# 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**

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Study contact

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**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

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**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

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**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)

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**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.

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**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