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The addition of clopidogrel as a third agent in patients with PAD undergoing lower extremity revascularization treated with rivaroxaban and aspirin is associated with higher rates of bleeding during exposure, with no added benefit

The benefit and safety of rivaroxaban plus aspirin versus aspirin alone is consistent regardless of background clopidogrel. However, the addition of clopidogrel did increase bleeding overall, particularly immediately after the procedure when patients were taking clopidogrel

Aurora, CO, March 29, 2020 – CPC Clinical Research, an affiliate of the University of Colorado Anschutz campus, announced yesterday that the VOYAGER PAD trial demonstrated a benefit for an antithrombotic strategy in reducing major adverse limb and cardiovascular event risk in patients with peripheral artery disease (PAD) after lower extremity revascularization. The data found that rivaroxaban along with aspirin reduced the risk of major adverse limb and cardiovascular events by 15% compared with aspirin alone for PAD patients after revascularization. In a prespecified subgroup analysis of this trial, researchers discovered that adding clopidogrel at the time of revascularization to this treatment strategy did not modify the efficacy of rivaroxaban plus aspirin on the primary outcome or key secondary endpoints or on safety but did increase the risk of bleeding, particularly immediately after the procedure when patients were taking clopidogrel. The subgroup analysis results were presented as a Late-Breaking Clinical Trial Session held during the American College of Cardiology's Annual Scientific Session Together with World Congress of Cardiology (ACC.20/WCC).

PAD affects an estimated 8 million people in the U.S. and over 200 million people worldwide. PAD is caused when there is limited blood flow to the limbs because of accumulation of plaque in the arteries. This limited blood flow condition causes health and lifestyle difficulties ranging from limb pain and trouble walking, to limb amputation, heart attack, ischemic stroke and/or cardiovascular death. As symptoms become increasingly severe for patients with PAD, the common treatment involves revascularization. There are currently no Class I recommendations for more intensive antithrombotic strategies to reduce the risk of limb and cardiovascular outcomes after intervention. Due to the absence of studies demonstrating efficacy for these outcomes in this high-risk population, there is a gap in clinical practice around PAD treatments following revascularization. Clinicians often treat revascularization in patients with PAD using dual antiplatelet therapy with aspirin and a P2Y12 receptor blocker such as clopidogrel, although there is limited evidence to support this.

“This was a prespecified subgroup analysis to look at whether the use of clopidogrel modified the benefits seen with rivaroxaban and aspirin or increased the risks [of bleeding],” said William R. Hiatt, MD, professor of medicine/cardiology, University of Colorado School of Medicine, Chief Science Officer, CPC Clinical Research, and the study’s lead author. “We found that in this [clinical] setting, where we are treating patients with symptomatic PAD with lower extremity revascularization procedures, the addition of clopidogrel [atop] rivaroxaban and aspirin does not provide any further benefit but did increase bleeding risk immediately after the procedure during the short time when clopidogrel was used, so there doesn’t seem to be a compelling reason to use it. Researchers continue to explore how increased bleeding with clopidogrel, may affect other outcomes. Patients were randomized during this study at a 1:1 ratio to receive either rivaroxaban 2.5 mg twice daily plus aspirin 100 mg once daily (n=3,286) or aspirin 100 mg once daily alone (n=3,278). Patients were classified by revascularization procedure type (endovascular vs. surgical) and use of clopidogrel, which was allowed at the treating physician’s discretion. Patients were followed for a median of 28 months.

“People with PAD tend to be undertreated, yet they are very high risk, particularly for ischemic limb events such as acute limb ischemia or major amputation after revascularization,” Hiatt said. “I hope that these data will lead to more education and improve how we care for these patients. From these unique data we see the benefit and risks of rivaroxaban plus aspirin were consistent regardless of concomitant use of clopidogrel. However, with higher short-term rates of bleeding when clopidogrel is added to rivaroxaban and aspirin these findings do not support the routine use of clopidogrel after lower extremity revascularization in these patients when we have an evidence-based strategy of rivaroxaban and aspirin.”

ABOUT CPC

CPC Clinical Research, an academic research organization and affiliate of the University of Colorado Anschutz Medical Campus, has led innovative research in cardiovascular disease and particularly peripheral artery disease and cardiometabolic disease for more than 30 years. Founded in 1989 to lead the Appropriate Blood Pressure Control in Diabetes (ABCD) trial (www.ncbi.nlm.nih.gov/pubmed/8960857), CPC is recognized for its expertise in comprehensive clinical trial management for both national and international clinical research. Over the past three decades, the organization’s services have evolved to stay at the forefront of the everchanging landscape of clinical research.

CPC also leads innovative programs to help vulnerable populations across Colorado to achieve health without disparities. As a result of these efforts, CPC Community Health has provided health education and/or coaching to over 82,000 individuals and made significant improvements in the lives of those at risk for cardiovascular disease. The results of these Community Health programs, focused on rural and Latino populations, have been recognized by the CDC.

CPC offers full-service clinical trial design, oversight, and management with rapid access to Key Opinion Leaders in a variety of therapeutic areas. These individuals are on the cutting edge of scientific, clinical and regulatory developments. Many of

CPC's leadership team have chaired and/or served on FDA advisory committees including the Cardiovascular and Renal, Endocrine and Metabolism, and Reproductive Health committees. For more information, go to www.cpcclinicalresearch.org/news-and-presentations/ and www.cpccommunityhealth.org

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