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A phase II trial of CY-101 in participants with adrenocortical cancer

Submission date
08/11/2025

Recruitment status
Recruiting

Registration date
03/02/2026

Overall study status
Ongoing

Last Edited
01/05/2026

Condition category
Cancer

[X] 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
In this clinical trial, researchers are testing a drug called CY-101. CY-101 is a type of drug called a peptide. CY-101 works in 2 ways: 1) It binds to cancer cells and destroys their outer layer (membrane), leading to the killing of the cells; 2) It enters into the cancer cells and activates a protein called Axin2, which in turn reduces the levels of another protein that helps cancer cells to survive, called β-catenin. Both these ways of working trigger the body's immune system to kill more cancer cells, both in the treated tumour and tumours that have spread elsewhere in the body.

CY-101 has been tested in clinical trials before and now researchers want to find out if it will be effective in treating people with adrenocortical carcinoma (ACC) that has spread to nearby tissues or to other organs. The main aims of the trial are to: find out the best dose of CY-101 that can be given safely to people with ACC; find out whether CY-101 is effective in treating people with ACC; learn more about the potential side effects of CY-101; learn about how CY-101 might affect the quality of life of people with ACC; and learn more about what happens to CY-101 inside the body.

Who can participate?
The trial aims to recruit 41 participants aged 16 years and over with ACC who have received at least 1 but no more than 2 previous lines of treatment for their cancer.

What does the study involve?
This clinical trial has 2 phases (Phase 2A and Phase 2B). In Phase 2A (dose optimisation), 2 different doses of CY-101 will be tested to decide which is the best dose to give to a larger number of participants with ACC in Phase 2B. Phase 2B (dose expansion) of the trial will help us gather more information on whether CY-101 is effective in treating people with ACC, CY-101's effects on the body and what happens to CY-101 as it moves through the body.

Due to the small size and type of molecule that CY-101 is, the only way to give the drug and get it close to cancer cells is to inject it directly into the tumour lesions (an area where cancer is present); this is called an intratumoural injection. In most cases, this will be under the guidance of an ultrasound or computed tomography (CT) scan.

What are the possible benefits and risks of participating?
Although the anticipated benefit for people with ACC participating in this trial is unknown at this stage, they will be contributing to the further understanding of how best to treat ACC, which may benefit patients in the future.

CY-101 is a new drug that has been tested in a small number of people. While some side effects are known, others may still be discovered. Participants will be closely monitored throughout the trial. Possible risks relevant to this trial include: reactions or pain at the place where the study drug is injected; allergic reactions; bleeding (haemorrhage); effects related to activation of the body's immune system; digestive problems such as nausea, vomiting or diarrhoea; changes in blood tests and liver function; and risks related to reproduction (i.e. relating to pregnancy and embryo development). Due to these risks, participants on the trial will be monitored closely to find out the effects of CY-101, and the trial has been carefully designed to keep participants safe. Participants will also be required to follow the trial contraceptive requirements and/or not be pregnant to ensure their unborn child is not exposed to any risks.

Other risks and burdens a participant may encounter are: radiation exposure from CT and positron emission tomography scans; discomfort or bruising from blood tests and biopsies; and the inconvenience of visiting the hospital for regular tests and visits.

Where is the study run from?
Cancer Research UK

When is the study starting and how long is it expected to run for?
March 2026 to July 2032

Who is funding the study?
Cancer Research UK

Who is the main contact?
Dr Debashis Sarker, drugdev@cancer.org.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-cy-101-adrenocortical-carcinoma-clarity

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Additional identifiers

Integrated Research Application System (IRAS)
1012105

Central Portfolio Management System (CPMS)
70063

Protocol serial number
CRUKD/25/001

Study information

Scientific Title
A Cancer Research UK phase II trial of CY-101 given via intratumoural administration in locally advanced or metastatic adrenocortical carcinoma (CLARITY)

Acronym
CLARITY

Study objectives

Main objectives of the trial:
1.To find the best dose of CY-101 to be injected into the tumours of people who have adrenocortical carcinoma (ACC) that has spread into nearby areas or to other organs.
2.To investigate whether CY-101 can shrink the tumours of people who have ACC that has spread into nearby areas or to other organs, when CY-101 is injected into their tumours.

