

EXPERT OPINION ON THE CLINICAL USE OF ANGIOTENSIN RECEPTOR BLOCKERS IN HYPERTENSIVE PATIENTS WITH ASSOCIATED COMORBIDITIES IN INDIAN SETTINGS

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Abstract

Objective: The present study aims to collect expert opinions on commonly used angiotensin receptor blockers (ARBs) for reducing blood pressure (BP) and managing associated comorbidities, with a specific emphasis on the use of olmesartan in Indian settings.

Methodology: The study used a 22-question questionnaire to gather insights from specialists across different Indian settings regarding their perspectives on ARBs for the management of hypertensive patients with concomitant comorbidities.

Results: The present survey study included 986 participants. Olmesartan monotherapy was strongly recommended by 88% of the clinicians for its outstanding BP reduction ability. According to 45% and 48% of the responders, olmesartan monotherapy resulted in a double-digit BP decrease in 25 to 50% and >0% of hypertensive individuals. According to 91% of the respondents, olmesartan offers early BP reduction within two weeks of medication, in terms of additional benefits, 68%, 23%, and 7% of respondents reported that olmesartan can reduce cardiovascular risk, proteinuria, and left ventricular hypertrophy (LVH), respectively. Majority

(82% and 80%) of the clinicians recommended olmesartan as the most preferred ARB therapy for hypertensive patients with comorbid diabetes and renal condition. A significant number of respondents (91%) noted that olmesartan treatment confers end-organ protection and a double-digit drop in BP.

Conclusion: According to the expert opinion, olmesartan is one of the best ARBs for reducing blood pressure quickly and effectively. The treatment also provides end-organ protection and a decrease in cardiovascular risk and is strongly advised in hypertension patients with concomitant renal and diabetic conditions.

Keywords: hypertension, angiotensin receptor blockers, ARBs, olmesartan, comorbidities, cardiovascular risk

Introduction

Hypertension affects an estimated 1.28 billion individuals aged 30-79 years globally and is a leading cause of premature mortality.¹ With an estimated burden of 200 million people, hypertension is the most significant non-communicable disease risk factor in India.² It is estimated that one in every four persons in India has hypertension, yet only approximately 12% of them maintain their blood pressure under control.³ In India, hypertension is the leading health risk factor, accounting for the greatest share of disease burden and death. It is responsible for an estimated 1.6 million fatalities in India each year, owing to ischemic heart disease and stroke.^{4,5} Globally, hypertension is the single most significant risk factor for cardiovascular (CV) mortality. It is responsible for more CV disease (CVDs) fatalities than any other modifiable risk factor. More than half of those who died from coronary heart disease (CHD) and stroke had high BP.^{6,7} Previous research has shown that hypertension is a major risk factor for heart failure, atrial fibrillation, heart valve illnesses, aortic syndromes, as well as coronary heart disease, and stroke.⁸ In conjunction with other CV risk factors, high blood pressure (BP) induces CV end-organ damage and increases the risk of chronic kidney disease (CKD) and stroke.⁹

Comorbidities such as type 2 diabetes mellitus (T2DM), obesity, and dyslipidemia coexist with hypertension making the disease management highly complicated because of overlapping pathophysiology and shared risk factors.⁹ T2DM is identified in up to 50% of hypertension patients in India. The incidence of isolated systolic hypertension is highest in individuals with diabetes and hypertension related to autonomic neuropathy, and they have a greater baseline heart rate and are at an elevated risk of CVDs.¹⁰ In addition, uncontrolled hypertension hastens the deterioration of kidney function. According to the 2017 American College of Cardiology and

American Heart Association (ACC/AHA) recommendations, 16% of individuals with hypertension individuals also have CKD. These hypertensive individuals have the highest incidence of resistant hypertension, as well as renal and cardiovascular conditions.^{11,12}

Angiotensin receptor blockers (ARBs) efficiently decrease blood pressure (BP) by inhibiting the renin-angiotensin system and are suggested as first-line drugs in the treatment of hypertension.¹³ Major randomized clinical trials have shown that ARBs improve outcomes in conditions such as diabetic nephropathy, chronic heart failure or heart failure after myocardial infarction, hypertension with left ventricular hypertrophy, and in patients with a history of previous events or complicated diabetes.¹⁴ Olmesartan is a long-acting ARB that has been shown to have a comparable or more effective activity in decreasing blood pressure when compared to other ARBs. Olmesartan, in fact, demonstrated a bigger and more prolonged antihypertensive impact over the course of 24 hours, as well as a buffering effect on short-term blood pressure fluctuation.¹⁵ Several studies revealed the clinical efficacy of olmesartan-based monotherapies at various doses in hypertensive outpatients with varying CV risk factors.¹⁶

The objective of the present study is to gather expert opinion on commonly used ARBs for the reduction of BP and associated comorbidities with a special focus on the use of olmesartan in Indian settings.

