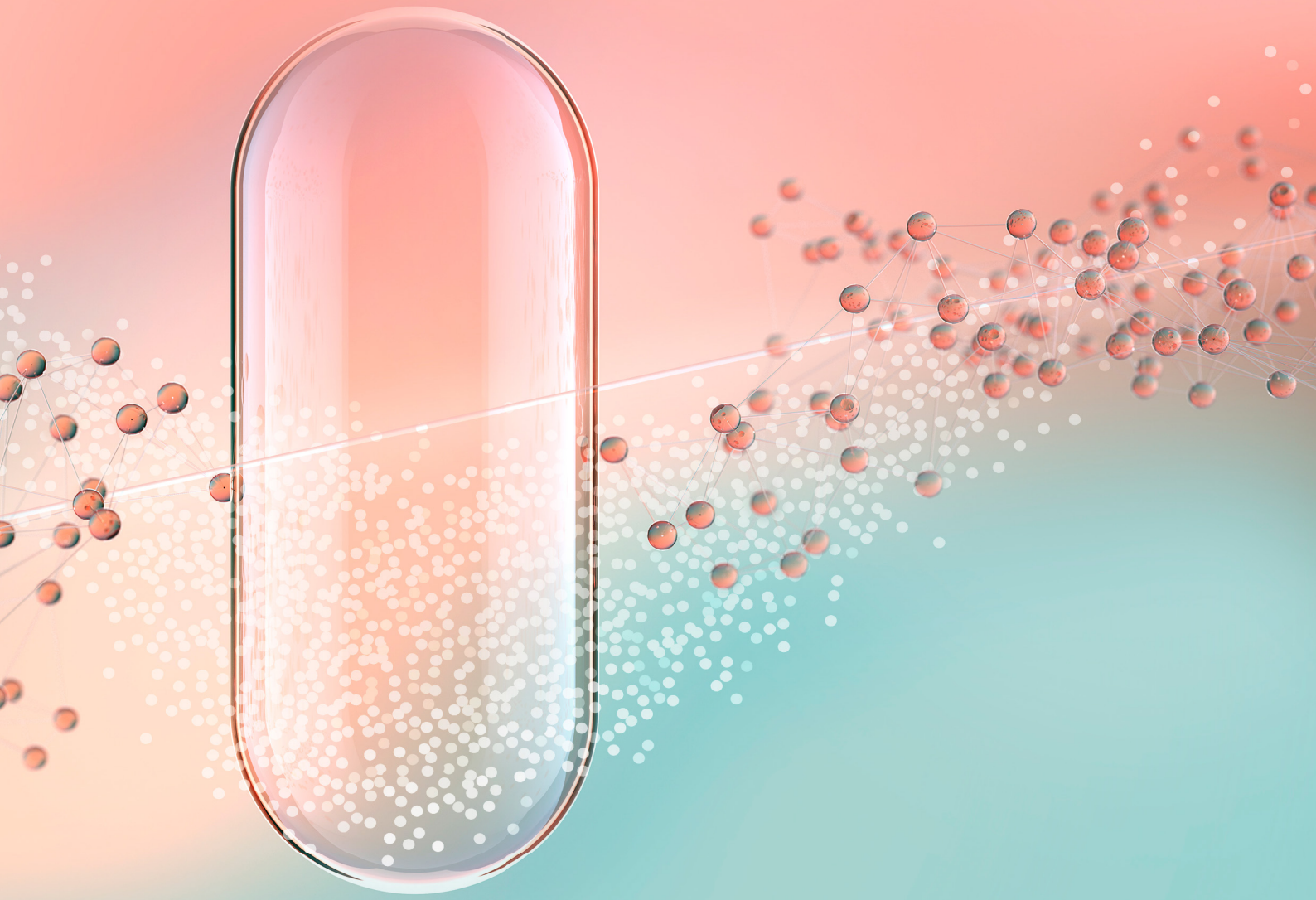
exploristics
INNOVATIVE ANALYTICS SOLUTIONS



KerusCloud Use Example

De-risking once a study has initiated, adapting to new information

Re-evaluating the probability of success (PoS).

KerusCloud®

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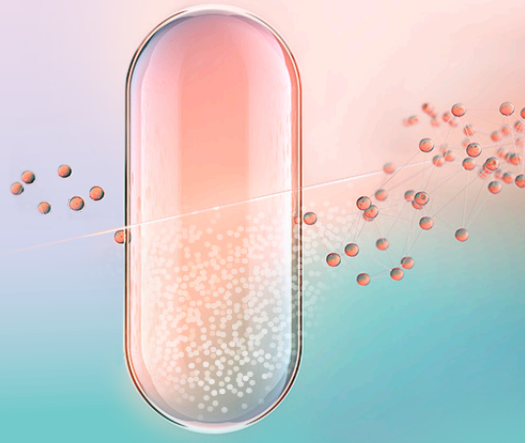


The Challenge

A sponsor biopharmaceutical company was running a clinical trial to examine the effect on an inflammatory biomarker of interest in patients treated with an investigative treatment versus placebo. Following initiation of the trial, two things changed:

Change 1

It emerged that the treatment effect was potentially larger than originally expected at the study design and planning stages. This meant that the original sample size was probably conservative.

Change 2

During the recruitment period the COVID-19 pandemic occurred, causing the planned sample size to become logistically difficult to achieve.

Considering these changing circumstances, the sponsor wished to re-evaluate the probability of success (PoS) for the study if it was adapted to include fewer patients than initially planned.

