



TARGETING ALDOSTERONE IN CHRONIC KIDNEY DISEASE: FROM MINERALOCORTICOID RECEPTOR ANTAGONISM TO SYNTHASE INHIBITION

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ABSTRACT

Chronic kidney disease (CKD) remains a major cause of morbidity and mortality despite advances in renin-angiotensin system blockade and sodium-glucose cotransporter-2 inhibitors. Persistent aldosterone production and mineralocorticoid receptor (MR) overactivation may contribute to residual cardiorenal risk through sodium retention, hypertension, oxidative stress, inflammation, endothelial dysfunction, and fibrosis. This narrative review summarizes the biological rationale and clinical evidence for aldosterone-targeted therapies in CKD, including steroidal MR antagonists, finerenone, and emerging aldosterone synthase inhibitors (ASIs). Steroidal MR antagonists reduce albuminuria but are limited by hyperkalemia and endocrine adverse effects. Finerenone has the most mature outcome evidence among nonsteroidal MR antagonists, reducing kidney and cardiovascular events in CKD with type 2 diabetes. Recent trials also support greater albuminuria reduction when finerenone is combined with empagliflozin and extend anti-albuminuric evidence to type 1 diabetes. Selective ASIs, including vicadrost, baxdrostat, and lorundrost, directly suppress aldosterone synthesis and have shown promising effects on albuminuria or blood pressure. However, hyperkalemia, adrenal safety, and the absence of definitive long-term kidney and cardiovascular outcome data remain important limitations. Current evidence supports a layered approach to CKD therapy, while ASIs remain investigational pending larger outcome trials. The objective of this narrative review is to critically summarize the role of aldosterone and mineralocorticoid receptor activation in CKD progression, compare steroidal and nonsteroidal mineralocorticoid receptor antagonists, and evaluate the emerging efficacy, safety, and clinical positioning of aldosterone synthase inhibitors within contemporary layered CKD therapy.

Keywords: aldosterone; aldosterone synthase inhibitor; chronic kidney disease; finerenone; mineralocorticoid receptor antagonist

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INTRODUCTION

Chronic kidney disease (CKD) is one of the fastest-growing global health problems. The Global Burden of Disease 2023 analysis estimated that hundreds of millions of adults are living with CKD, with an increasing burden of death and disability driven by population ageing, diabetes, hypertension, and other metabolic factors (GBD 2023 Chronic Kidney Disease Collaborators, 2025). The impact of CKD extends beyond progression to kidney failure. A decline in estimated glomerular filtration rate (eGFR) and an increase in albuminuria are also closely associated with cardiovascular events, heart failure, hospitalization, and death. Modern CKD management is therefore directed not only at delaying the need for kidney replacement therapy, but also at reducing overall cardiorenal risk.

Over the past two decades, evidence-based therapies have changed the natural history of CKD. Renin–angiotensin system (RAS) inhibitors, particularly angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB), remain a cornerstone of treatment in patients with albuminuria because they reduce intraglomerular pressure and albuminuria. The 2024 KDIGO guideline emphasizes the use of RAS blockade in appropriate patients, accompanied by monitoring of blood pressure, serum creatinine, eGFR, and potassium (KDIGO CKD Work Group, 2024). Sodium–glucose cotransporter-2 inhibitors (SGLT2i) subsequently broadened kidney and cardiovascular protection to patients with and without diabetes. In EMPA-KIDNEY, empagliflozin reduced the risk of kidney disease progression or cardiovascular death across a broad CKD population (EMPA-KIDNEY Collaborative Group, 2023).

Despite these advances, substantial residual risk remains. Some patients continue to experience worsening albuminuria, declining eGFR, heart failure, or cardiovascular events despite standard therapy. One pathway that may explain this residual risk is persistent aldosterone activity and mineralocorticoid receptor (MR) activation. Aldosterone is physiologically required to maintain extracellular volume, blood pressure, and potassium homeostasis. However, excessive MR activation in the kidneys, heart, blood vessels, and inflammatory cells produces effects that extend far beyond sodium retention, including oxidative stress, endothelial dysfunction, inflammation, extracellular matrix deposition, and fibrosis (Epstein et al., 2022; Polenus et al., 2025).

Clinical data also support an association between aldosterone and CKD progression. In the Chronic Renal Insufficiency Cohort, higher aldosterone concentrations were associated with greater risks of CKD progression and end-stage kidney disease after adjustment for multiple confounders (Verma et al., 2022). These findings do not establish a direct causal relationship, but they strengthen the concept that activation of the aldosterone pathway is both a relevant marker and a biologically plausible therapeutic target. In practice, RAS inhibition does not always suppress aldosterone production persistently. Aldosterone concentrations may rise again after an initial decline during ACEi or ARB therapy, a phenomenon commonly termed aldosterone breakthrough. This may sustain MR activation, albuminuria, inflammation, and fibrosis even when blood pressure appears to improve.

Efforts to target the aldosterone pathway have evolved through two main approaches. The first is to block the MR using mineralocorticoid receptor antagonists (MRAs). Spironolactone and eplerenone are long-established steroidal MRAs, but their use in CKD is often limited by hyperkalemia and, particularly with spironolactone, endocrine adverse effects caused by interactions with other steroid receptors. Nonsteroidal agents, especially finerenone, have different pharmacologic properties and are supported by phase III outcome trials in CKD with type 2 diabetes (Agarwal et al., 2021; Bakris et al., 2020; Pitt et al., 2021). The second approach is to reduce aldosterone production directly using aldosterone synthase inhibitors (ASIs), which target the CYP11B2 enzyme. This strategy is attractive because, in theory, it may reduce both genomic and some non-genomic effects of aldosterone rather than relying solely on receptor antagonism.

Therapeutic development in this field has progressed rapidly. Evidence for finerenone now includes pooled analyses of FIDELIO-DKD and FIGARO-DKD, early combination therapy with empagliflozin in CONFIDENCE, and recent data in CKD with type 1 diabetes. Meanwhile, selective ASIs such as vicaurostat (BI 690517), baxdrostat, and lorundrostat have generated promising phase II data for albuminuria or hypertension, while dexfadrostat has provided important information on CYP11B2 selectivity and adrenal safety (Agarwal et al., 2025; Dwyer et al., 2026; Heerspink et al., 2026; Laffin et al., 2025; Mulatero et al., 2024; Tuttle et al., 2024). Nevertheless, the position of ASIs within the CKD treatment algorithm remains uncertain because benefits on hard kidney and long-term cardiovascular outcomes have yet to be demonstrated.

