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From Molecular Design to Clinical Application: A Comprehensive Reviewof Aldosterone Synthase Inhibitors

Yurui Zhang

College of Pharmacy, South Medical University, Guangzhou, China
Ninetuzhang0101@gmail.com

Abstract. The aldosterone synthase inhibitors (ASIs) are a new approach to the treatment of hypertension and other disorders linked to aldosterone since they directly block the production of aldosterone in its enzyme synthesis site, CYP11B2. This upstream strategy presents potential benefits compared to the traditional mineralocorticoid receptor antagonists because it has the potential of inhibiting both the genomic and non-genomic effects of aldosterone. Recent developments have provided high-potency agents like lorundrostat and baxdrostat, that in spite of showing substantial blood pressure lowering, do not interfere with cortisol production, and thus can enhance the treatment window. ASIs have been shown to be effective in resistant hypertension and primary aldosteronism treatment based on clinical evidence. Besides, there is also an emergence of data that indicate possible cardio-renal protection advantages, such as a decrease in albuminuria. One of the most significant aspects of it still lacks a solution, such as the long-term safety evaluation, optimal patient selection, and integration into treatment algorithms. Further studies in the future should concentrate on organ-protective effectiveness in a long-term study, optimization of biomarkers-based therapy, and the implementation of combinations with other classes of drugs.

Keywords: aldosterone synthase inhibitors, hypertension, drug selectivity, resistant hypertension, mineralocorticoid receptor antagonists

1. Introduction

Hypertension is a major global risk factor for cardiovascular disease, stroke, and death, affecting approximately 1.3 billion people worldwide. Currently, nearly half of patients have suboptimal blood pressure control, and among those receiving treatment, 10% to 20% suffer from resistant hypertension, meaning their blood pressure remains elevated despite concurrent use of three or more antihypertensive medications, including a diuretic.

Aldosterone dysregulation plays a key role in hypertension pathogenesis. Traditional aldosterone antagonist therapy primarily relies on mineralocorticoid receptor antagonists (MRAs) such as spironolactone. While effective in lowering blood pressure, these drugs often cause sex hormone-related adverse reactions, including gynecomastia, erectile dysfunction in men, and menstrual irregularities in women, limiting their long-term use.

Aldosterone synthase inhibitors (ASIs) offer a mechanistically distinct approach by directly targeting CYP11B2 to suppress aldosterone synthesis at its source. Recent advances have yielded

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highly selective agents such as baxdrostat and lorundrostat. For instance, lorundrostat exhibits 374-fold selectivity for CYP11B2 over cortisol synthase, effectively reducing aldosterone levels with minimal impact on cortisol synthesis. Clinical studies have confirmed their significant efficacy.

This review summarizes the development of aldosterone synthase inhibitors for hypertension, covering their mechanism, drug development challenges, and emerging clinical evidence. As more research focuses on this area, ASIs are poised to bridge an important therapeutic gap, offering a new option for patients with resistant hypertension.

2. Pathophysiology of aldosterone synthase

2.1. Structure, encoding gene, and tissue distribution of aldosterone synthase

Aldosterone synthase (CYP11B2) is a mitochondrial cytochrome P450, which catalyzes the terminal stages of aldosterone production. The zone is designated as adrenal zona glomerulosa and it is expressed there. This enables the exact regulation of the synthesis of mineralocorticoids without interfering with glucocorticoids synthesis in the adjacent areas. Its action is dependent on several important structural elements: it has a heme-active site which transforms substrates of steroids; and it has a binding site in which its redox partner, adrenodoxin, provides the required electrons during catalysis.

The recent structural studies have helped to understand the interaction between CYP11B2 and adrenodoxin providing multiple salt bridges as well as hydrogen bonds stabilizing the protein protein interface and enabling the presence of substrate and inhibitors [1]. These findings provide novel treatment perspectives such as interventions that disrupt the CYP11B2 -adrenodoxin interactions in primary aldosteronism.

The epigenetic control of aldosterone synthase has also been explained in recent researches. There are prominent DNA methylation changes at the CYP11B2 promoter throughout adrenal localization locales with the zona glomerulosa hypomethylated relative to others. This distinctiveness of methylation adds to the zone-specific expression of CYP11B2 and introduces an additional layer of the regulation of aldosterone production. Interestingly, epigenetic derangements in disease conditions have been detected, and this suggests that epigenetics processes might contribute to the aldosterone maladjustment linked to hypertension [2].

2.2. Biosynthetic pathway and regulatory mechanisms of aldosterone

The biosynthesis of aldosterone is a multistep process in the mitochondria which converts cholesterol to the potent mineralocorticoid hormone. In this synthetic pathway, the tsunami of cholesterol into the inner mitochondrial membrane is the rate limiting step by means of the steroidogenic acute regulatory (StAR)-mediated cholesterol-carrying pathway. Within the mitochondria cholesterol is subjected to a series of enzymatic changes. The last three reactions then occur in the zona glomerulosa and include the 11-hydroxylation of 11-deoxycorticosterone to corticosterone, 18-hydroxylation of 18-hydroxycorticosterone, and 18-oxidation to form aldosterone which involves the CYP11B2 enzyme.

Several physiological variables rigorously control this pathway whereby angiotensin II (AngII) is the leading stimulator. AngII is acting via a set of intracellular signaling pathways mediating its activity via particular interaction with G protein-coupled receptors (AT1R) on zona glomerulosa cells. The evidence of recent studies indicated that the DNA methylation and microRNA regulation

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are connected with the expression of RAAS genes, e.g., angiotensinogen and CYP11B2, including salt-sensitive hypertension.

In addition to renin-angiotensin system, the electrolytes are important. Higher levels of serum potassium have a direct effect on stimulating cells in zona glomerulosa by depolarizing the cell membrane, opening the influx of calcium through the voltage-gated channels, and entering more calcium into the cell. The mechanism is crucial to offer a critical safety feedback loop which safeguards against hyperkalemia because of increased renal potassium excretion. Although the production of aldosterone can be temporarily stimulated by adrenocorticotropic hormone (ACTH), the potency of this effect is much smaller than those of AngII or potassium, and it has rather limited effects on the long-term regulation of aldosterone.

There is an emerging evidence of the presence of extra-adrenal production of aldosterone in some tissues. CYP11B2 expression was also shown in the adrenal medulla, pheochromocytomas, which suggests that aldosterone could be produced in locations other than the zona glomerulosa [3].

2.3. Similarities and challenges: aldosterone synthase and 11β-hydroxylase

A major challenge in developing specific aldosterone synthase inhibitors stems from the extraordinary structural similarity between CYP11B2 and its closely related isoenzyme, 11β-hydroxylase (CYP11B1). The two share approximately 93% amino acid identity and possess fully conserved active-site residues, making pharmacological discrimination extremely difficult. Despite their structural similarities, CYP11B2 in the zona glomerulosa drives aldosterone synthesis, whereas CYP11B1 in the zona fasciculata catalyzes the final step of cortisol production.

Recent crystallographic studies have elucidated the structural biology of these enzymes. High-resolution structures of CYP11B2 bound to inhibitors have revealed subtle differences in its substrate-binding pocket compared with that of CYP11B1. These insights enabled rational drug design that exploits architectural variations, leading to second-generation inhibitors with greatly enhanced selectivity. This selectivity is clinically crucial, as non-selective inhibitors that also block CYP11B1 can impair cortisol synthesis, disrupt the HPA axis, and risk adrenal insufficiency during stress—limiting the utility of early inhibitors. The clinical profile of osilodrostat underscores this point: initially developed as a CYP11B2 inhibitor, it was ultimately approved for Cushing's disease due to its potent CYP11B1 inhibition.

2.4. Core mechanisms of excess aldosterone in hypertension and related target organ damage

Chronic aldosterone excess, regardless of the context, triggers a series of pathophysiological processes. The traditional understanding of aldosterone's mechanism in hypertension has emphasized its renal actions on the distal nephron, where it binds to mineralocorticoid receptors and stimulates sodium reabsorption through the epithelial sodium channel (ENaC). This sodium-retaining effect expands plasma volume and increases cardiac output, ultimately elevating blood pressure. Simultaneously, aldosterone promotes renal potassium wasting, which can lead to hypokalemia in severe cases of primary aldosteronism.

Beyond these renal effects, aldosterone induces widespread cardiovascular injury through genomic and non-genomic pathways. In the cardiovascular system, aldosterone promotes myocardial fibrosis and diastolic dysfunction by stimulating collagen synthesis and fibroblast proliferation. It also induces endothelial dysfunction, reduces nitric oxide bioavailability, activates pro-inflammatory pathways in vascular smooth muscle cells, and increases vascular stiffness, contributing to hypertensive heart disease. Pathologically elevated aldosterone further impairs

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vascular reactivity, enhances sympathetic nervous system activity, and accelerates cardiomyocyte apoptosis. Due to its key role in hypertension and related disorders, targeting aldosterone synthase (CYP11B2) has become a crucial therapeutic strategy for conditions such as primary aldosteronism, congestive heart failure, and hypertension [4].

These mechanisms explain the disproportionate cardiovascular risk associated with hyperaldosteronism and underscore the therapeutic importance of targeting aldosterone production, particularly through selective inhibition of CYP11B2.

3. Development and pharmacological properties of aldosterone synthase inhibitors

3.1. Drug design strategies and development history

The design of an aldosterone synthase inhibitor represented the shortcoming of the classical mineralocorticoid receptor antagonist (MRA) spironolactone and eplerenone. Despite its effectiveness, MRAs are not devoid of the dangers such as hyperkalemia and cannot block the non-genomic action of aldosterone, which is not dependent on the receptor activation. These disadvantages shifted the treatment attention to the upstream block of aldosterone production. The original generation aldosterone synthase inhibitors, which were mainly steroidal analogue, did not exhibit specificity over the steroidogenic enzyme CYP11B1 as well as other steroidogenic enzymes and exhibited undesired hormonal side effects and restricted clinical use.

One of the most significant scientific achievements was made due to the development of structural biology. Direct identification of high-resolution crystal structures of CYP11B2 with its inhibitors showed slight variations in substrate-binding pockets in CYP11B2 and CYP11B1. These findings made it possible to design drugs rationally, targeting specific architectural attributes of the enzymes, and objectively the analyzes of the field switched to non-selective steroidal inhibitors, in favor of structure-directed identification of compounds highly selective.

The result of this rational design was the development of second-generation, non-steroidal inhibitors, which gave high selectivity a status in the industry. Most current inhibitors like baxdrostat and lorundrostat have significantly enhanced selectivity profiles, e.g. lorundrostat has 374 to 1 selectivity of CYP11B2 against CYP11B1 in vitro. Such increased specificity is translated into clinical safety, especially the maintenance of cortisol production, is a definite advance in the direction of targeted and safer treatment.

3.2. Introduction to representative drug molecules

Based on their selectivity profiles and clinical development trajectories, aldosterone synthase inhibitors can be categorized into distinct generations.

3.2.1. First generation: moderate selectivity

Represented by osilodrostat, this class demonstrated moderate selectivity for CYP11B2 over CYP11B1. It effectively lowered aldosterone and blood pressure but faced a key limitation: its insufficient selectivity often led to clinically significant cortisol suppression at higher doses. Nonetheless, it provided crucial proof-of-concept and was subsequently approved for Cushing's disease, leveraging its cortisol-lowering effect.

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3.2.2. Second generation: high selectivity

Exemplified by lorundrostat, these inhibitors were designed to overcome the selectivity issue. Lorundrostat shows a remarkable 374-fold preference for CYP11B2 over CYP11B1 in vitro. This translates to potent, dose-dependent aldosterone reduction (up to 70%) in humans without disrupting basal or stimulated cortisol production, offering a much-improved therapeutic window for hypertension.

3.2.3. Third generation: expanded indications / multi-target potential

Emerging compounds like BI 690517 define this generation by exploring indications beyond hypertension. In a phase 2 trial, it demonstrated efficacy in chronic kidney disease, dose-dependently reducing urinary albumin-to-creatinine ratio (UACR) by 22-39%. Its additive effect when combined with empagliflozin suggests potential for multi-target therapeutic strategies in cardio-renal diseases.

3.3. Mechanism of action: blocking at the source

3.3.1. ASIs: core mechanism and molecular basis

ASIs are a different perspective of antihypertensive agents, which is mechanically different in nature. In their mode of action, they directly and selectively suppress the enzyme aldosterone synthase (CYP11B2), which performs the last phase in aldosterone production in the adrenal cortex. ASIs amicably inhibit the systemic production of the major mineralocorticoid hormone, aldosterone, by acting on this enzymatic source.

