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Trials and tribulations: Rare disease research and the shifting care paradigm

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As aging populations grow and treatment paradigms shift, the industry must prepare for greater challenges in the rare disease clinical trial space, says CRO executive.

The National Institutes of Health (NIH), the US Food and Drug Administration (FDA) and National Organization for Rare Disorders (NORD) define a rare disease as affecting fewer than 200,000 people in the US. Currently, approximately 7,000 rare diseases listed by the NIH.

In the European Union, a disease is defined as rare when it affects fewer than 1 in 2,000 people.

To further discuss the challenges and future of clinical trials in rare diseases, we sat down with Lisa Dilworth, vice president of rare and orphan diseases at the contract research organization (CRO) Synteract.

For rare and orphan diseases – what are the biggest challenges?

Rare disease trials present multiple challenges, some more obvious than others. Thanks to novel solutions like

travel concierge services, harnessing data assets and telemedicine, we've been able to make great strides with some of the straightforward issues like geographic barriers, finding the right sites with access to the patient population and reducing the burden of clinical trial participation.

But, there are more subtle challenges still requiring expertise and attention, many of which have roots in the lack of understanding of the natural history of the disease itself.

Without robust natural history data and longitudinal disease modeling, we struggle to identify clinically meaningful outcomes for clinical trials. Furthermore, many rare diseases still lack a global consensus on the standard of care.

For example, depending on the region where a patient lives, they may be using different medications off-label, different steroid doses, or other supportive care. These things can introduce a high level of variability in clinical trial datasets, and we struggle to identify homogenous populations of these rare disorders.

Currently, we are seeing a renewed focus on collaboration between industry and patients to initiate natural history studies and patient registries.

> ***The value of sharing data to accelerate, inform and improve protocols can no longer be denied.***

The patient voice will continue to be heard, and advocates will continue their efforts to prepare the community for clinical trials. Advocates are also helping to push for standard of care consensus guidelines on a global scale, which will improve outcomes for patients.

Looking forward five years, do you expect these challenges to change or evolve?

Looking forward five years, we will see new challenges arise as the paradigm for treating many rare diseases shifts. Thanks to medical advances and access to new treatments, we are now seeing rare disease patients living into adulthood with diseases that were once lethal in childhood.

When it comes to treating these diseases, often pediatricians, currently, are the experts. But, as the next generation of patients grows older, they will need to transition from a specialty children's hospital/pediatrician to adult care. This may present challenges as the children's hospitals have access to multidisciplinary care centers that are not as common in adult care settings.

The collaborative and comprehensive care offered to rare disease patients suffering from a multitude of symptoms requires careful coordination across various departments at a site (e.g. neurologist, geneticist,

respiratory therapist, physical therapist, dietician).

Navigating this space will present challenges for young adults suffering from rare diseases as well as their extended care team.

As researchers, we will need to support this transition of care, and I expect to see adult physicians becoming principal investigators on trials that were once run solely by pediatricians.

How have new technologies and scientific advances helped improve potential clinical trial patient selection?

Many rare diseases are genetic in nature, making a profound impact on entire generations of families. The growing acceptance of, and access to, genetic testing means the potential for earlier intervention for these patients.

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This is of incredible importance because numerous investigational treatments show optimal benefit if initiated pre-symptomatically – thus delaying symptoms and preserving function.

For these trials, newborn genetic screening is powering clinical trial participation and, therefore, potentially enabling access to life-altering treatment.

How has the importance of including payers and others in the conversation changed, as some of the drugs for rare diseases can cost up to hundreds of thousands of dollars?

A clinical trial participant once told me *"You may know my disease, but I know my illness."* As researchers, it's imperative that we remember our study subjects are more than just data points.

In order to truly understand the disease burden, we need to look at things like impairment in activities of daily living, ability to maintain independence, quality of life, financial burden of expensive equipment, impacts on family income, housing modifications, missed school/work.

This holistic analysis of substantial cost burden to payers, patients, and society as a whole can help inform decisions regarding reimbursement. Too often, we are seeing rare disease treatments approved by regulators and, subsequently, patients denied access due to the cost.

Industry and patients need to continue proactive efforts to analyze the cost impact of leaving these diseases untreated to better understand the value of new drugs coming to market.

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