Retrospective cohort study to assess the increased risk of myelotoxicity due to the combined use of fluoropyrimidines and thiazides

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Study Finalised

Administrative details

EU PAS number

EUPAS1000000181

Study ID

1000000181

DARWIN EU® study

No

Study countries

☐ Spain

Study description

Retrospective cohort study to assess the increased risk of myelotoxicity due to the combined use of fluoropyrimidines and thiazides.

Study status

Finalised

Research institutions and networks

Institutions

Clinical Pharmacology Service, Puerta de Hierro-Majadahonda University Hospital (HUPHM)

Spain

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Institution | Educational Institution | Hospital/Clinic/Other health care facility

Contact details

Study institution contact

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Primary lead investigator

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Primary lead investigator

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Study timelines

Date when funding contract was signed
Planned: 21/03/2024

Actual: 21/03/2024

Study start date
Planned: 01/04/2024

Actual: 01/05/2024

Data analysis start date
Planned: 08/01/2025

Date of interim report, if expected
Planned: 15/01/2025

Date of final study report
Planned: 28/02/2025

Actual: 13/08/2025

Sources of funding

- No external funding

Study protocol

Mielotoxicidad fluoropirimidinas y tzd. V2 FINAL.pdf (204.62 KB)

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 topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

Retrospective cohort of patients treated with fluropyrimidines due to cancer in order to compare the incidence of mielotoxicity and other adverse events in patients thar are treated with thiazides or not.

Main study objective:

To compare the incidence of mielotoxicity of patients treated in combination with fluoropyrimidines and thiazides in comparision with patients not treated with thiazides.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

CAPECITABINE ACCORD

Medicinal product name, other

Tegafur

5-Fluorouracil

Hydrochlorothiazide

Bendroflumethiazide

Indapamide

Chlorthalidone

Study drug International non-proprietary name (INN) or common name

CAPECITABINE

HYDROCHLOROTHIAZIDE

INDAPAMIDE

OXALIPLATIN

Anatomical Therapeutic Chemical (ATC) code

(A) ALIMENTARY TRACT AND METABOLISM

ALIMENTARY TRACT AND METABOLISM

(C03AA01) bendroflumethiazide

bendroflumethiazide

(C03AA03) hydrochlorothiazide

hydrochlorothiazide

(C03BA11) indapamide

indapamide

(L01BC02) fluorouracil

fluorouracil

(L01BC03) tegafur

tegafur

(L01BC06) capecitabine

capecitabine

Medical condition to be studied

Anal cancer

Colon cancer

Chemotherapy

Population studied

Short description of the study population

Patients treated with capecitabine or capecitabine-oxaliplatin due to colorrectal/anal cancer

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Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Estimated number of subjects

192

Study design details

Setting

Patients treated in our hospital by the medical oncology department

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Comparators

Patients treated with thiazides and fluoropyrimidines versus treated only with fluoropyrimidines.

Outcomes

Myelotoxicity defined as: Anemia, leukopenia, neutropenia, lymphopenia and thrombocytopenia.
Clinical significance of those adverse events: febril neutropenia, hemorrhage, number of infections, oral mucositis and skin reactions

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Data analysis plan

Relative risk of mielotoxicity will be compared between both grups, those treated with thiazides and those not treated.

Summary results

We included 192 patients (mean age 68.6±13 years; 61.5% male); 37 (19.3%) were on thiazides at treatment start. Baseline characteristics, including chemotherapy type, did not differ between groups. Median follow-up was 125 days (IQR 75.8). Hemoglobin declined significantly in thiazide users at 1–3 months (-0.3 vs +0.11g/dL;p=0.006) and >6 months (-2.63 vs -0.75g/dL; p=0.002). Other hematologic parameters showed no significant differences. Myelotoxicity occurred in 83.8% of thiazide users vs 75.5% in controls (RR=1.11; 95%CI: 0.94–1.31;p=0.280).
No differences were seen in febrile neutropenia, mucositis, infections, or other AEs. Logistic regression did not identify any risk factor for myelotoxicity risk. Concomitant use of fluoropyrimidines and thiazides was not associated with higher myelotoxicity or adverse events. SmPC and drug-interaction warnings should be reconsidered.

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)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Not applicable