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CLINICAL TRIALS

High-impact session from kidney week

The high impact clinical trial session at this year's kidney week featured seven studies, all of which were widely commended for being well designed and conducted. Three of the study reports were simultaneously published in the *New England Journal of Medicine*. Although space here is limited, this research highlight will endeavour to provide an overview of the session.

The CORONARY study was presented by Amit Garg. In a randomized clinical trial, it has never been shown that reducing the risk of acute kidney injury (AKI) can improve outcomes in terms of long-term kidney damage. This trial aimed to address this gap in the literature by randomly assigning 2,932 patients to coronary-artery bypass grafting either with a beating-heart technique (off-pump) or with cardiopulmonary bypass (on-pump).

As expected, off-pump treatment significantly reduced the risk of AKI compared with on-pump (17.5% versus 20.8%); however, no significant difference in kidney function 1 year after surgery was evident between the two groups. Although this result is disappointing, the study indicates that mild AKI might not have a long-term effect on kidney function, calling into question its use as a marker in clinical trials.

Next, Glenn Chertow presented the results of the BEACON clinical trial in which patients with type 2 diabetes mellitus (T2DM) and stage 4 chronic kidney disease were randomly assigned to bardoxolone methyl or placebo. The trial was terminated on the recommendation of the data and safety monitoring committee because of the higher rate of cardiovascular events that occurred in the intervention group. What are the lessons to be learnt from this study? Chertow suggested that we should be cautious in the early phases of clinical trials. Although extra visits can be burdensome to staff and patients, we have a duty of care to the patients who take part in trials. That is, we must conduct rigorous research while

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preventing the possibility of approving drugs that should not be available to the general population.

The VA NEPHRON-D trial, presented by Linda Fried, also had a negative outcome. The study assigned 1,448 patients with T2DM and diabetic nephropathy to receive losartin. In the next stage of the study, the population was randomly divided into two arms: those who received lisinopril and those who received placebo. Again, the study was terminated early for safety concerns. Combination therapy in this patient population was not beneficial, prompting the question: is dual renin-angiotensin-aldosterone system blockade dead?

The fourth study compared the safety and efficacy of an angiotensin-converting enzyme (ACE) inhibitor-based therapy (lisinopril) with a β-blocker-based antihypertensive treatment (atenolol) in patients on maintenance haemodialysis with echocardiographic left ventricular hypertrophy and hypertension. Although blood pressure improved in both groups, no difference was evident between the treatments. Furthermore, this was the third study to be terminated for safety reasons. Despite early termination, the authors concluded that atenolol-based antihypertensive therapy might be superior to lisinopril-based therapy in preventing cardiovascular morbidity and all-cause hospitalizations.

Stephen Ash presented the results of a phase II clinical trial assessing ZS-9, a selective cation exchanger designed to preferentially entrap excess potassium. The drug was well tolerated, and the primary efficacy end point of reduction in serum potassium was met. A phase III trial has been initiated.

The ACCESS trial was another negative phase III study, this time assessing abatacept plus low-dose cyclophosphamide in patients with lupus nephritis. Although no improvement in complete response rate was evident by adding abatacept to the treatment, low-dose cyclophosphamide was shown to be efficacious in racially and ethnically diverse populations with lupus nephritis.

Finally, Afshin Parsa completed the session with a presentation of two studies (AASK and CRIC) that determined that variants of the gene *APOL1* were associated with the higher rates of end-stage renal disease in black patients compared with white patients. This association was independent of the diabetic status of the patients.

Taken together, although the majority of the studies were negative, the careful assessment of the results will help the design of future studies, and translational research in the field of kidney disease. Future trials will build on these results and the authors should be commended for making the full details of these negative trials available to the community.

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Original articles Garg, A. X. *et al.* Acute kidney injury from off-pump or on-pump coronary bypass grafting and kidney function one year later [abstract HI-OR01]. *J. Am. Soc. Nephrol.* **24**, 1059A (2013) | de Zeeuw, D. *et al.* Bardoxolone methyl in type 2 diabetes and stage 4 chronic kidney disease. *N. Engl. J. Med.* doi:10.1056/NEJMoa1306033 | Fried, L. F. *et al.* Combined angiotensin inhibition for the treatment of diabetic nephropathy. *N. Engl. J. Med.* doi:10.1056/NEJMoa1303154 | Agarwal, R. *et al.* Hypertension in hemodialysis patients treated with atenolol or lisinopril (HDPAL): a randomized controlled trial [abstract HI-OR04]. *J. Am. Soc. Nephrol.* **24**, 1059A (2013) | Ash, S. R. *et al.* Safety and efficacy of ZS9, a novel selective cation trap, for treatment of hyperkalemia in CKD patients [abstract HI-OR05]. *J. Am. Soc. Nephrol.* **24**, 1060A (2013) | Rovin, B. *et al.* Treatment of lupus nephritis with abatacept plus low-dose pulse cyclophosphamide: the results of the ACCESS trial [abstract HI-OR06]. *J. Am. Soc. Nephrol.* **24**, 1060A (2013) | Parsa, A. *et al.* APOL1 risk variants, race, and progression of chronic kidney disease. *N. Engl. J. Med.* doi:10.1056/NEJMoa1310345