# 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**

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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: 01/05/2020

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**Study start date**

Planned: 12/06/2021

Actual: 11/06/2021

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**Data analysis start date**

Planned: 01/09/2021

Actual: 08/09/2021

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**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

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**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

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**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

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**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.

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**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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**Special population of interest**

Hepatic impaired

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**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