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THE CRITICAL ROLE REGISTRIES PLAY IN RARE DISEASES SUCH AS CELLULAR AND GENE THERAPY

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Rare diseases with single gene mutations are now showing great potential for treatment and, in some cases, even the potential for a cure. Certain cancers are also being treated using these techniques. New products are rapidly being introduced to the marketplace, and the number of early stage assets are expanding rapidly. Several different treatment approaches are used, but all strategies aim to target the correction of a mutated or missing gene.

A well-established strategy employs a genetically engineered virus that is directly infused into the patient. The virus targets and infects a specific tissue where its genetic cargo is released and incorporated into the targeted tissue. A variety of different viruses have been used, such as adenovirus, adeno associated virus, lentivirus, and Maloney leukemia virus. Rare diseases currently being treated include Hemophilia, Duchenne Muscular Dystrophy, Pompe Disease, Fabry disease, thalassemia, and adenosine deaminase severe combined immunodeficiency (ADA SCID). Areas that are still under exploration with viral mediated therapies include accurate tissue targeting and duration of effect – often leading to pre- and post-marketing safety assessments and regulatory required commitments as they launch and commercialize into the real-world use in the market.

Genetic engineering of a patient's stem cells, so called gene and cell therapy, is another alternative to viral based therapies. In this method, the patient's stem cells are apheresed, transferred to the certified manufacturing site, transfected with the normal gene-containing virus, expanded, and then returned to an appropriate certified site of instillation and reinfused into the patient. While effective, additional complexities with this method include the time required to obtain the engineered stem cells, the need for conditioning chemotherapy, and of course the expense. The advantage, however, is the potential for an enduring response from the engineered stem cells. Off-the-shelf donor stem cells (allo stem cells) are being developed that could potentially impact the cycle time from drug ordering through instillation.

Availability of manufacturing facilities, costs, regulatory guidelines, timely availability of the product, and proven efficacy are common considerations to both of the aforementioned methods. Importantly, based on current regulatory guidance, "Long Term Follow-up After Administration of Human Gene Therapy Products" (U.S. Food and Drug Administration, 2018), all patients will require long-term safety monitoring through establishment of registries.

Emerging (gene) therapies raise numerous questions regarding the impact on standard of care. This includes items such as early identification of probable responders, disease specific prognostic factors, potential treatment outcomes, therapeutic response, and methods to integrating conventional and evolving therapies. Long-term patient follow-up with the patient population offers powerful insight to cost and care implications of treating all patients, both pre-symptomatic and symptomatic.

Data collected through registries play a critical role in defining disease modifying gene therapies and redefine the progression and treatment of natural diseases. It is critical to follow the evolution of rare diseases and measure the impact therapies have on patients, caregivers, and the overall healthcare system. In order to obtain and assess these long-term safety and effectiveness data, impact from patients receiving both standard, conventional drug therapies, and new emerging therapies needs to be collected and analyzed.

There are expected challenges with global disease registries. Registries normally collect data following a patient's "standard of care." There are no additional requirements beyond the standard of care, and each patient enrolled in a long-term global registry is followed by their participating physician, with no additional burden and no additional testing.

In many countries outside of the US, the registry must be designed as a strictly observational study. This may limit the type of data collected, as well as the continuity of assessments for developmental and functional milestones, especially for the more severely affected patients.

Overall, a well-designed registry will follow patients with a rare disease tailored to the assessment. The safety and effectiveness of new and evolving treatments can transform the future care of patients at varying stages of disease progression, and as importantly, analyze healthcare resource utilization and caregiver burden.

For more information on immunotherapy and registries, contact ubc.com/contact