Ambulatory Blood Pressure in ONTARGET

Ambulatory Blood Pressure Values in the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET)

Giuseppe Mancia, Gianfranco Parati, Grzegorz Bilo, Peggy Gao, Robert Fagard, Josep Redon, Istvan Czuriga, Martin Polák, José M. Ribeiro, Ramiro Sanchez, Bruno Trimarco, Paolo Verdecchia, Walter van Mieghem, Koon Teo, Peter Sleight, Salim Yusuf

Abstract—In the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial, telmisartan (T; 80 mg daily) and ramipril (R; 10 mg daily) caused similar clinic blood pressure (BP) reductions, with a similar incidence of cardiovascular and renal events. The R+T combination lowered clinic BP somewhat more with no further cardiovascular or renal protection. The aim of this substudy was to see whether these clinic BP changes reflected the changes of 24-hour BP, a BP with a better prognostic value. In 422 patients in whom 24-hour BP monitoring was performed either before or after 6 to 24 months of treatment, demographic and clinical characteristics were similar in the 3 treated groups. Twenty-four-hour systolic BP was similarly reduced by R (−2.0 mmHg) and T (−2.1 mmHg), whereas the reduction was more than twice as large in the T+R group (−5.3 mmHg), which showed a lower on-treatment 24-hour BP also in additional patients (n=408) in whom ambulatory BP was performed only on-treatment. Twenty-four-hour systolic BP was ≤14 mmHg lower than clinic systolic BP at baseline, whereas during treatment the 2 values became progressively closer as clinic systolic BP was more tightly controlled and superimposable when clinic systolic BP was <120 mmHg. Similar results were obtained for diastolic BP. These findings provide evidence on the relationship of clinic and ambulatory BP target drug treatment. They also show that in the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial, failure of the R+T combination to enhance cardiovascular and renal protection was not because of inability to more effectively control daily life BP.

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Key Words: ambulatory blood pressure ■ antihypertensive treatment ■ high cardiovascular risk ■ angiotensin-converting enzyme inhibitors ■ angiotensin receptor blockers

The Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) has shown that in patients at high cardiovascular (CV) risk a treatment regimen based on telmisartan or ramipril reduced to a similar degree clinic blood pressure (BP) and showed no significant difference in the incidence of CV morbid or fatal events. Clinic BP was reduced to a somewhat greater degree in patients treated with a combination of the 2 drugs (1.5–2.4 mmHg systolic BP [SBP] and 0.8–1.4 mmHg diastolic BP [DBP]), without, however, any significant difference in CV outcome. Because ramipril had been shown previously to reduce outcomes in high CV risk individuals; this led to the conclusion that telmisartan and ramipril have a similar protective effect, which is not enhanced by double blockade of the renin-angiotensin system, despite the potentially greater protection associated with a greater BP-lowering effect.

Evidence is available that BP reductions induced by antihypertensive treatment cannot be precisely quantified if BP is measured in the clinic environment because clinic BP is affected to a variable degree by a transient increase known as the white coat effect. Furthermore, clinic BP values are poorly reproducible, and their treatment-induced changes reflect to only a modest degree the concomitant changes in daily life BP, that is, a more reproducible and prognostically important BP, which relates more steeply to CV morbidity and mortality.

The ONTARGET included a prespecified substudy focusing on ambulatory BP (ABP) to determine whether and to what extent treatment-induced changes in clinic BP correspond to daily life ABP. This article reports the results.

Methods

Patients and Monitoring Procedures

The protocol of the ONTARGET has been described in detail previously. Briefly, men and women aged ≥55 years without symptomatic heart failure at entry and with a history of coronary...
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**Table 1. Demographic, Clinical, and Laboratory Characteristics of Patients Who Had an Ambulatory BP Monitoring Either at Baseline and Between 6 and 24 Months After Randomization to Treatment**

| Demographic/Clinical Variables | ONTARGET, ABPM (n=25,498) | Overall, ABPM (n=422) | Telmisartan, ABPM (n=139) | Ramipril, ABPM (n=142) | Combination, ABPM (n=141) | Overall ABPM (n=141) | P Value
<table>
<thead>
<tr>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, %</td>
<td>26.7</td>
<td>24.6</td>
<td>24.5</td>
<td>28.2</td>
<td>21.3</td>
<td>21.3</td>
<td>0.404</td>
</tr>
<tr>
<td>Age, y</td>
<td>66.4 (7.2)*</td>
<td>65.6 (6.9)</td>
<td>66.1 (7.2)</td>
<td>66.2 (6.7)</td>
<td>64.6 (6.6)</td>
<td>0.091</td>
<td></td>
</tr>
<tr>
<td>White, %</td>
<td>73.0</td>
<td>87.7</td>
<td>87.1</td>
<td>88.7</td>
<td>87.2</td>
<td>0.895</td>
<td></td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>68.7*</td>
<td>57.1</td>
<td>53.2</td>
<td>62.7</td>
<td>55.3</td>
<td>0.243</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>37.5*</td>
<td>30.1</td>
<td>27.3</td>
<td>26.8</td>
<td>36.2</td>
<td>0.155</td>
<td></td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>12.6</td>
<td>10.7</td>
<td>9.4</td>
<td>12.0</td>
<td>10.6</td>
<td>0.776</td>
<td></td>
</tr>
<tr>
<td>Angina, %</td>
<td>44.9</td>
<td>44.5</td>
<td>41.7</td>
<td>48.6</td>
<td>43.3</td>
<td>0.477</td>
<td></td>
</tr>
<tr>
<td>CAD, %</td>
<td>74.6*</td>
<td>68.7</td>
<td>66.9</td>
<td>72.5</td>
<td>66.7</td>
<td>0.484</td>
<td></td>
</tr>
<tr>
<td>PAD, %</td>
<td>13.5</td>
<td>15.6</td>
<td>15.8</td>
<td>14.8</td>
<td>16.3</td>
<td>0.937</td>
<td></td>
</tr>
<tr>
<td>Stroke/TIA, %</td>
<td>20.9</td>
<td>18.0</td>
<td>18.7</td>
<td>18.3</td>
<td>17.0</td>
<td>0.929</td>
<td></td>
</tr>
<tr>
<td>CCBG or PTCA, %</td>
<td>46.1</td>
<td>45.7</td>
<td>47.5</td>
<td>47.2</td>
<td>42.6</td>
<td>0.648</td>
<td></td>
</tr>
<tr>
<td>ß-Blockers, %</td>
<td>56.9</td>
<td>54.5</td>
<td>47.5</td>
<td>57.0</td>
<td>58.9</td>
<td>0.122</td>
<td></td>
</tr>
<tr>
<td>Calcium antagonists, %</td>
<td>33.1</td>
<td>37.0</td>
<td>38.8</td>
<td>32.4</td>
<td>39.7</td>
<td>0.378</td>
<td></td>
</tr>
<tr>
<td>Diuretics, %</td>
<td>28.0</td>
<td>28.0</td>
<td>21.6</td>
<td>31.7</td>
<td>30.5</td>
<td>0.120</td>
<td></td>
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<tr>
<td>Angiotensin II antagonists, %</td>
<td>8.6</td>
<td>9.2</td>
<td>8.6</td>
<td>9.9</td>
<td>9.3</td>
<td>0.939</td>
<td></td>
</tr>
<tr>
<td>Statins, %</td>
<td>61.6*</td>
<td>48.3</td>
<td>38.8</td>
<td>49.3</td>
<td>56.7</td>
<td>0.011</td>
<td></td>
</tr>
<tr>
<td>ASA, %</td>
<td>75.7*</td>
<td>67.3</td>
<td>64.0</td>
<td>72.5</td>
<td>65.2</td>
<td>0.257</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors, %</td>
<td>57.6</td>
<td>60.2</td>
<td>53.2</td>
<td>59.9</td>
<td>67.4</td>
<td>0.054</td>
<td></td>
</tr>
<tr>
<td>Ankle-arm BP ratio</td>
<td>1.1 (0.2)</td>
<td>1.1 (0.2)</td>
<td>1.1 (0.2)</td>
<td>1.1 (0.2)</td>
<td>1.1 (0.1)</td>
<td>0.873</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.1 (4.5)</td>
<td>28.1 (3.8)</td>
<td>28.0 (3.9)</td>
<td>28.4 (3.9)</td>
<td>28.1 (3.5)</td>
<td>0.646</td>
<td></td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.94 (0.08)</td>
<td>0.95 (0.08)</td>
<td>0.95 (0.08)</td>
<td>0.94 (0.08)</td>
<td>0.94 (0.07)</td>
<td>0.317</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine, mmol/L</td>
<td>94.2 (24.3)</td>
<td>93.7 (22.7)</td>
<td>90.5 (19.8)</td>
<td>96.3 (24.7)</td>
<td>94.4 (23.2)</td>
<td>0.095</td>
<td></td>
</tr>
<tr>
<td>Serum glucose, mmol/L</td>
<td>6.7 (2.6)</td>
<td>6.4 (2.2)</td>
<td>6.3 (2.1)</td>
<td>6.4 (2.3)</td>
<td>6.5 (2.2)</td>
<td>0.653</td>
<td></td>
</tr>
<tr>
<td>Serum cholesterol, mmol/L</td>
<td>5.0 (1.1)</td>
<td>5.1 (0.9)</td>
<td>5.2 (1.0)</td>
<td>5.1 (1.0)</td>
<td>5.0 (0.9)</td>
<td>0.119</td>
<td></td>
</tr>
</tbody>
</table>

ONTARGET indicates Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial; ABPM, ambulatory blood pressure monitoring; CAD, coronary artery disease; PAD, peripheral artery disease; TIA, transient ischemic attack; CCBG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; ASA, antiplatelet drugs; ACE, angiotensin-converting enzyme. Data are shown as % or mean±SD (in parenthesis). Drugs refer to use before the run-in period. Baseline characteristics of all ONTARGET patients (except the 422 involved in the substudy) are also shown for comparison.

*P<0.03 from overall ambulatory BP group.
and DBP smoothness indices,22,23 which were obtained by the ratio between the mean and the SD of the hourly BP changes induced by treatment. This provided a normalized measure of the homogeneity of BP reduction throughout the 24 hours, which has been shown to have a normal distribution, a high reproducibility, and an independent relationship with left ventricular mass and carotid intima-media thickness.22,23 ABP values were compared with clinic BP values (mean of 2 measurements in the sitting position 3 months apart) obtained by a semiautomatic device (OMRON, model HEM-757)19 at the visit when ABP monitoring was started. Between-group comparisons were made by unpaired (different treatments) or paired (treatment versus pretreatment) t tests. P values for the BP changes induced by treatment were calculated after adjustment for baseline BP. The t tests were 2 sided and the Tukey method was used for multiple comparisons. Data from the different groups were pooled to calculate clinic-ABP differences at baseline and during treatment according to the target clinic SBP values recommended by guidelines or used in trials on high CV risk patients.24,25 Pooled data were also used to calculate the correlations between clinic BP and ABP or daytime and nighttime BP values before and during treatment. A P<0.05 was taken as the level of statistical significance. Data are shown as mean+SD or 95% CIs.

Results

BP Changes With Treatment

ABP monitoring was performed in 422 patients either at baseline or after 6 or 24 months of treatment. Table 1 shows that demographic and clinical characteristics at baseline were comparable in the 3 treated groups. This was also the case for baseline clinic and 24-hour SBP and DBP, which were much lower than clinic SBP and DBP. Additionally, SBP and DBP values were much less during the night when compared with daytime (Figure 1). This was the case also for heart rate whose 24 hour values were similar to clinic values with no between-group differences. As shown in Figure 2, in these 422 patients treatment, significantly reduced 24-hour SBP and DBP from pretreatment values. The reduction was similar in the telmisartan and ramipril groups but significantly and markedly greater in the group under combination treatment, which also showed SBP and DBP smoothness index values that were almost twice as large as those seen in the monotherapy group (Figure 3). In all 3 groups, BP reduction induced by treatment was greater for clinic BP than for ABP, for the day than for the night (during which the BP reduction was small and often not significant) and for SBP than for DBP.

