

# Impact of cardiovascular comorbidities on the effectiveness of bevacizumab in elderly patients with metastatic colorectal cancer (IRAZU)

**First published:** 12/12/2019

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Study

Ongoing

## Administrative details

### PURI

<https://redirect.ema.europa.eu/resource/41349>

### EU PAS number

EUPAS32748

### Study ID

41349

### DARWIN EU® study

No

## Study countries

☐ France

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## Study description

Colorectal cancer is the third most frequent cancer with a median age at diagnosis of 73 years. About 40% of cases evolve to a metastatic colorectal cancer (mCRC). The arrival of targeted therapies from 2005 in the therapeutic strategy of mCRC has participated to the improvement of overall survival for these patients. However, randomized controlled trials (RCTs) on mCRC suffer from an underrepresentation of elderly patients, while they represent the most part of mCRC patients. Despite this huge gap between the population included in RCTs and the population with mCRC, these RCTs are used to elaborate international guidelines. Owing to the mechanism of action of bevacizumab (angiogenesis inhibitor), cardiovascular adverse events such as heart failure, malignant hypertension, myocardial infarction, and venous and arterial thromboembolism are expected events, and frequently reported in RCTs. Despite the exclusion of patients with cardiovascular comorbidities from RCTs evaluating bevacizumab, the presence of cardiovascular comorbidities does not represent formal contraindications, but only precautions of use. Besides, there are no specific guidelines for the treatment of elderly patients, especially those with cardiovascular comorbidities, which are highly prevalent at mCRC diagnosis. To date, no data related to their impact on mCRC treatment by bevacizumab are available. This study aims to evaluate the impact of the presence of cardiovascular comorbidities on effectiveness and safety in elderly mCRC patients treated with bevacizumab. A cohort of mCRC patients aged  $\geq 65$  years at diagnosis, and treated with bevacizumab in first-line treatment will be identified between 2009 and 2015 using the French National Claims Database (SNDS). The primary endpoint will be defined as the occurrence of death from any cause at 36 months, and the secondary endpoints will be the occurrence of serious cardiovascular events during the follow-up.

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## Study status

Ongoing

## Research institutions and networks

### Institutions

#### Bordeaux University Hospital (CHU de Bordeaux)

☐ France

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

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**Institution**

Hospital/Clinic/Other health care facility

#### Bordeaux PharmacoSpi, University of Bordeaux

☐ France

**First published:** 07/02/2023

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**Institution**

Educational Institution

Hospital/Clinic/Other health care facility

Not-for-profit

ENCePP partner

#### Bordeaux university hospital Bordeaux, France

## Contact details

### Study institution contact

Pernelle Noize

Study contact

[pernelle.noize@chu-bordeaux.fr](mailto:pernelle.noize@chu-bordeaux.fr)

### Primary lead investigator

Amandine Gouverneur

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Actual: 04/07/2019

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### Study start date

Planned: 01/09/2020

Actual: 05/11/2020

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### Data analysis start date

Planned: 01/12/2020

Actual: 10/12/2020

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### Date of final study report

Planned: 31/12/2021

## Sources of funding

- Other

## More details on funding

Ministère des Solidarités et de la Santé - Direction Générale de l'Offre de Soins -  
PHRC-K 2018

## 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 type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Effectiveness study (incl. comparative)

**Main study objective:**

The main objective of this study is to evaluate the impact of the presence of cardiovascular comorbidities at baseline on 36-month overall survival in elderly mCRC patients treated with bevacizumab.

## Study Design

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

Cohort

## Study drug and medical condition

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

(L01XC07) bevacizumab

bevacizumab

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### **Medical condition to be studied**

Colorectal cancer metastatic

## Population studied

### **Age groups**

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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### **Estimated number of subjects**

16000

## Study design details

## Outcomes

Occurrence of death from any cause at 36 months. Occurrence of death from any cause at 12 and 24 months. Occurrence of each of the following serious cardiovascular event: heart failure, malignant hypertension and thromboembolic events (including myocardial infarction, venous and arterial thrombosis, stroke and pulmonary embolism) during the follow-up. Occurrence of a composite endpoint of serious cardiovascular events during the follow-up.

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## Data analysis plan

The probability of death will be evaluated at 12, 24 and 36 months using Kaplan-Meier analyses and will be compared across groups using the log rank test. The impact of cardiovascular comorbidities on 36-month risk of death and on the occurrence of serious cardiovascular events will be evaluated using time-dependent multivariable proportional hazards Cox regression models (for death) and Fine and Gray models taking into account death as a competing risk (for occurrence of cardiovascular events only). A sensitivity “on-treatment” analysis will be carried-out. The safety will be assessed between the first dispensing of bevacizumab and the date of the considered cardiovascular events (separately or combined) or the last dispensing of first-line bevacizumab during the follow-up whichever came first. All analyses will be stratified according to age at mCRC diagnosis: <75 versus  $\geq 75$  years old.

## Data management

### Data sources

#### Data sources (types)

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

### 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