Observational Patient Evidence for Regulatory Approval and uNderstanding Disease (OPERAND)

First published: 17/04/2019

Last updated: 31/05/2019

Study Ongoing

Administrative details

EU PAS number

EUPAS29415

Study ID

29944

DARWIN EU® study

No

Study countries

United States

Study description

The OPERAND program will study the conditions under which it may be possible to replicate the findings of two previously published randomized clinical trials (RCTs) with observational data. Such evidence would set the stage for improving confidence in estimates of treatment effectiveness for patient populations beyond those originally studied in RCTs. Two project teams will independently replicate the same two trials, the ROCKET Atrial Fibrillation and the LEAD-2 studies, using their own methodology. If the data confirms the previously published RCT results, the teams will extend the use of the data to estimate the ATE for the populations actually treated within the original indication. All analyses will be conducted using the OptumLabs Data Warehouse (OLDW)—a database of more than 120 million lives of claims data linkable to over 50 million lives of electronic medical record data.

Study status

Ongoing

Research institutions and networks

Institutions

Harvard Pilgrim Health Care Institute

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Brown University

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Harvard Pilgrim Health Care Institute Boston, MA, USA, Brown University Providence, RI, USA, OptumLabs, Multiregional Clinical Trials Center of Brigham and Women's Hospital and Harvard

Contact details

Study institution contact

Darren Toh Darren_Toh@harvardpilgrim.org

Study contact

Darren_Toh@harvardpilgrim.org

Primary lead investigator

Darren Toh

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 10/04/2019

Actual: 09/04/2019

Study start date
Planned: 01/05/2019

Actual: 27/05/2019

Data analysis start date
Planned: 17/06/2019

Date of interim report, if expected
Planned: 17/07/2019

Date of final study report
Planned: 31/10/2019

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Amgen, AstraZeneca, Pfizer, UCB, Sanofi, Merck

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:

Non-interventional study

Scope of the study:

Effectiveness study (incl. comparative)

Main study objective:

To replicate 2 previously published RCTs of pharmacological products used as the basis of marketing approval by the FDA. For each trial, we will first mimic the inclusion/exclusion criteria, endpoint definitions, exposure windows, and other study design features and then use state-of-the-art causal inference methods to estimate ATE and compare to those reported in the original publications

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(B01AA03) warfarin

warfarin

(B01AF01) rivaroxaban

rivaroxaban

(A10BJ02) liraglutide

liraglutide

(A10BB12) glimepiride

glimepiride

Medical condition to be studied

Type 2 diabetes mellitus

Atrial fibrillation

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

9999

Study design details

Outcomes

For the first study, primary outcome is a composite of the occurrence of stroke (ischemic or hemorrhagic) and systemic embolism. For the second study, primary outcome is change in hemoglobin A1C at the end of the study compared with baseline.

Data analysis plan

In this first study, to mimic the primary analysis in the ROCKET AF trial, we will conduct analyses to obtain the analog of intention-to-treat and per-protocol treatment effect estimates. Cox proportional hazards regression model will be used to estimate hazard ratios for treatment effects. We will use different analytical approaches that control for baseline confounding. The 95% confidence interval (CI) for estimates in all approaches will be obtained via nonparametric bootstrap. In the second study, to mimic the primary analysis in the LEAD-2 trial, we will conduct analyses to obtain the analog of intention-to-treat treatment effect estimates. We will use a linear regression model to estimate the mean difference in change in A1C from baseline. We will use different analytical approaches that control for confounding due to baseline characteristics. The 95% CI for estimates in all approaches will be obtained via nonparametric bootstrap.

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.

Conflicts of interest of investigators

DoIForm_DarrenToh.pdf (903.5 KB)

Composition of steering group and observers

OPERAND Steering Committee.pdf (134.17 KB)

Data sources

Data sources (types)

Administrative healthcare records (e.g., claims)

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