Abstract Final Report - EUPAS9977

Note: The study report is under the PRAC review and it will be posted as soon as the review is complete and the procedure is closed.

Title
An Observational Post-authorization Safety Specialist Cohort Event Monitoring Study (SCEM) to monitor the Safety and Utilization of rivaroxaban (XARELTO®) initiated in secondary care for the prevention of atherothrombotic events in patients who have had acute coronary syndrome (ACS) in England and Wales (The ROSE-ACS study).

Keywords
Rivaroxaban – Post-marketing – Safety – SCEM – ROSE-ACS

Rationale and background
Rivaroxaban 2.5mg twice daily, co-administered with daily dose of 75-100mg acetylsalicylic acid (ASA) alone or with ASA plus daily dose of 75mg clopidogrel or standard daily dose of ticlopidine, is indicated for the prevention of atherothrombotic events in adult patients after an ACS with elevated cardiac biomarkers in the EU.

Research question and objectives
The primary objective was to quantify the cumulative incidence of major bleeding according to the TIMI classification occurring during the study period, overall and stratified by intracranial, gastrointestinal and urogenital sites. In addition there were several secondary and exploratory objectives aimed at understanding the patient population prescribed rivaroxaban in combination with standard oral antiplatelet therapy for ACS including drug utilisation characteristics as well as describing changes in the health profile of patients over the course of the study and the risk of other major and minor bleeds and other events of interest.

Study design
An observational, population-based cohort design of two cohorts (rivaroxaban and a contextual cohort of patients receiving the current standard treatment of care; dual antiplatelet therapy) with data collection at start of treatment with rivaroxaban or contextual medication (index date) and 12-weeks post-index date.

Setting
Secondary care hospital setting in England and Wales.

Subjects and study size, including dropouts
Six hundred and ninety-nine patients have provided consent to participate in the study within the period from September 2015 to October 2018. Forty-seven patients were subsequently found to be ineligible for participation; 33 incorrectly identified, 10 had insufficient clinical information, and four patients were withdrawn. Baseline and Outcome Data case report forms (CRFs) were provided for 652 (93.3%) patients of which 528 (81.0%) were prescribed standard oral antiplatelet

combination therapy alone i.e. the contextual cohort, and 124 (19.0%) were prescribed rivaroxaban in combination with standard oral antiplatelet therapy.

Variables and data sources
Patient data were derived by healthcare professionals from medical charts at index date and 12-weeks post-index date.

Results
Participants
A total of 47 HCPs from 26 sites recruited 652 evaluable patients (124 rivaroxaban and 528 contextual) to the study.

Descriptive data
The majority of both rivaroxaban and contextual cohorts were male (83.1% and 75.2% respectively) and overall, the rivaroxaban cohort tended to be slightly younger than the contextual cohort (mean age 60.2 vs. 64.3 years). In both treatment cohorts females were older than males (mean age: rivaroxaban 61.1 vs. 60.0 years; contextual 68.2 vs. 63.0 years). The majority of patients were treated for STEMI in the rivaroxaban cohort (51.6%) and NSTEMI (56.6%) in the contextual cohort.

Patient general health characteristics were broadly similar between the rivaroxaban and contextual cohorts. The majority of patients had their treatment initiation in the inpatient setting however in the rivaroxaban cohort, patients were most frequently initiated on rivaroxaban within three days of being admitted (82.3%) whereas in the contextual cohort 69.7% were initiated treatment the same day of admission.

Outcomes
The cumulative incidence of major bleeding according to the TIMI classification of non-CABG Related Bleeding was 0.8% (n=1) in the rivaroxaban cohort and 0.9% (n=5) in the contextual cohort. In the rivaroxaban cohort, the major bleed occurred within the gastrointestinal site. In the contextual cohort, four of the major bleeds occurred within the gastrointestinal site (cumulative incidence 0.8%) and one occurred in another site (0.2%). No bleeding events were reported within urogenital or intracranial sites in either of the cohorts.

Deaths
Three (2.4%) deaths occurred on treatment in the rivaroxaban cohort and eight (1.5%) occurred in the contextual cohort. For both cohorts, all causes of death (where specified) were cardiac related.

Discussion
The ROSE-ACS study shows that rivaroxaban is largely being prescribed to populations in accordance with prescribing recommendations and national clinical guidelines. In terms of the primary outcome risk of major bleeding, the numbers of bleeds in the rivaroxaban cohort which fulfilled the TIMI definition of non-CABG related major bleeding were low (<1%). However, interpretation of the results needs to consider the small sample size of patients treated with rivaroxaban due to low usage in ACS. The SCEM design provides a framework suitable to evaluate the safety of newly marketed medicines in secondary care setting.

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