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A trial to test CAR-T cells for glioblastoma in adults when standard treatment is not effective or stops working

Submission date 17/05/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/08/2024	**Overall study status** Ongoing	
Last Edited 09/04/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Glioblastoma is the most common type of brain tumour and despite continued research, remains incurable with little improvement in clinical outcomes over the last three decades. Current treatment for glioblastoma includes surgery, radiotherapy and chemotherapy. While these treatments can be successful in the short term, cancer often returns or progresses (increases) within a year. New treatments for glioblastoma are urgently needed.
The CARGO trial will treat glioblastoma patients with a form of CAR-T cells called CARGO-T cells if standard treatment has failed or their cancer has returned. CAR-T cells are T cells (a type of white blood cells) genetically modified in a lab to target tumour cells. In leukaemia and myeloma, CAR-T cells have shown promising results, and several products are now NHS approved.
CARGO-T cells target the mutated protein EGFRvIII which can be found on glioblastoma tumour cells in some patients.
The trial is a phase I, dose finding and safety study. This means the treatment has never been studied before in this disease and a safe or effective dose is unknown. CARGO will test whether CARGO-T cells can be successfully manufactured and used to treat GBM.

Who can participate?
Adults aged 16+ with glioblastoma that has not responded to or has returned following standard treatments.

What does the study involve?
The initial study procedure is confirming EGFRvIII tumour positivity via a biopsy. If eligibility is confirmed, participants will undergo an insertion of an Ommaya reservoir (or similar catheter) for monitoring intracranial pressure and possible ICV CARGO-T cells administrations, procurement of starting material for the CARGO-T cells and treatment to control disease whilst the CARGO-T cells are being manufactured. This treatment may include proton beam therapy. Once the CARGO-T cells are manufactured, patients will be given lymphodepletion in preparation for the IV CARGO-T cells infusion.
Up to 4 ICV CARGO-T cells infusions may be given if disease does not respond to or returns

following the previous infusion.
Participants will be followed up for up to 15 years following their last infusion.

What are the possible benefits and risks of participating?
Benefits:
There may be no benefit in taking part in this study. If the CARGO-T cells 'work', which is not yet known, this may help shrink the tumour or stop it from growing. The information we receive from those taking part in the study may help improve our knowledge of treating glioblastoma which may benefit the treatment of patients with high-grade gliomas, including glioblastoma, in the future.
Risks:
This patient population has exhausted standard treatments and the largest risk they face is disease progression.
The main risk of participating on the trial is the side effects of the interventions. Neurological side effects such as seizures, headaches and cognitive changes may be experienced. Immune-related side effects are also possible such as increased infections, flu-like symptoms and autoimmune reactions. The surgical procedures carry similar risks to any surgery such as infection and bleeding with the additional possibility of neurological side effects. Participants will be closely monitored, and treatment/supportive care provided where necessary.

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
May 2024 to June 2034

Who is funding the study?
Jon Moulton Charity Trust (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2022-003747-10

IRAS number
1007305

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
UCL/126897, IRAS 1007305, CPMS 57214

Study information

Scientific Title
Immunotherapy using CAR T-cells to target EGFRvIII for relapsed/refractory adult Glioblastoma

Acronym
CARGO

Study objectives
To evaluate the feasibility of ATIMP manufacture and the safety of administration in this setting.
To evaluate how effectively CARGO-T cells grow and persist in the body following administration.
To evaluate proton beam therapy as a bridging therapy to facilitate CARGO-T cells administration.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/08/2024, London - West London & GTAC Research Ethics Committee (2 Redman Place, London, E20 1JQ, United Kingdom; +44 (0)207 104 8184; westlondon.rec@hra.nhs.uk), ref: 24/LO/0471

Study design
Phase I dose-finding and safety study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Safety, Efficacy

Participant information sheet

Health condition(s) or problem(s) studied
Relapsed/refractory glioblastoma

Interventions
Whilst the CARGO-T cells are being manufactured, bridging therapy will be given to maintain disease control which may include proton beam therapy.
Following a lymphodepleting regimen of fludarabine & cyclophosphamide, patients will receive an infusion of IV CARGO-T cells at one of the following doses (Theme 1):
- Cohort 1: 50 million CARGO-T cells
- Cohort 2: 100 million CARGO-T cells
- Cohort 3: 100 million CARGO-T cells plus a single dose of 3mg/kg ipilimumab the day before their CARGO-T cell infusion

Subsequently, patients may be eligible for up to 4 doses of 10 million CARGO-T cells via intracerebroventricular (ICV) infusion (Theme 2) if they do not achieve complete remission at day 28 or experience frank relapse beyond day 28, and have not experienced significant /persistent toxicity following previous infusion(s).

Intervention Type
Drug

Pharmaceutical study type(s)
Prophylaxis, Therapy

Phase
Phase I

Drug/device/biological/vaccine name(s)
CARGO-T cells [INN not proposed yet]

Primary outcome measure
1. Toxicity following CARGO-T cells administration will be evaluated by the number of grade 3-5 adverse events causally related to the ATIMP at 28 days post ATIMP infusion
2. Feasibility of leukapheresis collection and generation of CARGO-T cells as evaluated by the number of therapeutic products generated following ATIMP manufacture

3. Feasibility of administration of CARGO-T cells therapy measured by the number of successful CARGO-T cells administrations, firstly as an IV agent (Theme 1) and in the event of non-response /relapse following IV, as an ICV agent, with option for repeated dosing (Theme 2)

Secondary outcome measures
1. Efficacy will be measured by the proportion of patients achieving responses and depth of response following the RANO 2.0 criteria at 1, 3 and 6 months post ATIMP infusion
2. Persistence and frequency of circulating CARGO-T cells in peripheral blood will be assessed by the number of CARGO-T cells in blood samples as per flow cytometry and qPCR at several timepoints between ATIMP infusion to 24 months post infusion
3. Relapse rate, progression-free survival and overall survival will be assessed at 12 and 24 months post ATIMP infusion
4. The feasibility of proton beam therapy as a bridging therapy will be assessed by the proportion of patients who complete PBT as planned at the time of completion of PBT, and the proportion of patients who then undergo CARGO-T cells administration on Day 0 (infusion)

Overall study start date
15/05/2024

Completion date
30/06/2034

Eligibility

Key inclusion criteria
1. Age ≥16 years
2. Disease status:
2.1. Relapsed or recurrent IDH-wildtype GBM confirmed by pathology review of surgically resected tissue, and
2.2. Tumour tissue is positive for EGFRvIII expression as performed by immunohistochemistry (IHC)
3. Written informed consent (or where applicable, consent by a legal representative)
4. Agree to undergo a pregnancy test and use adequate contraception (where applicable)
Trial inclusion criteria: for radiotherapy:
5. ≥6 months since completion of primary radiotherapy.
6. Prior history of standard dose, conventionally fractionated brain radiotherapy (i.e. 54 - 60Gy in 28 - 33 fractions).
7. Up to and including three enhancing lesions.
8. Predicted re-irradiation Gross Tumour Volume <50cm^3
9. Maximum diameter of enhancing disease must be ≤6cm

Participant type(s)
Patient

Age group
Mixed

Lower age limit
16 Years

Sex

Both

Target number of participants
12

Key exclusion criteria
1. ECOG 3 - 4
2. Metastatic or primary spinal GBM
3. Organ function:
3.1. Cardiac: Serious and uncontrolled cardiac arrhythmias despite medical management, history of ischemic heart disease within the last 6 months before eligibility confirmation and left ventricular ejection fraction (LVEF) <40%
3.2. Pulmonary: Requirement for supplemental oxygen and/or oxygen saturation ≤90% on air
3.3. Renal: Creatinine clearance <50 ml/min
3.4. Hepatology: Bilirubin >2x upper limit of normal
3.5. Neurologic: Pre-existing significant neurological disorders unrelated to the CNS malignancy investigated in this study
4. Active hepatitis B, C or HIV
5. Active severe infection
6. History of or active medical or psychiatric condition that is uncontrolled with current treatment or deemed by the investigators to be severe enough to preclude participation in this study
7. Unable to undergo leukapheresis due to contraindications, inability to tolerate procedure and /or issues with adequate venous access for the procedure
8. Known allergy to study product excipients (albumin, DMSO, dextran)
9. Cohort 3 only: Any contraindications to receiving ipilimumab including history of clinically significant pneumonitis or lung fibrosis <24 weeks before registration
10. History of auto-immune disease or connective tissue disease requiring systemic immunosuppression/disease-modifying agents within 24 months before registration or resulting in end-organ damage
11. Steroid therapy requiring >2 mg dexamethasone (or equivalent) daily
12. Women who are pregnant or breastfeeding

Date of first enrolment
25/03/2025

Date of final enrolment
25/03/2027

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University College London Hospital
University College London Hospitals NHS Foundation Trust

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Sponsor information

Organisation
University College London

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Sponsor type
University/education

Website
https://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Jon Moulton Charity Trust

Alternative Name(s)
The Jon Moulton Charity Trust

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Other

Anonymised trial data will be published as part of the trial publication in a peer-reviewed scientific journal. Trial data will also be included in the accompanying documents for any conference where final trial results are presented.

Intention to publish date
30/06/2035

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

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