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A Phase I trial of LY3143921 hydrate in solid tumours

Submission date
30/09/2025

Recruitment status
No longer recruiting

Registration date
09/12/2025

Overall study status
Completed

Last Edited
13/04/2026

Condition category
Cancer

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
This clinical trial is looking at a drug called LY3143921 (a Cdc7 inhibitor, used as a hydrate) in adult patients with advanced solid tumours. Cdc7 helps cells replicate correctly. Cdc7 is usually found at a low level in normal cells but can reach higher levels in cancer cells. This is often the case in certain types of solid tumour cancers, which are the focus of this trial. It is thought that giving LY3143921 will block the function of Cdc7 and will affect cancer cells by stopping their replication and causing them to die. The main aims of this trial are to find out the maximum dose of LY3143921 hydrate that can be given safely to patients, and to assess the potential side effects and how they can be treated.

Who can participate?
Patients aged 18 years and over with advanced solid tumours where there is no suitable treatment available for their cancer, their treatment has stopped working or they don't want to have the treatment that has been offered to them.

What does the study involve?
This clinical trial has two parts:
Part 1 – a 'dose escalation' phase where groups of patients will receive increasing doses of LY3143921 hydrate to find a safe dose and a dose that best targets the cancer cells.
Part 2 – an 'expansion' phase where a larger group of patients will receive the highest dose of LY3143921 hydrate, considered to be safe from Part 1, to find out more about how the drug is working.

In the dose escalation part of the trial, the first few patients joining have a low dose of LY3143921 hydrate. Vital signs, including heart rate, temperature and blood pressure, will be monitored. If they don't have any serious side effects, the next few patients will have a higher dose. This process continues until the doctors find the best dose to give to patients to target cancer cells. Blood samples will be taken frequently to see how quickly the drug appears in the patient's body and how quickly their body gets rid of (excretes) the drug.

In the dose expansion part of the trial, patients will receive the highest dose of LY3143921 hydrate considered to be safe from the dose escalation part of the trial, to find out how the

drug is working. For this stage, there are three cohorts: Cohort 1: patients with CRC; Cohort 2: patients with NSCLC; and Cohort 3: patients with solid tumours commonly associated with P53 (a tumour suppressor protein) mutation or loss of function. Tissue samples (biopsies) of the patient's cancer are taken before treatment, and again during the first cycle of treatment, to find out how LY3143921 hydrate works, and which cancers benefit the most from this drug.

What are the possible benefits and risks of participating?
This is the first time that LY3143921 hydrate is being used in humans. The possible direct benefit is that the study drug may help treat the patient's cancer, although the chances of this are unknown. The trial will also give information that may help improve the treatment for patients with cancer in the future.

The information derived on the potential effects in humans is based on laboratory tests and research in animals.

Possible side effects include:
• feeling dizzy or lightheaded due to low blood pressure
• eye pain and/or eyesight changes due to abnormal growth of blood vessels in the eyes

Where is the study run from?
The Cancer Research UK Centre for Drug Development, based in London, UK

When is the study starting and how long is it expected to run for?
December 2016 to April 2025

Who is funding the study?
Cancer Research UK

Who is the main contact?
Cancer Research UK Centre for Drug Development; drugdev@cancer.org.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-ly3143921-hydrate-for-advanced-cancer

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT03096054

Clinical Trials Information System (CTIS)
2016-001245-80

Integrated Research Application System (IRAS)
216105

Central Portfolio Management System (CPMS)
35213

Protocol serial number
CRUKD/17/004

Study information

Scientific Title
A Cancer Research UK Phase I trial of LY3143921 hydrate (a Cdc7 inhibitor) given orally in adult patients with advanced solid tumours

Study objectives
Primary Objectives:
1. To propose a recommended dose for Phase II (RP2D) evaluation by determining the maximum tolerated dose (MTD) and schedule of LY3143921 hydrate
2. To assess the safety and toxicity profile of LY3143921 hydrate

