ISRCTN94783078 https://doi.org/10.1186/ISRCTN94783078

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
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
[X] 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

Type(s)
Public, Scientific

Contact name
Prof Alberico Catapano

ORCID ID
https://orcid.org/0000-0002-7593-2094

Contact details
Via Giuseppe Balzaretti, 7
Milano
Italy
20133
+39 (0)2 49637591
alberico.catapano@unimi.it

Type(s)
Principal Investigator

Contact name
Dr Jaimini Cegla

ORCID ID
https://orcid.org/0000-0003-1168-0366

Contact details
Cane Road
London
United Kingdom
W12 0HS
+44 (0)7775557295
j.cegla@imperial.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
345905

ClinicalTrials.gov number
NCT06832371

Secondary identifying numbers
Nil known

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

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

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

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 measure
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.

Secondary outcome measures
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

Overall study start date
01/02/2024

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
72

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
England

France

Greece

Italy

Netherlands

United Kingdom

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
United Kingdom
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
Viale del Policlinico 155
Roma
Italy
00161

Study participating centre
Prof. Paolo CALABRO' Dipartimento Scienze-Cardiovascolari AO "Sant'Anna e San Sebastiano" di Caserta
Via Ferdinando Palasciano
Caserta
Italy
81100

Study participating centre

U.O. ASTANTERIA/MCAU AOU Policlinico “Paolo Giaccone” di Palermo
Via del Vespro, 129
Palermo
Italy
90127

Study participating centre
Medicina Interna Cardiovascolare Dipartimento Malattie Cardio-Toraco-Vascolare Policlinico Sant’Orsola di Bologna
via Albertoni 15
Bologna
Italy
40138

Study participating centre
DAI di Medicina Clinica Centro di Riferimento Regionale di Lipidologia e Dislipidemie AOU Federico II di Napoli
Via Sergio Pansini, 5
Napoli
Italy
80131

Study participating centre
Direttore Nefrologia e Emodialisi Centro Aterosclerosi e Dislipidemie Ospedale Bassini ASST Nord Milano
Via M. Gorki, 50
Cinisello Balsamo
Italy
20092

Study participating centre
U.O. Nutrizione Clinica AOU Mater Domini di Catanzaro
Via Tommaso Campanella 115
Catanzaro
Italy
88100

Study participating centre
S.S. Servizio Trasfusionale A.O.U. Ospedale S. Luigi Gonzaga
Regione Gonzole, 10
Orbassano

Italy
10043

Study participating centre
SC di Medicina ad indirizzo Metabolico Nutrizionale Ospedale Civile di Baggiovara AOU di Modena
Via Pietro Giardini, 1355
Modena
Italy
41124

Study participating centre
Dipartimento di Medicina Traslazionale e per la Romagna Università degli Studi di Ferrara
Via Aldo Moro, 8
Ferrara
Italy
44124

Study participating centre
Endocrinologia, Diabetologia e Malattie del Metabolismo Ospedale Maggiore di Borgo Trento A. O.U.I di Verona
Piazzale Aristide Stefani, 1
Verona
Italy
37126

Study participating centre
U.O.C. di Medicina Interna P.O. Nesima ARNAS Garibaldi
Via Palermo, 636
Catania
Italy
95122

Study participating centre
U.O.C. Medicina Interna Ambulatorio DISLIPIDEMIE e PREVENZIONE dell'ATEROSCLEROSI Ospedale Regionale Generale "F. Miulli"
S.P. Acquaviva/Santeramo Km 4.100
Acquaviva delle Fonti
Italy
70021

Study participating centre
U.O.C. Clinica Medica I A.O.U. di Padova
Via Giustiniani, 2
Padova
Italy
35128

Study participating centre
Di.M.I. Genova Università degli Studi di Genova
Viale Benedetto XV, 6
Genova
Italy
16132

Study participating centre
Medicina Interna Ospedale Molinette AOU Città della Salute e della Scienza
Corso Bramante, 88
Torino
Italy
10126

Study participating centre
Lipoapheresis Unit CENTRO DI RIFERIMENTO PER LA DIAGNOSI E IL TRATTAMENTO DELLE DISLIPIDEMIE EREDITARIE Fondazione Toscana Gabriele Monasterio
Via Moruzzi, 1
Pisa
Italy
56124

Study participating centre
Unité de Lipidologie et Prévention Cardiovasculaire Centre de Compétence Dyslipidémies Rares (CEDRA) Service de Nutrition, Hôpital Pitié-Salpétrière
APHP 83 bd de l'hôpital
Paris
France
75013

Study participating centre

Hôpitaux Universitaires de Strasbourg – Hôpital de Hautepierre Unité de Nutrition Thérapeutique Service d'Endocrinologie – Diabétologie et Nutrition - 1
Avenue Molière BP 49
Strasbourg
France
67098

Study participating centre
Service Médecine Interne et de Médecine Polyvalente-post-Urgences Centre de compétences dyslipidémies rares (CEDRA) Hôpital Claude Huriez
CHU Lille Rue Michel Polonovski
LILLE
France
59037

Study participating centre
Department of Nutrition- Metabolic disease and Endocrinology (Pr Valéro), La Conception Hospital
147 went Baille
MARSEILLE
France
13385

Study participating centre
Erasmus University Medical Center
Dr. Molewaterplein 40
Rotterdam
Netherlands
3015 GD

Study participating centre
Radboud University Medical Centre
Geert Grooteplein Zuid 10
Nijmegen
Netherlands
6525 GA

Study participating centre
METROPILITAN Hospital
Ethnarchou Makariou 9 & Eleftheriou Venizelou 1
Piraeus

Greece
185 47

Study participating centre
University General Hospital of Ioannina
Leoforos Stavrou Niarchou
Ioannina
Greece
455 00

Sponsor information

Organisation
Fondazione S.I.S.A.

Sponsor details
Via Giuseppe Balzaretti 7
Milano
Italy
20133
+39 (0)2 49637591
fondazione@sisa.it

Sponsor type
Research organisation

Website
http://www.sisa.it

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan

The sponsor will present the results of this trial in a final Clinical Study Report (CSR) in accordance with GCP and all other regulatory obligations. The study results will be published and /or presented at scientific meetings. The sponsor is the owner of the data resulting from this clinical trial. Once the study has been closed and the Study Coordinator has presented the main study publication, any participating Centre may use its own data (data generated in its own centre) for educational purposes, publications and presentations. These may be sent to the sponsor for approval with a 15-day notice for abstracts, presentations or educational material and a 30-day notice for publications.

Intention to publish date
01/09/2028

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