Clinical Therapeutics/Volume ▮, Number ▮, 2018

# Efficacy and Safety of Fixed-dose Combination Therapy With Telmisartan and Rosuvastatin in Korean Patients With Hypertension and Dyslipidemia: TELSTA-YU (TELmisartan-rosuvaSTAtin from YUhan), a Multicenter, Randomized, 4-Arm, Double-blind, Placebo-controlled, Phase III Study

Gyu Chul Oh, MD[1]; Jung-Kyu Han, MD, PhD[1]; Ki Hoon Han, MD, PhD[2]; Min-Su Hyon, MD, PhD[3]; Joon Hyung Doh, MD, PhD[4]; Moo Hyun Kim, MD, PhD[5]; Jin-Ok Jeong, MD, PhD[6]; Jang-Ho Bae, MD, PhD[7]; Sang Hyun Kim, MD, PhD[8]; Byung-Su Yoo, MD, PhD[9]; Sang Hong Baek, MD, PhD[10]; Moo-Yong Rhee, MD, PhD[11]; Sang-Hyun Ihm, MD, PhD[12]; Jung Hoon Sung, MD, PhD[13]; Young Jin Choi, MD, PhD[14]; Soo-Joong Kim, MD, PhD[15]; Kyung-Soon Hong, MD, PhD[16]; Byoung Kwon Lee, MD, PhD[17]; JangHyun Cho, MD, PhD[18]; Eun Seok Shin, MD, PhD[19]; Jay Young Rhew, MD, PhD[20]; Hyunsu Kim, MD, PhD[21]; and Hyo-Soo Kim, MD, PhD[1]

*[1]Division of Cardiology, Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea; [2]Division of Cardiology, Department of Internal Medicine, Asan Medical Center, Seoul, Republic of Korea; [3]Division of Cardiology, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea; [4]Division of Cardiology, Department of Internal Medicine, Inje University Ilsan-Paik Hospital, Goyang, Republic of Korea; [5]Division of Cardiology, Department of Internal Medicine, Dong-A University Hospital, Busan, Republic of Korea; [6]Division of Cardiology, Department of Internal Medicine, Chungnam National University Hospital, Daejon, Republic of Korea; [7]Division of Cardiology, Heart Center, Konyang University Hospital, Daejon, Republic of Korea; [8]Division of Cardiology, Department of Internal Medicine, Seoul Metropolitan Government–Seoul National University Boramae Medical Center, Seoul, Republic of Korea; [9]Division of Cardiology, Department of Internal Medicine, Wonju Christian Hospital, Wonju, Republic of Korea; [10]Division of Cardiology, Department of Internal Medicine, Seoul St. Mary's Hospital, Seoul, Republic of Korea; [11]Division of Cardiology, Department of Internal Medicine, DongGuk University International Hospital, Goyang, Republic of Korea; [12]Division of Cardiology, Department of Internal Medicine, Bucheon St. Mary's Hospital, Bucheon, Republic of Korea; [13]Department of Cardiology, CHA Bundang Medical Center, Seongnam, Republic of Korea; [14]Department of Cardiology, Sejong General Hospital, Bucheon, Republic of Korea; [15]Division of Cardiology, Department of Internal Medicine, Kyung Hee University Hospital, Seoul, Republic of Korea; [16]Division of Cardiology, Department of Internal Medicine, Chuncheon Sacred Heart Hospital, Chuncheon, Republic of Korea; [17]Division of Cardiology, Department of Internal Medicine,*

*Accepted for publication March 14, 2018.*
https://doi.org/10.1016/j.clinthera.2018.03.010
0149-2918/$ - see front matter

*Gangnam Severance Hospital, Seoul, Republic of Korea; [18]Department of Cardiology, Heart Center, Saint Carollo Hospital, Sun-cheon, Republic of Korea; [19]Division of Cardiology, Department of Internal Medicine, Ulsan University Hospital, Ulsan, Republic of Korea; [20]Division of Cardiology, Department of Internal Medicine, Presbyterian Medical Center, Jeonju, Republic of Korea; and [21]Division of Cardiology, Department of Internal Medicine, Kosin University Gospel Hospital, Busan, Republic of Korea*

## ABSTRACT

**Purpose:** Hypertension and dyslipidemia are 2 risk factors of cardiovascular disease that often present simultaneously. Traditionally, treatment of these multiple conditions required separate medications for each disease, which may result in poor compliance and thus lead to possible treatment failure. Fixed-dose combination (FDC) therapy with a single pill may be a solution in these situations.

