Title: A pharmacoepidemiological study of rivaroxaban use and potential adverse outcomes in routine clinical practice in Sweden

Progress Report - EUPAS9895

This PASS category 1 study is being conducted using secondary data from Swedish Data Sources (Swedish Drug Register, the national Swedish Patient Register and the national Cause of Death Register and the LISA Register), maintained by the national Board of Health and Welfare in Sweden. This study is conducted in collaboration with Leif Friberg, MD, PhD, Friberg Research AB, Sweden, a member of ENCePP. The primary objective of this prospective cohort study is to characterize the drug utilization, safety and effectiveness of rivaroxaban in approved indications under clinical practice conditions. The study is currently ongoing.

Results from the second interim report for the cohorts accrued from 09 Dec 2011 to 31 Dec 2016 included baseline characteristics of new users of rivaroxaban and warfarin with information on prior medical history, comorbidities, comedications, and unadjusted incidence rates of bleeding, were submitted to EMA in Q4/2017.

In total, 50,104 first-time users of rivaroxaban and 116,812 first-time users of SOC in the comparison group had been identified. Of all the exposed patients according to index drug definition, 88% (44,424/50,372) and 40% (114,133/282,531) were naïve users (no use of any oral anticoagulant) of rivaroxaban and SOC, respectively.

Although the proportion of patients for each cohort differed, the most common indication in first-time users of rivaroxaban or SOC was SPAF (34% or 53% of patients, respectively), followed by VTE treatment (21% and 15%, respectively). The proportion of patients with TKR/THR was much higher in the rivaroxaban cohort than in the SOC cohort (16% vs 0.1%). Only 55 (0.1%) rivaroxaban users could be assigned to the ACS indication. In first time users of rivaroxaban, 0.1% (n=61), 23.5% (n=11,756), 30.9% (n=15,460), 45.6% (n=22,827), were prescribed an initial daily dose of 2.5 mg, 10 mg, 15 mg, 20 mg, respectively. Thus the majority of patients were prescribed the 20 mg dose.

Among the first-time naïve users the median age was 71 years in the rivaroxaban cohort and 73 years in the SOC cohort, 51% and 56% of the cohorts were male, respectively. Uptake of rivaroxaban increased over time (e.g. there were only 4% rivaroxaban users in the first year of study going up to ~30% by 2016), whereas uptake of SOC has decreased over time (30% in 2012 to 6% in 2016).

The median CHA2DS2VASc score were similar between the rivaroxaban group and the SOC group with SPAF (overall median CHA2DS2VASc score of 3 with IQR of 2-5). Overall, the proportions of patients at different levels of bleeding risk were similar between cohorts. Almost one third of all users had a HAS-BLED score of 3 and above indicating a high risk of bleeding. Assessment of eGFR status in the 12 months prior to the index date suggested that the majority of patients had normal or near normal renal function (99% for rivaroxaban and 97% for SOC users). More patients in the SOC cohort were moderately to severely impaired.

During the current reporting period, the investigator did not have access to any new data releases. Nevertheless, he has already requested the last and final data release to the national Board of Health and Welfare in Sweden, which will capture information from the national registers up until 31 Dec 2018. It is estimated this dataset will be available for analysis by Aug/Sept 2019, at the earliest.

Study finalization is estimated for 2020.