Metamizole and risk of hepatotoxicity –comparative cohort study of incidence of hepatic events in patients treated with metamizole vs. patients treated with paracetamol in IMS Disease Analyzer Germany between January 2009 and December 2018 (Metamizole and hepatotoxicity)

First published: 18/10/2019

Last updated: 02/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS31864

Study ID

31865

DARWIN EU® study

No

Study countries

☐ Germany

Study description

Metamizole is a medication with analgesic, antipyretic, spasmolytic, and weak anti-inflammatory effects, used for acute and chronic pain management, and in some countries, fever management. Cases of drug-induced liver injury (DILI) have been reported in association with metamizole treatment, however the evidence from epidemiological studies is very limited (one case-control only). This study aims to quantify the incidence of hepatic events in patients treated with metamizole compared to patients treated with paracetamol or NSAIDs (chosen as an active comparator).

Study status

Finalised

Research institutions and networks

Institutions

European Medicines Agency (EMA)

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Institution

Contact details

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Study contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/06/2018

Actual: 01/06/2018

Study start date

Planned: 01/01/2019

Actual: 01/04/2019

Data analysis start date

Planned: 15/04/2019

Actual: 15/06/2019

Date of final study report

Planned: 01/01/2020

Actual: 01/01/2020

Sources of funding

- EMA

Study protocol

Study-protocol -IMS DE-Metamizole_DILI 4 september 2019.pdf(233.46 KB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

This study aims to quantify the incidence of hepatic events in patients treated with metamizole compared to patients treated with paracetamol.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Comparative study

Study drug and medical condition

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

METAMIZOLE

Medical condition to be studied

Drug-induced liver injury

Population studied

Short description of the study population

The study focused on incident users of metamizole and paracetamol from 1 January 2009 to 31 December 2018.
Patients with less than 365 days of observation and those with a history of cancer, HIV, viral hepatitis, liver disease, or Budd-Chiari syndrome was excluded from the study.

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

Hepatic impaired

Estimated number of subjects

600000

Study design details

Outcomes

Drug-induced liver injury, classified as a composite outcome of various hepatic terms (see protocol). in case of sufficient data, we will analyse separately toxic liver disease (ICD 10 code K71), hepatic failure not elsewhere classified (ICD 10 code K72) and other hepatic events (ICD 10 codes K75-K76).

Data analysis plan

A comparative cohort will be created, where the relative risk will be calculated with the Cox Proportional Hazards models. all variables will be recorded at baseline and not integrated as time-dependent. The analysis will be adjusted for age (continuous), gender and the identified confounders that will show an effect on the risk estimate (significant association in univariate models and more than 10% change in risk estimate). Missing data will be dealt with through list-wise deletion (complete case analysis).

Documents

Study publications

Hedenmalm K, Pacurariu A, Slattery J, Kurz X, Candore G, Flynn R. Is there an i...

Data management

Data sources

Data source(s), other

IQVIA Disease Analyzer Germany

Data sources (types)

Electronic healthcare records (EHR)

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