

# Does metamizole cause less kidney injury than non-steroidal anti-inflammatory drugs when administered in combination with diuretics and antihypertensives? (Triple whammy with metamizole)

**First published:** 26/04/2023

**Last updated:** 15/04/2024

Study

Planned

## Administrative details

### EU PAS number

EUPAS104667

---

### Study ID

104941

---

### DARWIN EU® study

No

---

### Study countries

 Spain

---

## Study description

The term "triple whammy" (TW) corresponds to the concurrent use of diuretics, renin-angiotensin-aldosterone system inhibitors (RAASI) and non-steroidal anti-inflammatory drugs (NSAIDs). These therapeutic classes have an impact on kidney function in various ways, such as by causing hypovolemia and decreasing glomerular perfusion and thus filtration rate. The objective of this study is to compare the impact of the exposure to the TW combination that includes metamizole as compared to the TW that includes an NSAID in terms of risk of hospitalisation for AKI, need for renal replacement therapy (RRT) and all-cause mortality during hospitalisation. The difference between the TW that includes metamizole and that which includes an NSAID on the change in serum creatinine (sCr) and the estimated glomerular filtration rate (eGFR) during the first year after the beginning of the exposure to TW will also be analyzed.

---

## Study status

Planned

## Research institutions and networks

### Institutions

#### Navarre Health Service

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

**Last updated:** 01/02/2024

Institution

## Contact details

### **Study institution contact**

Dulce Maria Calvo Barbado [dulcemaria.calvo@autonoma.cat](mailto:dulcemaria.calvo@autonoma.cat)

Study contact

[dulcemaria.calvo@autonoma.cat](mailto:dulcemaria.calvo@autonoma.cat)

### **Primary lead investigator**

Dulce Maria Calvo Barbado

Primary lead investigator

## Study timelines

### **Date when funding contract was signed**

Planned: 18/11/2019

---

### **Study start date**

Planned: 01/05/2023

---

### **Data analysis start date**

Planned: 25/09/2023

---

### **Date of final study report**

Planned: 11/03/2024

## Sources of funding

- Other

## More details on funding

Government of Navarre

## 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 type:**

Non-interventional study

---

#### **Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

#### **Main study objective:**

to compare the impact of the exposure to the TW combination that includes metamizole as compared to the TW that includes an NSAID in terms of risk of hospitalisation for AKI

## Study Design

## **Non-interventional study design**

Case-control

# Study drug and medical condition

## **Anatomical Therapeutic Chemical (ATC) code**

(C03X) OTHER DIURETICS

OTHER DIURETICS

(C09C) ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs), PLAIN

ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs), PLAIN

(M01A) ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

(N02BA) Salicylic acid and derivatives

Salicylic acid and derivatives

---

## **Medical condition to be studied**

Acute kidney injury

# Population studied

## **Age groups**

- Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
  - Adults (65 to < 75 years)
  - Adults (75 to < 85 years)
  - Adults (85 years and over)
- 

## **Special population of interest**

Renal impaired

---

### **Estimated number of subjects**

50000

## Study design details

### **Outcomes**

hospitalization for AKI, Need for RRT during hospitalization due to AKI (analyzed in the participants who suffered hospitalization for AKI-cases) All-cause mortality during hospitalization (analyzed in the participants who suffered hospitalization for AKI-cases) Change in sCr and eGFR

---

### **Data analysis plan**

The comparison of categorical variables between cases and controls will be analyzed through the Chi-square test or Fisher's test, and in the case of quantitative variables through the t-Student or Mann-Whitney test. The association between the exposure and the risk of hospitalization due to AKI will be analyzed using conditional logistic regression models, adjusting for possible confounding factors. The adjusted Odds Ratio and 95% confidence interval will be estimated. Sensitivity analyses of the primary outcome restricting to cases and controls with eGFR or sCr data in the 12 months prior to the index date. A subgroup analysis of the risk of hospitalisation for AKI will be performed in: patients older than 75 year and patients with eGFR <60 mL/min

## 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), other

BIFAP Spain

---

### Data sources (types)

[Disease registry](#)

[Electronic healthcare records \(EHR\)](#)

[Other](#)

---

### Data sources (types), other

Case-control surveillance database

## 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