ISRCTN14986389 https://doi.org/10.1186/ISRCTN14986389

Investigating the feasibility of a clinical trial to test using irreversible electroporation to treat locally advanced pancreatic cancer following initial chemotherapy

Submission date
04/02/2021

Recruitment status
No longer recruiting

Registration date
09/02/2021

Overall study status
Completed

Last Edited
25/03/2025

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Surgery (pancreatic resection) is the only treatment with the potential to cure pancreatic cancer. Only 10 to 20 out of every 100 people are eligible for surgery. One of the major reasons is that the cancer has spread into the surrounding structures, which is known as locally advanced pancreatic cancer (LAPC). Currently, the recommended treatment for LAPC is chemotherapy (drugs which destroy cancer). Those in whom the chemotherapy prevents the growth or spread of cancer have a chance of improved survival.
Irreversible electroporation (IRE) is a new method of treating cancer. IRE treatment destroys cancer cells by electricity. Under general anaesthetic, IRE probes, which are similar to needles, are inserted into the pancreas and an electrical charge is passed through the cancer.
Early studies in pancreas cancer suggest that IRE treatment may increase how long people with LAPC live. However, there has been no trial to provide evidence of how effective IRE treatment is in people with LAPC that is unsuitable for surgery.
This study aims to find out how feasible it would be to carry out a trial of IRE treatment following initial chemotherapy for LAPC.
The study will also investigate the safety, practicality, and technical success of IRE treatment, how acceptable IRE treatment is to patients and their doctors, how many participants are recruited and withdraw from the study, participant survival, and participant quality of life.

Who can participate?
Adults with locally advanced pancreatic cancer who are not suitable for surgical resection

What does the study involve?
Following first-line chemotherapy with Folfirinox, participants will be allocated to one of two groups, with an equal chance of being in either group (like tossing a coin). One group will receive the IRE procedure followed by standard-of-care chemotherapy, and the other group will receive standard-of-care chemotherapy alone. Patients will be followed up every 3 months for 12 months where they will undergo blood tests and CT scans.

What are the possible benefits and risks of participating?
The aim of IRE for LAPC is to provide an improvement in life expectancy and a better quality of life. There is data to suggest this may be effective but it has not yet been proven.
Risks associated with IRE that may rarely occur in a small number of participants include: pain at the treatment site; acute pancreatitis; local vascular occlusion from thrombosis; leakage of fluid from the pancreas, bile duct or duodenum at the insertion point of the IRE probes; and cardiac arrhythmias.

Where is the study run from?
Liverpool Clinical Trials Centre (UK)

When is the study starting and how long is it expected to run for?
From October 2020 to February 2025

Who is funding the study?
National Institute for Health Research (NIHR) Research for Patient Benefit programme (UK)

Who is the main contact?
Dr Kellie Platt, lappie@liverpool.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Brian Davidson

Contact details
Wellington Hospital
8A Wellington Place
London
United Kingdom
NW8 9LE
+44 (0)208 0168 096
b.davidson@ucl.ac.uk

Type(s)
Public

Contact name
Dr Kellie Platt

Contact details
Liverpool Clinical Trials Centre
University of Liverpool
Block C
Waterhouse Building
1-5 Brownlow Street
Liverpool

United Kingdom
L69 3GL
+44 (0)151 794 8897
lappie@liverpool.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
272784

Central Portfolio Management System (CPMS)
46763

Study information

Scientific Title
Treatment of unresectable Locally Advanced Pancreas cancer with Percutaneous Irreversible Electroporation following initial systemic chemotherapy (LAP-PIE): a randomised controlled feasibility trial

Acronym
LAP-PIE

Study objectives
It is feasible to conduct a randomised controlled trial of irreversible electroporation (IRE) in patients with locally advanced pancreatic cancer (LAPC)?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved, London Brent Research Ethics Committee (80 London Road, Skipton House, London, SE1 6LH; +44 (0)207 104 8129; brent.rec@hra.nhs.uk), ref: 21/LO/0077

Study design
Multi-centre randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Malignant neoplasm of pancreas, locally advanced pancreas cancer

Interventions
Patients will be recruited to the study following screening and consent, where they will then have baseline assessments in order to ensure suitability and their health state prior to treatment.

All patients on the study will have completed a standard of care regimen of FOLFIRINOX given prior to registration and then be randomised (1:1) to one of two arms. Randomisation will be carried out by the Liverpool Clinical Trials Centre using the TARDIS system. The control arm will simply receive the physician's choice of chemotherapy (per their oncologist's decision), whereas the other will receive one IRE procedure as well as their physician's choice of chemotherapy.

All patients will be re-staged following treatment for surgery on the Advanced Pancreatic Cancer to see if their tumour remains unresectable. If not, the patient will go on to have pancreatic surgery as they would have as standard for this disease.