Methods

We carried out a cross sectional, questionnaire based survey among clinicians specialized in treating hypertension and associated comorbidities in the major Indian cities from June 2022 to December 2022.

Questionnaire

The questionnaire booklet titled HOPS (**H**ypertension and **O**lmesartan clinical **P**erspectives from Indian **S**pecialists) study was sent to the physicians who were interested to participate. The HOPS study questionnaire included questions on the current practices, preferences, clinical observations, and experiences related to the use of ARBs in routine settings, particularly olmesartan, for the management of hypertension and associated cardiovascular comorbidities. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which is recognized by the Indian Regulatory Authority, Drug Controller General of India.

Participants

An invitation was sent to leading doctors in managing GERD in the month of March 2022 for participation in this Indian survey. 986 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provided necessary data. Physicians were asked to complete the questionnaire without discussing with peers. A written informed consent was obtained from each physician prior initiation of the study.

Statistical Methods

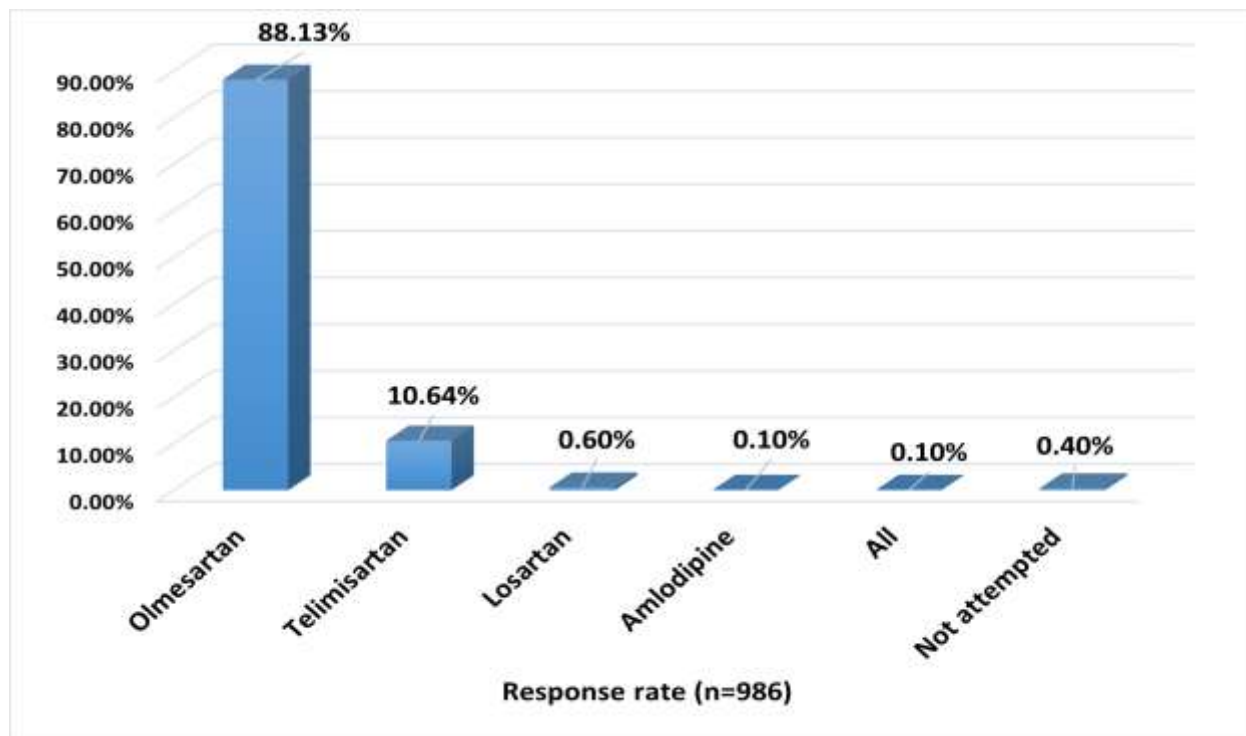
Descriptive statistics were used for the analysis, with percentages representing categorical variables. Bar charts were created using Excel 2013 (version 16.0.13901.20400) to depict the frequency and percentage distributions for each variable.