Secondary objectives of the trial:
1.To learn more about the side-effects of CY-101 when it is injected into the tumours of people who have ACC that has spread into nearby areas or to other organs.
2.To learn more about whether, and for how long, CY-101 can shrink tumours when it is injected into the tumours of people who have ACC that has spread into nearby areas or to other organs.
3.To learn about how CY-101 might affect the quality of life of people who have ACC that has spread into nearby areas or to other organs, when CY-101 is injected into their tumours.
4.To find out more about the pharmacokinetics (PK) of CY-101, i.e., what happens to the drug in the body over time, when it is injected into the tumours of people who have ACC that has spread into nearby areas or other organs.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/01/2026, London – Westminster (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; 0207 104 8169; westminster.rec@hra.nhs.uk), ref: 25/LO/0815

Primary study design
Interventional

Allocation
N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Treatment

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Adrenocortical carcinoma

Interventions
This clinical trial has 2 phases (Phase 2A and Phase 2B). It is a Phase II multi-centre open-label randomized dose-optimisation and single-arm dose expansion trial design

In Phase 2A, a total of 16 evaluable participants (i.e. people for whom the main aims of the trial can be assessed) will be recruited and randomised in a 1:1 ratio (i.e. in equal numbers) into 2 cohorts of 8 participants each to compare 20 mg and 40 mg dose levels of CY-101 given via IT injection at a volume of 4 mL once every 2 weeks (Q2W) in cycles consisting of 14 days. Participants will be randomised using an electronic data capture system.

In Phase 2B, participants will be treated at the chosen best dose level from Phase 2A. CY-101 will be administered via IT injection at a volume of 4 mL Q2W in cycles consisting of 14 days. Phase 2B will include 33 evaluable participants, which may include eligible participants from Phase 2A who received the selected dose and are evaluable for whether their ACC responded to CY-101. In total, the trial requires 41 evaluable participants across both phases to complete the trial.

Participants may receive CY-101 for up to 52 weeks (maximum of 26 cycles) unless there are unacceptable side effects, there is evidence that their cancer is progressing, or the Investigator decides it is in the participant's best interests to be withdrawn. Participants may be allowed to continue for a further 26 weeks or 13 cycles (whichever is shorter) if they are found to be benefiting from CY-101; however, this depends on whether there are enough supplies of CY-101. It is expected that after this, CY-101 will be permanently discontinued.

If a participant is withdrawn from the trial, the trial doctor will discuss further treatment options with the participant and will arrange for their care to continue outside of the clinical trial. Participants will be followed up for safety for 28 days after their last dose of CY-101 and for survival for at least 12 months after their last dose.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
CY-101

Primary outcome(s)
Phase IIa: Determining an optimal dose of CY-101 based upon review of all clinically relevant data including but not limited to toxicity, efficacy, quality of life data and PK parameters at the end of Phase IIa and EoT
Phase IIb: Overall Response Rate (ORR) defined as the proportion of participants who achieve complete response (CR) or partial response (PR) according to intratumoural immunotherapy Response Evaluation Criteria in Solid Tumours (itRECIST) at the end of the trial

Key secondary outcome(s)
Phase 2a and 2b
1. Frequency and causality of adverse events, including relatedness, seriousness and severity graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 assessed at the end of Phase IIa and end of trial.
2. Participant reported quality of life outcomes using European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 assessed at the end of Phase IIa and end of trial.
3. PK parameters including, where possible, maximum concentration, area under the curve, time

to reach maximum concentration, terminal elimination half-life, clearance and volume of distribution assessed at the end of Phase IIa and end of trial.

Phase 2b
4. ORR defined as the proportion of participants who achieve immune complete response (iCR) or immune partial response (iPR) according to immune-related Response Evaluation Criteria in Solid Tumours (iRECIST) assessed at the end of trial.
5. Duration of response defined as the time from date of first confirmed CR or PR according to itRECIST, or iCR or iPR according to iRECIST, to date of disease progression or death from any cause assessed at the end of trial.
6. Disease control rate defined as best response of CR, PR or stable disease ≥12 weeks according to itRECIST and iCR, iPR or immune stable disease ≥12 weeks according to iRECIST assessed at the end of trial.
7. Progression free survival (PFS) defined as the time from date of first dose of CY-101 to date of disease progression or date of death from any cause assessed at the end of trial.
8. PFS at 18 weeks assessed at the end of trial.
9. Overall Survival (OS) defined as time from date of first dose to date of death from any cause assessed at the end of trial.
10. OS at 6 and 12 months assessed at the end of trial.
11. Growth modulation index defined as the ratio of PFS on trial to PFS from previous treatment assessed at the end of trial.
12. Time to next treatment defined as the interval from commencement of CY-101 on the trial to initiation of the next line of therapy assessed at the end of trial.

