

Case Study

Adapting to recruitment difficulties

Driving Decision Making With An Adaptive Clinical

KerusCloud®

KerusCloud® is a revolutionary simulation-guided study design tool that ensures clinical trials are designed effectively to collect the right data, from 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 Challenge

A sponsor was experiencing recruitment difficulties in an ongoing clinical trial, making the original sample size difficult to complete. During conduct of the trial, external evidence emerged indicating that the treatment effect was likely to be larger than the effect assumed in the initial sample size calculation.

The Sponsor needed alternative adaptive approaches that would maintain study integrity and control the false positive rate (alpha), while allowing the possibility of stopping early – for efficacy or for futility – with fewer patients than initially planned.

The Approach

KerusCloud® was used to compare a range of group sequential designs against a fixed design with no interim analysis, quantifying the ability of each to stop the study early for efficacy or futility. The design space explored included:

- **Efficacy stopping rules:** Pocock and O'Brien-Fleming
- **Futility:** with and without a futility stopping rule
- **Interim timing:** 60% and 75% through recruitment
- **Assumed true treatment effect:** null, the initially expected 10%, and the updated expected 12%

For each combination, KerusCloud® quantified the overall probability of success (PoS) and the operating characteristics of the design.

The Results

KerusCloud® quantified overall PoS and operating characteristics under different assumed true treatment effect sizes and different design choices (interim timing and stopping rules). This enabled a multidisciplinary team to:

- Quantify and debate the merits of each design option against a common set of metrics.
- Make an informed design decision that explicitly described the elements of the study design that remained uncertain.
- Decide where to spend the “alpha”, and understand the implications for the overall study of looking at the data part way through for decision-making.

The Impact

The work gave the project team the evidence to de-risk the study on two fronts.

First, it clarified the value of an interim analysis: the team understood what the most likely outcome of that interim would be, so appropriate plans could be put in place in advance, and could proceed with confidence that the chosen recruitment path was what was needed to achieve the appropriate PoS.

Second, it identified the adaptive design offering the right balance of benefit (a smaller average sample size) against risk (the probability of making an incorrect decision at the interim or final analysis).

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 mmsholdings.com or get in touch info@mmsholdings.com