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A trial testing the safety and effectiveness of treating patients with kidney cancer that has spread to other parts of the body with a tumour freezing treatment (called cryoablation) and immunotherapy

Submission date
06/09/2025

Recruitment status
Not yet recruiting

Registration date
05/01/2026

Overall study status
Ongoing

Last Edited
05/01/2026

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
The current management of kidney cancer that has spread beyond the kidney to surrounding organs includes giving immunotherapy, which is medication designed to boost the immune system by training the body to better recognise and attack cancer cells.

Unfortunately, a quarter of kidney cancers do not respond to this treatment (called resistance) and half of patients will develop further cancer spread within a year of treatment. These medications can also give patients side-effects such as diarrhoea, skin rashes and trouble breathing.

Better ways to treat advanced kidney cancer are required and new approaches are needed to overcome drug resistance and make treatment more effective. One way to do this is to find ways to better prepare the immune system for immunotherapy, by offering other treatments first.

Cryoablation involves freezing cancer cells by inserting small needles into the cancer using x-ray guidance. This has been shown to kill cancer cells but also help the body to familiarise itself with the cancer and provide a spark for the immune system. Based on previous research, it has been shown that if immunotherapy is given after cryoablation then it can be more effective by strengthening the immune system’s ability to recognise and attack cancer cells. In other words, it is hypothesised that the combination of cryoablation and immunotherapy works together to amplify the body's natural ability to fight cancer.

Who can participate?
Patients with advanced kidney cancer.

What does the study involve?
In this trial, we will investigate whether it is safe to combine cryoablation with standard immunotherapy in patients with advanced kidney cancer. Patients will be closely monitored to see how they respond and if they develop any side effects. The trial will also help improve our understanding of how this combination therapy impacts the body's immune response so that future treatments can be refined and improved.

What are the possible benefits and risks of participating?
We already know that nivolumab plus ipilimumab is an effective treatment in some, but not all, patients with advanced kidney cancer. All participants will receive combination nivolumab plus ipilimumab in this trial. We hope that combining immunotherapy with cryoablation will improve the chances of the treatment working. However, we do not know whether this will be the case. Therefore, your participation in this study may not be of direct benefit to you personally but it is possible that it may be of benefit to future cancer patients. Without research of this sort, improvements in cancer treatments are not possible.
These patients would normally receive immunotherapy as part of standard of care treatment; however, the additional risk stems from the ablation treatment which requires a general anaesthetic and treatment to their kidney cancer which carries risks of bleeding, pain and infection. Patients will be monitored closely throughout the trial and will be asked to attend regular outpatient appointments. The frequency of appointments will be greater than standard care, both during treatment cycles and afterwards if needed.

Where is the study run from?
University of Leeds (UK)

When is the study starting and how long is it expected to run for?
March 2026 to June 2028

Who is funding the study?
Varian Medical Systems

Who is the main contact?
marta.kurzawa@nhs.net

Lay summary under review with external organisation

Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1010229

Protocol serial number
2023-CT02

Study information

Scientific Title
A Phase I study of tumour cryOabLAtIon in combination with ipilimumab and nivolumab in front-line treatment of metastatic Renal cell carcinoma

Acronym
POLAR trial

Study objectives
The primary aim is to characterise the safety of immunotherapy plus cryoablation in patients with advanced kidney cancer.
The key secondary aim is to characterise the immune and inflammatory response to ICI plus cryoablation.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 12/11/2025, Yorkshire & The Humber - Leeds East Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8357; leedseast.rec@hra.nhs.uk), ref: 25/YH/0204

Study design
Interventional non randomized

Primary study design

Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Metastatic renal cell carcinoma

Interventions
This is a single arm study
All participants will receive nivolumab 3mg/kg plus ipilimumab 1mg/kg intravenously, every 3 weeks, x4 cycles
This will be followed by single agent nivolumab, 480mg IV or 1200mg subcutaneously, every 4 weeks
Treatment will continue until disease progression, intolerable toxicity or participant withdrawal of consent
Between cycles 1 and 2 of nivolumab plus ipilimumab, participants will undergo cryoablation of a tumour lesion
Participants will undergo 12-weekly CT scans (up to 24 months)

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Nivolumab, ipilimumab

Primary outcome(s)
Incidence of grade 3-5 adverse events, as per CTCAE V5.0 criteria, measured continuously and for up to 100 days post cessation of trial therapy

