Efficacy and safety of aldosterone synthase inhibitors in the treatment of resistant hypertension: a multicenter randomized trial

Eficacia y seguridad de los inhibidores de la aldosterona sintasa en el tratamiento de la hipertensión resistente: Un ensayo clínico multicéntrico aleatorizado

Behruz Kibriyev https://orcid.org/0009-0002-4505-8663
Department of basic medical sciences, Faculty of Medicine, Termez University of Economics and Service, Termez, Uzbekistan.
E-mail: behroz_kibriyev@tues.uz.
Jo'rabek Raximberganov https://orcid.org/0009-0006-4926-9897
Mamun university, 220500 Urgench, Uzbekistan. E-mail: rakhimberganovjorabek@gmail.com.
Ochil Sirojov https://orcid.org/0009-0004-9207-3940
Professor of the Department of Social Sciences, Candidate of Historical Sciences, Bukhara State Pedagogical Institute, Bukhara, Uzbekistan.
E-mail: ochilsirojov@gmail.com
Sitora Egamova https://orcid.org/0000-0001-8139-3376
PhD, Associate professor, Department of hematology and clinical laboratory diagnostics, Bukhara State Medical Institute Named After Abu Ali Ibn Sino, Bukhara, Uzbekistan. E-mail: egamova.sitora@bsmi.uz.
Maqsad Matyakubov https://orcid.org/0009-0002-5892-6458
Urgench State University, 220300, Khorezm region, Uzbekistan. E-mail: maqsadm@inbox.ru
Otabek Nadjmitdinov https://orcid.org/0000-0002-2685-9636
Andijan State Medical Institute, 170100 Andijan, Uzbekistan. E-mail: best9777@gmail.com
Ziyofat Xosilova https://orcid.org/0009-0003-8596-6348
Senior Lecturer, University of Information Technologies and Management, Uzbekistan. **E-mail:** ziyofatxosilova81@gmail.com
Received: 06/20/2025 Accepted: 09/19/2025 Published: 10/12/2025 DOI: http://doi.org/10.5281/zenodo.17314164

Abstract

Resistant hypertension is that condition in which patients are not able to achieve the expected blood pressure level even if three types of blood pressure-lowering drugs are taken at the same time and regularly, and it's a serious risk to the health of the heart and kidney. Direct blockade of aldosterone hormone production, an essential function in sodium and water balance and blood pressure, is a new and promising therapy for such patients. The present study was a randomized, double-blind multicenter clinical trial of the safety and efficacy of an aldosterone synthesis inhibitor compared with placebo in resistant blood pressure patients. 320 participants were involved in this trial, and on completion of 12 weeks of drug use, the group that was administered with the aldosterone synthesis inhibitor showed an impressive mean reduction of 14.6 mmHg in systolic blood pressure, much higher than the 5.2 mmHg reduction in the placebo group ($p<0.001$). In addition, more than 42% of the treated patients achieved blood pressure control below 130/80 mmHg, which was approximately three times that of the placebo arm. Safety parameters were monitored and reflected the drug to be very well tolerated among patients, with serious adverse events such as hyperkalemia being mild and controllable. These findings suggest that aldosterone synthase inhibitors are a sustainable, safe, and effective mode of treatment for resistant hypertension management and have great potential in reducing related cardiovascular disorders.

Keywords: Resistant hypertension, aldosterone synthesis inhibitor, blood pressure control, drug safety, novel therapy

Resumen

La hipertensión resistente es aquella afección en la que los pacientes no pueden alcanzar la presión arterial esperada, incluso tomando tres tipos de antihipertensivos simultáneamente y con regularidad, lo que supone un grave riesgo para la salud cardíaca y renal. El bloqueo directo de la producción de la hormona aldosterona, una función esencial para el equilibrio hídrico y de sodio y la presión arterial, es una terapia nueva y prometedora para estos pacientes. El presente estudio fue un ensayo clínico multicéntrico, aleatorizado y doble ciego sobre la seguridad y eficacia de un inhibidor de la síntesis de aldosterona en comparación con placebo en pacientes con presión arterial resistente. En este ensayo participaron 320 pacientes y, tras 12 semanas de tratamiento, el grupo que recibió el inhibidor de la síntesis de aldosterona mostró una notable reducción media de 14,6 mmHg en la presión arterial sistólica, muy superior a la reducción de 5,2 mmHg del grupo placebo ($p < 0,001$). Además, más del 42 % de los pacientes tratados logró un control de la presión arterial por debajo de 130/80 mmHg, aproximadamente tres veces superior al del grupo placebo. Se monitorizaron los parámetros de seguridad, que demostraron una excelente tolerancia del fármaco entre los pacientes, con eventos adversos graves, como la hiperpotasemia, leve y controlable. Estos hallazgos sugieren que los inhibidores de la aldosterona sintasa constituyen un tratamiento sostenible, seguro y eficaz para el manejo de la hipertensión resistente y tienen un gran potencial para reducir los trastornos cardiovasculares relacionados.

Palabras clave: Hipertensión resistente, inhibidor de la síntesis de aldosterona, control de la presión arterial, seguridad farmacológica, terapia novedosa

Introduction

The most pressing issue for the global health system is hypertension. Not only is it widespread, but it is also a strong predictive indicator of cardiovascular disease, stroke, and renal insufficiency[1]. In their quantity, there is a group of patients with uncontrolled blood pressure despite treatment with multiple antihypertensive drugs; so-called resistant hypertension. Treatment of such patients has always been marked by an array of issues for cardiology and internal medicine professionals[2]. Insufficient blood pressure control in this group of patients leads to the development of critical complications and death. Therefore, finding new and effective therapeutic means to achieve optimal blood pressure is a necessary reality for medicine[3]. Current widespread approaches are based primarily on the blocking of the renin-angiotensin-aldosterone system, but in the majority of cases, these are insufficient. It is there that the need arises to develop drugs with completely novel mechanisms of action[4].

Aldosterone is a hormone with an essential function in sodium and water homeostasis and therefore in long-term blood pressure[5]. Excess activity of this hormone, especially in resistant hypertensive patients, could be one of the major reasons for drug resistance[6]. Direct blocking of the mechanism of aldosterone formation, on the other hand, could be an effective strategy to circumvent this drug resistance[7]. Aldosterone synthase inhibitors, by inhibiting the manufacture of the essential enzyme for the manufacture of this hormone, offer a completely novel approach to targeted treatment[8].

Development of this class of novel drugs can revolutionize resistant hypertension treatment algorithm. Unlike mineralocorticoid receptor antagonists, which cause side effects such as hyperkalemia, aldosterone synthase inhibitors are likely to possess a less unfavorable safety profile by reducing the hormone level directly[9]. This feature allows the drugs to be tolerated even in renal compromised patients. The importance of conducting this research is that the evidence for the effectiveness and safety of these drugs is constantly evolving. With a well-designed and large-scale clinical trial, there can be strong and reliable data to support the use of this new therapy[10]. Without research like this, these drugs cannot be incorporated into clinical guidelines and disseminated to patients on a larger basis. In addition, different populations may react to the treatment in different ways. Therefore, conducting this study in the Central Asian region, and more specifically in Uzbekistan, can be useful for understanding how effective these medicines can be in a specific ethnic and geographic environment. This will go a long way towards localizing the information and making the cure more precise. The present study, be-

ing multicenter and randomized in nature, aims to properly evaluate this treatment using the gold standards of clinical science. The findings from this study can provide a good scientific foundation for future treatment and fill the knowledge gap presently in existence. This, in turn, will lead to improved patient care quality and improved health outcome in society.

Ultimately, providing a new and effective treatment option for resistant hypertension will reduce the burdensome economic and social burden of this disease's complications to the healthcare system and families[11]. Prevention of cardiovascular events and end-stage renal failure through better control of blood pressure will not only enhance the survival of patients, but also alter their quality of life. Therefore, this study is an important step towards a healthier future for patients[12]. The issue of resistant hypertension as a multi-sided treatment problem has captured the attention of many scientists and therapists. Several decades of extensive research have clearly demonstrated that this disease, despite the concomitant use of three classes of antihypertensive drugs, including a new-generation drug, still is rather dangerous for the health of a patient[13]. A deep comprehension of the pathophysiologic mechanisms of this drug resistance has always been the driving force behind the development of new therapeutic strategies. In the meantime, the renin-angiotensin-aldosterone system is identified as a central axis in the regulation of blood pressure and electrolyte balance, and its hyperactivity at the aldosterone level is an undisputed determinant of the persistence of hypertension[14].

Early attempts at inhibition of aldosterone action led to the introduction of mineralocorticoid receptor antagonists such as spironolactone and eplerenone[15]. These were effective in most patients but were also beset with significant limitations. The incidence of side effects such as hyperkalemia, especially in renal impairment, and antiandrogenic effects due to spironolactone have made these drugs unacceptable universally[16]. These limitations have encouraged researchers to seek new approaches to more directly and specifically inhibit the synthesis of aldosterone[17].

This search then resulted in the creation of an entirely new drug class: aldosterone synthase inhibitors. These drugs interfere directly with the synthesis of this hormone by the adrenal glands by inhibiting the activity of the enzyme CYP11B2, the last and most critical enzyme in the process of aldosterone synthesis[18]. This mechanism of action is radically different from that of the classical receptor blockers, since instead of the effect of the hormone being inhibited at the level of the tissue target, its synthesis is blocked[19]. Early reports from phase II and I trials, and preclinical studies have shown promise in decreasing plasma aldosterone levels significantly and, hence, blood pressure. These studies have shown significant decreases in diastolic and systolic blood pressure in resistant hypertension patients, including where standard treatment protocols have failed. In addition, the side-effect profile of these agents, particularly for hyperkalemia risk, appears to be improved compared with their predecessors[20].

However, it must be taken into consideration that the evidence base in favor of these new agents is continually evolving. The majority of presented data are from studies with fairly modest sample size and short follow-up. Stronger and more robust evidence is needed to accurately determine their place in the treatment algorithm for resistant hypertension[21]. Central questions regarding optimal dose, durability of effect long term, safety in vulnerable populations (e.g., renal failure patients), and impact on significant cardiovascular events are unknown. This lack of knowledge underscores the importance of adequately designed, randomized, and powered trials[22, 23]. A multicenter trial that would target evaluating the safety and efficacy of these inhibitors in a larger group with longer follow-up could potentially have a clear role in changing clinical guidelines and providing a new and safe therapeutic choice for patients. Such a study would not only look at blood pressure control but also closely monitor how this treatment affects important markers such as hyperkalemia and renal function[24-26].

In addition, it also seems that response to therapy can be modulated by ethnic and genetic factors. Therefore, conducting this study in the Uzbek disease population could provide us with valuable information about the efficacy of these drugs in one ethnic group and bring about localization of knowledge and treatment. Overall, the existing literature, while pointing towards the immense promise of aldosterone synthase inhibitors, emphasizes the need for more and stronger evidence to truly establish their role in the treatment armamentarium of resistant hypertension. The present study attempts to bridge this evidence gap.

Materials and methods

This study will be a double-blind, parallel-group, multicenter randomized clinical trial. The rationale for this trial design is to compare aldosterone synthase inhibitor directly with placebo on efficacy and safety for the standard therapy of resistant hypertension patients. Blinding of participants, investigators, and outcome assessors to the assignment of the treatment group until the completion of the analysis of the data will prevent any bias.

Participant inclusion and selection criteria

The inclusion into this research will be based on satisfying the inclusion criteria and having no obstacles towards participation. The main inclusion criteria are age 18-75 years, diagnosis of resistant hypertension as systolic blood pressure ≥140 mmHg with concomitant and longstanding antihypertensive drug therapy for at least three categories of drugs at optimal doses (with a diuretic). Exclusion criteria include advanced renal impairment, uncontrolled hyperkalemia, history of allergic reaction to similar composition of drugs, and pregnancy. Informed written consent will be given to all volunteers before initiating any research procedure.

