# 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:** 19/12/2025

Institution | Non-Pharmaceutical company | ENCePP partner

## Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

Sweden

**First published:** 24/03/2010

**Last updated:** 02/06/2026

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:** 17/08/2026

Institution | Other | ENCePP partner

## Contact details

### Study institution contact

Pasi Korhonen pasi.korhonen@epidresearch.com

Study contact

pasi.korhonen@epidresearch.com

### 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

---

**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**

760.000

## 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

---

**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

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.

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