Serious Liver Injury and Interstitial Lung Disease Occurrences in Patients Diagnosed with Atrial Fibrillation Treated with Selected Antiarrhythmics

First published: 07/03/2017

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Study Finalised

Administrative details

EU PAS number

EUPAS18129

Study ID

36375

DARWIN EU® study

No

Study countries

☐ United States

Study description

Prospective population monitoring will be employed to conduct the surveillance portion of the program and an observational retrospective cohort study will be conducted to compare rates of serious Liver injury/disease and interstitial lung disease, separately, in patients exposed to other selected anti-arrhythmic comparator cohorts versus dronedarone-exposed patients. Two administrative claims databases (OptumInsight formerly i3 Drug Safety/United Health Care and HealthCore/WellPoint) and one electronic health record (EHR) system (Health ResearchTx/Department of Defense, or DoD) will be used to monitor the use of dronedarone in the general population and The HealthCore Integrated Research Database (or HIRD) and the DoD databases will be used for the retrospective study. Retrospective and prospective population monitoring of defined exposures and outcomes will commence in each database as of July 20, 2009 (dronedarone launch date). Monitoring will continue through 2015 or until a sufficient number of dronedarone users are identified for the initiation of a targeted pharmacoepidemiology study. The study population will be comprised of patients treated for atrial fibrillation or flutter (AF/AFL) who are treated with anti-arrhythmic drugs (dronedarone, amiodarone, sotalol, flecainide, dofetilide, and propafenone). In addition to prospectively capturing the number of new users of dronedarone and comparator drugs, the surveillance component of this study will capture the number of serious liver injury and interstitial lung disease occurrences after the index date in the study population.

Study status

Finalised

Research institutions and networks

Institutions

Sanofi

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Institution

Contact details

Study institution contact

Trial Transparency Team contact-us@sanofi.com

Study contact

contact-us@sanofi.com

Primary lead investigator

Trial Transparency Team

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 08/01/2011

Actual: 08/01/2011

Study start date

Planned: 15/08/2011

Actual: 15/08/2011

Data analysis start date
Actual: 15/08/2011

Date of final study report
Planned: 30/06/2017

Actual: 09/05/2017

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Sanofi U.S.

Study protocol

DRONEC05917 protocol.pdf(245.99 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

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:

1. To count the number of new users of dronedarone and comparators identified from administrative claims databases and electronic health records (EHR) on a quarterly basis.
2. To identify the number of serious liver injury occurrences among new users of dronedarone and comparators.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

MULTAQ

Study drug International non-proprietary name (INN) or common name

DRONEDARONE

Anatomical Therapeutic Chemical (ATC) code

(C01BD07) dronedarone

dronedarone

Medical condition to be studied

Atrial fibrillation

Population studied

Short description of the study population

The study population will be comprised of patients treated for newly occurring atrial fibrillation or flutter (AF/AFL), including those who are treated with anti-arrhythmic drugs (dronedarone, amiodarone, sotalol, flecainide, dofetilide) as well as a population not treated with these anti-arrhythmic drugs (but could be treated with rate control drugs e.g., digoxin or beta blockers).

Overall patient inclusion criteria were:

• 365 days of continuous eligibility in the health plan prior to and including the Index Date;
• A new prescription for any one of the following six anti-arrhythmic agents: dronedarone, amiodarone, sotalol, flecainide, dofetilide, or propafenone, dispensed between 20 July 2009 (the dronedarone launch date in the US) and 31 March 2014. The first of these drugs of interest dispensed during the patient selection period determined a patient's study cohort assignment and was referred to as the patient's Index Drug. The date on which that first study medication was dispensed was defined as the patient's Index Date, and the 365 days prior to and including the patient's Index Date defined their baseline period;
• Diagnosed with atrial fibrillation (AF, ICD-9-CM diagnosis code 427.31) during the baseline period;
• No use of the Index Drug during the baseline period. Use of non-index study drugs during the baseline period was allowed;
• Patient aged 18 years or older as of their Index Date.

Overall patient exclusion criteria were:
• Unknown gender;
• Index Drug use during the baseline period;
• Multiple study drugs on the Index Date;
• Less than 365 days of continuous eligibility in the health plan prior to and including the Index Date;
• Absence of a diagnosis of AF during the baseline period;
• A diagnosis of cancer, organ transplant, or HIV during the baseline period;
• Women who were pregnant during the 280 days prior to and including the Index Date, or became pregnant during the 280 days following the Index Date, or
• Date of death preceding Index 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

80524

Study design details

Outcomes

Serious liver injury/disease, interstitial lung disease

Data analysis plan

Tables summarizing baseline characteristics of patients in each of the cohorts were generated. Patients in the dronedarone cohort and those in the other anti-arrhythmic drug cohorts were matched on the propensity of being treated with the drug of interest. The number of patient-years of observation, the number of incident events, raw event rate with its 95% confidence interval, and the p-value for the comparison of event rates between the comparator drugs and dronedarone were calculated. In order to compare rates of outcome events over time, if enough events were identified separate Cox Proportional Hazards

regression analyses were conducted for each outcome (i.e. SLD and ILD). Hazard ratios, with their 95% confidence intervals and p-values, for each comparator drug relative to dronedarone were reported, if data warranted. Kaplan-Meier curves were generated to display the risk of each out.

Documents

Study results

DRONEC05917 Study report_Part 1.pdf(6.99 MB)

Study report

DRONEC05917 Study report_Part 1.pdf(6.99 MB)

DRONEC05917 Study report_Part 2.pdf(5.29 MB)

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