THE DIFFERENCE IS IN THE DATA®

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Case Study

Adapting to recruitment difficulties

Driving decision making with an adaptive clinical trial in the face of recruitment difficulties

KerusCloud® is a revolutionary simulation-guided study design tool that ensures clinical trials are designed effectively to collect the right data, in the right patients, in the right way. Its use supports evidence-based design decisions to extensively de-risk real clinical studies, reducing development time, costs and patient burden.

The Software

KerusCloud® allows multiple study uncertainties to be explored simultaneously, in minutes, within a virtual environment. Study outcomes are visualized with an interactive heatmap where detailed results help identify the pros and cons of different design options. This allows the key drivers of study success to be pinpointed rapidly so that the best design and analysis approach can be selected, first time.

Diverse information and data types inform the simulations with sources including the scientific literature, disease registries, historical trials and real-world data. These data are captured in the platform as synthetic data sets, avoiding privacy constraints, and used to build virtual patient populations to answer 'what if' study scenarios questions.

KerusCloud's synthetic data driven simulations are uniquely informative. They best represent the complexity found in real studies by accurately mimicking the quirks found in real patient-level data, like missingness. Therefore, KerusCloud® provides exceptional advanced analytical insights able to deliver the smarter studies needed to address today's complex clinical research challenges.

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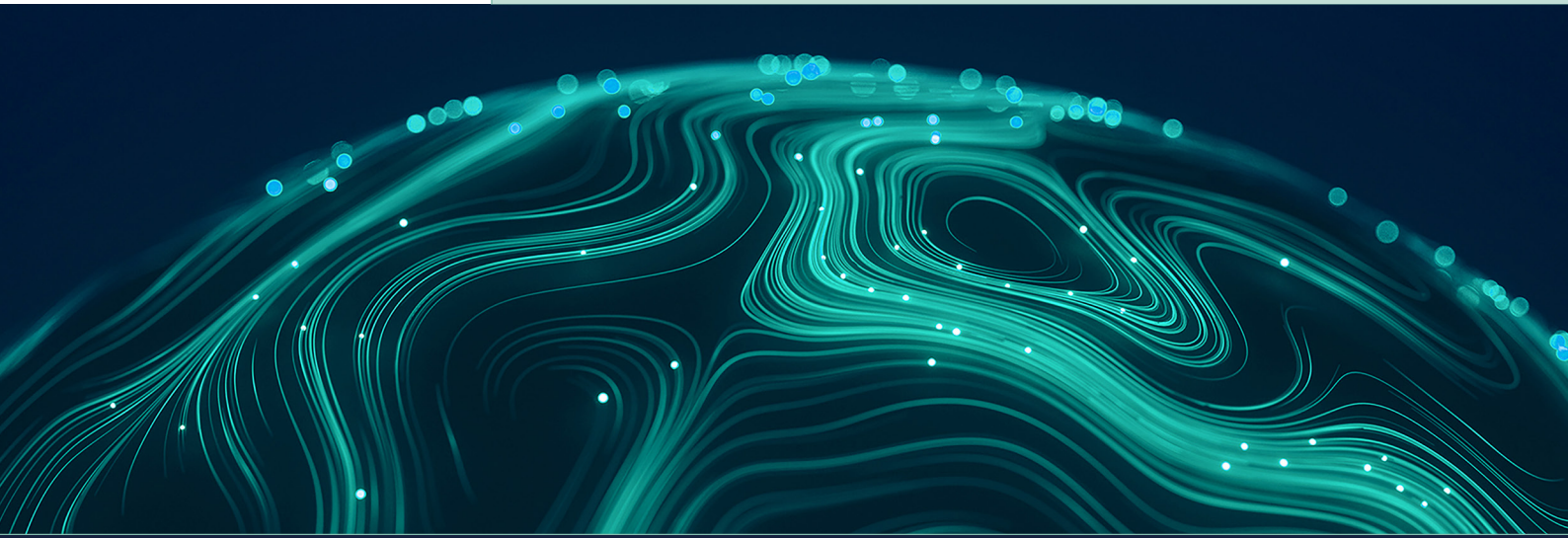
The Challenge

A Sponsor was experiencing recruitment difficulties for an ongoing clinical trial. This meant that it would be difficult to complete the original sample size. External evidence then emerged during conduct of the trial indicating the treatment effect was likely to be larger than assumed in the initial sample size calculation. The Sponsor wished to explore alternative adaptive approaches to the study which would maintain integrity, controlling for false positive rate (alpha) but enabling the possibility of stopping the study early with fewer patients than initially planned, either for efficacy or for futility.



