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Trial to investigate if the addition of two novel immunotherapy agents in combination with a chemotherapy agent can reduce the size of the cancer and how long they can delay the growth of the cancer in patients with metastatic pancreatic cancer.

Submission date 30/03/2023	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 31/03/2023	**Overall study status** Stopped	
Last Edited 11/06/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

The prognosis for patients with advanced pancreatic cancer (when potentially curative surgery is not a possibility) is extremely poor, with most patients dying within one year of diagnosis or earlier. Combinations of two or three chemotherapy agents are the standard of care for metastatic pancreatic cancer patients with good performance status only, due to the potential side effects. However, almost 50% of the patients presenting with advanced disease have lower performance status and have limited options in terms of active treatment, which is in general single agent chemotherapy such as gemcitabine or 5-FU. Even then this offers modest benefits with the trade-off of the limited quality of life for patients. Due to this, a large proportion of patients in this category end up receiving the best supportive care only. In addition, this subgroup of patients is traditionally poorly served in the clinical trial setting as they are excluded due to lower performance status. Therefore, novel tolerable combination therapies are urgently needed for these patients. Despite the early success of novel agents that “modulate” the immune system (immunotherapy) to fight cancers such as melanoma and lung, the results for the single-agent approach in pancreatic cancer has been disappointing to date. The main aim of the study will be to determine how much this drug combination reduces the size and how long it can delay the growth of cancer.

Who can participate?

Up to 50 patients with metastatic pancreatic ductal adenocarcinoma will be treated in the study from approximately 25 hospital sites in the UK.

What does the study involve?

This study will be testing the effects of two novel immunotherapy agents that work together to

“re-wire” the immune system to fight cancer cells, IMM-101 and pembrolizumab in combination with gemcitabine.

What are the possible benefits and risks of participating?
There may or may not be direct medical benefits to patients from taking part in this study. A potential benefit is that patients may respond well to the study treatment and their cancer may be controlled for longer. The study may also provide information on the treatment of pancreatic cancer which will benefit others in the future. Patients who agree to take part in this study may benefit from closer monitoring and regular contact with the study team, as they will have extra scans and blood tests. Participants will give written informed consent. The patient information sheet will outline all potential risks and burdens associated with trial participation. The main risks are the potential side -effects of the drug treatments which include: low white blood cells, decrease in platelets, anaemia, nausea and sickness, hair loss, diarrhoea, constipation, skin rash, feeling tired, pain in muscles and bones, and fever.
Patients will be seen regularly during the study to make sure they are tolerating the study treatment. All participants in the trial will be closely monitored for side effects and, where required, additional treatment may be given to control any side effects that develop.
Participants will be advised they can stop the trial at any time if they feel the side effects are a problem to them.
There may be pain/discomfort experienced at the time of taking blood samples.
Although some additional blood samples are being collected from patients in the study, these are scheduled to be taken when patients would be attending the hospitals to avoid additional visits for patients.
Overall the potential inconvenience and adverse effects are thought to be balanced by the potential benefit that participants may gain from receiving treatment in this trial.

Where is the study run from?
Glasgow Clinical Trials Unit, The University of Glasgow (UK)

When is the study starting and how long is it expected to run for?
March 2023 to December 2026

Who is funding the study?
Immodulon Therapeutics Ltd (UK)
Merck Sharp and Dohme (UK)

Who is the main contact?
Karen Carty (Project Manager), karen.carty@glasgow.ac.uk (UK)

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-gemcitabine-pembrolizumab-and-imm-101-for-pancreatic-cancer-primus-006

Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
2020-004701-31

Integrated Research Application System (IRAS)
1005296

Protocol serial number
PRIMUS006-2022

Study information

Scientific Title
PRIMUS-006: A phase II trial of gemcitabine, pembrolizumab and IMM-101 as first-line treatment in patients with metastatic pancreatic cancer

Acronym
PRIMUS 006

Study objectives
To determine the objective response rates of gemcitabine in combination with IMM-101 and pembrolizumab in patients with metastatic pancreatic cancer
1. To explore the safety and tolerability of this regimen in patients with metastatic pancreatic cancer
2. To describe the Duration of Response, Progression – Free Survival (PFS), Disease Control Rate (DCR), and Overall Survival (OS) of patients with metastatic pancreatic cancer treated with this combination

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 22/09/2023, North East - Newcastle & North Tyneside 2 Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, Newcastle, NE2 4NQ, United Kingdom; +44 (0)207 104 8086; NewcastleNorthTyneside2.REC@hra.nhs.uk), ref: 23/NE/0079

Primary study design
Interventional

Study design
Interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Metastatic pancreatic cancer

Interventions
This study is a single-arm phase II study. All patients registered for the study will receive the study intervention which is the following three drugs in combination: IMM-101, pembrolizumab and gemcitabine.

Details of the treatment regimen are provided below:
1. IMM-101: will be administered at a dose of 1mg intra-dermal (ID) between 2 to 7 days before the first cycle of pembrolizumab (MK-3475)/gemcitabine then 1mg ID on day 8 of cycle 1, 1mg

on day 1 of cycle 2, 1mg on day 8 of cycle 3 then 1mg on day 8 of each cycle thereafter.
2. Pembrolizumab (MK-3475): will be administered at a dose of 200mg by IV infusion every 3 weeks starting from cycle 1, day 1.
3. Gemcitabine: will be administered at a dose of 1000mg/m2 by IV infusion on day 1 and day 8 of every 3 week-cycle starting from cycle 1, day 1.

Treatment will continue for all patients until the patient decides to withdraw, progressive disease, unacceptable toxicity, or at the investigator's discretion, and up to a maximum of 2 years

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
Gemcitabine, pembrolizumab (MK-3475) and IMM-101

Primary outcome(s)
The proportion of patients achieving an objective response, defined by RECIST 1.1, measured using CT scans for radiological assessment of disease until disease progression at baseline, 6 weekly (eg., weeks 6, 12, 18, 24, 30, 36, 42 and 48) during year 1 of treatment then 12 weekly during the second year of treatment and until progression after discontinuation of study treatment for reasons other than disease progression.

Key secondary outcome(s)
1. Evaluation of safety and tolerability of gemcitabine in combination with IMM-101 and pembrolizumab, (Occurrence and frequency of grade 1-5 adverse events) measured using NCI-CTCAE Version 5.0 during combination treatment and for up to at least 30 days after the last dose of study therapies. In addition, immune-mediated adverse events that occur up to 90 days after the last dose of pembrolizumab will also be recorded.
2. Evaluation of progression-free survival (PFS), disease control rate (DCR) and overall survival (OS) rates of gemcitabine in combination with IMM-101 and pembrolizumab; PFS and DCR are defined by RECIST V1.1. and measured using CT scans for radiological assessment of disease until disease progression at baseline, 6 weekly (eg., weeks 6, 12, 18, 24, 30, 36, 42 and 48) during year 1 of treatment then 12 weekly during the second year of treatment and until progression after discontinuation of study treatment for reasons other than disease progression. OS is assessed every 3 months after discontinuation of study treatment.

Completion date
01/12/2026

Reason abandoned (if study stopped)
Lack of staff/facilities/resources

Eligibility

Key inclusion criteria
The principal inclusion criteria are noted below:
1. Patients aged > or = 18 years for age

2. Patient has given written informed consent to participate in the trial
3. Histologically or cytologically confirmed metastatic pancreatic ductal adenocarcinoma or its variants
4. Patient has been enrolled in the Precision-Panc Master Protocol and their tissue has been deemed suitable for NGS analysis
5. No prior systemic anti-cancer therapy for metastatic pancreatic cancer. Patients may have received prior pre-, peri-, or post-operative systemic anti-cancer therapy for operable disease with curative intent provided that the last dose of systemic anti-cancer therapy was completed > 6 months before the recurrent disease was documented
6. ECOG performance status 1, but not sufficiently fit to potentially tolerate treatment with a combination treatment regimen consisting of two or more cytotoxic chemotherapy agents in the opinion of the investigator
7. Measurable disease by RECIST 1.1
8. Estimated life expectancy > 3 months
9. Adequate haematological and biochemical function
10. Willingness to comply with study procedures including administration of study therapies
11. Females of childbearing potential must have a negative pregnancy test within 72 hours of the first dose of study treatment and agree to use highly effective contraceptive measures during the study and for 6 months after the last administration of the study drug
12. Male patients with partners of childbearing potential must agree to use highly effective contraceptive measures during the study and for 6 months after the last administration of the study drug
13. Patients with a history of HCV infection are eligible for the study if HCV viral load is undetectable at screening. Patients who have been treated for HCV infection must have completed curative anti-viral therapy at least 4 weeks before registration to the trial.
14. Patients who are hepatitis B positive will be eligible as long as they meet the following criteria:
14.1. Patients who are HBsAg positive are eligible if they have received HBV antiviral therapy for at least 4 weeks and have an undetectable HBV viral load before registration to the trial
14.2. Patients should remain on anti-viral therapy throughout study treatment and follow local guidelines for HBV anti-viral therapy post-completion of study treatment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
0

Key exclusion criteria

The principal exclusion criteria are noted below:
1. Pregnant or breast-feeding women.
2. Patients with cardiovascular disease defined as Stage II to IV congestive heart failure (CHF) as determined by the New York Heart Association (NYHA) classification system, or history of myocardial infarction (MI), or cardiac arrhythmia associated with haemodynamic instability, or unstable angina, or cerebral vascular accident, or transient ischemia, if any have occurred within the previous 12 months prior to study treatment.
3. Any other serious medical or psychiatric disorder that would be, in the opinion of the investigator, a contra-indication to either the trial procedures or to therapy with gemcitabine, IMM-101 or pembrolizumab.
4. Any prior therapy with IMM-101 or an immune checkpoint inhibitor.
5. Major surgery within 28 days of starting study treatment and patients must have recovered from any effects of major surgery.
6. Patients with a known hypersensitivity to gemcitabine, IMM-101, or pembrolizumab or any of the excipients of the products, including patients who have previously experienced an allergic reaction to any mycobacterial product.
7. Current or prior use of immunosuppressive medication within 14 days before the first dose of IMM-101 or pembrolizumab. The following are exceptions to this criterion:
7.1. Intranasal, inhaled, or topical steroids; or local steroid injections (e.g., intra-articular injection)
7.2. Systemic corticosteroids at physiologic doses not to exceed 10 mg/day of prednisolone or equivalent
7.3. Steroids as premedication for hypersensitivity reactions (e.g., CT scan premedication) and chemotherapy-induced nausea and vomiting
8. History of allogenic organ transplant.
9. Previous severe or life-threatening skin adverse reaction with other immune-stimulatory anticancer agents.
10. Active autoimmune disorders, or prior documented severe autoimmune or inflammatory disorders requiring immunosuppressive treatment in the last 2 years (including inflammatory bowel disease [e.g., colitis, Crohn's disease], diverticulitis with the exception of diverticulosis, coeliac disease, irritable bowel syndrome, or other serious gastrointestinal chronic conditions associated with diarrhoea); systemic lupus erythematosus; Wegener syndrome (granulomatosis with polyangiitis), Graves' disease; rheumatoid arthritis, hypophysitis, uveitis or other evidenced autoimmune disorders. The following are exceptions to this criterion:
10.1. Patients with vitiligo or alopecia
10.2. Diabetes mellitus type I or resolved childhood asthma/atopy
10.3. Patients with hypothyroidism (e.g., following Hashimoto syndrome) stable on hormone replacement
10.4. Any chronic skin condition that does not require systemic therapy
10.5. Patients with coeliac disease controlled by diet alone
11. History of (non-infectious) interstitial lung disease or pneumonitis that required steroids or current pneumonitis.
12. Patients with an active infection requiring systemic therapy.
13. Concurrent active Hepatitis B (defined as HBsAG positive and/or detectable HBV/DNA) or Hepatitis C virus (defined as anti-HCV Ab positive and detectable HCV RNA) infection.
14. History of (non-infectious) interstitial lung disease or pneumonitis that required steroids or current pneumonitis.
15. Patients with an active infection requiring systemic therapy.
16. Receipt of the last dose of an approved (marketed) anticancer therapy (chemotherapy, targeted therapy, biologic therapy, monoclonal antibodies, etc.) or radiotherapy within 28 days or 5 half-lives, whichever is the longest, prior to the first dose of study treatment.
17. Received prior radiotherapy within 2 weeks of the start of the study intervention.

Participants must have recovered from all radiation-related toxicities, not require corticosteroids, and not have had radiation pneumonitis. A 1-week washout is permitted for palliative radiation (≤2 weeks of radiotherapy) to non-CNS disease.
18. Other malignancy within 3 years except for non-invasive malignancies such as cervical carcinoma in situ, non-melanoma carcinoma of the skin, or ductal carcinoma in situ of the breast that has/have been surgically cured or treated/biochemically-stable, organ-confined prostate cancer (patients can remain on treatment for this indication as long as not contraindicated with study treatment).
19. Receipt of a live attenuated vaccine within 30 days prior to the first dose of study therapy.

Date of first enrolment
17/06/2024

Date of final enrolment
30/06/2026

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Beatson West of Scotland Cancer Centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre
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Study participating centre

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Study participating centre
Queen Elizabeth Hospital
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Sponsor information

Organisation
NHS Greater Glasgow and Clyde

ROR
https://ror.org/05kdz4d87

Funder(s)

Funder type
Industry

Funder Name
Immodulon Therapeutics Ltd

Funder Name
Merck Sharp and Dohme

Alternative Name(s)
MSD United Kingdom, Merck Sharp & Dohme, Merck Sharp & Dohme Corp., MSD

Funding Body Type
Private sector organisation

Funding Body Subtype

For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the Clinical Trials Unit (CTU). The CTU is committed to furthering cancer research by sharing de-identified individual-patient data (IPD) from its studies with others in the field who wish to use the data for high-quality science. They are happy to consider proposals from researchers and will share IPD to the maximum extent, subject to individual study constraints relating to:
1. Ethical approval and informed consent
2. Contractual and legal obligations
3. Publication timelines (data will not normally be shared before the publication of the primary results)
In addition, all proposals will be reviewed for their scientific merit by the CTU and the study Chief Investigator. Only data relevant to the objectives of a particular proposal will be provided. An independent review process will be undertaken in cases of disagreement between the applicant and the CTU/Chief Investigator.

IPD sharing plan summary
Available on request