

Efficacy and Safety of Ezetimibe and Rosuvastatin Combination Therapy Versus Those of Rosuvastatin Monotherapy in Patients With Primary Hypercholesterolemia

Woohyeun Kim, MD¹; Yeonyee E. Yoon, MD²; Sung-Hee Shin, MD, PhD³; Jang-Whan Bae, MD, PhD⁴; Bum-Kee Hong, MD, PhD⁵; Soon Jun Hong, MD, PhD⁶; Ki Chul Sung, MD, PhD⁷; Seung Hwan Han, MD, PhD⁸; Weon Kim, MD, PhD⁹; Moo-Yong Rhee, MD, PhD¹⁰; Sang-Hyun Kim, MD, PhD¹¹; Sang Eun Lee, MD¹²; Min Su Hyon, MD, PhD¹³; Gyo-Seung Hwang, MD, PhD¹⁴; Jang Won Son, MD, PhD¹⁵; Jang-Young Kim, MD, PhD¹⁶; Min Kyu Kim, MD, PhD¹⁷; Sang Wook Kim, MD, PhD¹⁸; Jae-Hyeong Park, MD, PhD¹⁹; Jin Ho Shin, MD, PhD²⁰; and Chang Gyu Park, MD, PhD¹

¹Department of Cardiology, Cardiovascular Center, Korea University Guro Hospital, Seoul, Republic of Korea; ²Department of Cardiology, Cardiovascular Center, Seoul National University Bundang Hospital, Seongnam, Republic of Korea; ³Division of Cardiology, Department of Internal Medicine, Inha University College of Medicine, Incheon, Republic of Korea; ⁴Division of Cardiology, Department of Internal Medicine, Chungbuk National University College of Medicine, Cheongju, Republic of Korea; ⁵Division of Cardiology, Heart Center, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea; ⁶Department of Cardiology, Cardiovascular Center, Korea University Anam Hospital, Seoul, Republic of Korea; ⁷Division of Cardiology, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; ⁸Division of Cardiology, Gachon University Gil Medical Center, Incheon, Republic of Korea; ⁹Division of Cardiology, Department of Internal Medicine, Kyung Hee University, Kyung Hee University Hospital, Seoul, Republic of Korea; ¹⁰Cardiovascular Center, Dongguk University Ilsan Hospital, Goyang, Republic of Korea; ¹¹Division of Cardiology, Department of Internal Medicine, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Republic of Korea; ¹²Division of Cardiology, Asan Medical Center, Seoul, Republic of Korea; ¹³Division of Cardiology, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Seoul, Republic of Korea; ¹⁴Department of Cardiology, Ajou University School of Medicine, Suwon, Republic of Korea; ¹⁵Division of Cardiology, Department of Internal Medicine, Yeungnam University Hospital, Daegu, Republic of Korea; ¹⁶Department of Cardiology, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea; ¹⁷Division of Cardiology, Department of Internal Medicine, Hallym University Dontan Sacred Heart Hospital, Hwaseong, Republic of Korea; ¹⁸Division of Cardiology, Department of Internal Medicine, Chung-Ang University Hospital, Seoul, Republic of Korea; ¹⁹Division of Cardiology, Department of Internal Medicine, Chungnam National University College of Medicine, Chungnam National University Hospital, Daejeon, Republic of Korea; and ²⁰Division of Cardiology, Department of Internal Medicine, Hanyang University Hospital, Seoul, Republic of Korea

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ABSTRACT

Purpose: The aim of this study was to evaluate the safety and efficacy of combination treatment of rosuvastatin with ezetimibe in patients with primary hypercholesterolemia.

Methods: This multicenter, randomized, double-blind study comprised a main study and an extension study. In the main study, the efficacy and safety of a combination of rosuvastatin (5, 10, and 20 mg) with ezetimibe (10 mg) were compared with those of rosuvastatin (5, 10, and 20 mg) alone. The subjects who achieved the National Cholesterol Education Program Adult Treatment Panel III LDL-C goal in the main study and agreed to a further study were enrolled for the extension study. In the extension study, ezetimibe 10 mg was also administered to subjects who had received rosuvastatin (5, 10, and 20 mg) alone in the main study, and the same treatment was continued for subjects who had received a combination of rosuvastatin with ezetimibe in the main study.

Findings: At the end of the main study (week 8), LDL-C levels were significantly lower in subjects receiving combination therapy than in those receiving rosuvastatin monotherapy. Other lipid profiles also significantly improved in the combination therapy group. These improvements continued in the extension study. The combination therapy of rosuvastatin and ezetimibe was generally well tolerated. At the end of the main study, more subjects achieved the National Cholesterol Education Program Adult Treatment Panel III LDL-C goal in the combination therapy group than in the monotherapy group. The increased dosage of rosuvastatin was also well tolerated in the combination treatment.

Implications: Combination therapy of ezetimibe 10 mg with varying doses of rosuvastatin that are commonly used in the clinical field improved the lipid profile and allowed more subjects to reach the LDL-C goal in primary hypercholesterolemia compared with rosuvastatin monotherapy. In addition, the efficacy of the combination therapy was maintained for the extended period. Additional beneficial changes were also achieved with combination therapy even in patients who responded well to rosuvastatin monotherapy. ClinicalTrials.gov identifier: NCT03288038. (*Clin Ther.* 2018;■:■■■-■■■) © 2018 Published by Elsevier HS Journals, Inc.

Key words: cardiovascular diseases, combination therapy, ezetimibe, LDL-C, rosuvastatin.

INTRODUCTION

Primary hypercholesterolemia is a lipid disorder characterized by high levels of cholesterol in the blood. Hypercholesterolemia is closely associated with an increased risk of coronary heart disease (CHD).¹⁻⁷ The National Cholesterol Education Program (NCEP) established guidelines in which LDL-C was identified as the causative factor for CHD and the main target in lipid-lowering treatment.⁸ Furthermore, the 2013 American College of Cardiology/American Heart Association guideline on the treatment of elevated blood cholesterol recommended the use of statins, along with lifestyle modification, for prevention of atherosclerotic cardiovascular disease.⁹

Although the percentage of population that consumes lipid-lowering medications has increased, the overall prevalence of hypercholesterolemia has not decreased. According to data from the National Health and Nutrition Examination Surveys in the United States, the prevalence of hypercholesterolemia in adults aged ≥ 20 years increased to 27.8% in 2011–2014 from 22.8% in 1988–1994. In the Korean population, the prevalence of hypercholesterolemia increased to 17.9% in 2015 from 13.5% in 2010 and from 8.0% in 2005.¹⁰ Despite use of lipid-lowering medications, a significant number of patients do not reach the NCEP Adult Treatment Panel III (NCEP ATP III) LDL-C goal.¹¹⁻¹³ This finding indicates that LDL-C is poorly controlled in patients diagnosed with hypercholesterolemia, possibly due to poor compliance, inadequate response to therapy, and side effects, particularly at higher doses.¹⁴⁻¹⁸

In previous studies, the ezetimibe (EZE) and statin combination therapy was effective in lowering LDL-C levels and was safe and tolerable. Rosuvastatin (RSV) in combination with EZE demonstrated better efficacy in the EXPLORER (EXamination of Potential Lipid-modifying effects Of Rosuvastatin in combination with Ezetimibe versus Rosuvastatin alone). and ACTE (EfficACy and SafeTy of Ezetimibe Added On to Rosuvastatin Versus Up Titration of Rosuvastatin in Hypercholesterolemic Patients at Risk for Coronary Heart Disease) studies

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