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WIN OVER study: Efficacy and safety of olmesartan in Indian hypertensive patients: Results of an open label, non-comparative, multi-centric, post marketing observational study

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ABSTRACT

Background: Hypertension is a global health problem. Multiple classes of drugs including angiotensin receptor blockers (ARBs) are available for the treatment of hypertension. Olmesartan is a relatively newer ARB used in hypertension management.

Objective: To assess the efficacy and safety of WIN-BP (Olmesartan 20 mg/40 mg) tablet in Indian patients with hypertension.

Material and methods: An open label, non-comparative, multi-centric, real world post marketing observational study included Indian adult hypertensive patients who were treated with olmesartan 20 mg/40 mg tablet once daily for six months. The primary outcome was reduction of systolic blood pressure (SBP) to <140 mmHg and diastolic BP (DBP) to <90 mmHg at 3 and 6 months after initiation of treatment with olmesartan. All reported adverse events were recorded.

Results: A total of 8940 patients were enrolled in this study. Baseline SBP of 164 mmHg was reduced to 153, 145, 134 and 130 mmHg at the end of 15 days, 1, 3 and 6 months respectively. Similarly, baseline DBP of 100 mmHg was reduced to 93, 89, 84 and 82 mmHg at the end of 15 days, 1, 3 and 6 months respectively. The reduction in both systolic and diastolic blood pressure from day 15 to month 6 was statistically significant ($p < 0.0001$) with olmesartan treatment. The percentage of responders for both systolic and diastolic blood pressure increased consistently from day 15 to month 6. Only 0.08% patients reported the adverse events. No serious adverse event was reported in the study.

Conclusion: Olmesartan 20 mg/40 mg is effective and well tolerated without any serious adverse events in patients with hypertension.

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1. Introduction

High blood pressure is a major public health problem in many countries including India.[1] The prevalence of hypertension in India among urban and rural populations is 25% and 10% respectively and continues to increase rapidly.[1] Changing socioeconomic milieu with consequent changes in the lifestyles of general public are believed to be the major determinants of the rise in the prevalence of hypertension in India.[2]

Hypertension is one of the major contributors of cardiovascular morbidity and mortality worldwide. It is therefore important to adequately control the blood pressure (BP) to reduce the complications associated with hypertension. The treatment of hypertension has been shown to significantly reduce the incidence of stroke, myocardial infarction and heart failure.[3]Various treatment modalities including non-pharmacological and pharmacological are available for the management of hypertension.[1] Among the pharmacological treatment options, multiple classes of drugs with different mechanism of action are available which can be selected based on individual patient characteristics. Given the important role of renin–angiotensin–aldosterone system in regulating blood pressure, it becomes an important target of therapy aimed at treating hypertension. Angiotensin receptor blockers (ARBs) are modulators of the renin–angiotensin–aldosterone system and act by blocking the receptor responsible for the action of angiotensin II. ARBs have been shown to be highly effective in the management of hypertension as monotherapy or in combination with other drugs.[4] Olmesartan medoxomil is an ARB with excellent efficacy and tolerability profile. It has long half-life which ensures effective BP control over the 24 h dosing interval. As a result, once daily dosing is required making the dosing regimen simple and improving patient compliance.[5] Other advantages of olmesartan include a lower incidence of drug interactions and lack of the effect of age on its pharmacokinetic profile.

2. Objective

The objective of this study was to evaluate the efficacy and safety of WIN-BP (Olmesartan 20 mg/40 mg) tablet in Indian patients with hypertension.

3. Material and methods

An open label, non-comparative, multi-centric, real world post marketing observational study was conducted in existing or newly diagnosed hypertensive Indian patients. Adults patients (>18 years) of either sex, with essential hypertension or hypertension with co-morbidities such as angina, diabetes mellitus, dyslipidemia or mild to moderate heart failure were included in this study. The patients whose BP was not controlled with single antihypertensive agent were also included in this study. Pregnant and lactating women, patients with history of hypersensitivity to olmesartan, those with severe cardiac failure, renal artery stenosis, chronic renal failure, clinically significant hepatic or renal impairment, varicose veins, chronic venous insufficiency associated with edema or any significant uncontrolled illness were not included in the study. Patients who were on concomitant medications like oral contraceptives, non-steroidal anti-inflammatory drugs, diuretics, vasodilators, digoxin, anticoagulants were also excluded from the present study.