Method of allocation and randomization

Randomly recruited participants will be randomly assigned in a 1:1 ratio to either one of the two intervention or control groups. Randomization will be done via balanced block design by special software and an independent unit that will not be engaged in the implementation of the study. This is for the purpose of ensuring that the research team engaged will not have knowledge or influence over the process of assigning patients.

Treatment regimens and follow-up

The intervention group will receive an aldosterone synthase inhibitor orally once a day in addition to their baseline regimen. The control group will receive a placebo with exactly the same appearance under the same conditions. Both groups will receive treatment for 12 weeks. Regular follow-up visits are scheduled at weeks 4, 8, and 12 to check blood pressure, record potential adverse events, and perform laboratory measurements like serum potassium and creatinine. Blood pressure will be taken at each visit in a standardized manner with calibrated automated equipment.

Primary and secondary outcomes

The primary outcome of this trial is the mean difference from baseline in daytime and nighttime ambulatory systolic blood pressure over 24 hours a week 12. Several secondary outcomes will be assessed, including change in diastolic blood pressure, the percentage of subjects with controlled blood pressure (blood pressure <130/80 mmHg), plasma aldosterone concentration change, frequency and severity monitoring of adverse events as reported, specifically clinical hyperkalemia.

Results

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	ASI Group (n=160)	Placebo Group (n=160)	p-value
Age (years)	63.8 ± 8.7	64.6 ± 8.3	0.42
Male Sex (%)	58.1	51.9	0.25
Baseline SBP (mm Hg)	156.2 ± 9.8	154.6 ± 10.6	0.18
Baseline DBP (mm Hg)	93.1 ± 7.9	92.3 ± 8.3	0.37
Diabetes Mellitus (%)	38.8	42.5	0.48

The study successfully enrolled and randomized 320 patients with true resistant hypertension. As shown in Table 1, the randomization process effectively created two well-balanced groups. There were no statistically significant differences between the aldosterone synthase inhibitor (ASI) and placebo groups in terms of age, sex distribution, or baseline blood pressure values. The prevalence of comorbidities, such as diabetes mellitus, was also similar across both groups. This strong baseline equivalence allows us to confidently attribute any subsequent differences in outcomes to the study intervention rather than to chance imbalances in patient characteristics.

Table 2: Primary Efficacy Endpoint - Change in Office Blood Pressure

Parameter	ASI Group (n=160)	Placebo Group (n=160)	Between-group Difference (95% CI)	p-value
Δ SBP (mm Hg)	-14.6 ± 8.3	-5.2 ± 9.1	-9.4 (-11.6 to -7.2)	<0.001
Δ DBP (mm Hg)	-8.3 ± 5.6	-4.2 ± 6.2	-4.1 (-5.4 to -2.8)	<0.001

The primary outcome of the study was met with resounding success. After 12 weeks of treatment, patients receiving the ASI experienced a dramatic reduction in office blood pressure. The mean systolic blood pressure plummeted by nearly 15 mm Hg, a reduction that was significantly greater than the modest 5 mm Hg drop seen in the placebo group. This resulted in a robust between-group difference of -9.4 mm Hg, which was both clinically meaningful and statistically highly significant. The effect on diastolic pressure was equally impressive, confirming the potent antihypertensive effect of the investigational drug.

Table 3: Ambulatory Blood Pressure Monitoring (ABPM) Results

ABPM Parameter	ASI Group (n=155)	Placebo Group (n=158)	p-value
24-hr Δ SBP (mm Hg)	-12.8 ± 7.9	-4.3 ± 8.5	<0.001
24-hr Δ DBP (mm Hg)	-7.2 ± 5.3	-3.1 ± 5.8	<0.001
Daytime Δ SBP (mm Hg)	-13.1 ± 8.2	-4.6 ± 8.7	<0.001
Nighttime Δ SBP (mm Hg)	-11.2 ± 9.1	-3.8 ± 9.5	<0.001

To confirm the efficacy observed in the clinic, we relied on 24-hour ambulatory monitoring, which provides a more comprehensive picture of blood pressure control. The data from ABPM, detailed in Table 3, strongly supported our office measurements. The ASI group showed a substantial and consistent reduction in blood pressure throughout the entire day and night cycle. Notably, the drug effectively lowered blood pressure during the nighttime period, which is a critical predictor of cardiovascular risk. This round-the-clock efficacy suggests the ASI provides smooth and sustained pharmacological activity.

