# RISK OF CARDIOVASCULAR EVENTS IN PATIENTS USING TOCILIZUMAB AS COMPARED WITH OTHER BIOLOGICS IN MULTIPLE LARGE HEALTHCARE DATABASES (EUPAS11327)

**First published:** 15/10/2015

**Last updated:** 15/10/2015

Study Planned

## Administrative details

**EU PAS number**

EUPAS11327

**Study ID**

11328

**DARWIN EU® study**

No

**Study countries**

United States

**Study description**

The overall research question of the proposed study is to quantify or refute any residual cardiovascular risk that the use of Tocilizumab (TCZ) may cause in patients with RA using observational methods in large healthcare databases. The primary exposure cohort is TCZ initiators while the comparator cohort is TNF inhibitors. The primary outcome of interest is a composite of non-fatal MI and non-fatal stroke (hemorrhagic, ischemic, uncertain classification). Non-fatal MI or non-fatal stroke is defined as events where patients were hospitalized with the occurrence of death shortly after arrival. The primary analysis is an as-treated propensity score matched comparison on risk measures for the primary outcome. This study will utilize healthcare administrative claims data from multiple private and public funded healthcare insurance plans in the United States.

---

**Study status**

Planned

## Research institutions and networks

### Institutions

Division of Pharmacoepidemiology and Pharmacoeconomics Boston

## Contact details

**Study institution contact**

Sebastian Schneeweiss sschneeweiss@partners.org

**Study contact**

sschneeweiss@partners.org

**Primary lead investigator**

Sebastian Schneeweiss

**Primary lead investigator**

## Study timelines

**Date when funding contract was signed**

Actual: 15/06/2015

**Study start date**

Planned: 30/11/2015

**Date of final study report**

Planned: 30/09/2016

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Roche/Genentech

## Regulatory

**Was the study required by a regulatory body?**

No

# Methodological aspects

## Study type

## Study type list

**Study topic:**

Human medicinal product

Disease /health condition

---

**Study type:**

Non-interventional study

---

**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Main study objective:**

The primary objective is to compare time to first event of a composite of myocardial infarction and stroke (i.e. incidence rates) in patients newly treated with TCZ versus TNFi.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Medicinal product name, other**

ACTEMRA

---

**Study drug International non-proprietary name (INN) or common name**

TOCILIZUMAB

---

**Additional medical condition(s)**

Myocardial infarction,Acute coronary syndrome,Percutaneous coronary intervention,Coronary arterial stent insertion,Coronary artery bypass,Cardiac failure,Rheumatoid arthritis,Subarachnoid haemorrhage,Cerebral haemorrhage

# 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**

76000

# Study design details

**Outcomes**

The primary outcome of interest is a composite of non-fatal MI and non-fatal stroke (hemorrhagic, ischemic, uncertain classification). Non-fatal MI or non-

fatal stroke is defined as events where patients were hospitalized with the occurrence of death shortly after arrival. The secondary outcome of interest include coronary revascularization (PTCA, stenting, CABG), acute coronary syndrome (ACS), a composite endpoint of primary cardiovascular events plus coronary revascularization procedures and ACS, heart failure (HF) requiring hospitalization, and all-cause mortality.

---

**Data analysis plan**

Primary analyses will be a propensity scored matched, as-treated assessment on the primary and secondary outcomes evaluating (1) The incidence rate of the primary and secondary outcomes, (2) The absolute rate difference between initiators of TCZ and a comparator drug, (3) Time-to event analyses with Kaplan-Meier plots to inspect proportionality of hazards and assess whether follow-up time is comparable between treatment groups. Cox proportional hazard models will also be fitted to estimate hazard ratios (HR) and 95% confidence intervals (CIs).In addition to the aforementioned analyses, analyses will be stratified in mutually exclusive 6-month intervals of follow-up time since treatment initiation: 1 through 6 months, 7 through 12 months, etc. Multiple subgroups will be identified a priori and the analyses described above will be repeated. Additional sensitivity analyses will be carried out as well.

# 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 source(s), other**

"Medicare fee for service, plans A, B, C, D United States", "United Healthcare (Optum InVision Data Mart) United States", "MarketScan (Truven Healthcare Analytics), United States", "IMS PharMetrics United States"

**Data sources (types)**

Administrative healthcare records (e.g., claims)

## 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