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

First published: 12/12/2019

Last updated: 24/07/2024

Study Ongoing

Administrative details

EU PAS number

EUPAS32748

Study ID

41349

DARWIN EU® study

No

Study countries

☐ France

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 ≥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.

Study status

Ongoing

Research institutions and networks

Institutions

Bordeaux University Hospital (CHU de Bordeaux)

France

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Hospital/Clinic/Other health care facility

Bordeaux PharmacoEpi, University of Bordeaux

France

First published: 07/02/2023

Last updated: 08/02/2023

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 pernelle.noize@chu-bordeaux.fr

Study contact

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

Study start date

Planned: 01/09/2020

Actual: 05/11/2020

Data analysis start date

Planned: 01/12/2020

Actual: 10/12/2020

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

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
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

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)

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.

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 ≥75 years old.

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)

Administrative healthcare records (e.g., claims)

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