Survey Report

Perception Mapping of Indian Clinicians on Patient Profiling of Telmisartan + Hydrochlorothiazide Versus Telmisartan + Chlorthalidone

Version No.: 1.1

The study was conducted according to the approved protocol and in compliance with the protocol, Good Clinical Practice (GCP), and other applicable local regulatory requirements.

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Table of content

1 INTRODUCTION

Hypertension (HTN) is a significant contributor to cardiovascular (CV) disease and mortality worldwide [1]. About one-third of the world's 8 billion people suffer from HTN [2]. The main cause of morbidity and mortality in HTN stems from vascular damage, affecting the heart, brain, and kidneys. Changes in the structure and function of arterial walls occur early in the disease, leading to increased arterial stiffness [3]. Hypertension is a leading risk factor for various CV conditions, including coronary artery disease, congestive heart failure, atrial fibrillation, cerebrovascular disease, peripheral arterial disease, aortic aneurysm, and chronic kidney disease (CKD) [4]. The management of HTN involves both lifestyle modifications and pharmacological interventions, with combination therapy often recommended when monotherapy fails to adequately control blood pressure (BP).

Among the most commonly prescribed antihypertensive combinations, Telmisartan, an angiotensin II receptor blocker (ARB), is frequently paired with a diuretic to enhance its efficacy. Two such combinations are Telmisartan + Hydrochlorothiazide (HCTZ) and Telmisartan + Chlorthalidone (CT), each with distinct pharmacodynamic properties and clinical outcomes.

Telmisartan + HCTZ is one of the most widely prescribed combinations for HTN due to its proven efficacy in lowering BP, favorable safety profile, and well-established use in clinical practice. Hydrochlorothiazide, a thiazide diuretic, works by reducing sodium and water reabsorption in the kidneys, thereby decreasing blood volume and vascular resistance. This combination has been shown to be effective for both essential and resistant HTN, making it a popular choice in clinical settings [5]. In contrast, Telmisartan + CT, another common antihypertensive combination, uses CT, a thiazide-like diuretic. Chlorthalidone has a longer half-life and potentially superior BP-lowering effects compared to HCTZ. Research has suggested that CT is more effective at reducing CV events due to its prolonged antihypertensive action and better 24-hour BP control, especially in high-risk populations [6]. Given the high burden of HTN in India, which is also marked by a high prevalence of CV diseases, understanding clinician perceptions of Telmisartan + HCTZ versus Telmisartan + CT is essential for optimizing treatment strategies [7].

2 RATIONALE OF THE STUDY

The rationale behind studying the perception mapping of Indian clinicians on patient profiling of Telmisartan + HCTZ versus Telmisartan + CT lies in understanding the preferences, clinical outcomes, and therapeutic decisions that shape HTN management in India. Both combinations are commonly prescribed for the treatment of HTN, but the choice between them depends on various factors, including drug efficacy, safety profile, patient comorbidities, and clinician experience.

Telmisartan, an ARB, is combined with diuretics to provide complementary antihypertensive effects. Hydrochlorothiazide and CT are both thiazide-like diuretics, but they differ in their pharmacodynamics and side effect profiles. Hydrochlorothiazide is often preferred for its mild diuretic effect and shorter duration of action, whereas CT is considered more potent and has a longer half-life, leading to more sustained BP control. Understanding how clinicians perceive the use of these two combinations can provide insights into prescribing patterns and their impact on patient outcomes.

Indian clinicians, who often face challenges such as polypharmacy, high rates of comorbidities like diabetes and CV disease, and varying patient adherence, play a critical role in treatment choice. Clinician perspectives on patient profiling, such as which patient subgroups benefit from each combination, and how adverse effects are managed, can help in tailoring more effective treatment regimens. Additionally, this research can guide future clinical guidelines and improve personalized care for hypertensive patients in India. Ultimately, mapping clinician perceptions will contribute to better treatment strategies, improved patient satisfaction, and enhanced healthcare outcomes.

3 STUDY OBJECTIVE

To assess the perception mapping of indian clinicians on patient profiling of telmisartan + HCTZ versus telmisartan + CT.

4 METHODS

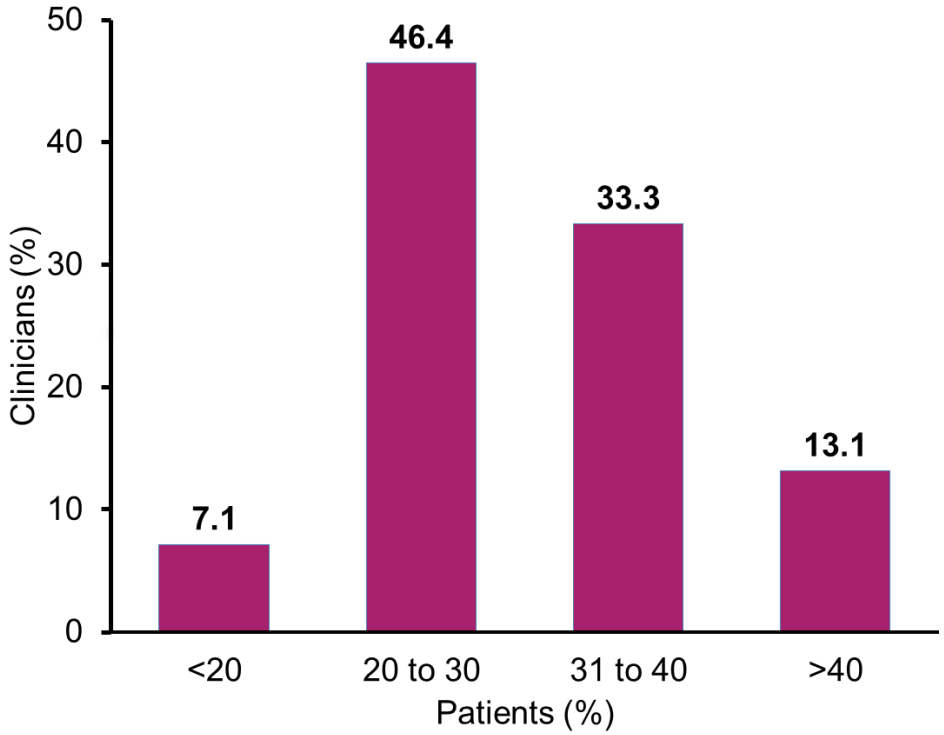
This study employs a cross-sectional, questionnaire-based survey method to assess Indian physicians' perceptions, practices, and clinical experiences regarding the use of Telmisartan + HCTZ versus Telmisartan + CT in HTN management. A structured 13-

