CALYX™

CASE STUDY

LG Chem Randomization Challenge Resolved by Calyx IRT

SITUATION

LG Chem was looking to outsource two trials, one of which had a complex randomization design: the randomization ratio was 10:10:10:10:1 and it included three stratification factors. Some strata targets were relatively low, increasing the risk of not fulfilling the allocation ratio within each possible stratum level. In addition, the protocol design stated that at month six, subjects randomized to the placebo arm would stop treatment and be considered as having completed the study.

CHALLENGE

A typical randomization design using a blocked list would require a very large block size of 41, which was not appropriate, considering the low recruitment target for some strata. Although a list could be built to meet those requirements, the sample size was not large enough to fill a block for each stratum, which would inevitably result in an imbalance of the allocation ratio at the end of the trial.

LG Chem was was also concerned that the population in a stratum may be too low to include all treatment arms. Without the right randomization design, LG Chem might need to increase recruitment targets, subsequently increasing study timelines and budget.

An additional challenge was the potential partial unblinding of the subjects within the same block as a placebo subject who reaches month six.

SOLUTION:

One of Calyx's randomization experts was engaged in discussions with LG Chem during the IRT vendor selection process and throughout the study setup phase. They shared their point of view from a biostatistical aspect, and challenged the randomization design to confirm what could and could not be achieved through a blocked list.

They concluded that the risk of imbalance was too high to use a typical blocked list randomization approach and discussed the concept of minimization with LG Chem.

To highlight the relevance of a minimization design, they ran a simulation through a proprietary SAS program, which provided an idea of the balance across treatment arms and strata. The simulation was used to demonstrate the impact of various minimization algorithm parameters, helping the study team select the right settings in IRT.

For example, when using a dynamic randomization method such as minimization, the ICH-e9 advises that a random element is used within the process to make it non-deterministic. The size of the random element was investigated through simulation, along with the usual stratum weights, for the given populational characteristics of stratum recruitment. The random element is a powerful tool to reduce the predictability of assignment but can also affect the allocation ratio achievable with a small recruiting stratum group.

The simulation exercise provided a useful visualization of how minimization parameters would impact the study outcome, giving the LG Chem team confidence that the IRT randomization design would be suitable. The Calyx project team used Calyx's own pre-validated parameterized minimization module for the 'Pocock and Simon Method of Minimization with Biased Coin Assignment,' which reduces the risk usually associated with 'bespoke programming' of such complex randomization methods. The module includes a full audit trail of each randomization event, allowing one to review why a patient was assigned to a specific treatment arm, and what calculations were done by the system.

RESOLUTION:

The LG Chem study team trusted Calyx to meet the protocol's complex randomization design, with adequate settings that ensured the right balance between treatment arms. Calyx's expertise was a key component to the success of the trial setup.

> "We relied heavily on Calyx's IRT expertise and followed their recommendations for overcoming our studies' challenges, resulting in a solution that perfectly met our RTSM needs for two complex gout trials."
>
> LG Chem

Book a meeting with Calyx randomization experts to learn more about minimization and other advanced RTSM algorithms to drive your trial's success.

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Reliably solving the complex.

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