CASE STUDY

George Clinical
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George Clinical's Scientific Leadership Achieves Exceptional Integration Between Science and Operations with Unprecedented Low Rates of Loss to Follow Up and Withdrawal of Consent

Landmark CREDENCE renal outcomes trial stopped early based on achievement of pre-specified efficacy criteria.

SITUATION

Five million people are predicted to have kidney failure by 2035. This is a global problem causing not only a diminished quality of life for patients, who are at risk for many adverse health outcomes, but also creating great societal and financial costs worldwide. Finding better ways to try and improve those outcomes, or more importantly, prevent people from reaching kidney failure, has been a real passion for the scientific leadership teams at George Clinical and The George Institute of Global Health for over 20 years, and it's an area where we have seen some real success.

CREDENCE was the first dedicated renal outcomes trial in patients with chronic kidney disease and type 2 diabetes. This randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial evaluated the efficacy and safety of canagliflozin versus placebo in preventing clinically important renal and cardiovascular outcomes in these patients. The trial enrolled approximately 4,400 patients in 34 countries.

Due to the global nature of CREDENCE and the critical importance of recruitment and retention to its success, it was extremely beneficial to have an experienced team of medical and scientific experts to oversee the trial globally from a top-tier level.

Aside from positioning the study on answering the fundamental scientific question aiming to address a key clinical need, George Clinical ensured that all scientific stakeholders remained engaged with the study and had clear roles, responsibilities and an accountability structure.

George Clinical was a natural fit to be selected to manage the academic-led steering committee and the broader scientific leadership team that provided oversight of CREDENCE. Our research scientists are leaders in the renal field with a track record of developing new strategies for the treatment and prevention of kidney disease across diverse populations. With over two decades of experience in renal research and multi-national collaboration, our teams are able to ensure effective study operations that are integrated with scientific focus, accelerate recruitment and ensure the most accurate outcomes possible. Their expertise in outcome studies includes the recent CANVAS and CANVAS-R trials exploring the same drug class. Their understanding of multi-national collaborations was a critical factor in making sure that despite language, cultural and clinical practice differences, all involved would be "speaking the same language" with regard to the key aspects of the trial.

CHALLENGES

Integration of scientific leadership with the operations of a large CRO across 690 sites in 34 countries posed significant challenges, from managing a large workforce to maintaining focus on the unified scientific purpose of the study and sustaining consistent and relevant communications. With so many stakeholders across multiple time zones, keeping everyone engaged in open dialogue was essential to understanding and adapting to the varying ways in which different countries manage kidney disease and define key endpoints.

Limiting loss to follow up and withdrawal of consent are always a major concern in any clinical trial, but in a trial of such magnitude that is endpoint driven, it was critical to keep this ultimate loss of data to a minimum. With so much at stake and so many variables, it was extremely important to ensure that at trial's end, there would be no questions as to the quality of the trial.

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SOLUTIONS

Organizational Structure

George Clinical's teams of scientific leaders and project management specialists are located across our operational hubs in the Asia-Pacific and globally and have extensive experience in multi-national collaboration. They were able to establish efficient organizational oversight of the trial through a coordinated structure for management and communications including Regional Scientific Leaders in the Americas, Asia and Europe, as well as National Leaders in each country represented in the study. This system ensured that there was a designated point of escalation between the sites and operational teams, the sponsor, and the steering committee, and guaranteed a smooth flow of both scientific and operational information between key stakeholders in both directions.

Training and Country-Level Planning

During the recruitment phase of the study, the George Clinical scientific managers worked closely with the sponsor to provide detailed and engaging training to investigators. Country-level recruitment plans were developed through close collaboration with National Leaders in order to hear their concerns and take into consideration specific situations, questions or needs related to their respective locations. As our scientific leadership team are also clinician researchers, they have a patient-focused approach to recruitment and retention that partnered well with the National Leaders to determine the best pathway for each country.

Peer-to-Peer Communication Strategy

George Clinical has always valued peer-to-peer communication to enhance operations and outcomes in research and clinical trials. Our team set up regular webinars that allowed investigators to discuss not only important study information, but also broader scientific issues of interest. George Clinical scientific teams supplemented the usual CRO operational escalation pathways through the site monitors which allowed additional issues to be identified and quickly resolved. Our teams maintained a close hands-on approach that included continuous review of recruitment and retention data with the scientific team to quickly identify any sites/countries of concern and to proactively address any potential problems.

Keeping Communications Current

George Clinical scientific leaders knew that National Leaders would have heavy workloads and that up-to-date information would be critical for a study of this

size and magnitude to be effective. Our team prepared important study communications for the National Leaders, as well as content for site engagement. This ensured that the National Leaders were working with the most current information possible and remained focused on investigator interactions and support.

"One very important element to the success of CREDENCE was having a really connected team with a unified purpose that stayed engaged with the science. Our medical and scientific leadership maintained open communication with our investigators and coordinators throughout the trial. With so many individual national characteristics and viewpoints from different kinds of practitioners, we shared a lot of unique insights into what the problem was and why we thought SGLT2 inhibitors might help. The result of all these discussions was a really engaged team. And now we have a once-in-a-generation result for the treatment of kidney disease. This trial has shown the SGLT2 inhibitor canagliflozin reduces kidney disease progression by around one third and even showed a reduced need for dialysis and transplantation. That's a transformational result." Meg Jardine, Program Head, Innovative Kidney Research at The George Institute for Global Health, Head, Renal Trials, George Clinical and member of the CREDENCE steering committee.

RESULTS

- CREDENCE was so successful that the study was stopped early by the data safety monitoring board on an interim analysis when they found overwhelming efficacy. Canagliflozin is the first new therapy in more than 15 years for slowing the progression of chronic kidney disease in patients with type 2 diabetes.
- High degree of engagement of all investigators throughout the study was achieved.
- Unprecedented subject retention was achieved through to endpoint determination.
- VERY low rates of withdrawal of consent (0.1% – ALL BUT SIX PARTICIPANTS).
- 90% of participants agreed to full follow up as per the protocol.

George Clinical is proud of our participation in CREDENCE where we ran the operations in India, provided medical monitoring for the APAC region, and managed endpoint adjudication and scientific leadership for all 690 sites in 34 countries. The successful integration between scientific leadership and operations provides an excellent model for future trials.