A Post-marketing Database Surveillance to Investigate the Risk of Hyperglycemia and Diabetes Mellitus in Hypercholesterolemic Patients Treated with ATOZET or Ezetimibe Atorvastatin coadministration in Japan (MK-0653C-855)

First published: 15/06/2021

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS41414

Study ID

46433

DARWIN EU® study

No

Study countries

Japan

Study description

The purpose of this study is to investigate diabetes health outcomes of interest (HOI) hyperglycemia and diabetes mellitus in participants who receive ATOZET compared to participants who receive coadministration of ezetimibe and atorvastatin. The study will also investigate these risks in participants with hepatic impairment.

Study status

Finalised

Research institutions and networks

Institutions

Merck Sharp & Dohme LLC

United States

First published: 01/02/2024

Last updated: 08/07/2025

Institution **Pharmaceutical company**

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Clinical Trials Disclosure Merck Sharp & Dohme Corp.

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 21/08/2020

Study start date

Planned: 12/06/2021

Actual: 11/06/2021

Data analysis start date

Planned: 01/09/2021

Actual: 08/09/2021

Date of final study report

Planned: 31/12/2021

Actual: 21/12/2021

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Merck Sharp & Dohme Corp.

Study protocol

MK-0653C-855-00-v2_Final Redaction.pdf(1.49 MB)

Regulatory

Was the study required by a regulatory body?

Yes

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

Non-EU RMP only

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

To compare the incidence rates of HOI between those taking ATOZET and those taking the coadministration of ezetimibe and atorvastatin. The HOI for this study are hyperglycemia and diabetes mellitus.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Post-marketing database surveillance

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(C10AA05) atorvastatin

atorvastatin

(C10AX09) ezetimibe

ezetimibe

(C10BA05) atorvastatin and ezetimibe

atorvastatin and ezetimibe

Medical condition to be studied

Hypercholesterolaemia

Population studied

Short description of the study population

The surveillance population is hypercholesterolemic patients with no past history of diabetes mellitus who are prescribed with ATOZET or coadministration of ezetimibe and atorvastatin between 1-APR-2018 and 30-SEP-2020 (selection period).

Inclusion criteria

1) Patients who have a hypercholesterolemia diagnosis (ICD code: E78.5) during the selection period, AND

2) Patients who have received ATOZET (ATC code: C10BA05) or coadministration of ezetimibe and atorvastatin (ATC code: C10AX09 and C10AA05) during the selection period.

The exclusion criteria are as follows:

• For the ATZ-group

1) Patients given ezetimibe monotherapy (C10AX09) as a pre-treatment drug, OR

2) Patients given other lipid modifying agents (C10) as a pre-treatment drug except atorvastatin (C10AA05), OR

3) Patients who were not given any pre-treatment drug, OR

4) Patients who had ATOZET treatment before April 2018, OR

5) Patients who do not have a 6-month lookback period prior to the index date, OR
6) Patients who have any missing information on critical variables (e.g., gender, age), OR
7) Patients who have severe liver dysfunction considered as the contraindication for the use of ATOZET, OR
8) Patients who were diagnosed with diabetes mellitus (ICD-10 codes: E10-E14) or were using antidiabetic drugs (A10) during the lookback period, OR
9) Patients whose blood glucose level was >200 mg/dL during the 6-month lookback period prior to the index date, OR
10) Patients whose HbA1c level was >6.5% during the 6-month lookback period before the index date will be excluded.
• For the EZE-ATV-group
1) Patients given ezetimibe (C10AX09) as a pre-treatment drug, OR
2) Patients given other lipid modifying agents (C10) as a pre-treatment drug except atorvastatin (C10AX09), OR
3) Patients who were not given any pre-treatment drug, OR
4) Patients who had Ezetimibe/Atorvastatin coadministration treatment before April 2018, OR
5) Patients who do not have a 6-month lookback period prior to the index date, OR
6) Patient

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)

Special population of interest

Hepatic impaired

Estimated number of subjects

2000

Study design details

Outcomes

The primary outcomes for diabetes and hyperglycemia are defined as: diagnostic code for hyperglycemia or diabetes mellitus AND (blood glucose > 200 mg/dL AND HbA1c >6.5%) OR (blood glucose > 200 mg/dL two times on different days). The secondary outcomes for diabetes and hyperglycemia are defined as: 1) (blood glucose > 200 mg/dL AND HbA1c >6.5%) OR (blood glucose > 200 mg/dL two times on different days) . 2) diagnostic code for hyperglycemia or diabetes mellitus AND (blood glucose > 200 mg/dL once or more than once).

Data analysis plan

- Calculation of number of diabetes or hyperglycemia HOI (based on various definitions) per 1,000 person years for the ATOZET and ezetimibe/atorvastatin coadministration groups - Calculation of incidence rate ratios (IRR) of various diabetes or hyperglycemiaHOI, adjusting for covariates, for the ATOZET and ezetimibe/atorvastatin coadministration groups

Documents

Study results

MK0653C-855-CSR_final redaction.pdf(2.69 MB)

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 sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

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