A Post-marketing Database Surveillance to Investigate the Risk of Hepatic Events in Hypercholesterolemic Patients Treated with ATOZET or Ezetimibe Atorvastatin coadministration in Japan (MK-0653C-853)

First published: 15/06/2021

Last updated: 23/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS41295

Study ID

46425

DARWIN EU® study

No

Study countries

☐ Japan

Study description

The purpose of the study is to investigate hepatic health outcomes of interest (HOI) fulminant hepatitis, hepatitis, jaundice in participants who receive ATOZET compared to participants with coadministration of ezetimibe and atorvastatin. It will also study 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

Clinical Trials Disclosure Merck Sharp & Dohme Corp.
datasharing@organon.com

Study contact

datasharing@organon.com

Primary lead investigator

Clinical Trials Disclosure Merck Sharp & Dohme Corp.

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 01/05/2020

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-853-00-v2-Prot_Final Redaction.pdf(1.46 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 hepatic health outcomes of interest (HOI) between those taking ATOZET and those taking the coadministration of ezetimibe and atorvastatin.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Post-marketing database surveillance (PMS)

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 populations will include patients with hypercholesterolemia who are: 1) undergoing treatment with ATOZET, or 2) undergoing treatment with coadministration of ezetimibe and atorvastatin, between 1-APR-2018, and 30-SEP-2020, (selection period) in the MID-NET database.

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 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) Patients who have any missing information (e.g., gender, age), OR
7) Patients who have severe liver dysfunction considered as the contraindication for the use of Ezetimibe or Atorvastatin will be excluded.

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 hepatic HOI is the combination of hepatic diagnoses (fulminant hepatitis, hepatitis, jaundice) AND laboratory test values (AST > 3 × ULN or ALT > 3 × ULN). The secondary hepatic HOI is hepatic diagnoses (fulminant hepatitis, hepatitis, jaundice) AND/OR various definitions of abnormal AST or ALT.

Data analysis plan

- Calculation of number of hepatic 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 hepatic HOI, adjusting for covariates, for the ATOZET and ezetimibe/atorvastatin coadministration groups

Documents

Study results

MK0653C-853-CSR_final redaction.pdf(2.72 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