Cohort Study of the Incidence of Major Cardiovascular Events in New Adult Users of Lisdexamfetamine and Remote Adult Users of Other ADHD Treatments

First published: 05/09/2017

Last updated: 02/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/43216

EU PAS number

EUPAS20546

Study ID

43216

DARWIN EU® study

No

Study countries

☐ Denmark

☐ Sweden

Study description

This study will consist of multiple observational (non-interventional) population-based cohort studies of patients initiating Lisdexamfetamine dimesylate (LDX) compared with patients with remote use of other attention deficit and hyperactivity disorder (ADHD) medications, in three electronic health care data sources: the Danish National Registries, and the Swedish National Registers. The main objective of this study is to estimate the incidence rate (IR) and the adjusted incidence rate ratios (IRRs) of the composite major adverse cardiovascular events (MACE) endpoint in a cohort of adult patients who are current new users of LDX compared with a cohort of remote users of other ADHD treatments. Current use for LDX new users is defined as the duration of the LDX prescription or dispensing plus 30 days. The remote use of other ADHD treatments will be generated by selecting adult patients with at least one prescription/dispensing for a medication indicated for ADHD, other than LDX, during the 24 months prior to the index date and with no prescriptions or dispensings of these medications in at least the last 180 days before index date. The analysis will be conducted separately in each data source, and overall estimates of effect will be obtained using meta-analytic techniques as appropriate. The primary endpoint, MACE, will comprise the first occurrence of any of its individual components during follow-up: hospitalisation for acute myocardial infarction, fatal or non-fatal, hospitalisation for stroke, fatal or non-fatal, out-of-hospital coronary heart disease death, and out-of-hospital cerebrovascular death. Secondary endpoints are an extended MACE (EMACE) endpoint that includes hospitalisation for either unstable angina or TIA, the composite coronary and stroke components of EMACE, and an additional secondary endpoint that will be a composite of sudden cardiac death and

serious ventricular arrhythmias.

Study status

Finalised

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)

- ☐ France
- ☐ Spain
- ☐ Sweden
- ☐ United Kingdom
- ☐ United Kingdom (Northern Ireland)
- ☐ United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution **Not-for-profit** **ENCePP partner**

Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

- ☐ Sweden

First published: 24/03/2010

Last updated: 23/04/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | Not-for-profit | 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: 13/03/2025

Institution | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Cristina Rebordosa

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 01/06/2017

Actual: 01/06/2017

Study start date
Planned: 01/12/2019

Actual: 30/09/2019

Date of final study report
Planned: 30/06/2020

Actual: 18/12/2020

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Shire Human Genetic Therapies, Inc., a wholly owned subsidiary of the Takeda Pharmaceutical Company Limited

Study protocol

0304010 - LDX Protocol Final Version (v2.0)- 08March2016_redacted.pdf(6.91 MB)

LDX protocol_final version 3.0_final_3Jun2019_Redacted.pdf(2.29 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 2 (specific obligation of marketing authorisation)

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:

The primary objective of this study is to estimate, in real-world settings, the incidence rate (IR) and the adjusted incidence rate ratios (IRRs) of the

composite major adverse cardiovascular events (MACE) endpoint in a cohort of adult patients who are current new users of LDX compared with a cohort of remote users of other ADHD treatments in three European data sources.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N06BA12) lisdexamfetamine

lisdexamfetamine

Additional medical condition(s)

Major Cardiovascular Events (MACE)

Population studied

Short description of the study population

The source population will be all individuals aged 18 years or older registered in the study databases from the date LDX will become available for the treatment of ADHD in adults in each country until the end of study period. To be eligible for inclusion into the study population, individuals should have at least 12 months of data available prior to cohort entry. The study will include two cohorts identified from all eligible individuals in the study data sources: the LDX

cohort and the remote use of other ADHD treatments cohort.

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

170940

Study design details

Outcomes

Major cardiovascular events (MACE). MACE, will comprise hospitalisation for acute myocardial infarction (AMI), fatal or non-fatal, hospitalisation for stroke, fatal or non-fatal, out-of-hospital coronary heart disease death, and out-of-hospital cerebrovascular death. Extended MACE (EMACE). EMACE comprises all MACE components plus hospitalisation for either unstable angina or transient ischaemic attack (TIA), the composite coronary and stroke components of EMACE, and a composite of sudden cardiac death and serious ventricular arrhythmias.

Data analysis plan

Each research partner will conduct country-specific analyses within each data source to (1) select the study population, (2) describe the study cohorts, including patterns of demographics, medical history, exposures, and endpoints, (3) within its data, estimate exposure propensity scores that will be used to control for confounding, (4) create a summary of aggregated data set based on

counts of patients, person-years, and outcome events according to the strata of age, sex and propensity scores, (5) analyse IR and standardised IRs, and (6) analyse crude and adjusted IRRs. IRs will be standardised to the distribution of person-time of LDX users by age, sex, quintiles of the propensity score, and data source. The coordinating centre activities include conducting a (1) pooled description analysis of study cohorts, (2) pooled analysis of IR and standardised IRs, and (3) pooled analysis of crude and adjusted IRRs. Mantel-Haenszel methods will be used to summarise IRRs across strata.

Documents

Study results

4765_Elvanse PASS_exec summary_FINAL_18Dec2020_Redacted.pdf(173.25 KB)

Data management

Data sources

Data source(s)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

Data sources (types)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Other

Data sources (types), other

Hospital discharge data

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