Use of inhaled long acting beta2 adrenoceptor agonists and the risk for Acute Myocardial Infarction (AMI). A methodological comparison across data sources and epidemiological design

First published: 26/10/2012

Last updated: 02/07/2024

Study Ongoing

Administrative details

PURI

https://redirect.ema.europa.eu/resource/6882

EU PAS number

EUPAS2561

Study ID

6882

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 inhaled long acting beta2 adrenoceptor agonists associated with the risk of myocardial infarction 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

Ongoing

Research institutions and networks

Institutions

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

Novartis Pharmaceuticals

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 de Medicamentos y Productos Sanitarios (AEMPS) Spain, Lægemiddelstyrelsen (DKMA) Denmark, Ludwig-Maximilians-Universität-München (LMU Muenchen) Germany, European Medicines Agency (EMA) United Kingdom, Novartis Pharma AG (Novartis) 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

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Study contact

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Primary lead investigator

Marietta Rottenkolber

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: 01/02/2013

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 Beta2_AMI 30 March 2012_Amendment1_22Aug2012.pdf(1.24 MB)

PROTECT_WP2 Final protocol Beta2_AMI_Amendment2_clean_Version_withAppendix2_130220.pdf(1.2 MB)

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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Other

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

Analysis of discrepancies in results between different databases

Main study objective:

To assess the association between the use of inhaled long acting beta2adrenoceptor agonists and the risk of acute myocardial infarction 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

Case-control

Cohort

Other

Non-interventional study design, other

Case-crossover, Descriptive study = description of exposure and/or outcome in the whole database during a defined period of time

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(R03AC) Selective beta-2-adrenoreceptor agonists

Selective beta-2-adrenoreceptor agonists

(R03BB) Anticholinergics

Anticholinergics

(R03CK) Adrenergics and other drugs for obstructive airway diseases

Adrenergics and other drugs for obstructive airway diseases

Medical condition to be studied

Acute myocardial infarction

Population studied

Age groups

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

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

DescriptivesExtensive descriptive studies will be performed to characterize and compare exposure and outcome in the databases.Cohort studyIncidence density will be calculated as the number of AMI divided by person-time. Stratified relative risk will be graphically shown with the Ramlau-Hansen method. Time-dependent Cox-regression models will be used for confounding factor adjusted analysis. Hazard ratio's will be calculated for current use of LABA compared to the control group.Nested case controlConditional logistic

regression analysis will be used to estimate the risk (OR) of AMI with current use of LABA compared to the control group. OR for AMI will be estimated by comparing inhaled LABA with the control group (No-LABA) using conditional regression analysis.CCOThe Nonparametric Multiple Intervals Approach will be used. OR will be calculated with the use of conditional logistic regression, as described above

Data management

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