Safety and efficacy of IMM-101 combined with stereotactic radiotherapy in patients with limited MEtastatic PANcreatic Cancer (MEPANC-1)

Published: 14-12-2020
Last updated: 30-01-2025

This study has been transitioned to CTIS with ID 2024-514598-23-00 check the CTIS register for the current data. This is an open-label, non-randomized, multicentre phase II study with an initial safety-run in. During the safety run-in phase, we will...

Ethical review	Approved WMO
Status	Completed
Health condition type	Exocrine pancreas conditions
Study type	Interventional

Summary

ID

NL-OMON54853

Source
ToetsingOnline

Brief title
MEPANC-1

Condition

- Exocrine pancreas conditions

Synonym
metastatic pancreatic cancer, pancreatic ductal adenocarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Ministerie van OC&W,Immodulon Therapeutics

Intervention

Keyword: IMM-101, Immunotherapy, Metastatic pancreatic cancer, SBRT

Outcome measures

Primary outcome

Safety run-in phase endpoint. The primary endpoint for this part of the study is safety. Safety is defined as maximum of 6 out of 20 patients experiencing a grade 3/4/5 events related to the IMM-101 vaccination or SBRT before, during and after IMM-101 and SBRT. These will be considered significant events for this endpoint. Safety will be evaluated at completion of the 6 injections.
Phase II endpoint The primary endpoint is efficacy and will be calculated for the overall study. Efficacy is defined as 1-year progression free survival (PFS). Progression-free survival will be calculated from the start of FOLFIRINOX (PFS 1) to the date of progressive disease of the primary tumour or locoregional recurrence, progression of previously treated lungs and/or liver metastasis, the occurrence of new metastases or death. Efficacy is defined as an increase of 12 to 24% in patients which received at least 8 cycles of FOLFIRINOX (standard cohort) and of 5 to 15% in 1-year progression-free survival in patients with less than 8 cycles (expansion cohort), will be the main endpoint.

Secondary outcome

Secondary endpoints are PFS calculated from the start of the first IMM-101 injection (PFS 2), overall survival (from start FOLFIRINOX and IMM-101 untill

death (OS1 and OS2)), quality of Life, the effects of IMM -101 administered

with SBRT on circulating immune cells and tumour markers CA 19-9, CEA and

radiological response (as determined by RECIST and iRECIST).

Study description

Background summary

Approximately 40% to 50% of patients diagnosed with pancreatic cancer present with metastatic disease. In addition, 80% of patients with resected pancreatic ductal adenocarcinoma (PDAC) develop recurrent disease due to its aggressive nature and its tendency to develop early metastases. Around 25% of patients with recurrence develop liver only metastases. Lung-only recurrence is seen in 14,7% of the patients. All these patients including those who develop metastases after resection are currently treated with palliative chemotherapeutic drugs, regardless of their pattern of metastases. Median overall survival in these metastatic patients treated with FOLFIRINOX, the most effective chemotherapeutic regimen is shorter than 11 months with a 1-year progression free survival of 12%.
Patients with limited hepatic and/or pulmonary metastases could potentially benefit from additional multimodality treatment after standard palliative treatment. This treatment could be effective for patients with few metastases to limited organ sites, also known as oligometastatic disease. Recently, a new definition of oligometastatic disease in PDAC was proposed, which includes anatomical and biological criteria. We define limited metastatic disease as <=5 metastases in the liver and/or lungs with a total tumour size per organ of < 9 cm. The concept of limited metastatic disease creates extra treatment approaches for each patient*s individual metastatic state. The addition of Stereotactic Body Radiation (SBRT) with immunotherapy (IMM-101) after FOLFIRINOX will harness the immune system in a synergistic approach. SBRT can act as an in- situ vaccine, increasing the expression of cell surface receptors and tumour antigen presentation and can even produce anti-tumour cytotoxic T cell response. In addition, IMM-101 (suspension of heat-killed whole cell Mycobacterium obuense) activates and maturates antigen presenting cells. Especially dendritic cells can aid in the antigen processing and T-cell cross priming, processes that are deficient in the setting of metastatic pancreatic cancer. IMM-101 immunotherapy thereby has the potential to optimize the immunogenic anti-tumour effect of radiation therapy. The combination of boosting the immune responses with immunotherapy in the presence of an increased exposure to tumour antigen will provide sufficient induction of the immune system to counter further metastatic burden. We hypothesize that treatment of IMM-101 combined with SBRT in patients with limited metastatic

hepatic or pulmonary disease of PDAC induces a durable local and systemic anti-tumour immune response to obtain disease control. This IMM-101 and SBRT protocol will start 4 weeks after standard chemotherapy treatment (FOLFIRINOX).

Study objective

This study has been transitioned to CTIS with ID 2024-514598-23-00 check the CTIS register for the current data.

This is an open-label, non-randomized, multicentre phase II study with an initial safety-run in. During the safety run-in phase, we will investigate the safety of combining IMM-101 administration with SBRT in 20 patients with limited metastatic disease in the liver and/or lung. If deemed safe, we will continue inclusion in the second phase of the study with an additional 80 patients in order to evaluate the efficacy of combining IMM-101 treatment with SBRT based on a 100% improvement of progression free survival.
The primary objective of the safety run-in is to determine safety of IMM-101 combined with SBRT in patients with limited metastatic disease from PDAC. When this combination is found to be safe, the second phase of the study will be initiated, the primary objective of the phase II is to investigate the potential efficacy of IMM-101 combined with SBRT. Secondary objectives are biochemical immune response, the effect on tumour markers, radiological tumour response and quality of life.

Study design

An open-label, non-randomized with an initial safety run-in followed by a phase II multicentre study looking at the efficacy of IMM-101 administered with SBRT.