question electronic survey will be distributed to a representative sample of 100 physicians, including cardiologists and general practitioners from various regions in India. Participants will be identified through professional networks and medical associations, ensuring a diverse and representative sample. The questionnaire will capture data on HTN treatment frequency, prescribing preferences, efficacy and safety perceptions, and factors influencing therapeutic choices. Inclusion criteria require physicians to be actively treating HTN and familiar with both drug combinations, while those with no experience or incomplete responses will be excluded. Ethical approval will be obtained, and informed consent will be secured before participation. Responses will be anonymized, securely stored, and analyzed using statistical methods to identify key trends. Although randomization and blinding are not applicable, efforts will be made to minimize selection bias by reaching a broad participant pool. The study findings will be compiled into a comprehensive report and disseminated through scientific publications or conferences, contributing to improved HTN management guidelines.

5 RESULTS

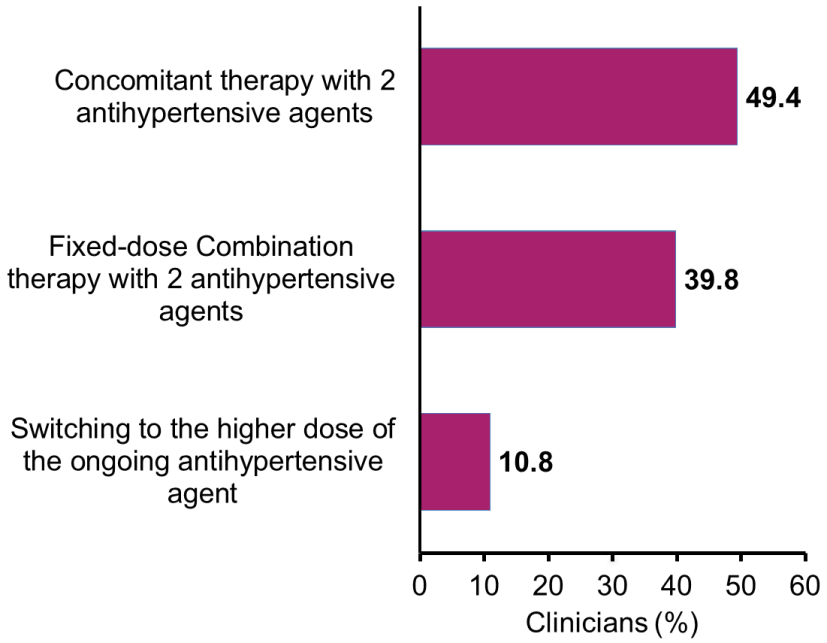
A total of 84 HCPs participated in the survey. Below is the summary of the responses.

Question 1. What percentage of patients are diagnosed with Hypertension in your clinical practice?



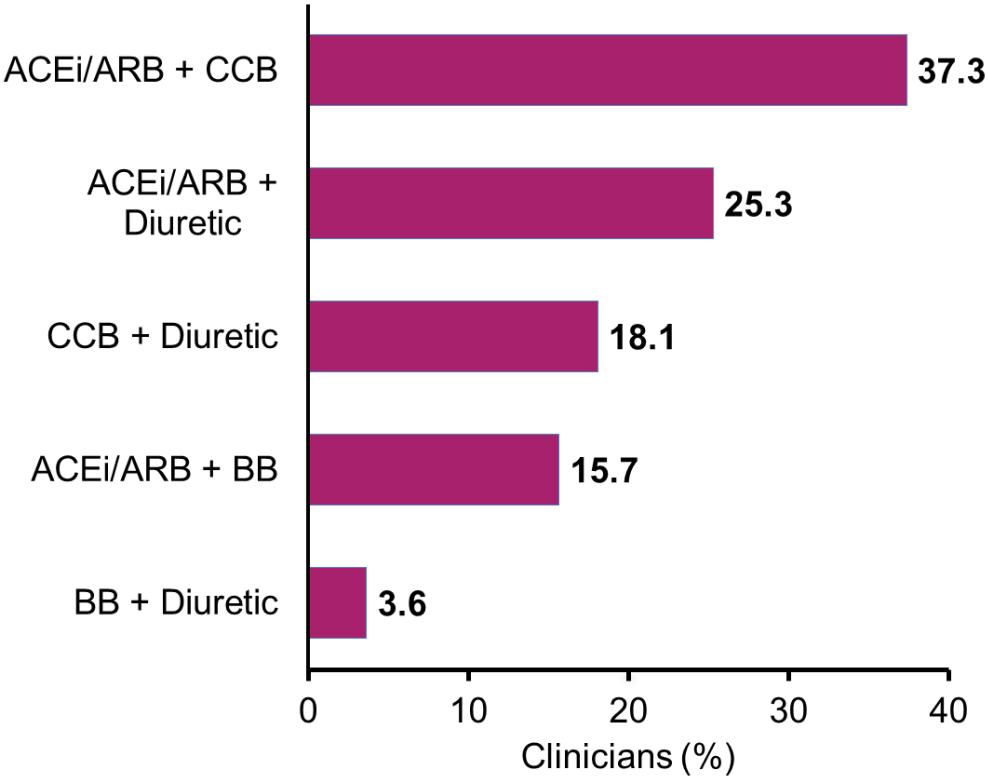
- Around 46.4% of clinicians reported that 20-30% of their patients were diagnosed with HTN during clinical practice.
- A significant portion (33.3%) of clinicians reported that 31-40% of their patients were diagnosed with HTN during clinical practice.
- Approximately 13% of clinicians reported that >40% of their patients were diagnosed with HTN during clinical practice.
- A small portion (7.1%) of clinicians reported that <20% of their patients were diagnosed with HTN during clinical practice.

