implementation** of the study finding

Recruitment goal: 60 each country
20 patients/40 caregivers (360 total)

Method: Discreet Choice Experiment
Wave 1 potential for Wave 2

Funding support

Thank you!