

# RESET-Myositis: An Open-Label Study to Evaluate the Safety and Efficacy of CABA-201 in Subjects With Active Idiopathic Inflammatory Myopathy

<b>Submission date</b> 12/04/2024	<b>Recruitment status</b> Recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/07/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 02/08/2024	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

This study is testing the safety and effectiveness of CABA-201 in adults with Idiopathic Inflammatory Myopathy, including dermatomyositis (DM), anti-synthetase syndrome (ASyS), and immune-mediated necrotizing myopathy (IMNM), who are not getting improvement from other treatments. CABA-201 is a chimeric antigen receptor T cell therapy (CART) that is intended to find and temporarily remove B cells in the patient's body, including those that are thought to cause their disease.

### Who can participate?

Adults up to age 65 years who have the DM, ASyS or IMNM forms of IIM, muscle weakness and signs of active disease despite prior treatment with standard of care may participate. Additional tests will be performed to determine if a patient can participate.

### What does the study involve?

The study involves screening so the participant meets the participation criteria, collection of the participant's white blood cells by a process called leukapheresis, manufacture of CABA-201 using the collected white blood cells. Once the CABA-201 is made, the participant will be given preconditioning with fludarabine and cyclophosphamide starting 5 days before CABA-201. Cyclophosphamide and fludarabine are both approved in the UK for the treatment of certain cancers and are often given as part of a "preconditioning" regimen prior to infusion of CART cell therapies used to treat certain cancers to help the CART cell therapies work better

CABA-201 is given via the vein on Day 1. Immediately following CABA-201 infusion, participants are monitored in the hospital for approximately 10 days. Follow-up after this time will be done in the outpatient clinic. Participants will be expected to remain in the study for up to 3 years, including screening, pre-treatment, CABA-201 infusion and follow up, with an additional long-term follow-up period for a total of 15 years after CABA-201 infusion.

What are the possible benefits and risks of participating?

There is a possibility that symptoms of IIM may get better after CABA-201. It is not known how long this improvement may last. It is also possible that the IIM does not get better, or even gets worse after CABA-201.

There are risks associated with CABA-201, the preconditioning medications fludarabine and cyclophosphamide and the study assessments. The safety of CABA-201 is still being studied. The risks are based on studies and the experience of other people who have received other CAR-T cell therapy with preconditioning.

Low blood counts may occur and it is unknown how long this will last. CABA-201 and the preconditioning may increase the risk of infection. It is not known how long this will last. After they are infused into the body, CABA-201 cells can release compounds such as cytokines which are chemical messengers to other cells. Release of large amounts of certain cytokines can cause "cytokine release syndrome," a severe flu-like syndrome. Symptoms of these severe flu-like syndromes include high fevers, chills and shaking, muscle aches, joint aches, sweating, nausea, vomiting, loss of appetite, fatigue, headache, and fast heart rate. Other similar therapies have been associated with immune effector cell-associated neurotoxicity syndrome (ICANS), which may be serious and require treatment. Infusion and hypersensitivity reactions may occur after CABA-201 infusion. CABA-201 is made using a non-live, inactive lentivirus. It is theoretically possible that a new virus which can multiply may be made during CABA-201 manufacture or after infusion, called replication-competent lentivirus (RCL). RCL has never been detected during any phase of manufacture of CABA-201 or other similar products which use an inactive lentivirus. It has also not been found in patients who received these products. Participants treated with these products may have false positive HIV test results due to the similarity between HIV and the lentivirus used.

The CABA-201 T cells could divide and multiply without control of normal control mechanisms. People may develop new tumors which come from their genetically modified T cells. The occurrence of a new autoimmune disease (AD) or worsening of myositis after CAR T therapy could be due to the CABA-201. To date, no worsening of AD has been reported after infusion of CAR T cells with cyclophosphamide and fludarabine.

Risks associated with preconditioning include: cough, fatigue, fever, chills, weakness, vision change, swelling of arms and feet, gastrointestinal upset, hair loss, skin rash or discoloration, changes in fingernails, sores and inflammation along the gastrointestinal tract, bleeding, bladder irritation, blood clots, heart damage or abnormal heart rhythm, lung damage, birth defects, confusion, abnormal levels of liver and pancreas enzymes, lymph system disorders, coma, seizures, agitation, blindness, inflammation of eye nerves and cancer, including blood cancer.

Risks associated with study procedures include pain, bleeding, swelling or bruising where blood is drawn or intravenous catheters are placed, radiation exposure with certain tests, and fear of small spaces from certain tests.

There is a risk that participant privacy is breached. Data will have a code number which will be provided to Cabaletta and other individuals and/or companies that act on the sponsor's behalf. Access to your un-coded information will be restricted to the study doctor, study staff, health authorities and staff authorized by the sponsor (i.e., study monitors, auditors), when they need it to verify the data and procedures of the study.

Where is the study run from?  
Advanced Clinical (UK)

When is the study starting and how long is it expected to run for?  
June 2023 to July 2028

Who is funding the study?  
Cabaletta Bio (USA)

Who is the main contact?  
1. Dr Christina Shepherd, cshepherd@advancedclinical.com  
2. Dr Hector Chinoy, hector.chinoy@nca.nhs.uk

## Contact information

**Type(s)**  
Scientific

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Dr Christina Shepherd

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## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**  
1008852

**ClinicalTrials.gov number**

NCT06154252

### **Secondary identifying numbers**

CAB-201-002, IRAS 1008852, CPMS 58719

## **Study information**

### **Scientific Title**

A Phase 1/2, Open-label Study to Evaluate the Safety and Efficacy of Autologous CD19-specific Chimeric Antigen Receptor T cells (CABA-201) in Subjects with Active Idiopathic Inflammatory Myopathy

### **Study objectives**

The main objective of the trial is to determine the safety of CABA-201 and to identify the appropriate dose to be administered to participants with idiopathic inflammatory myopathy.

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

Approved 11/06/2024, North East – York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ , United Kingdom; +44 (0)207 104 8079; York.rec@hra.nhs.uk), ref: 24/NE/0081

### **Study design**

Interventional non-randomized

### **Primary study design**

Interventional

### **Secondary study design**

Non randomised study

### **Study setting(s)**

Hospital, Other

### **Study type(s)**

Safety, Efficacy

### **Participant information sheet**

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

### **Health condition(s) or problem(s) studied**

Active Idiopathic Inflammatory Myopathy including dermatomyositis, anti-synthetase syndrome, and immune-mediated necrotizing myopathy

### **Interventions**

A single intravenous infusion of CABA-201 at a single dose level following preconditioning with fludarabine and cyclophosphamide

## **Intervention Type**

Biological/Vaccine

## **Pharmaceutical study type(s)**

Pharmacokinetic, Pharmacodynamic, Pharmacogenetic, Therapy

## **Phase**

Phase I/II

## **Drug/device/biological/vaccine name(s)**

CABA-201, fludarabine, cyclophosphamide

## **Primary outcome measure**

AEs occurring within 28 days after CABA-201 infusion, including DLTs and AEs related to CABA-201

## **Secondary outcome measures**

Within 156 weeks post CABA-201 infusion:

1. AEs, vital signs, physical examination, and clinical laboratory tests occurring within 156 weeks after CABA-201 infusion.
2. Changes from baseline in WBC with differential, including B cell counts.
3. Frequency of reaching released product at target dose.
4. Fold cell expansion, transduction efficiency, vector copy number per cell, and product phenotype.
5. Total number of CABA-201 positive cells in each manufacturing run.
6. Percent of CAR-transduced cells in the total number of cells for infusion.
7. Number and percentage of CABA-201 positive cells in the peripheral blood of subjects over time.
8. Changes in muscle enzymes (CK, LDH, AST, ALT or aldolase).
9. Changes in myositis-specific antibody (MSA) levels.
10. Changes from baseline in TIS.
11. Proportion of subjects achieving major (TIS  $\geq 60$ ), moderate (TIS  $\geq 40$ ), and minimal (TIS  $\geq 20$ ) response.
12. Change in individual 6 core set measures (CSMs).
13. Time to minimal, moderate and major response.
14. Proportion of subjects with maintenance of TIS response.
15. Change in IIM-related rashes or lesions on CDASI.
16. Muscle changes as demonstrated on MRI evaluation.
17. Change in PFTs.
18. Change in HRCT chest assessments.
19. Change from baseline in the dose of concomitant corticosteroids and other IIM-related therapies.
20. Proportion of subjects achieving a dose of  $\leq 5$  mg/day oral prednisone or equivalent.
21. Proportion of subjects who require no IIM-related therapies.
22. Changes from baseline in FACIT-F, pain NRS, PROMIS physical function 20a v2.0, PGIC, SF-36v2, and EQ-5D-5L scores.
23. Proportion of subjects who meet confirmed deterioration criteria.
24. Time to confirmed deterioration.
25. Proportions of subjects achieving drug-free major, moderate and minimal responses.
26. Time to achievement of drug-free major, moderate and minimal responses.

