Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care
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Aldosterone Synthase Inhibitors in Development: Current and Upcoming Data

Jamie Dwyer
University of Utah, United States

Despite contemporary guideline-directed medical therapy that includes renin-angiotensin system inhibitors and SGLT2 inhibitors, patients with chronic kidney disease (CKD) and hypertension continue to face substantial residual cardiorenal risk. Pivotal trials such as CREDENCE, DAPA-CKD, and EMPA-KIDNEY established the benefits of SGLT2 inhibition, yet a high burden of kidney progression, heart failure, and cardiovascular death persists, underscoring the need for complementary mechanisms of action. Aldosterone dysregulation, a recognized driver of vascular stiffness, fibrosis, sodium retention, and adverse cardiorenal remodeling, remains an undertreated therapeutic target. This presentation reviews the emerging class of aldosterone synthase inhibitors (ASIs), which suppress aldosterone production upstream at CYP11B2 and, with improved CYP11B2:CYP11B1 selectivity, avoid the off-target cortisol suppression that hampered earlier compounds. We compare the pharmacokinetic and pharmacodynamic profiles of three agents, lorundrostat, baxdrostat, and vicadrostat, and synthesize the contemporary evidence base across uncontrolled, treatment-resistant, and CKD-associated hypertension. Phase 2 and Phase 3 trials, including ADVANCE-HTN, LAUNCH-HTN, Explore-CKD, Explore-OSA, FigHTN, BaxHTN, Bax24, and the vicadrostat Phase 2 program, demonstrate clinically meaningful, placebo-corrected reductions in systolic blood pressure of approximately 8 to 14 mm Hg, along with substantial reductions in urine albumin-to-creatinine ratio in CKD populations. Hyperkalemia is the dominant safety signal, particularly when ASIs are layered atop RAAS inhibition and SGLT2 inhibition, whereas no clinically significant cortisol effects have been observed. We then frame the mechanistic rationale for pairing ASIs with SGLT2 inhibitors and preview the ongoing pivotal outcome programs, ARCTIC, PACIFIC, EASi-Kidney, and Prevent-HF, which will evaluate whether ASIs durably

reduce kidney progression, heart failure, and cardiovascular death. Implications for nephrologists managing high-risk CKD, near-term regulatory milestones, and outstanding scientific questions are discussed.

Keywords: aldosterone synthase inhibitors