

## Candesartan and Amlodipine: Effect on the Incidence of Cardiovascular Events and New-Onset Diabetes

The 3-year extension of the Candesartan Antihypertensive Survival Evaluation in Japan (CASE-J) Study demonstrated comparable efficacy of the angiotensin receptor blocker candesartan and the calcium channel blocker amlodipine on the incidence of cardiovascular (CV) events in high-risk hypertensive Japanese patients. As observed in the earlier phase of the study, candesartan exhibited sustained superiority over amlodipine with regards to reduction in new-onset diabetes throughout the 3-year extended follow up. Kazuwa Nakao, MD, Kyoto University, Kyoto, Japan, presented findings from the CASE-J extended follow-up study.

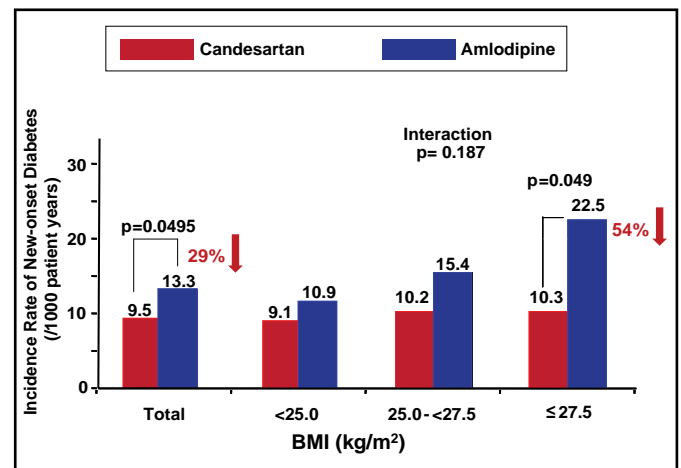
The Case-J Extension included 2232 hypertensive patients from the original trial who were randomized to either candesartan (n=1140) or amlodipine (n=1092). The two groups were characteristically well-matched at baseline with a mean systolic blood pressure (SBP) of 163 mm Hg and a mean diastolic blood pressure (DBP) of 92 mm Hg. The mean age of study participants was 64 years and the mean body mass index (BMI) was ~24.5. The two groups also had similar comorbidities and risk factors at baseline. The primary composite endpoint was the incidence of CV mortality and morbidity, defined as sudden death and CV, cardiac, renal, and vascular events. The secondary endpoints included the incidence of all-cause death, CV death, and new-onset diabetes.

BP was well-controlled in both treatment groups throughout the duration of the early trial and this benefit was maintained over the extended course of follow-up. There was no significant difference in the incidence of CV events between the two groups. Analysis of the single primary endpoint components (sudden death, CV events, cardiac events, renal events, and vascular events) found no significant difference between candesartan and amlodipine treatment. The incidence of all-cause death was also comparable for both treatment groups.

Treatment with candesartan significantly reduced the incidence of new-onset diabetes compared with amlodipine during the original study arm (p=0.031) and this benefit was demonstrated further in the extension arm of the study. A 29% relative risk reduction of new-onset diabetes was observed in the candesartan group compared with amlodipine (HR, 0.71; 95% CI, 0.51 to 1.00; p=0.0495; Figure 1). There also appeared to be an interaction between BMI and new-onset diabetes (interaction p=0.187). Increases in risk reduction

correlated with increased BMI, particularly in patients with BMI  $\geq 27.5$  (p=0.049; Figure 1).

**Figure 1. Relationship Between New-onset Diabetes and BMI.**



Findings from the CASE-J Extension study provided valuable long-term data regarding the efficacy of candesartan and amlodipine on the incidence of CV events and new-onset diabetes in high-risk hypertensive patients. While results were comparable for both treatments concerning CV events, the incidence of new-onset diabetes was significantly reduced with candesartan compared with amlodipine and this benefit was sustained over time.

## First-Line Treatment with Combination Aliskiren/Amlodipine Improves Blood Pressure Control Over Amlodipine Alone in Moderate and Severe Hypertension

First-line combination therapy with aliskiren and amlodipine provided greater reductions in blood pressure (BP) levels and higher rates of BP control compared with amlodipine monotherapy in patients with moderate or severe hypertension, according to new findings from a prospective trial. Combination therapy was also well tolerated, suggesting an important role for aliskiren/amlodipine in the management of patients with type 2 hypertension.

For many patients with moderate or severe hypertension, effective treatment requires combination antihypertensive therapy using agents with complementary mechanisms of action. This 8-week, double-blind, randomized trial was designed to compare the effectiveness of first-line