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# Studying how lomitapide treatment affects the risk of serious heart problems in people with a rare inherited high cholesterol condition

**Submission date**
12/06/2025

**Recruitment status**
No longer recruiting

**Registration date**
07/07/2025

**Overall study status**
Ongoing

**Last Edited**
18/08/2025

**Condition category**
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

## Plain English summary of protocol

Background and study aims
Homozygous familial hypercholesterolemia (HoFH) is a rare, life-threatening condition characterized by a severe elevation of LDL cholesterol (LDL-C) and accelerated atherosclerosis. In these patients, an aggressive therapy to reduce LDL-C is mandatory to control the high risk of CHD associated with this disease. Lomitapide has been demonstrated to be very effective in reducing LDL-C in HoFH in both clinical trial and real-world experience. However, limited information is available on how this drug affects cardiovascular risk. Due to the rarity of the disease, a randomized controlled trial testing the effect of lomitapide on the incidence of major adverse cardiovascular events (MACE) is not feasible.
To overcome this, an observational study with the aim of analyzing the occurrence of MACE in HoFH patients exposed to lomitapide will be performed. In the Italian network of lipid centres, information about MACE in HoFH patients exposed to lomitapide is available for more than 30 patients. The duration of follow-up among these patients was not homogenous. In fact, there was a group of patients with barely 1 year of treatment and this may not represent a sufficient time to observe any detectable benefit on cardiovascular risk, especially in adult HoFH patients exposed to high levels of LDL-C since birth. Therefore, to provide a better estimation of the effect of lomitapide therapy on MACE, we have designed this observational study with a retrospective phase in which the data available will be collected, followed by a prospective phase where all patients will be followed up to completion of at least 3 years of treatment. As a parallel cohort of untreated HoFH is not available, we have decided to compare the occurrence of MACE during the 3-year period of lomitapide treatment with that which occurred in the same cohort during the 3-year period before initiation of lomitapide.

Who can participate?
Patients aged 18 years and over with homozygous familial hypercholesterolemia treated with lomitapide at any dosage for at least 12 months

What does the study involve?
All the tests and observations are made according to standard of care:
Patient demographic information (weight, BMI): sex, age, ethnicity and height.

Physical examination, vital signs (blood pressure and heart rate).
Medical history, including the genetic diagnosis (if available).
MACE assessment, Serious Adverse Events (SAEs).
Prior and concomitant lipid-lowering therapies.
Laboratory data: e.g. plasma lipids and liver function tests.
Liver MRI or ultrasound to assess the presence and severity of hepatic steatosis at baseline, if available (within the year before first lomitapide prescription).
Liver elastography or fibroscan at baseline, if available (within the year before first lomitapide prescription).
The maximum duration of the study will be about 3 years.

What are the possible benefits and risks of participating?
Benefits: There is no direct benefit from taking part in this study. However, the study can contribute to improving scientific knowledge of lomitapide therapy, HoFH clinical conditions, including its treatment management and quality of life in patients with HoFH.
Risks: As the registry is an observational study, the patients are not required to take any additional medication, treatment procedures or diagnostic tests as part of their study participation. About the risks and side effects associated with lomitapide (Lojuxta®), please refer to the Summary of Products Characteristics.

Where is the study run from?
More than 26 sites from Europe (Italy, Greece, France, the Netherlands and the United Kingdom) will participate in the study. The study is run from an Italian Sponsor (Fondazione SISA).

When is the study starting and how long is it expected to run for?
February 2024 to December 2027

Who is funding the study?
Fondazione SISA (Italy)

Who is the main contact?
Prof. Alberico Catapano, alberico.catapano@gmail.com

# Contact information

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Public, Scientific


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## Additional identifiers

### ClinicalTrials.gov (NCT)
NCT06832371

### Integrated Research Application System (IRAS)
345905

## Study information

### Scientific Title
Evaluation of the effect of lomitapide treatment on major adverse cardiovascular events in patients with homozygous familial hypercholesterolemia

### Acronym
LILITH

### Study objectives
Due to the rarity of the disease, a randomized controlled trial testing the effect of lomitapide on the incidence of major adverse cardiovascular events (MACE) is not feasible. To overcome this, an observational study with the aim of analyzing the occurrence of MACE in HoFH patients exposed
to lomitapide will be performed.

