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)

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22166

Source
Nationaal Trial Register

Brief title
LAPC-2

Health condition

Locally advanced pancreatic cancer (LAPC)

Sponsors and support

Primary sponsor: Erasmus MC, Surgery department
Source(s) of monetary or material Support: Erasmus MC

Intervention

Outcome measures

Primary outcome

Phase I
The main endpoint of the first inclusion phase is to determine safety/toxicity of IMM-101 administration in LAPC patients undergoing SBRT. Safety/toxicity of the IMM-101 intervention will be determined according to CTCAE version 5.0. All grade 4 and 5 events related to the administration of the IMM-101 product will be considered events for this endpoint.

Phase II
The main endpoint of the second inclusion phase is to asses efficacy of IMM-101 therapy in combination with SBRT in LAPC patients. Efficacy will be determined using 1-year PFS rates. PFS is defined as survival without locoregional progressive disease, the occurrence of distant metastases, the occurrence of second or recurrent pancreatic cancer from the date of inclusion. All included patients (i.e. 38 patients) will be analyzed for this endpoint.

Secondary outcome

For all patients the following secondary endpoints will be determined:
• Overall survival.
• Time to locoregional progression, defined as the period of time without locoregional progression after inclusion.
• Time to distant metastasis, defined as the period of time without distant metastases after inclusion.
• Radiological response rate after IMM-101 and SBRT using RECIST criteria (version 1.1)
• Resection rate defined as the percentage of included patients that underwent a curative-intent resection.
• Feasibility of receiving IMM-101 treatment and performing follow-up. Defined as feasibility of treatment procedures in order to be able to administer IMM-101 to patients and follow up these patients (e.g. ability to collect extra blood samples at designated time points).
• Safety/Toxicity according to CTCAE 5.0.
• Tumor-specific immune responses.
• Quality of sleep and sleep duration.
• Quality of life.

Study description

Background summary

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 (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 phase II with 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 objective

Approximately 30-40% of patients with pancreatic cancer present with locally advanced pancreatic cancer. 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 the use of neoadjuvant chemotherapy such as 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. 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 of the body’s 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, and 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 design

Screening, baseline, week 2/4/8/10/12/14 and 26. Following study week 26 standard FU will be performed at month 9/12/15/18/21/24/36/42/48/54 and 60.

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.

Contacts

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Eligibility criteria

Inclusion criteria

• Histologically confirmed pancreatic cancer, as indicated by a definite cytology report.
• Tumor considered locally advanced after diagnostic work-up including CT-imaging, using the DPCG criteria for locally advanced disease 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 size < 7 cm x 7 cm x 7 cm.
• 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 an Actiwatch device on non-dominant arm.
• Effective contraceptive methods.
• Written informed consent.

* If bilirubin is higher than 35 umol/L placement of a metal biliary stent is mandatory.

Exclusion criteria

• Prior radiotherapy, chemotherapy other than FOLFIRINOX or pancreatic resection.
• Current or previous treatment with immunotherapeutic drugs.
• Previous allergic reaction to any mycobacterial product.
• Prolonged systemic corticosteroid or immunosuppressant medication use (i.e. >2 weeks).
• 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 5 years previously to diagnosis of pancreatic cancer and 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 type:	Interventional
Intervention model:	Other
Allocation:	N/A: single arm study
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-08-2019
Enrollment:	38
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion
Date: 04-03-2019
Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 49825
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL7578
CCMO	NL68762.078.19
OMON	NL-OMON49825

Study results