REVIEW ARTICLE

CONTENTS

Hopes and doubts about zilebesiran, a new antihypertensive drug

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ABSTRACT

The aim of this work is to critically evaluate the benefits and risks of zilebesiran. A comprehensive literature search was conducted in PubMed and Google Scholar databases to identify relevant studies on zilebesiran and other small-interfering RNA (siRNA)-based therapies for hypertension. The search covered publications from January 2010 to December 2025. The following keywords and combinations were used: "zilebesiran", "siRNA therapy", "angiotensinogen inhibition" "hypertension". Hypertension is one of the most prevalent cardiovascular diseases worldwide**.** The effectiveness of the therapy is still unsatisfactory, which is caused, among other things, non-adherence to pharmaceutical treatment. A long-acting drug could reduce this non-adherence to some extent. The mechanism of action of zilebesiran is based on silencing the angiotensinogen gen by activation the RNA-induced silencing complex (RISC). In animal studies and then in patients with hypertension (KARDIA I and KADRIA 2), zilebesiran after a single subcutaneous administration reduced angiotensinogen concentrations in blood by 90% and a systolic blood pressure by 10-20 mm Hg compare to placebo for a period of 3-6 months. In the studies conducted so far, apart from a few cases of orthostatic hypotension and a slight increase in creatinine in the blood, no serious side effects were found. A large study, KARDIA 3, is currently underway to assess the antihypertensive efficacy and reduction of cardiovascular complications. Despite the promising results of previous studies further observation are still necessary regarding long-term hypotensive effectiveness, reduction of risk cardiovascular complication and side effects.

KEYWORDS: zilebesiran, small interfering RNA, low level of angiotensinogen, new drugs on hypertension

Wiad Lek. 2026;79(7):1646-1653. doi: 10.36740/WLek/221451 DOI

INTRODUCTION

EFFECTIVENESS OF TREATMENT AND ADHERENCE TO THERAPY OF ARTERIAL HYPERTENSION

Numerous studies indicate that over 1.3 billion to 1.4 billion people worldwide suffer from hypertension, but less than 16% of them have blood pressure below 140/90 [1-3].

It is estimated that hypertension is a leading factor in cardiovascular disease and death [4]. As the population of developed countries ages, the number of people with hypertension is expected to increase further. This will also be facilitated by increased obesity, air pollution, exposure to noise, and poor diet [3, 4]. The higher the blood pressure, the higher the risk of serious cardiovascular events [4, 5]. Intensive treatment of hypertension with a reduction in blood pressure from 140/81 to 133/76 mm Hg significantly reduces the risk of serious cardiovascular complications by 10%. Each drop in blood pressure by 5 mm Hg reduces this risk by 10% [6].

Therefore, the latest guidelines of the European Society of Hypertension recommend lowering blood pressure to below 130/80 mm Hg, but not below 120/80 mm Hg [7]. However, the beneficial effects of hypertension therapy described above depend on long-term, sustained blood pressure reduction. Not only discontinuation of effective hypertension therapy but also poor adherence to antihypertensive therapy leads to a significant increase in the risk of cardiovascular complications and increased mortality [8-10]. However, large meta-analyses covering tens of thousands of patients with hypertension have shown that the rate of patients discontinuing hypertension therapy or low adherence to antihypertensive medications is high, ranging from 31-83%, and usually 30% greater in men than in women [11-13].

Overall, nearly two-thirds (62.5%) of the medication nonadherence was noticed in Africans and Asians. A particularly high rate of discontinue therapy is observed in young people [5, 11].

Many years ago, it was noted that the simultaneous use of several antihypertensive drugs leads to more

frequent, irregular use of these medications, or even complete discontinuation of these medications. This is one reason why guidelines for the treatment of hypertension recommend the use of several antihypertensive medications in a single tablet as a fixed-dose combination pill (FDC) [7]. This therapeutic approach has improved the effectiveness of hypertension therapy, but in many patients, satisfactory therapeutic efficacy has still not been achieved [14]. Low effectiveness of hypertension therapy is still observed not only in Africa but also in Europe and the United States [11, 13, 14]. According to the research by Bruner et al. [13] the unsatisfactory effectiveness of therapy is influenced by stress, emotions, insomnia and multimorbidity. The lowest effectiveness of therapy related to non-adherence to treatment recommendations is observed in low- to middle-income and non-income countries and non-Western countries. No significant positive trend in adherence was detected between 2010 and 2020 [11].

