Effects of Olmesartan-Based Treatment on Masked, White-Coat, Poorly Controlled, and Well-Controlled Hypertension: HONEST Study

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The authors examined the effects of olmesartan-based treatment on clinic systolic blood pressure (CSBP) and morning home systolic blood pressure (HSBP) in 21,340 patients with masked hypertension (MH), white-coat hypertension (WCH), poorly controlled hypertension (PCH), and well-controlled hypertension (CH) using data from the Home Blood Pressure Measurement With Olmesartan Naive Patients to Establish Standard Target Blood Pressure (HONEST) study. MH, WCH, PCH, and CH were defined using CSBP 140 mm Hg and MHSBP 135 mm Hg as cutoff values at baseline. At 16 weeks, the MH, WCH, PCH, and CH groups had changes in CSBP by −1.0, −15.2, −23.1, and 1.8 mm Hg, and changes in morning HSBP by −12.5, 1.0, −20.3, and 2.0 mm Hg, respectively. In conclusion, in "real-world" clinical practice, olmesartan-based treatment decreased high morning HBP or CBP without excessive decreases in normal morning HBP or CBP according to patients' BP status. *J Clin Hypertens (Greenwich).* 2014;16:442–450. ©2014 The Authors. *The Journal of Clinical Hypertension* Published by Wiley Periodicals, Inc.

Hypertension status is classified as masked hypertension (MH), white-coat hypertension (WCH), poorly controlled hypertension (PCH, or sustained hypertension), and well-controlled hypertension (CH) based on thresholds of clinic blood pressure (CBP) and out-of-clinic blood pressure (BP). Of these types of hypertension status, the treatment of MH is often neglected.[1] Its prevalence varies widely, with estimates ranging between 10% and 48%, with the substantial differences being due to the reference population and the specific criteria.[2–5] The cardiovascular risk for patients with MH is approximately 2 to 3 times higher than that for people with normotension and is the same or more than that for patients with sustained hypertension.[6,7] These facts imply that standard antihypertensive management guided only by CBP is not sufficiently adequate to achieve hypertension control.

The opposite of MH is WCH, in which CBP is increased but out-of-clinic BP is normal.[8] In some studies, the prognosis for patients with WCH was about the same as that for those with normotension.[5,6,9] However, results from an international study showed a tendency for increased stroke incidence in patients with WCH,[10] and the lack of a significant association between WCH and stroke incidence cannot negate such an association.[11] WCH may progress to sustained hypertension[12] and antihypertensive treatment should be considered, at least in patients at high cardiovascular risk, such as those with complications including diabetes mellitus or the metabolic syndrome.

Cardiovascular events tend to occur most frequently in the morning, along with a peak in ambulatory BP,[13] and the morning home systolic BP (HSBP) is the strongest independent predictor for stroke among clinic, 24-hour, awake, sleep, evening, pre-awake, and morning BPs.[14]

Home BP (HBP) monitoring is the simplest way to measure out-of-clinic BP and thus identify patients with MH or WCH using both morning HBP and CBP. Few large-scale studies have investigated the effects of antihypertensive therapy on patients with MH and WCH. Until now there were findings on the association between cardiovascular events and hypertension status using CBP and ambulatory BP in untreated patients, but there were fewer findings on the association between cardiovascular events and hypertension status using CBP and HBP in treated patients. For the treatment of hypertension in clinical practice, the use of HBP to determine the association between cardiovascular events and hypertension status is more important. Hence, the Home Blood Pressure Measurement With Olmesartan Naive Patients to Establish Standard Target Blood Pressure (HONEST) study was conducted to obtain the evidence. The HONEST study is a prospective observational study following up >20,000 patients receiving olmesartan-based antihypertensive treatment for 2 years.[15] We analyzed the data from the HONEST study to investigate the effects of 16 weeks of olmesartan-based treatment on the 4 groups: the MH group, the WCH group, the PCH group, and the CH

group using systolic BP (SBP), clinic SBP (CSBP) 140 mm Hg, and morning HSBP 135 mm Hg as cutoff values. In our previous report using data from the HONEST study, we showed how the distribution of patients changed across the 4 groups.[16] In the present study, we performed a more detailed analysis by comparing baseline patient characteristics between the 4 groups. It will be possible to offer more meaningful suggestions on the whole concept of antihypertensive treatment in clinical care settings when the final results are revealed, knowing how CBP and HBP changed, and how hypertension status such as MH and WCH changed after 16-week olmesartan-based treatment.