**Overall study start date**

05/06/2023

**Completion date**

31/07/2028

## Eligibility

**Key inclusion criteria**

1. Age  $\geq 18$  and  $\leq 65$  years
2. A clinical diagnosis of IIM, based on the 2017 European League Against Rheumatism/American College of Rheumatology classification criteria
3. Diagnosis of DM, ASyS, IMNM based on the presence of serum myositis-specific antibodies
4. Evidence of active disease, despite prior or current treatment with standard of care treatments, as defined by the presence of elevated creatine kinase (CK), DM rash, or active disease on muscle biopsy, magnetic resonance imaging (MRI), or electromyography
5. Presence of muscle weakness

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Upper age limit**

65 Years

**Sex**

Both

**Target number of participants**

18

**Key exclusion criteria**

1. Contraindication to leukapheresis
2. History of anaphylactic or severe systemic reaction to fludarabine, cyclophosphamide or any of their metabolites
3. Active infection requiring medical intervention at screening
4. Current symptoms of severe, progressive, or uncontrolled renal, hepatic, hematological, gastrointestinal, pulmonary, psychiatric, cardiac, neurological, or cerebral disease, including severe and uncontrolled infections, such as sepsis and opportunistic infections.
5. Concomitant medical conditions that, in the opinion of the investigator, might place the subject at unacceptable risk for participation in this study, interfere with the assessment of the effects or safety of the investigational product or with the study procedures
6. Significant lung or cardiac impairment
7. Previous CAR T cell therapy
8. Prior solid organ (heart, liver, kidney, lung) transplant or hematopoietic cell transplant

**Date of first enrolment**

20/12/2023

**Date of final enrolment**

31/07/2025

## **Locations**

**Countries of recruitment**

England

United Kingdom

United States of America

**Study participating centre****Northern Care Alliance NHS Foundation Trust**

Salford Royal Hospital, Division of Surgery & Tertiary Medicine

Ground Floor Offices, Clinical Sciences Building

Stott Lane

Salford

United Kingdom

M6 8HD

**Study participating centre****Kings College Hospital NHS Foundation Trust**

Department of Rheumatology, Portocabin B

Caldecott Road

London

United Kingdom

SE5 9RS

**Study participating centre****National Hospital for Neurology and Neurosurgery**

UCLH NHS Foundation Trust

Queen Square

London

United Kingdom

WC1N 3BG

**Study participating centre****Manchester Royal Infirmary**

Manchester University NHS Foundation Trust

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United Kingdom  
M13 9WL

## Sponsor information

### Organisation

Advanced Clinical

### Sponsor details

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### Sponsor type

Industry

## Funder(s)

### Funder type

Industry

### Funder Name

Cabaletta Bio

### Alternative Name(s)

Cabaletta Bio, Inc., Cabaletta

### Funding Body Type

Government organisation

### Funding Body Subtype

For-profit companies (industry)

### Location

United States of America



# Results and Publications

## Publication and dissemination plan

- Peer-reviewed scientific journals
- Internal report
- Conference presentation
- Publication on website
- Other publication
- Submission to regulatory authorities

The study will be registered on ClinicalTrials.gov. Both websites are publicly accessible. After processing the data, the participants have the right to be informed of the overall results of the study. If the results of the study are published, then the subject’s identity will remain confidential. The investigator will maintain a list to enable subjects to be identified. However, this list will not be shared or distributed. All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. Subject names will not be supplied to the sponsor. Only the subject number will be recorded in the eCRF, and if the subject name appears on any other document, then it must be redacted before a copy of the document is supplied to the sponsor. As part of the informed consent process, the subjects will be informed in writing that representatives of the sponsor, Independent Ethics Committee (IEC), or regulatory authorities may inspect their medical records to verify the information collected, and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws. In addition, all investigators in the study may have access to raw data for publication purposes with permission from the sponsor.

## Intention to publish date

31/07/2029

## 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

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version 1.0	02/06/2024	11/07/2024	No	Yes