

# Pan European Multi-Database Bladder Cancer Risk Characterisation Study

**First published:** 07/03/2013

**Last updated:** 30/03/2024

Study

Finalised

## Administrative details

### PURI

<https://redirect.ema.europa.eu/resource/19338>

### EU PAS number

EUPAS3626

### Study ID

19338

### DARWIN EU® study

No

### Study countries

☐ Finland

☐ Netherlands

☐ Sweden

☐ United Kingdom

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### 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.

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### 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

Pasi Korhonen

**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

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### Study start date

Planned: 30/07/2013

Actual: 29/07/2014

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### 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

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### **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

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**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

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**Medical condition to be studied**

Type 2 diabetes mellitus

## Population studied

## Short description of the study population

Patients  $\geq 40$  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  $\geq 40$  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)

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## Special population of interest

Other

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## Special population of interest, other

Type 2 diabetes mellitus patients

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## 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)

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### 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 ...](#)

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## **Data management**

### **ENCePP Seal**

**This study has been awarded the ENCePP seal**



## **Conflicts of interest of investigators**

[2013-0017-DolForm\\_Pasi Korhonen-SDPP-3626.pdf](#)(399.86 KB)

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## Composition of steering group and observers

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

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## Signed code of conduct

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

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## Signed code of conduct checklist

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

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## Signed checklist for study protocols

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

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# Data sources

## Data source(s)

Clinical Practice Research Datalink

Sweden National Prescribed Drugs Register / Läkemedelsregistret

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## Data source(s), other

CPRD, The Swedish prescribed drug register

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## Data sources (types)

[Administrative healthcare records \(e.g., claims\)](#)

[Drug dispensing/prescription data](#)

[Electronic healthcare records \(EHR\)](#)

[Other](#)

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## 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

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### Check completeness

Unknown

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### Check stability

Unknown

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### Check logical consistency

Unknown

## Data characterisation

### Data characterisation conducted

Unknown