Follow up visits will begin following surgery in order to assess the quality of life for the patients for up to 12 months following randomisation.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Ability to recruit patients measured using the following from participant records at screening, randomisation, IRE visit (if allocated), restaging visit, surgery visit, follow up visits, end of treatment, and end of the study:
1.1. Rate of recruitment
1.2. Number of screening failures
1.3. Number of patients that complete the study pathway as per protocol
1.4. Rate of withdrawal from trial, the reasons why, and at which stage

Key secondary outcome(s))
1. Practicality and the technical success of IRE measured using the following:
1.1. Mortality rate from patient records at 6 weeks, 3, 6, 9, and 12 months post-randomisation and overall
1.2. Technical success rate (complete local therapy) at the time of IRE procedure and operative CT
1.3. Surgical rate from patient records at surgery visit and follow up visits
1.4. Resection rate (R0/R1) from patient records at restaging visit
1.5. Local or systemic disease progression on follow up rate from patient records, at restaging visit and follow up visits
1.6. Adherence to protocol from patient records at the IRE visit, surgery visit, follow up visits, and end of the study
2. The acceptability of treatment to patients and their clinicians measured using the following:
2.1. Health-related quality of life measured using the EurolQol 5-dimension (EQ-5D) questionnaire at randomisation, 3, 6, 9, and 12 months post-randomisation
2.2. Indicative costs related to health resource use in both treatments (IRE and chemotherapy vs chemotherapy alone) assessed across all timepoints
2.3. Social costs of attending for both the IRE treatment and Standard of Care group (travel, time off work, social support costs) assessed across all timepoints
2.4. Return to normal activity rate within 12 months post-randomisation recorded in the case report form at 12 months follow up visit
2.5. Return to employment rate (in those who work) within 12 months post-randomisation recorded in the case report form at 12 months follow up visit
2.6. Number of work days lost (in those who work) within 12 months post-randomisation

recorded in the case report form at 12 months follow up visit
3. Safety of the IRE and chemotherapy measured using serious adverse events recorded following randomisation and adverse events recorded in the case report form at follow up visits

Completion date
06/02/2025

Eligibility

Key inclusion criteria
1. Able to provide informed consent
2. Aged ≥18 years
3. Locally advanced pancreatic cancer anywhere in the pancreas
3. Tissue confirmation of pancreatic adenocarcinoma by biopsy or cytology/pathology
4. Cancer not amenable to surgical resection (following pancreas surgeon/multidisciplinary team review)
5. Completed systemic chemotherapy with FOLFIRINOX (standard or modified). This must be the only regimen of chemotherapy the patient has had since diagnosis.
6. Considered amenable to irreversible electroporation (IRE) therapy by pancreas interventional radiologist
7. WHO Performance status 0 or 1
8. Maximum cancer diameter 3.5 cm at the time of IRE treatment
9. Considered fit for general anaesthetic following pre-assessment.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. First line chemotherapy other than FOLFIRINOX
2. Concomitant malignancy (except skin and prostate cancers)
3. Metastatic disease including distant (i.e. non-local) nodal metastases
4. Borderline resectable disease
5. Occlusion or >180° involvement of the portal vein (superior mesenteric vein/portal vein)
6. Arterial involvement with <180° of the superior mesenteric artery, celiac axis, or common hepatic artery
7. Untreated gastric outlet or biliary obstruction
8. Co-morbidity precluding general anaesthesia
9. Indwelling electrical devices such as pacemakers and Left Ventricular Assist Devices (LVADs)

10. Chronic Kidney Disease stage 3, 4, or 5
11. History of epilepsy or other neurological diseases
12. Abdominal varices preventing safe access to pancreas cancer
13. Unable to tolerate general anaesthetic with neuromuscular blockade
14. Subjects who are actively bleeding, anticoagulation which cannot be discontinued, coagulopathy defined as an international normalized ratio (INR) of ≥1.5, or have any one of the following haematology results:
14.1. Haemoglobin <8 g/dl
14.2. Absolute neutrophil count <1500 cells/ml
14.3. Platelet count <50,000.

Date of first enrolment
01/03/2024

Date of final enrolment
30/11/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Free London NHS Foundation Trust
Royal Free Hospital
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
King's College Hospital NHS Foundation Trust
King's College Hospital
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston

Birmingham
United Kingdom
B15 2GW

Study participating centre
Leeds Teaching Hospitals NHS Trust
St. James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle-upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Royal Liverpool and Broadgreen University Hospitals NHS Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
United Kingdom
L7 8XP

Study participating centre
The Clatterbridge Cancer Centre NHS Foundation Trust
Clatterbridge Road
Bebington
Wirral
United Kingdom
CH63 4JY

Sponsor information

Organisation

Royal Free London NHS Foundation Trust

ROR
https://ror.org/04rtdp853

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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

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 article		12/05/2022	16/05/2022	Yes	No
HRA research summary			28/06/2023	No	No