Patient engagement in clinical trial design for rare neuromuscular disorders: impact on the DELIVER and ACHIEVE clinical trials

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OUR OBJECTIVE

Engaging individuals living with disease in drug development and regulatory processes leads to more thoughtful and sensitive trial designs, drives more informative and meaningful outcomes from clinical studies, and builds trust between the public, government, and industry stakeholders. This engagement is especially important in the case of rare diseases, where affected individuals and their families face many difficulties getting information, treatment, and support.

Dyne Therapeutics is developing therapies for people with genetically-driven muscle diseases. During the development of potential treatments for Duchenne muscular dystrophy (DMD) and myotonic dystrophy type 1 (DM1), Dyne sought the opinions of individuals living with these diseases to inform its clinical trial design and to decrease the difficulties that participants and families might experience participating in them.

WHAT WE DID TO ACCOMPLISH OUR OBJECTIVE

Dyne internal planning meetings to determine key objectives and questions and create materials to facilitate dialogues on participant and caregiver preferences, clinical development plans, and clinical trials

Community Advisory Boards (CAB)*

Participants are trained Duchenne advocacy leaders, as well as caregivers, from 12 countries

Patient and Care Partner Advisory Workshops

Participants (n = 8 for DMD and n = 18 for DM1) were identified by Dyne based on relationships with individuals living with disease and/or care partners experienced with burden of disease

Input regarding considerations for selecting clinical trials and importance of and burden associated with stie locations and trial design elements; accessibility of content in informed consent forms; optimizing trial participant support

Summary and interpretation

Implementation

DISCUSSION TOPICS

Considerations for enrollment in clinical trials | **Clinical trial protocol elements** | **Study visits**

WHAT DID WE LEARN?

Considerations for enrollment in clinical trials

- The DMD and DM1 communities are willing to participate in trials because of significant need for therapies
- Participants were supportive of efforts to reduce travel burden
- Shorter placebo duration and asymmetrical trial design (i.e., more participants on active drug vs. placebo) is preferable and also supported by the CAB
- Understanding of the investigational therapy's mechanism of action and any prior data
- Support in enrollment decision-making from medical care provider, advocacy communities, other families living with the disease

Clinical trial protocol elements

- Care providers valued functional assessments that measure improvements in the ability to perform an activity and prefer video assessments
- Workshop participants helped Dyne identify appropriate measures to mitigate anxiety that younger participants may experience with clinical assessments such as MRI, biopsies, and blood draws
- Workshop participant were supportive of endpoints related to activities of daily living as illustrative and useful in assessing the impact of an investigational therapeutic
- The DMD CAB was supportive of defining a sequential order of assessments for all outcome measures for consistency and Dyne's intentions for modifying endpoint and outcome measures

WHAT DID WE LEARN? (*CONT'D*)

Study visits

Advisory participants recommended that Dyne:

- Provide a detailed itinerary and schedule to ensure a smooth clinic visit
- Build flexibility in the timing of assessments to help with individual participant needs
- Minimize travel burden through financial and organizational support (critically important): have travel and patient support programs that provide fit-for-purpose, long-distance and cross-border travel, meals, housing, insurance, and related support programs
- Provide age-appropriate communication to engage participants
- Communicate trial status information through research coordinators

KEY THEMES

Considerations for trial selection, protocol elements, study visits

Ability to participate
- Develop a comprehensive concierge program to minimize travel, administrative and financial burden on participants and care providers

Perception of benefit and risks
- Placebo ratio and duration
- Reduce the invasiveness of procedures and tests
- Provide an upfront rationale for tests

Clear communication from Sponsor
- Engage participants directly in an age-appropriate way
- Develop a clear communication plan for updates and share upfront

Flexibility
- Provide options for timing and location of assessments based on participant and care provider needs
- Consider the unique needs of participants

Information from trusted sources
- Engage and educate patient advocacy organizations and health care providers

Enrollment
- Enroll diverse patient groups

WHAT WE DID BASED ON LEARNINGS

- **Refined clinical trial inclusion/exclusion criteria and clinic visit design based on perceptions of benefits and risks of trial participation;**
- **Developed travel service program to address the burden of clinical trial travel and enable long-distance and cross-border participation for increased access to the clinical trial;**
- **Planned for home visits when feasible; ensuring adequate rest before clinic visit initiation and between assessments;**
- **Developed and implemented a transparent and consistent communications plan for trial participants and community members;**
- **Assessed and adjusted procedures to provide maximum participant comfort and lower anxiety, particularly with younger participants, including age-appropriate communication content.**

Thank you to our communities!

These engagement activities provide valuable insights into the participant experience and have helped Dyne initiate clinical trials that better meet the needs of affected community members.

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DISCLOSURE INFORMATION

MW and AD are employees of and may hold stocks in Dyne Therapeutics, Inc.