The approach of preventing the upstream and inhibiting of the receptor has some important theoretical benefits over conventional MRAs such as spironolactone, which work downstream to block the receptor. Blockade of Both Genomic and Non-Genomic Aldosterone Effects: Aldosterone has deleterious actions (both genomic slow, receptor-mediated and rapid non-genomic). Angiogenic Potential of Better Safety: MRAs leave the genomic actions of mineralocorticoid receptor intact, whereas traditional steroidal ASIs reduce the levels of circulating aldosterone itself, potentially preventing all the consequences of mineralocorticoid action, including non-genomic action (not specifically through the mineralocorticoid receptor). ASIs can result in more desirable side effect profile by decreasing the levels of aldosterone at its source. Clinical trials with high selectivity ASIs have demonstrated adequate blood pressure lowering with only slight rises in serum potassium and no impact on cortisol secretion levels implying a decreased risk of clinically significant hyperkalemia and endocrine adverse events. Nevertheless, this possible benefit should be legitimized by conducting bigger, long-term outcome studies.

3.3.2. Molecular basis for high selectivity and emerging research

The therapeutic utility of ASIs depends on superb selectivity against the closely related enzyme CYP11B1 (11 1 -hydroxylase): the enzyme that synthesizes cortisol. These two enzymes are about 93 percent identical in terms of sequence which makes effective design of drugs a huge challenge. The great selectivity of contemporary non-steroidal ASIs are products of exact molecular engineering appropriate due to the understanding of the structure: Active Site Coordination: The majority of inhibitors are tailored to coordinate the red blood cell at the site in an embodiment of the enzyme and inhibit its catalytic power. Exploitation of Subtle Structural Differences: Two distinct

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key differences of adjacent accessory binding pockets (substrate-access channels) in CYP11B2 and CYP11B1 are exploited despite near-identical active sites. The inhibitors are designed to establish the most ideal hydrogen bonds, salt bridges, and Van der Waals interactions with the original topology of the CYP11B2 pocket thus being selective towards CYP11B2 and incompatible to CYP11B1. As an example, the novel ASI lorundrostat is selective in vitro 374-fold with respect to CYP11B2 compared to CYP11B1.

4. Clinical evidence and application prospects of aldosterone synthase inhibitors

4.1. Essential hypertension and specific subgroups (low-renin/salt-sensitive)

The target population of essential hypertension is large and ASIs have obtained the largest and most credible clinical trials in the hypertension area and have proven to be stable and produce antihypertensive activity. A meta-analysis that was published in 2024 and included seven randomized controlled trials (including 1440 patients in total) gave detailed evidence on the effectiveness of ASIs [5]. These agents were found to be able to decrease office systolic blood pressure by an average of 6.3mmHg and office diastolic blood pressure by 2.2mmHg, and also they did not increase the risk of adverse events significantly. The patient subgroup with inhibited plasma renin activity targeted in a specific study, reported in 2023, in the Target-HTN trial, was shown to be significantly lowered in systolic blood pressure by the ASI lorundrostat (50 mg/day) [6]. This continues to be supported in 2025, by the Advance-HTN trial, which found that the effectiveness of lorundrostat was comparable across the racial line in a resistant hypertension group in which 53% were African American patients [7]. The clinical implications of this finding are very important because African American populations are more burdened with low-renin and resistant hypertension. These results suggest that, through the biomarkers, including the aldosterone-to-renin ratio, ASIs can be used to stratify therapy of hypertension.

4.2. Resistant hypertension

Cardiovascular risk is extremely high in the patients with resistant hypertension, and there is an unmet therapeutic need. Taking of traditional Mineralocorticoid Receptor Antagonist (MRA, e.g. spironolactone) is commonly restricted due to the side effects of the sex hormone and a risk of hyperkalemia. ASIs provide another approach to dealing with this issue by inhibiting the secretion of aldosterone in the first place.

As seen, pivotal Phase II clinical trials have validated the major effectiveness of ASIs in this segment of patients. Clinical trial at Phase II showed that Baxdrostat is effective in reducing blood pressure in patients with resistant hypertension [8]. In 2025, the Advance-HTN trial was a Phase IIb study in patients whose blood pressure was not optimized with triple-drug therapy, which reported that lorundrostat (50 mg/day) was to offer an extra decrease of about 8 mmHg in mean systolic blood pressure during 24 hours [7]. It was also discovered in this trial that further dose increase of antihypertensives of dose ranging between 50 mg and 100mg was not accompanied by any additional antihypertensive effect though accompanied by increased adverse events and therefore moderate dose of antihypertensives may form the best balance between efficacy and safety. Moreover, this synergistic effect could also be observed with ASIs that are combined with Renin-Angiotensin System inhibitors that would otherwise trigger the compensatory increase in angiotensin II due to decreasing the aldosterone level.

