The European Drug-induced Agranulocytosis Consortium Study (The EuDAC Study)

First published: 18/12/2013

Last updated: 18/12/2013

Study Ongoing

Administrative details

EU PAS number

EUPAS3847

Study ID

3848

DARWIN EU® study

No

Study countries

France

Germany

Netherlands

Spain

Sweden

United Kingdom

Study description

Studies show that adverse drug reactions (ADRs) are one of the most common reasons for hospitalisation in the adult population. It has also been proposed that ADRs are the fourth to sixth leading cause of death in hospitalised patients. Most ADRs are dose-dependent and pharmacologically predictable (type A reactions), while others have no known pharmacological cause (type B reactions). Agranulocytosis (unless due to chemotherapy) belongs to this second type that commonly is serious and sometimes leads to withdrawal of drugs from the market. The current knowledge about possible genetic causes of drug-induced agranulocytosis is minimal. The aim of EuDAC is to identify genetic factors that predispose to drug-induced agranulocytosis, enabling us to test and predict the individual risk before starting a drug treatment.

Study status

Ongoing

Research institutions and networks

Institutions

Uppsala University

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Clinical Pharmacology,Department of Medical Sciences

Centro de Estudios sobre la Seguridad de los Medicamentos (CESME), Universidad de Valladolid

Spain

First published: 22/02/2010

Last updated: 02/08/2013

Institution | Outdated | Educational Institution | ENCePP partner

Fundació Institut Català de Farmacologia (FICF)

Spain

First published: 29/03/2010

Last updated: 17/09/2019

Institution | Outdated | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Division of Clinical Pharmacology, Karolinska Institutet

Sweden

First published: 31/05/2010

Last updated: 07/02/2012

Institution | Outdated | Educational Institution | Hospital/Clinic/Other health care facility | Laboratory/Research/Testing facility | ENCePP partner

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution | Educational Institution | ENCePP partner

Electronic Health Records (EHR) Research Group, London School of Hygiene & Tropical Medicine (LSHTM)

United Kingdom

First published: 19/04/2010

Last updated: 30/10/2024

Institution | Educational Institution | ENCePP partner

Institute of Clinical Pharmacology and Toxicology (PVZ FAKOS), Charite Universitaetsmedizin Berlin

Germany

First published: 16/04/2010

Last updated: 02/05/2012

Institution | Outdated | Educational Institution | ENCePP partner

Institute of Clinical Pharmacology and Toxicology (PVZ FAKOS), Charite Universitaetsmedizin Berlin

Germany

First published: 16/04/2010

Last updated: 02/05/2012

Institution | Outdated | Educational Institution | ENCePP partner

Clinical Pharmacology Service, University of Málaga Spain, Medical Products Agency Sweden, Instituto de Parasitología y Biomedicina López Neyra Avda Spain, Clinical Pharmacology, Uppsala University Sweden, Laboratoire de Pharmacologie Médicale et Clinique, Faculté de Médecine de

l’Université de Toulouse France, Charité - University Medicine, Institute of Clinical Pharmacology and Toxicology, Berlin Germany

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Pär Hallberg

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 01/04/2008

Actual: 01/04/2008

Study start date

Planned: 01/03/2009

Actual: 01/03/2009

Data analysis start date
Planned: 01/06/2014

Date of final study report
Planned: 01/12/2015

Sources of funding

- Other

More details on funding

Swedish Medical Products Agency, Uppsala County Council Research Fund, Sweden, Swedish research council, Swedish Society of Medicine, Serlander's Fund, Sweden, Thereus' Fund, Sweden

Study protocol

The EuDAC Study 2013-12-03.pdf (536.09 KB)

Regulatory

Was the study required by a regulatory body?
No

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Other

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

Genome-wide association study

Main study objective:

To identify genetic factors that predispose to drug-induced agranulocytosis.

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A07EC) Aminosalicylic acid and similar agents

Aminosalicylic acid and similar agents

(H03B) ANTITHYROID PREPARATIONS

ANTITHYROID PREPARATIONS

(J01) ANTIBACTERIALS FOR SYSTEMIC USE

ANTIBACTERIALS FOR SYSTEMIC USE

(N03) ANTIEPILEPTICS

ANTIEPILEPTICS

(M01A) ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS, NON-STEROIDS

(B01AC) Platelet aggregation inhibitors excl. heparin

Platelet aggregation inhibitors excl. heparin

(D01B) ANTIFUNGALS FOR SYSTEMIC USE

ANTIFUNGALS FOR SYSTEMIC USE

(C07) BETA BLOCKING AGENTS

BETA BLOCKING AGENTS

(N06A) ANTIDEPRESSANTS

ANTIDEPRESSANTS

Medical condition to be studied

Agranulocytosis

Population studied

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

300

Study design details

Outcomes

Proportion of individuals who are carriers of investigated genetic polymorphisms.

Data analysis plan

Association analyses with genetic and clinical factors will be performed for the agranulocytosis group as a whole and stratified for each drug or class of drugs. A total of about 4000 population and treated controls will be used. To correct for population stratification, controls will be recruited from all countries and principal component analysis will be performed. To correct for multiple testing, the level of significance will be set at around p<1*10-8, which is equivalent to a Bonferroni correction for 1 million independent tests. We will make an effort to collect 100 new cases and controls for replication of the 10-20 top hits. We will then need to correct for 10-20 multiplied tests, i.e. a p-value of 0.0025-0.005 will suffice. We will perform single SNP tests with logistic regression with adjustment for population stratification by including significant principal components as covariates in the logistic-regression model. Results are illustrated with Q-Q and Manhattan plots.

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)

Spontaneous reports of suspected adverse drug reactions

Other

Data sources (types), other

Prospective patient-based data collection

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