Key secondary outcome(s))
Detection of immunogenic cell death, measured by plasma calreticulin ELISA, at 4-8h, 12-24h post cryo-ablation and pre-cycle 2 and pre-cycle 4 of study therapy

Completion date
01/06/2028

Eligibility

Key inclusion criteria
1. Aged 18 years or above
2. Diagnosed with metastatic RCC
3. Histologically confirmed clear cell renal cell carcinoma (or a component of clear cell)
4. Intermediate- or poor-risk disease according to IMDC classification
5. Evidence of measurable disease as per RECIST v1.1
6. Karnofsky score at least 70%
7. Eligible and planned for standard of care immunotherapy (nivolumab + ipilimumab)

8. Required laboratory values within 14 days prior to C1D1:
a. WBC ≥ 2 × 10^9/L
b. Neutrophils ≥ 1.5 × 10^9/L
c. Platelets ≥ 100 × 10^9/L
d. Haemoglobin > 9.0 g/dL
e. Serum creatinine ≤ 1.5 × ULN or calculated creatinine clearance (CrCl) ≥ 40 mL/min (Wright formula)
f. ALT ≤ 3 × ULN
g. Total Bilirubin ≤ 1.5 × ULN (except subjects with Gilbert Syndrome, who can have total bilirubin < 50 µmol/L)
9. Tumour lesion amenable to cryoablation in the opinion of the investigator (if a metastasis is ablated, at least one other measurable lesion must be present)
10. Female participants of childbearing potential and male participants whose partner is of childbearing potential must be willing to ensure that they or their partner use effective contraception during the study and for 5 months thereafter
11. Participant is able (in the Investigator's opinion) and willing to comply with all study requirements
12. Participant willing to allow their General Practitioner and consultant to be notified of participation in the study
13. Participant is willing and able to provide written informed consent for the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Female participant who is pregnant, lactating, or planning pregnancy during the study.
- Negative serum pregnancy test required for females of childbearing potential at screening and to be reconfirmed 24 hours pre-treatment.
2. Participant is enrolled in another investigational trial and/or is taking investigational medication and/or has been treated with an investigational device ≤30 days prior to planned procedure date.
3. In the Investigator's opinion, the participant has co-morbid disease(s) or condition(s) that would cause undue risk and preclude safe use of the Cryocare Touch system.

4. Prior systemic therapy for metastatic RCC (mRCC).
5. Prior adjuvant immunotherapy for RCC at any time.
6. Participant has a concurrent condition that, in the Investigator’s opinion, could jeopardize the safety of the subject or compliance with the protocol.
7. Participants who test positive for hepatitis B virus surface antigen (HBV sAg) or hepatitis C virus ribonucleic acid (HCV antibody), indicating acute or chronic infection.
8. Participants who test positive for human immunodeficiency virus (HIV) or have known acquired immunodeficiency syndrome (AIDS).
9. Active, known, or suspected autoimmune disease.
- Subjects are permitted to enrol if they have vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger.
10. Current or prior use of immunosuppressive medication within 14 days before the first dose of nivolumab or ipilimumab.
- Exceptions:
a. Intranasal, inhaled, topical steroids, or local steroid injections (e.g., intra-articular injection)
b. Systemic corticosteroids at physiologic doses
c. Steroids as premedication for hypersensitivity reactions
11. Major surgical procedure within 28 days prior to the first dose of immunotherapy.
12. Unable to undergo general anaesthesia (e.g., allergies to anaesthesia or history of adverse reactions to anaesthesia).
13. Untreated brain metastases or brain metastases treated only with whole brain radiotherapy.
- Patients are eligible if previous brain metastases were treated with complete surgical resection, Stereotactic Brain Radiation Therapy (SBRT), or gamma knife with no subsequent evidence of progression and are asymptomatic.

Date of first enrolment
01/03/2026

Date of final enrolment
30/08/2027

Locations

Countries of recruitment
United Kingdom

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
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Sponsor information

Organisation
University of Leeds

ROR
https://ror.org/024mrxd33

Funder(s)

Funder type
Industry

Funder Name
Varian Medical Systems

Alternative Name(s)
Varian Medical Systems, Inc., Varian Associates,

Funding Body Type
Private sector 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