Efficacy and Safety of 30-Mg Fimasartan for the Treatment of Patients With Mild to Moderate Hypertension: An 8-Week, Multicenter, Randomized, Double-Blind, Phase III Clinical Study

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ABSTRACT

Purpose: The standard 60-mg dose of fimasartan, a newly developed selective angiotensin II receptor blocker, is effective and safe for use in patients with mild to moderate hypertension. This study aimed to compare the efficacy and safety of low-dose (30 mg) fimasartan and placebo or valsartan (80 mg) for 8 weeks in patients with mild to moderate hypertension.

Methods: In this randomized trial, 293 patients (219 men; mean age, 54.24 [9.77] years) with mild to moderate hypertension were enrolled. After randomization to receive 30-mg fimasartan (n = 115), placebo (n = 117), or 80-mg valsartan (n = 61), the treatment dose was kept constant without dose escalation for 8 weeks. The primary end point was improvement in sitting diastolic blood pressure (SiDBP) from baseline to 8 weeks that was compared between treatments with low-dose fimasartan and placebo. The secondary end point was the overall efficacy and safety of low-dose

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fimasartan compared with that of placebo or valsartan.

Findings: At week 8, SiDBP changed by –9.93 (8.86) mm Hg in the fimasartan group and by –2.08 (9.47) mm Hg in the placebo group, which indicated significant antihypertensive efficacy ($P < 0.0001$). Efficacy was shown at week 4 as measured by SiDBP (–9.96 [7.73] vs –2.27 [7.85] mm Hg; $P < 0.0001$) or sitting systolic blood pressure (SiSBP) (–16.18 [14.44] vs –1.95 [13.48] mmHg; $P < 0.0001$) and at week 8 as determined by SiSBP (–15.35 [16.63] vs –2.30 [14.91] mm Hg; $P < 0.0001$). The fimasartan group exhibited more potent antihypertensive efficacy than the valsartan group both at week 4 (SiDBP, –9.96 [7.73] vs –6.53 [9.58] mm Hg [$P = 0.0123$]; SiSBP, –16.18 [14.4] vs –7.65 [12.89] mm Hg [$P = 0.0002$]) and at week 8 (SiDBP, –9.93 [8.86] vs –5.47 [8.96] mm Hg [$P = 0.0021$]; SiSBP, –15.35 [16.63] vs –7.49 [13.68] mm Hg [$P = 0.0021$]). Most treatment-emergent adverse events (TEAEs) were mild (89 of 95), and there were no serious TEAEs. The incidence of TEAEs was 19.1% in the fimasartan group, 22.6% in the placebo group, and 13.6% in the valsartan group, with no significant differences.

Implications: Low-dose fimasartan (30 mg) was well tolerated during the study period with no significant TEAEs. Low-dose fimasartan had an effective blood pressure–lowering effect that was greater than that of 80-mg valsartan in patients with mild to moderate hypertension. ClinicalTrials.gov identifier: NCT01672476. (*Clin Ther*. 2014;36:1412–1421)

Key Words: fimasartan, hypertension, placebo, valsartan.

INTRODUCTION

Fimasartan is a newly developed angiotensin II receptor blocker (ARB).[1–3] A Phase IIb study using 20 to 240 mg of fimasartan once daily for 8 weeks was conducted to determine the dosage for antihypertensive efficacy in patients with essential hypertension. Good efficacy and safety were observed at doses between 60 and 240 mg.[4] An ambulatory blood pressure–monitoring study was performed in which 60- or 120-mg fimasartan was orally administered for 8 weeks to patients with mild to moderate essential hypertension, and the 24-hour antihypertensive effect was compared with those of 80-mg valsartan. Fimasartan at 60 mg and 120 mg was found to be safe, with an antihypertensive effect that was maintained for >24 hours.[5] A Phase III study comparing the antihypertensive effects and safety of 60- to 120-mg fimasartan and 50- to 100-mg losartan for 12 weeks in patients with mild to moderate essential hypertension showed that the antihypertensive effect of fimasartan was superior to that of losartan, with a similar safety profile.[6]

In the present study, we conducted a double-blind, multicenter, randomized Phase III trial to compare the antihypertensive efficacy and safety of low-dose fimasartan (30 mg), valsartan (80 mg), or placebo in patients with mild to moderate essential hypertension. This study was conducted to determine an extended dose range of fimasartan for use in patients who require low-dose treatment.

PATIENTS AND METHODS

Study Design

The study was a randomized, double-blind, multicenter, placebo-controlled, parallel-group, Phase III clinical trial to compare the antihypertensive efficacy and safety of low-dose fimasartan and placebo in patients with mild to moderate essential hypertension. It complied with the Declaration of Helsinki and the International Conference on Harmonisation/Good Clinical Practice Guideline. The study was approved by the Korea Food and Drug Administration and the institutional review board of each participating study center. After voluntary agreement to participate in the study, subjects went through a screening period, including a 7-day washout period for those patients who had been taking another medication. Thereafter, subjects underwent a 14- to 21-day placebo run-in period, during which eligibility was confirmed based on the inclusion/exclusion criteria. The subjects were randomized into the study group (30-mg fimasartan), placebo group, and reference group (80-mg valsartan) at a 2:2:1 ratio, and the treatments were orally administered for 8 weeks. Subjects were asked to visit the study center at weeks 4 and 8 after treatment initiation for efficacy and safety assessments.

Patients

Male and female subjects aged 19 to 75 years with mild to moderate hypertension during the placebo run-in period were eligible for the study if they had not received treatment for hypertension at study entry