SEARCHING FOR NEW DRUGS FOR HYPERTENSION

Here is an intensive search for new pharmacological preparations that would improve the effectiveness of hypertension therapy [15-17] . The pharmaceutical industry is conducting in-depth research on compounds that potentially influence the mechanisms leading to hypertension. They are currently focusing on the use of, among others, activation of the AT2 receptor agonist, angiotensin (1-7) analogs., vasoactive intestinal peptide receptor agonists, intestinal L-type calcium channel blocker/ endothelin A/B2 receptor antagonist, antihypertensive vaccines. These studies did not lead to the introduction of any new antihypertensive drug into therapy, except for Baxdrostat, which inhibits aldosterone synthesis (similarly to the already known spironolactone), and Aprocitentan, a drug that inhibits endothelin receptors and is already used in hypertension resistant to antihypertensive therapy. Increased activity of the renin-angiotensin-aldosterone system (RAS) in the brain of patients with hypertension has also been noted [18]. Stimulation of this system increases the activity of the sympathetic nervous system, causes vasoconstriction, and increases the release of arginine vasopressin, which leads to an increase in blood pressure. Aminopeptidase (APA), located in the brain, converts angiotensin II to angiotensin III, responsible for the increase in blood pressure [18]. The drug firibastat, which inhibits aminopeptidase, lowers blood pressure by reducing the release of arginine vasopressin from the posterior pituitary gland into the bloodstream, which increases diuresis, reduces the activity of the sympathetic nervous system, and enhances baroreceptor function [18]. Firibastat, previously named QGC001 or RB150, is an orally active brain-penetrating prodrug of EC33, a selective and specific inhibitor of APA. Upon entry into the brain, it is cleaved by brain reductases to generate two active molecules of EC33, which inhibit brain APA activity, block brain angiotensin-III formation, and decrease BP. The decrease in blood pressure following firibastat administration depends not only on the drug's inhibitory effect on aminopeptidase but also on the conversion of angiotensin II to angiotensin 1-7, which lowers blood pressure. Initially, high hopes were placed on this drug. The first clinical trial, designated NEW-HOP, on the effects of firibastat included 256 overweight or obese patients with hypertension [19, 20]. After 8 weeks of firibastat administration, systolic blood pressure in the study patients decreased statistically significantly by 9.5 mm Hg and diastolic blood pressure by 4.2 mm Hg. In the black patients participating in this study, systolic blood pressure decreased by 10.5 mm Hg, and in the remaining patients by 8.9 mm Hg ($P<0.0001$). Furthermore, it was found that the higher the baseline hypertension, the more the study drug lowered blood pressure [19,20]. However, subsequent studies in patients with resistant hypertension did not demonstrate a significant reduction in blood pressure, and the study was discontinued [20, 21]. The low effectiveness of hypertension therapy may also be due to a small extent to patients who are resistant to antihypertensive therapy. However, it has been shown that only 10% of patients with hypertension are resistant to the inhibitors ACEIs, calcium antagonists, diuretics [22]. However, the lack of effectiveness of hypertension therapy in society is primarily due to irregular use of antihypertensive medications or temporary or even permanent discontinuation of antihypertensive therapy. This situation could be prevented by a drug that, after a single administration, would work for much longer than a day and would not cause adverse effects. It is possible that such a drug would significantly improve regular and long-term treatment of hypertension, and therefore the effectiveness of this therapy. For this reason, recent clinical trials of a new drug called zilebesiran have generated considerable interest and hope.

AIM

The aim of this work is to critically evaluate the benefits and risks of zilebesiran.

MATERIALS AND METHODS

A comprehensive literature search was conducted in PubMed and Google Scholar databases to identify relevant studies on zilebesiran and other small-inter-

fering RNA (siRNA)-based therapies for hypertension. The search covered publications from January 2010 to December 2025. The following keywords and combinations were used: "zilebesiran", "siRNA therapy", "angiotensinogen inhibition" "hypertension".

REVIEW

ZILEBESIRAN - MECHANISM OF ACTION

This drug inhibits the release of angiotensinogen in the liver. It is administered by subcutaneous injection once every 3 months or once every 6 months and produces a significant and long-lasting reduction in blood pressure. It is the first antihypertensive drug to modify the function of the gene responsible for angiotensinogen synthesis in the liver [23, 24].

Angiotensinogen secreted by the liver is converted into angiotensin-1 under the influence of renin, moreover small amounts angiotensinogen are also synthesized in adipose tissue, the kidney and the brain [24]. Angiotensin-1 is in turn converted into angiotensin II by angiotensin-converting enzyme (ACE). Angiotensin II exerts a powerful vasoconstrictor effect, stimulates the sympathetic nervous system, and stimulates the action of aldosterone and vasopressin. Both of these compounds also significantly increase blood pressure. Drugs such as ACE inhibitors or sartans significantly lower blood pressure and are frequently used in clinical practice. However, after prolonged use, due to the so-called escape phenomenon, a compensatory increase in renal renin secretion occurs, which weakens the antihypertensive effect of ACE inhibitors [24]. The relatively frequent side effects of ACE inhibitors and the insufficient antihypertensive effect of these drugs (due to the so-called escape mechanism) discourage many patients from long-term use of these drugs [25]. As indicated above, angiotensinogen plays a key role in the mechanism of action of the RAAS system., Andrew Fire and Crayg Mello discovered a method for gene silencing, for which they were awarded in 2006 the Nobel Prize. This discovery enabled the development of two methods for silencing the gene: antisense oligonucleotides (ASos) and small interfering RNAs (siRNAs). The latter method was used to develop the drug zilebesiran that silences the angiotensinogen gene [24]. These methods were used to synthesize several drugs successfully used in clinical practice. These include patisiran and vutrisiran, used for polyneuropathy associated with hereditary transthretin-mediated amyloidosis; givosiran, used for acute hepatic porphria; lumasiran and nedosiran, used for primary hyperoxaluria type 1; and inclisiran, used for primary hyperlipidemia [24].

Zilebesiran – a combination of a small RNA molecule composed of approximately 20 pairs of nucleosome binds to N-actylgalactosam. The latter compound ensures connection with liver cell receptors. The drug is then transported into the liver cell *via* clathrin-mediated endocytosis and is stored in endosomes, from where it slowly penetrates into the cytoplasm. As a result of further complex processes, the anti-sense strand binds to the RNA-inducing complex (RISC) molecule, thus forming an active RISC. The active RISC with the quide strand is recycled [24]. Thus, the modified RNA (siNRA) long-term silences the activity of the gene responsible for the production of angiotensinogen by liver cells, thanks to which a single administration of zilebesiran lowers blood pressure for a period of many weeks. The details of the operation of zilebesiran are, among others described, in Morosan's work [24].

ANIMAL STUDY

The first studies on the effect of zilebesiran on blood pressure were conducted in spontaneously hypertensive male rats fed a standard HIFH-sodium diet. SiRNA was administered by injection every two weeks at a dose of 10 mg/kg body weight. Following such administration, the drug is absorbed within approximately 8-16 hours. The half-life of the drug in blood serum is 3-5 days, while the half-life of pharmacological action is 3-6 months due to the slow return of RISC to its normal activity [24] .This drug was shown to induce a 98% reduction in serum angiotensinogen concentration. Zilebesiran at a dose of 400-800 mg also significantly reduces angiotensin I and angiotensin II concentrations and moderately reduces aldosterone concentrations, proportionally to the drug dose. All doses of zilebesiran moderately increase plasma renin activity [24]. The rats' blood pressure decreased by 14 mm Hg. In a similar study, where the animals received only valsartan, blood pressure decreased by 10 mm Hg [24].

Unlike angiotensin-converting enzyme inhibitors, zilebesiran does not interfere with bradykinin degradation and therefore does not cause dry cough or angioedema [26].

In the group of animals co-administered with zilebesiran and valsartan, blood pressure decreased by 70 mm Hg. As expected, the decreases in blood pressure following zilebesiran administration were greater in animals receiving the low-sodium diet than the high-sodium diet [24]. After zilebesiran the pressure drop was constant, no escape effect was observed [27].

The effect of zilebesiran can be reversed by subcutaneous administration of an siRNA fragment that reverses the drug's action (the REVERSIR effect). Such

studies were conducted in animals [28]. As a result of this approach, blood pressure returned to baseline values after 4-7 days. Another study demonstrated that acute administration of norepinephrine rapidly raised blood pressure. Other methods for terminating prolonged hypotension following zilebesiran administration include administration of fludrocortisone, a high-sodium diet, or administration norepinephrine. However, administration of midodrone did not increase the reduced blood pressure [29].

