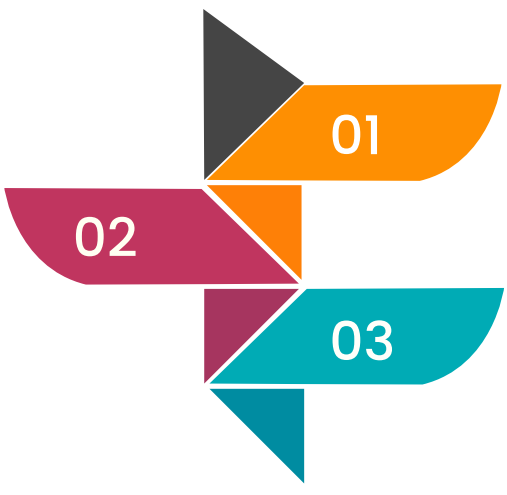
Are we ready for life cycle management using real-world evidence?

The process of life cycle management ensures realization of the commercial and clinical value of a drug right from the development stage to the end of the products' life. Indication expansion is one of the most successful life cycle management strategies, but is costly, time consuming, and can be high risk.

The FDA has a framework under section 505F to the Federal Food, Drug, and Cosmetic Act (FD&C Act) to evaluate the potential use of real-world evidence (RWE) to support the approval of a new indication for an already approved drug or to support or satisfy post approval study requirements. A preliminary guidance document for the industry was introduced in September 2021.

The key elements of the framework include:

The methodology adopted must be adequate to provide scientific evidence to answer the regulatory questions



The data must be fit for use in regulatory decision making

To adopt a validated approach that must meet the standards of data collection, monitoring, and integrity

Such an approach for using RWE data to support indication expansion may be extremely helpful in oncology and rare diseases where the unmet need is extremely high and compounded with complexities of clinical trial design. Some recent examples of the use of RWE include:

Prograf *(Tacrolimus)*

In July 2021, FDA approved Prograf in combination with other immunosuppressant drugs for the new indication of preventing organ rejection for patients who have received a lung transplant. The real-world data was extracted from U.S. Scientific Registry of Transplant Recipients registry data. The outcomes were analyzed based on discharge immunosuppression treatment regimen in recipients of a primary lung transplant between 1999 and 2017 who were alive at the time of discharge. These outcomes were with historical controls for lung transplant patients with no or minimal use of immunosuppressants.

Zolgensma *(Onasemnogene abeparvovec-xioi)*

Generation of historical control data becomes even more important in rare diseases to understand disease progression to support drug development and compare the effectiveness of the new intervention. This approach was utilized for Zolgensma (approved for spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene), where the data was analyzed from a longitudinal, multi-center, prospective natural history study enrolling 26 SMA infants, and 27 control infants less than 6 months of age and following them up for 24 months to analyze progression and co-relationship between motor function and biomarkers.

Ibrance *(Palbociclib)*

In April 2019, Pfizer announced Ibrance received supplemental indication approval for male breast cancer (index approval was for post-menopausal women with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced or metastatic breast cancer). This indication expansion was based on electronic health records data, claims data, and post-marketing safety reports to support clinical efficacy and safety in a new patient population.

The challenges of RWD include data quality, reproducibility, and accuracy which may affect validity. RWD and RWE must be fit for purpose and account for FDA requirements. The regulatory filing for Rozlytrek (entrectinib, approved for NTRK-fusion positive solid tumors, and adults with ROS1-positive metastatic non-small cell lung cancer [mNSCLC]) included RWD meant to establish data for additional clinical outcomes. The FDA did not consider the real-world data due to methodological limitations which included post-hoc analysis, selection bias, confounding bias and lack of statistical power due to limited cohort size. The resulting FDA label of Rozlytrek excluded time to treatment discontinuation, progression-free survival, overall survival outcomes, and only referenced improvements in overall response rate.

The environment is evolving for integration and success of RWE in clinical development and life cycle management for both new drugs as well as indication expansion for already marketed drugs.

We at SmartAnalyst, help major pharma and biotech companies to conduct RWE studies during the clinical development program for a new drug as well as for life cycle management. Our extensive experience is used to assist our clients in appropriate study design, choice of suitable databases and execution of the study.

Sources:

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