Patients satisfying the enrollment criteria were enrolled after written informed consent and were started treatment with olmesartan 20 mg/40 mg tablet once daily for six months. Dose titration was allowed as per the discretion of the treating physician. The patients were followed for six months which included a total of six visits (baseline, 15 days, 1 month, 2 month, 3 month, 6 month).

The primary outcome of the study was reduction in systolic BP (SBP) to ≤140 mmHg and diastolic BP (DBP) to ≤90 mmHg at 3 and 6 months of treatment with olmesartan. Global assessment for efficacy and tolerability was done by the treating physician and the patient himself/herself at the end of 6 months. All reported adverse events were recorded.

The study was conducted as per the applicable local and national regulatory laws and guidelines and as per the GCP guidelines of ICMR. The study protocol was approved by an independent ethics committee.

3.1. *Evaluation criteria*

Percentage of patients who achieved SBP ≤140 mmHg and DBP ≤90 mmHg at 3 months and 6 months of treatment were calculated. The absolute reduction in SBP and DBP at each visit compared to baseline was also studied for the significance of the difference. Global assessment of efficacy was done by both the patient and the doctor on a four-point scale i.e. 4 = excellent, 3 = good, 2 = moderate and 1 = poor. The tolerability was also assessed by both the patients and the doctors and was graded as – "good: mild/no adverse effects", "moderate: adverse events of moderate intensity" and "poor: adverse events-severe or discontinuation of therapy".

3.2. *Statistical analysis*

The analysis was done on intention-to-treat basis and included all patients who received at least one dose of study medication. Paired *t*-test and repeat measures ANOVA were used to assess the statistical significance of the differences in SBP and DBP between the baseline and the follow up visits. Chi-square test was used to compare the proportion of the patients achieving adequate BP control (defined above). A p value <0.05 was considered statistically significant.

4. Results

4.1. *Baseline characteristics*

A total of 8940 patients were enrolled in this study. The mean age, height and weight of the study patients are given in Table 1. Most of the patients included in the study were between 18 and 65 years of age while 11.2% patients were above 65 years of age. Nearly two-thirds (65.2%) of all study patients were males.

Table 1 – Baseline characteristics.

Parameter	n	Mean (SD)
Age (years)	8931	53.26 (10.34)
Height (cm)	4628	164.2 (9.74)
Weight (kg)	7196	69.98 (18.63)

Overall 19.9% patients had concomitant diabetes and 2.0% had ischemic heart disease. A substantial proportion of the patients were previously on antihypertensive agents with ARBs being the most common (87.2%) followed by beta blockers (14.2%), calcium channel blockers (13.8%), diuretics (9.7%), angiotensin converting enzyme (ACE) inhibitors (5.3%), vasodilators (2.0%) and others (13.4%). Olmesartan was added to existing antihypertensive treatment for controlling blood pressure, if found suitable.

4.2. *Antihypertensive efficacy of olmesartan*

Olmesartan was used in two strengths (20 mg/day and 40 mg/day). Out of 8940 patients, 56.6% patients received olmesartan 20 mg/day while 40.9% patients received 40 mg/day. Concomitant medications received by more than 1% patients included oral hypoglycemic agents (2.83%), statins (1.76%), angiotensin receptor blockers (1.32%) and beta blockers (1.15%).

The baseline BP of the study patients was 164 mmHg systolic and 99.84 mm of Hg diastolic. Olmesartan significantly reduced the BP throughout the study period. Statistically significant reductions in both SBP and DBP were seen from day 15 itself and the magnitude of reduction continued to increase till the end of the study (i.e. 6 months' follow-up) (Repeat measures ANOVA $p < 0.0001$) (Figs. 1 and 2). At each of the visit the difference i.e. reduction in blood pressure compared to baseline was significant.

Mean change in the SBP from the baseline at the end of first, third and six months were 19.08, 29.79 and 34.53 mm of Hg respectively.

Mean change in DBP from baseline at the end of first, third and six months were 11.07, 16.3 and 18.08 mm of Hg respectively.

The percentage of responders for SBP defined as patients with SBP ≤140 mmHg increased consistently from day 15 to month 6 as shown in Fig. 3.

Similarly, there was a constant increase in the percentage of DBP responders (patients with DBP ≤90 mmHg blood pressure) also, from day 15 to month 6 (Fig. 4).

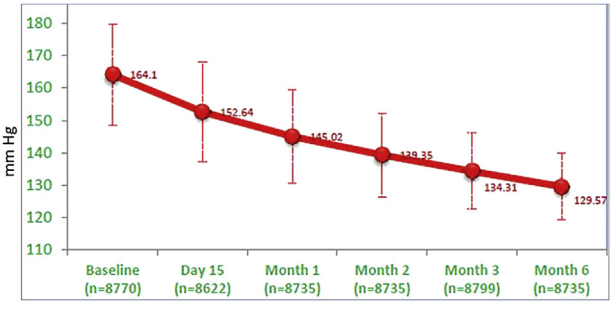

Fig. 1 – Reduction in systolic blood pressure.

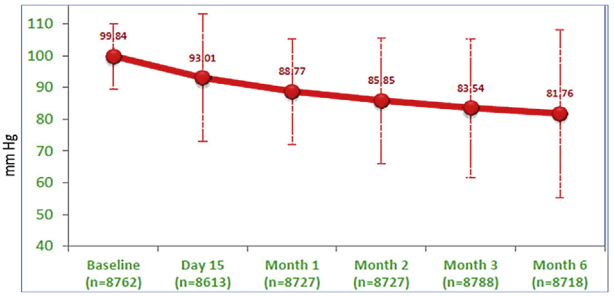

Fig. 2 – Reduction in diastolic blood pressure.

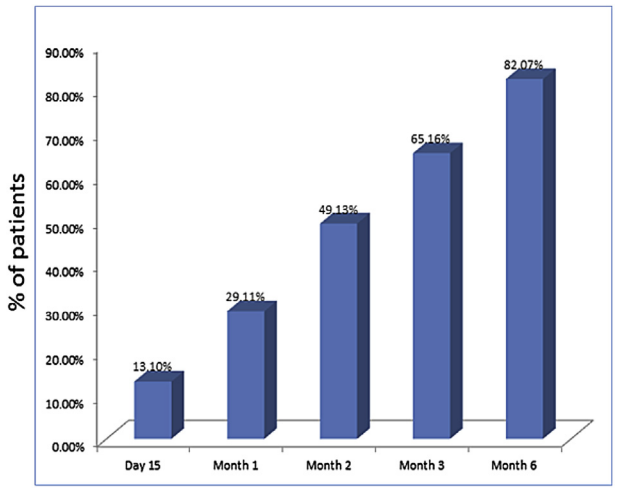

Fig. 3 – Responders for systolic blood pressure (≤140 mmHg).

When assessed by patients, the global assessment of response to therapy was good to excellent in most of the patients at six months (Fig. 5). Three forth of the patients at the end of six months rated the response as "excellent".

Similarly, the global assessment of response to therapy was rated as good by most (96.5%) of the treating physicians also (Fig. 6).

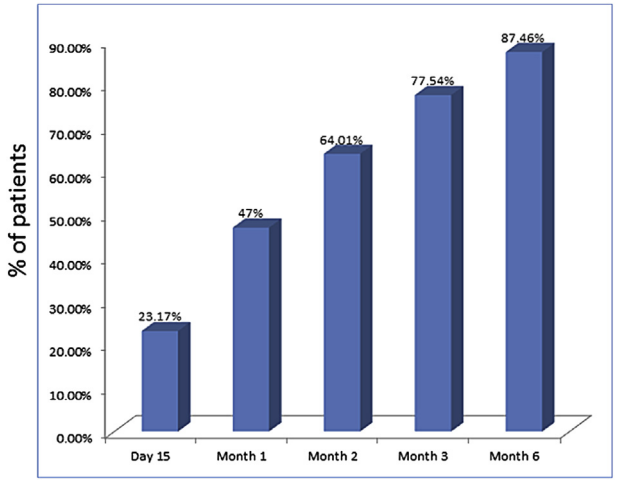

Fig. 4 – Responders for diastolic blood pressure (≤90 mmHg).

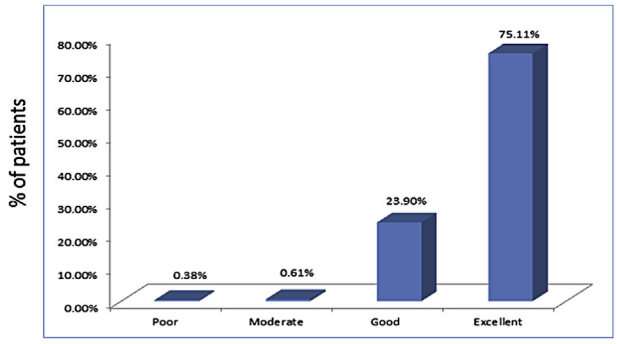

Fig. 5 – Global assessment of response to therapy by patients at 6 months (n = 8788).

4.3. *Safety*

Olmesartan was extremely well tolerated in the study patients. Adverse events were reported by only 3 (0.08%) patients. The reported adverse events included edema, dizziness, uncontrolled hypertension and vertigo (Table 2). No serious adverse event was reported in this study.

As per the global assessment, the tolerability at 6 months was rated as good by 96.49% and 96.48% patients when assessed by the patients and the treating physicians respectively (Figs. 7 and 8).

5. Discussion

ARBs are very commonly used agents in the management of hypertension. They are particularly preferred in numerous clinical conditions such as left ventricular hypertrophy, renal dysfunction, microalbuminuria, patients with previous myocardial infarction, heart failure, metabolic syndrome as well as diabetes mellitus.[6] Among all the ARBs, olmesartan is considered to be one of the most powerful antihypertensive agents. In a previous multicenter, randomized, double-blind clinical study, the antihypertensive efficacy of olmesartan 20 mg once daily was compared with recommended starting doses of other ARBs i.e. losartan 50 mg, valsartan 80 mg, and irbesartan 150 mg. The results demonstrated that olmesartan at its starting dose was more effective than the starting doses of the other studied ARBs in reducing cuff DBP in essential hypertension.[7]

Olmesartan has been available in India for several years now for the treatment of hypertension. However, its safety and efficacy has not been specifically assessed adequately in Indian patients. Rana et al studied the efficacy and safety of olmesartan 20 mg/d in an open label, multicentre, observational, post-marketing surveillance in adult Indian patients with stage 1 hypertension.[8] Olmesartan 20 mg once daily was found to be effective in BP reduction and also showed an excellent tolerability profile. Our results from this much larger study are in line with these previous observations. In addition, our study also evaluated the efficacy

Table 2 – Incidence of adverse events (n = 8940).

Adverse event	Percentage of patients
Edema	0.05%
Uncontrolled hypertension	0.03%
Dizziness	0.03%
Vertigo	0.03%

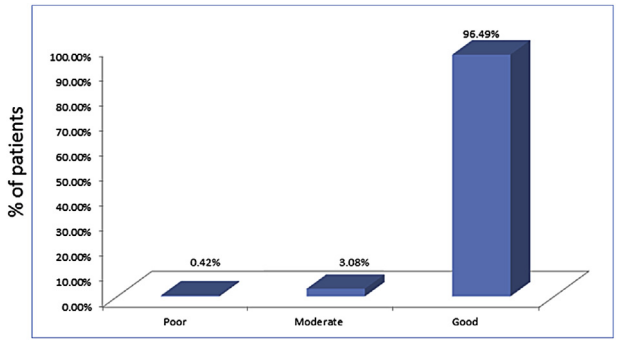

Fig. 7 – Global assessment of tolerability by patients at 6 months (n = 8804).

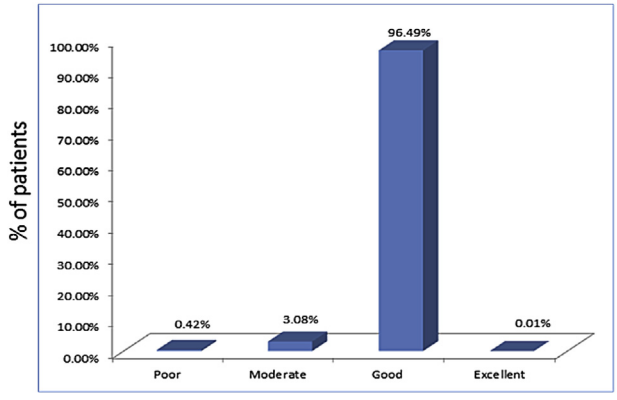

Fig. 6 – Global assessment of response to therapy by doctors at 6 months (n = 8804).