Question 2. What is the most commonly preferred approach to manage uncontrolled HTN?



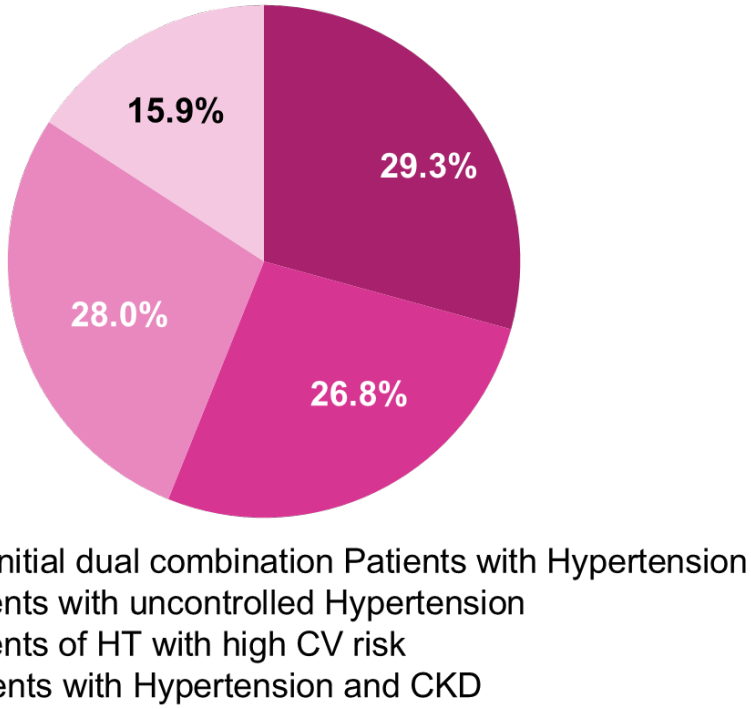
- A significant portion (49.4%) of clinicians preferred concomitant therapy with two antihypertensive agents to manage uncontrolled HTN.
- Around 39.8% of clinicians preferred fixed-dose combination therapy with two antihypertensive agents to manage uncontrolled HTN.
- Only 10.8% of clinicians preferred switching to a higher dose of the ongoing antihypertensive agents to manage uncontrolled HTN.

Question 3. Which of the Antihypertensive dual drug combination is commonly preferred by you in patients with uncontrolled HTN?



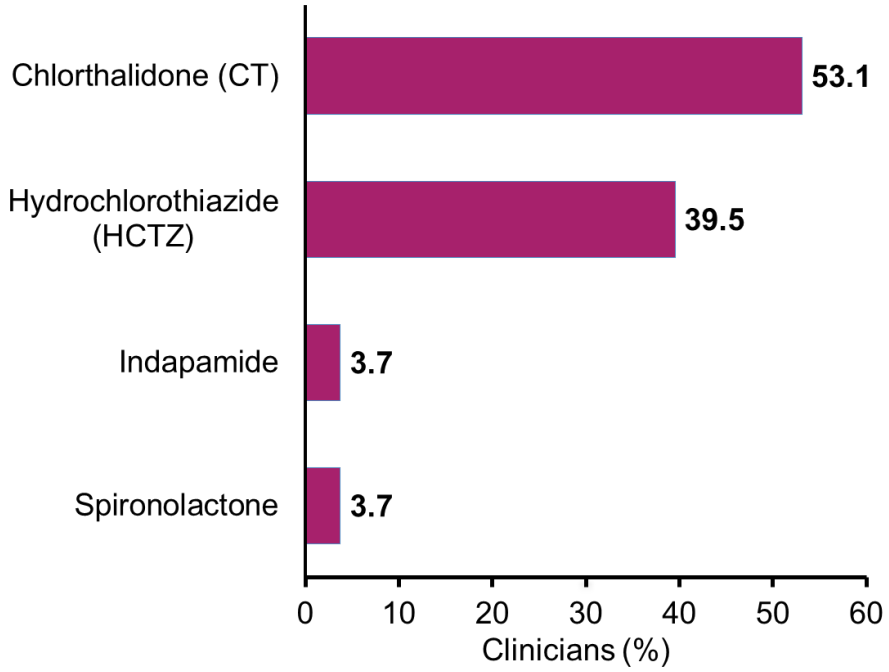
- The most commonly preferred ACEi/ARB + CCB antihypertensive dual-drug combination in patients with uncontrolled HTN was reported by 37.3% of clinicians.
- A significant portion (25.3%) of clinicians reported preferring the ACEi/ARB + Diuretic antihypertensive dual-drug combination in patients with uncontrolled HTN.
- Around 18.1% of clinicians reported preferring the CCB + Diuretic antihypertensive dual-drug combination in patients with uncontrolled HTN.
- A small portion (15.7%) of clinicians reported preferring the ACEi/ARB + BB antihypertensive dual-drug combination in patients with uncontrolled HTN.
- Only 3.6% of clinicians reported preferring the BB + Diuretic antihypertensive dual-drug combination in patients with uncontrolled HTN.

Question 4. What is the place of ARB + Diuretic combination in Hypertension therapy?