METHODS

Study Protocol

This study was a large-scale prospective observational study with a 2-year follow-up by September 30, 2012. The aims and protocol have already been previously reported.[15] The study protocol was approved by the In-House Ethical Committee of Daiichi Sankyo Co, Ltd, and by the Ministry of Health, Labour and Welfare of Japan (MHLW) before study commencement. The study was carried out in medical institutions registered in compliance with Good Post-marketing Study Practice in Japan and internal regulations for clinical studies at each institution. The study is registered at http://www.umin.ac.jp/ctr/index.htm under the unique trial number UMIN000002567.

In brief, participants were olmesartan-naive with essential hypertension and no history of recent acute cardiovascular events (eg, myocardial infarction, stroke, and cardiovascular interventions) and with no planned cardiovascular interventions. Diagnosis of essential hypertension was made by attending physicians without specific criteria regarding BP cutoff values or patients' use of antihypertensive treatment. Written informed consent was obtained from them at the start of the study. Olmesartan (generally 10 mg/d or 20 mg/d) was administered at each participating physician's discretion. The selection of target CBPs and HBPs was left to the discretion of individual physicians. No restriction was placed on prior antihypertensive drug treatment, with the exception of prior use of olmesartan, or on the use of combination antihypertensive drug treatment during the study. The data included patient characteristics (eg, disease history and complications), CBP and HBP, clinic pulse rate, home pulse rate, clinical laboratory test values, and the incidence of cardiovascular events and adverse events during the study period. The present analysis used data from the HONEST study for patients who received olmesartan in the first 16 weeks.

HBP Measurements

Patients who already owned electronic arm-cuff devices based on the cuff-oscillometric method were registered. All such devices available in Japan have been validated

and approved by MHLW. At the time of obtaining informed consent, patients were asked to measure HBP twice in the morning and twice at bedtime according to the Japanese Society of Hypertension,[17] namely, within 1 hour of waking in the morning (after urinating, before their dose of antihypertensive agents, before breakfast, and after 1 to 2 minutes of rest in a sitting position) and at bedtime (after 1 to 2 minutes of rest in a sitting position). We analyzed only the first measurement of morning HBP at baseline and at 16 weeks. Only the first measurement was used, because the present analysis was based on the previous report of the HONEST study,[16] in which we used data for the first measurement of morning HBP to compare our results with those of the Azelnidipine Treatment for Hypertension Open-Label Monitoring in the Early Morning (At-HOME) study.[18] Morning HBP at each measurement point was defined as an averaged value over 2 days.

Definition of Hypertension Status by CSBP and Morning HSBP

The BP control status of patients was defined based on European Society of Hypertension guidelines for BP monitoring at home, which state that HBP monitoring can provide information about BP control outside the office, thereby allowing the identification of treated hypertensive patients with WCH and MH.[19]

In this report, we defined hypertension status as CSBP and morning HSBP at the first measurement using SBPs (CSBP <140 mm Hg, morning HSBP <135 mm Hg) as follows: MH, CSBP <140 mm Hg and morning HSBP ≥135 mm Hg; WCH, CSBP ≥140 mm Hg and morning HSBP <135 mm Hg; PCH, CSBP ≥140 mm Hg and morning HSBP ≥135 mm Hg; and CH, CSBP <140 mm Hg and morning HSBP <135 mm Hg (Figure 1).

We divided the analysis population into 4 groups by hypertension status at baseline as follows: MH group, WCH group, PCH group, and CH group. At baseline, each defined hypertension group included patients both receiving and not receiving treatment. We reported the same criteria for the diagnosis and classification of patients, including treated patients, in a previous article regarding the protocol of this study.[15]

Statistical Analysis

The analysis population was defined as eligible patients and excluded patients with poor compliance with olmesartan, which was reported by the study investigator as "almost never taken the study drug" and/or with missing data of BP at baseline (Figure 2).

