

Case Study

Composite Biomarker

Building and validating a composite biomarker model to predict emphysema progression.

KerusCloud®

Building and validating a composite biomarker model to predict emphysema progression.

KerusCloud is a ground-breaking new clinical study design and analytics software platform which delivers smarter real-time studies for today's clinical research challenges.

Using powerful cloud-based processing, **KerusCloud** can handle the diverse and complex data now collected routinely, to deliver advanced analytics which simplify the study planning and decision-making process.

With unique second-generation study simulation capabilities, **KerusCloud** provides exceptional support in developing robust evidence packages for drug approval.

The Challenge

- + The ability to identify patients with worsening of emphysema is important for selecting the right population in COPD studies.
- + Working in collaboration with GSK COPD Clinical Discovery, the GSK Eclipse study was used as a basis for building a predictive model involving multiple baseline biomarkers.
- + 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.
- + Could the simulation capabilities of **KerusCloud** be used to design the study given the constraints?



Testimonial

“ We were extremely pleased with the results of the work. Until Exploristics 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

Building a predictive biomarker model with KerusCloud

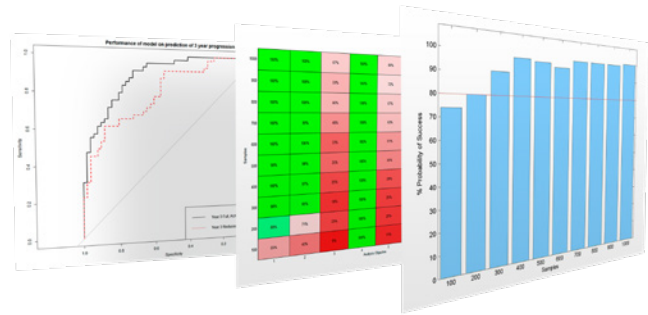
The Approach

The biomarker and clinical characteristics as well as the correlation structure was extracted from 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.

Various metrics were derived from 1000 simulated studies including AUC (of ROC curve) for model performance and p-values for individual biomarkers.



- + Kerus Cloud generated realistic data which could be used to evaluate the overall performance of the model and individual markers.
- + The full model required > 200 samples whilst the reduced model required 60 samples.

The Impact

The study demonstrated that **KerusCloud** could generate realistic data *in silico* and that it is feasible to use **KerusCloud** to design validation studies for multivariate predictive models.

- + It showed that we could optimize the model building and validation strategy given the available samples.
- + The strategy involving the reduced model required 70% fewer samples for the same probability of success.
- + It avoided the risk of attempting a study with a low chance of success.



Discover the power of cloud-based simulation.

Generate Robust Evidence

Develop strong evidence packages to support regulatory engagement or investment, increasing the value of development pipelines.

Optimise Studies for Success

Identify the right development path, optimising the number of patients required to generate the evidence needed to reduce approval timelines, costs and the risk of failure.

Accelerate Development

Accelerate access to novel treatments through better targeting of patient population and selection of outcome measures.

De-Risk Investment

Rapidly evaluate and test the impact of key assumptions to de-risk investment.

Transform Study Planning

KerusCloud transforms study planning with quick and convenient optimisation of study parameters to support the design of complex clinical research trials so you can:

- + Simulate data with correlations and missing values reflecting real-world patients and studies
- + Assess the probability of success for real-world objectives involving tradeoffs between several factors
- + Identify the critical study aspects impacting on the probability of success
- + Compare analysis plans with selections from