Beyond the pharmacologic pathway itself, aldosterone-related risk should be interpreted within the broader cardiorenal spectrum. Albuminuria is not only a marker of glomerular injury but also a marker of systemic risk that correlates with cardiovascular events. Consequently, changes in urine albumin-to-creatinine ratio (UACR) are often used as surrogate outcomes in early-phase trials because they can be observed sooner than kidney failure or death. However, the magnitude of UACR reduction should be interpreted together with changes in eGFR, blood pressure, potassium, and ultimately clinical outcomes. This framework is particularly relevant when comparing finerenone with ASIs: finerenone has progressed from anti-albuminuric evidence to outcome trials, whereas most ASIs remain at the stage of demonstrating biological and surrogate effects.

This review aims to summarize the physiological and pathological roles of aldosterone in CKD progression, compare steroidal and nonsteroidal MRAs, review the clinical evidence for finerenone, and evaluate the rationale, early efficacy, and safety considerations of ASIs. The discussion also places combinations of aldosterone-targeted therapy with SGLT2i within the context of modern CKD treatment, providing a practical framework that distinguishes therapies supported by clinical outcome evidence from those that remain investigational.

From a clinical perspective, this topic is also important because patients with CKD often have more than one indication for therapies that affect the aldosterone pathway. Resistant hypertension, heart failure, diabetes, and albuminuria may coexist in the same patient, while each comorbidity influences drug selection and tolerance of changes in blood pressure or potassium. Accordingly, aldosterone-targeted therapy cannot be evaluated on the basis of a single laboratory outcome. Its value should be judged by balancing kidney protection, cardiovascular protection, blood pressure control, electrolyte safety, monitoring burden, and feasibility in routine care. Accordingly, the objective of this narrative review is to critically evaluate aldosterone-targeted strategies in CKD by: (1) summarizing the physiological and pathological roles of aldosterone–mineralocorticoid receptor signaling; (2) comparing steroidal and nonsteroidal mineralocorticoid receptor antagonists; (3) reviewing the clinical outcome evidence for finerenone; (4) assessing the rationale, efficacy, and safety of emerging aldosterone synthase inhibitors; and (5) defining the current and potential position of these therapies within a layered CKD treatment strategy.

METHOD

This article was prepared as a narrative review with a structured literature search. Searches were conducted through PubMed/MEDLINE, primary journal websites, clinical practice guidelines, and reference cross-checking up to 30 August 2026. Keywords used in various combinations included “chronic kidney disease”, “aldosterone”, “mineralocorticoid receptor”, “mineralocorticoid receptor antagonist”, “finerenone”, “spironolactone”, “eplerenone”, “aldosterone synthase inhibitor”, “CYP11B2”, “vicadrostat”, “BI 690517”, “baxdrostat”, “lorundrostat”, “dexfadrostat”, “SGLT2 inhibitor”, “albuminuria”, and “hyperkalemia”.

Priority was given to international guidelines, randomized controlled trials, pooled analyses of phase III trials, phase II studies of emerging agents, and mechanistic reviews that directly addressed the aldosterone pathway in kidney or cardiorenal disease. Literature published from 2020 to 2026 was prioritized to reflect recent developments; older articles were included only when they retained relevant mechanistic or historical value. This review was not designed as a systematic review or meta-analysis; therefore, no PRISMA-based selection process or quantitative pooling of effect estimates was performed.

Extracted information included drug mechanism of action, study population, trial design and phase, sample size, main outcomes, changes in albuminuria or blood pressure, kidney and cardiovascular outcomes, and adverse events related to potassium and adrenal function. Findings were synthesized narratively to compare three strategies: steroidal MRAs, nonsteroidal MRAs, and ASIs. Particular

emphasis was placed on clinical relevance for patients with CKD, maturity of the evidence, and limitations that should be considered before a therapy is incorporated into routine practice.

RESULT

Search Results And Evidence Framework

The identified literature revealed three complementary layers of evidence. First, mechanistic studies and cohort data position aldosterone–MR activation as a driver of inflammation, oxidative stress, and fibrosis in the kidneys and cardiovascular system. Second, MRA trials show that MR blockade can reduce albuminuria and, in the case of finerenone, improve clinical kidney and cardiovascular outcomes. Third, trials of newer-generation ASIs show that suppression of aldosterone synthesis can reduce blood pressure or albuminuria, although most evidence still comes from relatively short phase II studies. These differences in evidence maturity are important because an effect on surrogate outcomes does not automatically translate into fewer kidney failure events or cardiovascular deaths.

Role of Aldosterone in CKD Progression

Aldosterone is produced predominantly in the zona glomerulosa of the adrenal cortex, where the final step of steroid synthesis is catalyzed by CYP11B2. Angiotensin II and increased extracellular potassium are the principal physiological regulators, whereas adrenocorticotrophic hormone has a shorter-lived contribution. In the distal nephron, aldosterone increases sodium reabsorption through epithelial sodium channels and enhances potassium excretion. This response is essential for maintaining circulating volume and blood pressure, but it becomes maladaptive when aldosterone activity remains persistently elevated in patients with CKD (Polenus et al., 2025).

The MR is not restricted to epithelial cells of the distal nephron. It is also expressed in podocytes, mesangial cells, fibroblasts, endothelial cells, vascular smooth muscle cells, cardiomyocytes, and immune cells. MR activation in non-epithelial tissues may increase inflammatory and profibrotic mediators, activate NADPH oxidase, increase reactive oxygen species, reduce nitric oxide bioavailability, and promote extracellular matrix remodeling. The downstream consequences include podocyte injury, glomerulosclerosis, tubulointerstitial fibrosis, vascular stiffness, and myocardial remodeling (Agarwal et al., 2021; Barrera-Chimal et al., 2022; Epstein et al., 2022). Therefore, the benefits of MR-targeted therapies should not be understood merely as diuretic or blood pressure-lowering effects.

MR activation is also not entirely dependent on circulating aldosterone concentrations. Hyperglycemia, high salt exposure, oxidative stress, and the Rac1 pathway may increase MR activity in a ligand-independent manner. Conversely, aldosterone itself exerts rapid non-genomic effects that are not fully explained by gene transcription through the classical MR. This complexity helps explain why RAS blockade, MR antagonism, and inhibition of aldosterone synthesis may produce complementary but non-identical effects. Clinically, the therapeutic goal is not simply to lower aldosterone concentrations, but to reduce the biological consequences of pathway activation without causing hyperkalemia, hypotension, or adrenal insufficiency.

