CASE STUDY

George Clinical
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George Clinical's Renal Experience Proves Valuable in Largest Corticosteroid Study in IgA Nephropathy

The determination of strong scientific leaders keeps trial on track to provide valuable data.

SITUATION

Despite optimal current care, up to 30% of people suffering from IgA nephropathy (IgAN) will develop kidney failure requiring dialysis or kidney transplantation. The largest corticosteroid trial in IgAN completed to date provided valuable and much needed evidence on the risks and benefits of corticosteroids regimens when used in IgAN to delay progression of this disease. This international, multicenter, double-blind, randomized clinical trial enrolled 500+ participants from nearly 70 sites around the world. Although the study was temporarily halted due to high levels of side effects among participants receiving the therapy, recruitment recommenced after trial modifications to a lower-dose regimen.

This unusual study was investigator initiated by the George Institute for Global Health with George Clinical contracted to conduct the study worldwide. Among the George Institute scientific leaders who developed the study and led the Steering Committee (SC) were George Clinical collaborators Prof. Vlado Perkovic (Steering Committee co-chair), Prof. Vivekanand Jha (India National Lead), Prof. David C. Wheeler and Assoc. Prof. Muh Geot Wong (Global co-lead) who also served as a lead investigator.

Largest corticosteroid trial in IgAN completed to date provided much needed evidence.

	An unusual investigator-initiated study by the George Institute for Global Health with George Clinical contracted to conduct the study worldwide.
	George Clinical's renal KOLs were pioneers in getting patients enrolled in the Asia-Pacific, where IgAN is known to be more common and more likely to lead to dialysis.
	The high caliber and deep experience of the involved scientific leadership meant that protocol amendments were made with a clear rationale and great consideration for patient safety.
	The evidence generated provided concrete and valuable information on corticosteroids use in people with IgAN at high risk of disease progression, despite maximum standard of care.

CHALLENGES

Recruitment was the major challenge, with over 900 patients screened at nearly 70 sites. Based on the advice of the Data Safety and Monitoring Committee (DSMC), the study was halted due to excess adverse events, and an interim analysis of data collected was performed and published. Under the leadership of the SC, the study protocol was modified with ongoing follow-up of all participants. Ultimately only a few more than 500 participants were randomized.

SOLUTIONS

In a decades long relationship between The George Institute and George Clinical, the best renal scientific minds in the world have collaborated in a peer-to-peer network to explore new avenues for kidney disease treatments. George Clinical's renal KOLs were pioneers during recruitment of this study, getting patients enrolled in the Asia-Pacific region where IgAN is known to be more common and more likely to lead to dialysis.

When the trial had to be suspended due to the safety concern of adverse events, participants recruited up to that point were unblinded, and a transitional analysis was published. The trial was then modified and transitioned to a lower-dose regimen. The sound decision making of the SC and the regional and local influence of the renal scientific leaders—as well as dedication and efficiency of the medical monitors, investigators and site staffs—were instrumental in ensuring that the study was able to continue to successful completion despite the setbacks.

RESULTS

This landmark study was able to be completed after modification, with a majority of patients followed up on until the end of the trial. The evidence generated provided concrete and valuable information of corticosteroids use in people with IgAN. This information is likely to strengthen the evidence-based KDIGO 2021 Glomerular Diseases Guidelines and the need for an informed choice discussion between the patient and clinician in using corticosteroids in IgAN.

The high caliber and deep experience of the involved scientific leadership meant that protocol amendments were made with a clear rationale and with great consideration for patient safety. As these researchers were also experienced clinicians, they balanced their strong awareness of the patients' priorities against the importance of completion of a well-designed investigator-initiated trial to address the dilemma in corticosteroid use in IgAN.

Despite the setbacks, this trial did suggest that a course of reduced-dose corticosteroid can effectively protect kidney function in people with IgAN at high risk of disease progression, despite maximum standard of care. The lower dosage also comes with a lower risk of adverse events.