Data are expressed as mean±standard deviation or percentage. For each comparison of baseline patient characteristics of the 4 groups, categorical data were analyzed by chi-square test and quantitative data by *t* test. The level of statistical significance was $P=.05/6=.0083$ after Bonferroni correction for multiple comparisons. Paired *t* tests and analyses adjusting for the number of add-on or discontinued antihypertensive medications and baseline characteristics were
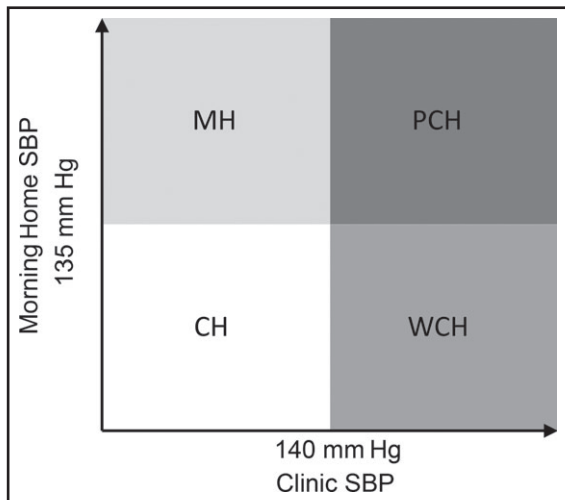
FIGURE 1. Definitions of hypertension status. CH indicates well-controlled hypertension; MH, masked hypertension; PCH, poorly controlled hypertension; SBP, systolic blood pressure; WCH, white-coat hypertension.

performed on data for BP and pulse rate changes. For all analyses, $P<.05$ was considered significant, and a two-sided test was used. SAS System release 9.2 software (SAS Institute, Cary, NC) was used for all statistical analyses.

RESULTS

Study Profile

The reasons for excluding data from the analysis are shown in Figure 2. The dataset in this analysis was used as of April 2012. Data for the first 16 weeks were collected from 22,162 patients. Data from 21,340 patients were used for the analyses.

Patients

The baseline characteristics of the 4 groups are presented in Table I. The proportions of patients in the MH, WCH, PCH, and CH groups were 11.7%, 5.5%, 74.8%, and 8.0%, respectively, at the start of the study. Most patients were in the PCH group, followed by the MH, CH, and WCH groups. The percentages of patients who had previously been treated with antihypertensive agents in the MH,WCH, PCH, and CH groups were 72.3%, 72.9%, 42.0%, and 79.9%, respectively.

We compared each group individually with the Bonferroni correction (data not shown). In the PCH group, the duration of hypertension was shorter and the percentage of history of cerebrovascular or cardiovascular disease, complications, and previously used antihypertensive agents were lower than in other groups (all $P<.0001$). In the MH group, the mean age was higher than in other groups ($P<.001$), and the proportion of regular alcohol drinkers was higher in the CH group
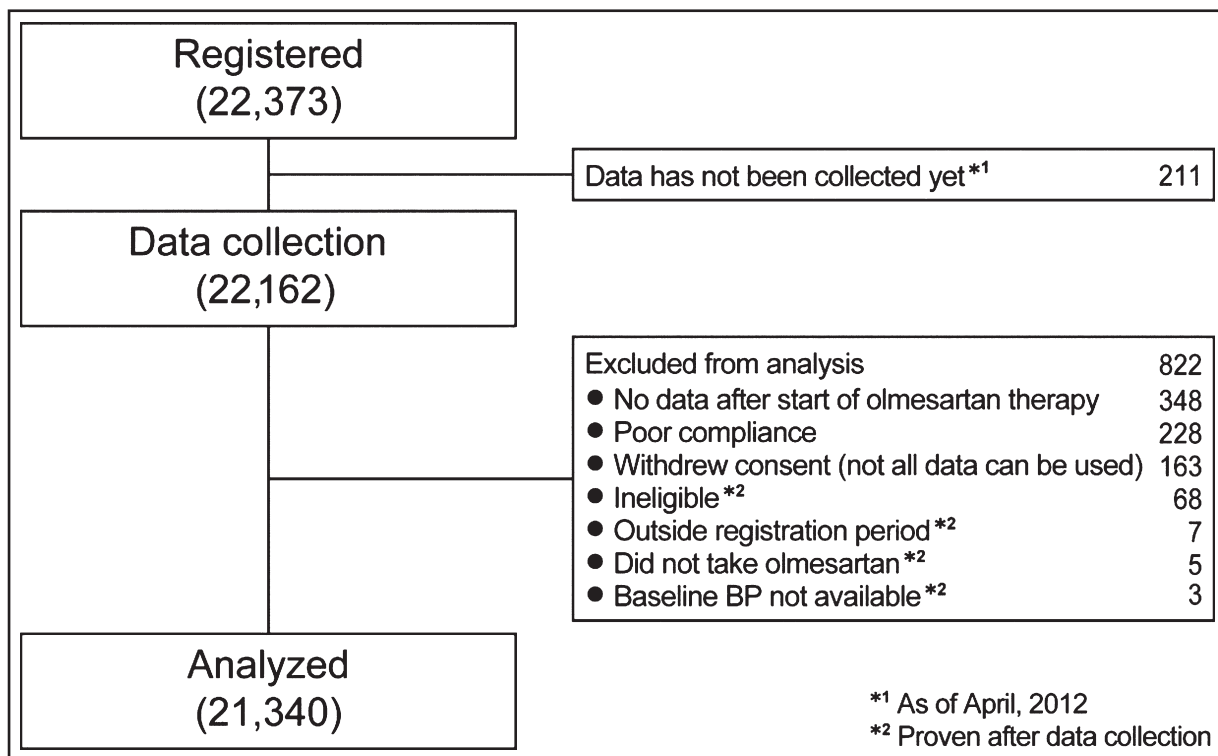
FIGURE 2. Profile of the Home Blood Pressure Measurement With Olmesartan Naive Patients to Establish Standard Target Blood Pressure (HONEST) study. BP indicates blood pressure.