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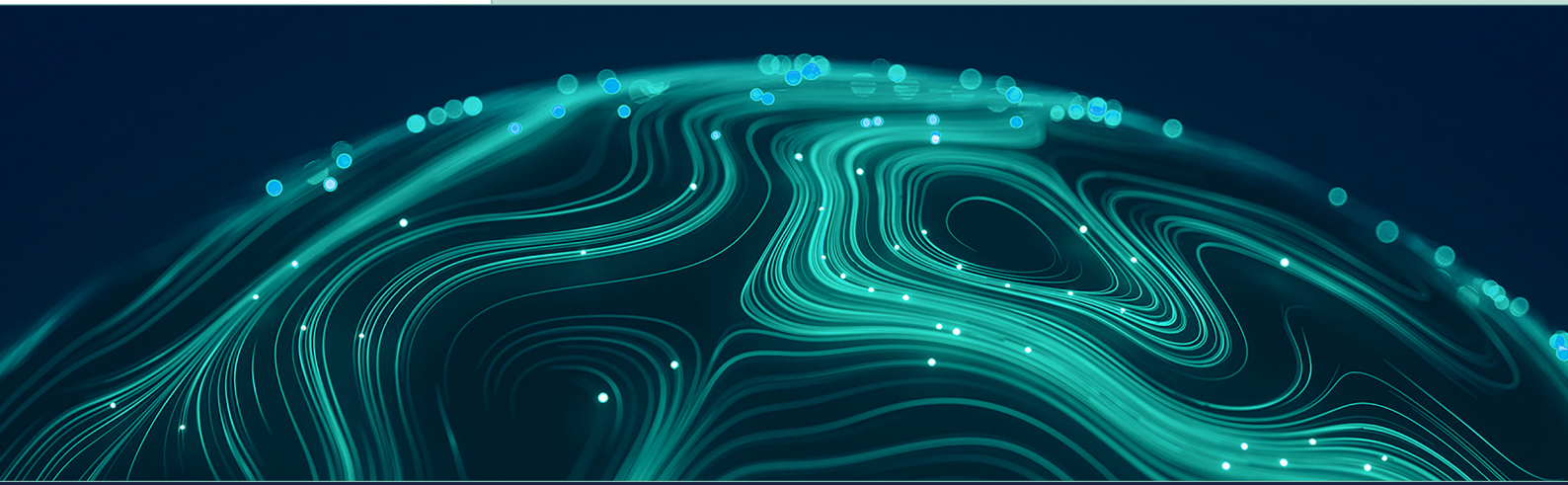
The Approach

KerusCloud® was used to explore different group sequential designs compared to a fixed design with no interim analysis, which would allow the study to stop early for futility or efficacy. This included:

- Different stopping rules for efficacy; Pocock and O'Brien-Fleming
- Whether to include a futility stopping rule or not
- Different timing of the interim analysis; 60% through recruitment, 75% through recruitment
- Different assumed true treatment effect; null, initially expected 10%, updated expected 12%



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The Results

KerusCloud® quantified the overall probability of success (PoS) and operating characteristics (OC) under different true treatment effect size assumptions, and under different design choices (timing of interim and stopping rules. This allowed a multidisciplinary team to:

- **Quantify and debate the merits of different design options.**
- **Make an informed decision which also described elements in the study design which were uncertain.**
- **Decide where they wanted to spend the "alpha" and understand the implications for the overall study in looking at the data part way through for decision-making.**

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The Impact

KerusCloud® provided key insights on sample size and allowed the project team to derisk their study by:

Understanding the benefits of an interim analysis which could ensure:

- **cruiting, then the sponsor could do so with the confidence that this was necessary to obtain the appropriate PoS**
- **an understanding of what the most likely outcome from this interim analysis would be, so that appropriate plans could be put into place**

Identifying the adaptive design that gave the right balance of benefit (smaller average sample size) and risk (probability of making an incorrect decision at interim or final analysis).

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Why MMS?

Expertise In Early Development

The development of investigational drugs is a complex and expensive process with many risks. For over ten years our teams have been supporting and de-risking clinical development with their in-depth statistics and modelling expertise. Our study planning, statistical analysis and programming services add value to early stage development programs by ensuring they deliver the robust evidence needed for incisive, informed decision-making.

With many of our development solutions built around our unique KerusCloud® platform, we can provide exceptional, bespoke, end-to-end biostatistics support from strategic decision-making and protocol development to analysis, reporting and stakeholder engagement.

Robust Evidence Packages

The unique offering of our comprehensive biostatistics services in combination with KerusCloud® ensures that MMS can help to generate strong evidence packages to support regulatory engagement or investment, accelerating development timelines and increasing the value of pipelines.

Let's talk!

If you'd like to discuss this case study further or learn more on how our technology enabled services can support your development project, please visit our website: mmsholdings.com

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