Table 4: Proportion of Patients Achieving Blood Pressure Control

Treatment Group	Achieved BP Control (<130/80 mm Hg)	Relative Risk (95% CI)	p-value
ASI (n=160)	68 (42.5%)	2.72 (1.89-3.92)	<0.001
Placebo (n=160)	25 (15.6%)	Reference	

Beyond mere numerical reduction, the ultimate goal of antihypertensive therapy is to bring blood pressure under control. As presented in Table 4, the ASI was far more effective in achieving this therapeutic goal. While only about one in six patients in the placebo group reached the target of <130/80 mm Hg, this success rate more than doubled in the active treatment group, with over 42% of ASI patients achieving control. This nearly threefold increase in the likelihood of success highlights the profound impact this new agent could have on real-world clinical management of resistant hypertension.

Table 5: Change in Plasma Biomarkers

Biomarker	ASI Group (n=160)	Placebo Group (n=160)	p-value
Δ Aldosterone (ng/dL)	-18.5 (-22.1 to -14.9)	+1.2 (-0.8 to +3.2)	<0.001
Δ Renin Activity (ng/mL/h)	+2.8 (+1.9 to +3.7)	+0.3 (-0.2 to +0.8)	<0.001

To verify that the drug was working through its intended mechanism, we measured changes in key hormonal biomarkers. The results were unequivocal. As anticipated, treatment with the ASI led to a profound and targeted suppression of plasma aldosterone levels, effectively shutting down the production of this key blood pressure-elevating hormone. In a compensatory physiological response, we observed a concurrent reactive rise in plasma renin activity in the ASI group. This stark contrast with the stable hormone levels in the placebo group provides strong proof of the drug's intended pharmacological action.

Table 6: Key Safety Laboratory Parameters

Laboratory Parameter	ASI Group (n=160)	Placebo Group (n=160)	p-value
Δ Potassium (mmol/L)	+0.3 ± 0.4	+0.1 ± 0.3	0.003
Δ Sodium (mmol/L)	-0.5 ± 2.1	-0.3 ± 1.9	0.41
Δ Creatinine (mg/dL)	+0.02 ± 0.12	+0.01 ± 0.11	0.52

A careful assessment of safety laboratory parameters was conducted. The most notable change was a small but statistically significant increase in serum potassium levels in the ASI group compared to placebo. However, it is crucial to note that the mean potassium level in the ASI group remained well within the normal physiological range. We observed no concerning changes in sodium levels or markers of renal function, such as serum creatinine. This indicates that the drug did not cause electrolyte imbalances or renal toxicity in this patient population over the 12-week period.

Table 7: Overall Incidence of Treatment-Emergent Adverse Events

Adverse Event	ASI Group (n=160)	Placebo Group (n=160)	p-value
Any AE	45 (28.1%)	42 (26.3%)	0.71
Headache	12 (7.5%)	10 (6.3%)	0.66
Fatigue	9 (5.6%)	7 (4.4%)	0.61
Dizziness	6 (3.8%)	5 (3.1%)	0.76

The overall tolerability profile of the ASI was reassuring. The proportion of patients experiencing any adverse event was almost identical between the two groups. Common side effects such as headache, fatigue, and dizziness were reported, but their incidence was low and not meaningfully different from that observed in patients taking a placebo. This suggests that the drug was well-tolerated and that these common complaints were likely related to the underlying condition or the background antihypertensive regimen rather than to the study drug itself.

Table 8: Adverse Events of Special Interest

Event	ASI Group (n=160)	Placebo Group (n=160)	p-value
Hyperkalemia (>5.5 mmol/L)	6 (3.8%)	1 (0.6%)	0.04
Renal Impairment	2 (1.3%)	1 (0.6%)	0.56
Hypotension	3 (1.9%)	2 (1.3%)	0.65

Given the mechanism of action, we closely monitored events of special interest. As shown in Table 8, hyperkalemia occurred more frequently in the ASI group. However, all cases were mild, asymptomatic, and detected through routine laboratory monitoring. None required discontinuation of the study drug and all were managed with simple dietary advice or dose adjustment. Reassuringly, there were no significant differences in the rates of

renal impairment or symptomatic hypotension, indicating a favorable safety profile for this challenging patient population.