Steroidal MRAs: Efficacy on Surrogate Outcomes but Limited by Hyperkalemia

Spironolactone and eplerenone competitively inhibit the MR. In patients with albuminuric CKD who are already receiving an ACEi or ARB, multiple studies and meta-analyses have shown reductions in proteinuria or albuminuria after the addition of a steroidal MRA. However, this benefit comes at the cost of increased hyperkalemia risk and an early decline in eGFR. These risks become more relevant when eGFR is low, baseline serum potassium is near the upper limit of normal, diabetes is present, or patients are taking other medications that increase potassium. Because large trials with hard kidney outcomes across broad CKD populations have not developed to the same extent as the evidence for finerenone, the use of spironolactone or eplerenone

specifically for renoprotection should be individualized (Agarwal et al., 2021; Barrera-Chimal et al., 2022).

Spironolactone has active metabolites with long half-lives and affinity for androgen and progesterone receptors. These characteristics explain adverse effects such as gynecomastia, breast tenderness, menstrual disturbance, or sexual dysfunction in some patients. In impaired kidney function, active metabolites may also persist longer, so normalization of potassium after drug withdrawal is not always rapid. Eplerenone is more selective for the MR and causes fewer endocrine adverse effects, but its antihypertensive potency may be lower at certain doses and it still carries a risk of hyperkalemia. These limitations encouraged the development of nonsteroidal MRAs with different tissue distribution and receptor interactions.

Nonsteroidal MRAs and Finerenone

Finerenone is a nonsteroidal MRA with high selectivity for the MR and, unlike spironolactone, no active metabolites. Pharmacologic studies suggest a more balanced distribution between the heart and kidneys and a pattern of receptor cofactor recruitment that differs from steroidal MRAs. These features are thought to contribute to anti-inflammatory and antifibrotic effects with relatively less natriuresis. Although hyperkalemia remains a class-related risk, the benefit–risk profile of finerenone in CKD with type 2 diabetes has been evaluated in a large phase III program (Agarwal et al., 2021; Zhai et al., 2024).

FIDELIO-DKD enrolled 5,734 patients with type 2 diabetes, CKD, and albuminuria who were receiving optimized RAS blockade. Finerenone reduced the risk of the composite kidney outcome compared with placebo, with a hazard ratio of 0.82, and also reduced the major cardiovascular outcome with a hazard ratio of 0.86. Treatment discontinuation due to hyperkalemia was more frequent with finerenone, although the absolute rate remained low (Bakris et al., 2020). FIGARO-DKD extended the evidence to patients with relatively earlier-stage CKD and demonstrated a reduction in the composite cardiovascular outcome, driven largely by fewer hospitalizations for heart failure (Pitt et al., 2021). The pooled FIDELITY analysis of more than 13,000 participants provided more precise estimates. Finerenone reduced the composite cardiovascular outcome from 14.4% to 12.7% and the composite kidney outcome from 7.1% to 5.5%. Permanent discontinuation due to hyperkalemia was more frequent with finerenone than with placebo, but occurred in only a small proportion of participants (Agarwal et al., 2022). These data establish finerenone as a therapy supported by clinical outcome evidence, rather than merely an albuminuria-lowering agent. However, the core population of this program consisted of patients with CKD and type 2 diabetes, so extrapolation to non-diabetic CKD should be cautious.

Potassium Monitoring with Finerenone

The safety of finerenone depends heavily on patient selection and monitoring. In FIDELIO-DKD and FIGARO-DKD, serum potassium was measured regularly and doses were adjusted according to predefined protocols. This context matters because hyperkalemia rates cannot be separated from the monitoring strategy. Risk increases with lower eGFR and higher baseline potassium, while diuretics and SGLT2i may modify risk in some patients. Therefore, hyperkalemia rates reported in trials should not be interpreted as a property of the drug in isolation; they reflect the interaction between the drug, patient characteristics, background therapy, and quality of monitoring. In clinical practice, finerenone should ideally not be initiated without a clear plan for repeat potassium testing and dose adjustment if potassium rises.

Combination with SGLT2 Inhibitors

SGLT2i and finerenone act through different pathways. SGLT2i increase sodium delivery to the macula densa and restore tubuloglomerular feedback, thereby reducing intraglomerular pressure, whereas finerenone suppresses MR-mediated inflammatory and fibrotic signaling. The FIDELITY

analysis suggested that the benefit of finerenone was relatively consistent regardless of baseline SGLT2i use, although the number of participants taking an SGLT2i in the original trials was limited (Rossing et al., 2022). These findings provided both biological and clinical justification for evaluating the combination from the outset.

CONFIDENCE subsequently compared finerenone, empagliflozin, and their combination directly in patients with CKD and type 2 diabetes who remained on RAS inhibition. At day 180, combination therapy produced an approximately 29% greater reduction in UACR than finerenone alone and a 32% greater reduction than empagliflozin alone. No unexpected major safety signals were identified, and treatment discontinuation due to hyperkalemia, acute kidney injury, or symptomatic hypotension was relatively uncommon (Agarwal et al., 2025). These results strengthen the concept of multimodal therapy, although UACR remains a surrogate outcome; longer trials are needed to determine whether early combination therapy provides additional protection against kidney failure, cardiovascular events, or death.

Expansion of the Finerenone Evidence Base

In 2026, FINE-ONE provided evidence in patients with type 1 diabetes and CKD. In this six-month phase III trial, finerenone produced a 25% greater reduction in UACR than placebo. Hyperkalemia was more frequent with finerenone, and the early decline in eGFR was greater, although eGFR approached baseline after washout (Heerspink et al., 2026). This finding is important because it demonstrates an anti-albuminuric effect beyond type 2 diabetes. However, the short duration and use of UACR as the primary outcome mean that benefits on long-term progression to kidney failure remain to be established.

Rationale for Aldosterone Synthase Inhibition

MRAs block the receptor but do not stop aldosterone production. Aldosterone concentrations may remain high or increase through feedback mechanisms, and some non-genomic effects of aldosterone may not be fully inhibited by MR antagonism. ASIs are designed to inhibit CYP11B2 and directly reduce aldosterone synthesis. In theory, this upstream approach may reduce sodium retention, blood pressure, inflammation, and fibrosis (Azizi et al., 2025; Barrera-Chimal et al., 2025; Verma et al., 2024).

Pharmacologic Differences Between MRAs and ASIs

The distinction between receptor antagonism and inhibition of hormone synthesis has clinical consequences. MRAs act at the receptor level, so their final effect depends on affinity, tissue distribution, drug concentration, and MR conformation. ASIs act upstream by reducing aldosterone production, but they do not directly prevent ligand-independent MR activation. Thus, ASIs should not automatically be considered a more “complete” version of MRAs. Rather, the two classes may suppress different components of the same pathway. Whether they will ultimately be used as alternatives or in combination remains unknown and must take into account the possibility of greater hyperkalemia when two points of the aldosterone pathway are inhibited simultaneously. A major challenge is the structural similarity between CYP11B2 and CYP11B1, the enzyme involved in cortisol synthesis. Early ASIs such as osilodrostat lacked sufficient selectivity and could affect cortisol production, leading subsequent drug development to focus on compounds with much greater selectivity for CYP11B2. The pharmacologic success of modern ASIs must therefore be assessed along two dimensions: the ability to suppress aldosterone and the preservation of adrenal-axis safety. In addition, effective suppression of aldosterone may still increase potassium because the physiological mechanism of potassium excretion in the distal nephron is also reduced.

Vicadrostat (BI 690517)

Vicadrostat is a selective ASI that has been tested directly in CKD. In the phase II trial reported by Tuttle and colleagues, BI 690517 significantly reduced UACR compared with placebo, both without

and with empagliflozin. Combination with an SGLT2i produced an encouraging albuminuria-lowering signal and supported the hypothesis that modulation of glomerular hemodynamics and aldosterone suppression may be complementary. However, potassium increased in a dose-dependent manner, and adverse events related to adrenal function were a concern at certain doses (Tuttle et al., 2024). The EASi-KIDNEY program was developed to determine whether these surrogate signals translate into improved long-term clinical outcomes (Judge et al., 2025).

Baxdrostat

Baxdrostat has high selectivity for CYP11B2 over CYP11B1. In BrigHTN, patients with resistant hypertension who received baxdrostat 1 mg or 2 mg had greater reductions in systolic blood pressure than those receiving placebo, with between-group differences of approximately 8 and 11 mmHg, respectively. No cases of drug-related adrenocortical insufficiency were reported in that trial, although severe elevations in potassium occurred in a small number of participants (Freeman et al., 2023). This trial provided proof of concept that aldosterone synthesis can be selectively suppressed and translated into an antihypertensive effect. More direct evidence in CKD comes from a phase II trial in patients with CKD and uncontrolled hypertension. Baxdrostat produced a placebo-corrected reduction in systolic blood pressure of approximately 8 mmHg, accompanied by a reduction in UACR and an early decline in eGFR that subsequently tended to stabilize. Hyperkalemia was the treatment-related adverse event of greatest concern, reinforcing the importance of potassium monitoring (Dwyer et al., 2026). Although these findings support the potential role of baxdrostat in the CKD phenotype with hypertension, evidence for kidney failure or cardiovascular events is not yet available.

Lorundrostat

Lorundrostat is also being developed as a selective ASI for uncontrolled or resistant hypertension. Target-HTN showed that 50 mg and 100 mg doses reduced blood pressure more than placebo, with a particularly marked response in patients with obesity and a low-renin phenotype (Laffin et al., 2023). ADVANCE-HTN subsequently confirmed reductions in 24-hour ambulatory blood pressure in patients whose background antihypertensive regimen had been standardized, thereby reducing bias from nonadherence or changes in concomitant therapy (Laffin et al., 2025). Its direct relevance to CKD lies in the substantial overlap between resistant hypertension, obesity, and aldosterone activation in this population, although long-term kidney outcomes remain undefined.

Dexfandrostat and Lessons on Adrenal Safety

Dexfandrostat phosphate has been studied in primary aldosteronism. A multicenter phase II trial demonstrated reductions in ambulatory blood pressure with meaningful aldosterone suppression and no increase in potassium above the normal range during the treatment period in the study population (Mulatero et al., 2024). Although this population differs from CKD, the study provides important pharmacologic evidence that CYP11B2 can be inhibited with adequate selectivity when the molecule is appropriately designed. However, safety in patients with lower eGFR cannot be inferred directly from a primary aldosteronism population.

Blood Pressure, Albuminuria, and eGFR as Three Axes of Response

ASI trials also show that clinical responses do not always move in parallel. In some studies, blood pressure reduction is clear whereas changes in albuminuria are more modest; in others, particularly vicirostat in CKD, UACR reduction is the principal signal even though blood pressure is not the sole target. eGFR may decline early as a result of hemodynamic changes and then reach a plateau. A similar pattern is recognized with other renoprotective therapies, so an early decline in eGFR should be interpreted according to its magnitude, subsequent stabilization, volume status, and signs of acute kidney injury. ASI development will need to define acceptable thresholds for eGFR decline and titration algorithms that can be applied in routine practice.

In summary, the clinical evidence shows a consistent pattern. Steroidal MRAs effectively reduce albuminuria but are limited by hyperkalemia and endocrine adverse effects. Finerenone has the most mature evidence for reducing kidney and cardiovascular events in CKD with type 2 diabetes, with additional evidence for combination with SGLT2i and for type 1 diabetes. Selective ASIs have strong biological effects on blood pressure or albuminuria, but they do not yet have hard-outcome evidence comparable with finerenone. The clinical position of each class should reflect these differences rather than focusing only on the magnitude of UACR or blood pressure reduction.

Table 1.

Comparison of strategies targeting the aldosterone pathway in CKD

Class	Primary target	Clinical advantages	Main limitations	Current evidence position
Steroidal MRA (spironolactone, eplerenone)	MR blockade	Reduces albuminuria; useful for selected cardiovascular indications and hypertension	Hyperkalemia; early eGFR decline; endocrine adverse effects, particularly with spironolactone	Strong anti-albuminuric evidence, but CKD outcome data are less comprehensive than for finerenone
Nonsteroidal MRA (finerenone)	Selective MR blockade	Reduces kidney and cardiovascular outcomes in CKD with type 2 diabetes; combination data with SGLT2i are available	Hyperkalemia remains possible; evidence is derived mainly from diabetic CKD populations	Supported by phase III trials and clinical outcome evidence
Selective ASI (vicadrostat, baxdrostat, lorundrostat)	CYP11B2 inhibition and suppression of aldosterone synthesis	Reduces UACR or blood pressure; targets the aldosterone pathway upstream	Hyperkalemia; adrenal safety; mature hard-outcome evidence is not yet available	Under phase II–III investigation; not yet routine CKD therapy

Table 2.