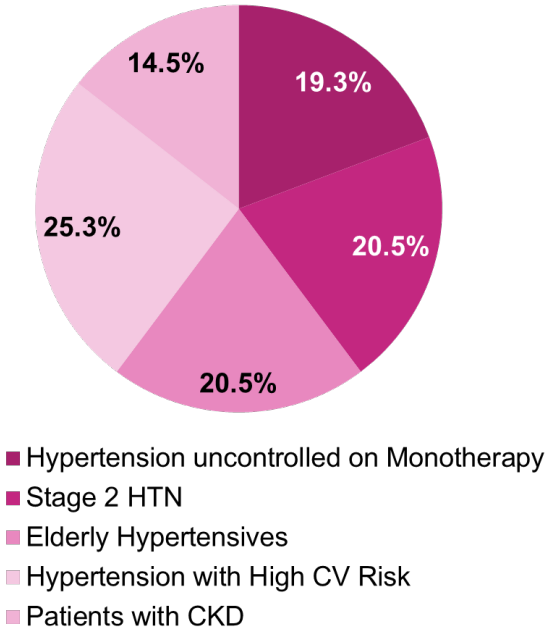
- As an initial dual combination for patients with HTN, the ARB + Diuretic combination was preferred in HTN therapy by 29.3% of clinicians.
- A significant portion (28.0%) of clinicians reported that for patients with HTN and high CV risk, the ARB + Diuretic combination had a place in HTN therapy.
- Around 26.8% of clinicians reported that for patients with uncontrolled HTN, the ARB + Diuretic combination was used in HTN therapy.
- Only 15.9% of clinicians reported that for patients with HTN and CKD, the ARB + Diuretic combination was utilized in HTN therapy.

Question 5. Which diuretic do you mostly prefer to use in combination with Telmisartan in patients with Hypertension?



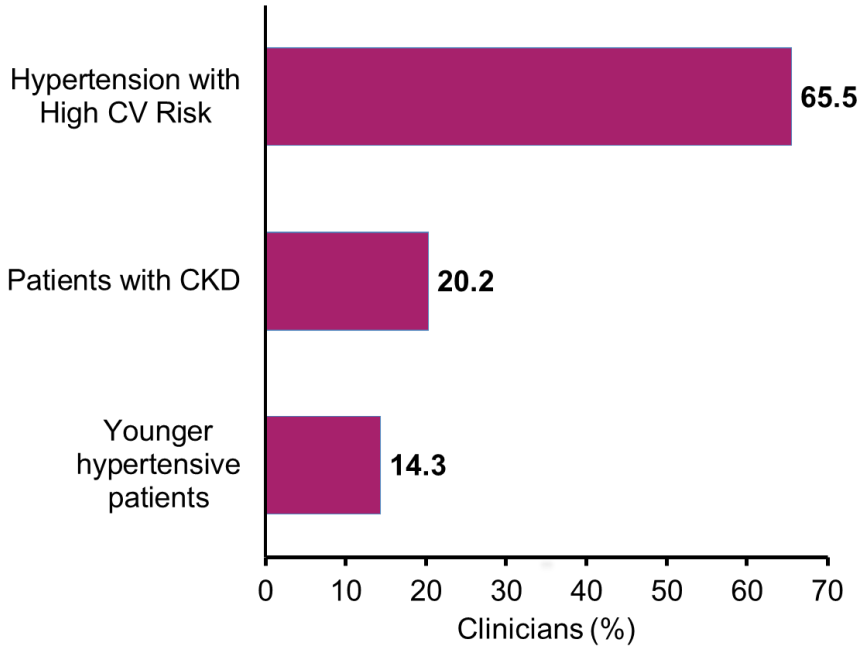
- A majority (53.1%) of clinicians reported that CT was the diuretic most commonly preferred for use in combination with telmisartan in patients with HTN.
- A significant portion (39.5%) of clinicians reported that HCTZ was the diuretic most commonly preferred for use in combination with telmisartan in patients with HTN.
- Indapamide was mostly preferred for use in combination with telmisartan in patients with HTN, as reported by 3.7% of clinicians.
- Similarly, spironolactone was mostly preferred for use in combination with telmisartan in patients with HTN, as reported by 3.7% of clinicians.

Question 6. In which patient profile do you see the key role of Telmisartan + HCTZ?



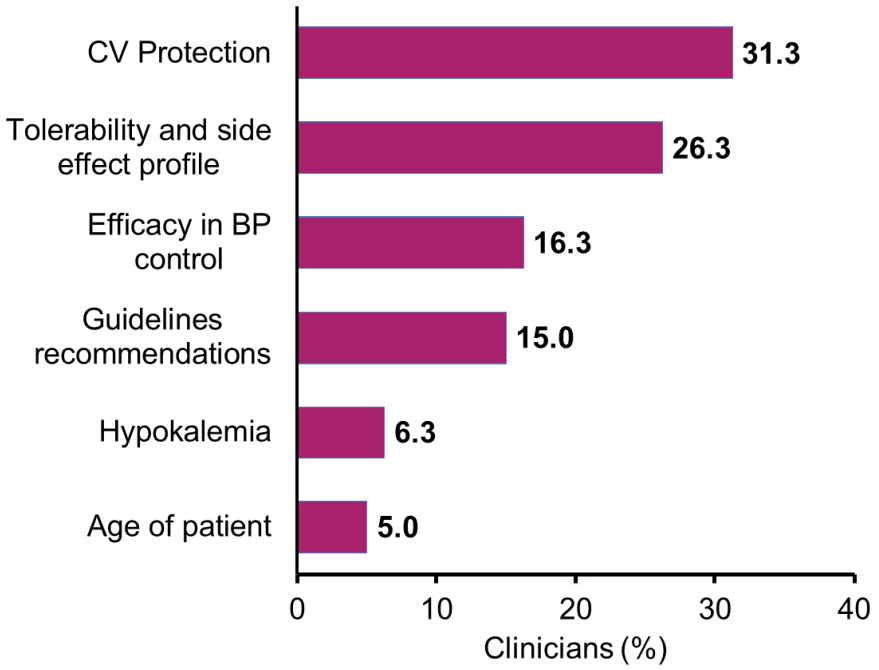
- A significant portion (25.3%) of clinicians reported that HTN with high CV risk played a key role in the use of telmisartan + HCTZ.
- Around 20.5% of clinicians reported that both stage 2 HTN and elderly hypertensive patients played a key role in the use of telmisartan + HCTZ.
- A notable portion (19.3%) of clinicians reported that uncontrolled HTN on monotherapy played a key role in the use of telmisartan + HCTZ.
- Only 14.5% of clinicians reported that patients with CKD played a key role in the use of telmisartan + HCTZ.

