

# Cohort Study of Pioglitazone and Cancer Incidence in Patients with Diabetes Mellitus

**First published:** 21/07/2015

**Last updated:** 02/07/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS10335

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### Study ID

14909

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### DARWIN EU® study

No

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### Study countries

 United States

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### Study description

The correlation between thiazolidinedione usage among diabetic patients and cancer risk has been studied previously. However, the most important limitation was the very short-term exposure to pioglitazone. In this cohort study, a large

population of diabetic patients was identified from the Kaiser Permanente of Northern California (KPNC) Diabetes Registry. The patients were originally planned to be followed-up from January 1, 1997 to December 31, 2005 for the usage of pioglitazone and incidence of cancer. Based on the discussion with Advisory board, it was recommended to increase the study population and duration of follow-up. The follow-up period was extended to June 30, 2012 for the study on pioglitazone usage and cancer incidence in diabetes patients (Study 1). The need to conduct an epidemiology study of diabetes and cancer risk (Study 2) was also identified in order to assess the association between diabetes severity and cancer risk. The Study 2 included diabetes patients who were KPNC members between 1997 and 2011. It also included a subset of patients who took the 1996/7 diabetes survey and Member Health Survey (MHS) in 1993, 1999, 2001 or 2003.

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### **Study status**

Finalised

## Research institutions and networks

### Institutions

**Takeda**

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**Institution**

Keiser Permente Northern California USA,  
University of Pennsylvania USA

## Contact details

### Study institution contact

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Study contact

[trialogdisclosures@takeda.com](mailto:trialogdisclosures@takeda.com)

### Primary lead investigator

Assiamira Ferrara

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 01/01/1996

Actual: 01/01/1996

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### Study start date

Planned: 01/01/1997

Actual: 01/01/1997

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### Date of interim report, if expected

Planned: 01/09/2011

Actual: 01/09/2011

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### **Date of final study report**

Planned: 01/09/2011

Actual: 29/05/2015

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Takeda

## Study protocol

[AD4833-403 Protocol KPNC other malignancies\\_4.pdf](#) (60.33 KB)

## Regulatory

### **Was the study required by a regulatory body?**

No

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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  
Disease epidemiology

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To evaluate whether treatment with pioglitazone was associated with risk of incident cancer at the 10 most common sites (prostate, female breast, lung/bronchus, endometrial, colon, non-Hodgkin lymphoma NHL, pancreas, kidney/renal pelvis, rectal, and melanoma) in a cohort of patients with recognized diabetes.

## 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 from Kaiser Permanente of Northern California (KPNC) Diabetes Registry who were followed up from January 1, 1997 to December 31, 2005 for the usage of pioglitazone and incidence of cancer.

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### **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)
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### **Special population of interest**

Other

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### **Special population of interest, other**

Diabetes mellitus patients

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### **Estimated number of subjects**

252467

## Study design details

## **Outcomes**

Hazard ratio of the 10 most common cancers associated with ever use of pioglitazone. Hazard ratio of the 10 most common cancers associated with time since first use, duration and dose of pioglitazone. Age, gender, calendar year-specific cancer incidence rates stratified by diabetes status. Age-, gender-adjusted incidence rates stratified by diabetes status, calendar year.

Association between diabetes and risk of the 10 most common cancers for full KPNC member and survey responder.

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## **Data analysis plan**

Study 1: Cox proportional hazards regression modeling was used to provide point and interval estimates of the relative hazard of the 10 most common cancers associated with ever use of pioglitazone (primary analysis) and time since first use, cumulative duration, and dose (secondary analyses). In all regression analyses, these measures of exposure to pioglitazone were treated as time-dependent covariates and time since entry into the cohort was the time scale. Study 2: Cancer incidence rates were calculated with attention to the proper allocation of at-risk person-time. The association between diabetes and risk of each of the 10 most common cancers was assessed using Cox proportional hazards regression models with control for available potential confounders: age, gender, calendar year. Similarly, Cox regression technique was used to examine the association between diabetes status and cancer risk among survey responders with adjustment for additional potential confounding variable.

## **Documents**

### **Study results**

[AD-4833-403 \(KPNC 10 common cancers\) 10-yr study report.pdf](#) (807.92 KB)

## Study publications

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

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## 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.

## Data sources

### Data sources (types)

Administrative healthcare records (e.g., claims)

Electronic healthcare records (EHR)

Other

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### Data sources (types), other

Prospective patient-based data collection

## 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**

No