Results

The present survey study included 986 participants. Around 41% of the physicians stated that 10 or more patients are newly diagnosed with hypertension every month. According to 50% of the respondents, the average age of hypertension patients visiting per day is 31-50 years, while 43% suggested it to be 51-60 years. Among 56% of the respondents highlighted that both males and females were equally susceptible to develop hypertension whereas only 38% of respondents reported an increased likelihood for hypertension in males than females. Nearly, 44% of responders said that the majority of newly diagnosed individuals belong to systolic blood pressure (SBP) range of 160-179 mm Hg, and diastolic blood pressure (DBP) range of 100-109 mm Hg. Majority of the respondents reported patient adherence to dietary requirements (42%) and physical activity (43%) as average, whereas 39% and 35% evaluated it to be good. On the other hand, 49% reported good patient adherence to antihypertensive medication, while 32% evaluated it to be average. According to 54% of the respondents, patient adherence is high among urban-educated subjects.

Majority of the respondents (53%) reported diabetes as the common co-morbid condition observed in patients with hypertension, while 32% and 9% reported it to be CKD and dyslipidemia respectively. Approximately 63% noted that 11-20% of hypertension patients have comorbid angina, whereas 21% and 16% reported the incidence as <10% and 21-30%, respectively. More than half of responders (56%) reported that 21-30% of hypertension patients have diabetes. According to 53% of respondents nearly 11-20% of hypertension patients are obese, whereas 34% and 13% noted the incidence to be 21-30% and <10%, respectively. According to 44% of respondents 11-20% of hypertension patients experience hypotension symptoms. Approximately 51% of the respondents noted that monotherapy is effective for managing hypertension in 21 to 40% of the patients whereas, nearly 58% clinicians stated that 21 to 40% of hypertensive patients require more than two antihypertensive medications.

Around 75% of the participants preferred ARBs as the first-line antihypertensive therapy, whereas 19% recommended calcium channel blockers (CCBs). Among the ARBs, nearly 88% recommended olmesartan as the monotherapy for achieving excellent BP reduction, whereas telmisartan was recommended by a minor percentage of respondents (11%) (Fig. 1).

Fig. 1: Response distribution to most recommended ARB monotherapy for effective BP reduction

According to 48% of the respondents, olmesartan monotherapy helped in achieving double-digit BP reduction in >50% of hypertensive patients. Nearly 45% of clinicians also reported achievement of a similar reduction in 25-50% of the patients. Approximately 51% of the respondents found that olmesartan is superior to telmisartan in terms of achieving goal BP. Nearly 91% of the clinicians reported that among ARBs, olmesartan offers early BP reduction within two weeks of therapy (Table 1).

Table 1: Distribution of response to recommended ARB monotherapy that offers early BP reduction within two weeks of therapy

ARBs	Responses (n=986)
Olmesartan	897 (90.97%)
Telmisartan	72 (7.30%)
Losartan	2 (0.20%)
Amlodipine	3 (0.30%)
Not attempted	12 (1.21%)