Zilebesiran also reduced cardiac hypertrophy [30]. Bovee et al. observed the effect of zilbesiran on the behavior of blood pressure in rats in which profound renal failure was induced by removing one kidney and in the other one a partial nephrectomy was performed. Administration of zilebesiran prevented the increase in blood pressure in the course of uremia [31]. Crus-Lopez et al. also noted the preventive effect of zilebesiran on the increase in blood pressure in rats with experimentally induced diabetes [32].

CLINICAL STUDY

The first clinical trials were conducted between 2019 and 2022 [33]. The study was conducted at four sites in the United Kingdom. The study participants were divided into several groups from group A, B and E. In Part A, eligible patients (12 per cohort) were randomly assigned in a 2:1 ratio to receive a single subcutaneous dose of zilebesiran (10, 25, 50, 100, 200, 400, or 800 mg) or placebo. Zilebesiran reduced angiotensinogen concentrations by more than 90% from a 100 mg dose. The decrease in blood pressure correlated with decreasing angiotensinogen levels (r=0.52). A single dose of 20 mg of zilebesiran reduced systolic blood pressure by more than 10 mm Hg and diastolic blood pressure by more than 5 mm Hg.

In Part B, after sequential administration of a low-salt diet (0.23 g per day) and a high-salt diet (5.75 g per day) from days − 21 through − 8, patients were randomly assigned in a 2:1 ratio to a single dose of 800 mg zilebesiran or placebo. After administration of 800 mg of zilebesiran, the corresponding changes systolic blood pressure after a low-salt diet were − 18.8±4.3 mm Hg and only -8,4 mm Hg on high-salt diet [33].

In part E all the patients received a single 800 mg dose of zilebesiran. Six patients had a mean decrease from baseline in systolic blood pressure of 21.8±2.9 mm Hg at week 6 after administration of 800 mg of zilebesiran and at week 24 change in the mean systolic and diastolic blood pressure was - 22,5 mm Hg and - 10,8 mm Hg respectively, among the eight patient [33].

No hypotension or worsening of renal function was observed. The increase in blood pressure observed due to the escape phenomenon in patients treated with RAAS inhibitors was not observed after zilebesiran administration [33].

The second phase of the randomized, placebo-controlled trial, KARDIA-1 was conducted between 2021 and 2023 in 78 centers in the USA, Canada, Great Britain, and Ukraine [33]. People aged 18-75 years with moderate hypertension were invited to participate in the study. The study included 394 patients, including 167 women and 93 Black patients. The study participants were divided into 5 groups. Patients in one group received only a placebo injection once every 3 months. Patients in the other groups received zilebesiran in doses of 150, 300, 600 mg every 6 months, or 300 mg every 3 months. The study lasted ½ year. In the first, third, and sixth months of the study, ABPM was performed. Automatic office BP measurement was performed on the first day of the study, then weekly, and finally monthly until the end of the study. In the group of patients receiving only placebo, blood pressure increased significantly, while in the groups treated with zilebesiran, it decreased. Redness (erythema) accompanied by pain at the injection site was observed in 5 patients. Mild hyperpotassemia (above 5.2 mmol/l) was noted in 5 percent of patients and hypotension in 13 patients. In four patients discontinued the drug due to orthostatic hypotension [33].

The randomized KARDIA-2 study evaluated the efficacy and safety of zilebesiran administered in combination with other antihypertensive drugs in hypertensive patients with uncontrolled hypertension [34, 35]. Specifically, the study included patients with previously untreated hypertension (systolic blood pressure 155-180 mm Hg) and patients treated with one or two antihypertensive drugs whose systolic blood pressure was 145-180 mm Hg. The study was conducted between 2022 and 2023 in 150 centers in Canada, Estonia, Germany, Latvia, Lithuania, Poland, England, and the USA. During the run-in period, previously used medications were discontinued and monotherapy with indapamide, amlodipine, or olmesartan was initiated once daily. A total of 667 patients were recruited, divided into indapamine groups (n=127), amlodipine groups (n=239), and olmesartan groups (n=301). Indapamine was administered at a dose of 2.5 mg once daily, amlodipine 5 mg once daily, and olmesartan 40 mg once daily. Additionally, patients in each group were randomly assigned to receive either zilebesiran or placebo. After three months of zilebesiran therapy systolic blood pressure decreased by 12,1 mm Hg in indapamide group ($p< 0,0001$), 9,7 mm Hg in amlodipine group ($p<0,0001$)

