Comparative Effectiveness of Ticagrelor vs. Prasugrel in Patients with Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention

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Background

Dual antiplatelet therapy (DAPT), comprising aspirin and a P2Y12 inhibitor, is pivotal in managing acute coronary syndrome (ACS) in patients undergoing percutaneous coronary intervention (PCI). While ticagrelor and prasugrel have both shown superior efficacy compared to clopidogrel in initial clinical trials, direct comparative evidence between ticagrelor and prasugrel remains mixed and inconclusive. Notably, the ISAR-REACT 5 trial unexpectedly demonstrated a significant reduction in major cardiovascular events with prasugrel over ticagrelor, influencing European Society of Cardiology guidelines to recommend prasugrel as the first-line therapy preferred over ticagrelor.[1,2] However, guidelines from the American College of Cardiology/American Heart Association continue to recommend either agent without preference, reflecting ongoing clinical uncertainty.[3] This discrepancy between guidelines highlights the need for rigorous real-world comparative evidence to inform optimal treatment strategies.

Methods

We designed a retrospective cohort study utilizing electronic health records and claims data standardized to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). Eligible participants are adults (≥18 years) diagnosed with ACS who underwent PCI and initiated treatment with either ticagrelor or prasugrel. Patients with exposure to warfarin or direct oral anticoagulants within 6 months, or prior history of stroke and gastrointestinal bleeding are excluded. The index date is defined as the PCI procedure date. The primary outcome is 1-year Major Adverse Cardiovascular Events (MACE), defined as a composite of all-cause mortality, acute myocardial infarction, and stroke. Secondary outcomes include 1-year Net Adverse Clinical Events (NACE), ischemic events, hemorrhagic events, and cardiovascular mortality. Sensitivity analyses assessing these outcomes at 1-month and 3-month time-at-risks, as well as as-treated analysis are also included. Baseline patient characteristics are balanced using propensity score stratification, and Cox proportional hazards models are applied. Results from multiple databases will be integrated through Bayesian random-effects meta-analysis. All steps of the study are conducted following a pre-specified, publicly available protocol to enhance transparency and reproducibility.

Anticipated Impact

As a major collaborative effort within the OHDSI network, this study addresses critical evidence gaps highlighted by conflicting international guidelines. Currently in the data collection phase, this study is anticipated to provide comprehensive insights into the comparative effectiveness and safety profiles of ticagrelor and prasugrel. The findings will address current guideline discrepancies and support clinicians in making informed decisions regarding optimal antiplatelet therapy for ACS patients undergoing PCI.

References

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