DARWIN EU® - Characterisation of acute renal outcomes and diabetic complications among patients with concomitant use of metformin and iodinated contrast agents

First published: 03/07/2025

Last updated: 15/07/2025

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000662

Study ID

1000000662

DARWIN EU® study

Yes

Study countries

- [ ] Denmark
- [ ] Finland
- [ ] Spain

United Kingdom

Study description

Art.31 CHMP referral in 2016 on metformin and use in patients with reduced kidney function led to PI updates including introduction of a warning and interaction with concomitant use with iodinated agents for patients undergoing imaging procedures.
Based on the evidence reviewed in the PSUSA, it was considered premature to delete the warning and interaction in the metformin PIs, at this stage. PRAC suggested the possibility to conduct a RWD study to gather more data on this specific issue and understand better if further regulatory action would be deemed necessary

Study status

Ongoing

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution **Educational Institution** **ENCePP partner**

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

- [ ] Belgium
- [ ] Croatia
- [ ] Denmark
- [ ] Estonia
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Greece
- [ ] Hungary
- [ ] Italy
- [ ] Netherlands
- [ ] Norway
- [ ] Portugal
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom

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Last updated: 30/04/2025

Network

Contact details

Study institution contact

Natasha Yefimenko study@darwin-eu.org

Study contact

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Primary lead investigator

Wanning Wang

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 20/03/2025

Actual: 20/03/2025

Study start date

Planned: 26/06/2025

Actual: 26/06/2025

Date of final study report

Planned: 31/10/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P4_C1_004_Metformin_ICA_V3.0.pdf (677.72 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

Study type:

Non-interventional study

Scope of the study:

Disease epidemiology

Data collection methods:

Secondary use of data

Study design:

Retrospective cohort studies will be conducted using routinely collected health data from 4 databases.

Main study objective:

1. To characterise patients with type 2 diabetes initiating treatment of metformin in terms of:

a. Demographics (age, sex)

b. Recorded comorbidities

c. Recorded duration from first diabetes diagnosis

d. Previous procedures with ICA, including phenotyping

e. CKD stage (most recent in past year), including phenotyping

2. To characterise patients with type 2 diabetes with a first procedure requiring ICA with ongoing metformin use in terms of :

a. Demographics (age, sex)

b. Comorbidities

c. Recorded duration from first diabetes diagnosis

d. CKD stage

e. ICA type

f. Time from metformin initiation to first procedure requiring ICA

3. To quantify the occurrence of renal dysfunction and of acute diabetes decompensation among patients with type 2 diabetes with a first procedure requiring ICA during metformin use specifically:

a. AKI, including phenotyping

b. Lactic acidosis

c. Diabetic ketoacidosis

d. Change in eGFR and CKD status before and after date of first procedure requiring ICA

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name, other

Metformin, iodinated contrast agents

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

METFORMIN

Population studied

Short description of the study population

1) Cohort 1: Patients with type 2 diabetes initiating metformin.

2) Cohort 2: Patients with type 2 diabetes on metformin undergoing their first procedure requiring ICA.

Age groups

- **In utero**
- **Paediatric Population (< 18 years)**
  - Neonate
    - Preterm newborn infants (0 – 27 days)
    - Term newborn infants (0 – 27 days)
  - Infants and toddlers (28 days – 23 months)
  - Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)
- **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)

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 source(s)

The Information System for Research in Primary Care (SIDIAP)

Hospital District of Helsinki and Uusimaa patient cohort (FinOMOP)

Danish Health Data Registries

Clinical Practice Research Datalink (CPRD) GOLD

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

CDM version

https://ohdsi.github.io/CommonDataModel/index.html

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown