Health Informatics Data: Connecting Patients to Investigators

Why are Clinical Trials in Rare Diseases Challenging Today?
From the perspective of a clinical trial, a rare disease suggests the available patient and site population is quite small and distributed diffusely. Likewise, any challenge related to study logistics, competitive landscape or patient recruitment is magnified as compared to trials in other indications. The paucity of sites and patients is an ongoing theme in rare disease trials beyond simply locating sites to participate in a trial. There may also be local patient treatment differences, particularly in children, that vary by region and country, which can further complicate any feasibility effort.

The current regulatory landscape in rare disease research is another area to consider. Major regulatory agencies encourage the development of treatments for patients with rare diseases, which, while accomplishing that larger goal, can also result in greater research competition for populations being studied.

Site and Patient Identification in Rare Disease Clinical Trials: Every Patient Matters

When planning rare disease trials, one must first understand the patients, then use this knowledge as a roadmap to identify and characterise the sites and countries where these patients live. The mechanisms by which this can be done are many, but the central theme is the same: when every patient matters, knowing the right investigators is essential. Collectively, these objectives have driven the development of physician and patient networks, consortia, and advocacy groups focused on individual diseases, as well as on classifications of disease, which are key collaborators in defining the pathway for success in rare disease clinical trials. Such networks are often critical partners in the conduct of rare disease trials, and early engagement with them can carry substantial benefits with regard to study conduct. It cannot be overstated that finding patients, sites and countries are intertwined and in the majority of cases, separating each pillar from the other can potentially jeopardise study delivery.

Operational efficiency becomes more difficult to balance with the realities of enrolment and feasibility in rare disease trials. This is because there are generally more sites required to achieve enrolment in a reasonable timeframe, particularly in larger trials. Objectively, this is inefficient from a trial delivery perspective but must be accepted as an outcome of feasibility. But what ultimately drives the development of a rare disease trial delivery strategy? The answer is multi-dimensional, considering the treatment landscape, site feedback, standards of care, competitive landscape, individual population's availability for a clinical trial, and most importantly, investigator and patient/family engagement in the clinical trial enrolment process.

Lastly, the advent of health informatics data has shown the potential to revolutionise the recruitment of trial participants in general, but in particular for rare diseases. There are a number of organisations accessing de-identified patient records, lab results, medical claims and prescription data, which have potential to generate site and patient efficiencies by removing uncertainty from the site and patient availability equation. However, many of the sources are largely unproven in the clinical trial space, and they are localised to the United States for the time being.

Future Challenges in Rare Disease Site Selection and Patient Recruitment

Moving deeper into the 21st century and beyond, site identification in rare disease clinical trials is likely to increase in complexity for several reasons, including:

- The rate of innovation in personalised medicine and novel techniques such as gene therapy, and certainly soon, CRISPR will further warrant a highly-specialised site identification strategy that extends beyond the simple matching of potential patients to potential sites.
- Assuming the regulatory landscape remains consistent, more developers will enter the rare disease space – not only addressing conditions without current treatment, but also to improve upon existing therapies in indications.

Further specificity in cancer and other indications to identify specific gene mutations and expression patterns effectively create hyper-personalised targets for new treatments. In this way, many cancers will become rare diseases, and the identification of these patients in clinical studies may precede clinical practice patterns because of the early development of new diagnostic modalities.

Ultimately, identifying patients and sites with appropriate patient access is likely to undergo a paradigm shift in order to accommodate these innovations. Although the future may see additional complexities, there are undoubtedly going to be even more opportunities to utilise health informatics data connecting patients to investigators. The path forward to success is bright, and one must embrace this innovation and understand that while the potential exists, challenges will accompany our collective journey to enhance our ability to effectively plan and recruit rare disease clinical trials.

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