Summary Interim Report - EUPAS9895

Acronym/Title	A pharmacoepidemiological study of rivaroxaban use and potential adverse outcomes in routine clinical practice in the Sweden – Second interim analysis
Report version and date **Author**	Second Interim Report and 08 November 2017 Leif Friberg, MD, PhD Friberg Research AB, Stockholm, Sweden.
Keywords	Population-based, rivaroxaban, standard of care, Sweden
Rationale and background	Rivaroxaban is an oral, direct Factor Xa inhibitor with multiple indications, including: venous thromboembolism prevention in adult patients undergoing elective hip or knee replacement surgery (TKR/THR); treatment and prevention of recurrent deep vein thrombosis and pulmonary embolism (VTE-T); stroke prevention in atrial fibrillation (SPAF); and prevention of atherothrombotic events following an acute coronary syndrome (ACS). As anticoagulant use is associated with bleeding risk, monitoring of the safety profile and patterns of rivaroxaban use in routine care is required. This study programme forms part of the overall rivaroxaban post-authorization safety monitoring activities in several European countries.
Research question and objectives	To describe patients prescribed oral rivaroxaban or standard of care (SOC) for the first time, explore characteristics of rivaroxaban use and determine unadjusted cumulative incidences and incidence rates for the primary outcomes (hospitalization for intracranial haemorrhage, gastrointestinal bleeding or urogenital bleeding) and one secondary safety outcome (all-cause death).
Study design	This study has a cohort design.
Setting	All patients who filled a first-time prescription for rivaroxaban or SOC (warfarin) in any pharmacy in Sweden between 09 Dec 2011 and 31 Dec 2016.
Subjects and study size, including dropouts	After applying exclusion criteria, there were 50,372 and 282,531 individuals in the rivaroxaban and SOC cohorts,

	respectively.
Variables and data sources	Detailed descriptive variables were captured, including co-medications and comorbidities. Unadjusted cumulative incidences and rates for the safety outcomes of interest were calculated.
Results	Among first-time users of rivaroxaban or SOC, the proportion of males were 50.7% and 55.7%, and median age was 71 years and 73 years, respectively. For both groups, the main indication was SPAF. Very few ACS patients were captured in this study but those that were tended to have more comorbidities. Medical histories of intracranial and urogenital bleeding were similar between the rivaroxaban and SOC groups, while gastrointestinal bleeding was more frequent in the SOC group compared with the rivaroxaban group, as were a history of ischaemic stroke, transient ischaemic attack, myocardial infarction and revascularization. Conversely, a history of VTE was more frequent in the rivaroxaban group than the SOC group. For the SPAF cohort, the unadjusted incidences of intracranial haemorrhage and all-cause death were lower with rivaroxaban than with SOC, whilst the incidences of gastrointestinal and urogenital bleeding were lower with SOC than with rivaroxaban. For the VTE cohort, the incidences of intracranial, gastrointestinal, and urogenital bleeding, and all-cause death were lower or similar with rivaroxaban than with SOC, while the rates only remained lower with rivaroxaban versus SOC for intracranial bleeding.
Discussion	Uptake of rivaroxaban increased over time. Based on available data, observed patterns of rivaroxaban use were largely in accordance with label recommendations for the respective indications. This interim report captured only the beginning of the ACS indication, therefore few patients were identified. The posology and outcomes presented a mixed picture; however, this might reflect the fact that the indication was not well-defined and that this cohort is very ill. Although the results in terms of risk for the different types of bleeding considered varied, these should be interpreted with caution and may differ from the final analysis, once

	adjustments for confounders have been performed.
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