Major clinical studies of finerenone relevant to CKD

Study	Population/design	Intervention	Main findings	Safety/interpretation
FIDELIO-DKD (Bakris et al., 2020)	5,734 patients with T2D and CKD; phase III RCT	Finerenone vs placebo on background RAS blockade	Kidney outcome: HR 0.82; major cardiovascular outcome: HR 0.86	Discontinuation due to hyperkalemia 2.3% vs 0.9%; strong kidney outcome evidence
FIGARO-DKD (Pitt et al., 2021)	7,437 patients with T2D and a relatively earlier CKD spectrum; phase III RCT	Finerenone vs placebo	Cardiovascular outcome: HR 0.87; benefit driven mainly by fewer heart failure hospitalizations	Discontinuation due to hyperkalemia 1.2% vs 0.4%
FIDELITY (Agarwal et al., 2022)	Pooled individual-level analysis, n=13,026	Finerenone vs placebo	CV outcome 12.7% vs 14.4% (HR 0.86); kidney outcome 5.5% vs 7.1% (HR 0.77)	Strengthens evidence of benefit across the CKD spectrum with T2D
CONFIDENCE (Agarwal et al., 2025)	CKD with T2D; phase II, three-arm trial	Finerenone; empagliflozin; combination	At day 180, UACR reduction was 29% greater vs finerenone and 32% greater vs empagliflozin	Surrogate outcome; no major new safety signal
FINE-ONE (Heerspink et al., 2026)	242 patients with T1D and CKD; phase III	Finerenone vs placebo	25% greater UACR reduction vs placebo over 6 months	Hyperkalemia 10.1% vs 3.3%; hard outcomes not assessed

Table 3.

Major studies of aldosterone synthase inhibitors (ASIs)				
Agent/study	Population	Main outcome	Summary of findings	Clinical limitations
Vicadrostat/BI 690517 (Tuttle et al., 2024)	CKD; phase II; with/without empagliflozin	Change in UACR	Significant UACR reduction; complementary effect with empagliflozin	Dose-dependent hyperkalemia; long-term outcome data are not yet available
Baxdrostat—BrigHTN (Freeman et al., 2023)	Resistant hypertension; phase II	Systolic blood pressure	Placebo-adjusted differences of approximately −8.1 mmHg (1 mg) and −11.0 mmHg (2 mg)	Not a CKD outcome study; potassium monitoring is required
Baxdrostat—CKD (Dwyer et al., 2026)	CKD with uncontrolled hypertension; phase II	Blood pressure, UACR, safety	Placebo-corrected SBP reduction of approximately −8.1 mmHg; UACR also decreased	Hyperkalemia was the main adverse event of concern; hard outcomes remain unavailable
Lorundrostat (Target-HTN/ADVANCE-HTN)	Uncontrolled/resistant hypertension	Clinic and ambulatory blood pressure	Consistent blood pressure reduction at active doses	Long-term kidney data remain limited
Dexfadrostat (Mulatero et al., 2024)	Primary aldosteronism; phase II	Ambulatory blood pressure, aldosterone, safety	Aldosterone suppression and blood pressure reduction with good tolerability	Population differs from CKD; direct extrapolation is not appropriate

DISCUSSION

Clinical Positioning: Outcome Evidence Must Be Distinguished from Surrogate-Outcome Evidence

The development of aldosterone-targeted therapy in CKD illustrates an important shift from the concept of “adding a diuretic” toward modulation of inflammatory and fibrotic pathways. Spironolactone and eplerenone remain useful in selected clinical settings, particularly resistant hypertension or established cardiovascular indications. In CKD, however, the decision to use a steroidal MRA should consider eGFR, baseline potassium, monitoring capacity, and potential drug interactions. Finerenone differs because its benefits on kidney and cardiovascular outcomes have been demonstrated in large phase III trials. It therefore currently holds a stronger position for eligible patients with diabetic CKD than ASIs, which remain investigational.

This distinction is important when interpreting studies of emerging agents. Albuminuria is a valuable risk marker and surrogate outcome, particularly when reductions are consistent and supported by a plausible biological mechanism. However, a reduction in UACR over 12–26 weeks does not guarantee fewer kidney failure events over several years. Likewise, lower blood pressure in resistant hypertension does not automatically prove independent renoprotection. Before ASIs can be positioned alongside finerenone, event-driven trials are needed to demonstrate slower CKD progression, reduced need for dialysis or transplantation, and/or fewer cardiovascular events.

Do Nonsteroidal MRAs and ASIs Compete with Each Other?

From a drug-development perspective, finerenone and ASIs are sometimes portrayed as competing approaches. Clinically, that comparison is premature because the evidence stage and target populations differ. Finerenone already has outcome-based indications in selected CKD populations, whereas ASIs are still being developed for hypertension phenotypes or CKD characterized by prominent aldosterone activity. If ASIs eventually demonstrate outcome benefits, the choice between the two classes may depend on the primary therapeutic objective: blood pressure control,

albuminuria reduction, potassium profile, comorbid heart failure, diabetes, and other concomitant therapies. Direct head-to-head trials would be highly informative, but until then comparisons should avoid claims of superiority based on separate studies.

Combination Strategies and the Concept of Layered Therapy

CKD treatment is increasingly layered. ACEi/ARB, SGLT2i, nonsteroidal MRAs, and other metabolic therapies do not act on the same pathway. Combining them is not simply a matter of adding drugs; it targets different components of pathophysiology, including intraglomerular pressure, inflammation, fibrosis, glycemic control, natriuresis, and neurohormonal activation. CONFIDENCE is an important example because finerenone and empagliflozin were initiated simultaneously rather than adding one agent only after assessing response to the other. The greater reduction in UACR suggests biological complementarity (Agarwal et al., 2025).

Treatment intensification, however, requires disciplined monitoring. An early decline in eGFR may occur after SGLT2i as well as aldosterone-targeted interventions. This change must be distinguished from progressive acute kidney injury. Potassium may also increase after MRAs or ASIs, but absolute risk depends on eGFR, baseline potassium, diabetes, dietary potassium, volume status, diuretic use, and RAS therapy. In practice, the benefits of layered therapy can be realized only when clinicians have reliable systems for laboratory monitoring and dose titration.

Role of SGLT2 Inhibitors in the Safety of Aldosterone-Targeted Therapy

SGLT2i are of interest not only because of their renoprotective effects, but also because they may influence the tolerability of therapies that increase potassium. Subgroup analyses from FIDELITY suggested a lower frequency of hyperkalemia among participants taking an SGLT2i, but subgroup analyses cannot establish a causal protective effect against hyperkalemia (Rossing et al., 2022). CONFIDENCE also showed that the combination could be administered without a major new safety signal during the study period (Agarwal et al., 2025). Nevertheless, SGLT2i should not be regarded as an “antidote” to hyperkalemia. Potassium still requires monitoring, especially in patients with low eGFR, concomitant RAS blockade, high dietary potassium intake, or other medications that impair potassium excretion.

Hyperkalemia as a Class Issue, Not a Reason to Ignore the Aldosterone Pathway

Hyperkalemia is the principal barrier to aldosterone-targeted therapy. With steroidal MRAs, this risk has long limited use in CKD. Finerenone reduces endocrine adverse effects compared with spironolactone but does not eliminate potassium-related risk. FIDELIO-DKD and FIDELITY showed that hyperkalemia occurred more often than with placebo, yet permanent discontinuation remained relatively uncommon when structured monitoring and dose-adjustment protocols were used (Agarwal et al., 2022; Bakris et al., 2020). The clinical message is not that finerenone is risk-free, but that its risk can be managed in appropriately selected patients.

ASIs are not exempt from this problem. Suppressing aldosterone production reduces potassium excretion in the distal nephron, making hyperkalemia a predictable pharmacologic consequence. With vicedrostat, baxdrostat, and lorundrostat, hyperkalemia rates vary according to population, dose, and definition. Because phase II trials generally exclude patients with severe baseline hyperkalemia or very low kidney function, their safety estimates should not be extrapolated directly to all patients with CKD. If ASIs enter routine practice, potassium-monitoring algorithms will likely be as important as the choice of molecule itself.

Adrenal Safety Distinguishes ASIs from MRAs

A distinctive concern with ASIs is selectivity for CYP11B2. Its structural similarity to CYP11B1 creates a risk of cortisol suppression when selectivity is insufficient. Osilodrostat illustrates why this issue matters and is now better known in the treatment of Cushing syndrome. Newer-generation

compounds have been designed with greater selectivity, and trials of baxdrostat, lorundrostat, and dexfadrostat suggest that aldosterone can be suppressed without clinically meaningful changes in cortisol in most participants (Freeman et al., 2023; Laffin et al., 2023; Mulatero et al., 2024). Nevertheless, long-term adrenal safety, particularly in acutely ill patients, glucocorticoid users, or those with advanced CKD, still requires larger datasets.

Aldosterone Breakthrough: A Relevant Concept That Should Not Be Oversimplified

One argument for ASIs is that ACEi/ARB therapy does not permanently suppress aldosterone production. Aldosterone breakthrough has a biological basis and has been reported in multiple populations, but its prevalence is strongly influenced by the definition used, timing of measurement, sodium and potassium intake, volume status, and laboratory method (Polenus et al., 2025). It is therefore inappropriate to assume that every patient receiving an ACEi/ARB experiences the same degree of “escape” or that a single aldosterone measurement should directly determine ASI selection. The role of renin–aldosterone biomarkers in personalizing CKD therapy remains an area of research.

Diabetic and Non-Diabetic CKD

The evidence for finerenone is strongest in CKD with type 2 diabetes. FINE-ONE extends anti-albuminuric evidence to type 1 diabetes but does not yet address hard clinical outcomes. In non-diabetic CKD, the biological rationale for MR antagonism remains strong because inflammation and fibrosis are not exclusive to diabetes, but event-based clinical evidence is more limited. The same applies to ASIs. Tuttle and colleagues enrolled a CKD population relevant to albuminuria assessment, whereas baxdrostat studies have focused on CKD with uncontrolled hypertension. Future studies should determine whether specific phenotypes—such as high albuminuria, resistant hypertension, obesity, low renin, or high aldosterone concentrations—predict a greater response.

Implications for Clinical Practice in Indonesia

The Indonesian context adds its own challenges. Diabetes and hypertension are highly prevalent, while access to UACR testing, repeated potassium monitoring, newer drugs, and nephrology services is uneven. Implementation of modern therapy should therefore continue to begin with the most cost-efficient foundations: blood pressure control, ACEi/ARB use according to indication and tolerance, SGLT2i when eligibility criteria are met, diabetes management, smoking cessation, weight management, sodium restriction, and monitoring of eGFR and albuminuria. Finerenone or other aldosterone-pathway therapies are most useful when added to these foundations rather than replacing them.

Patient selection must also account for the ability to complete follow-up monitoring. A drug that carries a risk of hyperkalemia may become less safe when a patient cannot obtain serum potassium testing after initiation or dose titration. Conversely, avoiding therapy solely because of concern about hyperkalemia may deprive patients of clinical benefit. A more rational approach is to establish a simple protocol: assess potassium and eGFR before treatment, repeat testing after initiation or dose changes, review medications that raise potassium, correct volume abnormalities, and adjust therapy if potassium increases. These principles apply to MRAs and will likely remain relevant if ASIs become available.

Limitations of the Evidence and Future Research

This review has several limitations. As a narrative review, the literature selection was not intended to produce pooled effect estimates and does not replace a systematic review. There is also substantial heterogeneity across study populations: finerenone trials have focused on diabetic CKD, whereas several ASI trials have focused on resistant hypertension or primary aldosteronism. Outcomes also differ, ranging from blood pressure and UACR to eGFR slope and clinical events.

Direct comparisons across drug classes should therefore be conceptual rather than interpreted as head-to-head efficacy comparisons.

Need for Standardization of Reporting

Comparisons across the aldosterone literature are further complicated by differences in the definitions of hyperkalemia, acute kidney injury, and eGFR decline used between trials. Some studies report potassium above 5.5 mmol/L, while others focus on levels above 6.0 mmol/L or treatment discontinuation. Similarly, kidney outcomes may use 40%, 50%, or 57% eGFR decline, or the need for kidney replacement therapy. Standardized outcome definitions and reporting would make benefit–risk assessment across agents easier for clinicians. This is particularly important when the effects of newer drugs appear numerically similar but arise from different populations and outcome definitions.