The Approach

Exploristics carried out additional literature searches to obtain relevant background information on the clinical biomarker of interest to inform the strategy for the simulation work. This identified two critical design assumptions that were not considered at the initial design stage:

- **Assumption 1** correlation between baseline and post dose biomarker value
- **Assumption 2** truncation of biomarker data due to values outside lab range

KerusCloud study simulation software was used to quantify the Probability of Success (PoS), going beyond the original sample size calculations to simultaneously evaluate multiple design and efficacy 'what if' scenarios. KerusCloud simulates patient level data and so was able to create virtual patient populations which could reflect the real-life data we would collect in the study, for example the truncation of biomarker data. The following scenarios were considered:

- a range of assumed expected effect sizes (including larger than originally planned)
- a range of assumed correlations between baseline and post dose (given the true underlying value was unknown)
- different recruitment design decisions between 60% and 100% of the planned sample size

The Results

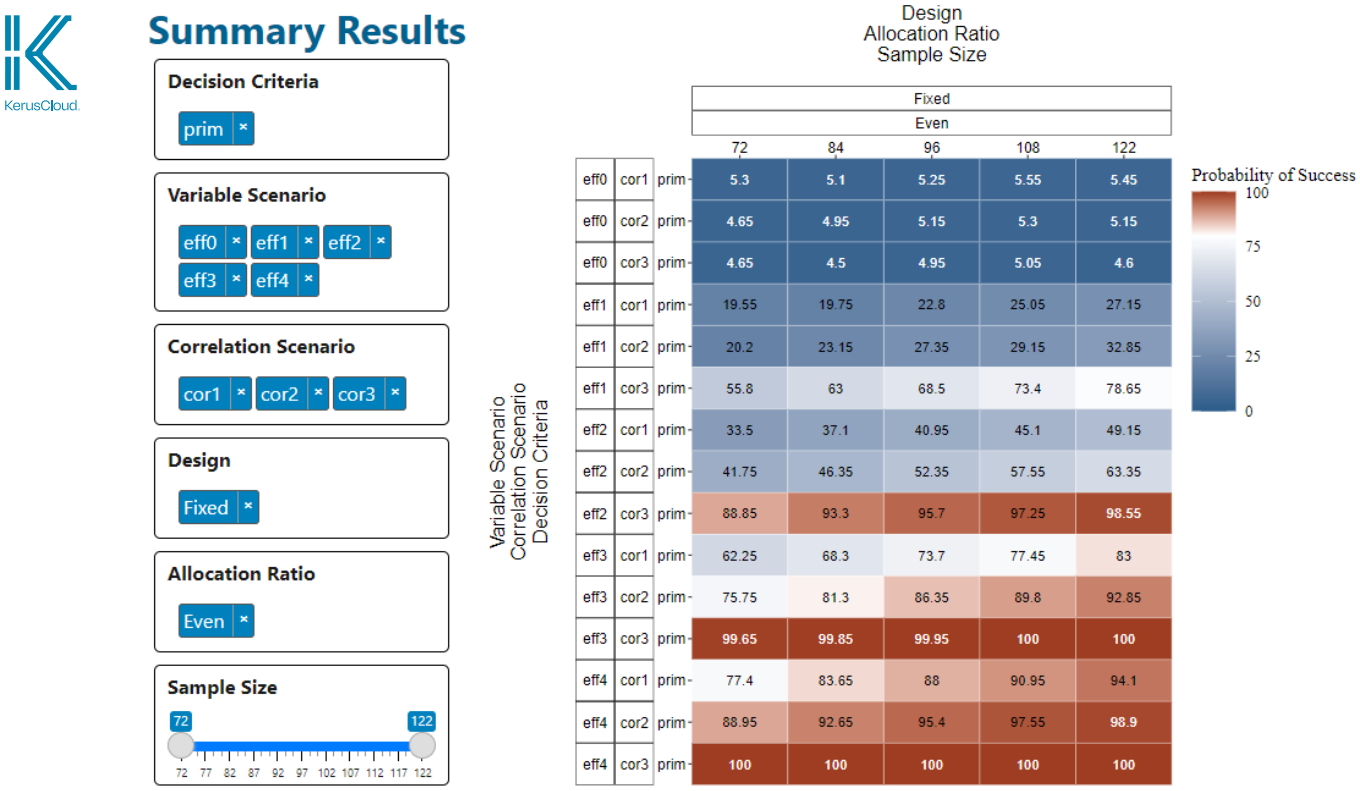
KerusCloud was used to rapidly quantify the PoS for these scenarios and then visualise in an interactive heatmap (Figure 1).

The PoS heatmap **identified a previously hidden risk;** the importance of the baseline to post dose correlation.

Simulated scenarios indicated that **this correlation was a key driver of success** and the study as **originally planned was underpowered** if the correlation was below 0.9.

The risk associated was **quantified** and the team could plan to **mitigate** this; by examining the correlation between baseline and post dose in a blinded fashion to provide **key information for planning.**

Figure 1. A KerusCloud heatmap showing the PoS values for different study scenarios, where dark blue indicates very low PoS and dark red indicates very high PoS.



The Impact

Simulation with KerusCloud provided key insights for the team when making decisions around the required sample size to support the design of this clinical trial, highlighting the benefits of simulation to fully explore the risks for a study.

- Its use identified the importance of the baseline to post dose correlation in this study, enabling mitigation for this risk to be put in place through a blinded ongoing review of the data.
- KerusCloud identified a viable design with an improved recruitment/risk profile relative to the original sample size calculation.
- These insights gave the company a more flexible recruitment strategy, de-risking the study while saving time and costs.