Abstract: Final study results - EUPAS15961

Title

An observational post-authorization Modified Prescription-Event Monitoring (M-PEM) safety study to monitor the safety and utilization of rivaroxaban (XARELTO®) for the prevention of stroke in patients with AF, treatment of DVT and PE, and prevention of recurrent DVT and PE following an acute DVT in the primary care setting in England, extended to include Acute Coronary Syndrome patients.

Primary author: Sandeep Dhanda- Drug Safety Research Unit (DSRU), Southampton, UK

Keywords

Rivaroxaban- Observational- Cohort- Safety- Utilisation

Rationale and background

Rivaroxaban (XARELTO®) is a highly selective direct factor Xa inhibitor. This post authorisation safety study (PASS) was carried out as part of a Risk Management Plan for rivaroxaban.

Research question and objectives

The primary objective was to quantify the cumulative incidence of major haemorrhage within gastrointestinal, urogenital and intracranial sites among rivaroxaban treated patients followed for up to 12 months.

Secondary and exploratory objectives aimed to explore the prevalence of non-clinical reasons for prescribing, prognostic and clinical risk factors for haemorrhage, changes in patient health profile and the risk of non-major bleeding events.

Study design

An observational cohort study using a M-PEM design.

Setting

Primary care in England.

Subjects and study size, including dropouts

The cohort was identified from dispensed rivaroxaban prescriptions from January 2012 - June 2016. GPs were contacted and asked to recruit patients into the study. The total evaluable cohort comprised of 17546 patients, with approximately an equal proportion of males and females.

Variables and data sources

Information on drug utilisation, relevant past medical history and events was requested from general practitioners at ≥3, and ≥12 months after the first rivaroxaban prescription issued for each patient.

Results

Baseline characteristics:

Stroke prevention in atrial fibrillation (AF) was the most frequent indication for prescribing (58.3%), followed by DVT/PE (34.0%). Patients in the DVT/PE cohort were on average younger than those with AF. The ACS indication group contained very few patients (0.2%), and the "Mixed", "Other" and "Not specified" indications contributed to 1.8%, 3.8% and 1.9% of the cohort, respectively.

The prevalence of prior bleeding was higher in the AF cohort as compared to DVT/PE (3.1% vs. 2.2%), but was highest in the "Mixed" group (5.0%). Prior history of CVA/TIA was most common for AF patients (19.8%).

Outcomes:

For all indications, the cumulative (twelve-month) incidence of major bleeding within gastrointestinal, urogenital and intracranial sites was 1.0% (n=168), 0.2% (n=34), and 0.3% (n=56), respectively. The cumulative incidence for clinically relevant non-major bleeds (CRNM), major bleeds (all), and a composite (major plus CRNM) was 4.7% (n=805), 2.0% (n=344), and 6.7% (n=1139), respectively.

After stratifying by indication, the cumulative incidence of major bleeding (inclusive of gastrointestinal, urogenital and intracranial) was higher in the AF group as compared to DVT/PE (1.7% vs. 1.2%).

In total, 1537 patients (8.8%) died during the twelve-month observation period and 1099 of these deaths (71.5%) occurred on treatment. Proportion of deaths were similar between AF and DVT/PE cohorts.

Discussion and conclusion

Rivaroxaban is largely being prescribed in accordance with prescribing recommendations in primary care. The estimates of risk of major bleeding at any specific site in the AF and DVT/PE rivaroxaban user populations are generally in line with prior knowledge based on clinical trial and observational data. This study is part of a broader literature on the safety of rivaroxaban and any conclusions on safety should be put into context with results from other post-marketing studies.

Marketing Authorisation Holder(s)

Bayer AG, 51368, Leverkusen, Germany

Names and affiliations of principal investigators

SAW Shakir MB ChB LRCP&S FRCP FFPM FISPE MRCGP, Director

DSRU, Bursledon Hall, Southampton SO31 1AA, UK