Question 7. In which patient profile do you prefer Telmisartan + CT?



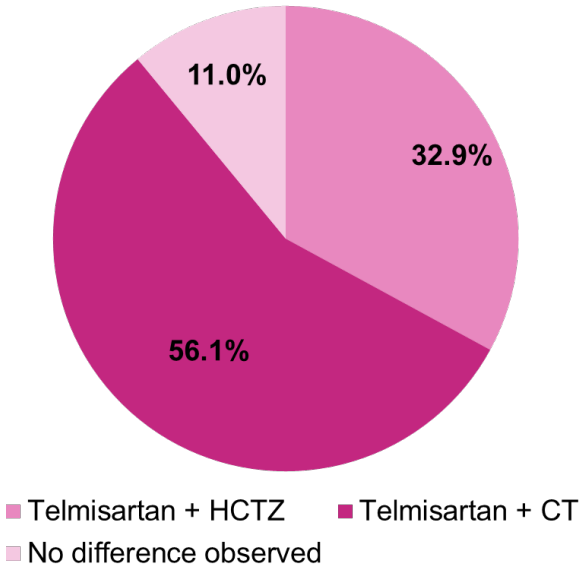
- The majority (65.5%) of clinicians reported that telmisartan + CT was preferred for patients with HTN and a high CV risk profile.
- Meanwhile, 20.2% of clinicians reported that telmisartan + CT was preferred for patients with a CKD profile.
- A small portion (14.3%) of clinicians reported that telmisartan + CT was preferred for younger hypertensive patients.

Question 8. What factors influence your choice between Telmisartan + Hydrochlorothiazide Versus Telmisartan + Chlorthalidone?



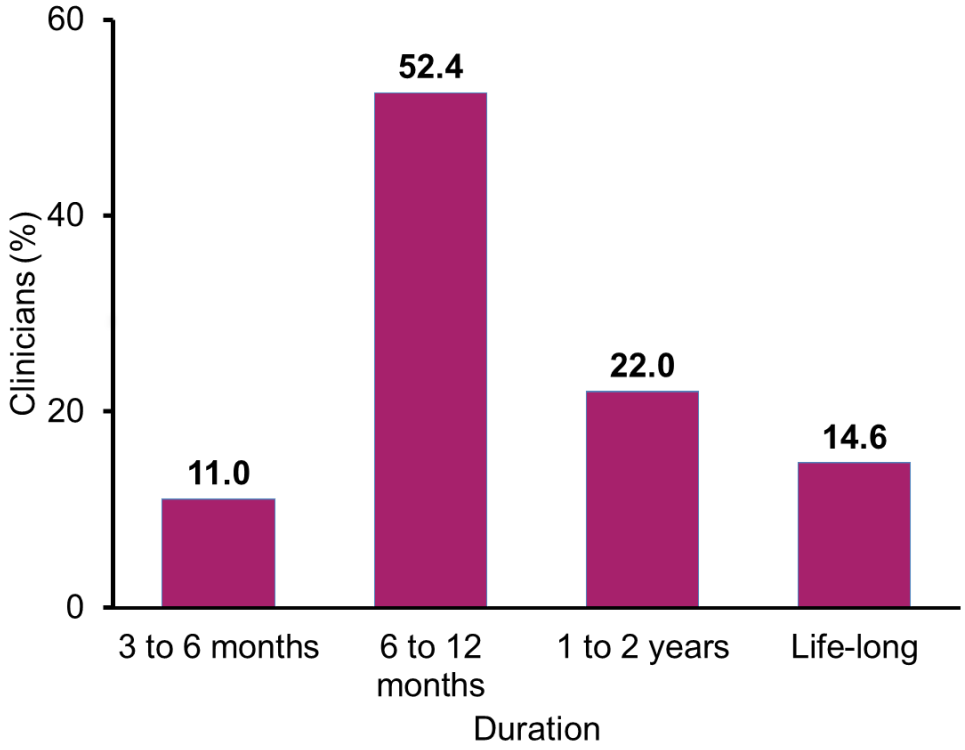
- A significant portion (31.3%) of clinicians reported that CV protection factors influenced their choice between Telmisartan + HCTZ and Telmisartan + CT.
- Around 26.3% of clinicians reported that tolerability and side effect profiles influenced their choice between Telmisartan + HCTZ and Telmisartan + CT.
- A notable portion (16.3%) of clinicians reported that efficacy in BP control influenced their choice between Telmisartan + HCTZ and Telmisartan + CT.
- Meanwhile, 15.0% of clinicians reported that guideline recommendations influenced their choice between Telmisartan + HCTZ and Telmisartan + CT.
- Hypokalemia influenced the choice between Telmisartan + HCTZ and Telmisartan + CT, as reported by 6.3% of clinicians.
- Only 5.0% of clinicians reported that the age of the patient influenced their choice between Telmisartan + HCTZ and Telmisartan + CT.

Question 9. In your clinical practice, which combination shows better long-term cardiovascular outcomes?



