Risks and benefits of bisphosphonate use in patients with chronic kidney disease: a population-based cohort study

First published: 08/07/2015

Last updated: 13/02/2019

Study Finalised

Administrative details

EU PAS number

EUPAS10029

Study ID

28025

DARWIN EU® study

No

Study countries

Denmark

United Kingdom

Study description

AIMS: We aim to study, in chronic kidney disease (CKD) patients, the association between oral bisphosphonate (BP) use and:1.CKD progression (WP1), 2.fracture risk (WP2), 3.hypocalcemia/hypophosphoatemia and adverse events (WP3), and 4.bone mineral density (BMD)(WP4).DESIGN: Population-based cohort studies using routinely collected data.POPULATION: Participants aged 40 years or older, with CKD stage 3B or above (eGFR<45ml/min/1.73m2). Previous users of anti-osteoporosis medications and those with <2 years follow-up data available will be excluded.OUTCOMES: For WP1: CKD progression based on stage progression or requirement ofhaemodialysis/transplantation (primary outcome) and change in eGFR (secondary outcome). WP2: READ/OXMIS(CPRD) codes will be used to ascertain osteoporotic (all but face/skull/fingers/toes) fracture/s. WP3: ICD10/OPCS codes(HES) will be used to identify:1.acute kidney injury, 2.hospitalization for hypocalcemia/hypophosphataemia, and 3.upper gastro-intestinal events. WP4: annualized hip BMD % change.SAMPLE SIZE: According to feasibility counts from CPRD, the number of eligible participants is of 204,528, with 34,127 being BP users. These numbers would provide 90% power to detect as significant a =15% fracture reduction, a =10% increase in CKD progression and a =20% excess risk of adverse events associated with BP use. The Danish database includes >35,000 patients. We expect to identify at least 500 CKD patients defined as BP users matched 1:5 to 2,000 non-users, which would provide >80% power to detect as significant a >25% bone loss reduction.STATISTICAL ANALYSES: BP use will be introduced as a time-varying exposure. Cox regression stratified by propensity matched sets will be used to estimate the association between BP use and the study outcomes(WP1/2/3). Linear regression models will be fitted to study the association between BP use and hip BMD in CKD patients(WP4).

Study status

Finalised

Research institutions and networks

Institutions

National Perinatal Epidemiology Unit (NPEU), University of Oxford

United Kingdom

First published: 15/03/2010

Last updated: 19/03/2010

Institution | Outdated | Educational Institution | ENCePP partner

NA (database study]

Contact details

Study institution contact

Daniel Prieto-Alhambra

daniel.prietoalhambra@ndorms.ox.ac.uk

Study contact

daniel.prietoalhambra@ndorms.ox.ac.uk

Primary lead investigator

Daniel Prieto-Alhambra

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 25/03/2015

Study start date
Planned: 01/03/2016

Actual: 01/03/2016

Data analysis start date
Planned: 01/09/2016

Actual: 01/09/2016

Date of interim report, if expected
Planned: 30/11/2016

Actual: 30/11/2016

Date of final study report
Planned: 14/09/2018

Actual: 30/09/2018

Sources of funding

- Other

More details on funding

NIHR, University of Oxford

Regulatory

Was the study required by a regulatory body?

No

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

Non-EU RMP only

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

Effectiveness study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To study the association between oral bisphosphonate use and 1.fracture risk (ie benefits) and 2.known adverse events amongst patients with CKD.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(M05BA) Bisphosphonates

Bisphosphonates

Medical condition to be studied

Chronic kidney disease

Osteoporosis

Osteoporotic fracture

Population studied

Short description of the study population

Participants aged 40 years or older, with chronic kidney disease (CKD) stage 3B or above (eGFR<45ml/min/1.73m2).

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

Renal impaired

Estimated number of subjects

204.528

Study design details

Outcomes

1. CKD progression, 2 osteoporotic (all but face/skull/fingers/toes) fracture/s. 3.acute kidney injury, hospitalization for hypocalcemia/hypophosphataemia, or upper gastro-intestinal events, and 4: annualized hip BMD % change. CKD progression as based on eGFR changes over time.

Data analysis plan

BP use will be introduced as a time-varying exposure. Cox regressionstratified by propensity matched sets will be used to estimate the association between BP use and the study outcomes(WP1/2/3). Linear regression models will be fitted to study the association between BP use and hip BMD in CKD patients(WP4).A more detailed analysis plan is available in the enclosed study protocol.

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)

Clinical Practice Research Datalink

Danish registries (access/analysis)

Data source(s), other

HES United Kingdom, UK Renal Registry United Kingdom, Odense University Hospital database Denmark

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Data sources (types)

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Other

Data sources (types), other

Odense University Hospital (OPEN) data on bone mineral density and biochemistry results

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