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A Phase II clinical trial to compare the effectiveness of gemcitabine and nab-paclitaxel administered in combination with ATRA vs without ATRA in patients with locally advanced treatment-naïve pancreatic cancer

Submission date
27/01/2021

Registration date
09/02/2021

Last Edited
27/01/2025

Recruitment status
Recruiting

Overall study status
Ongoing

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
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-atra-and-chemotherapy-for-pancreatic-cancer-starpac-2-or-primus-005

Background and study aims
Pancreatic cancer is a cancer that's found anywhere in the pancreas. The pancreas is an organ in the top part of your tummy. It helps you digest your food and makes hormones, such as insulin. Pancreatic cancer (PDAC) is the fourth-highest cancer killer worldwide and is responsible for 6% of cancer deaths. Around 80% of patients are diagnosed at a late stage when cancer has spread and surgical removal is no longer possible. Most patients appear with advanced disease, with approximately 35% of patients having locally advanced (laPDAC), for which the current treatment options are minimally effective.

Who can participate?
Patients aged 16 years or above, with pancreatic cancer.

What does the study involve?
Patients will be randomised to receive gemcitabine + nab-paclitaxel or gemcitabine + nab-paclitaxel + ATRA. ATRA (if allocated), gemcitabine and nab-paclitaxel will be administered in 28-day cycles. ATRA will be administered for 6 cycles whereas gemcitabine/nab-paclitaxel will be administered until the disease worsens, and all patients will be followed up every 3 months via telephone or patient medical records until death, loss to follow-up, or study termination by the Sponsor, whichever occurs first. Eligible patients will be identified through Precision-Panc, a national initiative for pancreatic cancer funded by CRUK, or in the normal NHS setting when undergoing exploratory surgery for their pancreatic cancer.

What are the possible benefits and risks of participating?
This trial aims to find out information that may help people with locally advanced pancreatic cancer who have not had prior treatment for this disease. It cannot be guaranteed that there will be a benefit to participants during their treatment as this is unknown at this stage.
Participants may have side effects from the drugs or procedures carried out in this study and they will vary from person to person. Everyone taking part in the study will be followed carefully for any side effects through regular checks such as blood tests, vital signs, physical examinations and review of any illnesses or symptoms. Common side effects (though not an exhaustive list) include hair loss, nausea, vomiting, diarrhoea, low platelets in the blood, low white blood cells, nerve damage that can cause pain, numbness or weakness, lack of energy, body pains, fever, cough and abnormal liver function tests.

Where is the study run from?
St Bartholomew's Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2019 to February 2029

Who is funding the study?
1. Medical Research Council (UK)
2. Celgene Corporation (USA)

Who is the main contact?
Professor Hemant Kocher, bci-starpac2@qmul.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Hemant Kocher

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Additional identifiers

EudraCT/CTIS number

2019-004231-23

IRAS number
1003111

ClinicalTrials.gov number
NCT04241276

Secondary identifying numbers
CPMS 44007

Study information

Scientific Title
Phase IIb randomised clinical trial repurposing ATRA as a stromal targeting agent in a novel drug combination for pancreatic cancer

Acronym
STARPAC2

Study objectives
Primary:
1. To assess the efficacy of ATRA when given in combination with gemcitabine and nab-paclitaxel based on PFS

Secondary:
1. To assess the efficacy of ATRA when given in combination with gemcitabine and nab-paclitaxel based on objective response rate (ORR)
2. To assess the efficacy of ATRA when given in combination with gemcitabine and nab-paclitaxel based on overall survival (OS)
3. To assess the safety and tolerability of ATRA when given in combination with gemcitabine and nab-paclitaxel over the first 6 cycles
4. To assess the surgical resection rate of ATRA when given in combination with gemcitabine and nab-paclitaxel
5. To assess the resection margin negative (R0) surgical resection rate of ATRA when given in combination with gemcitabine and nab-paclitaxel
6. To assess quality of life (QOL) of patients receiving ATRA in combination with Gemcitabine and Nab-Paclitaxel

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/05/2020, South Central - Oxford A Research Ethics Committee (Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 (0)207 104 8284; oxforda.rec@hra.nhs.uk), ref: 20/SC/0136

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Pancreatic cancer

Interventions
Active Comparator: Gemcitabine + nab-paclitaxel
Experimental: Gemcitabine + nab-paclitaxel + ATRA

Gemcitabine: 1000 mg/m2 IV on days 1, 8 and 15 of a 28-day cycle
Nab-paclitaxel: 125 mg/m2 IV on days 1, 8 and 15 of a 28-day cycle
ATRA: 45 mg/m2 orally (in two divided doses) from days 1 to 15 of each cycle

Patients will be randomised to receive gemcitabine + nab-paclitaxel or gemcitabine + nab-paclitaxel + ATRA. ATRA (if allocated), gemcitabine and nab-paclitaxel will be administered in 28-day cycles. ATRA will be administered for 6 cycles whereas gemcitabine/nab-paclitaxel will be administered until disease progression. Treatment may be discontinued earlier due to unacceptable toxicities or death or because the patient requests to be withdrawn from study treatment. If treatment with gemcitabine/nab-paclitaxel is stopped prior to the patient completing 6 cycles of treatment with ATRA (if allocated), the patient may continue on treatment with ATRA alone until the 6 cycles are completed, at the discretion of the treating physician. On completion of the study treatment patients will attend a safety visit 30 days (+7 days) after the last dose of gemcitabine/nab-paclitaxel. Patients will subsequently enter a survival follow-up period for a minimum of 12 months from the date of the safety visit.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Gemcitabine, nab-paclitaxel, ATRA

Primary outcome measure
PFS defined as the time from the date of randomisation to the date of first documented tumour progression using Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 or death from any

cause, whichever occurs first evaluated at baseline and 8 weekly thereafter until progression or death

Secondary outcome measures
1. ORR defined as the number of patients with an objective response (OR) divided by the number of patients analysed assessed by RECIST 1.1 every 8 weeks until progression or death
2. OS defined as the time from the date of randomisation to death from any cause assessed by patient contact or medical until end of treatment and then 3 monthly for at least 12 months
3. Safety and tolerability as assessed by AEs (CTCAE v5.0). collected from the time the patient gives informed consent until the safety visit
4. Surgical resection rate defined as the number of patients undergoing complete resection of known pancreatic primary and associated lymph nodes as per medical records at any point after enrolment, in each arm
5. R0 surgical resection rate defined as histologically confirmed complete resection of known pancreatic primary from those resected as per histopathology at any point after enrolment, in each arm
6. Patient reported outcomes as measured by questionnaire EQ-5D_5L at the beginning of each cycle until progression

Overall study start date
30/08/2019

Completion date
28/02/2029

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/11/2024:
1. Written informed consent prior to admission to this study
2. Age ≥16 years. No upper age limit
3. ECOG performance status 0 or 1
4. Histologically proven pancreatic ductal adenocarcinoma (PDAC) as part of the Precision-Panc Master Protocol, or for patients who have undergone exploratory laparotomy and found to have locally advanced disease
5. Locally advanced disease which is measurable according to the Response Evaluation Criteria in Solid Tumours (RECIST v1.1)
6. CT chest abdomen and pelvis within 28 days as well as PET-CT within 42 days of randomisation (MRI Liver only if indeterminate liver lesions) to confirm absence of metastatic disease.
7. Received no prior systemic therapy for pancreatic cancer
8. Adequate haematologic and end organ function, defined by the following laboratory results obtained within 14 days prior to the first study treatment:
8.1. Absolute Neutrophil Count ≥1.5 x 10^9/l (without granulocyte colony-stimulating factor support within 2 weeks prior to the first study treatment)
8.2. Platelet count ≥100 x 10^9/l (without transfusion within 2 weeks prior to the first study treatment)
8.3. Haemoglobin ≥10 g/dl (transfusion permitted to establish target haemoglobin levels prior to the first study treatment)
8.4. Calculated creatinine clearance (e.g. Cockcroft-Gault) ≥ 50 ml/min
8.5. Bilirubin level ≤1.5 ULN (patients with known Gilbert disease who have bilirubin levels ≤3 x ULN may be enrolled). Patients must be able to undergo biliary stenting if required before or, if

required, during the trial
8.6. AST or ALT <2.5 x ULN
8.7. Alkaline phosphatase (ALP) <2.5 x ULN
8.8. INR and aPTT ≤1.5 x ULN this applies only to patients who are not receiving therapeutic anticoagulation patients receiving therapeutic anticoagulation should be on a stable dose
9. Female patients of child-bearing potential are eligible, provided they have a negative serum pregnancy test within 7 days prior to the first dose of study treatment, preferably as close to the first dose as possible. All patients with reproductive potential must agree to use a medically acceptable method of contraception throughout the treatment period and for 1 month after discontinuation of ATRA and/or gemcitabine/nab-paclitaxel (whichever is the latest) and for 6 months after discontinuation for male patients. Acceptable methods of contraception include IUD, oral contraceptive, sub-dermal implant and double barrier (condom with a contraceptive sponge or contraceptive pessary). Micro-dosed progesterone preparations ("mini-pill") are an inadequate method of contraception during treatment with ATRA. If patients are taking this pill they should be instructed to stop and another form of contraceptive should be prescribed instead
10. Able to follow protocol requirements as assessed by the Principal Investigator

Previous inclusion criteria:
1. Written informed consent prior to admission to this study
2. Age ≥16 years. No upper age limit
3. ECOG performance status 0 or 1
4. Histologically proven pancreatic ductal adenocarcinoma (PDAC) as part of the Precision-Panc Master Protocol, or for patients who have undergone exploratory laparotomy and found to have locally advanced disease
5. Locally advanced disease which is measurable according to the Response Evaluation Criteria in Solid Tumours (RECIST v1.1)
6. CT chest abdomen and pelvis as well as PET-CT within 28 days of day 1 of treatment (MRI Liver only if indeterminate liver lesions) to confirm absence of metastatic disease.
7. Received no prior systemic therapy for pancreatic cancer
8. Adequate haematologic and end organ function, defined by the following laboratory results obtained within 14 days prior to the first study treatment:
8.1. Absolute Neutrophil Count ≥1.5 x 10^9/l (without granulocyte colony-stimulating factor support within 2 weeks prior to the first study treatment)
8.2. Platelet count ≥100 x 10^9/l (without transfusion within 2 weeks prior to the first study treatment)
8.3. Haemoglobin ≥10 g/dl (transfusion permitted to establish target haemoglobin levels prior to the first study treatment)
8.4. Calculated creatinine clearance (e.g. Cockcroft-Gault) ≥ 50 ml/min
8.5. Bilirubin level ≤1.5 ULN (patients with known Gilbert disease who have bilirubin levels ≤3 x ULN may be enrolled). Patients must be able to undergo biliary stenting if required before or, if required, during the trial
8.6. AST or ALT <2.5 x ULN
8.7. Alkaline phosphatase (ALP) <2.5 x ULN
8.8. INR and aPTT ≤1.5 x ULN this applies only to patients who are not receiving therapeutic anticoagulation patients receiving therapeutic anticoagulation should be on a stable dose
9. Female patients of child-bearing potential are eligible, provided they have a negative serum pregnancy test within 7 days prior to the first dose of study treatment, preferably as close to the first dose as possible. All patients with reproductive potential must agree to use a medically acceptable method of contraception throughout the treatment period and for 1 month after discontinuation of ATRA and/or gemcitabine/nab-paclitaxel (whichever is the latest) and for 6 months after discontinuation for male patients. Acceptable methods of contraception include

IUD, oral contraceptive, sub-dermal implant and double barrier (condom with a contraceptive sponge or contraceptive pessary). Micro-dosed progesterone preparations (“mini-pill”) are an inadequate method of contraception during treatment with ATRA. If patients are taking this pill they should be instructed to stop and another form of contraceptive should be prescribed instead
10. Able to follow protocol requirements as assessed by the Principal Investigator

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
Planned Sample Size: 170; UK Sample Size: 170

Key exclusion criteria
1. Patient has known metastases
2. Patient has experienced a significant reduction in performance status between the screening/ baseline visit and within 72 hours prior to commencement of treatment as per trial protocol, and as per the Investigator’s assessment
3. Patients with pre-existing sensory neuropathy >grade 1
4. History of other malignancies (except cured basal or squamous cell carcinoma, superficial bladder cancer, prostate cancer in active surveillance, or carcinoma in situ of the cervix) unless documented free of cancer for ≥2 years
5. Patient has active, uncontrolled bacterial, viral, or fungal infection(s) requiring systemic therapy
6. Patient has known active, uncontrolled HIV, or active, uncontrolled hepatitis B or C infection. Patients with undetectable viral load are eligible
7. Patient has undergone major surgery, other than diagnostic surgery (i.e. surgery done to obtain a biopsy for diagnosis without removal of an organ), within 4 weeks prior to Day 1 of treatment in this study
8. Patient has a history of allergy (including soya bean or peanut allergies) or hypersensitivity to any of the study drugs or any of their excipients, or the patient exhibits any of the events outlined in the Contraindications or Special Warnings and Precautions sections of the products or comparator SmPC or Prescribing Information
9. History of connective tissue disorders (e.g., lupus, scleroderma, arteritis nodosa)
10. Patient with a history of interstitial lung disease, history of slowly progressive dyspnoea and unproductive cough, sarcoidosis, silicosis, idiopathic pulmonary fibrosis, pulmonary hypersensitivity pneumonitis or multiple allergies
11. Patient with high cardiovascular risk, including, but not limited to, recent coronary stenting or myocardial infarction in the past year. A high cardiovascular risk is defined as person having recent (within last 12 months) coronary stenting or myocardial infarction or unstable angina which in the opinion of Principal Investigator, with or without a cardiologist opinion, is deemed to have an absolute risk for cardiovascular death of ≥ 5% over next 10 years. (ESC/ESH

guidelines)
12. History of Peripheral Artery Disease (e.g., claudication, Leo-Buerger's disease)
13. Patient has serious medical risk factors involving any of the major organ systems, or serious psychiatric disorders, which could compromise the patient's safety or the study data integrity
14. Concurrent treatment with other experimental drugs or participation in another clinical trial with any investigational drug ≤30 days prior to study entry depending on the half-life of the investigational drug and/or guidance issued by the IMP manufacturer. Please contact the STARPAC2 coordinating team for further information
15. Patient is taking any prohibited concurrent medication, including vitamin A supplements, and is unwilling to stop use prior to and during the trial
16. Patient is pregnant, planning to become pregnant or breast feeding
17. Patient has received a live vaccine within four weeks prior to receiving their first dose of study treatment
18. Patient is unwilling or unable to comply with study procedures, as assessed by the Principal Investigator

Date of first enrolment
30/04/2020

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
St Bartholomew's Hospital
Barts Health NHS Trust
West Smithfield
London
United Kingdom
EC1A 7BE

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

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
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NW1 2PG

Study participating centre
The Christie NHS Foundation Trust
550 Wilmslow Road
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M20 4BX

Study participating centre
NHS Lothian
Waverley Gate
2-4 Waterloo Place
Edinburgh
United Kingdom
EH1 3EG

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Guys and St Thomas's Hospital
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre

NHS Greater Glasgow and Clyde
J B Russell House
Gartnavel Royal Hospital
1055 Great Western Road Glasgow
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Sponsor information

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research.governance@qmul.ac.uk

Sponsor type
University/education

Website
http://www.qmul.ac.uk/

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council; Grant Codes: MR/S036601/1

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Celgene

Alternative Name(s)
Celgene Corporation

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/12/2027

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
HRA research summary			28/06/2023	No	No
Protocol article		20/01/2025	27/01/2025	Yes	No