DARWIN EU® - Association between genetic polymorphisms of interest and risk of myopathy among statin users

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Last updated: 06/01/2025



Study countries

] Estonia



Administrative details

PURI
https://redirect.ema.europa.eu/resource/1000000369
EU PAS number
EUPAS100000369
Study ID
100000369
DARWIN EU® study
Yes

United	Kingdom
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Study description

Around 1% to 30% of statin users report mild muscle symptoms including pain and/or weakness, usually

without significant creatine kinase (CK) elevation. Severe myopathy (CK elevation <10 times normal) occurs

in 0.1% of cases, while rhabdomyolysis (>40 times normal CK) is even rarer (<0.01%).

There is current regulatory interest in exploring the role the OATP1B1 (SLCO1B1 c.521CC) gene

polymorphism in atorvastatin users (treated with a fixed dose combination of acetylsalicylic acid/atorvastatin/ramipril) with regards to the risk of myopathy. SLCO1B1 encodes the liver-expressed OATP1B1

protein, which clears statins like rosuvastatin, atorvastatin, simvastatin, and pravastatin from the blood.

The SLCO1B1 521T>C polymorphism (rs4149056) reduces hepatic clearance of these statins, with

simvastatin being most affected, and fluvastatin and rosuvastatin less so.

Atorvastatin, a first-line lipid

lowering drug for cardiovascular disease, is widely prescribed but often discontinued due to muscle complaints.

More broadly, the aim of this study is to inform whether genetic testing could help predict the risk of

myopathy in users of atorvastatin and other selected statins, and whether dose adjustment would help

minimise risk for carriers of known polymorphisms. In addition, this study serves as a proof-of-concept of

the capacity of DARWIN EU to generate pharmacogenomic evidence to support

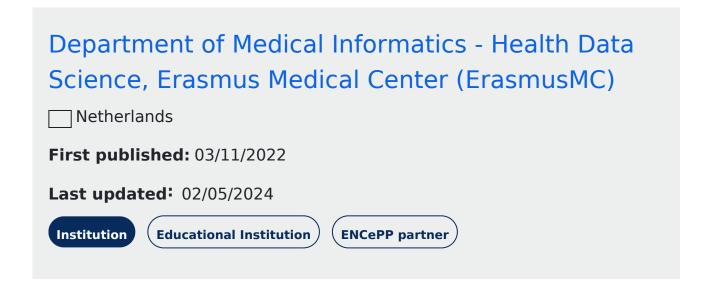
regulatory d	cision ma	king.
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Study status

Ongoing

Research institutions and networks

Institutions



Networks

Data Analysis and Real World Interrogation Network
(DARWIN EU®)
Belgium
Croatia
Denmark
Estonia
Finland
France

Germany
Greece
Hungary
Italy
☐ Netherlands
Norway
Portugal
Spain
Sweden
United Kingdom
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Network

Contact details

Study institution contactIlse Schuemie

Study contact

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Primary lead investigatorJunging Xie

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 06/06/2024 Actual: 06/06/2024

Study start date

Planned: 06/11/2024 Actual: 06/06/2024

Date of final study report

Planned: 17/03/2025

Sources of funding

EMA

Study protocol

DARWIN EU_Protocol_P3-C3-004_Statins_V6.pdf(775.56 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study topic, other:

pharmacogenetics

Study type:

Non-interventional study

Scope of the study:

Other

If 'other', further details on the scope of the study

To estimate the association between SLCO1B1 (and additionally ABCG2) genetic variants and the risk of statin-associated myopathy

Data collection methods:

Secondary use of data

Study design:

New User Cohorts

Main study objective:

Primary objectives

- 1a To estimate the risk of myopathy in new users of atorvastatin (any dose) according to genotype status
- 1b To estimate the risk of myopathy in new users of lower-dose atorvastatin according to genotype status
- 1c To estimate the risk of myopathy in new users of higher-dose atorvastatin according to genotype status

Secondary objectives

2a - To estimate the risk of myopathy in new users of simvastatin (separately for any dose, lower-dose and higher-dose) according to genotype status
2b - To estimate the risk of myopathy in new users of rosuvastatin (separately for any dose, lower-dose and higher-dose) according to genotype status if feasible (See Section 8.7 "Study Size" for more details on how to determine if this analysis is feasible)

2c - To estimate the risk of myopathy in new users of fluvastatin (separately for any dose, lower-dose and higher-dose) according to genotype status if feasible (See Section 8.7 "Study Size" for more details on how to determine if this analysis is feasible)

2d - To estimate the risk of myopathy in new users of pravastatin (separately for any dose, lower-dose and higher-dose) according to genotype status if feasible (See Section 8.7 "Study Size" for more details on how to determine if this analysis is feasible).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

Statins

Medical condition to be studied

Myopathy

Population studied

Short description of the study population

The source population will comprise of all incident statin users during the study period.

Age groups

Adult and elderly population (≥18 years)

Study design details

Setting

This study will be conducted using two prospective Biobank cohorts with primarily collected genetic data linked to routinely collected electronic health records in two European countries. Except for the genetic information, all other data have been previously mapped to the OMOP CDM to allow for federated analytics, and DARWIN EU data quality controls have been completed during onboarding to the network.

- 1. UK Biobank (UKBB), United Kingdom
- 2. Estonian Biobank (EBB), Estonia

Data management

Data sources

Data source(s)

UK Biobank

Estonian Biobank

Other	
Data sources (types), other Biobank	
Use of a Common Data Model (CDM)	
CDM mapping Yes	
CDM Mappings	
CDM name OMOP	
CDM website	
https://www.ohdsi.org/Data-standardization/	
CDM version	
https://ohdsi.github.io/CommonDataModel/index.html	
Data quality specifications	
Check conformance	
Unknown	

Data sources (types)

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown