Safety Evaluation of Adverse Reactions in Diabetes - Comparative studies (SAFEGUARD)

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Study | Finalised

Administrative details

Contact details

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PURI
https://redirect.ema.europa.eu/resource/20765

EU PAS number
EUPAS2895

Study ID
20765

DARWIN EU® study
No

Study countries
Germany
Italy
Netherlands
Spain
United Kingdom
United States

Study description
Safety issues associated with blood glucose lowering drugs are not new, the safety of these treatments has been questioned and highly publicized. It has been reported that some of them increase the risk or modify the prognosis of cancer, cardiovascular (CVD) or pancreatic diseases.The primary objective of the comparative studies in SAFEGUARD is to estimate the risk of myocardial infarction (MI), heart failure (HF), ventricular arrhythmia (VA)/sudden cardiac death (SCD), ischemic stroke (IS), hemorrhagic stroke (HS), acute pancreatitis (AP), pancreatic cancer (PC), bladder cancer (BC) and total mortality (TM) associated with the use of non-insulin blood glucose lowering drugs (NIBGLD), insulins and insulin analogs in subjects with T2DM.Data collected in 9 different electronic health databases from 5 different European countries the USA will be used. Nested case control studies in a cohort of T2DM patients will be conducted to assess the association of NIBGLD, insulins, and insulin analogs with MI, HF, VA/SCD, IS, HS, AP, BC and PC and a dynamic retrospective cohort study to estimate the association with TM.For the estimation of the risk, in the case control studies, cases will be compared with matched controls and adjusted for potential confounders. Conditional logistic regression will be used to calculate the unadjusted and adjusted odds ratios (ORs) with their 95% confidence intervals (CIs) with reference to another active compound.For the cohort studies, hazard ratios and incidence rates (IR) and the relative risk for TM with their 95% CIs will be estimated using Cox-regression. Time varying analyses will be conducted for estimation of the effect of duration of treatment. All analyses will be performed for each database separately and the heterogeneity among databases will be examined (e.g., I2). Advanced methodologies, subanalyses and sensitivity analyses will be carried out to deal with methodological issues.(i.e propensity scores, etc).

Study status
Finalised

Research institution and networks

Institutions

Erasmus Medical Centre Rotterdam

First published: 01/02/2024
Last updated 01/02/2024

Institution

Novo Nordisk

Consorzio Mario Negri Sud (CMNS)

Italy
First published: 17/01/2011
Last updated 27/08/2013

Institution

Not-for-profit

ENCePP partner

Health Search, Italian College of General Practicioners

Italy
First published: 02/03/2010
Last updated 25/06/2014

Institution

Educational Institution

Other

ENCePP partner

Leibniz Institute for Prevention Research and Epidemiology - BIPS

Germany
First published: 29/03/2010
Last updated 26/02/2024

Institution

Not-for-profit

ENCePP partner

Pharmacy & Pharmacology, University of Bath

United Kingdom
First published: 30/04/2010
Last updated
08/04/2019

Institution

Educational Institution

Hospital/Clinic/Other health care facility

ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands
First published: 07/01/2022
Last updated
10/01/2022

Institution

Laboratory/Research/Testing facility

ENCePP partner

RTI Health Solutions (RTI-HS)

France
Spain
Sweden
United Kingdom
United Kingdom (Northern Ireland)
United States
First published: 21/04/2010
Last updated
19/02/2024

Institution

Not-for-profit

ENCePP partner

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands
First published: 03/11/2022
Last updated
02/05/2024

Institution

Educational Institution

ENCePP partner

AEMPS Spain, UNIMIB Italy, BWH United States of America

Study timelines

Date when funding contract was signed
Planned:
23/08/2011
Actual:
23/08/2011

Data collection
Planned:
20/09/2012
Actual:
20/09/2012

Date of final study report
Planned:
30/09/2015
Actual:
30/09/2015

Sources of funding

- EU institutional research programme

More details on funding

Health Area of the European Commission under the VII Framework Programme

Study protocol

ENCEPP_SDPP_2895_Finalprotocol.pdf(968.53 KB)

