ISRCTN16728593 https://doi.org/10.1186/ISRCTN16728593

A study to assess the efficacy and safety of OATD-01 for the treatment of active pulmonary sarcoidosis

Submission date
23/09/2023

Recruitment status
No longer recruiting

Registration date
20/11/2023

Overall study status
Completed

Last Edited
16/10/2025

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
The study will test OATD-01, an experimental medicine, for the first time in patients with pulmonary sarcoidosis. The study goal is to evaluate OATD-01 in the reduction of inflammation and assess its safety. OATD-01 is a novel small molecule, which affects the activity of CHIT1. CHIT1 also known as chitotriosidase is an enzyme (a catalyst of chemical reactions) which has been shown to be involved in several lung diseases including pulmonary sarcoidosis. Therefore OATD-01 blocks this enzyme to reduce inflammation. OATD-01 has been tested in 129 healthy volunteers and has been shown to block CHIT1. It has also shown that it has an acceptable safety level to move to the next stage of clinical trials.

Who can participate?
Patients aged 18 years and over with pulmonary sarcoidosis

What does the study involve?
Up to 42 days of screening, 12 weeks of treatment and 4 weeks follow-up after the last dose per subject that is not withdrawn prematurely (subject to one or more unscheduled follow-up visits in case of premature withdrawal from the study treatment due to an adverse event that has not resolved or stabilized by week 12).

What are the possible benefits and risks of participating?
The main ethical issue related to this study is exposing participants to an experimental drug which involves the possibility of unknown side effects. Consequently, all participants are well informed of the risks involved and sign a consent form acknowledging this prior to starting the study. They are able to withdraw their consent and participation in the study at any time, without reason, although we would request a final discharge visit if they withdrew after the administration of the study drug. The PET/CT scan will require the administration of a radioactive isotope to improve the imaging results. Most of these will be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your body which provide your doctor with clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. MRI scans use a magnetic signal

sent through your body. If the patient has any metal parts in their body, there is a risk of interference, including heating and injury. If the patient knows of metal within their body (for example, hip replacement, knee replacement, cardiac stents, pacemaker, heart valve), please tell your study doctor. The MRI scan makes noise, and leaves little space for movement, so you may feel anxious during the test. The procedure for blood collection may cause mild pain and bruising at the collection site. The placement of an indwelling catheter is proposed in order to minimise these effects for rapid sampling. Very rarely, a blockage of a vein or a small nerve injury can occur, resulting in numbness and pain. If this occurs, it will resolve with time. The patients' blood pressure and pulse will be measured using an inflatable cuff which will be placed on the arm. They may experience mild discomfort in the arm whilst the cuff is inflated. Small sticky pads will be placed on the patient's upper body before the ECG. Before the pads are applied, the skin needs to be cleaned. Like Elastoplast®, these sticky pads may be uncomfortable to remove.

Where is the study run from?
Molecure S.A. (Poland)

When is the study starting and how long is it expected to run for?
September 2023 to December 2025

Who is funding the study?
Molecure S.A. (Poland)

Who is the main contact?
Dr Nikhil Hirani, N.Hirani@ed.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Nikhil Hirani

Contact details
51 Little France Crescent
Edinburgh
United Kingdom
EH16 4SA
+44 (0)131 242 1873
N.Hirani@ed.ac.uk

Type(s)
Scientific

Contact name
Dr Simbec Orion

Contact details
Simbec-Orion Group
Merthyr Tydfil Industrial Park
Cardiff Road

Merthyr Tydfil
United Kingdom
CF48 4DR

Additional identifiers

ClinicalTrials.gov (NCT)
NCT06205121

Clinical Trials Information System (CTIS)
2023-506642-23

Integrated Research Application System (IRAS)
1008468

Central Portfolio Management System (CPMS)
57634

Protocol serial number
OATD-01-C-03

Study information

Scientific Title
A randomized, double-blind, placebo-controlled, multicenter study to assess the efficacy and safety of a 12-week administration of OATD-01, an oral inhibitor of chitinase-1 (CHIT1), for the treatment of active pulmonary sarcoidosis (the KITE study)

Acronym
KITE

Study objectives
To evaluate the response to a 12-week treatment with OATD-01 as a reduction of granulomatous inflammation in pulmonary parenchyma evaluated by [18F]FDG PET/CT imaging in subjects with active pulmonary sarcoidosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/11/2023, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; +44 (0)2071048227; leicestercentral.rec@hra.nhs.uk), ref: 23/EM/0237

Primary study design
Interventional

Study design
Double-blind randomized placebo-controlled adaptive trial

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Active pulmonary sarcoidosis

Interventions
Subjects will be randomized in a 1:1 ratio under double-blind conditions according to the IRT electronic system to receive either 25 mg film-coated oral OATD-01 tablets or oral placebo tablets. Randomization will be stratified by the previous active treatment status for sarcoidosis (previously treated/treatment-naïve).

