

# 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

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### Study ID

46433

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### DARWIN EU® study

No

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### Study countries

## 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.

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
## 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.  
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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

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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-855-00-v2\\_Final Redaction.pdf](#) (1.49 MB)

## Regulatory

### **Was the study required by a regulatory body?**

Yes

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### **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

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**Study type:**

Non-interventional study

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**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 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

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**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

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### **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
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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 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).

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## 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)

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## 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

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### Check completeness

Unknown

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### Check stability

Unknown

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### Check logical consistency

Unknown

## Data characterisation

## **Data characterisation conducted**

No