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## CPC's Research Captures Global Attention During The 70th European Society of Cardiology (ESC) Congress with Multiple Late-Breaking Science Presentations

CPC Clinical Research, an academic research organization (ARO) affiliated with the University of Colorado Anschutz Medical Campus, presented three late breaking scientific abstracts at The European Society of Cardiology's 'ESC Congress 2020 - The Digital Experience'. This was a global cardiovascular event that disseminated stimulating cardiovascular science with featured key opinion leaders from around the world. Three members of CPC's faculty presented new scientific data in the Late-Breaking Trial Sessions.

Patients with peripheral artery disease (PAD) are at high risk for limb and cardiovascular events, especially after lower extremity revascularization (LER). The VOYAGER PAD trial demonstrated that low dose rivaroxaban (2.5 mg twice daily) plus aspirin significantly reduces the risk of severe limb and cardiovascular events in PAD patients undergoing LER with acceptable bleeding risk. This groundbreaking research was initially presented by Dr. Marc Bonaca during the ACC Scientific Sessions in March 2020 and can be found on CPC's website linked below. Secondary analyses from VOYAGER PAD provide insight into additional benefit of rivaroxaban and may help identify patients that will benefit most from this therapy.

Dr. William Hiatt, Professor of Medicine in the Division of Cardiology at the University of Colorado School of Medicine and Chair of the VOYAGER PAD trial, presented novel findings on August 30th, 2020. Although patients with PAD have typically been lumped

into a single population with regards to risk, which is not true, new data from VOYAGER PAD highlighted heterogeneity in risk profile on the basis of known coronary artery disease (CAD). Only about one-third of patients with PAD have clinical evidence of concomitant CAD as was seen in VOYAGER PAD. In those patients with PAD plus CAD, the risk profile and absolute benefits of rivaroxaban differs from those with PAD alone. In those with CAD, there is a higher risk of myocardial infarction relative to limb events while in those without CAD, the risk is driven more by limb events. While rivaroxaban is efficacious regardless of concomitant CAD, the benefit profile and absolute benefits are different and this may be important when personalizing therapeutic decision making. Dr. Hiatt said relative to the subgroup with PAD plus CAD, "With greater absolute benefit, fewer patients need to be treated to prevent an event. This makes the combination of rivaroxaban plus aspirin an attractive therapy in these very high-risk patients."

Dr. Connie Hess, Associate Professor of Medicine in the Division of Cardiology at the University of Colorado School of Medicine and one of CPC's Clinician Scientists, presented "Acute Limb Ischemia after Lower Extremity Revascularization: Insights From VOYAGER PAD" on September 1st, 2020. Acute limb ischemia (ALI) is a limb-threatening event typically caused by sudden thrombotic occlusion of an artery and is a major cause of morbidity in patients with PAD. In patients with stable, chronic PAD, a remote history of LER is associated with a 4-fold increased risk for ALI. ALI in the acute setting of LER has not been described, and effective therapies to reduce risk of ALI after LER have been lacking. In a subgroup analysis of patients with PAD and ALI, ALI was the most frequent ischemic event after LER for symptomatic PAD, and the risk for ALI started early post-procedure and continued over time. Rivaroxaban 2.5 mg twice daily with aspirin compared to aspirin alone significantly reduced the risk of ALI, regardless of the type of LER procedure and whether concomitant clopidogrel was used. Therefore, rivaroxaban plus aspirin should be considered early after LER for symptomatic PAD to reduce ALI.

The third late breaking presentation from CPC faculty was presented by Dr. Marc Bonaca, Professor of Medicine in the Division of Cardiology at the University of Colorado School of Medicine and CPC's Executive Director. This abstract was based on limb outcomes adjudicated in the Effect of Ticagrelor on Health Outcomes in DiabEtes Mellitus Patients Intervention Study (THEMIS trial). This was a large trial led by Drs. Deepak Bhatt and P. Gabriel Steg including over 19,000 patients with diabetes and coronary disease, but no history of myocardial infarction randomized to ticagrelor or placebo on a background of low dose aspirin and followed long-term. Overall, the trial showed that ticagrelor reduced myocardial infarction and stroke and increased bleeding. In addition, Limb ischemic events were adjudicated at CPC clinical research and this was the focus of this late breaking abstract. Overall ticagrelor reduced limb ischemic events including acute limb ischemia, major vascular amputation and peripheral revascularizations. The benefit was consistent regardless of PAD status, but absolute benefits appeared greater in those with PAD. These data expand the risk and benefit information for ticagrelor in patients with diabetes and coronary disease including those with concomitant PAD. These data also support the role of more potent antithrombotic strategies to reduce limb risk in PAD; however, the efficacy and safety of ticagrelor after PAD intervention has not been established.

**About VOYAGER PAD**

The Phase 3 VOYAGER PAD study included 6,564 patients from 534 sites across 34 countries worldwide. Patients were selected on the basis of symptomatic lower extremity PAD requiring revascularization without further enrichment for cardiovascular or limb risk. Patients were randomized 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 included regardless of the mode of revascularization (surgical or endovascular) and use of concomitant clopidogrel was allowed for up to 6 months. Patients were followed for a median of 28 months. The primary efficacy endpoint was a composite of acute limb ischemia and major amputation of a vascular etiology, heart attack (myocardial infarction, MI), ischemic stroke or cardiovascular death. The primary safety outcome was major bleeding according to the TIMI

classification. The study was funded by Bayer AG and Janssen Research and Development.

**About THEMIS**

Phase III THEMIS (Effect of Ticagrelor on Health Outcomes in DiabEtes Mellitus Patients Intervention Study) is a global, randomized, double-blinded trial in patients with CAD and T2D that have had no prior myocardial infarction or stroke. The trial was initiated in early 2014, across 42 countries and with more than 19,000 randomized patients. Over the duration of the study, 1,385 independently-adjudicated primary endpoint events were collected. The primary endpoint was met and demonstrated that compared to aspirin alone, ticagrelor when taken alongside aspirin, showed a statistically-significant reduction of major adverse cardiovascular events (MACE). The THEMIS study was funded by AstraZeneca.

**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 scientific leadership in study design and 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 urban 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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