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

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Study Planned

Administrative details

EU PAS number

EUPAS18510

Study ID

18511

DARWIN EU® study

No

Study countries

☐ Spain

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 subrogate 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.

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 | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Primary lead investigator

Xavier Vidal

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 01/07/2016

Study start date
Planned: 01/09/2016

Data analysis start date
Planned: 01/03/2017

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

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

Not applicable

Methodological aspects

Study type:

Non-interventional study

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

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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)

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

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 proporcionality 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

Data sources

Data source(s)

The Information System for Research in Primary Care (SIDIAP)

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

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No