TABLE I. Baseline Characteristics of Patients

	Group at Baseline[a]			
	MH (n=2502)	WCH (n=1177)	PCH (n=15,955)	CH (n=1706)
Women	1186 (47.4)	656 (55.7)	8140 (51.0)	802 (47.0)
Age, y	66.6±11.4	65.2±11.5	64.5±11.9	65.3±11.8
Body mass index, kg/m²	24.26±3.56	24.15±3.97	24.37±3.72	23.93±3.48
Duration of hypertension, y[b]	5.72±4.29	6.13±4.27	4.65±4.43	6.57±4.09
Disease history				
Cerebral or cardiovascular disease	401 (16.0)	155 (13.2)	1367 (8.6)	318 (18.6)
Cerebrovascular disease	249 (10.0)	104 (8.8)	863 (5.4)	199 (11.7)
Cardiovascular disease	185 (7.4)	66 (5.6)	574 (3.6)	141 (8.3)
Complications				
Dyslipidemia	1222 (48.8)	629 (53.4)	6751 (42.3)	882 (51.7)
Diabetes mellitus	600 (24.0)	314 (26.7)	3050 (19.1)	400 (23.4)
Chronic kidney disease	565 (22.6)	287 (24.4)	2971 (18.6)	460 (27.0)
Heart disease	338 (13.5)	122 (10.4)	1306 (8.2)	217 (12.7)
Hepatic disease	174 (7.0)	76 (6.5)	1047 (6.6)	111 (6.5)
Cerebrovascular disorder	20 (0.8)	11 (0.9)	61 (0.4)	13 (0.8)
Modifiable lifestyle factors				
Regularly drinks alcohol	402 (16.1)	159 (13.5)	2657 (16.7)	221 (13.0)
Current smoker	271 (10.8)	98 (8.3)	2098 (13.1)	151 (8.9)
Previously used antihypertensive agents				
≥1	1808 (72.3)	858 (72.9)	6702 (42.0)	1363 (79.9)
Calcium channel blockers	1313 (52.5)	580 (49.3)	4899 (30.7)	897 (52.6)
Angiotensin II receptor blockers	859 (34.3)	455 (38.7)	2429 (15.2)	792 (46.4)
β-Blockers	240 (9.6)	107 (9.1)	812 (5.1)	177 (10.4)
Diuretics	255 (10.2)	113 (9.6)	630 (3.9)	232 (13.6)
Angiotensin-converting enzyme inhibitors	134 (5.4)	68 (5.8)	469 (2.9)	109 (6.4)
α-Blockers	93 (3.7)	36 (3.1)	253 (1.6)	72 (4.2)
Other	17 (0.7)	4 (0.3)	57 (0.4)	12 (0.7)

Abbreviations: CH, well-controlled hypertension; MH, masked hypertension; PCH, poorly controlled hypertension; WCH, white-coat hypertension.
[a]Values expressed as mean±standard deviation or number (percentage). [b]Recorded as 10 years for patients who had hypertension for ≥10 years.

(P=.0056). In the WCH group, the proportion of women was higher than in the other groups (all P<.005).

In addition, we classified by baseline hypertension status the 228 patients who were excluded from the analysis because of poor compliance. The distribution of hypertension status of these patients (MH, 13.6%; WCH, 6.1%; PCH, 72.4%; and CH, 7.9%) was similar to that of the patients included in the present analysis.

Administration Status of Antihypertensive Agents

Administration status of olmesartan is shown in Table II. At the start of olmesartan treatment, the average dosage of olmesartan (mg/d) and number of antihypertensive agents including olmesartan in the MH, WCH, PCH, and CH groups were 18.4±7.7 and 1.7±0.8, 18.1±7.2 and 1.6±0.8, 18.2±6.8 and 1.4±0.7, and 18.0±7.7 and 1.7±0.8, respectively. At 16 weeks, they were 19.1±8.7 and 1.8±0.9, 18.1±8.4 and 1.6±0.8, 19.0±8.1 and 1.5±0.7, and 17.5±8.5 and 1.7±0.9, respectively.

