SYNOPSIS

Name of sponsor/company	Daiichi Sankyo Co., Ltd.
Name of finished product	REZALTAS® COMBINATION TABLETS LD・COMBINATION TABLETS HD
Name of active ingredient	CS-866AZ (Olmesartan medoxomil/Azelnidipine)
Title of study	A randomized-controlled, double-blinded phase III study of CS-866AZ
Study centre(s)	Thirty-eight sites in Japan
Publication (reference)	Hypertension Research **32**: 1148-1154, 2009
Studied period	July 2006 to August 2007
Phase of development	Phase III
Objectives	The antihypertensive effect and safety of co-administration of olmesartan medoxomil (OLM) and azelnidipine (AZL) were compared to those of administration of OLM or AZL alone in patients with mild to moderate essential hypertension to verify the superiority of combination therapy to monotherapies.
Methodology	A multicenter, randomized, double-blind, 4-group, parallel, comparative study
Number of patients (planned and analysed)	Number of patients planned: 760 Number of patients analyzed: Full analysis set; 862 Safety analysis set; 866
Diagnosis and main criteria for inclusion	Main inclusion criteria: ・ Age ≥20 years ・ Baseline BP during the run-in period was stable and fulfilled the criterion: "systolic BP ≥ 140 mmHg and < 180 mmHg, and diastolic BP ≥ 90 mmHg and < 110 mmHg." ・ The 24-hour BP determined by ambulatory blood pressure monitoring (ABPM) during the run-in period met the criterion: "systolic BP ≥ 135 mmHg and diastolic BP ≥ 80 mm Hg." Main exclusion criteria: ・ Secondary or malignant hypertension ・ Myocardial infarction or cerebrovascular disorder ・ Night-shift workers
Test product, dose and mode of administration	Co-administration of OLM 20 mg tablet and AZL 16 mg tablet Co-administration of OLM 10 mg tablet and AZL 8 mg tablet

	Study drugs were administered orally once a day after breakfast.
Duration of treatment	Run-in period, 4 weeks; Treatment period, 12 weeks
Reference therapy	OLM 20 mg and AZL 16 mg
Criteria for evaluation	Efficacy (primary endpoint): The difference between sitting BP (systolic BP and diastolic BP) during the run-in period and that at the end of treatment (ΔBP) Safety: Adverse events (occurrence or exacerbation of subjective symptoms/objective findings and abnormal changes in clinical laboratory values)
Statistical method	Efficacy (primary endpoint): In the treatment comparison for ΔBP, P-values were calculated by an analysis of covariance with the BP value at baseline and gender and weight as covariates. The adjusted mean value for each treatment group and the 95% confidence interval were also calculated. Safety: The number and percentage of patients who developed AEs with a possible causal relationship to the study drug and all AEs were determined.
Summary-conclusions	The difference in sitting BP during the run-in period and that at the end of treatment was -23.6/-14.2 mmHg (systolic/diastolic BP) in the OLM 20 mg/AZL 16 mg group, and -20.3/-13.0 mmHg in the OLM 10 mg /AZL 8 mg group, which was a significantly greater reduction in BP compared with either monotherapy groups (-15.7/-9.9 mmHg in OLM 20 mg [$p<0.001$] or -15.0/-9.4 mmHg in AZL 16 mg [$p<0.001$]). The incidence of adverse events in the OLM/AZL combination groups was similar with the monotherapy groups. These results showed that combination therapy with OLM/AZL was well tolerated and exerted a stronger antihypertensive effect compared to monotherapy with OLM or AZL in patients with essential hypertension.
Date of report	October 14, 2010