Secondary Objectives:
1. To determine the pharmacokinetic (PK) profile of LY3143921
2. To assess the efficacy of LY3143921 hydrate

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 17/02/2017, Office for Research Ethics Committees Northern Ireland Health and Social Care Research Ethics Committee A (Unit 4, Lissue Industrial Estate West, Rathdown Walk, Moira Road, Lisburn, BT28 2RF, United Kingdom; +44 (0)2895361400; RECA@hscni.net), ref: 17/NI/0005

Primary study design
Interventional

Study design
Multi-centre dose-escalation dose-expansion first-in-human phase I trial

Study type(s)
Efficacy, Safety, Treatment

Health condition(s) or problem(s) studied
Colorectal Cancer (CRC), High Grade Serous Ovarian Cancer (HGSOC), Non-Small Cell Lung Cancer (NSCLC; Squamous Cell Variant), Squamous Carcinoma of the Oesophagus, Squamous Carcinoma of the Head and Neck (Human Papillomavirus Negative), Urothelial Cancer, Breast Cancer (Triple Negative Type), Pancreatic Cancer

Interventions
This is a multi-centre, dose escalation and expansion, first-in-human phase I trial in patients with advanced solid tumours.

The clinical trial consists of two parts: Part 1 (the dose escalation phase) and Part 2 (the dose expansion phase).

Patients will receive LY3143921 hydrate capsules orally for 21 days (one cycle) for up to 12 cycles. If the patient is showing benefit, they may continue beyond 12 cycles.

In Part 1, the starting dose for dose escalation will be 30 mg. A single dose will be administered seven days before Cycle 1 Day 1, on Cycle 1 Day -7 (dose escalation phase only); from Cycle 1 Day 1, each cycle of treatment will consist of 21 days of continuous dosing with LY3143921 administered once or twice daily.

Part 2 is an expansion phase with three cohorts planned at the RP2D. Cohort 1: patients with CRC administered LY3143921 hydrate on a continuous 21 day dosing schedule; Cohort 2:

patients with squamous NSCLC administered LY3143921 hydrate on a continuous 21-day dosing schedule; and Cohort 3: patients with solid tumours commonly associated with P53 mutation or loss of function administered LY3143921 hydrate on an intermittent, three days on, four days off per week (21-day cycle) dosing schedule.

Patients will be followed up for safety until resolution of drug-related adverse events (AEs) and for disease progression until database lock.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
LY3143921 hydrate

Primary outcome(s)
1. Determination of the MTD: determining the maximal dose at which no more than one patient out of up to six patients at the same dose level experiences a highly probable or probable drug-related DLT, and determining the schedule of administration at which the MTD is established. The time frame is 28 days from the first administration of LY3143921 hydrate in the dose escalation cohort, including the single dose on Cycle 1 Day-7, where applicable.
2. To assess the safety and toxicity profile of LY3143921 hydrate, the causality of each AE to LY3143921 hydrate will be determined, and the severity will be graded according to National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 4.02. The time frame is from the first administration of LY3143921 hydrate until the last patient's last visit (LPLV).

Key secondary outcome(s)
1. Determine the maximum observed plasma concentration (C^max), time to reach maximum observed plasma concentration (T^max), area under the curve (AUC), plasma half-life, volume of distribution and clearance of LY3143921, with plasma samples analysed using liquid chromatography mass spectrometry according to agreed standard operating procedures and validated methods. Not all participants were analysed at all time points. The time frame is up to 21 time points from the first dose of LY3143921 hydrate to the Off-Study Visit.
2. Overall Response Rate: the ratio of patients with any response to the total number of patients in the response population. A patient is considered a responder if they are assessed according to Response Evaluation Criteria in Solid Tumours (RECIST) version (v)1.1 as having either a complete response or partial response. The time frame is at the evaluation at LPLV.
3. Progression Free Survival: the median (range) number of days from first administration of LY3143921 hydrate to documented disease progression measured according to RECIST v1.1. Patients who are lost to follow-up or who withdraw consent for follow-up will be censored at the time of the last recorded disease assessment. Patients who start a new treatment will not be censored. The time frame is at the evaluation at LPLV.

