Effectiveness of PCSK9 Inhibitors in Familial Hypercholesterolemia: Feasibility Analysis

First published: 03/12/2024

Last updated: 03/12/2024

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000387

Study ID

1000000387

DARWIN EU® study

No

Study countries

☐ Canada

Study description

Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) are a relatively novel class of drugs used in the treatment of heterozygous familial hypercholesterolemia (hereafter, FH). However, data are limited on the real-

world use and effectiveness of PCSK9i for FH in Canada. The aims of this study are 1) to determine the percentage of patients with FH achieving Canadian public drug plan treatment goals for PCSK9i, and 2) to estimate the incidence of major adverse cardiovascular events among patients with FH who are prescribed PCSK9i. Using administrative healthcare data from the provinces of Alberta, British Columbia, and Ontario, we will identify patients who began treatment with a PCSK9i (alirocumab or evolocumab) between 2015 and 2023. PCSK9i initiators will be identified using prescription drug claims, and FH status will be inferred using a combination of public drug plan reimbursement (which is limited to those with FH) and laboratory test values for low-density lipoprotein cholesterol (LDL-C). Patient characteristics at the time of PCSK9i initiation will be described. We will determine the percentage of patients achieving the public drug plans' recommended treatment goal of at least 40% reduction in LDL-C levels during treatment with PCSK9i. The incidence of major adverse cardiovascular events during treatment will be estimated to support assessment of the feasibility of future observational studies of PCSK9i.

Study status

Ongoing

Research institutions and networks

Institutions

Lady Davis Institute

First published: 01/02/2024

Last updated: 01/02/2024

Institution

University of British Columbia

First published: 01/02/2024

Last updated: 01/02/2024

Institution

University of Alberta, Edmonton, Canada

ICES, Toronto, Canada

Networks

Canadian Network for Observational Drug Effect Studies (CNODES) and Alberta Drug and Technology Evaluation Consortium (ADTEC)

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Michael Paterson

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 08/08/2024

Actual: 08/08/2024

Study start date

Planned: 08/08/2024

Actual: 08/08/2024

Date of final study report

Planned: 14/04/2025

Sources of funding

- Other

More details on funding

CNODES and ADTEC are collaborating core network partners of CoLab funded for query-related activity by Canada’s Drug Agency (CNODES CDA grant number C222 360).

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

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Feasibility analysis

Data collection methods:

Secondary use of data

Study design:

Descriptive cohort study

Main study objective:

The main objectives are:
1. To determine the percentage of patients with FH who are achieving the public drug plans' recommended treatment goal of at least 40% reduction in LDL-C during treatment with PCSK9i.
2. To estimate the incidence of major adverse cardiovascular events among patients with FH who are prescribed PCSK9i.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

PRALUENT

REPATHA

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

ALIROCUMAB

EVOLOCUMAB

Anatomical Therapeutic Chemical (ATC) code

(C10AX13) evolocumab

evolocumab

(C10AX14) alirocumab

alirocumab

Additional medical condition(s)

Heterozygous Familial Hypercholesterolemia

Population studied

Short description of the study population

The study population will include all patients aged 10 years or older (66 years or older in Ontario) who began treatment with a PCSK9i in the study provinces between April 1, 2015 (or the date of the first claim for PCSK9i in each province) and March 31, 2023.

Age groups

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Adult and elderly population (≥18 years)

Estimated number of subjects

20000

Study design details

Setting

Using administrative healthcare data from the provinces of Alberta, British Columbia, and Ontario, we will identify patients who began treatment with a PCSK9i (alirocumab or evolocumab) between 2015 and 2023. PCSK9i initiators will be identified using prescription drug claims, and FH status will be inferred using a combination of public drug plan reimbursement (which is limited to those with FH) and laboratory test values for LDL-C (using an adaptation of Ruel et al.’s criteria). To ensure patients are new users, we will require a minimum of

365 days of data availability with no prescription for PCSK9i. Cohort entry will be defined as the date of the first dispensing of a PCSK9i. For the purposes of cardiovascular outcome assessment, patients will be followed from the date of cohort entry to the first of: a major adverse cardiovascular event, treatment discontinuation, loss of health insurance, death, or end of the study period.

Outcomes

We will study 4 sets of measures:

1. Patient characteristics at cohort entry (sociodemographic and clinical characteristics)

2. Duration of PCSK9i therapy

3. Attainment of LDL-C treatment targets: Among patients for whom the required laboratory data are available, we will determine the percentage who:
a. Achieve the public drug plan’s recommended 40% reduction in LDL-C within 8 weeks of PCSK9i initiation
b. Maintain the public drug plan’s recommended 40% reduction in LDL-C during PCSK9i therapy
c. Achieve the 2021 Canadian Cardiovascular Society post-treatment absolute LDL-C thresholds for primary prevention (no previous atherosclerotic cardiovascular disease (ASCVD)) or secondary prevention (previous ASCVD) within 8 of PCSK9i initiation
d. Achieve specific LDL-C thresholds within 8 weeks of PCSK9i initiation for primary and secondary prevention patients

4. Incidence of major adverse cardiovascular events (MACE): defined a composite outcome previously used in a CNODES study (Filion et al. 2020),

consisting of myocardial infarction, ischemic stroke, or cardiovascular death (using the algorithm previously validated by Lix et al. 2021)

The incidence of MACE during treatment will be estimated to support assessment of the feasibility of future observational studies of PCSK9i.

Data analysis plan

Analyses will be completed in each provincial database with measures pooled cross-provincially as appropriate. First, patient characteristics at the time of PCSK9i initiation will be described. Second, the mean and median duration of PCSK9i therapy will be estimated, from the date of treatment initiation to the date of discontinuation. Third, the percentage of patients achieving the LDL-C treatment targets (described above) will be determined. Fourth, the crude and age- and sex-standardized incidence rate and corresponding 95% confidence intervals of MACE will be estimated among all PCSK9i initiators and among the subset with and without a history of these events, and those with and without a history of ASCVD. MACE will also be computed by subgroups. Last, a sensitivity analysis will be conducted for the attainment of LDL-C targets in the subset of patients with baseline measures in a shorter timeframe preceding PCSK9i initiation.

Documents

Link to project page on CNODES website.
Major adverse cardiovascular events definition
Cardiovascular death algorithm definition

Data management

Data sources

Data source(s), other

Provincial administrative health databases

Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Laboratory tests and analyses

Population registry

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