Rare Disease Clinical Development: The Crucial Need for Patient and Parent Involvement

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Rare Disease Clinical Trials

February 28, 2017 was the tenth observance of Rare Disease Day worldwide. Rare Disease Day awareness events took place in over 80 countries through the collaboration of countless foundations and patient advocacy organizations. This year’s theme was research that inspires and empowers the rare disease community, as captured in the slogan, “With research, possibilities are limitless.”

While there is no universal definition for the term “rare disease,” in the United States, a condition is considered “rare” if it affects fewer than 200,000 persons combined in a particular rare disease group. There are approximately 7,000 different types of rare diseases and disorders, with more being discovered each day. Over 30 million people in the United States are living with rare diseases—50% of whom are children.

The people and families affected by rare diseases often feel isolated and helpless in the fight against their condition that is uncommon, complex, and often misunderstood by the people in their life, including healthcare providers in some cases. To cope with the lack of traditional resources, patients and their families become their own experts, tirelessly researching online and connecting with other rare families through social media communities and advocacy groups. This drive to learn and understand, coupled with their personal experiences living with a rare disease, makes their collaboration with researchers and industry experts especially productive. This partnership is essential to the success of rare disease clinical development programs.

Patient and Parent Participation in Clinical Trials

A family’s involvement in a clinical trial often calls for great sacrifice. In many cases, their home is not near a clinical site, which makes attending regular study visits a logistical challenge. Time away from work and travel costs can create financial strain. Then there is the discomfort and anxiety a patient experiences during regular visits and tests, and the burden of questionnaires and/or journals required throughout the trial. In order to be successful, a trial must be developed in a way that minimizes these hardships. Ultimately, the significant barriers families and caregivers may face should always be a key focus in tailoring study designs and expectations.

There are a number of steps that can be taken to help alleviate the significant physical, emotional, and financial impact on patients and families. They include utilizing best practices for recruiting and retaining participants, such as letting the prevalence of a rare disease in a geographic area drive patient recruitment and site activation, and increasing patient home support. There should also be a clearly-enunciated emphasis on identifying and collaborating on specific services or products to improve quality of life outside of the investigational environment. In addition, sponsors and CROs must collaborate with the patient community throughout a trial to learn from the feedback as the study progresses.

Incorporating the patient’s voice and needs from the start through a respectful and meaningful relationship must go beyond a research focus. A patient-centric approach of listening, understanding, adapting trial requirements, and giving back to the rare disease community can help ensure that there are adequate levels of participation to make the study as successful as possible. Collaboration and trust among families and disease-specific foundations, as well as support and advocacy groups, is essential.

What can empower patients and families is the opportunity to provide input on sometimes marginal or unconventional outcomes or endpoints that directly affect quality of life. It is powerful for patients to be involved in the study design and meaningful outcome decision-making processes, reaffirming that the trial is designed for them. Adapting to more customized research methodologies not only can increase participation, but also maximize retention, adherence, and data quality.
PROMETRIKA Interview with Ovid Therapeutics

Ovid Therapeutics is a young company but one with significant experience working with people battling rare diseases. It is a key part of the company’s Vision and Mission to first and foremost consider the impact on patients and families in every phase of the design and execution of studies. It approaches rare disease development programs by first taking the time to understand and build relationships with the patient communities that it serves and using that information, along with strong relationships with patients and families, to develop transformative therapies.

Recently, PROMETRIKA’s Head of Clinical Operations & Drug Safety, LuAnn Sabounijan, connected with Vice President of Global Market Access for Ovid Therapeutics, Raquel Cabo, to discuss how that approach has helped them recruit and connect with patients and families for their Angelman syndrome program. Raquel’s answers provide tremendous insight on the challenges and rewards of patient involvement in rare disease research.

L. Sabounijan: As a seasoned veteran in rare disease clinical trials with a passion for working with patients at all stages of product development, can you share with us your history of collaboration with the Angelman syndrome patient/parent groups at Ovid?

R. Cabo: Ovid Therapeutics’ philosophy is that we are involved with the Angelman syndrome community for the long haul. While we are working to create innovative treatments, we strive to establish meaningful partnerships with patients and families that go beyond developing the medicine. Connecting with caregivers is critical in our studies as the patients we work with are non-verbal.

To ensure we develop the right medicine and that it is accessible, we are working closely not only with the patient and their family, but also with related foundations and organizations that represent the broader rare disease community. It takes many united voices to get regulatory and market access approval. When a medicine is on the market, ongoing feedback will be important as well.

Our goal is not just to produce a product. We strive to create a collaboration in which patients and families know they are leaving their mark on a study that will affect others battling their rare disease. We want them to feel engaged and empowered, and to know that the trial is “for them and by them” so to speak.

In an example of engaging and empowering the people we work with, we held an online competition to design the logo for the STARS clinical trial program in Angelman syndrome. Approximately 50 logo designs were submitted from which we narrowed the field down to three finalists, and then asked the community to vote. The winner by 300 votes was a logo designed by the mother of an individual with Angelman syndrome who was inspired by the strength and bravery of her child and shows a figure reaching for the stars. We now use it on all patient materials related to the study.

