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

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 institution 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 02/07/2019
Institution
Laboratory/Research/Testing facility
ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)
Netherlands
First published: 07/01/2022
Last updated 10/01/2022
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 (GloDaSt), IQVIA

Czechia
Finland
Germany
Slovakia
Spain

First published: 17/01/2011
Last updated
16/02/2024

Institution
ENCePP partner
Other

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 data collection

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
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

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
National Prescribed Drugs Register / Läkemedelsregistret

Data source(s), other
CPRD, The Swedish prescribed drug register

Data sources (types)
Administrative data (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