The Life Raft Group Research Model

Real World Evidence in Action

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Although targeted medicine has brought about immense progress in cancer treatment, there are still enormous challenges regarding patient survival. Randomized clinical trials (RCTs) driven by lab-based research have been the gold standard for identifying new treatments. However, these traditional approaches often fail to take into consideration the patient perspective, especially in side effects management, and the vital role it plays in adherence and successful treatment outcomes.

With the increasing application of genomic profiling, the complexity of cancer diagnosis now dictates an unprecedented need for new drug development to target newly identified cancer subsets and to overcome resistance to existing treatments. As more mutations are discovered, most cancers will become "rare cancers". The better the science, more types and subtypes of cancers will be identified, creating smaller patient pools for clinical trials.

Increasingly, real world data and resultant real world evidence are being utilized to enhance and complement traditional research. The volume of real world data available in health care settings is growing exponentially.

Unfortunately, big data does not necessarily mean smart data. Smart data is often more timely, accurate, and takes into consideration the patient perspective which offers enormous potential in identifying trends that could lead to life-saving interventions and help improve the quality of life for cancer patients.

Real World Data

"Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources." -FDA

Real World Evidence

"The clinical evidence regarding the usage and potential benefits or risks of a medical product derived from the analysis of real world data (RWD)." -FDA

Real world evidence utilizes observational data to determine the perceived benefit of treatments to increase survival and improve quality of life for cancer patients.

Since our inception 18 years ago, we have generated real world data and real world evidence. By identifying not only interventions that are effective, but also those that are not, we can provide life-saving information in an accurate and timely manner, enhancing survival and quality of life for our GIST patient community. Our research model, Patient-Powered Science for Life, is a comprehensive approach that complements traditional research with real world evidence supported by data from our proprietary platforms, which include the GIST Patient Registry, GIST Collaborative Tissue Bank, and SideEQ, our side effects management tool.

Rare Cancer Research Landscape

The development of imatinib, the first targeted oral cancer treatment, transformed cancer care and set the stage for the growing reliance on genomic sequencing to develop targeted treatments. This means that most cancers will now be rare cancers defined by smaller subsets. As more oral cancer treatments become available, patients are often being treated away from major, academic, medical specialty centers. With oral treatments being taken 365 days a year, often indeterminately, adherence rates can be compromised.

Cancer research has traditionally relied upon randomized clinical trials (RCTs) and lab-based research to identify and bring life-saving treatments to market. Although this approach has resulted in breakthrough treatments, including the development of the first targeted oral chemotherapies, there are severe limitations to this process:

1. Drugs are expensive to bring to market. According to a 2017 study[2], the cost to develop a cancer drug from lab discovery through clinical trials, and finally, approval from the FDA, on average can cost $648 million to $1.3 billion[3] and can take up to take up to 12 years.[4]
2. There is a time lag between discovery of the efficacy and effectiveness of a drug, and the sharing of data with those impacted by the information.
3. Patient survival is not the primary objective and patients are not the primary stakeholders.
4. As combination therapies become more common with the utilization of genomic sequencing for targeted treatments, several pharmaceutical companies may need to be involved in the process rather than just one.
5. The process is driven by pharma. Although the desire to develop new treatments is generally altruistic, it is also driven by the business goals of creating revenue.
6. Physicians often have run out of options when their patients have developed resistance to the approved treatments.
7. It is just as important to learn what is ineffective as what is effective.
8. Post-approval studies are infrequent.

The Value of Real World Data and Real World Evidence

Valued as the yardstick by which clinical data is created, traditional randomized clinical trials take place in highly controlled settings with a small subset of the patient population. The subjects in such studies are generally healthier than patients with similar disease in a real world setting,

due to the rigorous screening processes for such trials. Although this assures the validity of comparative effectiveness research, it may not take into account data about outcomes from a broader set of patients in a real world setting. It is valuable for medical professionals, pharma companies, and payers to understand how treatments perform outside a trial setting.

With the volume of data now available both in clinical and non-clinical settings, the ability to gather evidence that can lead to life-saving treatments is more tangible. Real world data highlighting the patient perspective is an increasing necessity. In response to the 21st Century Cures Act, there is "additional focus on these types of data to support regulatory decision making." (FDA: Real World Evidence)[1]

Real world evidence utilizes observational data to determine the perceived benefit of treatments with the priority of increasing survival and improving quality of life. With the increasing demand for this type of data, especially in the world of rare diseases, rich sources of real world data are key to gathering empirical evidence to identify effective clinical interventions.

What are the sources of this real world data? Medical records, both electronic medical records and clinician records, have been the traditional, primary sources. There are multiple problems with this type of data. Systems are frequently not interoperable, and there are inherent difficulties in extracting the type of data needed to translate into real world evidence. Data systems are often designed primarily for billing purposes, and, most importantly, institutional records do not follow the patient over time across multiple treatment facilities.

The Life Raft Group Approach: Patient Powered Science for Life

Approved in 2001 as the first targeted oral chemotherapy treatment for CML (Chronic Myeloid Leukemia) and eventually for GIST, Gleevec (imatinib), hailed as "The Magic Cancer Bullet,"[5] heralded an age of precision medicine. A group of patients and caregivers (who eventually became the first members of The Life Raft Group), became the first patients to contribute to our real world evidence observational studies.

Our early patient and caregiver stakeholders were determined to learn as much about the disease as they could. The LRG began a Patient Registry on index cards, tracking as much patient information as possible.

Early on, we conducted a Side Effects Survey,[6] where we used our own quality of life scale, as opposed to the NCI Toxicity Scale. This survey provided evidence that in our patient population (patients with GIST on imatinib), many side effects improved over time. This information encouraged patients to adhere to treatment. This data was shared with Novartis, the pharmaceutical company that manufactured Gleevec (imatinib). This was information that complemented the data from the early clinical trials.

In 2008, we conducted an open cohort study to determine the effect of Gleevec (imatinib) dose on the survival of metastatic GIST patients. Data from our Patient Registry indicated that the best treatment strategy to maximize survival for patients with metastatic GIST consisted of initiating imatinib therapy at 400mg and slowly escalating the dose to a minimum of 600mg prior to the onset of progression. This was an example of how the rich data from the LRG registry can be utilized to provide evidence that may influence treatment protocols, but also serves as a catalyst for further research.[7]

A follow-up of this study resulted in publication in 2009, evaluating self-reported progression as a predictor of survival in metastatic patients.[8]

Today, the Life Raft Group maintains the largest GIST Patient Registry in the world, with over 1900 members from sixty-plus countries. With the support of the Patient Registry Team, this tool serves to empower patients to learn more and take charge of their care, which has led to higher survival rates. Simply stated, empowered and educated patients live longer.

Our members provide data for their GISTory, a portable record that tracks their GIST medical history. This gives them a centralized location for their records, across institutional boundaries and time. They can also compare their profile to others in the larger patient community, discovering practical real-world data for treatment decision making.

They become part of a global community by contributing their data. Using this data, the LRG identifies treatment response trends that can provide lifesaving information without the time lag of traditional research. Our registry undergoes rigorous quality control measures, assuring that clinical data is accurate and up-to-date.

Based on over 18 years of experience, we determined there was a need to create an encompassing strategy for capturing real world data through multiple vehicles. We established Project InterGR, a multi-faceted solution to foster collaboration and accelerate research through interactive platforms. Adding to a Patient Registry enhanced by GIST/PRIME (the web-based patient facing front end) we created a sophisticated tool to capture real-world data on side effects management. SideEQ[9], an interactive platform, enables cancer patients to track and manage their side effects. The monitoring of the SideEQ data is systematic and is integrated with the PRO-CTCAE Measurement System (Patient Reported Outcomes Common Terminology for Adverse Events). This is a system developed by the NCI to describe the frequency, severity and interference of 78 symptomatic treatment toxicities such as pain, fatigue, nausea, etc.[10]

The data collected allows the patient access to the input and perspective of other patients. It also provides information the patient can share with their own treatment team. Patients learn that side effects can change over time, and that they can learn to manage their side effects. This is empowering information that helps patients stay on their prescribed medication, particularly over long periods of time.

This data not only provides an opportunity to learn the patient perspective on side effects, but also provides a comparison to traditionally collected medical information. Most importantly, it provides critical insight into patient adherence. With the increasing use of targeted oral drugs, patient adherence is becoming an increasing problem, one that is compounded by relying on incomplete patient reporting of non-compliance.

Currently, the Life Raft Group's Real World Evidence Team is involved with several initiatives where our emphasis on real world data has initiated collaborations with leading GIST experts, academic medical centers, government and pharma, all in an effort to accelerate research through patient-powered science. Project Surveillance[11], an interactive platform for physicians and researchers, will soon provide a valuable tool for the collaborative sharing of data for GIST experts with a foundation of real world data from our Patient Registry, the largest GIST registry in the world.

Our data recently has shown a higher level of efficacy for a recognized treatment, which we intend to share with the pharmaceutical company. This may result in further studies or possibly changes in clinical recommendations.

We established the Pediatric and SDH-Deficient GIST Consortium[12], an innovative collaborative initiative designed to strengthen and advance research to find effective treatments of a rare subset of Gastrointestinal Stromal Tumor (GIST) patients who have been unresponsive to the current standard treatments. The consortium consists of experts with complementary skill sets who will team with patients and patient advocacy groups to find targeted solutions for this population.

The Consortium was recognized at the Biden Cancer Summit for its innovative approach.

Our early emphasis on real world data continues to place us at the forefront of the real world evidence research paradigm.

The LRG stands ready to expand our horizons by collaborating and sharing our expertise in real world evidence with the global community.

References

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