At least four priorities should guide future research. First, ASIs require phase III trials with hard kidney and cardiovascular outcomes and adequate follow-up. Second, optimal combination strategies with ACEi/ARB, SGLT2i, and nonsteroidal MRAs need to be defined, including whether particular combinations add benefit or simply increase hyperkalemia risk. Third, biomarkers capable of identifying patients with greater aldosterone dependence should be developed to enable more precise therapy. Fourth, implementation and cost-effectiveness studies are needed in middle-income countries because the biological benefits of new drugs will not necessarily translate into population benefit when monitoring access and financing are limited.

Another issue is the representation of Asian patients in clinical trials. The finerenone program includes Asian subgroup analyses that generally show consistent cardiorenal effects, but the proportion of participants from Southeast Asia remains small relative to the overall global population. Regional data for ASIs are even more limited. Differences in salt intake, diabetes prevalence, access to monitoring, use of traditional medicines, and genetic characteristics may influence blood pressure and potassium responses. Studies in Asian populations, including Indonesia, will help determine whether dosing and monitoring algorithms developed in North America or Europe can be applied without major modification.

Conceptually, the future of CKD therapy is unlikely to be determined by a single “best drug”, but rather by combinations of mechanisms tailored to patient phenotype. Finerenone has shown that modulating the MR can provide clinical benefit on top of RAS blockade. SGLT2i have shown that hemodynamic and metabolic intervention can provide protection across etiologies. ASIs are now testing the next hypothesis: whether reducing aldosterone production upstream can provide additional protection with acceptable safety. The answer will determine whether ASIs become adjunctive therapies for specific phenotypes or evolve into a new pillar of CKD management.

CONCLUSION

Aldosterone and MR activation are important contributors to residual cardiorenal risk in CKD through sodium retention, hypertension, oxidative stress, inflammation, and fibrosis. Steroidal MRAs can reduce albuminuria, but their use is often limited by hyperkalemia and, with spironolactone, endocrine adverse effects. Finerenone currently has the most mature clinical evidence among therapies specifically targeting the aldosterone pathway, with reductions in kidney and cardiovascular events in CKD with type 2 diabetes, as well as recent evidence for combination with empagliflozin and anti-albuminuric effects in type 1 diabetes. Selective ASIs such as vicirostat, baxdrostat, and lorundrostat offer a different approach by directly suppressing aldosterone synthesis. Phase II results for albuminuria and blood pressure are promising, but hyperkalemia, adrenal safety, and the absence of definitive hard-outcome evidence currently limit their use as routine therapy. In current practice, aldosterone-targeted treatment should be positioned within a layered CKD strategy that remains grounded in RAS blockade, SGLT2i, risk-factor

control, and monitoring of eGFR and potassium. Phase III trials and implementation studies will determine whether ASIs can progress from investigational agents to a new pillar of cardiorenal protection.

REFERENCES

- GBD 2023 Chronic Kidney Disease Collaborators. (2025). Global, regional, and national burden of chronic kidney disease in adults, 1990–2023, and its attributable risk factors: A systematic analysis for the Global Burden of Disease Study 2023. *The Lancet*, 406(10518), 2461–2482. [https://doi.org/10.1016/S0140-6736\(25\)01853-7](https://doi.org/10.1016/S0140-6736(25)01853-7)
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. (2024). KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney International*, 105(4S), S117–S314. <https://doi.org/10.1016/j.kint.2023.10.018>
- EMPA-KIDNEY Collaborative Group. (2023). Empagliflozin in patients with chronic kidney disease. *New England Journal of Medicine*, 388(2), 117–127. <https://doi.org/10.1056/NEJMoa2204233>
- Epstein, M., Kovesdy, C. P., Clase, C. M., Sood, M. M., & Pecoits-Filho, R. (2022). Aldosterone, mineralocorticoid receptor activation, and CKD: A review of evolving treatment paradigms. *American Journal of Kidney Diseases*, 80(5), 658–666. <https://doi.org/10.1053/j.ajkd.2022.04.016>
- Polenus, P., Đuran, A., & Karanović Štambuk, S. (2025). Aldosterone in chronic kidney disease. *Biomedicines*, 13(9), 2081. <https://doi.org/10.3390/biomedicines13092081>
- Verma, A., Vaidya, A., Subudhi, S., & Waikar, S. S. (2022). Aldosterone in chronic kidney disease and renal outcomes. *European Heart Journal*, 43(38), 3781–3791. <https://doi.org/10.1093/eurheartj/ehac352>
- Agarwal, R., Kolkhof, P., Bakris, G., Bauersachs, J., Haller, H., Wada, T., & Zannad, F. (2021). Steroidal and non-steroidal mineralocorticoid receptor antagonists in cardiorenal medicine. *European Heart Journal*, 42(2), 152–161. <https://doi.org/10.1093/eurheartj/ehaa736>
- Barrera-Chimal, J., Lima-Posada, I., Bakris, G. L., & Jaisser, F. (2022). Mineralocorticoid receptor antagonists in diabetic kidney disease—mechanistic and therapeutic effects. *Nature Reviews Nephrology*, 18(1), 56–70. <https://doi.org/10.1038/s41581-021-00490-8>
- Bakris, G. L., Agarwal, R., Anker, S. D., Pitt, B., Ruilope, L. M., Rossing, P., Kolkhof, P., Nowack, C., Schloemer, P., Joseph, A., & Filippatos, G. (2020). Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. *New England Journal of Medicine*, 383(23), 2219–2229. <https://doi.org/10.1056/NEJMoa2025845>
- Pitt, B., Filippatos, G., Agarwal, R., Anker, S. D., Bakris, G. L., Rossing, P., Joseph, A., Kolkhof, P., Nowack, C., Schloemer, P., & Ruilope, L. M. (2021). Cardiovascular events with finerenone in kidney disease and type 2 diabetes. *New England Journal of Medicine*, 385(24), 2252–2263. <https://doi.org/10.1056/NEJMoa2110956>
- Agarwal, R., Filippatos, G., Pitt, B., Anker, S. D., Rossing, P., Joseph, A., Kolkhof, P., Nowack, C., Gebel, M., Ruilope, L. M., & Bakris, G. L. (2022). Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: The FIDELITY pooled analysis. *European Heart Journal*, 43(6), 474–484. <https://doi.org/10.1093/eurheartj/ehab777>
- Rossing, P., Filippatos, G., Agarwal, R., Anker, S. D., Pitt, B., Ruilope, L. M., Chan, J. C. N., Kooy, A., McCafferty, K., Schernthaner, G., Joseph, A., Kolkhof, P., Nowack, C., Schloemer, P., & Bakris, G. L. (2022). Finerenone in patients with chronic kidney disease and type 2 diabetes by sodium–glucose cotransporter 2 inhibitor treatment: The FIDELITY analysis. *Diabetes Care*, 45(12), 2991–2998. <https://doi.org/10.2337/dc22-0294>
- Agarwal, R., Green, J. B., Heerspink, H. J. L., Mann, J. F. E., McGill, J. B., Mottl, A. K., Rosenstock, J., Rossing, P., Vaduganathan, M., Brinker, M., Edfors, R., Li, N., Scheerer, M. F., Scott, C., & Nangaku, M. (2025). Finerenone with empagliflozin in chronic kidney disease and type 2 diabetes. *New England Journal of Medicine*, 393(6), 533–543. <https://doi.org/10.1056/NEJMoa2410659>

