exploristics
INNOVATIVE ANALYTICS SOLUTIONS

Case Study

# Effective Precision Medicine Strategies

Improving success rates in a retrospective Precision Medicine (PM) study approach-based on Pharmacogenetics (PGx).

KerusCloud®

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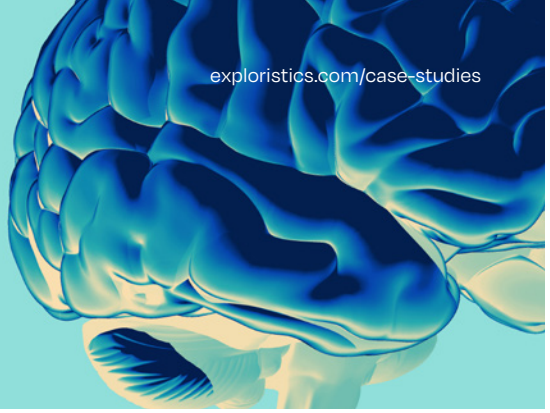

**Over 90% of treatments undergoing trials currently fail to reach the market. Effective study planning and analysis is essential to reduce these failure rates and maximise the chances of a successful treatment development programme.**

**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 diverse and complex data to deliver advanced analytics to support key decision-making within clinical research programs. With unique second-generation simulation capabilities, **KerusCloud** ensures that the best design and analysis approach can be chosen to meet clinical objectives and significantly increase the probability of success.

This case study demonstrates how **KerusCloud** can improve the chances of success for a study where a retrospective Precision Medicine (PM) approach based on Pharmacogenetics (PGx) has been implemented following failure of the main study to meet its primary objective. In this case, PGx may offer key insight into the influence of genetic factors on variability of patient response, allowing the identification of genetic subgroups that derive a meaningful response to treatment. Here, **KerusCloud** shows that prospective optimisation of the study design to meet its objectives could dramatically increase the probability of study success in Precision Medicine.

## The Challenge

- A Phase IIb study in Alzheimer's disease was conducted, comprising 500 subjects randomised into 4 treatment groups receiving a placebo or 2mg, 4mg or 8mg of Rosiglitazone. Subjects were equally divided (1:1:1:1) with 125 subjects per group and the study was powered to detect a difference in all-comers. The study failed to meet its primary objective so a retrospective PGx study was undertaken using banked blood samples from around 60% of the study participants. This analysis did not form part of any prospective power calculations, so it was considered to be exploratory.
- The objective of the PGx study was to evaluate ability of numerous candidate genetic markers to explain the variability in response and ultimately to identify a predictive marker that could be used to progress the treatment in a genetic subgroup. In this study, we construct some what-if scenarios in **KerusCloud** and evaluate their likelihood of success.

## Testimonial

"The early R&D for **KerusCloud** was specifically directed towards enabling precision medicine strategies within clinical development programmes. 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**.

**CEO, Exploristics**

# Increasing PM success with KerusCloud

## The Approach

Statistics on the population response 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.
These statistics were used to randomly generate patient level data consistent with the original characteristics and assumptions.

Study data was simulated 1000 times using **KerusCloud** for two scenarios: performing a retrospective analysis using the original study design; prospectively designing a smarter study where PGx was integrated into the design. For each scenario, we evaluated the probability to detect a genetically defined subgroup of patients who derive a clinically meaningful benefit.

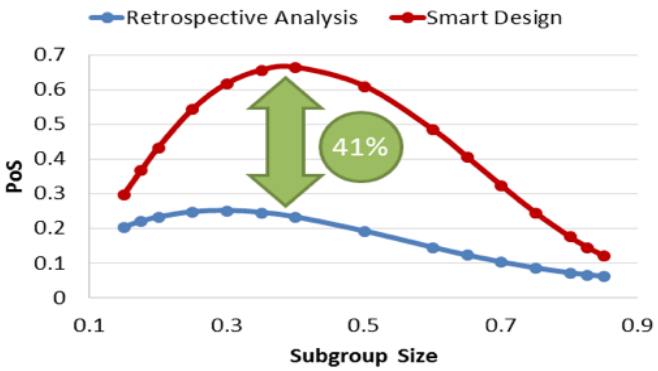


**Figure 1:** The Probability of Success (PoS) for each scenario evaluated on **KerusCloud**. A smarter design significantly outperforms the retrospective approach without increasing the cost.

## The Impact

**KerusCloud showed that:**

- **The original study design had a low chance of success (~20%) to detect a clinically meaningful subgroup.**
- **Increasing the sample collection rate could nearly double the PoS.**
- **PoS could be further increased by reducing the number of treatment groups and implementing dose response models whilst maintaining the total number of subjects.**
- **Overall, study success rate can be improved by as much as 41% without increasing sample size and cost, as shown in Figure 1.**
- **Therefore, prospective study planning with KerusCloud can increase the likelihood of study success over the retrospective approach alone and improve the chances of meeting study objectives.**
- **Using KerusCloud offers the potential to rescue a development programme costing £15-20M.**
- **KerusCloud enables the successful implementation of Precision Medicine Strategies.**

**Published in Drug Discovery Today**, 2011; **Preventive and Predictive Genetics**, 2015.

# KerusCloud®

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 the comprehensive analysis suite