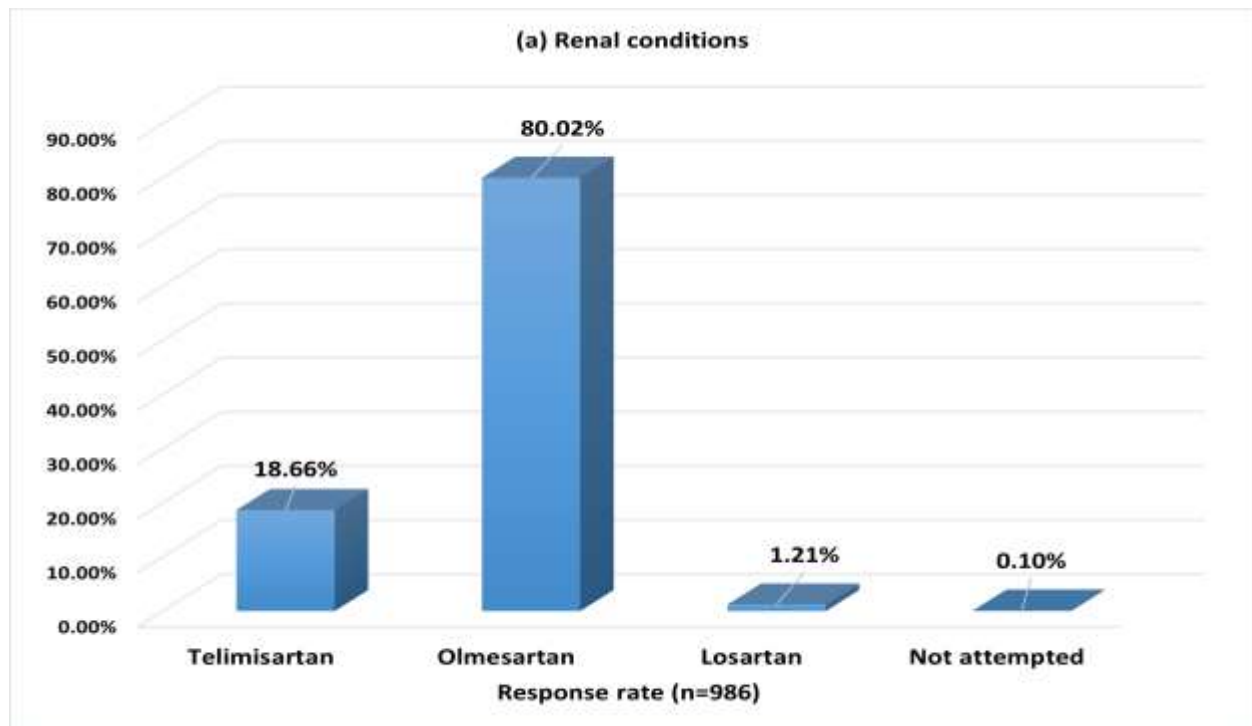
Majority of the respondents (68%) acknowledged that, in addition to BP control, olmesartan is effective in lowering cardiovascular risk, while the remaining 23% and 7% reported that olmesartan treatment can reduce proteinuria and LVH (Table 2).

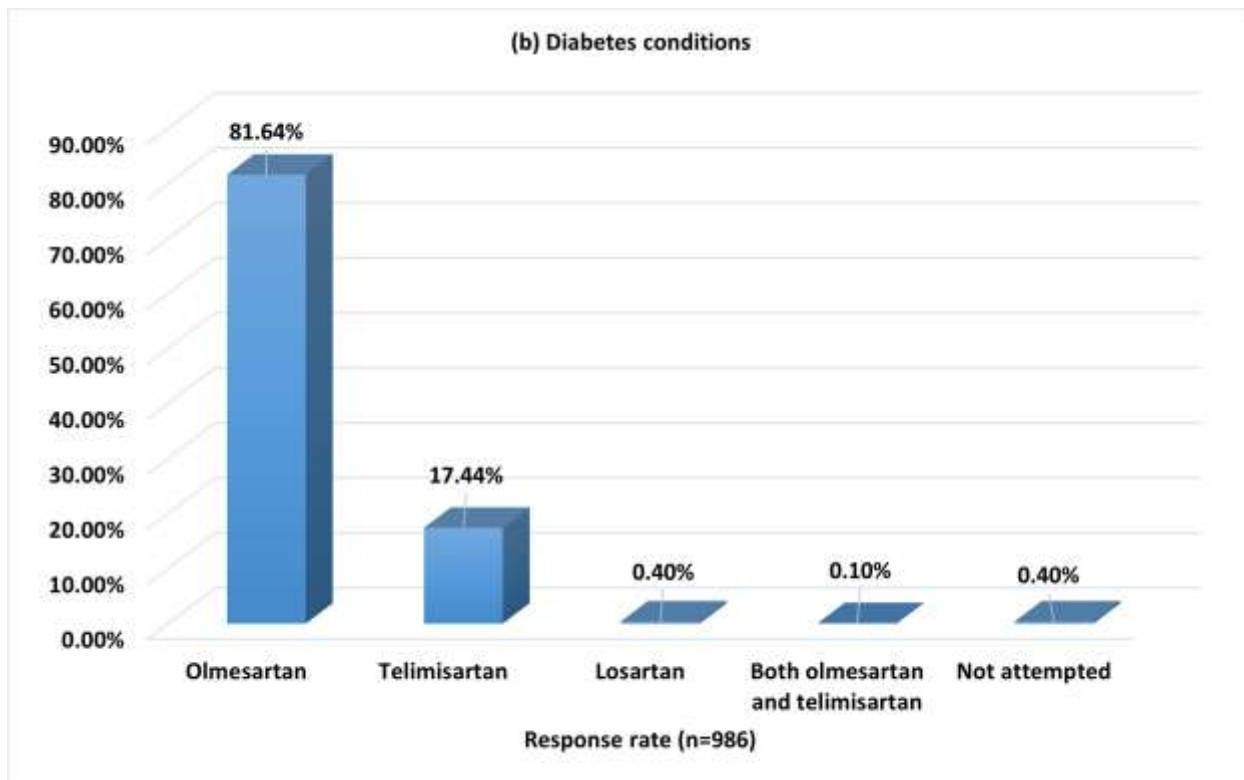
Table 2: Distribution of response to clinical outcomes of olmesartan treatment beyond BP control

Clinical outcomes	Responses (n=986)
Reduction in cardiovascular risk	675 (68.45%)
Reduction in proteinuria	228 (23.12%)
Reduction in left ventricular hypertrophy	72 (7.30%)
All	7 (0.70%)
Not attempted	4 (0.40%)

Among the ARBs, olmesartan was recommended by 80% of responders in hypertensive patients with comorbid renal conditions, whereas telmisartan was preferred by 19% (Fig. 2a). Nearly 82% of the clinicians recommended olmesartan as the most preferred ARB as initial therapy for hypertension with comorbid diabetes. On the other hand, 11% suggested telmisartan as the choice of therapy (Fig. 2b).

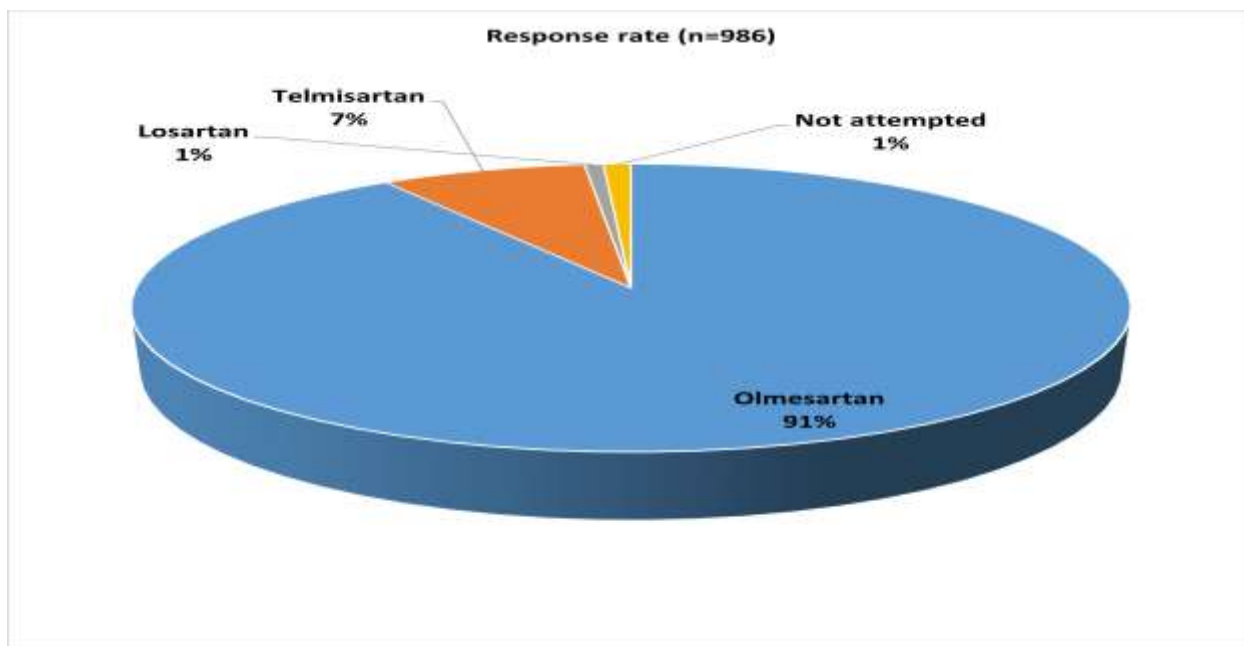
Fig. 2: Distribution of response to recommended ARBs for patients with comorbid renal conditions (a) and those with comorbid diabetes (b)





