Efficacy and safety of low-dose rivaroxaban on top of aspirin in patients with polypharmacy and multimorbidity: an analysis from the COMPASS trial

T. Vanassche¹, P. Verhamme¹, D. Leong², D.L. Bhatt³, O. Shestakovska², A.P. Maggioni⁴, K.A.A. Fox⁵, E. Muehlhofer⁶, S. Connolly², S. Yusuf², J. Eikelboom², J. Bosch⁷

¹ University Hospitals (UZ) Leuven, Leuven, Belgium; ² Population Health Research Institute, Hamilton, Canada; ³ Brigham and Women'S Hospital, Harvard Medical School, Boston, United States of America; ⁴ Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy; ⁵ University of Edinburgh, Center for Cardiovascular Science, Edinburgh, United Kingdom; ⁶ Bayer AG, Research & Development, Pharmaceuticals, TA Thrombosis & Hematology, Wuppertal, Germany; ⁷ McMaster University, School of Rehabilitation Science, Hamilton, Canada On behalf of The COMPASS investigators

Funding Acknowledgement: Type of funding source: Private company. Main funding source(s): The COMPASS trial was funded by Bayer AG.

Background: In patients with coronary or peripheral artery disease, intensified antithrombotic therapy with aspirin plus low dose rivaroxaban reduced cardiovascular outcomes compared with aspirin alone. Polypharmacy and multimorbidity are frequent in patients with vascular disease and are often perceived as barriers to more intensive pharmacotherapy by both patients and physicians.

Purpose: To report cardiovascular outcomes and the efficacy, safety, and net benefit of low dose rivaroxaban plus aspirin in patients with stable vascular disease by the number of concomitant cardiovascular drugs and by the number of comorbidities.

Methods: We reported ischemic events (cardiovascular death, stroke, or MI), major bleeding (ISTH modified criteria), and a prespecified net clinical outcome in participants from the randomised, double-blind COMPASS study by number of cardiovascular medications (0–2, 3, 4, 5–7) and by number of concomitant medical conditions. We compared rates and hazard ratios of patients treated with rivaroxaban plus aspirin vs aspirin alone by

category of number of medications and concomitant conditions and tested for interaction between polypharmacy and multimorbidity and antithrombotic regimen.

Results: Although patients with polypharmacy and multimorbidity have a higher risk of cardiovascular events (Figure) those who required many cardiovascular drugs derived the largest absolute reduction in the net clinical outcome when adding rivaroxaban on top of aspirin. The relative efficacy, safety, and net clinical benefit of adding low-dose rivaroxaban to aspirin in patients with stable vascular diseases were not affected by the number of cardiovascular drugs or by the number of comorbidities. Multimorbidity, but not polypharmacy, was related with a higher risk of major bleeding.

Conclusion: Addition of low-dose rivaroxaban conveyed a benefit irrespective of the number of concomitant drugs or comorbid conditions. Multiple comorbidities and/or polypharmacy should not dissuade the addition of low-dose rivaroxaban to aspirin in otherwise eligible patients.