Absolute On-Treatment SBP and DBP

A total of 830 patients had 1 ABP monitoring between 6 and 24 months after initiation of treatment. As shown in Table 2, clinic SBP was similar, whereas ambulatory SBP was lower in the telmisartan than in the ramipril group, the mean difference achieving statistical significance for 24-hour (−3.1 mm Hg) and nighttime (−4.1 mm Hg) values. Compared with patients on monotherapy, clinic and ambulatory SBP were lower in the group under combination treatment (Table 2 and Figure 4) although the mean differences were statistically significant mainly versus patients on ramipril (24-hour, −4.4 mm Hg; daytime, −4.8 mm Hg; nighttime, −3.8 mm Hg). On-treatment DBP displayed much smaller or no between-group differences, this being the case also for on-treatment heart rate (data not shown).

Correlations and Differences Between Baseline and On-Treatment Clinic and ABP

In the 422 patients in whom baseline and on-treatment values were available, correlations between clinic and 24-hour BP values were significant but not close either for SBP (correlation coefficient 0.39 and 0.58 at baseline and during treatment, respectively; P<0.0001 for both) or for DBP (correlation coefficient 0.51 and 0.49; P<0.0001 for both). Treatment-induced changes of clinic and 24-hour SBP and DBP were even less closely related (0.33 and 0.24, respectively; P<0.0001 for both). Figure 5 shows that in all available patients the marked differences between clinic and 24-hour or daytime SBP and DBP seen at baseline became progressively smaller in patients achieving a progressively lower target clinic SBP with treatment and that the 2 sets of values were substantially similar in the group in which clinic SBP was reduced to <120 mm Hg.

![Figure 1](http://hyper.ahajournals.org/)

**Figure 1.** Baseline clinic and ambulatory systolic blood pressure (SBP) and diastolic blood pressure (DBP) in 422 patients treated with ramipril (R), telmisartan (T), or their combination (R+T) in whom a 24-hour ambulatory BP was performed either before or during treatment (see Methods). Data are shown as mean±SD values. Baseline heart rate (HR) values are reported at the bottom of each panel. No between-group difference was statistically significant.
Discussion

Our study shows that in the ONTARGET patients of the ABP substudy, telmisartan caused a similar or only slightly greater reduction of ABP than ramipril. It also shows that the reduction was much more pronounced in patients under combination with the 2 drugs in whom the BP-lowering effect was at least twice as large as that associated with one or the other monotherapy throughout the day and night. This rules out the possibility that in ONTARGET the ramipril-telmisartan combination did not lead to a greater CV or renal protection because of a limited effect on daily life BP, a variable of important prognostic significance. On the contrary, the combination lowered daily life BP even more clearly than could be inferred from clinic BP measurements, with also a greater smoothness index and thus a greater between-hour consistency of the antihypertensive effect and a lower BP variability, a parameter that has been shown to have independent prognostic significance.27–30 This implies that other explanations should be sought for the failure of the combination to improve CV or renal outcome compared with the combination components in monotherapy.

We can speculate that at the doses used in ONTARGET, double blockade of the renin-angiotensin system had direct harmful effects that neutralized the protection associated with the greater ABP reduction. It is also possible, however, that because initial ABP values were largely within the normal range24,31 their relationship with events was flatter than at higher values, with thus no substantial effect of greater or smaller treatment-induced changes. We cannot exclude that larger ABP reductions from initially normal values had a detrimental effect, a J curve-like phenomenon32 that masked the greater ABP reduction. It is also possible, however, that double blockade of the renin-angiotensin system had direct harmful effects that neutralized the protection associated with the greater ABP reduction. We can speculate that at the doses used in ONTARGET, double blockade of the renin-angiotensin system had direct harmful effects that neutralized the protection associated with the greater ABP reduction.

An interesting additional finding of our study is that while in baseline conditions ABP values were markedly lower than the clinic ones, the difference was less during treatment and more so as clinic BP achieved a progressively lower target. Indeed, when the target was set at <130 mmHg (the value recommended by guidelines for high CV risk individuals such as those from ONTARGET),24 daytime ABP was <1 mmHg lower than clinic BP and day and 24-hour BP values were superimposable with clinic BP in patients in whom the clinic BP target was <120 mmHg, that is, the value aimed at in the more intensively treated high CV risk patients of the action to control cardiovascular risk in diabetes mellitus study.25 The reasons for this decreasing clinic-ABP difference from baseline to progressively more aggressive treatments are not explained by our study, although we can speculate that several factors (eg, regression dilution, waning of the white coat effect, and resistance to treatment of daily life BP) may be involved. The results, however, are relevant to the debated question of which ABP values should be recommended for treatment, an issue on which there is no direct evidence because no event-based trial has so far systematically measured ABP before and at various times during treatment.31 In this context, our study suggests that daytime or 24-hour BP targets for treatment may not be too different from the clinic ones, particularly when, as in patients at high CV risk, a tighter clinic BP control is pursued.

Figure 3. Smoothness index values in patients of Figure 1. SBP indicates systolic blood pressure; DBP, diastolic blood pressure; R, ramipril; T, telmisartan.
Several other results of our study are noteworthy. First, in the ONTARGET patients, the ambulatory SBP reductions induced by telmisartan, ramipril, and the combination of the 2 drugs were all greater than the 24-hour DBP reductions, which means that the BP-lowering effect includes a reduction of pulse pressure. Because in elderly patients like those of ONTARGET pulse pressure has prognostic significance, this can be regarded as a potentially favorable effect common to all treatments used. In line with the results of previous studies, daytime BP was reduced by treatment more than nighttime BP on which the effect was usually so small as to make differences from baseline values not statistically significant. This may have occurred because the drugs were given in the morning, which made their concentration in blood and tissues lower at night. It may also be explained, however, by the law of initial value, that is, irrespective of the treatment used, the magnitude of a BP reduction is directly related to the initial BP value, which is much lower during the night than during the day. Clinic BP and ABP values were significantly related to each other, but the correlation coefficients were low. This was even more the case for their treatment-induced changes, which confirms previous evidence that individual patient measurements made in the clinic environment do not provide an accurate assessment of daily life BP, including its modification by treatment. This represents an additional argument in favor of an extensive use of ABP in future trials of the beneficial effects of antihypertensive drugs.

Our study has strengths and limitations. An important strength is that BP data were carefully checked for quality, which led to the inclusion in the data analysis of only ABP with adequate data. An important limitation, on the other hand, is that, as in all previous ABP data collected in trials, ABP data were collected from nonrandomized patients who were a small fraction of the overall ONTARGET population. This raises the question of whether the present findings are representative of those of the ONTARGET as a whole. Although remaining unproven, we suggest that this may be the case, because most baseline demographic and clinical characteristics of the patients did not differ significantly from those reported in the main study (Table 1). Furthermore, in the overall ONTARGET patients, the clinic BP values at run-in (141.8/82.1 mm Hg) were not substantially different from those of the ABP monitoring patients. This was the case also for the BP reductions between 6 and 24 months of treatment which in all ONTARGET patients were on average 5.4/4.4, 4.4/3.3, and 7.8/4.9 mm Hg for the telmisartan, ramipril, or their combination groups, respectively.

Table 2. Clinic and Ambulatory Blood Pressure Mean Values and SDs (in Brackets) in the 3 Treatment Groups After 6 to 24 Months of Treatment (n=830)

<table>
<thead>
<tr>
<th></th>
<th>Telmisartan</th>
<th>Ramipril</th>
<th>Combination</th>
<th>Overall P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>275</td>
<td>284</td>
<td>271</td>
<td></td>
</tr>
<tr>
<td>Clinic SBP, mm Hg</td>
<td>135.5 (16.0)†</td>
<td>136.3 (16.6)‡</td>
<td>131.9 (16.7)*</td>
<td>0.005</td>
</tr>
<tr>
<td>Clinic DBP, mm Hg</td>
<td>77.1 (9.9)</td>
<td>78.4 (10.1)</td>
<td>76.6 (10.5)</td>
<td>0.080</td>
</tr>
<tr>
<td>24-h SBP, mm Hg</td>
<td>124.0 (14.8)</td>
<td>127.1 (14.9)*‡</td>
<td>122.7 (16.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>24-h DBP, mm Hg</td>
<td>70.8 (8.0)</td>
<td>71.9 (8.9)</td>
<td>70.6 (9.2)</td>
<td>0.162</td>
</tr>
<tr>
<td>Daytime SBP, mm Hg</td>
<td>126.0 (15.4)</td>
<td>128.5 (14.7)*‡</td>
<td>123.7 (16.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Daytime DBP, mm Hg</td>
<td>72.9 (8.7)</td>
<td>74.0 (9.2)</td>
<td>72.4 (9.6)</td>
<td>0.099</td>
</tr>
<tr>
<td>Nighttime SBP, mm Hg</td>
<td>117.6 (16.4)</td>
<td>121.7 (18.3)*†</td>
<td>117.9 (18.8)</td>
<td>0.011</td>
</tr>
<tr>
<td>Nighttime DBP, mm Hg</td>
<td>65.3 (8.7)</td>
<td>66.6 (10.3)</td>
<td>65.6 (10.4)</td>
<td>0.267</td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.
*P<0.05 vs telmisartan.
†P<0.05.
‡P<0.01 vs combination.

Figure 4. Hourly systolic blood pressure (SBP) and diastolic blood pressure (DBP) profiles in 830 patients under treatment with ramipril (R), telmisartan (T), or their combination (R+T) for 6 to 24 months. Data are shown as hourly mean values.
The ONTARGET ABP monitoring substudy shows that the telmisartan/ramipril combination induced a substantially greater ABP reduction compared with telmisartan or ramipril alone. This rules out the possibility that the combination did not protect patients more than the monotherapies because it failed to more effectively control a variable of important prognostic significance, such as daily life BP. Furthermore, our data confirm that, in individual patients, significant discrepancies exist between the information offered by clinic BP and ABP monitoring both at baseline and during treatment, which emphasizes the need to obtain systematic information on daily life BP in outcome trials. Finally, our data shed light on the quantitative relationship between clinic BP and ABP before and during treatment. The main finding is that, whereas before treatment ABP is much lower than clinic BP, the 2 sets of values come closer during treatment and are similar in patients under stricter clinic BP control. This is relevant to the debated question of what should be the ABP target.

Disclosures
Giuseppe Mancia, Gianfranco Parati, Robert Fagard, Josep Redon, Paolo Verdecchia, Koon Teo, and Salim Yusuf received consulting, lecture fees, and research grants from Boehringer Ingelheim and from other companies manufacturing angiotensin receptor blockers. The other authors have no conflicts to report.

References

Figure 5. Absolute clinic and 24-hour blood pressure (BP) values (top) and differences at baseline and at different BP targets with treatment. Data are from all available patients. SBP indicates systolic blood pressure; S, systolic; D, diastolic.

**What Is New?**

- This is a detailed report on the long-term effect of double blockade (angiotensin receptor antagonist + angiotensin converting enzyme inhibitor) of the renin-angiotensin system on ambulatory blood pressure, vis-a-vis the blockade provided by angiotensin receptor antagonist or angiotensin converting enzyme inhibitor only. A thorough description of the relationship between the effect of antihypertensive treatment on clinic and ambulatory blood pressure (BP) is provided, including the quantitative difference between the 2 sets of values at different tightness of clinic BP control.

**What Is Relevant?**

- The results show that in ONTARGET double blockade of the renin-angiotensin system lowered ambulatory BP more than predictable based on clinic BP data. This rules out the possibility that an insufficient BP reduction was responsible for the disappointing effect of this treatment strategy on outcome reported in the main study. The results also provide the novel evidence that, whereas clinic BP is markedly greater than ambulatory BP at baseline drug treatment, the difference becomes progressively less (and eventually superimposable) as clinic BP control becomes tighter. This is relevant to the issue of which should be the target ambulatory BP with treatment, on which little or no evidence is available.

**Novelty and Significance**

The article provides a detailed description of the ambulatory BP effects of the 3 different treatments used in the ONTARGET. It highlights the limited relationship between these effects and those on clinic BP. It also provides evidence on which may be the ambulatory BP values that correspond to the different target clinic BP recommended by guidelines for treatment.
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