Adverse drug reactions (ADRs) result in approximately 200,000 deaths per year and contribute to about 5% of all hospital admissions, in Europe.\(^1\)

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### INTRODUCTION

Adverse drug reactions (ADRs) result in approximately 200,000 deaths per year and contribute to about 5% of all hospital admissions, in Europe.\(^1\)

The efficacy of antithrombotic medications such as aspirin may vary between patients and alternative medications need to be identified. Novel oral anticoagulants (NOACs) provide alternative options for thromboprophylaxis.

#### AIMS

- To conduct a comparative analysis of ADRs reported for aspirin and ADRs reported for the NOACs as documented in pharmacovigilance (PV) reports
- To observe ADRs following the use of aspirin and NOACs in the Maltese population and compare them to ADRs from PV reports
- To identify studies on the use of NOACs in PAD
- To analyse consumption trends for NOACs.

### METHOD

1. **Individual Case Safety Reports (ICSRs)** from Eudravigilance were used to compare fifteen ADRs listed as commonly occurring in the Summaries of Product Characteristics, for aspirin and the three NOACs: apixaban, dabigatran and rivaroxaban. ADRs reported between 2013 and 2017 were used for the study.

2. A questionnaire was developed to collect information related to ADRs encountered by patients while taking aspirin or NOACs. Fifty patients were recruited (25 taking aspirin, 25 taking rivaroxaban).

3. Documented ADRs from PV reports (ICSRs) were compared to patient reported ADRs in the questionnaire.

4. A literature search was carried out to identify studies on the use of NOACs in patients with peripheral artery disease (PAD). The search for articles was conducted until April 2018.

5. The consumption trends of NOACs for approved indications were evaluated from literature.

### RESULTS

- For the fifteen ADRs analysed, 51,391 ICSRs were reported to Eudravigilance, with bleeding-related ADRs (n=38,826) being the most frequently reported ADRs.
- Gastrointestinal bleeding (n=25,892) was the most frequently reported ADR for rivaroxaban (n=12,974), aspirin (n=5,855), dabigatran (n=5,321), and apixaban (n=1,742).
- Reported ADRs were highest for rivaroxaban (n=24,832). Consumption trends show that rivaroxaban is the most used NOAC.
- Aspirin, apixaban, dabigatran and rivaroxaban differ with regards to the safety profile. For all fifteen ADRs investigated, statistically significant differences were observed between reported cases of ADRs for the four medications.
- Thirty-six patients (aspirin=18 patients, rivaroxaban=18 patients) who completed the questionnaire reported at least one ADR. Bleeding-related ADRs were least reported by patients (aspirin=11 ADRs, rivaroxaban=4 ADRs).
- Eight studies analysing the use of NOACs in PAD patients were identified. Two studies on PAD showed that when added to aspirin, NOACs demonstrated favourable efficacy compared to aspirin alone.
- Consumption trends show that rivaroxaban is the most commonly used NOAC.

### CONCLUSION

- Bleeding-related ADRs were highest in PV reports and the lowest reported in questionnaires, suggestive of under-reporting of ADRs considered as minor or less serious by patients. Results reflect a bias on the reporting of ADRs to PV databases.
- High numbers of reported ADRs for rivaroxaban compared to dabigatran and apixaban are possibly related to consumption trends.
- Differences in reported ADRs could be due to differences in consumption trends, differences in safety profiles of medication or reporting bias.
- ADRs are more likely to be reported for novel medications such as NOACs, for which clinical experience may be limited when compared to conventional drugs such as aspirin.
- NOACs may be used in patients in whom other treatment options are not effective or causing considerable ADRs.
- More data on the safety and efficacy of NOACs is necessary to help determine the risk-benefit ratio of therapy.