**Methods:** This multicenter, 8-week, randomized, double-blind, Phase III study evaluated the efficacy and safety of FDC treatment with telmisartan (80 mg) and rosuvastatin calcium (20 mg) in Korean patients with mild to moderate hypertension and dyslipidemia. Patients were randomly assigned to 4 groups: (1) FDC drug (80 mg of telmisartan and 20 mg of rosuvastatin); (2) 80 mg of telmisartan; (3) 20 mg of rosuvastatin; or (4) placebo. After 8 weeks of treatment, the change in mean sitting systolic blood pressure (MSSBP) and mean sitting diastolic blood pressure (MSDBP) between the FDC group and the rosuvastatin group, and the percent change in LDL-C between the FDC group and the telmisartan group, were compared.

**Findings:** A total of 210 patients were enrolled in the study (84 in the FDC group, 42 in the rosuvastatin group, 43 in the telmisartan group, and 41 in the placebo group). The reduction in blood pressure was significantly greater in the FDC group than in the rosuvastatin group after 8 weeks of treatment (least squares mean change from baseline, –16.1 [1.6] mm Hg vs –1.7 [2.2] mm Hg [$P < 0.001$] for MSSBP; –8.8 [1.0] mm Hg vs –1.6 [1.4] mm Hg [$P < 0.001$] for MSDBP). Least squares mean percent change in LDL-C from baseline was also significantly greater in the FDC group compared with the telmisartan group (–49.3% [2.2%] vs 1.5% [3.0%]; $P < 0.001$). FDC therapy also had a higher rate of achieving the treatment goal in both blood pressure (60% vs 45%; $P = 0.024$) and LDL-C (88.8% vs 16.3%; $P < 0.001$) compared with rosuvastatin or telmisartan alone, respectively. In regression analysis, higher baseline MSSBP, female sex, and lower body mass index were associated with increased reductions in MSSBP, whereas higher baseline LDL-C level and lower body mass index were associated with greater reductions in LDL-C. There were 48 adverse events in 36 patients (17.3% [36 of 208]), and 17 adverse drug reactions in 12 patients (5.8% [12 of 208]), indicating no significant differences in short-term safety among study groups.

**Implications:** Treatment with an FDC drug containing telmisartan and rosuvastatin showed similar efficacy in lowering blood pressure and LDL-C levels compared with that of each single drug. ClinicalTrials.gov identifier: NCT01914432. (*Clin Ther*. 2018;▮:▮▮▮–▮▮▮) © 2018 Published by Elsevier HS Journals, Inc.

**Key words:** dyslipidemia, fixed-dose combination, hypertension, rosuvastatin calcium, telmisartan.

## INTRODUCTION

Cardiovascular disease is the leading cause of death, accounting for 31% of global deaths.[1] Among risk factors for cardiovascular events, hypertension and dyslipidemia are 2 diseases that often present simultaneously.[2,3] Hypertension and dyslipidemia are both associated with endothelial dysfunction and insulin resistance, and they can have synergistic, deleterious effects on cardiovascular outcome.[4] Previous studies have suggested that targeting the renin-angiotensin-aldosterone system by adding 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) to angiotensin II receptor blockers (ARBs) can reinforce the antihypertensive effect of ARBs.[5] However, the increased number of pills can also result in lower compliance, in turn leading to treatment failure.[6] A single, fixed-dose combination (FDC) drug could improve patient compliance by reducing the number of pills, while effectively maintaining blood pressure–lowering and lipid-modifying efficacies.

Telmisartan, a unique member of the ARB class, not only inhibits the renin-angiotensin-aldosterone system but also partially activates peroxisome proliferator activated receptor-γ (PPAR-γ), giving it a