Nearly 91% of the clinicians reported that olmesartan offers double digit BP reduction and end organ protection, on the other hand 8% suggested telmisartan as the choice of therapy (Fig. 3).

Fig. 3: Distribution of response to ARB that offers double digit BP reduction and end organ protection



Discussion

The current study has provided further evidence supporting the efficacy of olmesartan as an ideal therapy for effectively reducing blood pressure and managing associated comorbidities in patients with hypertension. Due to its ability to offer benefits beyond blood pressure control, olmesartan emerges as a promising choice for enhancing the overall health outcomes of hypertensive patients.

In the present study, the experts have recommended the use of olmesartan as monotherapy for better, double-digit, and early BP reduction among the ARBs. In concurrence with this finding, The WINOVER study, comprising 8940 Indian adult hypertensive patients, reported that olmesartan significantly reduced BP and was effective and well-tolerated in patients with hypertension, without any severe side effects.¹⁷ Furthermore, several other studies have shown the effectiveness of olmesartan compared to other ARBs. Kalikar et al. noted that olmesartan is more effective at lowering SBP when compared to telmisartan and losartan and equally effective in lowering DBP.¹⁸ A comparative study by Nakayama et al. reported that olmesartan lowers arterial BP more effectively than telmisartan.¹⁹ Olmesartan reduced daytime and 24-hour DBP and SBP more efficiently than candesartan, according to Brunner's study.²⁰ In individuals with essential hypertension, olmesartan is more efficient at lowering cuff DBP compared to losartan, valsartan, and irbesartan.²¹ A meta-analysis conducted by Wang et al. further supported the superiority of olmesartan in terms of antihypertensive effectiveness compared to losartan and valsartan.²² These findings underscore the potential of olmesartan as a robust option for effectively managing hypertension and its associated comorbidities.²³

The current study has validated the pleiotropic effects of olmesartan, extending beyond blood pressure regulation. These additional benefits include decreased CV risk, reduced proteinuria, and end-organ protection. Based on these findings, the experts strongly recommended olmesartan therapy for hypertensive patients with diabetes and renal conditions. ARBs are considered first-line medications for T2DM with hypertension. A study by Nakayama et al. on early-stage type-2 diabetics with hypertension indicated that olmesartan has more effective anti-inflammatory and arterial blood pressure-lowering properties than telmisartan.¹⁹ A real-world data study by Khan et al. reported that olmesartan effectively lowered blood pressure in Indian patients with essential hypertension as well as in individuals with comorbid diabetes.²⁴ Ono et al. noted that olmesartan is more effective than other ARBs at reducing urinary protein in CKD patients, suggesting that its benefits in protecting the kidneys may be superior to those of other ARBs.²⁵ Additionally, olmesartan, when used as an add-on medication, has been found to reduce blood pressure preferentially at night while concurrently inhibiting renal damage in hypertensive individuals with CKD.²⁶

The current expert viewpoints underscore the significant role of olmesartan in managing hypertension and associated comorbidities. The study highlights the medication's adaptability and potential synergistic effects, providing a comprehensive understanding of its potential advantages. The expert opinion enhances the validity and applicability of using olmesartan in

routine hypertension therapy. However, it is important to note that differing opinions and preferences among the experts may have influenced the reported results, potentially introducing bias. Therefore, it is crucial to consider these limitations when evaluating the study findings.

Conclusion

The consensus among the clinician's favor olmesartan as the primary choice among ARBs for achieving early and excellent BP reduction. Additionally, the respondents recognized multifaceted benefits of olmesartan, including its ability to lower CV risk and provide end-organ protection, recommending the drug for managing hypertensive patients with comorbid diabetes and renal conditions.

Conflict of Interest

None

Acknowledgement

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