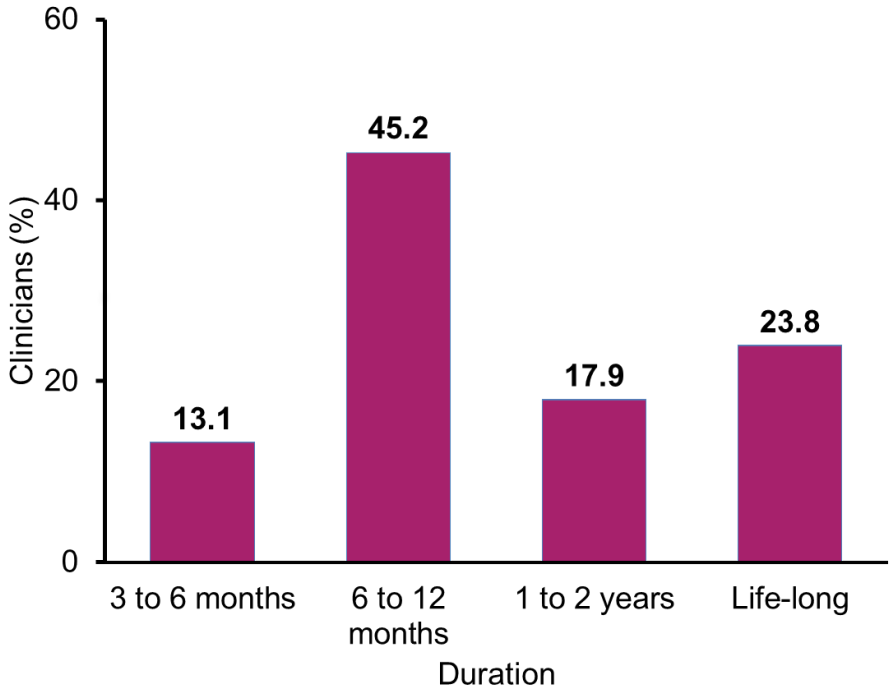
- A majority (56.1%) of clinicians reported that the telmisartan + CT combination showed better long-term CV outcomes in clinical practice.
- Around 32.9% of clinicians reported that the telmisartan + HCTZ combination showed better long-term CV outcomes in clinical practice.
- Only 11.0% of clinicians reported that no differences were observed between combinations in terms of long-term CV outcomes in clinical practice.

Question 10. What is the average duration of therapy for Telmisartan + Hydrochlorothiazide therapy in patients with uncontrolled HTN?



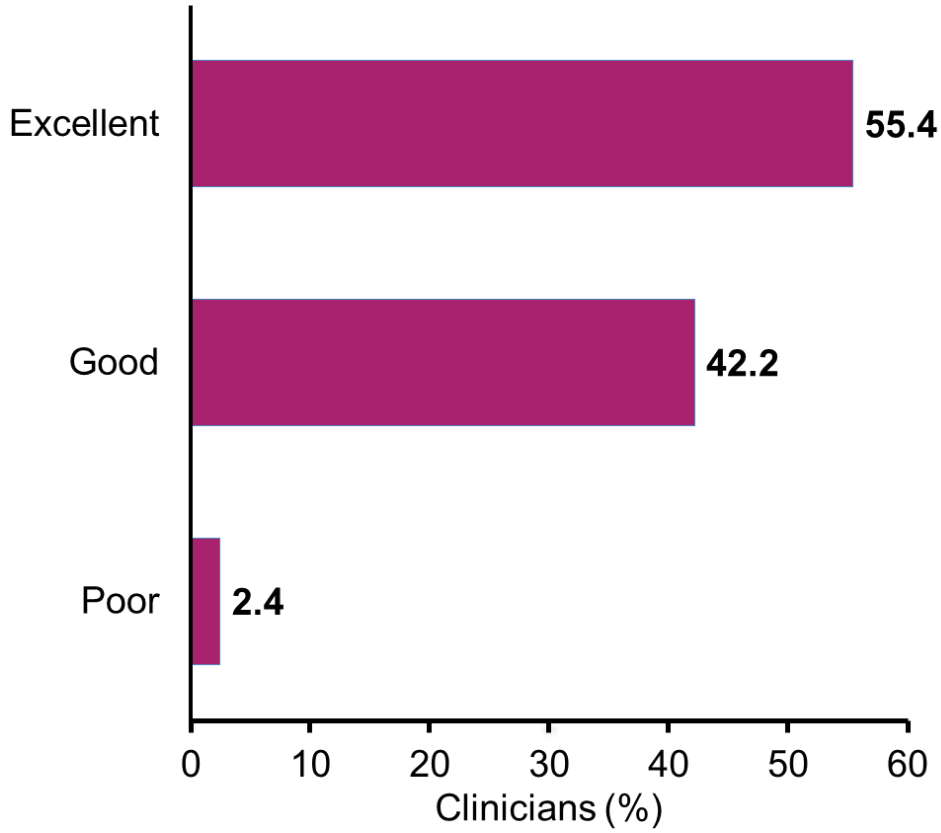
- The majority (52.4%) of clinicians reported that 6 to 12 months was the average duration of therapy for telmisartan + HCTZ in patients with uncontrolled HTN.
- Around 22.0% of clinicians reported that 1 to 2 years was the average duration of therapy for telmisartan + HCTZ in patients with uncontrolled HTN.
- A notable portion (14.6%) of clinicians reported that life-long was the average duration of therapy for telmisartan + HCTZ in patients with uncontrolled HTN.
- Only 11.0% of clinicians reported that 3 to 6 months was the average duration of therapy for telmisartan + HCTZ in patients with uncontrolled HTN.

Question 11. What is the average duration of therapy for Telmisartan + Chlorthalidone therapy in patients with uncontrolled HTN?



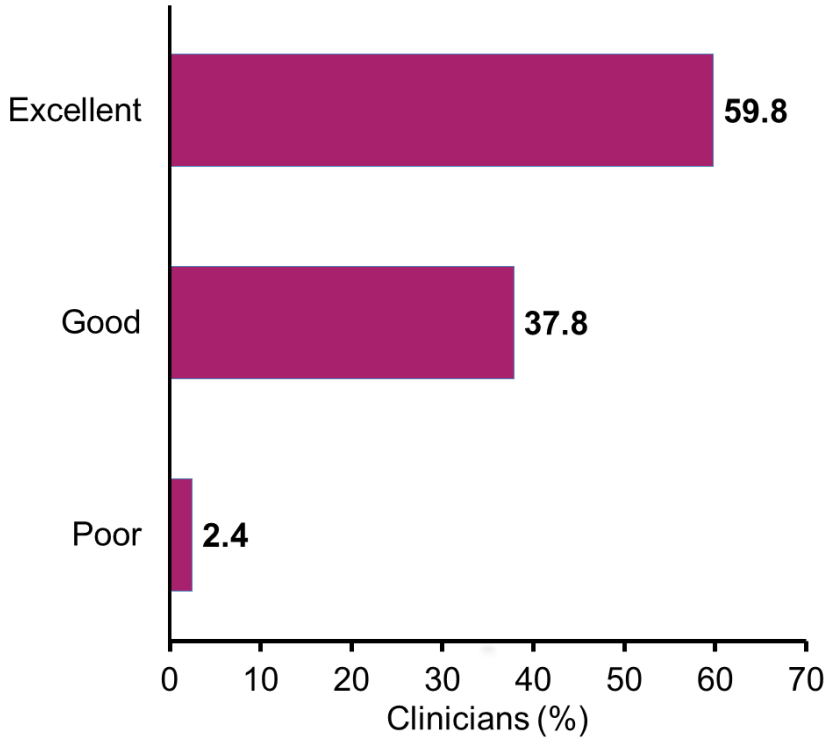
- The majority (45.2%) of clinicians reported that 6 to 12 months was the average duration of therapy for telmisartan + CT in patients with uncontrolled HTN.
- Around 23.8% of clinicians reported that life-long was the average duration of therapy for telmisartan + CT in patients with uncontrolled HTN.
- A notable portion (17.9%) of clinicians reported that 1 to 2 years was the average duration of therapy for telmisartan + CT in patients with uncontrolled HTN.
- Only 13.1% of clinicians reported that 3 to 6 months was the average duration of therapy for telmisartan + CT in patients with uncontrolled HTN.

Question 12. In your opinion, how is the long-term safety profile of Telmisartan + Hydrochlorothiazide therapy?



- A majority (55.4%) of clinicians reported that the excellent long-term safety profile of telmisartan + HCTZ therapy was their opinion.
- A significant portion (42.2%) of clinicians reported that the good long-term safety profile of telmisartan + HCTZ therapy was their opinion.
- Around 2.4% of clinicians reported that the poor long-term safety profile of telmisartan + HCTZ therapy was their opinion.

Question 13. In your opinion, how is the long-term safety profile of Telmisartan + CT therapy?



- A majority (59.8%) of clinicians reported that the excellent long-term safety profile of telmisartan + CT therapy was their opinion.
- A significant portion (37.8%) of clinicians reported that the good long-term safety profile of telmisartan + CT therapy was their opinion.
- Around 2.4% of clinicians reported that the poor long-term safety profile of telmisartan + CT therapy was their opinion.

6 SUMMARY

A large portion of clinicians (46.4%) reported that 20-30% of their patients were diagnosed with HTN during clinical practice, with 33.3% observing 31-40% of their patients diagnosed. The majority (49.4%) preferred concomitant therapy with two antihypertensive agents for managing uncontrolled HTN, while 39.8% favored fixed-dose combination therapy. ACEi/ARB + CCB was the most commonly preferred dual-drug combination (37.3%) for uncontrolled HTN. The ARB + Diuretic combination was often used in HTN therapy, especially in patients with high CV risk (28.0%) or uncontrolled HTN (26.8%). When combining with telmisartan, CT was the preferred diuretic (53.1%), followed by HCTZ (39.5%). For patients with high CV risk, telmisartan + CT was favored by 65.5% of clinicians. Factors influencing the choice between Telmisartan + HCTZ and Telmisartan + CT included CV protection (31.3%) and tolerability (26.3%).

In terms of long-term CV outcomes, telmisartan + CT was favored (56.1%), and the typical therapy duration for both combinations ranged from 6 months to 2 years. Clinicians largely agreed on the excellent safety profiles of both telmisartan + HCTZ (55.4%) and telmisartan + CT (59.8%), with few reporting poor safety profiles. Overall, clinicians prioritize dual therapy and combinations with good safety and efficacy profiles to manage HTN, particularly in patients with higher CV risk or uncontrolled HTN.

7 DISCUSSION

The data reveals key insights into the clinical management of HTN, with a focus on treatment preferences, dual-drug combinations, and factors influencing clinical decisions. A significant number of clinicians reported that a substantial portion of their patient population is diagnosed with HTN, with 46.4% of clinicians observing that 20-30% of their patients have this condition. This highlights the prevalence of HTN in clinical practice and the need for effective management strategies. Regarding treatment preferences, a majority (49.4%) of clinicians favored concomitant therapy with two antihypertensive agents for managing uncontrolled HTN, underscoring the importance of combination therapy in achieving optimal BP control. Additionally, 39.8% preferred fixed-dose combination therapy, which simplifies treatment regimens for patients, potentially improving adherence. Among the dual-drug combinations, ACEi/ARB + CCB was the most commonly preferred for uncontrolled HTN (37.3%), while the ARB + Diuretic combination also held prominence in clinical practice, especially for patients with high CV risk (28.0%) and uncontrolled HTN (26.8%).

When it comes to diuretics, CT and HCTZ were the most favored choices for use with telmisartan in HTN therapy. CT was preferred by 53.1% of clinicians, while 39.5% chose HCTZ. This suggests that CT's more sustained effects and favorable outcomes in clinical trials may contribute to its higher preference. Furthermore, clinicians considered various factors when choosing between combinations such as telmisartan + HCTZ and telmisartan + CT. CV protection, tolerability, and efficacy in BP control were prominent factors influencing these decisions. These preferences align with current guidelines emphasizing the importance of CV protection in managing HTN, particularly in high-risk populations.

In terms of long-term outcomes, the majority of clinicians (56.1%) believed that telmisartan + CT showed better long-term CV outcomes, reinforcing the growing recognition of CT's benefits in managing HTN with co-morbidities like CV disease. The safety profiles of both combinations were highly rated, with most clinicians acknowledging excellent long-term safety, further supporting their continued use in clinical practice.

Overall, the data underscores a preference for dual therapies with proven efficacy, safety, and CV benefits, reflecting current clinical trends in HTN management.