and 4,0 mm Hg in olmesartan group (p>0,006). Greater reductions in office SBP were observed. They were 18.5 mm Hg, 10.2 mm Hg, and 7 mm Hg, respectively. After 6 months, the reductions were 13.6 mm Hg in the indapamide group, 8.6 mm Hg in the amlodipine group, and 4.6 mm Hg in the olmesartan group (p<0.001). No serious complications were observed; only a transient trend toward hyperkalemia and increased serum creatinine was noted, which spontaneously resolved during further follow-up. A decrease in GFR of more than 30% was observed in 4.8% of patients in the indapamide and zilbesiran group, 0.8% in the amlodipine and zilebesiran group, and 2.7% in the olmesartan and zilebesiran group [34, 35].

Preliminary results of the KARDIA 3 study, currently comprising 270 patients with a mean age of 67 years, 77% of whom were at high cardiovascular risk, and 23% of whom had already been diagnosed with cardiovascular disease [36]. Baseline blood pressure in the study group was 142/70 mm Hg. Three months after subcutaneous administration of 300 mg of zilebesiran, blood pressure decreased by 5 mm Hg, and after 600 mg of zilebesiran, by 3.3 mm Hg (ABPM). Six months after administration of 300 mg of zilebesiran, blood pressure decreased by 3.9 mm Hg, and after 600 mg of zilebesiran, by 3.6 mm Hg. The decrease in blood pressure in ABPM measurements after 3 months was more pronounced: 5.5 mm Hg and 7.4 mm Hg. The nocturnal blood pressure decrease was greater, reaching 6.6 mm Hg and 8.2 mm Hg, respectively [36]. The drug's manufacturers plan to conduct another Phase III ZENIT CVT study involving 11,000 patients with uncontrolled hypertension despite the use of at least two antihypertensive drugs and cardiovascular disease or relatively high cardiovascular risk. The study is scheduled to be completed in 2030. The aim of this study will be not only to assess the drug's antihypertensive effect but also to assess the reduction in the number of heart attacks and strokes compared to placebo [36].

Lemine et al. conducted a meta-analysis of available studies on zilebesiran

that have been published until 2024 [37]. The study included 1,145 randomized patients whose blood pressure and serum angiotensinogen levels were assessed after treatment with zilebesiran and placebo. In all patients included in the meta-analysis, blood pressure was measured using ABPM. This meta-analysis showed that in patients treated with zilebesiran at doses greater than 250 mg and less than 500 mg, reduction of systolic blood pressure was the greatest (the difference compared to placebo was 16.40 mmHg.) (p<0.00001). Higher doses of zilebesiran above 500 mg of zilebesiran were found to be less effective [37].

Another meta-analysis conducted by Raza et al. showed that zilebesiran significantly lowers blood pressure after 12 weeks of treatment with ABPM (MD 11.9 nn Hg p<0.00000001 and after 24 weeks MD is 19.68 (p<0.00001). [38]. In office SBP measurements the difference compared to placebo after 12 weeks was 12.21 mmHg and after 24 weeks 8.49 mmHg p<0.00001. Zilebesiran caused mild side effects (OR 1.37) p<0.01, but with no serious side effects reported [38]. Changes in creatinine concentration and glomerular filtration rate proved statistically insignificant. A significant decrease in blood pressure was observed in both ABPM and office SBP [38]. Another meta-analysis by Singh et al. confirmed the results of the previous meta-analyses [39]. Twelve weeks after zilebesiran administration, a decrease in systolic blood pressure of 15.12 mm Hg and diastolic blood pressure of 7.34 mm Hg was observed in ABPM. The most common side effect were erythema (at the site of drug administration) and headache. A slight increase in potassium and creatinine levels was observed. Low titers of anti-zilebesiran antibodies in blood were detected in 5% of patients.