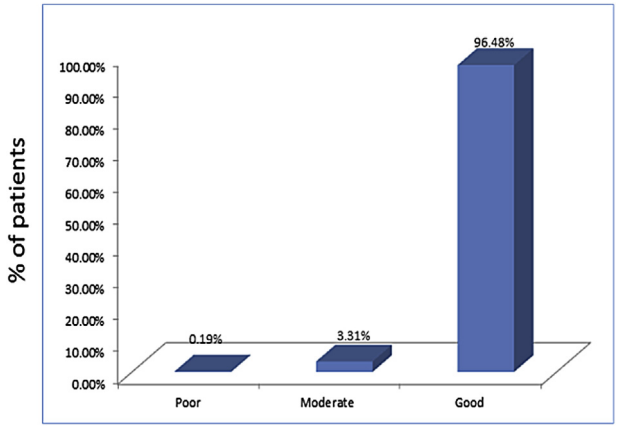

Fig. 8 – Global assessment of tolerability by doctors at 6 months (n = 8818).

and safety of olmesartan 40 mg/d. Analysis of 6 months data confirmed the efficacy and safety of olmesartan 40 mg/d in hypertension management. The consistent improvement in the efficacy of olmesartan was observed throughout the study period. Almost 96% physicians rated the global efficacy of olmesartan as "good", demonstrating its effectiveness in significantly reducing the BP. Furthermore, the therapeutic benefit was observed with once daily dosing which suggests that olmesartan is suitable for once daily administration. These findings are in accordance with the previous data showing sustained BP lowering during the entire 24-h dosage interval with olmesartan administered once daily.[9,10]

It has been reported that olmesartan has rapid onset of action, with significant BP lowering effect seen from 2 weeks onwards.[8] In our study also, significant reductions in SBP and DBP were seen from second visit (i.e. at 15 days) itself.

In terms of tolerability, the excellent safety profile of olmesartan was observed with no patient showing any serious adverse events and very low overall incidence of adverse events.

Olmesartan 20 mg and 40 mg per day is an excellent addition to the armamentarium of the antihypertensive drugs for managing hypertension in Indian patients.

6. Limitation

This study had some limitations that merit attention. The most important limitation was its open label and non-comparative study design. However, this is a recognized well-accepted limitation of all post-marketing surveillance studies. Though such study design introduces bias in the assessment of therapeutic response and safety of the drug being studied, post-marketing surveillances still provide valuable insights in to the performance of the study drug in real-life clinical setting. For this purpose, post-marketing surveillances remain the only option as this kind of information cannot be derived from any other form of study. Thus our study too demonstrated excellent safety profile and antihypertensive efficacy of olmesartan in regular clinical practice However, in order to provide a counter-check mechanism to mitigate, at least to some extent, the potential reporting bias, we also recorded the patients' own perception of the efficacy and tolerability of the drug. Consistency of the patients' assessment with that of the investigators provides further evidence of the accuracy and the validity of the study findings.

7. Conclusion

This post marketing, real world study demonstrates the efficacy and safety of olmesartan 20 mg/40 mg in Indian adult patients with hypertension, making olmesartan an effective and well tolerated suitable treatment option for both newly diagnosed patients as well as for patients whose BP is not adequately controlled with other antihypertensive agents.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Gupta R, Guptha S. Strategies for initial management of hypertension. *Indian J Med Res*. November 2010;132:531–542.
2. Mahmood SE, Srivastava A, Shrotriya VP, et al. Prevalence and epidemiological correlates of hypertension among labour population. *Natl J Community Med*. 2011;2:43–48.
3. Chobanian AV, Bakris GL, Black HR, et al. National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating committee. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *J Am Med Assoc*. 2003;289:2560–2572.
4. Catanzaro DF, Frishman WH. Angiotensin receptor blockers for management of hypertension. *South Med J*. 2010 Jul;103:669–673.
5. Volpe M, Tocci G. Olmesartan in the treatment of hypertension in elderly patients: a review of the primary evidence. *Drugs Aging*. 2013 Dec;30:987–998.
6. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension. *Eur Heart J*. Advance Access published 14.06.13.
7. Oparil S, Williams D, Chrysant SG, et al. Comparative efficacy of olmesartan, losartan, valsartan, and irbesartan in the control of essential hypertension. *J Clin Hypertens (Greenwich)*. 2001; Sep–Oct;3:283–291, 318.
8. Rana R, Singh A. Olmesartan medoxomil evaluated for safety and efficacy in Indian patients with essential hypertension: a real world observational post marketing surveillance. *J Assoc Physicians India*. 2010 Feb;58:77–83.
9. Neutel JM. Clinical studies of CS-866, the newest angiotensin II receptor antagonist. *Am J Cardiol*. 2001;8:37C–43C.
10. Scott LJ, McCormack PL. Olmesartan medoxomil: a review of its use in the management of hypertension. *Drugs*. 2008;68:1239–1272.