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Pharmacokinetic and Pharmacodynamic Profiles of BR-A657 in Patients with Essential Hypertension

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Background: BR-A657 is an angiotensin receptor blocker under clinical development. The purpose of this study was to investigate pharmacokinetic and pharmacodynamic profiles of BR-A657 in patients with hypertension.

Methods: A randomized, double-blind, placebo-controlled, parallel-group, multiple-dose study was conducted. In this study, 38 patients with essential hypertension received BR-A657 or placebo once daily for 4 weeks (10 subjects in 20 mg, 10 subjects in 60 mg, 10 subjects in 180 mg and 8 subjects in the placebo group). Serial blood samples were collected on Day 1 and Day 28. Steady-state tmax, t1/2, Cmax and AUC0-24 were estimated. Levels of plasma renin activity and plasma aldosterone were obtained.

Results: At steady-state, mean tmax and t1/2 ranged from 1.7?2.5 hours and 7.5?9.9 hours, respectively, across the 20 mg, 60 mg, and 180 mg dosage groups. Mean Cmax and average AUC0-24 values increased dose-proportionally. All doses resulted in increases in plasma renin activity around 6 hours post-dose. Plasma aldosterone levels decreased until 6 hours and increased afterwards. Neither plasma renin nor aldosterone showed any distinct pattern over time in the placebo group.

Conclusion: At steady state, mean Cmax and AUC0-24 of BR-A657 showed dose-proportional increases over a dosage range from 20 mg to 180 mg. The fact that plasma aldosterone level declined despite increased plasma renin activity implies BR-A657 inhibited the increase in aldosterone by blocking the action of angiotensin II in renin-angiotensin-aldosterone system (RAAS) effectively.