### Ethics approval required
Ethics approval required

### Ethics approval(s)
Approved 30/01/2025, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; +44 (0)207 104 8066, +44 (0)207 104 8227, +44 (0)207 104 8284; leicestercentral.rec@hra.nhs.uk), ref: 24/EM/0275

## Primary study design
Observational

## Study design
Observational multicenter international open-label retrospective and prospective study

## Study type(s)
Prevention

## Health condition(s) or problem(s) studied
MACE in patients with familial hypercholesterolemia

## Interventions
All the tests and observations are made according to standard of care:
Patient demographic information (weight, BMI); sex, age, ethnicity and height will be collected once at Y-3.
Physical examination, vital signs (blood pressure and heart rate)
Medical history will be collected once at Y-3, including the genetic diagnosis (if available).
MACE assessment, Serious Adverse Events (SAEs).
Prior and concomitant lipid-lowering therapies.
Laboratory data: for plasma lipids and liver function test (Total Cholesterol, HDL, Triglycerides, LDL-C, ALT, AST, GGT).
Apolipoprotein B, lipoprotein(a), hematology (i.e. complete blood count), glucose, glycated hemoglobin, albumin, coagulation (PT, PTT and fibrinogen), creatinine, BUN, CPK, C-reactive protein, and CK18F will be requested at baseline visit retrospectively only if these results are already available in medical records.

Liver MRI or ultrasound to assess the presence and severity of hepatic steatosis at baseline, if available (within the year prior to first lomitapide prescription). For liver MRI data, liver fat fraction will be assessed. For liver ultrasound, information on the severity of liver steatosis (absent, mild, moderate, severe) will be collected.

Liver elastography or fibroscan at baseline, if available (within the year prior to first lomitapide prescription). For liver elastography, information on Acoustic Radiation Forced Impulse (ARFI) and Controlled Attenuation Parameter (CAP). For fibroscan data, liver stiffness (Kpa) and CAP will be collected.

The maximum duration of the study will be 37 months, which is approximately 3 years.

## Intervention Type
Other

## Primary outcome(s)
The incidence of major adverse cardiovascular events (MACE) is assessed using medical records and hospital discharge summaries. Events are adjudicated by an independent expert committee.
Timepoints: retrospectively at each timepoint during the 3 years prior to lomitapide initiation, and prospectively during the 3 years of lomitapide treatment.

## Key secondary outcome(s)
1. LDL-C and plasma lipid levels (Total Cholesterol, HDL, Triglycerides, LDL-C) are measured using standard laboratory blood tests at each timepoint during the 3 years prior to lomitapide

initiation, and prospectively during the 3 years of lomitapide treatment
2. Liver function tests (ALT, AST, GGT) are measured using standard laboratory blood tests at each timepoint during the 3 years prior to lomitapide initiation, and prospectively during the 3 years of lomitapide treatment
3. Lipid-lowering treatment (LLT) changes, including discontinuation of LDL apheresis or addition of new agents, are collected via investigator medical records at each timepoint during the 3 years prior to lomitapide initiation, and prospectively during the 3 years of lomitapide treatment
4. MACE incidence assessed using alternative definitions (3-point and 4-point MACE), based on medical records and adjudicated by the expert committee at each timepoint during the 3 years prior to lomitapide initiation, and prospectively during the 3 years of lomitapide treatment

### Completion date
31/12/2027

## Eligibility

### Key inclusion criteria
1. Adult patients (age ≥18 years)
2. Patients with clinical or genetic diagnosis of HoFH who were treated with lomitapide at any dosage
3. On treatment with lomitapide for at least 12 months at the time of enrollment
4. Availability of 3 years medical records prior to the commencement of lomitapide treatment to confirm the occurrence of MACE events
5. Patients who have the ability to understand the requirements of the study and provide written informed consent to comply with the requirements

