

# Assessment of cardiovascular effects of non-insulin glucose-lowering agents. Major cardiovascular events in new users of non-insulin glucose-lowering agents: observational longitudinal study in the Catalan population-based electronic health record database, SIDIAP, 2010-2015

**First published:** 06/04/2017

**Last updated:** 06/04/2017

Study

Planned

## Administrative details

### EU PAS number

EUPAS18510

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### Study ID

18511

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### DARWIN EU® study

No

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## Study countries

 Spain

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## Study description

Cardiovascular (CV) risk is the leading cause of morbidity and mortality in T2DM population. The effect of control serum glucose levels on macrovascular complications remains uncertain. Glucose-lowering agents are currently marketed based on results of clinical trials with surrogate variables, mainly the percentage of glycated haemoglobin and other glucose markers. In 2007, concerns about CV safety of rosiglitazone led to regulatory recommendations regarding CV risk of new hypoglycemic agents, which are in force since 2008 (FDA, US) and 2012 (EMA, EU). In order to fulfill these recommendations, since 2008 a number of large randomized clinical trials have been designed and conducted, with a non-inferiority design as basis, with controversial results. Other ten large RCTs, on-going or recently completed, are currently assessing the CV effect of seven marketed agents are currently unavailable. Aim: To evaluate the effect of currently marketed non-insulin glucose-lowering agents on major CV outcomes in cohorts of Spanish population based on records of population-based EMR SIDIAP. Design: Longitudinal retrospective observational cohort study, period of observation of six years (1st January 2010- 31st Dec 2015) Material and Methods: Cohorts of patients aged 18 yrs. or older registered in the SIDIAP database, diagnosed of type 2 diabetes mellitus, and treated with approved glucose-lowering agents since their first prescription. Patients will be stratified by demographic and clinical variables. The incidence rate of the first major cardiovascular event will be calculated. The primary outcome (PCO) is the composite of CV death, non-fatal myocardium infarction (MI) and non-fatal stroke. Secondary outcomes are: composite (SCO) of CV death, a non-fatal myocardium infarction (MI), non-fatal stroke and hospitalization due to unstable angina or coronary revascularization procedures, individual components of SCO, hospitalization due to HF (HHF) and all-cause mortality.

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## Study status

Planned

## Research institutions and networks

### Institutions

#### Fundació Institut Català de Farmacologia (FICF)

 Spain

**First published:** 29/03/2010

**Last updated:** 17/09/2019

**Institution**

**Outdated**

**Educational Institution**

**Hospital/Clinic/Other health care facility**

**Not-for-profit**

**ENCePP partner**

## Contact details

### Study institution contact

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**Study contact**

[xvg@icf.uab.cat](mailto:xvg@icf.uab.cat)

### Primary lead investigator

Xavier Vidal

**Primary lead investigator**

# Study timelines

## **Date when funding contract was signed**

Planned: 01/07/2016

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## **Study start date**

Planned: 01/09/2016

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## **Data analysis start date**

Planned: 01/03/2017

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## **Date of final study report**

Planned: 01/03/2018

# Sources of funding

- Non-for-profit organisation (e.g. charity)

# More details on funding

IDIAP Jordi Gol

# Study protocol

[Protocol version April06.pdf](#) (372.69 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)?

Not applicable

## Methodological aspects

### Study type

### Study type list

#### **Study type:**

Non-interventional study

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#### **Scope of the study:**

Effectiveness study (incl. comparative)

#### **Main study objective:**

To evaluate the effect of currently marketed non-insulin glucose-lowering agents on major CV outcomes in cohorts of Spanish population based on records of population-based EMR SIDIAP

## Study Design

### **Non-interventional study design**

Cohort

## Study drug and medical condition

### **Anatomical Therapeutic Chemical (ATC) code**

(A10B) BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS

BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS

## Population studied

### 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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### Estimated number of subjects

270000

## Study design details

### Outcomes

Composite of three-components of mayor cardiovascular events (MACE): cardiovascular death, non-fatal myocardial infarction (MI) and non-fatal stroke. Secondary Composite Outcome is a MACE of four components: CV death, non-fatal MI, non-fatal stroke and hospitalization due to unstable angina or coronary revascularization procedures

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### Data analysis plan

Incidence rates of primary and secondary composite outcomes events and secondary outcomes events will be estimated for each cohort during follow-up. Incident rates will be presented per 1000 patient-years and their corresponding 95% confidence intervals (CIs). Hazard ratios of PCO, SCO and SO will be

calculated between cohorts (treated vs. non-treated) for each therapeutic group and, secondarily, for each given agent. Data will be analysed with multivariate Cox proportional-hazard regression models, once verified proportionality assumptions. To control potential biases for confounding factors, the differences between exposed and non-exposed populations to the different hypoglycemic agents will be adjusted by estimating a propensity index using a logistic regression model. In order to control the effect of time-dependent confounders the use of marginal structural models will be also considered.

## 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 source(s)**

The Information System for Research in Primary Care (SIDIAP)

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### **Data sources (types)**

[Drug dispensing/prescription data](#)

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

## 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