Changes in BP

Table III shows BP and pulse rate changes in all 4 groups of patients. At 16 weeks following the start of olmesartan administration vs baseline, morning HSBP in the MH group changed from 147.2±10.4 mm Hg to 134.7±13.7 mm Hg (P<.0001). CSBP in the WCH group changed from 152.6±11.9 mm Hg to 137.3±16.4 mm Hg (P<.0001). However, 16-week treatment with olmesartan had little effect on CSBP in the MH group and morning HSBP in the WCH group. There was a similar trend in diastolic BP (DBP) in the MH and WCH groups. At 16 weeks following the start of olmesartan treatment vs baseline in the PCH group, morning home SBP/DBP changed from 156.9±13.6/89.5±11.1 mm Hg to 136.4±13.5/79.4±9.9 mm Hg and clinic SBP/DBP changed from 160.4±15.2/90.3±12.4 mm Hg to 137.3±15.0/78.5±10.7 mm Hg (all P<.0001). At 16 weeks following the start of olmesartan treatment vs baseline in the CH group, morning home and clinic SBP/DBP had been well controlled. Similar results were obtained from further analyses including data adjusted for age, sex, dyslipidemia, diabetes, chronic kidney disease, history of cardiovascular disease, and changes in the number and dose of antihypertensive drugs (other than olmesartan) during the 16-week follow-up period.

TABLE II. Administration Status of Olmesartan

	Group at Baseline[a]			
	MH (n=2502)	WCH (n=1177)	PCH (n=15,955)	CH (n=1706)
At start of olmesartan treatment (0 week)				
Dose of olmesartan, mean±SD, mg/d	18.4±7.7	18.1±7.2	18.2±6.8	18.0±7.7
0 (discontinuation)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
>0–≤5 (mainly 5)	68 (2.7)	31 (2.6)	342 (2.1)	61 (3.6)
>5–≤10 (mainly 10)	656 (26.2)	315 (26.8)	3993 (25.0)	486 (28.5)
>10–≤20 (mainly 20)	1592 (63.6)	758 (64.4)	10,802 (67.7)	1040 (61.0)
>20–≤40 (mainly 40)	186 (7.4)	73 (6.2)	818 (5.1)	119 (7.0)
Antihypertensive drugs (including olmesartan), No.	1.7±0.8	1.6±0.8	1.4±0.7	1.7±0.8
At 16 weeks				
Dose of olmesartan, mean±SD, mg/d	19.1±8.7	18.1±8.4	19.0±8.1	17.5±8.5
0 (discontinuation)	57 (2.3)	32 (2.7)	368 (2.3)	55 (3.2)
>0–≤5 (mainly 5)	53 (2.1)	37 (3.1)	324 (2.0)	75 (4.4)
>5–≤10 (mainly 10)	555 (22.2)	288 (24.5)	3157 (19.8)	455 (26.7)
>10–≤20 (mainly 20)	1569 (62.7)	723 (61.4)	10,698 (67.1)	991 (58.1)
>20–≤40 (mainly 40)	268 (10.7)	97 (8.2)	1408 (8.8)	130 (7.6)
Antihypertensive drugs (including olmesartan), No.	1.8±0.9	1.6±0.8	1.5±0.7	1.7±0.9

Abbreviations: CH, well-controlled hypertension; MH, masked hypertension; PCH, poorly controlled hypertension; SD, standard deviation; WCH, white-coat hypertension.
[a]Values are expressed as number (percentage) unless otherwise specified.

Changes in Hypertension Status

At 16 weeks, 45.7% of the MH group, 44.9% of the WCH group, and 34.4% of the PCH group were classified as having CH; however, 33.6% of the MH group, 27.2% of the WCH group, and 29.1% of the PCH group remained in their original groups (Figure 3a–c). Conversely, 66.9% of the CH group remained in its original group at 16 weeks (Figure 3d).

DISCUSSION

The main finding of this study was that olmesartan-based treatment was effective in decreasing high morning HBP in patients with MH and PCH and high CBP in patients with WCH and PCH while normal CBP in patients with MH and CH and normal MHBP in patients with WCH and CH did not decrease excessively in "real-world" clinical practice.

Some papers[12,20] reported the reproducibility of the classification of hypertension status, MH, WCH, CH, and PCH after follow-up, but little is known concerning the reproducibility of the classification of hypertension status during antihypertensive treatment. This study showed the classification of hypertension status of patients with hypertension changed by olmesartan-based antihypertensive treatment.

Baseline Characteristics of Patients

In this study, approximately 8% of all registered patients were those with CH. The reasons they were prescribed add-on and/or switched to olmesartan were to receive additional clinical benefits, such as lowered BP, increased safety, and reduced cardiovascular risk. Overall, the CH group had proportionally more high-risk patients receiving proactive antihypertensive treatment. In contrast, the PCH group tended to be at relatively low risk. A large proportion of patients had PCH at baseline, probably because their physicians considered olmesartan-based treatment appropriate for patients with PCH or otherwise needing further antihypertensive treatment. In the MH group, the mean age was significantly higher than in other groups, although the differences were slight (1.3 to 2.1 years). The proportion of regular alcohol drinkers was higher in the MH group compared with the CH group, which is consistent with previous reports showing that the proportion of regular alcohol drinkers is high in patients with MH defined by morning HBP.[21,22] The proportion of women was higher in the WCH group than in other groups, which was also consistent with previous reports.[22,23]

Reclassification of Hypertension Status With Olmesartan-Based Treatment

Although about 30% of patients in the MH, WCH, and PCH groups remained in the same groups after 16 weeks of olmesartan-based treatment, about 45% in the MH and WCH groups and about 35% in the PCH group achieved CH. On the other hand, one third of patients in the CH group did not remain in the same group after 16 weeks. It is speculated that patients in the CH group included those switched from high-dose antihypertensive treatment to standard-dose olmesartan treatment or from a combination drug to olmesartan monotherapy because of adverse reactions. However, BP values in this group varied, and two thirds of patients remained well-controlled, with a mean SBP of 127 mm

TABLE III. BP and Pulse Rate Before and After 16 Weeks of Olmesartan Treatment

	Baseline[a]	16 Weeks[a]	⊿	P Value[b]	Adjusted⊿	P Value[c]
Home (morning)						
MH group						
Systolic BP, mm Hg	147.2±10.4	134.7±13.7	−12.5	<.0001	−13.9	<.0001
Diastolic BP, mm Hg	84.7±10.4	78.3±10.1	−6.3	<.0001	−5.1	<.0001
Pulse rate, beats per min	69.3±10.0	68.0±10.0	−1.5	<.0001	−1.9	.0782
WCH group						
Systolic BP, mm Hg	127.5±5.9	128.6±12.8	1.0	.0092	−1.6	.4783
Diastolic BP, mm Hg	76.5±9.2	76.0±9.9	−0.5	.0922	−1.5	.3355
Pulse rate, beats per min	68.0±9.5	67.5±9.5	−0.4	.1415	−2.0	.2852
PCH group						
Systolic BP, mm Hg	156.9±13.6	136.4±13.5	−20.3	<.0001	−16.0	<.0001
Diastolic BP, mm Hg	89.5±11.1	79.4±9.9	−10.0	<.0001	−7.2	<.0001
Pulse rate, beats per min	71.4±9.9	69.1±9.4	−2.3	<.0001	−1.2	.0550
CH group						
Systolic BP, mm Hg	125.0±7.4	127.0±11.9	2.0	<.0001	3.1	.0242
Diastolic BP, mm Hg	75.5±9.3	75.7±9.3	0.3	.1394	1.2	.2182
Pulse rate, beats per min	69.0±9.7	68.1±9.7	−1.0	.0002	−0.6	.6003
Clinic						
MH group						
Systolic BP, mm Hg	130.1±7.8	129.1±14.0	−1.0	.0007	−0.8	.5166
Diastolic BP, mm Hg	76.6±10.8	73.9±10.7	−2.6	<.0001	−2.1	.0265
Pulse rate, beats per min	72.4±10.9	71.6±10.4	−1.0	<.0001	0.4	.7140
WCH group						
Systolic BP, mm Hg	152.6±11.9	137.3±16.4	−15.2	<.0001	−14.3	<.0001
Diastolic BP, mm Hg	85.0±11.5	77.8±11.2	−7.0	<.0001	−7.6	<.0001
Pulse rate, beats per min	75.0±12.5	74.2±11.9	−0.8	.0366	2.8	.2579
PCH group						
Systolic BP, mm Hg	160.4±15.2	137.3±15.0	−23.1	<.0001	−17.6	<.0001
Diastolic BP, mm Hg	90.3±12.4	78.5±10.7	−11.8	<.0001	−9.1	<.0001
Pulse rate, beats per min	74.4±11.1	72.6±10.4	−1.9	<.0001	−0.4	.5351
CH group						
Systolic BP, mm Hg	125.1±9.6	126.9±13.9	1.8	<.0001	2.7	.0815
Diastolic BP, mm Hg	74.3±10.2	74.2±10.4	−0.2	.5576	1.0	.3433
Pulse rate, beats per min	72.6±11.3	72.4±10.8	−0.2	.5135	−1.7	.2547

