

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

**First published:** 26/01/2022

**Last updated:** 02/07/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS45385

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### Study ID

45386

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### DARWIN EU® study

No

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### Study countries

 Italy

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## 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.

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## Study status

Finalised

## Research institutions and networks

## Institutions

### Agenzia regionale di sanità della Toscana (ARS Toscana)

 Italy

**First published:** 01/02/2024

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**Institution**

**EU Institution/Body/Agency**

**ENCePP partner**

## Contact details

### Study institution contact

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**Study contact**

[rosa.gini@ars.toscana.it](mailto: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

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**Study start date**

Planned: 13/05/2021

Actual: 13/05/2021

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**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

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

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**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

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**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 ( $\geq 45$  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  $\geq 45$  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.
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## Age groups

- Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
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## 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

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### Data sources (types)

[Administrative healthcare records \(e.g., claims\)](#)

[Drug dispensing/prescription data](#)

[Other](#)

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### 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

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### **Check completeness**

Unknown

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### **Check stability**

Unknown

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### **Check logical consistency**

Unknown

## Data characterisation

### **Data characterisation conducted**

No