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A study to explore the effect of immunotherapy drug, tebentafusp, on patients with clear cell sarcoma (ultra-rare, aggressive type of soft tissue sarcoma that primarily affects young adults)

Submission date
17/10/2025

Recruitment status
Recruiting

Registration date
05/02/2026

Overall study status
Ongoing

Last Edited
05/02/2026

Condition category
Cancer

[_] 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

Clear cell sarcoma (CCS) is a rare type of soft tissue cancer which has very limited treatment options. In this research study patients with advanced CCS will be treated with tebentafusp, a drug which is approved for melanoma. Previous research showed that melanoma treatment could also work for patients with CCS. In this clinical trial the researchers will try to find out if the drug will work for patients with CCS and how long the effect will last for if it works. The researchers will also collect tissue and blood samples to learn about the effect of the drug and the mechanisms of action. The patients will have regular visits to clinic to have blood samples and other assessments including radiology assessments. Patients will be treated until disease progression, consent withdrawal or unacceptable toxicity. Patients who have clinical benefit can remain on the study after disease progression. At the end of the treatment the patients will have follow up every 3 months.

Who can participate?

Clear cell sarcoma patients aged 18 years and over who screen positive for HLA-A*02:01 and meet the eligibility requirements can participate in the treatment group. Clear cell sarcoma patients aged 18 years and over who screen negative for HLA-A*02:01 and meet the eligibility requirements can participate in the control group.

What does the study involve?

Patients who screen positive for HLA-A*02:01 and meet the eligibility requirements will be treated with weekly tebentafusp in 21-day cycles. The patients will have infusions at day 1, 8 and 15 of each cycle. The initial dose at cycle 1 day 1 will be 20 mcg, which will be increased to 30 mcg at cycle 1 day 8 and the final total dose of 68 mcg at cycle 1 day 15. The dose can be reduced in case of toxicity and not be escalated further. Patients who test negative for HLA-A*02:01 will be included in the control group with the physician's choice of treatment. All

patients could be treated beyond disease progression if they have clinical benefit. Radiographic assessment via computer tomography (CT) or magnetic resonance imaging (MRI) (where CT is not feasible or per the investigator's discretion) will occur at baseline and every subsequent 6 weeks through to 48 weeks, and then every 9 weeks thereafter. All patients treated with tebentafusp will undergo mandatory research biopsies at baseline and on-treatment (week 6) if it is safe and feasible to do so. Serial peripheral blood samples for correlative analysis will be collected at baseline and at various timepoints on treatment. The purpose of the biopsies is to assess baseline immune characteristics of clear cell sarcoma (CCS) tumours and to measure changes in peripheral blood T cells before and after treatment. The purpose of the genetic analysis of the blood samples is to identify which patients benefit from the treatment and potential mechanism of action. The genetic testing does not expect to produce results relevant for the patients' future treatment. Patients who are HLA-A*02:01-negative and ineligible to receive tebentafusp will be prospectively enrolled onto a separate study group and treated with physicians’ choice of treatment. They will also be radiographically assessed at the same schedule as patients treated with tebentafusp, if feasible, and kept on this treatment until progression of disease or unacceptable toxicity on the physicians’ choice regimen. At the end of the treatment the patients will have every 3 months follow up.

What are the possible benefits and risks of participating?
While there are no guaranteed benefits for the patients the researchers hope that some patients may have overall positive effect from the treatment on their lifestyle and their disease. Tebentafusp is a drug which is already approved on the market and in use in the clinical practice. Some of the common adverse events include fever, acute skin reactions and elevated liver enzymes.

Where is the study run from?
Royal Marsden NHS Foundation Trust (UK)

When is it starting and how long is it expected to run?
October 2025 to December 2032

Who is funding the study?
Sarcoma Alliance for Research through Collaboration (SARC) (USA)

Who is the main contact?
Mrs Meghan Blalock, mblalock@sarctrials.org

Plain English summary under review with external organisation

Contact information

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Public, Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06942442

Integrated Research Application System (IRAS)
1012905

Protocol serial number
SARC045

Study information

Scientific Title
A Phase II trial of tebentafusp in HLA-A*02:01 positive patients with advanced clear cell sarcoma

Acronym
SARC045

Study objectives
Primary objective:
To estimate the proportion of HLA-A*02:01-positive patients with metastatic or unresectable clear cell sarcoma and treated with tebentafusp who are progression free at 24 weeks by Response Evaluation Criteria in Solid Tumors (RECIST 1.1).

Secondary objectives:
1. To estimate the best overall objective response rate (ORR) by RECIST v1.1 and by Choi criteria
2. To estimate the median duration of response (DoR) among responders
3. To estimate the clinical benefit of rate (CBR), defined as the proportion of patients who achieve a best response of stable disease (SD), partial response (PR), or complete response (CR) by RECIST 1.1 for ≥6 months
4. To estimate the disease control rate (DCR), defined as the proportion of patients who achieve

a best response of SD, PR, or CR by RECIST 1.1
5. To estimate the median progression-free survival (PFS)
6. To estimate the median overall survival (OS)
7. To describe the safety of study treatment, as assessed by Common Terminology Criteria for Adverse Events (CTCAE) version 5.0
8. To estimate the progression-free survival of HLA-A*02:01-negative patients with unresectable or metastatic CCS treated with physician's choice compared to HLA A*02:01-positive patients treated with tebentafusp

Ethics approval required
Ethics approval required

Ethics approval(s)
Not yet submitted

Primary study design
Interventional

Study design
Interventional non-randomized study

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Clear cell sarcoma

Interventions
Patients who screen positive for HLA-A*02:01 and meet the eligibility requirements will be treated with weekly tebentafusp in 21-day cycle. The patients will have infusions at day 1, 8 and 15 of each cycle. The initial dose at cycle 1 day 1 will be 20 mcg, which will be increased to 30 mcg at cycle 1 day 8 and the final total dose of 68 mcg at cycle 1 day 15. The dose can be reduced in case of toxicity and not be escalated further. Patients who test negative for HLAA* 02:01 will be included in the control arm of the study with physician's choice treatment. All patients could be treated beyond disease progression if they have clinical benefit.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Tebentafusp

Primary outcome(s)
Disease progression measured by RECIST 1.1 at 24 weeks

Key secondary outcome(s)
1. Best overall response rate (ORR) measured by RECIST 1.1 at 12 and 24 weeks
2. Median duration of response (DoR) measured by RECIST 1.1 at 12 and 24 weeks

3. Clinical benefit rate (CBR) measured by number of patients achieving SD, PR or CR as per RECIST 1.1 at 12 and 24 weeks
4. Median progression free survival (PFS) measured by patient survival status collected every 3 months after study treatment period
5. Median overall survival (OS) measured by patient survival status collected every 3 months after study treatment period
6. Safety of study treatment, assessed by CTCAE V5.0
7. Progression-free survival of HLA-A*02:01-negative patients with unresectable or metastatic clear cell sarcoma treated with physician's choice compared to HLA-A*02:01-positive patients treated with tebentafusp, measured by patient survival status collected every 3 months after study treatment period

Completion date
31/12/2032

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Histologically confirmed diagnosis of HMB-45+ clear cell sarcoma which is unresectable and/or metastatic
3. HLA-A*02:01 positive
4. ECOG Performance Status of ≤2 at screening
5. At least one site of measurable disease on CT/MRI scan as defined by RECIST v 1.1 criteria. Baseline imaging must be performed within 28 days of Cycle 1 Day 1 of study.
6. Adequate organ function within 28 days of Day 1 of study defined as:
6.1. Absolute Neutrophil Count (ANC) ≥1.5
6.2. Platelets ≥75
6.3. ALT and AST ≤2.5 x institutional upper limit of normal (ULN) or ≤5.0 x institutional ULN if considered due to tumor
6.4. Alkaline phosphatase ≤2.5 x institutional ULN unless considered due to tumor
6.5. Serum bilirubin ≤1.5 x institutional ULN. NOTE: Patients with elevated bilirubin secondary to Gilbert's disease are eligible to participate in the study
6.6. Serum creatinine ≤1.5 x institutional ULN or 24-hour creatinine clearance ≥50 ml/min (calculated creatinine clearance using Cockroft formula is acceptable)
7. Written, voluntary informed consent
8. Patients must demonstrate progression of disease by RECIST 1.1 within 6 months of study enrollment. Newly diagnosed patients with unresectable or metastatic disease and only one baseline scan are eligible to screen and enroll.
9. All other relevant medical conditions must be well-managed and stable, in the opinion of the investigator, for at least 28 days prior to first administration of study drug

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. History of sever hypersensitivity reaction (eg. anaphylaxis) to other biologic drugs or monoclonal antibodies
2. Clinically significant cardiac disease or impaired cardiac function, including any of the following:
2.1. Clinically significant and/or uncontrolled heart disease such as congestive heart failure (New York Heart Association grade ≥2), uncontrolled hypertension, or clinically significant arrhythmia currently requiring medical treatment
2.2. QTcF >470 msec on screening electrocardiogram (ECG) or congenital long QT syndrome. NOTE: If the initial automated QTcF interval is >470 msec at screening, for the purpose of determining eligibility, the mean QTcF, based on at least 3 ECGs obtained over a brief time interval (i.e., within 30 minutes), should be manually determined by a medically qualified person.
2.3. Acute myocardial infarction or unstable angina pectoris < 6 months prior to Screening
3. Presence of symptomatic or untreated central nervous system (CNS) metastases, or CNS metastases that require doses of corticosteroids within the prior 3 weeks to study Day 1. Patients with brain metastases are eligible if lesions have been treated with localized therapy and there is no evidence of progression for at least 4 weeks by MRI prior to the first dose of study drug
4. Active infection requiring systemic antibiotic therapy. Patients requiring systemic antibiotics for infection must have completed therapy at least 1 week prior to the first dose of study drug
5. Known history of uncontrolled human immunodeficiency virus (HIV) infection (defined as CD4 count < 200 and/or a detectable viral load). Testing for HIV status is not necessary unless clinically indicated
6. Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection per institutional protocol. Testing for HBV or HCV status is not necessary unless clinically indicated or the patient has a history of HBV or HCV infection
7. Malignant disease, other than that being treated in this study. Exceptions to this exclusion include the following: malignancies that were treated curatively and have not recurred within 2 years prior to study treatment; completely resected basal cell and squamous cell skin cancers; any malignancy considered to be indolent and that has never required therapy; and completely resected carcinoma
in situ of any type
8. Any medical condition that would, in the investigator’s or Sponsor’s judgment, prevent the patient’s participation in the clinical study due to safety concerns, compliance with clinical study procedures or interpretation of study results
9. Patients receiving systemic steroid therapy or any other immunosuppressive medication at any dose level, as these may interfere with the mechanism of action of study treatment. Local steroid therapies (e.g., otic, ophthalmic, intra-articular or inhaled medications) are acceptable
10. History of adrenal insufficiency

11. Participants with clinically significant pulmonary disease or impaired lung function, including any of the following:
11.1. An oxygen saturation of <92% on room air, measured by pulse oximeter
11.2. History of interstitial lung disease
11.3. History of pneumonitis that required corticosteroid treatment or current pneumonitis
11.4. Ongoing requirement for intermittent or continuous oxygen supplementation
12. History of colitis or inflammatory bowel disease
13. Major surgery within 2 weeks of the first dose of study drug (minimally invasive procedures such as bronchoscopy, tumor biopsy, insertion of a central venous access device, and insertion of a feeding tube are not considered major surgery
and are not exclusionary)
14. Radiotherapy within 2 weeks of the first dose of study drug, with the exception of palliative radiotherapy to a limited field, such as for the treatment of bone pain or a focally painful tumor mass
15. Use of hematopoietic colony-stimulating growth factors (eg, G-CSF, GM-CSF, M-CSF) ≤ 2 weeks prior to start of study drug. An erythroid-stimulating agent is allowed as long as it was initiated at least 2 weeks prior to the first dose of study treatment and the patient is not red blood cell transfusion dependent
16. Women who are pregnant or nursing/breastfeeding. Where pregnancy is defined as the state of a female after conception and until the termination of gestation.
17. Women of childbearing potential who are sexually active with a non-sterilized male partner, defined as all women physiologically capable of becoming pregnant, unless they are using highly effective contraception during study treatment (defined in Section 7.2.3), and must agree to continue using such precautions for 6 months after the final dose of investigational product; cessation

Date of first enrolment
30/01/2026

Date of final enrolment
31/12/2032

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Royal Marsden NHS Foundation Trust
Fulham Road
London
England
SW3 6JJ

Sponsor information

Organisation
Sarcoma Alliance for Research through Collaboration

ROR
https://ror.org/04fnb9f41

Funder(s)

Funder type
Charity

Funder Name
Sarcoma Alliance for Research through Collaboration

Alternative Name(s)
The Sarcoma Alliance for Research through Collaboration, SARC

Funding Body Type
Government organisation

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

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?
Protocol file	version 3		22/10/2025	No	No