Completion date
31/07/2032

Eligibility

Key inclusion criteria
1. Written (signed and dated) informed consent and be capable of co-operating with CY-101 administration and follow-up.
2. Histologically confirmed ACC that is either locally advanced and not amenable to surgical resection or metastatic, with evidence of disease progression post the most recent line of therapy.
3. Participants must have received treatment with at least 1 line, but not more than 2 prior lines, of systemic therapy for established locally advanced or metastatic disease, and must have received mitotane therapy within these lines of therapy for advanced/metastatic disease (or as neoadjuvant/adjuvant therapy). Participants must have relapsed within 1 year of neoadjuvant /adjuvant therapy for this to be considered a line of treatment.
4. At least 1 lesion that is objectively evaluable or measurable, according to itRECIST. Previously irradiated lesions cannot be counted as target lesions unless they have clearly progressed after radiotherapy. Participants also require at least 1 separate lesion(s) amenable for IT injection by a clinician or interventional radiologist under ultrasound-assisted guidance. Refer to protocol for further details.
5. Adequate tissue available for biomarker testing, from either archival tissue or pre-treatment biopsy.
6. Life expectancy of ≥12 weeks.
7. Eastern Cooperative Oncology Group performance status of 0-2.
8. Haematological and biochemical indices within the prescribed ranges.
9. Aged 16 years or over at the time consent is given.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
16 Years

Upper age limit
99 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Radiotherapy (except for palliative reasons), endocrine therapy, chemotherapy or other Investigational Medicinal Products (IMPs) during the previous 28 days before the first dose of CY-101. Continued treatment with mitotane during the trial to control hormonal symptoms is permitted under certain conditions as specified in the trial protocol. Mitotane plasma level monitoring is to be maintained and documented during the trial.
2. Prior treatment with a Wnt inhibitor.
3. Ongoing toxic manifestations of previous treatments greater than Common Terminology Criteria for Adverse Events Grade 1 (other than alopecia of any grade or Grade 2 peripheral neuropathy). Exceptions apply.
4. Any central nervous system metastases (unless patients had local therapy and are asymptomatic, radiologically stable for 4 weeks and off steroids for the last 4 weeks).
5. Women who are pregnant or breastfeeding (or planning to breastfeed).
6. Women of childbearing potential. However, those patients who are not already pregnant or breastfeeding (or planning to breastfeed) are eligible, provided they have a negative highly sensitive serum pregnancy test ≤7 days before trial entry and agree to follow the trial's contraceptive requirements.
7. Male patients with partners of childbearing potential. However, those patients who agree to follow the trial's contraceptive requirements are eligible.
8. Major surgery from which the patient has not yet recovered.
9. At high medical risk because of non-malignant systemic disease, including active uncontrolled infection.
10. Serologically positive for hepatitis B virus or hepatitis C virus (HCV). Patients with previous HCV exposure but no current infection are eligible.
11. Known untreated human immunodeficiency virus (HIV) infection. Patients on established antiretroviral medication and who have well-controlled HIV infection/disease are eligible, provided they meet protocol-specified criteria.
12. Allergy or hypersensitivity to any of the ingredients/excipients in the CY-101 formulation.
13. Significant cardiovascular disease. As defined in the trial protocol.

14. Extensive radiotherapy to >25% of bone marrow within 12 weeks prior to the first dose of CY-101.
15. Participating in or plans to participate in another interventional clinical trial whilst taking part in this trial of CY-101. See protocol for more information.
16. Current malignancies of other types, with certain exceptions as per the trial protocol. Cancer survivors who have undergone potentially curative therapy for a prior malignancy, have no evidence of that disease for ≥5 years and are deemed at negligible risk for recurrence are eligible for the trial.
17. Any congenital immunodeficiency syndrome.
18. Active autoimmune disease that has required systemic treatment in the 2 years before trial entry.
19. Use of systemic corticosteroids (apart from replacement doses for endocrinopathy up to an equivalent of 10 mg QD prednisolone or 20 mg QD prednisolone if receiving mitotane concurrently).
20. Prior adverse reaction to cancer immunotherapy that required intravenous steroid treatment or other immunosuppressive treatment.
21. Live, attenuated vaccine within 28 days before the first dose of CY-101.
22. Evidence of bleeding diathesis, or anticoagulant or antiplatelet therapy (excluding prophylactic low molecular weight heparin or low-dose aspirin).
23. High burden of metastatic disease defined as ≥4 organs involved with metastases or greater than 12 individual metastases, including primary tumour.
24. Patients with uncontrolled hormonal secretion (according to the judgement of the Investigator), e.g. Cushing's or mineralocorticoid excess causing uncontrolled hypertension, diabetes, and hypokalaemia.
25. Any other condition that, in the Investigator’s opinion, would mean that the trial is not in the best interests of the patient.

Date of first enrolment
01/03/2026

Date of final enrolment
31/01/2030

Locations

Countries of recruitment
United Kingdom

England

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Sponsor information

Organisation
Cancer Research UK

ROR
https://ror.org/054225q67

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary

Available on request