Real World Evidence

Where and How It is Best Used

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Real World Evidence Emerges As A Viable Tool In The Pharmaceutical Industry

In recent years, the terms Real World Data (RWD) and Real World Evidence (RWE) have been repeatedly mentioned by the FDA in various channels. [1][2] In July 2018, the administration published a guideline to the industry for using RWE in clinical investigations [3]; and in December 2018, a framework for its own future RWE program [4]. Not only has the FDA been actively promoting the use of RWE to the biopharma industry, it has also been probing into how the incorporation of RWE can improve regulatory decision-making processes. More importantly, even before these regulatory endorsements, the biopharma industry has already taken its own initiatives on RWE in this past decade, adopting and increasing capacity in investigating RWE. According to a report published by Deloitte in June 2018[5], more than half of the leading biomedical science companies have developed or have improved their RWE capabilities in recent years. Inevitably, RWE will be the next big thing in biopharma intelligence. In this increasingly connected world, where everything ultimately becoming a data point is the daily reality, It is more important than ever for all participants in the health care industry to understand how RWE can be used and how it can shape the immediate future of the industry.

Stakeholders in the healthcare landscape – healthcare providers, payers, regulators, pharmaceutical companies, and most important of all, the patients – all can benefit from the use of RWE, and therefore, by their very nature, are driving the increasing interest. From the patients' perspective, publicly available results derived from RWE help them to understand the benefit and risk of an intervention in a day-to-day, real world setting. In the meantime, healthcare providers can optimize the quality of treatment as well as the quality of a patient's life by analyzing and learning from RWE results. Payers can use RWE to evaluate a product based on the value it brings to the patients and market in order to make pricing and reimbursement decisions. RWE is already a routine when submitting to regulators in the EU; and in the US, it has recently been accepted as part of regulatory submission to support and to enhance the submission process. The newly implemented FDA regulatory framework provides a guideline to evaluate RWE as support for approval of new indications and to fulfill post approval requirements. In response to the demands from other stakeholders, biopharma companies can use RWE to aid the drug development process, to support the product's value stories, as well as to optimize market access strategies.
In addition, for the rare diseases in which clinical trial patients are hard to recruit, RWE can be especially helpful.

How is RWE involved in a product life cycle, from pre-clinical to post-market?

What kinds of questions can be answered, and/or analysis done in each phase?

RWE can play many important roles in supporting and enhancing efficiency and potential efficacy during clinical trials. These include but are not limited to: regulatory submission, expanding indication and monitoring safety. Biopharma companies will need to work more closely with stakeholders such as CROs, sites, agencies, and regulatory committees so they can stay in trend. In order to prove the efficacy and cost benefits of RWE for these and other stakeholders, it is critical for biopharma to properly generate and utilize appropriate RWE, and do so to provide constant insights and value stories throughout the entire product life cycle, from pre-clinical to post market.

At the various stages of a therapeutic product's life cycle, RWE plays different roles. Even in the pre-clinical phase, when there is limited RWE available for the product of interest, it is still possible to use RWE to explore the status quo of the targeted patient population. Studies can be conducted to profile the prevalent and incident patient cohort of the medical condition of interest, to examine treatment patterns prescribed by physicians, and to assess the cost and effectiveness of current standards of care. With such information, biopharma could understand the overall health condition of the targeted patient cohort, and better situate itself to provide care for the neediest patients.

As the clinical stage progresses into later phases, more data is being generated; it then becomes feasible to gauge both the clinical and economic outcomes for various real world study objectives. It is possible to evaluate the competitiveness of the product even before it hits pharmacy shelves. We can design studies that explore the disease history, improve patient recruitment/patient selection, understand patient preference and gather evidence for FDA approvals among others. Moreover, complex models can be constructed to generate economic evidence, and therefore, guide various marketing and patient outreach strategies.

Entering the post-market stage, real world studies are constructed to monitor drug safety profiles, adherence/persistence rates, resource utilization in real world settings, and to measure effectiveness against other treatments. In recent years, we have also seen an increasing number of collaborations between biopharma and insurance providers in the US in developing outcome-based contracts based on RWE results, with the intention of extending the latest therapeutics to more patients.

