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)

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22166

Bron
NTR

Verkorte titel
LAPC-2

Aandoening

Locally advanced pancreatic cancer (LAPC)

Ondersteuning

Primaire sponsor: Erasmus MC, Surgery department
Overige ondersteuning: Erasmus MC

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

• 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• 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).

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-08-2019
Aantal proefpersonen:	38
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	04-03-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 49825
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten