Cohort Study of Pioglitazone and Bladder Cancer in Patients with Type II Diabetes

First published: 17/08/2012

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS2717

Study ID

15058

DARWIN EU® study

No

Study countries

United States

Study description

Following guidance from the United States Food and Drug Administration (FDA) and European Medicine Agency, the University of Pennsylvania and Kaiser Permanente Northern California (KPNC) designed and conducted this study from

the KPNC database to assess the potential association between pioglitazone and bladder cancer among patients with type 2 diabetes mellitus. The study was conducted over the course of 10 years, with a series of interim analyses provided to the sponsor (Takeda) and the appropriate regulatory agencies. In 2011, the planned 5-year interim analysis of this study was published in Diabetes Care. In 2012 an 8-yr interim analysis together with several sensitivity analyses and additional analyses requested by the FDA were undertaken. In 2014 the final 10-yr analysis was completed. In 2011, the planned 5-year interim analysis of this study was published in Diabetes Care. That report included data from 1 January 1997 to 30 April 2008. Following reporting of these data, there was a request from the FDA for an additional fourth interim analysis at 8 years including data from 1 January 1997 to 31 December 2010.In August 2011 the FDA requested a sensitivity analysis to assess change of cohort entry criteria to minimize left censoring of exposure.

Study status

Finalised

Research institutions and networks

Institutions

Kaiser Permanente Northern California,Division of Research

Contact details

Study institution contact

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Study contact

lewisjd@mail.med.upenn.edu

Primary lead investigator

James Lewis

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 01/01/1997

Study start date

Actual: 01/01/1997

Data analysis start date

Actual: 01/01/1997

Date of interim report, if expected

Actual: 30/03/2012

Date of final study report

Planned: 01/06/2014

Actual: 11/08/2015

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Takeda Global Research & Development Center, Inc

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:

Disease epidemiology

Other

If ‘other’, further details on the scope of the study

Association between pioglitazone and bladder

Data collection methods:

Secondary use of data

Main study objective:

The main objective of this study was to assess the potential association between pioglitazone and bladder cancer compared with non-pioglitazone users among patients with type 2 diabetes mellitus.

Study Design

Non-interventional study design

Case-control

Cohort

Study drug and medical condition

Medical condition to be studied

Type 2 diabetes mellitus

Population studied

Short description of the study population

Patients diagnosed with diabetes, who were age 40 or older and were still members of Kaiser Permanente on January 1, 1997.

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

Other

Special population of interest, other

Diabetes mellitus patients

Estimated number of subjects

193.099

Study design details

Outcomes

The primary outcome for this study was the incident diagnosis of bladder cancer identified from the Kaiser Permanente Northern California cancer registry from 01 January 1997 to 31 December 2012.

Data analysis plan

Continuous and categorical variables were compared with the Wilcoxon rank sum test and chisquare test or Fisher’s exact test, respectively. For the cohort study, Cox proportional hazards models were used for all calculations of the

relative hazard (HR) of bladder cancer with pioglitazone, adjusted for the covariates.. Other categories of diabetes medications were included in the baseline model to assess both for confounding and the association of the other medications with bladder cancer. To test for confounding, we separately added the other potential confounding variables to the baseline model to assess for a change in the hazard ratio for pioglitazone or for change in the highest category of pioglitazone exposure in models of dose and duration.

Documents

Study report

01-03-TL-OPI-524 10-Year Final Report.pdf (308.33 KB)

01-03-TL-OPI-524 8-year Interim Report.pdf (237.06 KB)

01-03-TL-OPI-524-4th_Interim_Report_(Additional_Sensitivity_Analysis).pdf (117.55 KB)

01-03-TL-OPI-524-Proteinuria Analysis.pdf (187.57 KB)

Study, other information

01-03-TL-OPI-524 8-year Interim Report.pdf (237.06 KB)

01-03-TL-OPI-524-4th_Interim_Report_(Additional_Sensitivity_Analysis).pdf (117.55 KB)

01-03-TL-OPI-524-Proteinuria Analysis.pdf (187.57 KB)

Study publications

Lewis JD, Habel LA, Quesenberry CP, et al. Pioglitazone Use and Risk of Bladder…

Lewis JD, Ferrara A, Peng T, Hedderson M, Bilker WB, Quesenberry CP Jr, Vaughn …

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.

Composition of steering group and observers

Steering Group.pdf (7.49 KB)

Data sources

Data sources (types)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Other

Data sources (types), other

Prescription event monitoring

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