One tablet daily, in the morning, is to be taken orally as a fixed regimen after breakfast for 12 weeks. The first dose will be taken onsite at the randomization visit W0; the study drug will be also taken at the onsite visits W4 and W8 and EOT visit (if coincides with the last day of treatment).

Treatment compliance will be source-documented in a subject's diary and recorded in the eCRF by the investigator.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
OATD-01

Primary outcome(s)
Response to treatment from baseline to End-of-Treatment (EOT) classed as Complete response, Partial response, Stable disease and Progressive disease based on Standard Uptake Volume (SUV) changes in the uptake for {18F]FDG-PET/CT above the background (pulmonary parenchyma /ascending aorta) in pulmonary target lesions and any new lesions

Key secondary outcome(s)
1. Granulomatous inflammation evaluated by [18F]FDG PET/CT imaging, quantified as the percent change of maximum, mean, peak SUV (SUVmax, SUVmean, SUVpeak), and volume of the lesions in pulmonary parenchyma, mediastinal/hilar nodes, and extrathoracic locations at Screening and EoT
2. Number of patients escaping to corticosteroids. Discontinuing the treatment with IMP and escaping to standard-of-care treatment will be captured promptly at EOT for efficacy evaluation. Subjects with study treatment discontinued and escape therapy prescribed will be followed up for safety up until W12 visit.
3. Absolute change in Forced Vital Capacity (FVC, % predicted) and Forced Expiratory Volume in the first second (FEV1) at Screening, W0, W4, W8 and EoT
4. Quality of life measured by the Kings Sarcoidosis Questionnaire General and Lung (KSQ GENERAL and LUNG) scores at W0, EoT and W12
5. Occurrence of Treatment-emergent Adverse Events (TEAEs), SAEs, Adverse Events of Special Interest (AESIs), TEAEs leading to discontinuation and TEAEs leading to death, recorded from the time of signature of informed consent until 30 days after the last of OATD-01/Placebo.

6. Occurrence of clinically significant laboratory (hematology and biochemistry) parameter abnormalities
7. Mean change in vital signs (systolic and diastolic blood pressure, heart rate, respiratory rate) at Screening, W0, W2, W4, W8, EoT, W12 and FUP
8. Occurrence of any clinically significant abnormalities in 12-lead electrocardiography (ECG) or 24-h ECG at Screening, W0, W2, W4, W8, EoT, W12 and FUP
9. Change from baseline and in between visits in cardiac safety parameters evaluated by 12-lead ECG [Heart Rate (HR) , PR QTcF and QRS] at Screening, W0, W2, W4, W8 and EoT
10. Occurrence of:
10.1. QTcF >450 ms (male), >470 ms (female) and >500 ms (any sex)
10.2. Change from baseline in QTcF >30 ms and >60 ms
11. Heart rhythm abnormalities including supraventricular arrhythmias, ventricular arrhythmias, and non-sustained ventricular tachycardias
12. Occurrence of a clinically significant abnormality of sperm parameters at W0, W8 and EoT
13. Occurrence of clinically significant abnormality of free testosterone concentration
14. Occurrence of TEAEs of sensation abnormalities or ataxia
15. Proportion of subjects with clinically significant thyroid parameters (Thyroid Stimulating Hormone [TSH], Free Triiodothyronine [FT3], and Free Thyroxine [FT4] and renal function parameters [blood urea nitrogen (BUN)/total urea, creatinine, creatinine clearance (CrCL)]
16. Pharmacokinetics: mean plasma concentrations of OATD-01 measured at W0, W4, W8 and EoT

Exploratory endpoints and biomarker evaluations:
1. Measured at baseline, W4, W8 and EOT:
1.1. CHIT1 activity in plasma
1.2. CHIT1 activity in sputum (induced collection, in subjects able to produce an analyzable sputum specimen)
2. Serum levels of CHIT1 protein, soluble interleukin-2 receptor [sIL-2R], chemokine (C-C motif) ligand 18 [CCL18] and Tumor Necrosis Factor α (TNF-α) levels
measured pre-dose at visit W0, at any timepoint post-dose at visits W4, W8 and EOT if on study treatment.

