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



## Administrative details

#### **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



### 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



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

Spain

First published: 01/02/2024



Ludwig-Maximilians-University Munich

First published: 01/02/2024

Last updated: 01/02/2024



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		
First published: 26/06/2013		
Last updated: 14/01/2025		
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

# 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