Use of antiepileptics and risk of suicidality. An exploratory study using the UK General Practice Research Database (GPRD) and data from the Danish registries with an evaluation of available data from further European data sources.

First published: 26/10/2012

Last updated: 02/07/2024

Study Finalised

Administrative details

EU PAS number

EUPAS2356

Study ID

13022

DARWIN EU® study

No

Study countries

- [ ] Denmark
- [ ] Germany
- [ ] Netherlands
- [ ] Spain
- [ ] United Kingdom

Study description

The studies described in this protocol are all performed within the framework of PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium) Work Package 2 and Working Group 1. The primary aim of these studies is to develop, test and disseminate methodological standards for the design, conduct and analysis of Pharmacoepidemiological (PE) studies applicable to different safety issues and using different data sources. To achieve this, results from PE studies on 5 key Drug / adverse events (D-AEs) pairs performed in different databases will be evaluated. The use of antiepileptics associated with the risk of suicidality is one of the key D-Ae pair of interest. Therefore, emphasis will be on the methodological aspects of the studies in this protocol and not on the clinical consequences of studying the association under investigation.

Study status

Finalised

Research institutions and networks

Institutions

F. Hoffmann-La Roche

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands

First published: 01/03/2010

Last updated: 23/05/2024

Institution | Educational Institution | ENCePP partner

European Medicines Agency (EMA)

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)

Spain

First published: 01/02/2024

Last updated: 04/09/2024

Institution | EU Institution/Body/Agency | Not-for-profit | Regulatory Authority | ENCePP partner

Ludwig-Maximilians-University Munich

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Agencia Espanola del Medicamento y Productos Sanitarios (AEMPS) Spain, European Medicines Agency (EMA) United Kingdom, Lægemiddelstyrelsen (Danish Medicines Agency (DKMA) Denmark, Ludwig-Maximilians-Universität-München (LMU MUNCHEN) Germany, F.Hoffmann-La Roche AG Switzerland

Networks

PROTECT

- [ ] Belgium
- [ ] Denmark
- [ ] France
- [ ] Germany
- [ ] Italy
- [ ] Netherlands
- [ ] Poland
- [ ] Spain
- [ ] Sweden
- [ ] Switzerland
- [ ] United Kingdom

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Network

Contact details

Study institution contact

Markus Schuerch markus.schuerch@roche.com

Study contact

markus.schuerch@roche.com

Primary lead investigator

Markus Schuerch

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 19/08/2009

Actual: 19/08/2009

Study start date
Planned: 03/10/2011

Actual: 03/10/2011

Date of final study report
Planned: 31/12/2013

Actual: 01/04/2016

Sources of funding

- EU institutional research programme
- Pharmaceutical company and other private sector

More details on funding

Amgen, AstraZeneca, Genzyme, GSK, MerckSerono, Novartis, Roche, Pfizer, Innovative Medicines Initiative (IMI)

Study protocol

PROTECT_WP2 Final Protocol_Suicide_Anticonvulsants_Dec 16 2011_Amend 1 approved 5Oct2012.pdf (457.19 KB)

PROTECT WP2 Final protocol_AED Suicidality_Amend3_15Feb2013approved.pdf (449.55 KB)

Regulatory

Was the study required by a regulatory body?

No

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

Disease epidemiology

Drug utilisation

Other

If ‘other’, further details on the scope of the study

Analysis of discrepancies in results between different databases

Data collection methods:

Secondary use of data

Main study objective:

To assess the association between the use of antiepileptics and the risk of suicidality with different study designs across different primary care databases and to compare the results between databases, across designs to evaluate the impact of design/database/population differences on the outcome of the studied association.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N03A) ANTIEPILEPTICS

ANTIEPILEPTICS

Medical condition to be studied

Suicidal behaviour

Suicidal ideation

Completed suicide

Suicide attempt

Population studied

Short description of the study population

Patients who have received a first prescription to at least one Antiepileptic drugs (AED) at 1-Jul-1996 or later in the UK or Denmark, age of 15 years and older at the index date, a registration history of at least 6 months prior to the index date (first date of AED prescription) and fulfilling research data criteria in General Practice Research Database (GPRD).

Age groups

- Adolescents (12 to < 18 years)
- Children (2 to < 12 years)
- Infants and toddlers (28 days – 23 months)
- 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

55700000

Study design details

Data analysis plan

Descriptive studies to compare the six European databases. We will estimate point and period prevalence overall and by AEDs for the study period between 1-Jan-2000 and 31-Dec-2009. Analytical studies to evaluate a possible association between anti-epileptic drugs and suicidalityWe will estimate risks of suicidality for all AEDs and by individual AEDs prescribed in UK and Denmark. We will apply two different study design: cohort study, and case-crossover studies. For the cohort study we will apply Cox regression analyses with the following potential confounding factors: gender, age, marital status, socio-economic status, BMI, smoking status, alcohol abuse, drug and medication abuse, number of different drugs prescribed in the six months prior to index date, a number of comorbidities associated with a higher risk for suicidality and calendar period. Exposure to AEDs and anti-depressives will be handled as time varying variables.

Documents

Study results

Abstract Schuerch et al (2016).pdf (9.75 KB)

Study publications

Schuerch M, Gasse C, Robinson NJ, Alvarez Y, Walls R, Mors O, Christensen J, He…

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.

Signed checklist for study protocols

Encepp checklist AED suicidality 31Aug2012 MS.pdf (359.49 KB)

Data sources

Data source(s)

THIN® (The Health Improvement Network®)

Clinical Practice Research Datalink

Danish registries (access/analysis)

Data sources (types)

Administrative healthcare records (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