Official Title: Efficacy and Safety of Different Ticagrelor Regimens Versus Clopidogrel in Patients With Coronary Artery Disease: a Retrospective Multicenter Study (SUPERIOR)

NCT number: 03381742

Document date: August 16, 2019

Objective

Current guidelines favor dual anti-platelet therapy with ticagrelor 90 mg BID (T90BID) over clopidogrel 75 mg QD (C75QD) in addition to aspirin for coronary artery disease (CAD). However, an increased risk of ticagrelor-related adverse events prompted evaluation of low-dose regimens. This study aimed to examine the efficacy and safety outcomes of two low-dose regimens of ticagrelor in a large-scale cohort of patients with CAD.

Design

This is a retrospective, multicenter, observational study of 3,043 consecutive inpatients and outpatients with CAD, who received either ticagrelor or clopidogrel therapy.

Methods

We retrospectively analyzed the data from 11 hospitals on 3,043 CAD patients, who received C75QD, T90BID, ticagrelor 45 mg BID (T45BID), or ticagrelor 90 mg QD (T90QD) for at least 5 consecutive days before thromboelastography test. The main efficacy outcome was the ADP-induced inhibition of platelet aggregation (IPA), and other efficacy outcomes included ADP-induced platelet-fibrin clot strength (MA), rate of high on-treatment platelet reactivity (HTPR), and cardiovascular event (cardiovascular death, new-onset myocardial infarction, or stroke) rates. The primary safety outcome was bleeding rate (major or minor bleeding), and rate of new-onset dyspnea was also studied. All the patients had a 5-day follow-up period after the first dosing of study drugs to assess the efficacy and safety outcomes. The outcomes were compared between patients with clopidogrel treatment and patients who received different ticagrelor regimens (T90BID, T45BID and T90QD) using logistic regression model for total population and propensity score–matching analysis.

Primary data analysis was performed by investigators with cooperation from the First Affiliated Hospital of Harbin Medical University and the other participating hospitals. The study was approved by the Ethics Committees of the First Affiliated

Hospital of Harbin Medical University.

Data are summarized as frequencies and percentages for categorical variables. Continuous variables are expressed as median and interquartile range. To compare differences in continuous variables among groups, Mann–Whitney U test or Kruskal–Wallis rank sum test was performed, followed by Dunn's multiple comparison test. The Fisher's exact test or χ^2 test was used to compare categorical variables, followed by Bonferroni adjustments for multiple comparisons test. Univariate and multivariate logistic regression analyses were conducted to evaluate the association between platelet inhibition (HTPR/non-HTPR) and treatment group or other clinical characteristics. Odds ratios (OR) and their 95% confidence intervals (CIs) are presented as a measure of association.

Propensity score matching was performed to reduce selection bias and confounders between two groups at baseline. The propensity scores were estimated using a multivariate logistic regression model that included the following variables: age; gender; weight; cigarette smoking; hypertension; diabetes mellitus; chronic kidney disease; previous PCI; previous coronary artery bypass grafting; serum levels of total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, creatinine and uric acid; aspirin use; and acute myocardial infarction. The propensity scores were used to match the clopidogrel and ticagrelor groups in a 1:1 ratio, with a caliper value of 0.05.

All statistical analyses were 2-tailed, and a P value < 0.05 was considered statistically significant. Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC, USA) and R version 3.2.1 (http://www.r-project.org).