CASE STUDY

EMERALD CLINICAL TRIALS

Emerald Clinical Meets Challenging Recruitment Targets in Complex Renal Trial

As a strong proponent of trial innovation with experience in quickly adapting to complex and fluid operations, Emerald Clinical was the ideal partner for the SONAR trial.

SITUATION

Emerald Clinical was contracted by a large biopharmaceutical company to run operations in the APAC region for SONAR, a randomized, multi-country, multicenter, double-blind, parallel, placebo-controlled study of the effects of a selective endothelin-A receptor antagonist on renal outcomes in subjects with type 2 diabetes and nephropathy. Emerald Clinical also provided scientific leadership and managed endpoint adjudication for the trial globally.

This class of drugs had never been tested to the full extent in patients, although in the pre-clinical work it was very promising despite potential risks.[1] In SONAR, researchers were able to minimize the known risk of sodium retention and optimize the efficacy of the drug on patients in two ways. One was a carefully selected drug dose. The second was an Enrichment Design which excluded sensitive patients, selecting patients for a substantial albuminuria reduction and minimal clinical signs of sodium retention.

Enrichment designs where randomization is based on biomarker expression, like in the SONAR trial, can be an efficient way of determining the benefit-risk in the biomarker-positive population. **Katherine Tuttle (University of Washington, Seattle, USA) said that SONAR "demonstrates a turning point in trial innovation," and "succeeded in shifting trial design to match patients with treatment on the basis of safety and response assessments during a pre-randomization enrichment period."**[2] This innovative approach to clinical trials can help to facilitate future clinical trial conduct leading to smaller and more efficient trials.

As a strong proponent of trial innovation with experience in quickly adapting to complex and fluid operations, Emerald Clinical was the ideal partner for the SONAR trial. As part of the Steering Committee of SONAR, our scientific leaders designed this complex study, and in the APAC region, helped maintain a strategic approach to engage sites, interacted with site personnel and helped minimize patient dropout and low retention. The level of hands-on support that Emerald Clinical's people are always willing to give was crucial in overcoming the many challenges faced.

CHALLENGES & SOLUTIONS

Challenge: Complex study design including enrichment phase; less complex competing studies recruiting at the same time.

Solution:

Emerald Clinical's Scientific Leadership model of operations was critical in overcoming this challenge in the APAC region as our Regional Scientific Leader on

---

[1] Endothelin receptor antagonist gives renoprotection in selected patients with T2DM and CKD: Prof. Dick de Zeeuw, MD: ISN World Congress of Nephrology, Melbourne, Australia, April 15, 2019.

[2] SONAR results support atrasentan for preserving renal function in type 2 diabetes: medwireNews: Medicine Matters diabetes.

this project, Dr Muh Geot Wong, who is also a clinician, engaged sites in discussions around recruitment strategies from a clinical perspective. Although novel trial designs provide unique opportunities to expedite drug development, they require thoughtful planning and implementation. Emerald Clinical met these challenges by ensuring rigorous engagement, communication and collaboration among all involved parties. Our scientific leaders with clinical experience helped sponsors/sites to maintain focus on scientific goals while enhancing patient involvement and recruitment efficiency.

In addition, a high potential program was set up for countries such as South Korea and China to engage sites in a way that signaled their preferential treatment as high recruiters. Specific strategies were devised to engage sites with large subject pools to maximize their recruitment capabilities. Multiple teleconferences with scientific leaders to keep communications flowing were scheduled to ensure that sites in all countries could easily participate at "best possible" times. Emerald Clinical's team encouragement and good experience sharing among all sites resulted in a successful recruitment strategy.

Challenge: Long study duration, risk of patient dropout and low retention.

Solution:

Emerald Clinical goes into every study strategically prepared to minimize patient dropout and maximize retention by pre-trial planning, including less burdensome protocol design, setting clear expectations for sites and patients, choosing the best patients for specific studies, and generally taking patient needs into consideration as much as possible. Continued/regular site engagement was assured with regular study newsletters, including shared experiences with other sites.

Emerald Clinical employs a concierge approach to site relationships and develops site partnerships built on consistency of engagement and trust that goes beyond site activity monitoring. These closer relationships in the SONAR study meant that sites could rely on their CRAs in a way that is unique to Emerald Clinical. Our low turnover of team members and regional medical monitors in the APAC region allowed site relationships to develop and ensured that best scientific support was being given to sites over the life of the study.

Emerald Clinical's Dedicated Global Endpoint Adjudication Team

Specializing in cardiovascular and renal endpoints, Emerald Clinical's endpoint adjudication team has managed the review of thousands of endpoints across a range of trials from smaller outcomes to large, global, registration studies. Our team consists of medically trained professionals to provide leadership and medical oversight, and specialized operational staff to coordinate the endpoint collection and adjudication process. Located at the best institutions across the globe, our adjudicators have extensive experience in adjudicating clinical endpoints, and often chair endpoint adjudication committees. Using a validated web-based endpoint management system, Emerald Clinical manages endpoint adjudication activities to the highest scientific and operational standards.

Challenge: Sponsor requirement for recruitment of a very specific population.

The sponsor required 200 Chinese patients for Chinese registration of the Investigational Product, which caused recruitment to continue in China beyond the Recruitment Open Window (ROW) timeline.

Solution:

In order to avoid demotivation of sites, Emerald Clinical prepared sites with early and clear communication that they would stay open for longer than ROW to meet recruitment goals in their site-level contracts. Sites clearly understood the importance to the success of the study of these additional requirements, felt fully supported and remained committed to completing the special recruitment successfully

RESULTS

Difficult recruitment goals for a complex trial met and global endpoint adjudication managed successfully. Although the trial was ended early, findings resulted in very beneficial information for future diabetic kidney disease research.

- Emerald Clinical was able to exceed the sponsor required recruitment target, including the recruitment of 200 patients from China, within study timelines.
- Emerald Clinical met original contracted metrics for sites and patients enrolled.
- Although trial was stopped early, trial results showed a 35% risk reduction in the primary endpoint over placebo in the enriched population of patients with a very good safety profile. The decision to close the SONAR study early was not related to any safety concerns.