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

Submission date
12/04/2024

Recruitment status
Recruiting

Registration date
16/07/2024

Overall study status
Ongoing

Last Edited
03/06/2026

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] 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 and children with idiopathic inflammatory myopathy, including dermatomyositis (DM), anti-synthetase syndrome (ASyS), and immune-mediated necrotizing myopathy (IMNM), or juvenile idiopathic inflammatory myopathy (JIIM) who are not getting improvement from other treatments. CABA-201 is a chimeric antigen receptor T cell therapy (CAR T) 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?
Children aged 6 years or older who have juvenile idiopathic inflammatory myopathy and adults up to age 75 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, and 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 CAR T-cell therapies used to treat certain cancers to help the CAR T-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 in the main study 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. Participants in the sub-studies will be expected to remain in the study for up to 1 year, 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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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06154252

Integrated Research Application System (IRAS)
1008852

Central Portfolio Management System (CPMS)
58719

Protocol serial number
CAB-201-002

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 or Active Juvenile Idiopathic Inflammatory Myopathy

Acronym
CAB-201-002

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

Primary study design
Interventional

Study design
Interventional non-randomized

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Active Idiopathic Inflammatory Myopathy including dermatomyositis, anti-synthetase syndrome, immune-mediated necrotizing myopathy, juvenile idiopathic inflammatory myopathy, juvenile dermatomyositis, juvenile polymyositis, juvenile myositis

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

Intervention Type
Biological/Vaccine

Phase
Phase I/II

Drug/device/biological/vaccine name(s)

CABA-201, fludarabine, cyclophosphamide

Primary outcome(s)
AEs occurring within 28 days after CABA-201 infusion, including DLTs and AEs related to CABA-201

Key secondary outcome(s)
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 ≥60), moderate (TIS ≥40), and minimal (TIS ≥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 ≤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.

Completion date
31/07/2028

Eligibility

Key inclusion criteria
Current inclusion criteria as of 03/06/2026:
Adult Cohorts:
1. Age ≥18 and ≤75 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, or IMNM
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
Other protocol-defined criteria apply.

Juvenile Cohort:
1. Age ≥6 and ≤17 years at enrollment
2. A clinical diagnosis of IIM, based on the 2017 The European League Against Rheumatism /American College of Rheumatology classification criteria
3. Evidence of active disease, despite prior or current treatment with standard of care treatments, as defined by the presence of elevated muscle enzymes, DM rash, or active disease on muscle biopsy, magnetic resonance imaging (MRI), or electromyography
Other protocol-defined criteria apply.

Previous inclusion criteria:
1. Age ≥18 and ≤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

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
6 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 03/06/2026:
Adult Cohorts:

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
Other protocol-defined criteria apply.

Juvenile Cohort:
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
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Date of first enrolment
20/12/2023

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Germany

Italy

Spain

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
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Study participating centre
Kings College Hospital NHS Foundation Trust
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Study participating centre
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Study participating centre
NIHR Great Ormond Street Hospital Clinical Research Facility
Great Ormond Street Hospital for Children NHS Foundation Trust
Great Ormond Street
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Sponsor information

Organisation
Advanced Clinical

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

Individual participant data (IPD) sharing plan

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?
Participant information sheet	version 1.0	02/06/2024	11/07/2024	No	Yes