Abbreviations: BP, blood pressure; CH, well-controlled hypertension; MH, masked hypertension; PCH, poorly controlled hypertension; WCH, white-coat hypertension. [a]Values are expressed as mean±standard deviation or number (percentage). [b]Data analyzed by paired *t* test. [c]Data adjusted for age, sex, dyslipidemia, diabetes mellitus, chronic kidney disease, history of cardiovascular disease, and changes in the number and dose of antihypertensive drugs (other than olmesartan) during the 16-week follow-up period. ⊿: Change in values after 16 weeks from baseline.

Hg. Moreover, for patients with concomitant diabetes, the proportion who achieved CBP <130/80 mm Hg increased from 45% to 51% in the CH group (data not shown).

The results that the classification of hypertension status changed after antihypertensive treatment suggest the importance of both CBP and morning HBP-guided antihypertensive treatment.

Antihypertensive Effects of Olmesartan-Based Treatment

Olmesartan seems to have a favorable antihypertensive profile, since olmesartan-based treatment was effective in decreasing high morning HBP in patients with MH and PCH and high CBP in patients with WCH and PCH, while normal CBP in patients with MH and CH and normal MHBP in patients with WCH and CH did not decrease excessively. Generally speaking, the higher the BP, the more antihypertensive drugs reduce it. Conversely, the lower the BP, the less they reduce it. However, clinicians often have difficulty with antihypertensive treatment for patients with MH or WCH as there are few reports concerning the effects of antihypertensive drugs in patients who had one high BP value and the other normal. Therefore, these results are considered to be useful for treatment in patients with MH or WCH in usual clinical care settings.

MH has a cardiovascular risk nearly equal to that of PCH.[6,7] In addition, WCH can be a risk factor for stroke in the long term.[10] Furthermore, patients with MH[12,24] and WCH[12,25] are more likely than normotensive individuals to develop sustained hypertension. In this way, BP control in patients with MH and WCH is clinically important, and olmesartan-based treatment is
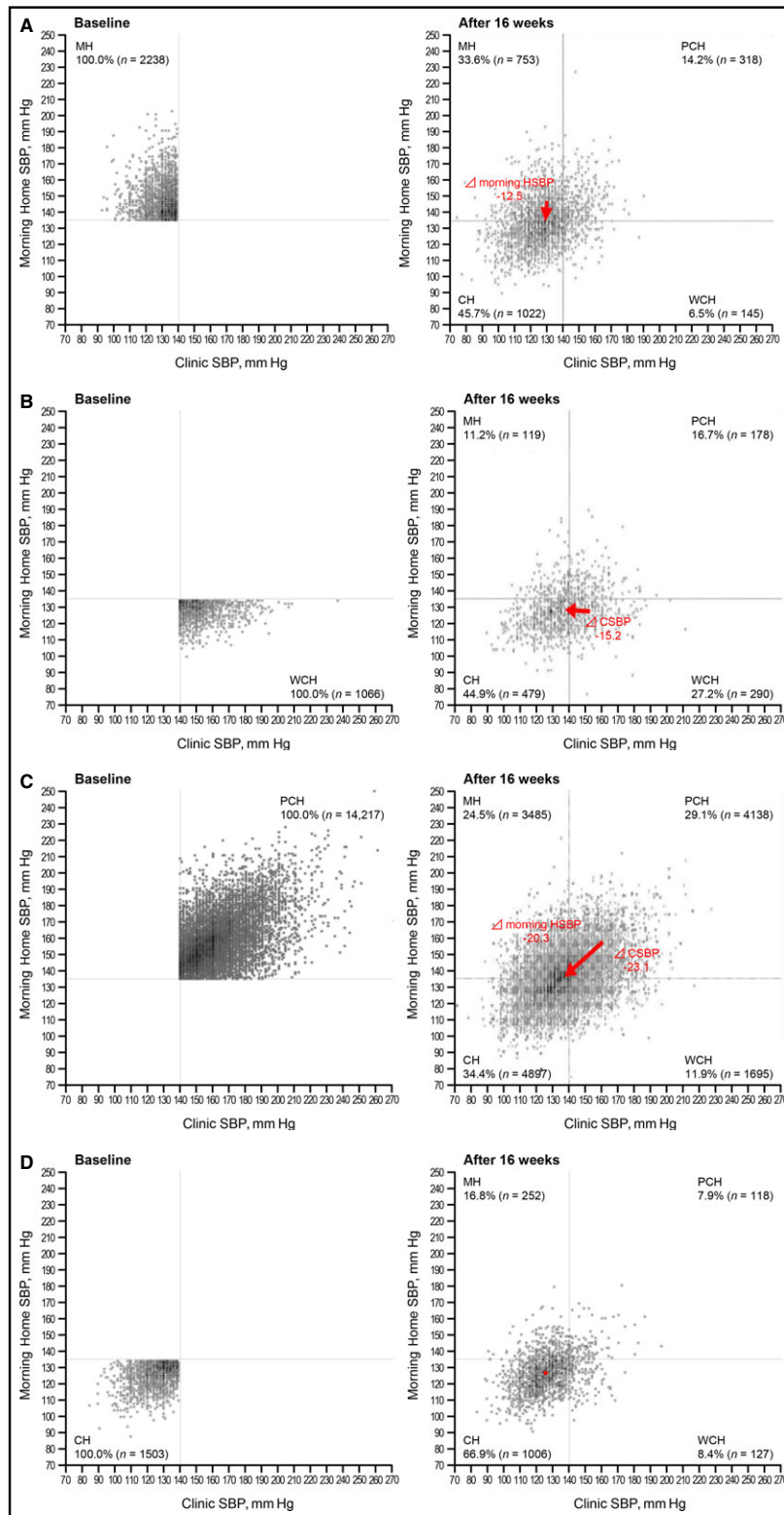
FIGURE 3. Changes in morning home systolic blood pressure (HSBP) and clinic systolic blood pressure (CSBP) in patients with masked hypertension (MH) (a), white-coat hypertension (WCH) (b), poorly controlled hypertension (PCH) (c), and well-controlled hypertension (CH) (d) after olmesartan-based treatment. The arrow in Figures 2a–c show the change in average systolic blood pressure (SBP) from baseline to 16 weeks. In Figure 2d, the dot is used, since the change in average SBP from baseline to 16 weeks is too small to be shown by an arrow. ΔMorning HSBP indicates change in morning HSBP; ΔCSBP, change in CSBP.

considered to contribute to reducing cardiovascular risk in patients with MH and WCH.

Saito and colleagues[26] have reported that olmesartan does not cause excessive reduction of DBP in elderly patients with isolated systolic hypertension. This indicates that olmesartan, which is effective in decreasing high BP but prevents controlled BP from decreasing excessively in hypertensive patients, has a favorable profile.

Olmesartan-based treatment decreased both high CSBP and morning HSBP in the PCH group to the same degree. These results suggest that olmesartan-based treatment has a sufficient sustained 24-hour BP-lowering effect and that it may be suitable for the treatment of a wide range of hypertensive patients.

Study Limitations

There are some limitations to this investigation. First, the HONEST study was designed to assess the treatment effects in the "real world" of clinical practice, and, consequently, patients were not blinded to treatment and there was no control group. Thus, the possibility of regression toward the mean cannot be excluded. Furthermore, the effects of olmesartan shown in this study may also be achieved by other antihypertensive drugs. Therefore, further randomized studies are needed to verify our findings. However, the results of the present study showing a sustained 24-hour BP-lowering effect of olmesartan were similar to those of previous double-blind clinical trials.[27–29] Second, the definitions of BP control status we used for both treated and untreated hypertensive patients in the present study are inconsistent with the stricter definitions used in previous studies involving general populations. Finally, because the present study lacks data for daytime BP and nocturnal BP, there was the potential for missing stress-induced hypertension and nocturnal hypertension. This may lead to underestimation of the prevalence of MH and overestimation of the prevalence of WCH. However, regarding diagnostic accuracy, home BP is deemed to be a reliable alternative to ambulatory BP in the diagnosis of hypertension and the detection of WCH and MH in both untreated and treated patients.[30] Nevertheless, the graphical analyses used in this study are a simple and useful method for both physicians and patients when evaluating BP control in daily clinical practice because the current BP status and changes in BP status are easily visualized.

CONCLUSIONS

The results of the HONEST study provide new findings relevant to the effectiveness of olmesartan-based treatment in patients with MH, WCH, PCH, and CH in the "real world" by guided CSBP and morning HSBP.

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