Science For A Better Life

Clinical Study Synopsis

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The study listed may include approved and non-approved formulations or treatment regimens. Data may differ from published or presented data and are a reflection of the limited information provided here. The results from a single trial need to be considered in the context of the totality of the available clinical research results for a drug. The results from a single study may not reflect the overall results for a drug.

Title	PROTECT-AF: A Post-marketing Retrospective nOn-interventional study using naTionwide registries and electronic medical records to investigate the real-life Effectiveness and major bleeding Complications of oral anTicoagulants in Norwegian non-valvular Atrial Fibrillation patients.
Keywords	
Rationale and background	Non-vitamin K antagonist oral anticoagulants (NOACs) are approved for the prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF) as they reduce the risk of these events. However, the anticoagulant effect of the drugs must be balanced against a risk of bleeding complications especially in patients with renal impairment and elderly who represent a large group of those affected by NVAF
Research question and objectives	This population-based study will assess the effectiveness and safety of NOACs (rivaroxaban, dabigatran and apixaban compared to warfarin in OAC naïve NVAF patients in Norway. In addition, this study will serve as a pilot project to evaluate the ethical and operational feasibility as well as the usefulness of linking the EMR data to the Norwegian Health Registers. Primary objective: to assess the incidence rates of: a. ischemic stroke (effectiveness) b. intracranial hemorrhage (safety) in OAC naïve NVAF patients who are dispensed individual NOACs for the first time and compare with the corresponding rates in OAC naïve users of warfarin in a propensity score matched population. Secondary objectives • To assess the incidence rates of: • overall stroke (ischemic, hemorrhagic, other unspecified) and systemic embolism outcomes; • myocardial infarction; • all-cause mortality;

	• major bleeding as defined by ISTH and the Cunningham algorithm (in a sub-set of patients; cohort 2) in OAC naïve NVAF patients who are dispensed individual NOACs and compare with the corresponding rates in OAC naïve users of warfarin in the overall population and separately for the elderly and renally impaired patient using a propensity score matched population. • To describe and compare demographic and clinical characteristics (age, gender, CHA_2DS_2-VASc and HAS-BLED score, bleeding history, concomitant medications and co-morbidities) as well as drug utilization patterns of NVAF patients who initiated an OAC (NOACs and warfarin) in the study period. Several exploratory objectives aim to assess: • differences in characteristics of NVAF patients receiving OACs or not • impact of adherence to NOACs on rates of ischemic stroke and bleeding • patient characteristics of NVAF patients receiving standard vs. reduced dose of NOACs and corresponding rates of ischemic stroke and bleeding in these sub-groups validate data on indications and outcomes derived from the national registers using Electronic Medical Records (EMR) available for a regional sub-set of patients (cohort 2).
Study Design	This study will be a population-based retrospective cohort study on de-identified individual-level data extracted from national registers and EMRs in Norway. It will be based on two partly overlapping cohorts of patients, one utilizing only nation-wide health registers (cohort 1) and one cohort based on EMR data from selected hospitals in Norway combined with the registry data (cohort 2).
Setting	The study will be undertaken in Norway and will comprise all adult patients with NVAF who initiated treatment with either a NOAC or warfarin during the study period for the first time (OAC naïve

	first-time users). Study endpoints, discontinuation, switch to another OAC, death or end of study period will serve as censoring criteria.
Subjects and Study Size, including dropouts	The study population will comprise all adult OAC naïve NVAF patients in Norway who filled a prescription for an OAC (rivaroxaban, apixaban, dabigatran, warfarin) in the study period, defined as from 1 January 2014 to 30 June 2018 (or later depending on availability of data). Based on the information regarding number of patients receiving listed drugs in the country, the sample size for the study will be approximately 70,000 patients.
Variables and Data sources	Norwegian Patient Register, Norwegian Prescription Database, and Electronic Medical Records from local hostials.
Results	None. Study terminated prior to data collection and data analysis.
Discussion	None. Study terminated prior to data collection and data analysis.
Marketing Authorisation Holder(s)	Bayer AG Muellerstr. 173 13353 Berlin Germany
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