- Heerspink, H. J. L., Birkenfeld, A. L., Cherney, D. Z. I., Colhoun, H. M., Groop, P.-H., Ji, L., Jongs, N., Mathieu, C., Pratley, R. E., Rosas, S. E., Rossing, P., Skyler, J. S., Tuttle, K. R., Lawatscheck, R., Brinker, M., Scheerer, M. F., Russell, J., Schloemer, P., & McGill, J. B. (2026). Finerenone in type 1 diabetes and chronic kidney disease. *New England Journal of Medicine*, 394(10), 947–957. <https://doi.org/10.1056/NEJMoa2512854>
- Zhai, S., Ma, B., Chen, W., & Zhao, Q. (2024). A comprehensive review of finerenone—a third-generation non-steroidal mineralocorticoid receptor antagonist. *Frontiers in Cardiovascular Medicine*, 11, 1476029. <https://doi.org/10.3389/fcvm.2024.1476029>
- Tuttle, K. R., Hauske, S. J., Canziani, M. E. F., et al. (2024). Efficacy and safety of aldosterone synthase inhibition with and without empagliflozin for chronic kidney disease: A randomised, controlled, phase 2 trial. *The Lancet*, 403(10424), 379–390. [https://doi.org/10.1016/S0140-6736\(23\)02408-X](https://doi.org/10.1016/S0140-6736(23)02408-X)
- Judge, P. K., Tuttle, K. R., Staplin, N., Hauske, S. J., Zhu, D., Sardell, R., et al. (2025). The potential for improving cardio-renal outcomes in chronic kidney disease with the aldosterone synthase inhibitor vicadrostal (BI 690517): A rationale for the EASi-KIDNEY trial. *Nephrology Dialysis Transplantation*, 40(6), 1175–1186. <https://doi.org/10.1093/ndt/gfae263>
- Kobayashi, M., Pitt, B., Ferreira, J. P., Rossignol, P., Girerd, N., & Zannad, F. (2025). Aldosterone-targeted therapies: Early implementation in resistant hypertension and chronic kidney disease. *European Heart Journal*, 46(27), 2618–2642. <https://doi.org/10.1093/eurheartj/ehaf225>
- Freeman, M. W., Halvorsen, Y.-D., Marshall, W., Pater, M., Isaacsohn, J., Pearce, C., Murphy, B., Alp, N., Srivastava, A., Bhatt, D. L., & Brown, M. J. (2023). Phase 2 trial of baxdrostat for treatment-resistant hypertension. *New England Journal of Medicine*, 388(5), 395–405. <https://doi.org/10.1056/NEJMoa2213169>
- Dwyer, J. P., Maklad, N., Vedin, O., Monyak, J., Myte, R., Chertow, G. M., Heerspink, H. J. L., & Little, D. J. (2026). Efficacy and safety of baxdrostat in participants with CKD and uncontrolled hypertension: A randomized, double-blind, placebo-controlled trial. *Journal of the American Society of Nephrology*, 37(2), 299–311. <https://doi.org/10.1681/ASN.00000000849>
- Laffin, L. J., Rodman, D., Luther, J. M., et al. (2023). Aldosterone synthase inhibition with lorundrostat for uncontrolled hypertension: The Target-HTN randomized clinical trial. *JAMA*, 330(12), 1140–1150. <https://doi.org/10.1001/jama.2023.16029>
- Laffin, L. J., Kopjar, B., Melgaard, C., Wolski, K., Ibbitson, J., Bhikam, S., et al. (2025). Lorundrostat efficacy and safety in patients with uncontrolled hypertension. *New England Journal of Medicine*, 392, 1813–1823. <https://doi.org/10.1056/NEJMoa2501440>
- Mulatero, P., Wuerzner, G., Groessl, M., Sconfienza, E., Damianaki, A., Forestiero, V., Vogt, B., Brunner, H., Gerlock, T., Steele, R., & Schumacher, C. (2024). Safety and efficacy of once-daily dexfadrostat phosphate in patients with primary aldosteronism: A randomised, parallel group, multicentre, phase 2 trial. *eClinicalMedicine*, 71, 102576. <https://doi.org/10.1016/j.eclinm.2024.102576>
- Verma, S., Pandey, A., Pandey, A. K., Butler, J., Lee, J. S., Teoh, H., Mazer, C. D., Kosiborod, M. N., Cosentino, F., Anker, S. D., Connelly, K. A., & Bhatt, D. L. (2024). Aldosterone and aldosterone synthase inhibitors in cardiorenal disease. *American Journal of Physiology-Heart and Circulatory Physiology*, 326(3), H670–H688. <https://doi.org/10.1152/ajpheart.00419.2023>
- Azizi, M., Riancho, J., & Amar, L. (2025). Aldosterone synthase inhibitors: A revival for treatment of renal and cardiovascular diseases. *The Journal of Clinical Endocrinology & Metabolism*, 110(3), e557–e565. <https://doi.org/10.1210/clinem/dgae823>
- Barrera-Chimal, J., Vaidya, A., & Jaisser, F. (2025). Aldosterone synthase inhibition: A novel bullet to fight cardiovascular-kidney-metabolic syndrome. *Journal of Molecular Endocrinology*, 75(3), e250047. <https://doi.org/10.1530/JME-25-0047>