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Lower age limit
18 Years

### Sex
All

### Key exclusion criteria
1. Patients who were prescribed lomitapide outside of the marketing authorization or in contraindicated patients
2. Patients who are receiving lomitapide in clinical trials
3. Patients receiving an investigational agent, defined as any drug or biologic agent other than lomitapide that has not received Market Authorization in the country of participation, at time of enrolment

### Date of first enrolment

09/09/2024

**Date of final enrolment**
30/11/2025

# Locations

**Countries of recruitment**
United Kingdom

England

France

Greece

Italy

Netherlands

**Study participating centre**
**Imperial College Healthcare NHS Trust**
Hammersmith Hospital
Cane Road
London
United Kingdom
W12 0HS

**Study participating centre**
**Guy's & St Thomas' NHS Foundation Trust Royal Brompton and Harefield Hospitals**
Great Maze Pond
London
United Kingdom
SE1 9RT

**Study participating centre**
**Queen Elizabeth Hospital**
Mindelsohn Way
Birmingham
United Kingdom
B15 2GW

**Study participating centre**

**University Department of Medicine Central Manchester University Hospitals NHS Foundation Trust**
Oxford Road
Manchester
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UK M13 9WL

**Study participating centre**
**Centro per le Malattie Rare del Metabolismo dei Lipidi Unità di Medicina Interna e Malattie Metaboliche Dipartimento di Medicina Traslazionale e di Precisione Sapienza Università di Roma**
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**Study participating centre**
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**Study participating centre**
**U.O. ASTANTERIA/MCAU AOU Policlinico "Paolo Giaccone" di Palermo**
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**Study participating centre**
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**Study participating centre**
**DAI di Medicina Clinica Centro di Riferimento Regionale di Lipidologia e Dislipidemie AOU Federico II di Napoli**

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**Study participating centre**
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**Study participating centre**
**U.O. Nutrizione Clinica AOU Mater Domini di Catanzaro**
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**Study participating centre**
**S.S. Servizio Trasfusionale A.O.U. Ospedale S. Luigi Gonzaga**
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**Study participating centre**
**SC di Medicina ad indirizzo Metabolico Nutrizionale Ospedale Civile di Baggiovara AOU di Modena**
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**Study participating centre**
**Dipartimento di Medicina Traslazionale e per la Romagna Università degli Studi di Ferrara**
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**Study participating centre**
**Endocrinologia, Diabetologia e Malattie del Metabolismo Ospedale Maggiore di Borgo Trento A. O.U.I di Verona**
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**Study participating centre**
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**Study participating centre**
**U.O.C. Medicina Interna Ambulatorio DISLIPIDEMIE e PREVENZIONE dell'ATEROSCLEROSI Ospedale Regionale Generale "F. Miulli"**
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**Study participating centre**
**U.O.C. Clinica Medica I A.O.U. di Padova**
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**Study participating centre**
**Di.M.I. Genova Università degli Studi di Genova**
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**Study participating centre**

**Medicina Interna Ospedale Molinette AOU Città della Salute e della Scienza**
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**Study participating centre**
**Lipoapheresis Unit CENTRO DI RIFERIMENTO PER LA DIAGNOSI E IL TRATTAMENTO DELLE DISLIPIDEMIE EREDITARIE Fondazione Toscana Gabriele Monasterio**
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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
**METROPILITAN Hospital**
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**Study participating centre**
**University General Hospital of Ioannina**
Leoforos Stavrou Niarchou
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# Sponsor information

**Organisation**
Fondazione S.I.S.A.

# Funder(s)

**Funder type**
Other

**Funder Name**
Investigator initiated and funded

# Results and Publications

**Individual participant data (IPD) sharing plan**
The datasets generated during and/ora analysed during the current studi will be available upon request from Prof. Alberico Luigi Catapano (fondazione@sisa.it)

**IPD sharing plan summary**
Available on request

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol file | version 2.2 | 14/02/2025 | 20/06/2025 | No | No |