Case Study

Composite Biomarker ————

Building and validating a composite biomarker model to predict emphysema progression

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

Global pharmaceutical company GSK was seeking to build a predictive model to identify patients with worsening emphysema for selecting the right population in chronic obstructive pulmonary disease (COPD) studies. They wanted to understand if KerusCloud® could be used to design the study given that:

- **+** There is no standard approach for designing a validation study for a multivariate model.

- **+** The ability to build and validate a model was limited by the number of available samples.
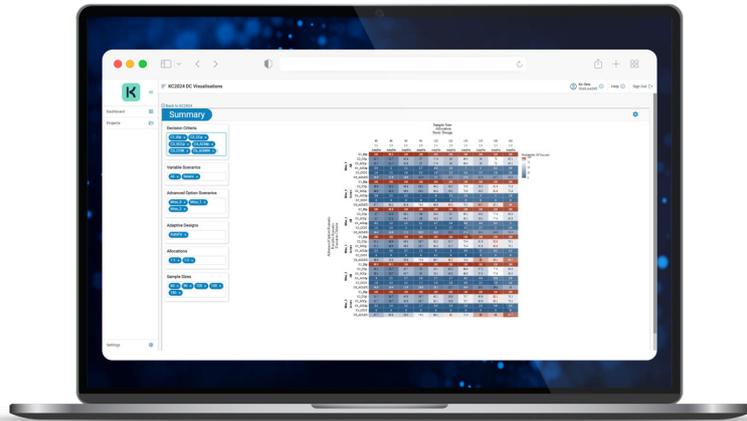
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The Approach

Working in collaboration with GSK COPD Clinical Discovery, MMS used the GSK ECLIPSE study as a basis for building a predictive model involving multiple baseline biomarkers.

+ The biomarker and clinical characteristics as well as the correlation structure was extracted from patient level ECLIPSE data.

+ Validation comprised multiple study objectives relating to the performance of individual markers as well as the overall model.

+ A range of study designs was evaluated for their ability to achieve multiple objectives and a full model (8 biomarkers) and a reduced model (5 biomarkers) were assessed with results explored via a heatmap (Figure 1).

+ Various metrics were derived from thousands of simulated studies including an assessment of the model performance and p-values for individual biomarkers.

Figure 1. A typical KerusCloud® results heatmap

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The Results

KerusCloud® generated realistic data which could be used to evaluate the overall performance of the model and individual markers (Figure 2).

The full model required > 200 samples whilst the reduced model required only 60 samples.

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The Impact

The study demonstrated that KerusCloud® could:

Generate realistic data in silico and be used to design validation studies for multivariate predictive models.

Optimize the model building and validation strategy given the available samples.

Deliver a strategy that required 70% fewer samples for the same probability of success.

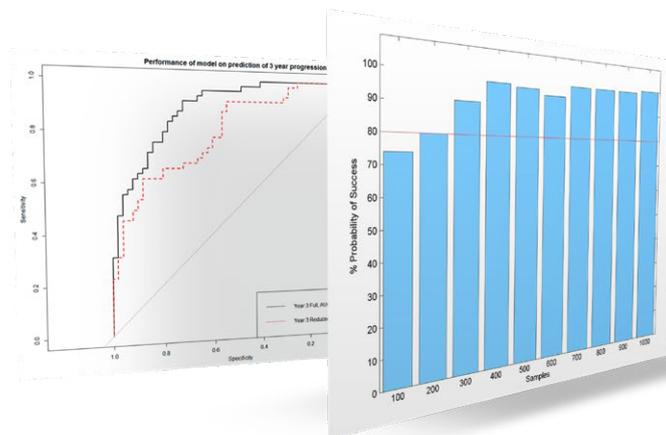Reduce the risk of attempting a study with a low chance of success.

Figure 2. Assessment of model performance and optimal sample size

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"We were extremely pleased with the results of the work. Until MMS became involved we were struggling to come to conclusions about the utility of the biomarkers being evaluated. The results with KerusCloud® provided our team with a solid understanding of the data allowing clear conclusions to be drawn."
Senior Scientific Director, Respiratory TAU, GSK

MMS | **KerusCloud**

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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

MMS. The Difference Is In The Data