Rivaroxaban real world effectiveness in patients with atrial fibrillation (GUARDIAN)

First published: 18/12/2025

Last updated: 28/09/2026

Study Finalised

Administrative details

EU PAS number

EUPAS1000000869

Study ID

1000000869

DARWIN EU® study

No

Study countries

Bosnia and Herzegovina

Serbia

Study description

Atrial fibrillation is the most common sustained cardiac arrhythmia in adults and is associated with substantial morbidity and mortality, portending significant

burden to patients, societal health and health economy. The currently estimated prevalence of AF in adults is between 2 % and 4 %, and a 2,3-fold rise is expected, owing to extended longevity in the general population and intensifying search for undiagnosed atrial fibrillation (AF). When AF is undetected or untreated, it can lead to serious complications, the most important is creation of blood clots that can lead to stroke. Overall AF increases the risk of stroke five-fold. Oral anticoagulants (OAC) represent the cornerstone therapy in stroke prevention. Rivaroxaban is one of four Non-Vitamin K Antagonist Oral Anticoagulants (NOAC) that have been approved for the reduction of stroke risk and systemic embolism in patients with AF and first in the class that directly inhibits both free and clot-bound Factor Xa and prevents the formation of new clots and the extension of existing clots. Non-interventional study with Krka's rivaroxaban evaluates its real-world effectiveness in heterogeneous population with atrial fibrillation and variety of risk factors. The study provides the therapeutic data, reflecting actual clinical aspects in the field of treatment with rivaroxaban and its role and value in improving patients' outcomes in treatment of AF.

Study status

Finalised

Research institutions and networks

Institutions

University Clinical Center of Serbia (UCCS)

Serbia

First published: 01/02/2024

Last updated: 19/04/2024

Institution | Hospital/Clinic/Other health care facility

Zenica Cantonal Hospital

Contact details

Study institution contact

Aljaž Kranjc aljaz.kranjc@krka.biz

Study contact

aljaz.kranjc@krka.biz

Primary lead investigator

Tatjana Potpara

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/05/2022

Actual: 25/05/2022

Study start date

Planned: 01/09/2022

Actual: 01/09/2022

Data analysis start date

Planned: 01/01/2025

Actual: 27/01/2025

Date of final study report

Planned: 01/07/2025

Actual: 21/11/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Representative offices or companies of Krka d.d., Novo mesto who participated in the study.

Study protocol

NIS_Guardian_protocol_summary.pdf (256.62 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Evaluation of patient-reported outcomes

Safety study (incl. comparative)

Data collection methods:

Primary data collection

Study design:

Observational, prospective, international, multicentre, non-interventional study. Only patients, who would be otherwise also treated with Krka’s rivaroxaban in line with local regular clinical practice were included in the study. Observation of patients lasted 12±1 month, divided in 4 data captures.

Main study objective:

Provide therapeutic data about effectiveness of Krka’s rivaroxaban across the broad range of patient risk profiles in routine clinical practice and to provide overview of the outcomes associated with therapy and factors influencing its use in the management of stroke prophylaxis in AF patients.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

This is an international, non-interventional, observational, prospective, multicentre study evaluating the effectiveness and safety of Krka’s rivaroxaban in patients with AF according to the investigator’s consideration and in compliance with indications stated in SmPC of Krka’s rivaroxaban. Only patients, who would be otherwise also treated with Krka’s rivaroxaban in local regular clinical practice, will be enrolled in this non-interventional study. The decision to prescribe Krka’s rivaroxaban is at the sole discretion of the treating investigator, including dose and duration of Krka’s rivaroxaban therapy.

Study drug and medical condition

Medicinal product name, other

Xerdoxo®

Study drug International non-proprietary name (INN) or common name

RIVAROXABAN

Anatomical Therapeutic Chemical (ATC) code

(B01AF01) rivaroxaban

rivaroxaban

Medical condition to be studied

Atrial fibrillation

Population studied

Short description of the study population

Patients with diagnosed non-valvular atrial fibrillation (NVAF) who were indicated for treatment with Krka’s rivaroxaban according to the valid SmPC. The patients could have been either naïve (patients who had never taken anticoagulants before) or patients that were already treated with anticoagulants (with exception of rivaroxaban). In the study were included patients who agreed with informed consent form and consent for statistical evaluation of personal data. Only patients who would also otherwise be treated with Krka’s rivaroxaban in local regular clinical practice were enrolled in the study.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Study design details

Setting

Routine clinical practice

Outcomes

Primary outcomes:

• Assessing the incidence of major bleeding events in the observed study period.

• Assessing the incidence of stroke and/or embolism mortality in the observed study period.

• Assessing the incidence of treatment-emergent adverse reactions in the observed study period.

Secondary outcomes: Includes 18 additional items. At the baseline this includes the assessment of the patient profiles, risk factors (sex, age, BMI, smoking habits, alcohol consumption), proportions of newly diagnosed patients, proportion of patients with comorbidities, evaluation of CHA2DS2-VASc score, evaluation of HAS-BLED score, proportion of patients previously treated with anticoagulants (except rivaroxaban) and proportion of treatment naïve patients. Secondary outcomes at each data capture include the assessment of incidence of symptomatic thromboembolic events (stroke, TIA and systemic embolism or myocardial infarction), the incidence of major bleeding events (fatal bleeding, symptomatic bleeding in a critical area or organ, or a bleeding caused by a fall of haemoglobin level of 1.24 mmol/l (20g/L) or more, or need for transfusion of 2 or more units of packed red blood cells or whole blood), the incidence of non-major bleeding events (any bleeding event that does not meet the criteria for major bleeding event), proportion of patients who need additional treatment of AF besides rivaroxaban, incidence of stroke and/or embolism mortality, incidence of treatment-emergent adverse reactions, evaluation of patient’s satisfaction to Krka’s rivaroxaban therapy in comparison to previous anticoagulant therapy, patient’s satisfaction with dosing regimen of Krka’s

rivaroxaban patient’s and investigator’s general satisfaction to Krka’s rivaroxaban therapy, evaluation of reasons for discontinuation of treatment and the incidence of all-cause mortality marked as either vascular or non-vascular.

Data analysis plan

The study characteristics of the protocol were entered into electronic data capture system - the eCRF application. All data and clinical information were collected in accordance with the country specific privacy laws, Helsinki declaration, protocol and regular clinical practice. Corrections made in eCRF by the investigator were captured in audit trail log. In case of missing, misleading or incomplete data during the study conductance, the monitor raised queries. These queries were forwarded to the investigator for clarification. Only the investigator or authorized study personnel were permitted to make data changes or corrections. Summary statistics consists of the number of patients/observations, frequencies and corresponding percentages for categorical variables, and of the number of patients/observations, mean, median, standard deviation, minimum and maximum, first and third quartile for numeric variables. Some variables (numeric discrete variables with few possible values) are summarized both as categorical variables and as numeric variables. For inferential assessment of proportions, the two-sided “equal-tails” Clopper-Pearson exact 95% - confidence interval will be employed. For the assessment of means and mean differences, the standard 95%-confidence interval for the mean (with unknown variance) based on the limiting distribution of the standardized sample mean will be employed.

Summary results

Part of separate document “Summary of final report”.

Documents

Abstract of study report

NIS Guardian_summary of final report_V3.pdf (550.64 KB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Non-interventional study

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

No

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes