Avoca Quality Consortium® Leading Change Collaborative Forum

Meeting Highlights

Topic: Innovative and Flexible Protocol Design

Meeting Date: January 19, 2021

Background Information

With the emergence of the COVID-19 pandemic, the pharmaceutical industry has had to rapidly develop modifications in clinical trial processes and adopt new technologies in order to continue studies, ensure compliance with regulations, and protect patient safety. While different companies adapted in various ways, protocol amendments have been required, and the creation of flexible protocols has become an attractive option both now and moving forward. As we approach the second and possibly third waves of COVID, current challenges will remain. When COVID passes, some of the technologies and processes originally developed to address the COVID-19 pandemic are likely to be continued.

Discussion Summary

Opening topics:

- In the COVID environment, companies must manage by taking calculated risks, including innovative protocol design, cross-functional organizational change management, and decentralized clinical trials. Considerations discussed:
    - Some companies are looking to decentralize trials quickly.
    - Understanding what qualification standards look like for technology providers and how qualification that is different than the standard trials must be considered.
    - Adding flexible language into the protocol is very helpful.
    - It's important to see things from site and patient perspectives; simple study designs.

What protocol development changes are being seen, including those required due to COVID?

- Study visits may need to be altered.
- Biostatistics in most cases should be involved in initial protocol development.
- Need to develop a best practices approach to Quality Tolerance Limits (QTLs).
- Scientific integrity is of paramount importance. If a QTL framework was previously in place, issues from COVID followed naturally. Also, estimands can be useful. What will be primary endpoints must be determined. Regarding interim events, if one has a protocol written using an estimand framework and QTL framework, the protocol and data coming can be reviewed for possible COVID impact on data integrity.

Protocol Simplification:

- Superfluous data is often collected just because we can. Some items make their way into the protocol because a prior study's similar protocol was used as the template/foundation for the new protocol.
- Perhaps the data collection can be simplified to capture only what is needed.

Platform Designs:

- Benefits: When the control log is shared, a lower proportion of patients are administered the placebo. If one company has two compounds or more, it's easier to understand early how a compound is performing, which can promote efficiency. It can lead to a seamless Phase III study.
- Challenges: It can be difficult to agree on the platform design if one or more Sponsors collaborate. It can be applied to different approaches; it is more common to look at drugs for similar indications which can add a competitive element.

What are key considerations in planning that are different than in traditional studies?

- If you are doing a basket type trial for a number of different indications, you can be essentially opening different sites at one institution. Groups tend to work independently from others and it's something to keep an eye on. This is similar to opening two studies in two different companies.
- In design, you have to simulate and project what the results could be.

Do you look at protocols holistically or in baskets to analyze QTLs?

- This depends on what QTLs would be around the primary efficacy endpoint.
    - You can have simplification and a relatively complex design.
    - The designs need good data at primary endpoints.
    - The best things about QTLs and estimands are the discussions across the team about why you are collecting certain data.
    - Teams need to look at study design to see if it's going to work for a patient and to ensure cross-functional stakeholders understand what introducing a new data point does to the patient and site. Amendments can have significant financial impact.
    - It's vital to find patients and keep them on a study as long as it's safe, and to make it easier for sites and patients to participate.

If you are interested in learning more about the Avoca Quality Consortium (AQC) or its Leading Change series, please contact Dawn.Auerbach@theavocagroup.com.