Maximize Phase I Study Timelines through Innovative Clinical Trial Design

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Early clinical research continues to be a high stakes industry requiring increasingly complex studies, procedures, and protocol designs all of which take longer to complete, which in turn drives up cost. The introduction of combined protocol designs—also called umbrella protocols—is gaining popularity among drug developers as a way to bring the first subject visit for the all-important proof-of-concept study forward by months, as well as saving significant cost.

Advantages of Umbrella Protocols

Reaching a first-in-human clinical trial is a major milestone, with years of preparation preceding it. Less than 10 years ago, Covance Clinic Research Units (CRUs) routinely conducted early clinical (Phase I) trials in a sequential manner. A single ascending dose (SAD) trial was typically carried out to completion, followed by a separate multiple ascending dose (MAD) trial. Additional studies to look at population differences, food effect or biomarkers may also have been performed alongside the MAD study. If these independent studies were successful, a transition into Phase II trials would follow.

Covance has over 25 years of experience conducting ascending dose studies. In the last five years we have conducted over 250 first-in-human ascending dose studies, two thirds of which were umbrella protocols.

Umbrella protocols offer many advantages as they not only serve to combine SAD and MAD phases into a single trial, they also can provide for the assessment of numerous other study components such as the evaluation of biomarkers, population differences (eg, elderly, ethnic groups), different drug formulations, and effect of food. When combined into one umbrella study, sponsors benefit with savings in both cost and time, as multiple objectives are achieved within a single protocol.

Application of Adaptive Designs

Applying a flexible, adaptive study design enables many aspects of the study to be modified based upon emerging data. In Covance, we routinely modify dose levels, numbers of subjects and sampling occasions, all without having to issue a protocol amendment and wait for ethics and/or regulatory approval. In fact, if the
protocol is carefully constructed and the communication between site and project manager is collaborative and highly effective, very few changes to a study design will require a protocol amendment. Such a cutting-edge approach to designing FIH ascending dose studies allows for the timely and rapid collection of value-adding data, refining and optimising the design whilst the study progresses.

An assessment comparing Covance umbrella studies with conventional sequential ascending dose studies concludes that umbrella protocols can result in a time savings of up to 4 months as shown below. For simplicity, this is based upon a UK CTA submission but similar time savings are applicable if the study is conducted in the US.
Our flagship CRUs for utilizing the umbrella protocol design are Leeds, UK; and Evansville, IN and Madison, WI in the US. Extensive experience with the process means that Covance can provide efficient and cost-effective trial designs for sponsors keen to progress their molecules swiftly through early clinical development. Beyond savings in time and cost however, Covance also offers the scientific and medical insight and confidence that is necessary to perform successful trials. Our proven ability in implementing umbrella protocols to provide rapid access to high quality data without compromising subject safety is a hallmark of Covance that our sponsors around the world have now come to expect.

Conclusion

Given the complexities of drug development, it’s imperative that contract research organisations offer innovative solutions that take time and cost out of the process. Covance has been at the forefront of the implementation of umbrella protocols and continues to be recognised for expertise in developing and executing complex study designs. Our CRUs in Leeds, UK and Evansville, IN and Madison, WI in the US are continually proving that their adaptive, customized approach to FIH study designs result in a savings in time and cost. We recognise the trust imparted to us as we transition a molecule from the nonclinical into the clinical arena, with our emphasis being placed on quality, safety and success.

For more information, please contact us.

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Karen Cornelissen is currently the Scientific Director at Covance Clinical Research Unit in Leeds, UK. As part of this role, Karen advises on study design and subsequent data interpretation, which draws upon her experience in analytical chemistry, drug metabolism and pharmacokinetics.

About Covance

Covance, with headquarters in Princeton, New Jersey, is one of the world’s largest and most comprehensive drug development services companies, with annual revenues greater than $2.2 billion and more than 11,000 employees in over 60 countries. Covance has the people, processes, client service, and global resource capabilities to respond to the toughest drug development challenges.

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