

# 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

**First published:** 08/03/2017

**Last updated:** 14/03/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS18153

---

### Study ID

36369

---

### DARWIN EU® study

No

---

### Study countries

## **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

**First published:** 01/02/2024

**Last updated:** 01/02/2024

Institution

### Contact details

#### Study institution contact

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

Study contact

[contact-us@sanofi.com](mailto: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**

32459

## **Study design details**

### **Outcomes**

Digitalis intoxication, Rhabdomyolysis and myopathy

---

### **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