

# A Post-marketing Database Surveillance to Investigate the Risk of Rhabdomyolysis and Myopathy in Hypercholesterolemic Patients Treated with ATOZET or Ezetimibe Atorvastatin coadministration in Japan (MK-0653C-854)

**First published:** 15/06/2021

**Last updated:** 23/04/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS41341

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### Study ID

46429

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### DARWIN EU® study

No

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## Study countries

☐ Japan

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## Study description

The purpose of this study is to investigate muscle health outcomes of interest (HOI) rhabdomyolysis and myopathy in participants who receive ATOZET compared to participants taking the coadministration of ezetimibe and atorvastatin. It will also study these risks in participants with hepatic impairment.

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## Study status

Finalised

# Research institutions and networks

## Institutions

**Merck & Co.**

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

## Contact details

### Study institution contact

Clinical Trials Disclosure Merck Sharp & Dohme Corp.  
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Study contact

[datasharing@organon.com](mailto: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: 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-854-00-v2-Final Redaction.pdf](#)(1.44 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

Safety study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To compare the incidence rates of muscle 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

## 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, OR
- (8) Patients whose CK level exceeded the ULN in the 6 months before index date, OR
- (9) Patients who were diagnosed with rhabdomyolysis or myopathy in the 6 months 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 (C10AA05), 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 a
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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 HOIs are the combination of a rhabdomyolysis diagnosis code AND laboratory test value (CK >10 x upper limit of normal) and the combination of a myopathy diagnosis code AND laboratory test value (CK > 10 x upper limit of normal). The secondary HOIs are a rhabdomyolysis or myopathy diagnosis code AND/OR various definitions of an abnormal CK laboratory test value.

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## Data analysis plan

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

# Documents

## Study results

[MK-0653C-854-CSR\\_final redaction.pdf](#)(2.68 MB)

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## Data management

## 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