# PROspective PioglitAzone Clinical Trial in MacroVascular Events (PROactive)

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Study Finalised

## Administrative details

**EU PAS number**

EUPAS10493

**Study ID**

10494

**DARWIN EU® study**

No

**Study countries**

- Austria
- Belgium
- Denmark
- Estonia
- Finland
- France

Germany
Hungary
Italy
Latvia
Lithuania
Netherlands
Norway
Poland
Slovakia
Sweden
Switzerland
United Kingdom

**Study description**

The risk reduction by pioglitazone in cardiovascular (CV) outcomes in high risk patients with Type 2 diabetes mellitus (T2DM) and pre-existing macrovascular disease was evaluated during the PROactive study. It was a multicenter, randomized, double-blind, placebo-controlled, parallel group study conducted in male and female patients between 35 and 75 years with a diagnosis of T2DM. Patients received 15 milligram (mg) dose of pioglitazone (or matching placebo), once daily along with the current diabetic medications. Doses were titrated from 15 mg to 30 mg in the first month visit, 30 mg to 45 mg in the second month visit and was maintained at 45 mg for a period of 2.5 to 3.5 years, unless there were any tolerability concerns. Visits were scheduled at 1,2,4,6,8,10 and 12 months following randomization and then every 3 months thereafter. Patients continued study medication until 30 months follow-up was reached or a study total of 760 macrovascular events had been reported, and final visits were completed.

**Study status**

Finalised

## Research institutions and networks

## Institutions

Multiple centres: 321 centres are involved in the study

## Contact details

**Study institution contact**

John Dormandy trialdisclosures@takeda.com

**Study contact**

trialdisclosures@takeda.com

**Primary lead investigator**

John Dormandy

**Primary lead investigator**

## Study timelines

**Date when funding contract was signed**

Actual: 28/05/2001

**Study start date**

Actual: 28/05/2001

**Date of final study report**

Actual: 29/11/2005

## Sources of funding

- Other

## More details on funding

Takeda Europe R&D Centre Ltd

## Regulatory

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

No

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**Is the study required by a Risk Management Plan (RMP)?**

Not applicable

# Methodological aspects

## Study type

## Study type list

**Study topic:**

Human medicinal product

Disease /health condition

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**Study type:**

Clinical trial

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Primary data collection

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**Main study objective:**

This study demonstrated that whether pioglitazone reduces total mortality and macrovascular morbidity in high-risk patients with type 2 diabetes mellitus.

## Study Design

**Clinical trial randomisation**

Randomised clinical trial

## Study drug and medical condition

**Study drug International non-proprietary name (INN) or common name**

PIOGLITAZONE HYDROCHLORIDE

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**Medical condition to be studied**

Type 2 diabetes mellitus

## Population studied

**Short description of the study population**

Patients aged 35-75 years old diagnosed with type 2 diabetes mellitus received pioglitazone with current diabetic treatment.

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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**

Patients with type 2 diabetes mellitus

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**Estimated number of subjects**

5238

## Study design details

**Outcomes**

Time from randomization to first occurrence of any of the events in the following composite: all-cause mortality, non-fatal MI (including silent MI), acute coronary syndrome, cardiac intervention including CABG or PCI, stroke, major leg amputation, and bypass surgery or revascularization in the leg., Secondary outcomes included: composite of all-cause mortality, non-fatal MI (excluding silent MI), and stroke; Cardiovascular mortality; individual components of the primary endpoint.

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**Data analysis plan**

For each endpoint, treatment-group differences were examined using a log rank test without covariates; a Cox proportional hazards model was fitted with

treatment as the only independent variable for estimate of the hazard ratio (95% confidence interval); Kaplan-Meier estimates of the survival functions were used to characterize treatment effects. Exploratory analyses were conducted using the proportional hazards model and incorporating additional covariates. 2 interim analyses were planned and conducted. The first was performed when approximately 50% of the anticipated final number of events had occurred and the second when approximately 75% of the events had occurred. These analyses were conducted by the Independent Statistical Centre and then reported to the Data and Safety Monitoring Committee. Each interim analysis for efficacy considered the 1-sided log rank test for the superiority of pioglitazone.

# 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)**

Other

**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

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

# Data characterisation

**Data characterisation conducted**

No