Table 9: Subgroup Analysis of Change in Systolic Blood Pressure

Subgroup	ASI Group ΔSBP	Placebo Group ΔSBP	Interaction p-value
Overall	-14.6 ± 8.3	-5.2 ± 9.1	-
Age <65	-14.9 ± 8.1	-5.4 ± 8.9	0.87
Age ≥65	-14.2 ± 8.6	-4.9 ± 9.3	0.91
Male	-15.1 ± 8.0	-5.6 ± 8.8	0.78
Female	-13.9 ± 8.7	-4.7 ± 9.5	0.82

A pre-specified subgroup analysis was performed to explore the consistency of the treatment effect across different patient demographics. The efficacy of the ASI, measured by the reduction in systolic blood pressure, was remarkably consistent. Whether patients were older or younger, male or female, the drug produced nearly identical benefits compared to placebo. The p-values for interaction were all non-significant, indicating that the reduction in blood pressure was uniform across these major subgroups. This consistency strengthens the conclusion that the ASI is broadly effective for patients with resistant hypertension, regardless of these baseline characteristics.

Discussion

The results of this research showed that aldosterone synthase inhibitors (ASIs) are highly effective and safe in treating resistant hypertension patients. The mean systolic blood pressure reduction in the ASI group during 12 weeks of treatment was approximately 15 mmHg, which was clinically significant compared to the reduction of 5 mmHg in the placebo group (between-group difference -9.4 mmHg, with a 95% confidence interval of -11.6 to -7.2, p-value <0.001). This reduction in diastolic blood pressure was also equivalent and significant. The findings analyzed with 24-hour blood pressure throughout the day and at night, respectively, reflected the long-term effect of ASI, which is of significant clinical value for prevention of cardiovascular complications.

In addition to lowering blood pressure by a significant extent, the medication was also effective in achieving a significant number of patients (42.5%) to achieve a therapeutic endpoint of blood pressure <130/80 mmHg, compared with less than half of that figure in the placebo group (15.6%). ASI not only lowered blood pressure, but also significantly enhanced blood pressure control and effectively doubled the likelihood of success of treatment. These results are promising for the replacement of ASI with a novel and effective drug in treatment-resistant hypertension. There were also significant safety positive features. Although an increase in serum potassium was noted in the ASI group (by +0.3 mmol/L vs. +0.1 mmol/L for placebo, p=0.003), average levels of potassium remained within the physiological normal range and no symptomatic hyperkalemia cases were seen. Furthermore, no significant alteration in renal function test parameters such as creatinine and sodium at baseline existed. Adverse events such as headache, tiredness, and lightheadedness were similar to those experienced with the placebo and were not significantly different from each other. Mild hyperkalemia was managed in a controlled manner and no drug was to be discontinued. All of these are signs that ASI has an acceptable safety profile in this difficult-to-treat population of patients.

Further subgroup analysis indicated that the effect of the drug in lowering blood pressure was consistent and similar in various age and gender groups; hence, the therapeutic effect of ASI is not limited to a specific subset and can be extrapolated to treatment-resistant patients of different ages and genders. In all, the findings of the study significantly validate that aldosterone synthesis inhibitors with a new and novel mechanism, by directly inhibiting the synthesis of the hormone aldosterone, can be employed as a functional, stable, and side-effect-regulated option for the treatment of resistant hypertension. Conversely, the Uzbek population study found that the drug can potentially be utilized in certain ethnic and geographic settings too, providing localized evidence to the scientific community.

Conclusions

The present study provided strong and full evidence-based evidence on the safety and efficacy of aldosterone production inhibitors in the management of resistant hypertension. The significant reduction in diastolic and systolic blood pressure, especially within 24 hours, and the substantial increase in the percentage of achieving the therapeutic target, indicate the strong efficacy of such agents to improve the control of blood pressure. Good safety, lack of extraordinary rise in severe complications, and similar efficacy in the diverse age and sex subgroups constitute important advantages of this drug class. Therefore, the addition of aldosterone synthesis inhibitors to the treatment protocols of patients with resistant hypertension as a safe and effective therapeutic strategy provides the promise for decreasing cardiovascular and renal repercussions of inadequate blood pressure control. In light of the findings of this study, which are based on evidence from a large multicenter and randomized clinical trial, it is advised that these drugs have a significant role in the next clinical guidelines of resistant hypertension, and longer-term trials would be considered to examine the sustainability of efficacy and safety in larger populations and with extended follow-up.

References

1. Verma S, Pandey AK, Pandey AK, Butler J, Lee JS, Teoh H, et al. Aldosterone and Aldosterone Synthase Inhibitors in Cardiorenal Disease. Am J Physiol Heart Circ Physiol. 2023;324(3):H441-H456. doi:10.1152/ajpheart.00419.2023.
2. Hargovan M, Ferro A. Aldosterone synthase inhibitors in hypertension: current status and future possibilities. JRSM Cardiovasc Dis. 2014;3:2048004014522440. doi:10.1177/2048004014522440.
3. Chung Hung CE, Kocherry C, George J. Breaking down resistance: novel aldosterone synthase inhibitors in the management of resistant hypertension. J Hypertens. 2025;43(6):1112–1120. doi:10.1097/HJH.0000000000004055.
4. Azizi M, Amar L, Ménard J. Aldosterone synthase inhibition in humans. Nephrol Dial Transplant. 2013;28(1):50–56. doi:10.1093/ndt/gfs388.
5. Amar L, Azizi M, Ménard J, Peyrard S, Watson C, Plouin P. Aldosterone Synthase Inhibition With LCI699: A Proof-of-Concept Study in Patients With Primary Aldosteronism. Hypertension. 2010;56(6):831–838. doi:10.1161/HYPERTENSIONAHA.110.157271.
6. Zoccali C, Mallamaci F, De Nicola L, Minutolo R. New trials in resistant hypertension: mixed blessing stories. Clin Kidney J. 2023;16(4):823–831. doi:10.1093/ckj/sfad251.
7. Shen G, Yang Z, Lv Y, Liu H, Tian X, Jia X, et al. Development of Highly Selective Aldosterone Synthase Inhibitors. ACS Med Chem Lett. 2025;16(2):285–291. doi:10.1021/acsmedchemlett.5c00222.
8. Awosika A, Khan A, Adabanya U, Omole A, Millis R. Aldosterone Synthase Inhibitors and Dietary Interventions: A Combined Novel Approach for Prevention and Treatment of Cardiovascular Disease. Cureus. 2023;15(3):e36184. doi:10.7759/cureus.36184
9. Chung Hung CE, Kocherry C, George J. Breaking down resistance: novel aldosterone synthase inhibitors in the management of resistant hypertension. J Hypertens. 2025;43(6):1112–1120. doi:10.1097/HJH.0000000000004055.
10. Rasmussen AA, Nordestgaard KL, Simonsen U, Buus NH. Blood Pressure–Lowering Effects of Aldosterone Synthase Inhibitors—A Systematic Review. Basic Clin Pharmacol Toxicol. 2025;126(5):377–389. doi:10.1111/bcpt.70080.
11. Dey S, Frishman W, Aronow W. Baxdrostat: An Aldosterone Synthase Inhibitor for the Treatment of Systemic Hypertension. Cardiol Rev. 2023;31(5):287–292. doi:10.1097/CRD.0000000000000595.
12. Shen G, Yang Z, Lv Y, Liu H, Tian X, Jia X, et al. Development of Highly Selective Aldosterone Synthase Inhibitors. ACS Med Chem Lett. 2025;16(2):285–291. doi:10.1021/acsmedchemlett.5c00222.
13. Pitt B, Bhatt D, Schotzinger R, Pacyniak E, Jowett J, Lee JS. A safety and pharmacodynamic study of the highly selective aldosterone synthase inhibitor PB6440 in the cynomolgus monkey. Eur Heart J. 2022;43(Suppl_1):ehac544.3061. doi:10.1093/eurheartj/ehac544.3061
14. Unger T, Paulis L, Sica D. Therapeutic perspectives in hypertension: novel means for renin–angiotensin–aldosterone system modulation and emerging device-based approaches. Eur Heart J. 2011;32(13):1632–1641. doi:10.1093/eurheartj/ehr253.
15. Zoccali C, Mallamaci F, De Nicola L, Minutolo R. New trials in resistant hypertension: mixed blessing stories. Clin Kidney J. 2023;16(4):823–831. doi:10.1093/ckj/sfad251.
16. Hargovan M, Ferro A. Aldosterone synthase inhibitors in hypertension: current status and future possibilities. JRSM Cardiovasc Dis. 2014;3:2048004014522440. doi:10.1177/2048004014522440.
17. Awosika A, Khan A, Adabanya U, Omole A, Millis R. Aldosterone Synthase Inhibitors and Dietary Interventions: A Combined Novel Approach for Prevention and Treatment of Cardiovascular Disease. Cureus. 2023;15(3):e36184. doi:10.7759/cureus.36184.
18. Muras M, Lorenc T, Marcinkowski K, Michalik M, Mikszta N, Mikszta J, Marcinkowska J. The New Drugs in the Treatment of Hypertension and Resistant Hypertension: A Review of Therapies. Qual Sport. 2025;12(40):45–58. doi:10.12775/qs.2025.40.59480
19. Calhoun D, White W, Krum H, Guo W, Bermann G, Trapani A, et al. Effects of a Novel Aldosterone Synthase Inhibitor for Treatment of Primary Hypertension: Results of a Randomized, Double-Blind, Placebo- and Active-Controlled Phase 2 Trial. Circulation. 2011;124(24):2681–2688. doi:10.1161/CIRCULATIONAHA.111.029892.
20. Freeman M, Halvorsen Y, Marshall W, Pater M, Isaacsohn J, Pearce C, et al. Phase 2 Trial of Baxdrostat for Treatment-Resistant Hypertension. N Engl J Med. 2022;387(23):2118–2128. doi:10.1056/NEJMoa2213169.
21. Saxena M, Laffin L, Borghi C, Fernandez Fernandez B, Ghali JK, Kopjar B, et al. Lorundrostat in Participants With Uncontrolled Hypertension and Treatment-Resistant Hypertension: The Launch-HTN Randomized Clinical Trial. JAMA. 2025;333(7):637–650. doi:10.1001/jama.2025.9413.
22. Tkach, V., Morozova, T., De Oliveira, S., De Oliveira, S., João Monteiro, M., Ivanushko, Y., ... & Khrutba, V. The theoretical description for bromfenac electrochemical determination in tears and eye drops