8 CLINICAL RECOMMENDATIONS

- Chlorthalidone is the most preferred diuretic (53.1%) for combination therapy with telmisartan, suggesting its long-term efficacy and CV benefits.
- Hydrochlorothiazide is also a commonly used diuretic (39.5%) and remains an important option for combination therapy.
- Concomitant therapy with two antihypertensive agents is preferred by the majority (49.4%) of clinicians for managing uncontrolled HTN.
- Fixed-dose combination therapy (39.8%) simplifies treatment and may improve patient adherence.
- ACEi/ARB + CCB (37.3%) and ARB + Diuretic (28.0%) are commonly used for managing uncontrolled HTN, particularly in patients with high CV risk.
- ARB + Diuretic combination is preferred in managing HTN with high CV risk (28%) and in uncontrolled HTN (26.8%).
- Cardiovascular protection (31.3%), tolerability and side effect profiles (26.3%), and efficacy in BP control (16.3%) are key factors in selecting between telmisartan + HCTZ and telmisartan + CT.
- Clinicians should prioritize these factors when choosing a treatment regimen, especially for patients at high CV risk.
- Telmisartan + CT is believed to offer better long-term CV outcomes (56.1%), making it a preferred option for patients with high CV risk.
- Both telmisartan + HCTZ (55.4%) and telmisartan + CT (59.8%) are viewed as having excellent long-term safety profiles, supporting their continued use in long-term HTN management.

9 CONSULTANT OPINION

The data highlights the evident that the majority of clinicians prefer dual antihypertensive therapy, particularly for managing uncontrolled HTN. This preference aligns with current clinical guidelines and underscores the importance of combining medications to achieve optimal BP control. Clinicians favor fixed-dose combination therapies, which not only enhance patient adherence but also simplify treatment regimens. The choice of drug combinations such as ACEi/ARB + CCB and ARB + Diuretic reflects a focus on maximizing efficacy, with a notable emphasis on CV protection, particularly in high-risk patients. The data also indicates that diuretics like CT and HCTZ are key components in combination therapy, with CT being the most frequently selected due to its sustained effect and positive long-term CV outcomes. The safety profiles of these combinations are also a significant consideration, with clinicians overwhelmingly reporting excellent safety for both telmisartan + HCTZ and telmisartan + CI, further reinforcing their place in clinical practice. Clinicians also consider factors like tolerability, side effects, and the long-term CV benefits when making treatment decisions, reflecting a patient-centric approach to managing HTN. The average duration of therapy for these combinations is typically 6 to 12 months, suggesting a careful approach to long-term management with reassessment at appropriate intervals. Overall, the consultant opinion would stress the importance of tailored combination therapy in managing uncontrolled HTN, prioritizing both efficacy and safety to achieve long-term CV health outcomes.

10 MARKET OPPORTUNITIES

The data highlights several market opportunities in the management of HTN, particularly for pharmaceutical companies focusing on combination therapies. The significant preference for dual antihypertensive treatments, such as ACEi/ARB + CCB and ARB + Diuretic combinations, presents an opportunity for companies to develop and market fixed-dose combination products that simplify treatment regimens, thereby improving patient adherence. Given the increasing prevalence of HTN, especially among high-risk CV patients, there is a growing demand for effective, safe, and convenient treatment options.

The high preference for CT and HCTZ as diuretics in combination with telmisartan suggests opportunities for manufacturers to further promote these diuretics as key components in HTN therapy. Additionally, with clinicians emphasizing long-term CV benefits and safety profiles, there is an opportunity for companies to position their products based on efficacy in reducing long-term CV risks. Clinicians' focus on managing HTN in high-risk populations, including those with CV disease and (CKD), provides an avenue for targeting specific patient groups with tailored therapies. Furthermore, the significant attention to treatment duration (6 to 12 months) suggests potential for ongoing therapy options that encourage long-term patient management. These factors present strong opportunities for market growth in both established and emerging antihypertensive treatments.

11 MARKET POSITIONING

- Position fixed-dose combination antihypertensive products as the primary solution for managing uncontrolled HTN, emphasizing ease of use and improved patient adherence.
- Highlight the most preferred combinations, such as ACEi/ARB + CCB and ARB + Diuretic, as effective strategies for BP control, particularly in high-risk CV patients.
- Emphasize the role of CT and HCTZ as key diuretics when combined with telmisartan, capitalizing on their widespread preference among clinicians for long-term management of HTN.
- Position CT as the preferred diuretic, focusing on its long-term efficacy and CV benefits, to attract high-risk patient populations.
- Market products based on their CV protection benefits, as 31.3% of clinicians consider this factor when choosing between treatment combinations. This positioning would cater to patients at high CV risk, a growing segment in HTN management.
- Position products like telmisartan + CT and telmisartan + HCTZ based on their excellent long-term safety profiles, as 55.4% and 59.8% of clinicians report these combinations as having excellent safety, appealing to patients needing sustained therapy.
- Focus marketing efforts on patients with high CV risk, CKD, and those with uncontrolled HTN, as these groups significantly influence the choice of therapy.

12 REFERENCES

1. Gupta R, Yusuf S. Towards better hypertension management in India. Indian J Med Res. 2014 May;139(5):657-60.
2. Charchar FJ, Prestes PR, Mills C, Ching SM, Neupane D, Marques FZ, Sharman JE, Vogt L, Burrell LM, Korostovtseva L, Zec M. Lifestyle management of hypertension: International Society of Hypertension position paper endorsed by the World Hypertension League and European Society of Hypertension. Journal of hypertension. 2024 Jan 1;42(1):23-49.
3. Sumbria M, Negi PC, Sahai AK, Kaundal PK. To compare the effect of Telmisartan with Metoprolol on arterial stiffness in hypertension: prospective randomized parallel group trial. Indian Heart J. 2014 Jul-Aug;66(4):415-21.
4. Tackling G, Borhade MB. Hypertensive Heart Disease. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539800/\
5. Bakris, George L., and Matthew Sorrentino, eds. Hypertension: A companion to braunwald's heart disease. Elsevier Health Sciences, 2017.
6. Williams, B., Mancia, G., Spiering, W., Agabiti Rosei, E., Azizi, M., Burnier, M., et al., … ESC Scientific Document Group (2018). 2018 ESC/ESH Guidelines for the management of arterial hypertension. European heart journal, 39(33), 3021–3104.