

Case Study

Precision Medicine

Effective Precision Medicine Strategies With KerusCloud®

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 completed Phase IIb study in Alzheimer's disease had randomised 500 patients across four treatment groups – placebo, or 2mg, 4mg or 8mg of rosiglitazone – equally divided 1:1:1:1 with 125 patients per group, and powered to detect a difference in all-comers.

After the main study failed to meet its primary objective, the standard retrospective approach followed:

- Banked blood samples from around 60% of study participants were analysed. This analysis formed no part of any prospective power calculation, so it was exploratory.
- The objective was to evaluate the ability of numerous candidate genetic markers to explain variability in response, and ultimately to identify a predictive marker that could be used to progress the treatment in a genetic subgroup.

The Sponsor wanted to use the data from this study to explore how the probability of success (PoS) for precision medicine (PM) and pharmacogenetics (PGx) research could be improved through a smarter study design.

The Approach

KerusCloud® was used to construct 'what if' scenarios and evaluate the likelihood of success of the planned retrospective analysis against a smarter prospective design in which PGx was integrated from the start.

To build the simulations, statistics on the population response and on characteristics within each treatment group were extracted from the published study data. Additional information on the interaction between genetic markers, treatment and response was obtained from the literature. KerusCloud® then simulated patient-level data consistent with the published data and literature for two scenarios:

1. **Retrospective analysis** using the original study design.
2. **Prospective design** in which PGx was integrated into the design from the outset.

For each scenario, the probability of detecting a genetically defined subgroup of patients deriving a clinically meaningful benefit was evaluated. Scenario outcomes were reviewed through KerusCloud's interactive heatmap.

The Results

- The original study design had a low chance of success (~20%) of detecting a clinically meaningful subgroup.
- Increasing the sample collection rate could nearly double the probability of success.
- PoS could be increased further by reducing the number of treatment groups and implementing dose-response models, while maintaining the total number of patients.
- Study success rate could be improved by as much as 41% without increasing sample size or cost.

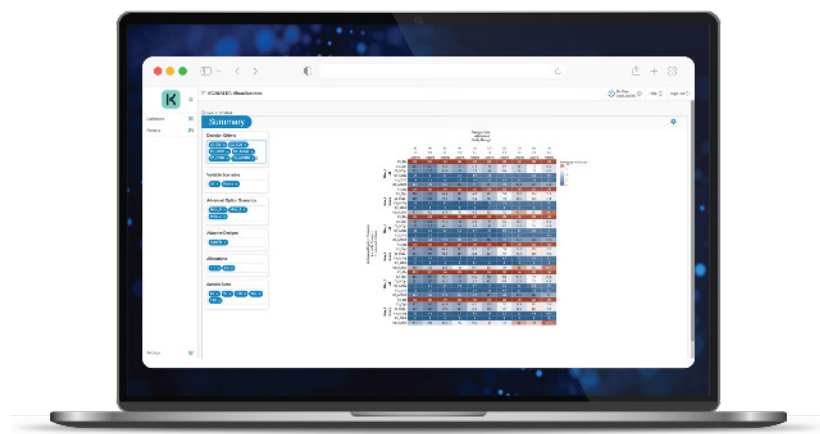
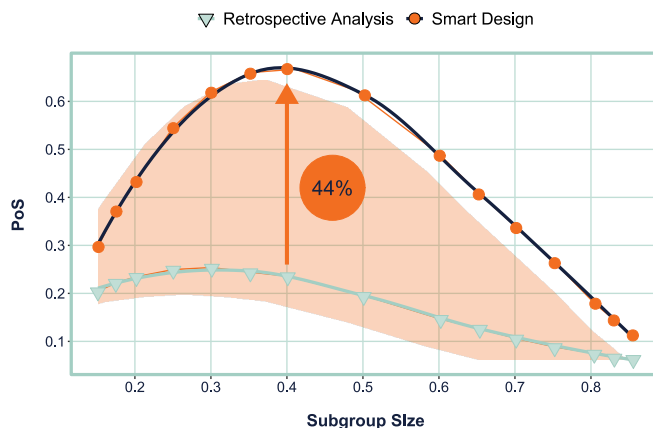


Figure 1. A typical KerusCloud® results

The Impact

Planning the pharmacogenetics prospectively – rather than relying on a retrospective analysis of banked samples – substantially increased the likelihood of study success and the chances of meeting study objectives, on the same sample size and cost base.

On this evidence, prospective simulation-led design offered a route to rescue a development program costing approximately £15–20M, and demonstrated how precision medicine strategies can be implemented successfully within a development program.



A KerusCloud® Smart Design increases Clinical Trial Probability of Success (PoS) by up to 44%

“The early R&D for KerusCloud® was specifically directed towards enabling precision medicine strategies within clinical development programs. This study demonstrated the power of simulation in complex study designs and the results were used as a proof of concept. This supported the continued development of the software platform which ultimately became KerusCloud®.”

SVP of Statistical Consulting, MMS

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