The STOP-ACEi Trial – Clinician's Summary

Recent research has indicated that discontinuing ACEi/ARB treatment may improve or stabilise renal function in patients with advanced progressive CKD. If confirmed, this observation has profound clinical implications. In the STOP-ACEi trial, participants with progressive stage 4 or 5 CKD will either continue with their existing ACEi/ARB therapy or discontinue these treatments, having their blood pressure controlled by other means.

Though the trial is driven by evidence showing that withdrawal of ACEi/ARBs may be beneficial for patients with advanced CKD, we recognise concerns you may have about this intervention, particularly for patients with high cardiovascular risk. This has been carefully considered in the trial design and we summarise the current evidence here.

A large meta-analysis of 26 randomised controlled trials provides strong evidence that while lowering blood pressure effectively reduces cardiovascular events, ACEi/ARBs do not have any superiority over other antihypertensives in reducing cardiovascular events in patients with or without kidney disease (Blood Pressure Lowering Treatment Trialists' Collaboration, BMJ 2013;347:f5680). A large study in patients with high cardiovascular risk indicates that combined ACEi/ARB therapy worsens renal outcomes (the ONTARGET study; Mann JF et al., Lancet, 2008. 372(9638): 547-53) and another recent study suggests that withdrawal of ACEi/ARB in advanced CKD may be beneficial (Ahmed AK et al., Nephol Dial Transplant 2010; 25 (12):3977-82). Additionally, multiple randomised controlled studies in dialysis patients have shown increased cardiovascular events with use of ACEi (Zannad F et al., Kidney Int 70; 1318-1324, 2006; Chan KE et al., Kidney Int 80; 978-985, 2011.).

Participants will be monitored throughout the study, including with an ECG every year and BP measurements at each visit. For participants that have stopped their ACEi/ARB treatments, blood pressure can be controlled by any other antihypertensive and if the clinical status of a participant requires use of ACEi/ARB at any time, these can be used. The trial is being overseen by an independent Data Monitoring and Ethics Committee who will be closely monitoring patient safety and incidence of cardiovascular events throughout the trial.

It is currently unknown whether withdrawal of ACEi/ARB could worsen outcomes and there is no evidence that ACEi/ARB withdrawal causes worse heart failure or an increase in cardiovascular events in patients with declining kidney function. Indeed, one could apply the reverse that continuing ACEi/ARB could make stable heart failure worse as a result of continued renal deterioration, worse fluid retention and higher cardiovascular risk. In practice, some clinicians withdraw these agents in patients with advanced CKD, but others do not. It is important for care of patients that controversy and debate evolves into evidence-based guidelines. The results of this trial are needed to better inform treatment of advanced CKD with ACEi/ARB.

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