Utilization Patterns of Lipid-lowering Therapies in Patients With Atherosclerotic Cardiovascular Disease or Diabetes: A Population-Based Study in South Korea

Siin Kim, PharmD, MS[1]; Hyungtae Kim, PharmD[1]; Eunju Kim, PhD[1]; Sola Han, PharmD, MS[1]; Pratik P. Rane, MBA, PhD[2]; Kathleen M. Fox, PhD[3]; Zhongyun Zhao, PhD[2]; Yi Qian, PhD[2]; and Hae Sun Suh, PhD[1]

[1]College of Pharmacy, Pusan National University, Busan, South Korea; [2]Amgen, Inc, Thousand Oaks, California; and [3]Strategic Healthcare Solutions, LLC, Aiken, South Carolina

ABSTRACT

Purpose: We aimed to study the utilization patterns of lipid-lowering treatment (LLT), including treatment modification, adherence, and possible statin intolerance, in patients with atherosclerotic cardiovascular disease (ASCVD) or diabetes using national claims data in South Korea.

Methods: A retrospective cohort study was conducted using data from the Korean Health Insurance Review & Assessment Service claims database. Patients aged ≥18 years with >1 outpatient pharmacy claim for a statin and/or ezetimibe dated January 1, 2012, to December 31, 2014, were identified and categorized into the following cohorts: patients with ASCVD, and patients with diabetes mellitus without ASCVD. LLT modification, adherence to index LLT, and possible statin intolerance were explored during the 12 months after the date of first prescription for a statin and/or ezetimibe.

Findings: Among 1,399,872 patients who met the eligibility criteria, 807,547 (57.7%) were patients with ASCVD and 592,325 (42.3%) were patients with diabetes without ASCVD. About half of the patients had no modification in their index treatment (46.2% in the ASCVD cohort and 48.9% in the diabetes cohort), and the most common modification was permanent discontinuation (19.6% in the ASCVD cohort and 21.4% in the diabetes cohort). The mean medication possession ratios were 0.77 in the ASCVD cohort and 0.73 in the diabetes cohort and showed a decreasing trend during the 12-month follow-up period. Among patients who initiated a statin and/or ezetimibe, possible statin intolerance was observed in 53,921 patients (6.7%) in the ASCVD cohort and 42,172 patients (7.1%) in the diabetes cohort.

Implications: In South Korea, a high rate of permanent discontinuation of statin therapy in patients with ASCVD or diabetes places these patients at high risk for cardiovascular events in the future. A decreasing trend of adherence to LLT implies that more intensive education and management are required to improve therapeutic effect and reduce the risk for ASCVD. The high rate of possible statin intolerance highlights an unmet need in the prevention and management of ASCVD in South Korea. (*Clin Ther.* 2018;■:■■■–■■■) © 2018 Elsevier HS Journals, Inc. All rights reserved.

Key words: adherence, atherosclerotic cardiovascular disease, diabetes, statin, statin intolerance, treatment pattern.

INTRODUCTION

Atherosclerotic cardiovascular disease (ASCVD) is a global health problem that results in ~17 million deaths worldwide each year.[1] The economic burden of ASCVD is estimated to be US $297.7 billion in the United States, which is higher than that of all cancers and benign neoplasms.[2] ASCVD is also a serious health care concern in South Korea, considering that heart disease, including myocardial infarction, angina,

and heart failure, as well as cerebrovascular disease, account for 1 in 5 deaths, and that the economic burden of coronary heart disease mounts to $2.5 billiion.[3,4]

Several risk factors, including diabetes mellitus, hypertension, peripheral arterial disease, and abdominal aortic disease, increase the risk for cardiovascular events.[5,6] Among these risk factors, diabetes has been clearly designated to be risk equivalent, and statin therapy is recommended for use in the disease.[7] Globally, the estimated medical cost of diabetes is $827 billion/y.[8] In South Korea, diabetes is the sixth-leading cause of death, and 7.6% of the Korean population has diabetes.[3,9]

Although statins are recommended for the primary and secondary prevention of ASCVD, some patients have difficulty maintaining statin therapy due to poor tolerability.[6,7,10,11] A recent analysis of data from a US claims database found that 27.1% of patients with a history of a cardiovascular event and 28.5% with a history of an coronary heart disease risk equivalent (eg, diabetes) were identified as having possible statin intolerance.[12] Thus, despite current, widely available lipid-lowering therapies (LLTs), there is an unmet medical need to provide additional LLT to reduce the risk for cardiovascular events and improve outcomes in high-risk patients requiring large reductions in low-density lipoprotein cholesterol (LDL-C) levels.

The lipid-lowering effectiveness of statins and the baseline lipid profile in the Korean population differ from those in Western populations.[13–15] Therefore, utilization patterns can be different between the 2 populations. Additionally, the effectiveness of LLTs is closely related to medication compliance, including adherence and persistence.[16–21] However, there is a lack of data on the utilization patterns of LLTs in the Korean population. Therefore, we aimed to study the utilization patterns of LLTs, such as treatment modification, adherence, and possible statin intolerance, in patients with ASCVD or diabetes.

MATERIALS AND METHODS
Study Design and Data Source
This retrospective cohort study used data from claims in the Korean Health Insurance Review & Assessment Service (HIRA) claims database, dated January 1, 2011, to December 31, 2015, which represented the most recent data available when the study was conducted. In Korea, the National Health Insurance (NHI) program, which is wage-based and compulsory, insures ~97% of the population. Those not covered by the NHI program are insured by Medical Aid, a government-subsidized public-assistance program for low-income and medically indigent individuals. Because HIRA reviews both programs, the HIRA database covers the entire population of South Korea.[22] This study was exempted by the institutional review board of Pusan National University (Busan, South Korea; PNU IRB/ 2016_04_HR).

Study Population
We identified patients aged ≥18 years with >1 outpatient pharmacy claim for a statin and/or ezetimibe dated from January 1, 2012, to December 31, 2014. The date of the first statin and/or ezetimibe prescription was defined as the *index date*. Eligible patients had a second claim for a statin and/or ezetimibe within 6 months after the index date.[12]

The following patients were excluded from the study: (1) those with claims for a statin or ezetimibe during the 12 months before the index date; (2) those who initiated multiple statins on the index date; (3) those with a medical claim indicating pregnancy or delivery during the 12 months before or after the index date; (4) those with a medical claim indicating death during the 12 months before or after the index date (see Supplemental Appendix A in the online version at https://doi.org/10.1016/j.clinthera.2018.04. 007)[23]; (5) those with outlier values on statin and/or ezetimibe prescriptions; and (6) those without ASCVD or diabetes during the 12 months before the index date. Regarding the 5th criterion, some patients had extreme outlier values in daily doses or units per administration; we considered those values to have resulted from errors in data entry, and excluded patients prescribed a statin and/or ezetimibe with a dosing schedule of 0 or ≥4 times daily, and those with a unit-dose other than 0.25, 0.5, 1, 2, or 3 tablets. Regarding the 6th criterion, patients with ASCVD were defined as having at least 1 medical claim with a diagnosis code for myocardial infarction, angina, coronary revascularization, peripheral artery disease, ischemic stroke, or transient ischemic attack. Patients with diabetes were defined as having at least 1 medical claim with a diagnosis code for diabetes