DISCUSSION

Despite the current availability of numerous antihypertensive medications, the effectiveness of hypertension therapy remains unsatisfactory. This is largely due to poor adherence to medical recommendations regarding hypertension therapy. The advantages of the possible introduction of zilebesiran to the treatment of hypertension were recently presented by Addison et al. [40] Will zilebesiran therapy solve this problem? Whether zilebesiran effectively reduces hypertension resistant to previously used medications has not been studied. There are also no studies of zilebesiran combined with beta-blockers and aldosterone antagonists. It is currently known that zilebesiran exerts its antihypertensive effect for at least a year. However, it is unknown whether longer-term administration (a few years) of this drug will result in a surrogate increase in angiotensinogen synthesis by adipose tissue or the kidneys. Zilebesiran only inhibits the synthesis of angiotensinogen produced in the liver. The promising observations that zilebesiran reduces cardiac fibrosis and slows the progression of chronic renal failure in experimental animals have not yet been verified in humans. If therapy with this drug significantly reduces hypertension and reduces the risk of cardiovascular complications we will only know after the completion of the KARDIA 3 study. Many issues related to adherence to medical recommendations will remain unresolved. How to convince patients to change their lifestyle, such

as a high-sodium diet and low physical activity, which also may lead to hypertension.

The smaller reduction in blood pressure following zilebesian administration in patients with cardiovascular disease in the first period of the KARDIA 3 study may already raise some concerns [36]. A similar situation occurred in the Firibastat study, when it was found that this drug demonstrated only marginal antihypertensive efficacy in patients with more treatment-resistant hypertension, and further study of the drug was discontinued. However, the final efficacy of zilebesiran cannot be determined based on the several-month duration of the KARDIA 3 study. The coming years will reveal the extent of the reduction in blood pressure and whether any adverse events are more frequent than previously reported. Special attention will be paid to the potential occurrence of chronic, irreversible renal failure, significant hyperkalemia, or uncontrolled hypotension. If zilebesiran proves to be free of these dangerous symptoms, it would be worthwhile to consider which patients with hypertension this drug would be most useful for. For many patients, zilebesiran may improve the effectiveness of hypertension therapy, but its limitations should be remembered. Zilebesiran lowers blood pressure 4-7 days after administration. Until zilebesiran takes effect, the patient must receive rapid-acting antihypertensive medications. An increase in blood pressure during therapy with zilebesiran at a dose of 500 mg requires the addition of another antihypertensive drug, not an increase in the dose of zilebesiran [37].

In patients with mild hypertension who were previously adequately treated with a single daily antihypertensive medication but subsequently were treated very irregularly, zilebesiran appears to be a good alternative, provided that no more severe hypotension develops. This situation may occur suddenly, for example in dehydration, diarrhea, sepsis. Therefore, the patient should be instructed to frequently monitor their blood pressure. A more profound drop in blood pressure will require emergency norepinephrine and a high-sodium diet [29]. This, in turn, may be more burdensome for the patient than taking the previous medication orally. This example indicates that zilebesiran will not always be readily used by patients and may even worsen the lack of patient compliance with the physician. In situations where several medications are used simultaneously, it would be advisable to use zilebesiran in combination with a diuretic or calcium channel blocker. This combination of drugs, as shown by the KARDIA 2 study [34,35] will provide greater blood pressure reduction than combining zilebesiran with an angiotensin-converting enzyme inhibitor or sartans. Furthermore, concomitant use of zilebesiran with an angiotensin-converting enzyme inhibitor can more easily lead to excessive serum potassium levels. The above examples indicate that even if zilebesiran proves to be an effective antihypertensive in everyday medical practice, it may not always be the ideal treatment for patients who do not adhere to treatment recommendations.

The large cardiology study KARDIA 3 will be completed in 2030. Only then will we know whether zilebesiran not only effectively lowers blood pressure but also reduces the risk of cardiovascular complications and whether it does not cause serious organ damage in some clinical situations. If zilebesiran successfully completes all these trials, we will have a drug that will expand our treatment options for hypertension.

CONCLUSIONS

The number of patients with hypertension is increasing worldwide, causing increasing cardiovascular complications and premature deaths. Despite numerous antihypertensive medications, the effectiveness of hypertension treatment has not improved sufficiently and remains unsatisfactory, primarily due to a lack of adherence to antihypertensive medications. Zilebesiran, administered as a subcutaneous injection twice a year, can improve adherence and effectiveness of hypertension therapy. We await the results of further studies with concern and hope to see whether zilebesiran will reduce the risk of cardiovascular complications and avoid serious side effects.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 30.01.2026
ACCEPTED: 05.05.2026