Regulatory

Was the study required by a regulatory body?
Yes

Is the study required by a Risk Management Plan (RMP)?
Not applicable

Methodological aspects

Study type

Study type list

Study topic:
Disease /health condition
Human medicinal product

Study type:
Non-interventional study

Scope of the study:
Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:
Secondary data collection

Main study objective:
The main objective of these observational studies is to estimate the risk of myocardial infarction (MI), heart failure (HF), ventricular arrhythmia (VA)/sudden cardiac death (SCD), ischemic stroke (IS), hemorrhagic stroke (HS), acute pancreatitis (AP), pancreatic cancer (PC), bladder cancer (BC) and

Study Design

Non-interventional study design
Case-control
Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
100000093996
DRUGS USED IN DIABETES

Medical condition to be studied
Type 2 diabetes mellitus

Population studied

Short description of the study population
All patients in the databases during the study period who have at least 365 consecutive days of valid data with at least one prescription/dispensing of a NIBGLD (ATC: A10B – Annex 1) or insulin or insulin analogues (ATC: A10A – Annex 1) in the study period.

Age groups
Term newborn infants (0 – 27 days)
Infants and toddlers (28 days – 23 months)
Children (2 to < 12 years)
Adolescents (12 to < 18 years)
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
2200000

Study design details

Outcomes
The primary objective of these observational studies is to estimate the risk of myocardial infarction (MI), heart failure (HF), ventricular arrhythmia (VA)/sudden cardiac death (SCD), ischemic stroke (IS), hemorrhagic stroke (HS), acute pancreatitis (AP), pancreatic cancer (PC), bladder cancer (BC) and total mortality (TM) associated with the use of NIBGLD and insulins and insulin analogs. To assess the background rates of the different events of

interest in the population of subjects with T2DM

Data analysis plan
The incidence rate (IR) and direct standardized incidence rates (SIRs) with the 95% confidence intercal (95%CI) of each outcome of interest in each database will be estimated at the population level for harmonization purposes. To assess the risk of the outcomes of interest (MI, HF, VA/SCD, HS, IS, AP, PC and BC), associated with the use of NIBGLD and insulins and insulin analogues, Conditional logistic regression will be used to calculate the unadjusted and adjusted odds ratios (ORs) with their 95% confidence intervals (CIs) with reference to another active compound which will be selected based on drug utilization studies. For the cohort studies, hazard ratios and incidence rates (IR) as well as the relative risk for TM with their 95% CIs will be estimated using Cox-regression analysis. All analyses will at first be performed for each database(DB) separately and the heterogeneity among DBs will be examined through heterogeneity indexes. Different sensitivity analyses will be performed

Documents

Results tables
Safety Evaluation of Adverse Reactions in Diabetes_report.pdf(954.98 KB)

Data management

ENCePP Seal

This study has been awarded the ENCePP seal

Conflicts of interest of investigators
DoI_MStukenboom_EMC.pdf(1.46 MB)

Composition of steering group and observers
ENCEPP_SDPP_2895_Scientific Advisory Board.pdf(77.91 KB)

Signed code of conduct
2012-0013_DoC Code of Conduce_SDPP-2895.pdf(33.53 KB)

Signed code of conduct checklist

2012-0013_Checklist of the CoC_SDPP-2895.pdf(1.05 MB)

Signed checklist for study protocols
2012-0013_Checklist Study Protocl_SDPP-2895.pdf(182 KB)

Data sources

Data source(s)
Clinical Practice Research Datalink
Health Search/IQVIA Health Longitudinal Patient Database
IPCI

Data source(s), other
CPRD, Health Search/CSD LPD, IPCI

Data sources (types)
Administrative data (e.g. claims)
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