Intervention

Six intradermal injections of IMM-101 (a vaccine adjuvant containing Heat-Killed Whole Cell Mycobacterium obuense) beginning 2 weeks prior to stereotactic body radiation therapy of all metastatic lesions. If present, SBRT will also be given on the primary tumour or on the local regional recurrence determined under strict conditions by the radiologist. Between the third and fourth injection of IMM-101 there will be a four-week break. Administration of IMM-101 will be performed at week -2, 0,2,4,8,10 and 12. This treatment starts 4 weeks after FOLFIRINOX for both groups.
Thereafter, IMM-101 will be given at a 4-week interval for up to 12 months (weeks 16, 20, 24, 28, 32, 36, 40, 44, 48, 52 and 56) or until the patient shows (clinical) progression, dies or withdraws from the study.

Study burden and risks

Patients will initially receive six intradermal injections with IMM-101 during

a 12- week period, followed by a monthly IMM-101 for up to 12 months. In addition, they will undergo additional blood collections in order to determine tumour- specific immune and tumour marker responses. These blood collections can cause bruising or slight short-term discomfort. In previously performed trials, IMM-101 administration proved to be safe showing a low toxicity profile. The main adverse reactions were limited to local skin reactions, so we do not expect any major side-effects of this treatment in our patient population. However, treatment with IMM-101 and SBRT on liver and/or lung metastases has not been investigated yet. Therefore, we will first include a limited number of patients (n=20) in the safety run-in, in order to establish the safety of IMM-101 administration before and during SBRT. Once the safety profile is established, we will enrol additional patients (n=80) in the subsequent second phase II of the trial.
Before FOLFIRINOX, and as part of the standard of care, all patients will undergo a CPTC-02 biopsy from one metastatic lesion in order to diagnose and confirm metastatic PDAC. The biopsy sample will also be used for Whole Genome Sequencing.
For SBRT, tumour tracking is enabled by the Synchrony® Respiratory Tracking System and requires the placement of radio- opaque markers in or near the tumour (fiducials). Fiducials are 3 mm gold objects frontloaded in a 19 Gauge FNA needle and pushed with the stylet through the entire length of the needle. Fiducials are consecutively placed in or close to every lesion in the liver (determined by the principal investigator) under endoscopic ultrasound or CT guidance. Complications of this procedure is 2% in consecutive series. In the lungs endovascular placement will be used to place fiducial markers.The success rate of endovascular coil rate is 99,8% with 10% of patients developing gr 1 complications: mild haemoptysis or small asymptomatic pulmonary infarction or haemorrhage. Since metastatic pancreatic cancer is a deadly disease with an extremely poor survival rate, we find that the above-mentioned risks and burden outweigh the potential benefit for patients participating in this trial.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's-Gravendijkwal 230
Rotterdam 3015 CE
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's-Gravendijkwal 230
Rotterdam 3015 CE

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Histologically confirmed (metastatic) pancreatic cancer, as indicated by a definite cytology/histology report.
• <=5 hepatic and/or pulmonary metastases in total.
• The combined diameter of all liver metastases AND the primary tumour or local recurrence in the pancreas is <9 cm.
• The combined diameter of all pulmonary metastases is <9 cm.
• CA 19-9 < 1000 IU/mL after completion of chemotherapy.
• Age > 18 years and < 75 years.
• WHO performance status of 0-2
• Tumour volume of the primary tumour <7cmx7cmx7cm. Each diameter must not exceed 7 cm.
• Adequate renal function (eGFR >= 30 ml/min).
• Adequate liver tests (bilirubin < 1.5 times normal; ALAT/ASAT < 5 times normal).
• Adequate bone marrow function (WBC > 3.0 x 109/L, platelets > 100 x 109/L and hemoglobin > 5.6 mmol/l).
• Effective contraceptive methods.
• Written informed consent.
• Patients who did not complete at least 8 cycles of FOLFIRINOX due to severe toxicity, will be included in the expansion cohort.

Exclusion criteria

• Metastasis in other organs than the lung and liver.
• Histopathologically proven extra regional lymph node metastasis.

• Malignant ascites.
• Liver function insufficient to tolerate the prescribed dose of radiotherapy.*
• Child-Pugh Classification grade B/C.
• Lung function insufficient to tolerate the prescribed dose of radiotherapy.*
• Diffuse liver metastasis pattern on CT scan.
• Current or previous treatment with immunotherapeutic drugs.
• Second primary malignancy except in situ carcinoma of the cervix, adequately treated non-melanoma skin cancer, or other malignancy treated at least 5 years previously to diagnosis of pancreatic cancer and without evidence of recurrence.
• Pregnancy, breast feeding.
• An active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or other immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
• Diagnosis of immunodeficiency or receiving systemic steroid therapy or any other form of immunosuppressive therapy within 7 days prior to the planned first dose of the study. The use of physiologic doses of corticosteroids may be approved after consultation with the Sponsor.
• History of Human Immunodeficiency Virus (HIV) (HIV-1/2 antibodies).
• Active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative] is detected).
• Positive PCR test for presence of SARS-CoV-2 during screening stage.
• Live virus vaccine within 30 days of planned start of trial treatment.
• Use of herbal remedies, including traditional Chinese herbal products (e.g., mistletoe).
• Allergic reaction to M. obuense or had previously received IMM-101.
• Otherwise deemed unsuitable by the Investigator.
*To be determined by the treating radiologist.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	09-02-2021
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	IMM-101
Generic name:	Mycobacterium obuense

Ethics review

Approved WMO Date:	14-12-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-12-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-07-2021

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-08-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	22-04-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 28039
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EU-CTR	CTIS2024-514598-23-00
EudraCT	EUCTR2020-003945-13-NL
CCMO	NL74985.078.20