SPEAKout
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Making your trial breakthrough:

How imaging can make — or break — your accelerated trial

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Breakthrough Therapy studies evaluate the effects of therapies on the most severe diseases, where patients have irreversible morbidity or mortality [IMM] or symptoms that represent serious outcomes of their sickness. The pressure to deliver quality data is immense because the cost of not delivering can result in patient deaths that may have been prevented.

The race is on

Earning the FDA's prized Breakthrough Therapy designation is just the beginning of the race, one that likely requires the use of an imaging surrogate for preclinical evidence or accelerated approval. For researchers who receive the coveted designation, this means getting clinical trial imaging done right, and fast.

But meeting the rigor of the FDA's accelerated review process can be complicated. When medical imaging is required, sponsors need to confidently navigate numerous challenges they'll face from an operational, regulatory, medical, and scientific point of view. And they must have the tools and processes in place in order to be able to move quickly.

"Unanticipated and complex imaging data may need to be submitted within just a few weeks, so having a solid process in place to ensure rapid, high-quality delivery is critical."

Proven processes and scalability are key

The design and demands of a Breakthrough Therapy trial can change practically overnight. Sponsors need to quickly collect patient images, onboard and train expert readers, and be prepared for the FDA's rolling review process. This is where individual application sections are sent to the FDA upon completion, as opposed to holding individual sections until the application is complete. In Breakthrough Therapy trials, validated imaging exports are likely required at each stage of the rolling review.

Breakthrough Therapy trial sponsors also need the flexibility to include both known and exploratory imaging biomarkers. We've seen Breakthrough Therapy trials require multiple, separate criteria per patient. Unanticipated and complex imaging data may need to be submitted within just a few weeks, so having a solid process in place to ensure rapid, high-quality delivery is critical.

Even more important, however, is the ability to quickly scale the number of readers who are trained and able to join the image review team when a study accelerates. Each reader needs to be specialized in the therapeutic area, trained on the trial's imaging charter and on proper application of the analysis criteria, and committed and available for the duration of the study. A plan for adjudicating disagreements and monitoring inter- and intra-reader variability also needs to be in place.

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Sponsors need to be prepared for potential, massive scope changes based on changes to the protocol, FDA requests, or need for additional studies. We have seen phase 1 trials evolve into the design of a complex phase 3 study, all through multiple protocol amendments. A study planned for a few dozen patients can quickly scale to over one thousand, and the reader team may need to grow tenfold.

Conclusion

These examples depict how every aspect of a trial is heightened, and how the challenges of medical imaging need to be addressed, with confidence, when a compound is designated a Breakthrough Therapy.

Everyone involved – from project managers to readers and scientists – needs to appreciate the importance of delivering flexibility, speed, and data quality that meet FDA standards in order to gain approval and bring important Breakthrough Therapies to patients whose lives depend on them.

To learn more about Calyx's extensive experience in supporting Breakthrough Therapy approvals, contact hello@Calyx.ai.

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