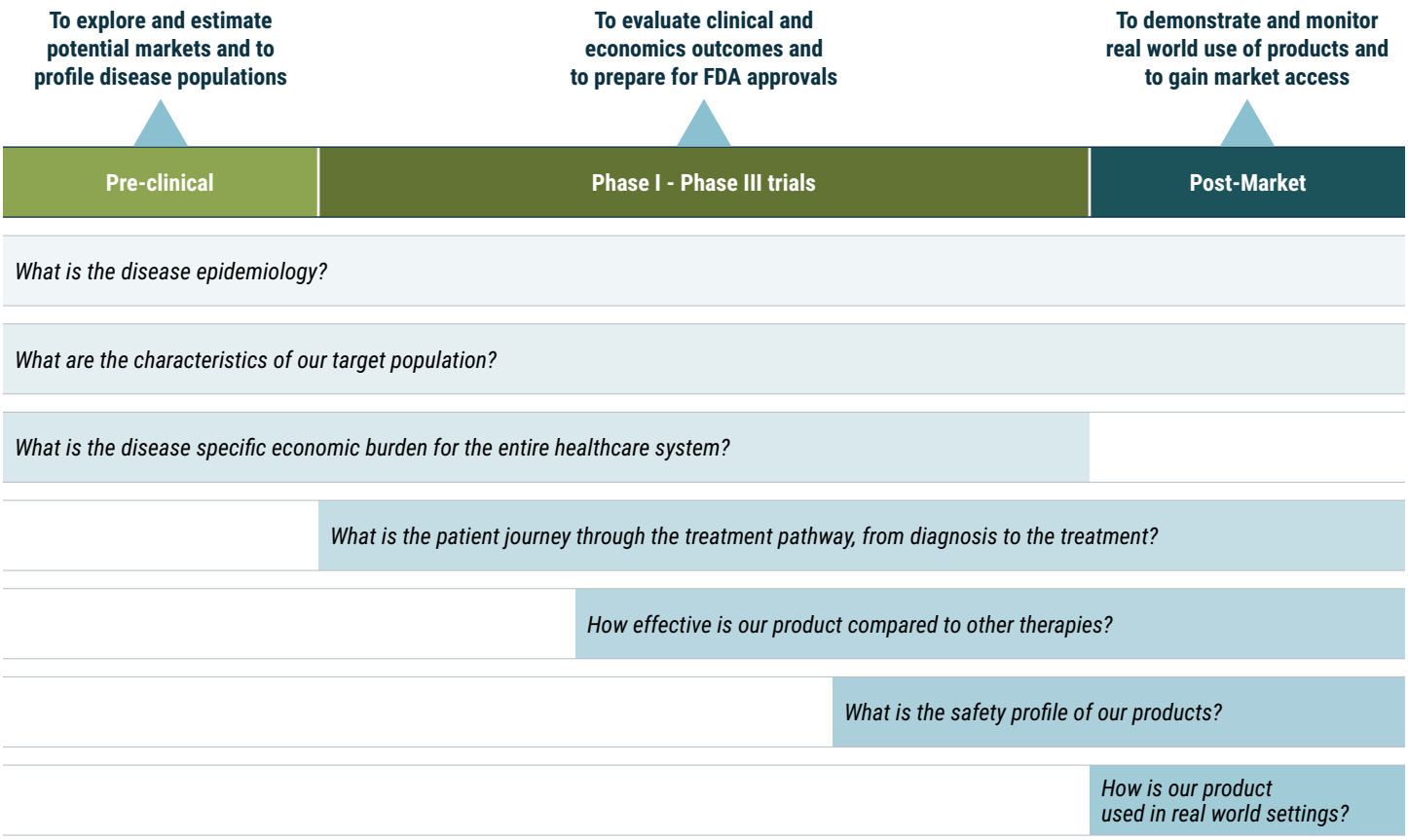

Figure 1: Sample business questions during different stages

Examples of Real World Evidence in Action

Case study 1: A Pre-clinical Study

Background: Allergic asthma (AA) is one of most common types of inflammatory diseases, and currently there is no cure for it. AA patients are subject to lifelong treatment. The purpose of the study was to examine and to understand the pattern of treatment for adolescent and adult patients.

Method: The objective was to analyze treatment patterns. A commercial claim database was found to be the most suitable for this kind of retrospective analysis, as it typically contains more patients than a data source with other origins. The study population was identified by indexing newly diagnosed AA patients. Then, they were divided into an adolescent cohort and an adult cohort, based on the age at diagnosis. The cohort was further dissected into moderate and severe subgroups by tabulating the dosage of treatment each patient received.

Finding and Solution: The study demonstrated that the gender distribution differs for adult and adolescent cohorts. The adult patients had a larger male percentage and an acute illness driven co-morbidity burden. More adolescents experienced acute respiratory infections. In terms of treatment patterns, more adolescent patients received SABAs and fewer received ICS/LABA and monoclonal antibodies as compared to adult patients.

The result of the study shows that considering the similar disease burden and availability of treatments, fewer adolescent AA patients received targeted treatment than adult patients did. This finding reveals the potential unmet need for adolescent AA patients, and it highlights the opportunity to incorporate targeted therapies as treatment options for this patient group.

Case Study 2: A Post-market Study

Background: A biopharma company launched drug D to treat patients with moderate to severe conditions X, Y, and Z. The company was particularly interested to find out how the real world usage of D impacted condition Z. They wanted to understand the patient profile and be able to monitor loading patterns with quarterly updates.

Method: The first step was to establish a patient cohort with condition Z only, and to remove patients who were not included in the label (i.e. underage, etc.). Any patient with condition X or Y was purged from the analysis along with any off-label patients. An open claims database was used to identify patients with condition Z who had submitted drug D claims during the identification period. Eligible patients receiving other treatments for Z prior to their start on drug D were also verified. The patient demographic profile and drug dosage at the index treatment date were recorded and calculated. Clinical characteristics, such as co-morbidities and treatment history in the 12 months prior to the index date, were also collected. The patient group was split in two: group one being based on whether the patient used the loading regimen within 4 weeks after the index date and group two having those patients who used the loading regimen more than 4 weeks after the index date.

Finding and Solution: In this specific study, about 80 percent of the patients received the loading regimen. However, there was no statistically significant difference between the demographics and clinical characteristics of the two groups. To monitor the cohort continuously, an interactive dashboard was developed and is updated quarterly. The company is using this to control the definition and length of the identification and follow-up period in order to better identify the real world impact of D usage on condition Z.

Conclusion

In recent years, biopharma companies have begun to invest heavily in RWE capabilities in both data generation and in-house technology development. RWE opportunities across all phases of the product life cycle are increasing at an unprecedented rate, which also means there are more opportunities to increase treatment efficiency and efficacy to improve patient quality of life. However, with richer resources and evolved technologies, the challenge remains on how to make appropriate use of all available RWE. To achieve such goals, there is increasing collaboration between the various healthcare stakeholders, in order to help improve both the quality and quantity of RWE utilization in the industry. The healthcare industry is quickly discovering, however, that a tremendous amount of expertise is required to navigate the seas of RWE and find the right course in generating and interpreting the data. Finding resources to do so has become as important as working with RWE in the first place.

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About Huanxue Zhou

Huanxue Zhou is Director of Health Economics & Outcomes Research (HEOR) at KMK Consulting, Inc. She obtained her Master's Degree in Statistics from Lehigh University. In her current role, she trains and leads HEOR analysts to execute HEOR studies to support clients. She is responsible for understanding clients' needs and ensuring the successful implementation of assigned projects. She provides consultation on appropriate research design, statistical analysis and interpretation of results. In the past seven years, she has worked with clients to develop many conference posters and peer-reviewed publications resulting from the execution of high-quality real-world data analyses in various therapeutic areas using a variety of observational databases.

About Bob Tian

Bob is a senior analyst at KMK Consulting, Inc. He joined the HEOR group at KMK in 2015. Since then he has been working with multiple large US and foreign real-world data projects, developing analytical methods for various goals. Bob has a Masters Degree in Industrial Engineering from ISyE at Georgia Institute of Technology.

KMK Consulting, Inc.

KMK Consulting, Inc. is a full-service consulting firm specializing in commercial operations support to the life science industry. Since our inception in 2000, KMK has grown to have more than 120 full-time employees, providing analytical support to clients on-site, as a project, or as SaaS that helps drive business decisions and improve the efficiency and effectiveness of commercial analytics and sales operations. We eliminate complexities for commercialization leaders by integrating:

- Accurate Marketing and Sales Analytics
- Market Research
- Sales Ops Software
- RWE/Health Economic & Outcome Research

The KMK HEOR team has extensive experience working with different RWD sources to solve assorted business questions. Our expertise in real-world evidence studies enables us to choose optimal data sources and to conduct sophisticated analysis to overcome data limitations. We are meticulous in how we balance selection bias and data quality issues in the design of a study, as well as how we conduct the analytical process. We always subject both the input data and the outcome to the highest level of scrutiny. Our dedicated team will turn the data into insights decision makers need ultimately leading to better efficiency.

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