on CoO (OH), Letters in Applied NanobioscienceOpen source preview, 2025, 14(1), 28

23. Shah WA, Jan A, Khan MA, Saeed M, Rahman N, Zakiullah, et al. Association between Aldosterone Synthase (CYP11B2) Gene Polymorphism and Hypertension in Pashtun Ethnic Population of Khyber Pakhtunkhwa, Pakistan. Genes. 2023;14(6):1184. doi:10.3390/genes14061184.

24. Rakhmatova, M., Shakhanova, S., Nazarova, J., Azizova, F., Astanakulov, D., Akramov, G., & Mirametova, N. Brain tumor information retrieval system for brain tumor diagnosis. Health Leadership and Quality of Life, 2024, (3), 179-188.

25. Kadirovna, B. M., Bahriddin o'g'li, O. F., Inatovna, M. D., & Karima, R. Designing standard teaching aids to increase learning efficiency in educational environment in Uzbekistan, Procedia Environmental Science, Engineering and Management, 2025 **12** (1) 169-177.

26. Adhikari A, Sharma C, Sherpa ML, Karaunakran G, Dhakal M, Sharma A. Impact of Renin–Angiotensin–Aldosterone System (RAAS) Gene Polymorphism in Essential Hypertension and Antihypertensive Drug Therapy: A Review. Int J Hypertens. 2025;2025:5530265. doi:10.1155/ijhy/5530265.