Supplementary analysis to describe any differences in the response in the subpopulation of subjects with the polymorphism of the 24-base rs3831317 pair duplication of the CHIT1 gene.

The anti-granulomatous effect of OATD-01 assessed using [18F]FDG PET/CT imaging will be additionally evaluated, as a secondary analysis, in the subpopulation of subjects with no such polymorphism in biallelic form. All subjects enrolled will be genotyped at randomization.

The primary and all secondary efficacy endpoints will be analyzed based on the following three subgroups.
1. Subjects with no biallelic mutation in the form of the 24-base pair duplication, rs3831317, of the CHIT1 gene (S1 subgroup)
2. Treatment-naïve subjects (S2 subgroup)
3. Subjects with previous potentially effective therapy (S3 subgroup)

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Male and female subjects with active symptomatic pulmonary sarcoidosis, (definite diagnosis of active pulmonary sarcoidosis per ATS guidelines)
2. Treatment-naïve or previously treated (no recruitment cap)
3. Parenchymal pulmonary involvement on [18F]FDG PET/CT

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Requirement for immediate start of standard of care therapy for pulmonary sarcoidosis
2. Cardiac or neuro- sarcoidosis
3. History of/active Löfgren syndrome
4. Clinically significant lung disease other than sarcoidosis (e.g. tuberculosis, asthma, Chronic Obstructive Pulmonary Disease, interstitial lung disease, lung cancer) or any current inflammatory or immunological systemic disease other than sarcoidosis
5. Potentially effective systemic or inhaled pharmacological (including investigational) therapy for sarcoidosis (whether pulmonary or other disease), with the exception of any of the following: a. corticosteroids received not later than 3 months prior to enrolment b. immunosuppressants or anti-TNF agents (or other anti-inflammatory/anti-fibrotic treatment) received not later than 4 months prior to enrolment
6. Systemic treatment indication being an extrapulmonary location of sarcoidosis (e.g., neurological)
7. Heart conditions: QTcF interval prolongation, cardiac arrhythmia (other than non-sustained supraventricular arrhythmia), heart failure (New York Heart Association class III or IV) and/or known myocardial hypertrophy or Left Ventricle Ejection Fraction <50% in the cardiac MRI
8. Known neurosarcoidosis or small fiber neuropathy or medical conditions causing primary ataxia
9. Lab abnormalities: Abnormal bilirubin, transaminases, alkaline phosphatase (ALP), Creatinine clearance (CrCL) Hypokalemia hypocalcemia (<2.1 mmol/L), marked fasting hyperglycemia at screening
10. Uncontrolled diabetes at Screening with plasma glucose exceeding 8.3 mmol/L, or other contraindication to [18F]FDG administration and/or PET procedure (including body temperature >37°C and any metabolic disease affecting the energy metabolism of muscles) as described in the separately provided PET protocol
11. Known positivity for Human Immunodeficiency Virus (HIV 1/2 antibodies), hepatitis B virus (HBV), or hepatitis C virus (HCV), or detected at screening
12. Severe, uncontrolled systemic disease (e.g., cardiovascular, pulmonary, thyroid, renal or metabolic disease) at Screening, or other condition, which in the opinion of the investigator,

would compromise the safety of the subject or the subject's ability to participate in the study
13. Current smoker of >5 cigarettes or e-cigarettes per day or user of nicotine-releasing alternatives (patches, chewing gums etc)
14. Prohibited medications: Current treatment with drug with QT prolongation effect, thiazide diuretics, strong CYP3A4 inhibitors and/or inducers, P-glycoprotein and/or BCRP strong inhibitors, drugs that are sensitive substrates of OCT1, MATE1, MATE2K, OAT3 with a narrow therapeutic index

Date of first enrolment
01/03/2024

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

England

Scotland

Denmark

France

Germany

Greece

Netherlands

Norway

Poland

United States of America

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
Royal Brompton Hospital
Sydney Street
London
United Kingdom
SW3 6NP

Sponsor information

Organisation
Molecure S.A.

Funder(s)

Funder type
Industry

Funder Name
Molecure S.A.

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date