Safety and efficacy of the addition of IMM-101 Heat-Killed Whole Cell Mycobacterium obuense to standard stereotactic radiotherapy in locally advanced pancreatic cancer patients (LAPC-2 trial).

Published: 20-05-2019
Last updated: 15-05-2024

This phase I/II study consists of 2 subsequent study parts. In the phase I part we will investigate the safety of combining IMM-101 administration with SBRT in 20 patients with locally advanced pancreatic cancer who have completed at least 4 cycles...

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

Summary

ID

NL-OMON49825

Source
ToetsingOnline

Brief title
LAPC-2

Condition

- Exocrine pancreas conditions

Synonym
locally advanced 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

Intervention

Keyword: IMM-101, Immunotherapy, Pancreatic cancer

Outcome measures

Primary outcome

For the first phase of 20 patients, safety defined as max 6 out of 20 patients experiencing a grade 4/5 toxicity related to the IMM-101 intervention, will be the main endpoint. Safety evaluation will take place after the 20th patients has received the 3rd vaccination. For the overall study efficacy, defined as an increase of 20% in 1-year progression free survival, will be the main endpoint.

Secondary outcome

Secondary endpoints for the overall study will be overall survival, time to locoregional progression, time to distant metastasis, safety/toxicity, feasibility, resection rate, immune responses and quality of life/sleep.

Study description

Background summary

Approximately 30-40% of patients with pancreatic cancer present with locally advanced disease. Patients with locally advanced pancreatic cancer cannot be surgically resected but at the same time have no clinically detectable distant metastasis. Current treatment regimens consist of neoadjuvant chemotherapy with FOLFIRINOX, followed by stereotactic body radiation therapy. Despite slow improvements in patient outcomes, this strategy results in only approximately a third of patients being surgically resectable and an overall survival of only

10-12 months due to the development of metastatic disease. Recently, improved understanding in the field of tumor immunology has led to progress and breakthroughs in cancer immunotherapeutic strategies. One such therapeutic strategy is immunotherapy using modulators of the immune system. Radiation therapy can act as an in-situ vaccine, increasing the expression of cell surface receptors and tumor antigen presentation and can even produce anti-tumor cytotoxic T cell response. However, optimal anti-tumor response requires an intact host*s immune system and without amplification, the anti-tumor immunity arising from radiation therapy is likely to be limited. It is hypothesized that the combination of boosting the immune responses in the presence of an increased exposure to tumor antigen will provide sufficient induction of the immune system to counter further tumor growth. IMM-101, through its activation and maturation of 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 advanced pancreatic cancer. IMM-101 immunotherapy thereby has the potential to optimize the immunogenic anti-tumor effect of radiation therapy.

Study objective

This phase I/II study consists of 2 subsequent study parts. In the phase I part we will investigate the safety of combining IMM-101 administration with SBRT in 20 patients with locally advanced pancreatic cancer who have completed at least 4 cycles of FOLFIRINOX chemotherapy. If deemed safe and feasible (safety evaluation will take place after the 20th patient has received the 3rd vaccination and safety will be defined as max 6 out of 20 patients experiencing a grade 4/5 toxicity related to the IMM-101 intervention) we will continue inclusion in the next pahse of the study with the inclusion of an additional 18 patients in order to be able to study efficacy of combining IMM-101 treatment with SBRT based on a 20% improvement of 1-year disease free survival. Secondary endpoints will be overall survival, time to locoregional progression, time to distant metastasis, feasibility, safety/toxicity, resection rate, tumor specific immune-responses and quality of life/sleep.

Study design

An open-label, non-randomized phase I/II single-center study.

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. Between the third and fourth injection will be a four-week break. Administration of IMM-101 will be performed at week 0,2,4,8,10 and 12.

Study burden and risks

Patients will receive six intradermal injections with IMM-101 during a 12-week period. In addition, they will undergo additional blood collections for determining tumor-specific immune responses. These blood collections can cause bruising or slight short-term discomfort. Furthermore, patients will be instructed to wear an Actiwatch during two 7-day periods to determine their activity level during daytime and duration of sleep during the night. In addition, they will be asked to complete questionnaires for quality of life (3 visits) and sleep (2 visits) during the study period. Apart from the time needed to complete these questionnaires no extra burden will be expected from these quality of life/sleep measurements.
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, since IMM-101 is composed of foreign material, not all reactions can be excluded and thus some uncertainty as to the safety of the product exists. Therefore, we will first include a limited number of patients (n=20) in a phase I study in order to establish safety and feasibility of IMM-101 administration before we will enroll more patients (n=18) in the subsequent phase II part of the trial.
Since locally advanced pancreatic cancer is a deadly disease with an extremely poor survival rate we find that the above-mentioned risks and burden do not outweigh the potential benefit for patients participating in this trial. The study has been designed to test the safety and feasibility of administration of the IMM-101 product, before a subsequent phase II study assessing safety and efficacy is undertaken. In this way we limit any unwanted adverse effects or lack of efficacy to as few patients as possible.

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 pancreatic cancer, as indicated by a definite cytology report
• Tumor considered locally advanced after diagnostic work-up including CT-imaging and diagnostic laparoscopy.
• Age > 18 years and < 75 years.
• WHO performance status of 0 or 1.
• ASA classification I or II.
• No evidence of metastatic disease.
• Largest tumor diameter < 7 cm x 7 cm x 7 cm.
• No direct tumor involvement oft he stomach, colon or small bowel.
• Normal renal function (Creatinine >= 30 ml/min).
• Normal liver tests (bilirubin < 1.5 times normal; ALAT/ASAT < 5 times normal).
• Normal bone marrow function (WBC > 3.0 x 10e9/L, platelets > 100 x 10e9/L and hemoglobin > 5.6 mmol/l).
• Ability to wear and Actiwatch device on non-dominant arm
• Written informed consent.

Exclusion criteria

• Previous allergic reaction to any mycobacterial product
• Prolonged systemic corticosteroid or immunosuppressant medication use
• Pregnancy
• Lymph node metastases from primary tumor outside the field of radiation.
• Second primary malignancy except in situ carcinoma of the cervix, adequately treated non-melanoma skin cancer, or other malignancy treated at least 3 years previously without evidence of recurrence.
• Pregnancy, breast feeding.

• Serious concomitant systemic disorders that would compromise the safety of the patient or his/her ability to complete the study, at the discretion of the investigator.
• An active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or 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.
• Known history of Human Immunodeficiency Virus (HIV) (HIV-1/2 antibodies).
• Known active Hepatitis B (e.g., HBsAg reactive) or Hepatitis C (e.g., HCV RNA [qualitative] is detected).
• Live virus vaccine within 30 days of planned start of trial treatment.
• Use of herbal remedies, including traditional Chinese herbal products (e.g., mistletoe).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-10-2019
Enrollment:	38
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	IMM-101
Generic name:	Mycobacetrium obuense

Ethics review

Approved WMO Date:	20-05-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-08-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-07-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-08-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-01-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-01-2021
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: 22166
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2019-000216-29-NL
CCMO	NL68762.078.19
Other	NTR NL7578
OMON	NL-OMON22166