Regulatory Matters

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Real-world by design: Considerations for designing clinical trials that include real-world evidence

The complexity of modern-day clinical trials has propelled trial design from being a consideration to now becoming what some experts believe is a science in and of itself. The United States Food and Drug Administration (FDA) sees immense potential in utilising real-world data in designing clinical trials. This article introduces real-world data and presents a few considerations for designing nonrandomised single-arm clinical trials and observational studies that include this design element.[1,2]

The FDA's Food, Drug and Cosmetics Act defines real-world data as data relating to patient health status and/or the delivery of healthcare routinely collected from a variety of sources, including data derived from electronic health records, medical claims and billing data, data from product and disease registries, patient-generated data, data from in-home-use settings, and data gathered from mobile devices.[2]

In a nonrandomised, single-arm trial setting, the following are some opportunities for the incorporation of real-world data:

1. external controls for studies wherein the disease evaluation criteria is well established;
2. historical records of vital signs, either as a pooled dataset or stratified according to any prespecified participant characteristic, collected from trial participants residing in different geographies; and
3. comparison datasets for those trials wherein a placebo or non-treatment arm is either not ethical or feasible.[2-4]

In an observational study setting, the following are some opportunities for the incorporation of real-world data:

1. because certain types of real-world data such as data from mobile health monitoring and wearable devices are captured in a noninterventional, purely observational, uncontrolled and 'natural' setting, they may be utilised to test hypotheses based on physical activity, caffeine consumption, and a variety of other lifestyle characteristics; and
2. postmarketing surveillance data and real-world data derived from medical claims, administrative claims, and electronic health records may be used not only to gain a deeper understanding of treatment-emergent adverse events in the long term, but also to validate safety and efficacy claims from randomised controlled trials.[3,4]

Despite the value that real-world data can offer, it may not be applicable to all types of trial designs. As a design element, the incorporation of real-world data in a clinical study often begins with a multifaceted discussion focusing on many considerations, including the following:

1. whether the treatment methodology is routine enough and the therapeutic area is established enough to gather sufficient real-world data before study initiation;
2. whether the available real-world data is of sufficient quality to lend itself to statistical comparisons against data gathered in a more traditional longitudinal study;
3. in trials focused on rare and ultra-rare diseases, whether the volume of available real-world data is sufficient for its utilisation as a trial design element; and
4. in cases where historical controls are being used as real-world evidence, whether clinical practice guidelines and data collection methods have remained consistent for the data to be useable as an accurate comparator dataset.[2]

In conclusion, the incorporation of real-world data as a design element in clinical trials can broaden our perspective, allow us to see the invisible, and potentially improve regulatory decision making.

References

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