Case Study: Using Real-World Data to Expand Eligibility Criteria for Phase III Endocrinology Study

It's no secret that starting out on the right foot with a well-designed protocol is a key factor in a clinical study's ultimate success. Protocol amendments after a study has launched are notorious timeline killers and cost inflators. Some are unavoidable, but most can be dodged with some smart strategizing. One solution increasingly used by study sponsors is the use of real-world data (RWD), or data collected during the routine care of patients, to determine a study's eligibility criteria. By applying RWD to pressure test the inclusion and exclusion criteria for protocols early in the game, these sponsors have been able to maximize eligibility requirements, saving themselves the substantial time and cost that comes with tweaking these standards later on down the line.

Challenge

In a global, Phase III endocrinology study, the study sponsor wanted to look at their anticipated access to patient populations across countries in Asia, Europe, and North America. They needed to ensure the protocol's eligibility requirements were not unnecessarily excluding potentially relevant populations and that they could expect to recruit these populations at the assumed recruitment rate. At the same time, they also wanted to ensure that the populations they selected aligned with the protocol's unique medication requirements. This study mandated patients to be on a stable dose of a specific background medication, and the team needed to know if this therapy was on the market and robustly prescribed in the countries they approached.

Solution

Starting early in the draft protocol stage (with primary endpoints locked, but secondary and exploratory endpoints still flexible), the study team began looking at two distinct federated electronic health record (EHR) systems: one with a combination of United States and European data and the other with European data only. They also examined historical studies and competitor trials using publicly available sources. The goal was to target the most representative population in the least restrictive manner that still achieved the study's endpoints.

Upon review, the study team found that one criterion seemed to be eliminating a significant number of patients. A comparison of screen failure rates of historical studies alongside the EHRs confirmed what they suspected: this was a problematic criterion. Because it was aligned with a primary endpoint of the study, the criterion could not be changed, but the team was able to let the sites know, allowing them to prepare for the impact on eligibility. The data also showed that a major inclusion criterion around background medication that the team had presumed was needed could in fact be opened up, expanding patient eligibility.

Next, the team brought their findings to investigators, sites, and patients to determine whether they aligned with these stakeholders' experiences. Data are valuable, but they may never tell the whole story. For example, sites can give important insights into the burden of procedures or other requirements that should be factored into eligibility considerations. That's why this stakeholder consult is an important validation step, the team says, that should not be bypassed.

Once the team received all of the various external data sources, including the RWD, the team met to review the findings and potential opportunities to optimize the design. The

entire study team, including physicians, feasibility, biostatistics, operations, and therapeutic experts, had a voice in these final decisions.

Outcomes

The study is now complete, and the sponsor saw major gains that can be attributed to the use of RWD as well as other strategic tactics to determine eligibility. Those gains include:

- A 71 percent increase in enrollment rates compared to a previous study in the same population that did not use RWD
- A 2.1-month reduction in recruitment timelines compared to the same previous study that did not use RWD
- A 33 percent increase in patient eligibility as a result of an inclusion criterion change flagged by the use of RWD

The Big Picture

The sponsor has used the strategies implemented in this example across its entire portfolio for two years with great success. The process has substantially improved site productivity—in fact, this sponsor's time from protocol sent to site agreement is now averaging eight days versus the industry average of six weeks. At the same time, fewer sites are now needed to recruit patients, with the organization averaging around 20 percent more patients per site than one year ago. Importantly, the inability to adequately recruit is now the organization's least cited reason to file an amendment.

With an eye to the future, the sponsor hopes to soon see full patient tagging to match up claims and EHR data, allowing even richer, more meaningful insights to improve trial delivery. Emerging market data is another critical gap that, when filled, will strengthen the case for RWD. With new technology unlocking data access every day, the application of RWD across the study spectrum will only continue to become more powerful.

Success Factors

This sponsor's advice for others hoping to apply RWD to determine eligibility requirements:

- *Don't Choose* – Sometimes there is a tendency to use either claims or EHR data to support a study when, in fact, they are complementary. Use both whenever you can.
- *Data Never Tell the Whole Story* – Yes, EHR and claims data are useful, but don't forget about the other form of "real-world data": talking to people, and particularly patients, PIs and study coordinators. Their insights can help you better understand the disease burden and what may or may not be feasible for your effort.
- *Let the Outcomes Do the Convincing* – The use of RWD to make trial decisions is still fairly novel to many organizations, and some stakeholders may not yet see the value. However, the real gains can happen when these strategies are adopted, standardized, and mandated across a portfolio. Take the initiative to pilot them on a clinical study, even if only in an exploratory arm, and then let the outcomes speak for themselves.

This case study is part of CTTI's Recommendations on Use of Real-World Data to Plan Eligibility