Safety clinical outcomes associated with the use of Idarucizumab for severe bleeding/emergency surgery: an observational population based study (Idarucizumab use)

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Study Finalised

Administrative details

EU PAS number

EUPAS45385

Study ID

45386

DARWIN EU® study

No

Study countries

☐ Italy

Study description

Background and Rationale The European Medicines Agency (EMA) approved a new monoclonal antibody called idarucizumab, a reversal agent for dabigatran. Findings from the pivotal trial (RE-VERSE trial) showed that idarucizumab reversed the anticoagulant effect of dabigatran in 98% of treated individuals. However, some case reports and case series reported potential rebound effect in dabigatran levels after an initial dose of the drug. So far, evidence on effectiveness and safety of idarucizumab in clinical practice is still limited. Therefore, new real-world studies are warranted to assess the relationship between idarucizumab use and safety clinical outcomes (i.e, mortality and re-hospitalization). Objectives • The risk of hospital mortality among idarucizumab treated individuals compared to non-treated individuals. • The length of hospitalization among idarucizumab treated individuals compared to non-treated individuals. • The risk of 30 days all-cause re-hospitalization among idarucizumab treated individuals compared to non-treated individuals. Study Design This will be a retrospective cohort study based on Healthcare administrative database (HAD). Methods • Baseline demographic and clinical characteristics will be reported and compared across exposure cohorts. • The relationship between idarucizumab status and in-hospital mortality will be estimated by using univariate and multivariate logistic regression model. • The relationship between idarucizumab status and re-hospitalization, within 30 days, for any reasons will be estimated by using a Cox proportional hazard model with competing risk with death as the competing risk factor. • The relationship between idarucizumab status and length of hospital stay will be estimated by using a general linear regression model with negative binomial distribution.

Study status

Finalised

Research institutions and networks

Institutions

Agenzia regionale di sanità della Toscana (ARS)

Italy

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Institution | EU Institution/Body/Agency | ENCePP partner

Contact details

Study institution contact

Rosa Gini rosa.gini@ars.toscana.it

Study contact

rosa.gini@ars.toscana.it

Primary lead investigator

Rosa Gini

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 05/03/2021

Actual: 05/03/2021

Study start date
Planned: 13/05/2021

Actual: 13/05/2021

Date of final study report
Planned: 15/12/2021

Actual: 15/12/2021

Sources of funding

- Other

More details on funding

Self-funded by ARS

Study protocol

Safety clinical outcomes associated with the use of Idarucizumab.pdf(485.86 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:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To describe (1) the risk of hospital mortality among idarucizumab treated individuals compared to non-treated individuals, (2) the length of hospitalization among idarucizumab treated individuals compared to non-treated individuals, (3) the risk of 30 days all-cause re-hospitalization among idarucizumab treated individuals compared to non-treated individuals

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AE07) dabigatran etexilate

dabigatran etexilate

(B01AF01) rivaroxaban

rivaroxaban

(B01AF02) apixaban

apixaban

(B01AF03) edoxaban

edoxaban

(V03AB37) idarucizumab

idarucizumab

Population studied

Short description of the study population

The study population will include adults (≥45 years old) under dabigatran treatment (ATC code: B01AE07) with emergency department access/hospitalization within the period January 1st, 2015 and December 31st, 2020. The date of emergency department access/hospitalization will be considered as index date to define the patient's clinical characteristics and exposure assessment.

Inclusion criteria

• All individuals aged ≥ 45 years;

• Actively registered in the demographic registry at least one year prior to the index date;

• Emergency department access/hospitalization due to life-threatening bleeding or due to surgery or other invasive procedures that could not be delayed and

for which normal haemostasis was required

Exclusion criteria

• Use of dabigatran less than 90 days before the index date;

• Patients with less than 2 years of lookback prior the index date.

Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

2000

Study design details

Outcomes

To describe (1) risk of hospital mortality among idarucizumab treated individuals compared to untreated individuals, (2) length of hospitalization among idarucizumab treated individuals compared to untreated individuals, (3) thirty-day all-cause re-hospitalization risk in idarucizumab treated and untreated individuals

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Data analysis plan

• The relationship between idarucizumab status and in-hospital mortality will be estimated by using univariate and multivariate logistic regression model. The results will be expressed as Odds Ratio (OR) with 95% confidence intervals (95%CI) • The relationship between idarucizumab status and re-hospitalization, within 30 days, for any reasons will be estimated by using a Cox proportional

hazard model with competing risk with death as the competing risk factor. Results will be expressed as unadjusted and adjusted Hazard Ratio (HR) with 95% confidence intervals (95%CI) • The relationship between idarucizumab status and length of hospital stay will be estimated by using a general linear regression model with negative binomial distribution. The results will be expressed as Incidence Rate Ratio (IRR) with 95%CI

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 source(s)

ARS Toscana

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Other

Data sources (types), other

Demographic registry Hospital discharge records Emergency department records Outpatient care records Prescription claims database Database of

diseases - specific exemption codes from co-payment to health care

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No