STAR CAST: Preliminary Results of Trial to Regress Hypertension

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Results from animal models have shown that hypertension can be regressed to normal blood pressure (BP) levels [Smallegange C et al. *Hypertension* 2004] and that this reduction can be maintained after pulse treatment with an angiotensin receptor blocker [Ishiguro K et al. *Hypertension* 2009]. The Short Treatment With Angiotensin Receptor Blocker Candesartan Surveyed by Telemedicine study [STAR CAST; Sasamura H. *Hypertens Res* 2008; UMIN-CTR UMIN000000941] tested the feasibility of regressing hypertension in humans. Hiroyuki Sasamura, MD, PhD, Keio University, Tokyo, Japan, presented the preliminary results.

In this prospective, randomized, open-label, blinded-endpoint study, 124 patients were randomized to candesartan 4 to 12 mg daily and 120 patients to nifedipine controlled release (CR) 10 to 40 mg daily for a 12-month active treatment period. Trichlormethiazide 2 mg daily was added to reach target BP levels after maximizing active treatment. During the subsequent 13-month withdrawal phase, the active treatment was reduced according to a predefined dosing schedule, and surveillance conducted using a telemedicine system that transferred home BP readings real-time to the research center.

The patients were young (mean age, 51; range, 30 to 59 years), with a family history of hypertension (within 2 degrees of consanguinity), and had been recently diagnosed with Grade 1 hypertension (systolic BP [SBP] 140 to 159 mm Hg and/or diastolic BP [DBP] 90 to 99 mm Hg on two consecutive occasions). The patients had not taken antihypertensive medication during the 3 months preceding the study and had provided informed consent. Most patients were men (60.5% and 65.8% of the candesartan and nifedipine CR groups, respectively). The baseline BP was 152/91 mm Hg.

The End BP was defined as an office SBP ≥140 mm Hg and/or ≥90 mm Hg at two consecutive visits; office SBP ≥160 mm Hg and/or DBP ≥100 mm Hg at any one visit; mean weekly home SBP ≥140 mm Hg and/or DBP ≥90 mm Hg for 2 consecutive weeks; or mean weekly SBP ≥160 mm Hg and/or DBP ≥100 mm Hg at any 1 week.

The office and home BP levels were significantly and similarly reduced below target levels with both candesartan and nifedipine CR.

The primary endpoint was the antihypertensive drug withdrawal success rate, defined as the proportion of patients who discontinued active treatment but did not reach End BP and did not restart antihypertensive treatment. All patients, except one in the candesartan arm, reached the End BP within 1 year. The Kaplan-Meier curve revealed a statistically significant difference in the candesartan arm compared with the nifedipine CR arm (log-rank p=0.0001).

The probability of not reaching the End BP was significantly higher in the candesartan arm at 1 month (RR, 1.874; 95% CI, 1.283 to 2.736; p=0.0008) and 3 months (RR, 9.080; 95% CI, 1.169 to 70.497; p=0.0099) after starting drug withdrawal compared with nifedipine CR. For the secondary endpoint of median duration of drug withdrawal, no significant difference was found (candesartan arm, 27 days [range, 27 to 34 days]; nifedipine CR arm, 27 days [range, 26 to 27 days]).

The withdrawal of candesartan was associated with a small but significantly longer delay before restarting antihypertensive medication compared with nifedipine CR, which was statistically significant for office SBP (p=0.003).

The standard doses of active treatment were not associated with regression of hypertension. Further studies with larger doses of candesartan for a longer time may be warranted to evaluate whether a sustainable and clinically relevant reversal of hypertension can be obtained and its natural history altered.