Another initiative we’ve sponsored is a “Make-a-thon” that encouraged industrial designers and engineers to collaborate on ideas to develop products for individuals with disabilities. In the Angelman Syndrome Make-a-thon the goal was to help a family save money on customized and expensive retrofitting. One of the results is a grid that can be placed over an iPad to frame icons so patients with poor fine motor skills can avoid touching two icons at once. The design of the accessory considered very specific details like the fact that a matte finish and sturdy materials would be much better for the patients with sensory and coordination challenges. Similar items sell online for $70 and are often made of more breakable materials, but the collaboration of the Make-a-thon allowed Ovid and its partners to manufacture their grids for a fraction of the price. This project really showcased the fact that there are creative and compassionate people outside the clinical space who are eager to help. Thanks to the teamwork and collaboration of all involved; it was a highly successful undertaking.

L. Sabounijan: In my experience working with patients and families at clinical research centers, I have seen the value of securing patient and family involvement in rare disease clinical trials. At a high level, can you share the key differences in outcomes with early patient/parent involvement in clinical development programs vs. non-involvement?
R. Cabo: Our development program in Angelman syndrome is our first sponsored program, and from the very beginning we have placed a huge importance on early patient and parent involvement. Parents are the experts when it comes to their children and what change would be most meaningful. Their input has helped us understand what aspects of the syndrome impact their child’s life, and their life, the most. Speaking with parents has helped us better understand the unmet needs given the current treatment pathway and the natural history of the syndrome. As is the case with many orphan conditions, there are limited established outcome assessments, working with parents and the foundations has helped us prioritize outcome assessments that are most relevant and feasible. Their input based on their experience, as well as what they’ve heard from other parents, has provided valuable insight.

When patients and parents are involved, it’s a much different story. You are able to co-create and navigate uncharted territory together.

L. Sabounijan: What are some best practices you have seen to involve parents/caregivers of children and young adults with rare developmental disabilities in clinical development planning?

R. Cabo: From our perspective, the key is transparency, communication, and collaboration. You need to have an efficient mechanism for collecting feedback at all stages of the development program. It’s also critical to build trust and mutually beneficial relationships with the community and the foundations. It is also really helpful to share insights with other stakeholders, such as payers, clinicians, and regulators.

In one example, one insight that was truly eye opening was one mother’s explanation that any fine motor improvement which would enable her daughter, who communicates with hand signals, to go from two to three signals in her “vocabulary” would be truly life-changing for the family. This perspective helps to define what impactful “improvement” really looks like to a patient, especially in a rare indication without widely established or recognized efficacy endpoints.

We’ve been fortunate to have family input in many areas of our studies — from mapping out the patient journey to helping define inclusion/exclusion criteria and more. Their feedback on what makes it easier or more difficult for a family to participate is also key. We even ask for their assistance in reviewing brochures and other literature to ensure that it makes sense to them and uses the right wording and imagery. Patient and parent assistance can also be invaluable for clinicians working on natural history studies and registries.

L. Sabounijan: What do you see as some potential challenges of involving parents in decisions about clinical trial planning? What suggestions do you have for dealing with these challenges?

R. Cabo: While each family is unique, most are very eager to give input and feedback. Providing them with education on what a clinical trial is and how it will progress is crucial as you get started. It is important to explain that while you do all you can to accommodate the patient’s unique needs, the protocol does have to be standardized to a degree. They should also understand how their time and effort will benefit the patient and the broader community, and that their feedback is necessary for the study to achieve its goal.

We hosted a series of webinars designed to answer family’s questions and found it to be an effective way to disseminate information about who can participate, how to enroll, and other aspects of the study. It’s also a good idea to talk with foundation leaders and ask if you can record those interactions and make them available to families on the internet.
Parting Thoughts

Ultimately, as Ovid Therapeutics and PROMETRIKA understand, rare disease development programs must be built on a foundation of deep respect and appreciation for all that patients and families are doing to help improve the quality of life of others with the disease. The best way to demonstrate that gratitude is to be as accommodating as possible in the study requirements, to provide exceptional support to patients and families, and to give back to the community whenever and wherever possible.

It has been said that too often “research is performed on patients, not with patients.”¹ Especially in the case of rare diseases, an adaptable and collaborative approach to clinical trials is essential. As patient advocacy groups contend, patients and families should have a greater say in the decisions that affect them—an idea summed up in the phrase “nothing about me without me.”²

From initial planning and design through all phases of clinical trial management, there are several challenges unique to patient participation in rare disease trials. By involving patients and parents more extensively at all stages of a study and by learning more from their personal experiences and their hope for changes that matter, we can produce a broader, deeper, and more complete body of knowledge. Patient-centric rare disease clinical trials have greater potential to accelerate meaningful treatment and prevention breakthroughs that help patients and their families lead longer, healthier, and happier lives.

1. Thornton S. Beyond rhetoric: we need a strategy for patient involvement in the health service. BMJ. 2014;348:g4072. [PubMed]