Completion date
09/04/2025

Eligibility

Key inclusion criteria

1. Histologically proven advanced or metastatic solid tumours, refractory to conventional treatment, or for which no conventional therapy exists or is declined by the patient.
1.1. For Phase Ia (dose escalation): Enriched for patients with tumours commonly associated with p53 mutation or loss of function:
1.1.1. CRC
1.1.2. HGSOC
1.1.3. NSCLC (squamous cell variant)
1.1.4. Squamous carcinoma of the oesophagus
1.1.5. Squamous carcinoma of the head and neck (Human Papillomavirus negative)
1.1.6. Urothelial cancer
1.1.7. Breast cancer (triple negative type)
1.1.8. Pancreatic cancer
1.2. For Phase Ib (expansion cohorts): Cohort 1: patients with metastatic CRC; Cohort 2: patients with squamous NSCLC, and Cohort 3: patients with solid tumours commonly associated with p53 mutation or loss of function (as described above for the Phase Ia part of the trial).
1.2.1 Consent for pre-treatment and post-treatment fresh tumour biopsy samples in a minimum of six patients in expansion Cohorts 1 and 3, optional for all other patients.
1.2.2. Consent for pre- and post-treatment skin punch biopsy in a minimum of six patients in each expansion cohort, optional for all other patients.
2. Life expectancy of at least 12 weeks.
3. Written (signed and dated) informed consent and be capable of co-operating with treatment and follow-up.
4. World Health Organization performance status of 0 or 1.
5. Haematological and biochemical indices within the ranges shown below:
5.1. Haemoglobin (Hb) ≥9.0 g/dL (no prior transfusion) or ≥10.0 g/dL (transfusion within last four weeks)
5.2. Absolute neutrophil count ≥1.5 × 10^9/L
5.3. Platelet count ≥100 × 10^9/L
5.4. Serum bilirubin ≤1.5 × upper limit of normal (ULN)
5.5. Alanine aminotransferase and aspartate aminotransferase ≤2.5 × ULN (or ≤5 × ULN in the presence of liver metastases)
5.6. Calculated creatinine clearance (using the Wright or Cockcroft-Gault formula) >50 mL/min
5.7. Prothrombin time and activated partial thromboplastin time** ≤1.5 × ULN
5.8. Albumin ≥ 80% of the lower limit of normal

**Therapeutic international normalised ratio values of 2.0-3.0 are acceptable for patients who are taking concomitant warfarin or other oral anticoagulants.

6. Age 18 years or over.
7. Consent must be given for the use of archived tumour samples for all patients.
8. Disease must be either evaluable or measurable using RECIST v1.1 criteria.

