Pan European Multi-Database Bladder Cancer Risk Characterisation Study

First published: 07/03/2013

Last updated: 30/03/2024

Study Finalised

Administrative details

EU PAS number

EUPAS3626

Study ID

19338

DARWIN EU® study

No

Study countries

- [ ] Finland
- [ ] Netherlands
- [ ] Sweden
- [ ] United Kingdom

Study description

This observational study is being undertaken to further assess the association between pioglitazone use and bladder cancer risk among patients with type 2 diabetes mellitus in four European countries: Finland, Netherlands, Sweden, and United Kingdom.

Study status

Finalised

Research institutions and networks

Institutions

EPID Research Oy

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Clinical Practice Research Datalink (CPRD)

United Kingdom

First published: 15/03/2010

Last updated: 17/01/2025

Institution | Laboratory/Research/Testing facility | ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 24/07/2024

Institution | Laboratory/Research/Testing facility | ENCePP partner

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

Sweden

First published: 24/03/2010

Last updated: 23/04/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | ENCePP partner

Global Database Studies, IQVIA

Czechia

Finland

Germany

Slovakia

Spain

First published: 17/01/2011

Last updated: 31/07/2024

Institution | Other | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Pasi Korhonen

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 30/03/2012

Actual: 30/03/2012

Study start date

Planned: 30/07/2013

Actual: 29/07/2014

Date of final study report

Planned: 30/09/2016

Actual: 30/09/2016

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Takeda Global Research & Development Centre (Europe) Ltd

Study protocol

Appendices 1-5.pdf(1008.28 KB)

ER12-9433-Actos Pan-European bladder cancer protocol Version 2.0 20Jun2013_NEW CLEANwith signatures.pdf(796.82 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

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:

To estimate and compare the absolute and relative risk of bladder cancer in patients with type 2 diabetes who are ever exposed to pioglitazone vs. never exposed to pioglitazone.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

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

PIOGLITAZONE

Medical condition to be studied

Type 2 diabetes mellitus

Population studied

Short description of the study population

Patients ≥ 40 years with type 2 diabetes mellitus in four European countries: Finland, Netherlands, Sweden, and United Kingdom whose antidiabetic treatment at cohort entry was modified to include pioglitazone or another antidiabetic medication.

Patients with following criteria were included:

• Treatment with any oral antidiabetic drugs at any time in the available medication records.

• Baseline is modified (cohort entry point) to include pioglitazone (exposure group) or another antidiabetic medication (reference group)

• Age ≥ 40 years at cohort entry

• At least 12 months of medication database membership during baseline period prior to cohort entry

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Age groups

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Special population of interest

Other

Special population of interest, other

Type 2 diabetes mellitus patients

Estimated number of subjects

760000

Study design details

Outcomes

Date of diagnosis of the first incidence of bladder cancer after the entry into the study cohort. - All cause mortality- Bladder cancer mortality

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Data analysis plan

Crude bladder cancer incidence and mortality rates with 95% CI will be estimated for each pioglitazone exposure definition separately within the strata of gender, age, year of cohort entry, duration of disease, medication and disease history. Crude incidence rates for each country will be provided separately. In the propensity score matched cohort analysis HR estimates with 95% CIs for each pioglitazone exposure definition will be estimated using Cox model with a counting process approach which enables the follow-up time of each patient to be split into several periods and thus allows adjustments for relevant baseline and time-dependent covariates in the model specification. Separate analyses of bladder cancer incidence, bladder cancer mortality and all-cause mortality will be performed for each country/dataset. In meta-analysis the pooled data set will be used and analysed using the similar methods as the individual cohort analyses.

Documents

Study results

Korhonen et al_pioglitazone use and bladder cancer risk_BMJ_2016.pdf(718.21 KB)

Study, other information

9433-2013-02-14-ENCePPProcessWithoutSealLetterFinalSigned.pdf(58.49 KB)
ER-9515-Cause_of_Death_Analysis_Protocol-21-April-2016_signed_Korhonen.pdf (540.56 KB)

ER12-9433-Actos-Pooled Analysis Protocol and Statistical Analysis Plan-Appendices 1-6.pdf(1.28 MB)

ER12-9433-Actos-Pooled Analysis Protocol and Statistical Analysis Plan-Appendix 7.pdf(1.89 MB)

ER12-9433-Pan_EU_bladder_cancer_Pooled_Analysis_Protocol_and_Statistical_Analysis_plan - 12-Feb-2014.pdf(457.17 KB)

Study publications

Korhonen P, Heintjes EM, Williams R, Hoti F, Christopher S, Majak M, Bezemer I,...

Korhonen P, Heintjes EM, Williams R, Hoti F, Christopher S, Majak M, Kool-Houwe...

Strongman H, Korhonen P, Williams R, Bahmanyar S, Hoti F, Christopher S, Majak ...

Data management

ENCePP Seal

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

2013-0017-DoIForm_Pasi Korhonen-SDPP-3626.pdf(399.86 KB)

Composition of steering group and observers

2013-0017-Composition of SG-SDPP-3626.pdf(106.91 KB)

Signed code of conduct

2013-0017-Declaration-CoC-SDPP-3626.pdf(44.84 KB)

Signed code of conduct checklist

2013-0017-Checklist CoC-SDPP-3626.pdf(1.1 MB)

Signed checklist for study protocols

2013-0017-ChecklistforStudyProtocols-SDPP-3626.pdf(283.42 KB)

Data sources

Data source(s)

Clinical Practice Research Datalink

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Data source(s), other

CPRD, The Swedish prescribed drug register

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Other

Data sources (types), other

Prospective patient-based data collection, Prescription event monitoring,

Population-wide registers in Finland and Sweden contain information e.g. on

medication purchases, hospitalisations, cancers and deaths. The PHARMO database network contains info on drug dispensings, hospital morbidity, clinical labs etc. UK CPRD contains the anonymised longitudinal medical records managed by GPs working the NHS primary care setting.

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

Unknown