Efficacy and Safety of Low-Dose Antihypertensive Combination Drugs Including Amlodipine, Telmisartan, and Chlorthalidone: A Multicenter, Randomized, Double-Blinded, Parallel, Phase II Clinical Trial

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Abstract:

Background and Objective: Although single pill high-dose triple antihypertensive combinations are already available on South Korea, there are no reports evaluating the efficacy and safety of the low-dose combination of amlodipine, telmisartan, and chlorthalidone. The aim of this clinical trial was to assess the efficacy and safety of low-dose combination drug containing telmisartan (20 mg), amlodipine (2.5 mg), and chlorthalidone (6.25 mg).

Methods: This study was a randomized, double-blinded, parallel, multicenter, phase II clinical trial. In total, 221 subjects from 21 clinical trial sites in South Korea were randomly assigned to groups 1 (AD-209; telmisartan 20 mg/amlodipine 2.5 mg/chlorthalidone 6.25 mg), 2 (AD-209-1A; telmisartan 20 mg/amlodipine 2.5 mg), 3 (AD-209-1B; amlodipine 2.5 mg/chlorthalidone 6.25 mg), and 4 (AD-209-1C; telmisartan 20 mg/chlorthalidone 6.25 mg) in a 1:1:1:1 ratio, and the treatments lasted 8 weeks. After the initial drug administration, the subjects visited the clinical trial sites at weeks 4 and 8 to evaluate drug efficacy and safety.

Results: In patients with mild-moderate hypertension, the mean change in MSSBP from baseline to week 8 between group 1 and groups 2, 3, and 4 was -5.93, -8.69, and -1.51 mmHg, respectively. The blood pressure of the subjects in group 1 was significantly lower than that of those in groups 2 and 3. It was also lower than that of subjects in group 4 although this difference was not significant. Among the 221 subjects enrolled, 20 (9.05%) experienced 25 treatment-emergent adverse events (TEAEs); of these, 14 (6.33%) experienced 17 adverse drug reactions (ADRs). No significant differences in the TEAE or ADR incidence rates were found between group 1 and groups 2, 3, and 4.

Conclusions: AD-209 (telmisartan 20 mg/amlodipine 2.5 mg/chlorthalidone 6.25 mg), a low-dose triple combination drug, demonstrated a higher blood pressure lowering effect than the corresponding a low-dose dual combination drugs in patients with essential hypertension. Its safety was similar to that of the dual-combination drugs.