

# RISK OF AGRANULOCYTOSIS ASSOCIATED WITH THE USE OF DRUGS

**First published:** 07/05/2012

**Last updated:** 03/09/2024

Study

Planned

## Administrative details

### EU PAS number

EUPAS2548

---

### Study ID

10857

---

### DARWIN EU® study

No

---

### Study countries

 Spain

---

### Study description

The objective of this study is to estimate the risk of agranulocytosis associated with the use of drugs. Agranulocytosis is a serious condition, with an estimated incidence of 1.6:1 million to 7.0:1 million inhabitants per year.<sup>1,2</sup> Case fatality

is around 10%, but this may depend to a large extent on the availability of prompt antibiotic treatment. Almost all classes of medicines have been implicated in agranulocytosis. Since 1980, a case-control surveillance study of Agranulocytosis has been carried out in the metropolitan area of Barcelona. With the aim of identifying all cases of agranulocytosis occurring in the study population. Our centre maintains regular contact with a designated hematologist of all hospitals in the area. Potential cases are patients with a granulocyte count of  $<500/\text{mm}^3$ , or a total white series count of  $<3,000/\text{mm}^3$  in two consecutive counts, with a hemoglobin level of 10 g/dl and a platelet count of  $100,000/\text{mm}^3$ .

---

### Study status

Planned

## Research institutions and networks

### Institutions

#### Fundació Institut Català de Farmacologia (FICF)

 Spain

**First published:** 29/03/2010

**Last updated:** 17/09/2019

Institution

Outdated

Educational Institution

Hospital/Clinic/Other health care facility

Not-for-profit

ENCePP partner

## Bellvitge University Hospital

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

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

**Institution**

## University Hospital Vall d'Hebron (HUVH)

 Spain

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

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

**Institution**

**Educational Institution**

**Hospital/Clinic/Other health care facility**

## Clinical Pharmacology Department, Area del Medicament, Hospital Clínic de Barcelona

 Spain

**First published:** 29/03/2010

**Last updated:** 24/08/2023

**Institution**

**Hospital/Clinic/Other health care facility**

**ENCePP partner**

## Parc de Salut Mar Barcelona (PSMAR)

 Spain

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

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

**Institution**

Hospital/Clinic/Other health care facility

## Consorci Corporació Sanitària Parc Taulí

 Spain

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

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

**Institution**

Educational Institution

Hospital/Clinic/Other health care facility

## Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau – IIB Sant Pau

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

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

**Institution**

Hospital Universitari Vall d'Hebron Barcelona,  
Hospital de la Santa Creu i Sant Pau Barcelona,  
Hospital del Mar Barcelona, Hospital de Barcelona  
Barcelona, Fundació Hospital/Asil de Granollers


Granollers, Hospital de Mataró Mataró, Hospital  
Universitari Germans Trias i Pujol Badalona,  
Hospital de Terrassa Terrassa, Hospital  
Universitari de Bellvitge Bellvitge, Corporació  
Sanitària i Universitària Parc Taulí Sabadell

## Networks


### EUDRAGENE


 France

 Italy

 Netherlands

 Spain

 Sweden

 United Kingdom

**First published:** 04/06/2010

**Last updated:** 20/08/2024

**Network**

## Contact details

### Study institution contact

Luisa Ibáñez li@icf.uab.cat

**Study contact**

li@icf.uab.cat

**Primary lead investigator**

Joan-Ramon Laporte

**Primary lead investigator**

## Study timelines

**Date when funding contract was signed**

Planned: 01/01/1980

---

**Study start date**

Planned: 01/01/1980

---

**Data analysis start date**

Planned: 01/01/1986

---

**Date of final study report**

Planned: 31/07/2015

## Sources of funding

- Other

## More details on funding

Agencia Española del Medicamento

## 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:**

The main objective is to estimate the risk of Agranulocytosis associated to several drugs.

## Study Design

### **Non-interventional study design**

Case-control

## Study drug and medical condition

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

(N02) ANALGESICS

ANALGESICS

---

## **Medical condition to be studied**

Agranulocytosis

## Population studied

### **Age groups**

- Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)
  - 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)
- 

### **Estimated number of subjects**

1200

## Study design details

### **Outcomes**

Odds ratios are calculated after controlling for confounding by applying a multiple logistic regression model, including potential known confounders and drug terms. Case-fatality rate for drugs showing odds ratio values significantly higher than one, population attributable risks are calculated from the odds

ratio.

---

### **Data analysis plan**

The analysis is performed with an unconditional and conditional multiple logistic regression model. For increasing statistical power for risk estimation associated with drugs having a low prevalence of use, the analysis is done with all the cases for which information on drug exposures is available, and their respective controls of agranulocytosis. The model included sex, age, and interviewer as additional terms. Drug exposures are considered in different ways. The main analysis refers to any exposure during the week before the index day, this definition of exposure is decided after taking into account that for most of the cases of agranulocytosis, the time elapsed from injury of the bone marrow or of peripheral neutrophils to the appearance of the initial symptoms of infection is usually less than 7 days. The following 2 additional confirmatory analyses are performed: one, with the aim of exploring possible information bias, and the other, to evaluate protopathic bias.

## Documents

### **Study publications**

[Ibáñez L, Vidal X, Ballarín E, Laporte JR. Population-based drug-induced agranu...](#)

[Ibáñez L, Sabaté M, Ballarín E, Puig R, Vidal X, Laporte JR, Agranulocytosis an...](#)

[Ibanez L, Vidal X, Ballarín E, Laporte JR. Agranulocytosis associated with dipy...](#)

[Ibáñez L, Ballarín E, Vidal X, Laporte JR. Agranulocytosis associated with calc...](#)

[Ibáñez L, Ballarín E, Pérez E, Vidal X, Capellà D, Laporte JR. Agranulocytosis ...](#)

---

## 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)

[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