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4.3. Primary aldosteronism

The most popular cause of secondary hypertension is Primary Aldosteronism (PA). Pharmacological treatment is the predominant one in patients with bilateral adrenal hyperplasia, or those who are not operable. Existing conventional drugs (e.g., spironolactone) can only prevent the aldosterone receptor but not decrease the plasma levels. Non-genomic pathways are still able to result in cardiorenal damage secondary to excess aldosterone [4].

ASIs are a new technological resolution concerning the medical treatment of PA because they can approach the very way of this pathological process, i.e. the autonomous production of aldosterone. ASIs have the potential to inhibit the genomic and non-genomic effects of aldosterone simultaneously through inhibition of the CYP11B2 enzyme, and thus would provide a more comprehensive level of organ protection. New-generation agents (e.g., lorundrostat and baxdrostat) are more selective aldosterone synthase (rather than the cortisol pathway), and therefore more appropriate to individuals who need long-lasting therapy, unlike the previous generation (which potentially could have an impact on cortisol production) [8]. As such, ASIs offer a new specific alternative to patients of PA who cannot tolerate MRAs, or whose reaction to the latter is suboptimal, or would rather medications to manage their ailment.

4.4. Cardio-renal target organ protection

The possible advantages of ASIs go much beyond the blood pressure. Their highlighted importance is the fact that it may be possible to directly mitigate and even reverse the aldosterone-mediated target organ damage, which is one of the key future directions in the given drug type.

Cardiac Protection: (Excess) aldosterone enhances myocardial adaptation and diastolic dysfunction, which can result in heart failure, by other mechanisms including pro-inflammatory and pro-fibrotic. The ASIs can theoretically inhibit these endocrine processes in a more comprehensive way because of reducing the levels of circulating and local tissue aldosterone. ASIs have already been shown to have potential in attenuating myocardial fibrosis and enhancing cardiac activity by preclinical investigations.

Renal Protection: Aldosterone has a critical role in the development of chronic kidney disease resulting in signs of glomerular hyperfiltration, podocyte injury, and proteinuria. In 2024, a Phase II clinical trial (which used BI 690517) demonstrated that ASIs could lower Urinary Albumin-to-Creatinine Ratio (UACR) by 22-39 per cent. of patients with chronic kidney disease [9]. It is a strong suggestion of a renoprotective effect without lowering the blood pressure. ASIs might be more effective than receptor blockade since they decrease intrarenal aldosterone levels, which enhances renal protection.

Currently, large and long-term clinical studies are still under investigations into the effects of ASIs on hard cardio-renal outcomes (e.g., heart failure hospitalization, end-stage renal disease). Their findings will eventually define the place of these drugs in organ protection area.

5. Safety, tolerability, and drug interactions

5.1. Cortisol synthesis inhibition: a risk mitigated by high selectivity

The primary safety challenge in developing ASIs is achieving selectivity for aldosterone synthase (CYP11B2) over the nearly identical (93% homology) cortisol-synthesizing enzyme, 11β-hydroxylase (CYP11B1). Off-target inhibition of CYP11B1 can impair glucocorticoid production

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and trigger compensatory ACTH elevation. Early, less selective compounds demonstrated this liability. However, highly selective second-generation ASIs have effectively minimized this risk. For instance, lorundrostat has demonstrated a 374-fold in vitro selectivity for CYP11B2 over CYP11B1. In a first-in-human study, it showed no suppression of basal or cosyntropin-stimulated cortisol production across a wide dose range. This establishes that exceptional enzymatic selectivity can effectively dissociate aldosterone suppression from clinically significant hypocortisolism.

5.2. Hyperkalemia: a dose-dependent effect with a favorable profile compared to MRAs

One of the known class effects of renin-angiotensin-aldosterone inhibition is hyperkalemia. In case of ASIs, it is a dose dependent and usually mild risk. Most cases do not need intervention as revealed by clinical data. A phase 2 study of BI 690517 indicated the presence of investigator-reported hyperkalemia in 10-18% of active study participants versus 6% in placebo [9]. Mechanically, ASIs could provide a possible superiority of MRAs. ASIs will be able to facilitate a more balanced inhibition of mineralocorticoid activity by decreasing aldosterone and its precursors, and this fact may avoid the risk of extreme forms of electrolyte disruptions, and the hormone may not be completely neutralized, which may help to reduce the risk of severe electrolyte disturbances. This becomes possible with the evidence that mean serum potassium has only a significant increment with lorundrostat.

5.3. Pharmacokinetics and drug-drug interaction potential via CYP450 metabolism

The pharmacokinetic profile of non-steroidal ASIs introduces specific safety considerations. These small-molecule inhibitors are primarily metabolized by hepatic CYP450 enzymes. This creates a clear potential for drug-drug interactions when co-administered with strong inducers or inhibitors of these metabolic pathways. For example, the pharmacokinetics of BI 690517 (vicadrostat) have been characterized in phase 1 studies, confirming its metabolic pathway. Consequently, appropriate dose adjustments and monitoring are necessary when these agents are used concurrently with other medications that significantly affect CYP450 activity to maintain therapeutic efficacy and avoid toxicity.

6. Challenges and future directions

6.1. Challenges

Even though there has been substantial progress in the creation of aldosterone synthase (CYP11B2) inhibitors, a number of significant obstacles still exist. The first of them is the fact that it is intrinsically challenging to gain total specificity against the almost identical cortisol-producing enzyme CYP11B1, owing to their almost-identical active sites. This also implies unexplained concerns regarding the long-term effects of the slightest disruption of the cortisol axis under the influence of stress and the impact of chronically raised ACTH. The little known about the drugs is that the best place to put them into the treatment regimen is still to be determined and it is time to find predictive biomarkers that are reliable and not reliant on the aldosterone to renin ratio when it comes to making an accurate patient selection. Besides, although combination therapies, especially combined with SGLT2 inhibitors, may be potentially effective, they should still be carefully integrated with currently existing drug classes, in particular, the mineralocorticoid receptor antagonists, since such a combination may potentially cause critical safety issues, such as hyperkalemia. Lastly, the long-term efficacy and safety profile, i.e., the sustainability of blood

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pressure control, the impact of the intervention on hard cardiovascular and renal outcomes, and the risk linked to protracted chronic modulation of adrenal steroidogenesis remains to be fully defined, which necessitates long-phase III trials and close post-marketing surveillance.

6.2. Future directions

The potential solutions to the selectivity issue are creation of more targeted ASIs, which inhibit areas other than the active site, where the difference in enzymes are greater; or further dual-targeting which balances the inhibition of both CYP11B2 and CYP11B1 in the case of Cushing syndrome with mineralocortin excess. The structural studies of enzyme-inhibitor complexes that will be aimed at continuously will aid the development of next-generation compounds with improved selectivity.

Clinically, in the future, work on the identification of viable biomarkers, including steroid metabolomics patterns, should be conducted as a means of improved predictive response to treatment. Studies ought also to shed light on the ideal location of therapy by conducting comparative research and health economic researches.

In terms of combination therapy, the most promising solution is the combination of ASIs and SGLT2 inhibitors, initially there is certain evidence of increased renal effects (e.g., decreased UACR) when combined with these agents [10]. Phase III trials will be used to further test this strategy. The challenging issue of safety concerns is not the only reason why synergistic effects on target organ protection including the decrease in fibrosis and inflammation should be investigated.

Lastly, the efficacy and safety should be determined over the long term with the implementation of prolonged phase III trials and post-marketing surveillance to completely define the risk benefit profile of these inhibitors over the long term.

7. Conclusion

Aldosterone synthase inhibitors provide a new and still potentially promising approach to the treatment of hypertension and other ailments caused by aldosterones. These agents have the potential to provide superior inhibition of aldosterone pathological effects by preventing the activation of the downstream receptors and instead inhibiting aldosterone biosynthesis. Very specific chemicals such as lorundrostat and baxdrostat have formed a major step forward in treatment showing large blood pressure equalizing contrasting to previous inhibitors and lack the hormonal disturbances previously seen. The major issues are not resolved such as long-term safety, the best choice of patients, and the place in the treatment algorithms; nevertheless, nowadays, clinical evidence tends to suggest their possible value in the systems of resistant hypertension and primary aldosteronism. Future studies may involve establishment of long-term protective advantages of cardiovascular and renal, development of patient selection strategies on the basis of biomarkers and evaluation of combining strategies with present antihypertensive classes, especially SGLT2 inhibitors. Further progress in the study of the structure and pathophysiology of CYP11B2 is likely to promote the development of even selective and safer aldosterone-related disease inhibitors.

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