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
69

Key exclusion criteria
1. Systemic anti-cancer therapy (except life-long hormone suppression such as luteinising hormone-releasing hormone agents in prostate cancer) or another investigational agent during the previous four weeks (six weeks for nitrosureas, mitomycin-C) is not permitted. Previous use of radiotherapy is permitted except where there has been a large volume of bone marrow irradiated or where the irradiated lesion is the only one suitable for RECIST measurability.
2. Ongoing toxic manifestations of previous treatments (Grade 2 or greater according to NCI-CTCAE v4.02) except alopecia or certain Grade 2 toxicities, which, in the opinion of the Investigator and Sponsor, should not exclude the patient; these should be discussed on a case-by-case basis.
3. Symptomatic brain metastases or spinal cord compression.
4. Significant baseline hypotension (<90 mmHg systolic or <50 mmHg diastolic) or symptomatic hypotension at any level of blood pressure.
5. Uncontrolled hypertension (>160 mmHg/100 mmHg).
6. Patients with a known left ventricular ejection fraction <50%. An echocardiogram must be performed in all patients.
7. Women of child-bearing potential (or who are already pregnant or lactating). However, those patients who meet the following points are considered eligible:
7.1. Have a negative serum or urine pregnancy test before enrolment and;
7.2. Agree to use two forms of contraception (one effective form plus a barrier method [oral, injected or implanted hormonal contraception and condom; intra-uterine device and condom; diaphragm with spermicidal gel and condom]) or agree to sexual abstinence, effective from the first administration of LY3143921 hydrate, throughout the trial and for six months afterwards.
8. Male patients with partners of child-bearing potential. However, those patients who meet the following points are considered eligible:
8.1. Agree to take measures not to father children by using a barrier method of contraception (condom plus spermicide) or to sexual abstinence effective from the first administration of LY3143921 hydrate, throughout the trial and for six months afterwards.
8.2. Men with partners of child-bearing potential must also be willing to ensure that their partner uses an effective method of contraception for the same duration, for example, hormonal contraception, intra-uterine device, diaphragm with spermicidal gel or sexual abstinence.
8.3. Men with pregnant or lactating partners must be advised to use barrier method contraception (for example, condom plus spermicidal gel) to prevent exposure of the foetus or neonate.
9. No major surgery within four weeks prior to the patient receiving Cycle 1 Day -7 (for dose escalation) or Cycle Day 1 (for dose expansion). If minor surgery has been performed within 2 weeks of the start of trial treatment, then patients must have recovered, and the Sponsor and Chief Investigator should be notified of the nature of this and agree to patient inclusion.

10. At high medical risk because of non-malignant systemic disease, including active uncontrolled infection.
11. Known to be serologically positive for hepatitis B, hepatitis C or human immunodeficiency virus (mandatory testing not required).
12. Significant cardiovascular disease as defined by:
12.1. History of congestive heart failure requiring therapy
12.2. History of unstable angina pectoris or myocardial infarction up to six months before trial entry
12.3. Presence of severe valvular heart disease
12.4. Presence of a ventricular arrhythmia requiring treatment
13. Past history of corneal ulceration, dry eye syndrome, and glaucoma. Contact lenses should also be avoided during participation in the trial.
14. Is a participant or plans to participate in another interventional clinical trial, whilst taking part in this Phase I study of LY3143921 hydrate. Participation in an observational trial or interventional clinical trial, which does not involve administration of an Investigational Medicinal Product and which would not place an unacceptable burden on the patient in the opinion of the Investigator and Medical Advisor, would be acceptable.
15. Any other condition which, in the Investigator’s opinion, would not make the patient a good candidate for the clinical trial.

Date of first enrolment
28/06/2017

Date of final enrolment
24/11/2021

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Study participating centre
Western General Hospital
Crewe Road South
Edinburgh
Scotland
EH4 2XU

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road

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Scotland
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Study participating centre
Northern Centre for Cancer Care
Freeman Road
Newcastle Upon Tyne
England
NE7 7DN

Study participating centre
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Belfast City Hospital
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BT9 7AB

Sponsor information

Organisation
Centre for Drug Research and Development

ROR
https://ror.org/014v77g24

Funder(s)

Funder type
Charity

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
Data from this trial and the final clinical study protocol will be submitted to a public registry and will be available immediately following publication, with no end date. Individual deidentified participant data that underlie the results reported will be shared with researchers whose proposed use of the data is approved by a review committee of the Sponsor. All requests made within 5 years from the end of the trial will be considered; requests made subsequently will be considered where possible. Requests should be submitted to drugdev@cancer.org.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	09/03/2026	13/04/2026	No	No
Plain English results			07/04/2026	No	Yes
Protocol file		17/03/2026	07/04/2026	No	No
Study website		11/11/2025	11/11/2025	No	Yes