Concomitant use of dronedarone and digoxin (or statins) and the risk of digitalis intoxication (or rhabdomyolysis and myopathy)-- a post-marketing cohort study using the US Clinformatics DataMart® (formerly LabRx®) database

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Study | Finalised

Administrative details

EU PAS number

EUPAS18153

Study ID

36369

DARWIN EU® study

No

Study countries

United States

Study description

This was a cohort study using existing database to evaluate if the concomitant use of dronedarone increases the risk of dose-related digitalis intoxication in digoxin users and the risk of rhabdomyolysis and myopathy in statin users.The study population consisted of 2 cohorts of patients identified from the Clinformatics DataMart® (formerly LabRx®) database who were at least 18 years old, had a diagnosis of atrial fibrillation (AF) or flutter (AFL), and filled a prescription of digoxin or statins between July 20, 2009 and March 31, 2016 (the date of the latest data available for this study). The cohort entry date was the date on which the first prescription of digoxin or statins was dispensed in the study period.Exposure of interest was concurrent use of dronedarone in digoxin or statins users. The concomitant use of dronedarone and digoxin (or statins) was defined as the treatment period during which a patient was on both drugs. Digoxin (or statins) alone was defined as the treatment period during which a patient was on digoxin (or statins), but not on dronedarone.The respective outcomes of interest were digitalis intoxication in digoxin users and rhabdomyolysis/ myopathy in statin users. Digitalis intoxication was defined by the presence of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9) codes 972.1 or E942.1 or tenth Revision, Clinical Modification (ICD-10) codes T46,xxxA or T46.0X5x.The covariates in the multivariate analyses included age at baseline, gender, the number of diagnoses of AF/AFL and history of comorbidities including congestive heart failure (CHF), diabetes, hypertension, stroke, myocardial infarction, and renal failure within 180 days prior to a patient’s cohort entry date, average dose of digoxin (or statins), the use of major medications with potent interactions with digoxin (or statins), and the calendar year of cohort entry date.Cox proportional hazards regression models were fit to obtain.

Study status

Finalised

Research institutions and networks

Institutions

Sanofi

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Institution

Contact details

Study institution contact

Trial Transparency Team Trial Transparency Team contact-us@sanofi.com

Study contact

contact-us@sanofi.com

Primary lead investigator

Trial Transparency Team Trial Transparency Team

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/03/2011

Actual: 01/03/2011

Study start date

Planned: 20/07/2009

Actual: 20/07/2009

Date of final study report

Planned: 21/12/2016

Actual: 21/12/2016

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Sanofi

Study protocol

DRONEC05911 protocol.pdf (306.84 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

Other study registration identification numbers and links

Study code: DRONE_C_05911

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 use of data

Main study objective:

To evaluate if the concomitant use of dronedarone increases the risk of dose-related digitalis intoxication in digoxin users and the risk of rhabdomyolysis and myopathy in statin users.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C01AA05) digoxin

digoxin

(C01BD07) dronedarone

dronedarone

(C10AA) HMG CoA reductase inhibitors

HMG CoA reductase inhibitors

Medical condition to be studied

Atrial fibrillation

Population studied

Short description of the study population

The study population consisted of 2 cohorts (digoxin and statin cohorts) of patients identified from the Clinformatics DataMart® database who were at least 18 years old, had a diagnosis of atrial fibrillation (AF) or flutter (AFL), and filled a prescription of digoxin or statins between July 20, 2009 (the launch date of dronedarone in the US) and March 31, 2016. Statins of interest included atorvastatin, simvastatin, lovastatin, and pravastatin. Fluvastatin and rosuvastatin were not considered for potential interactions with dronedarone because they are not metabolized or only weakly metabolized by CYP3A4 and are not P-gP substrates. The cohort entry date was the date on which the first

prescription of digoxin or statins was dispensed. Excluded from the cohort were the patients with the following conditions on the cohort entry date: (1) less than 6 months of enrolment period in the managed care organization (United Healthcare), and (2) a diagnosis of the outcome of interest within six months prior to the cohort entry date.

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)

Special population of interest

Other

Special population of interest, other

Atrial fibrillation patients

Estimated number of subjects

32.459

Study design details

Outcomes

Digitalis intoxication, Rhabdomyolysis and myopthay

Data analysis plan

Incidence rates of outcomes the concomitant use cohort and the single-drug cohort (digoxin or statins) were calculated. Adjusted hazard ratios for outcomes

comparing concomitant use to the single-drug use were calculated.

Documents

Study results

DRONEC05911 Study report.pdf (148.39 KB)

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)

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