A new approach for post-marketing safety studies

Digital tools enable efficient surveillance

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The large quantity of digitized healthcare data in the U.S., combined with advancements in data collection and processing technologies, present an enormous opportunity to shift dramatically how post-marketing safety studies can and should be conducted.

The Traditional Approach

Post-marketing safety studies are a big business. Estimating 100 sites, a post-marketing safety study can easily cost a pharmaceutical manufacturer $50 million. In the last five years, 832 observational safety studies (of various sizes, length of follow-up, etc.) were registered on ClinicalTrials.gov. Of those, only 224 have been marked as completed. An EY report estimated that "on average, a large pharma company processes approximately 700,000 adverse event (AE) cases annually" and that "fifty percent of pharmacovigilance resources are currently spent on managing cases that require integration of data that varies in quality, structure and format." The report further projects that by automating some key processes "the typical top biopharma can reduce time spent by 45%, with potential multimillion-dollar annual savings."

While pharmacovigilance and post-marketing safety are not necessarily equal in function, the cost and time required to manage these large studies present many challenges, beyond simply the manual processing of adverse events. Manufacturers face challenges with enrolling potentially hundreds of research sites to ensure that patient enrollment meets a threshold to make safety findings statistically relevant, while also sustaining the program over a long enough time period to ensure the safety profile is understood beyond initial uptake. Participating sites face challenges with recruiting enough patients using the drug and then keeping patient participation as follow-up typically diminishes over time.

A Use Case for Change

The case of Janus Kinase (JAK) inhibitors highlights a glaring need for innovative and more dynamic safety approaches. In 2021, following the review of multiple large, randomized trials that demonstrated a higher rate of serious cardiac events, malignancies, mortality and thrombosis, the US Food and Drug Administration (FDA) took steps towards implementing class-wide safety requirements. Beginning with mandatory boxed warnings about the risks of drugs in this class, progressing to delays in approvals as data were further analyzed, and culminating with mandated post-marketing safety programs two JAK inhibitors were recently approved for the treatment of atopic dermatitis (AD) with these prerequisite safety requirements.

While AD is the current condition of regulatory focus with this therapeutic class, treatments in this class are currently being prescribed for rheumatoid arthritis and psoriatic arthritis with marketing approval being sought for other conditions including ankylosing spondylitis and ulcerative colitis. Although these treatments may pose higher risks, they are critical for many patients with unmet needs currently not addressed by available treatment alternatives. Pharmaceutical manufacturers are faced with finding a rapid solution to meet the safety monitoring requirements without significantly delaying access to these important, innovative treatments.

Technology Supports a New Way

Big data capabilities allow for a decentralized approach to post-marketing safety surveillance that broadens the opportunities for participation and removes the disadvantages and disparities in data collection. Rather than being dependent on patients who present at pre-selected study sites, a data-driven approach can be used to access and assess a broader, more diverse cohort of patients who have been prescribed a specific treatment.

For example, in the OM1 ClinSafe-AD program (**Fig. 1**), atopic dermatitis patients' data are routinely collected through EMR systems – independent of provider, geography or other characteristic that may prevent them from being enrolled in a post-marketing safety study. Patient enrollment can thus proceed either through the prescribing clinician or through a central site. Either way, a decentralized approach expands the reach of the study while simultaneously reducing the burden of data entry with EMR data used to pre-populate case report forms. As events of interest are flagged, additional safety monitoring and event adjudication processes are triggered. The focus is on supporting patient and site participation, while automating data capture and monitoring. (**Fig. 2**)

Figure 1

Decentralized Safety Surveillance Methodology (ClinSafe™-AD)

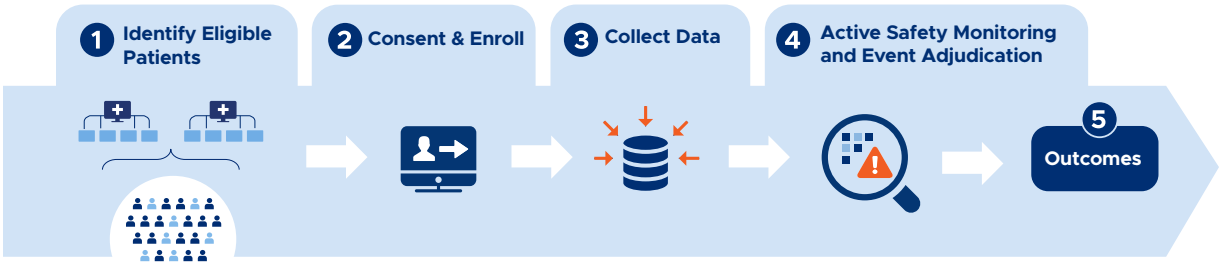

Figure 2

Utilizing purpose built, specialized data networks around conditions like AD, are an integral part of what is needed to move these types of programs forward. Many specialty societies and patient organizations have established registries to evaluate and measure the quality of care and clinical outcomes in their respective disease areas. These datasets, though currently under-utilized, can be an important piece of the puzzle when implementing safety programs. The American Academy of Dermatology's (AAD) DataDerm™ program is the largest clinical dermatology data registry. Through a collaboration between AAD and OM1, a program like ClinSafe-AD can connect and integrate specialty data from the registry with additional sources to expand the possibilities of patient reach and data sources that are available for safety monitoring and other important research initiatives.

Beyond the intended safety surveillance objectives, these automated programs also allow for evaluating effectiveness, the natural history of disease and other analyses due to the collection of longitudinal patient journeys and outcomes in an accessible database. They also allow for the evaluation of standardized outcome measures at scale, across a class of therapies in a way previously not possible.

Using patient-centric tools, such as electronic patient reported outcomes (ePRO) platforms, data can be collected directly from patients, allowing for easier access over time versus waiting on the patient to be seen by a physician. Electronic PROs add further depth around outcomes and events not typically available in EMR data. The ePRO data can then be linked into the broader dataset and continue to be collected prospectively.

The Future of Safety Surveillance

As regulators, pharmaceutical manufacturers and other healthcare stakeholders continue to search for better ways to meet unmet clinical needs, while balancing safety concerns, the ways in which safety is monitored and evaluated must evolve. Between large-scale healthcare datasets and advanced technology platforms, the shift to more dynamic, powerful and cost-efficient safety programs is becoming a reality. The case of JAK inhibitors may just be the impetus needed for the future of safety to take a giant step forward.