Autologous Dendritic Cells Loaded with Allogenic Tumor Lysate for Surgically Resected Pancreatic Cancer Patients (REACtiVe trial).

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

Summary

ID

NL-OMON52670

Source
ToetsingOnline

Brief title
REACtiVe

Condition

- Exocrine pancreas conditions
- Gastrointestinal neoplasms malignant and unspecified

Synonym
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,Amphera B.V.,TKI-LSH ondersteuning

Intervention

Keyword: Dendritic cell, Immunotherapy, Pancreatic cancer

Outcome measures

Primary outcome

The primary endpoint of this project proposal is to determine the feasibility of administering MesoPher after standard of care adjuvant therapy in patients with resected pancreatic cancer. We deem this treatment feasible in case 8 out of 10 patients are able to complete the proposed treatment.

Secondary outcome

As a secondary endpoint we will assess the safety of MesoPher in surgically resected pancreatic cancer patients.

In addition, we will determine the systemic immune profile, with emphasis on T lymphocytes, in surgically resected pancreatic cancer patients; and investigate how these immune profiles are affected by MesoPher treatment for individual patients.

W will also look at efficacy of the treatment.

Study description

Background summary

The annual incidence of patients developing pancreatic cancer in the Netherlands is approximately 3500. In 2030, pancreatic cancer is expected to be the second leading cause of cancer-related death. The 1-year overall survival (OS) for pancreatic cancer in the Netherlands is 20%; 5-year OS is only 3%.

Current treatments for pancreatic cancer include cytoreductive surgery, radio- and chemotherapy. To date, surgical resection is the mainstay of potentially curative treatment for patients with (borderline) resectable disease. However, ten years after resection, OS is 4%, demonstrating that cure is exceedingly rare. Apparently, the vast majority of patients with (borderline) resectable pancreatic cancer on imaging have occult metastatic disease. In the Netherlands, almost a third of these patients is found to have more advanced disease (locally advanced or metastatic) during surgical exploration and consequently does not undergo a resection. In the end, only 5-25% of all pancreatic cancer patients are eligible to undergo surgical resection.

We are in need of new treatments in order to curb the progression of pancreatic cancer. In contrast to radiotherapy and chemotherapy, dendritic cell vaccination may elicit specific anti-cancer responses without damaging surrounding healthy tissue and therefore would be a suitable complementary treatment to the current treatment regime.

While no clinical data is available concerning the efficacy and safety of allogenic tumor lysate pulsed DC vaccination in patients with pancreatic cancer, DC therapy with either autologous or allogenic tumor lysate has shown its feasibility and safety in patients suffering from MM. Here we propose to use PheraLys, a tumor lysate derived from five different malignant MM cell lines to load autologous DCs (MesoPher) for patient treatment. Microarray analysis of these five MM cell lines revealed that PheraLys contains a broad spectrum (>120) of tumor associated antigens (TAA) and cancer germline antigens (CGA) which are expected to induce high-avidity T cell responses within the patients. We argue that MesoPher possesses the potential to induce strong anti-tumor responses in patients suffering from pancreatic cancer as well, given the broad overlap of TAA and CGA expression between the two tumor types.

Compared to other cancer types, pancreatic cancer tissue specimens contain a relatively low number of cancer cells, making autologous tumor lysate for DC vaccination ineffective. We propose that the use of a lysate derived from five different MM cell lines to pulse DCs in pancreatic cancer patients has a higher feasibility than using autologous tumor lysate. Both MM and pancreatic cancer share multiple, clinically proven TAAs such as but not limited to: WT-1, mesothelin and MUC-1. In addition, unlike ACT with TCR transduced T cells which requires patients to have an HLA matching the therapeutic, whole tumor lysate therapy in the context of DC vaccination is applicable to all patients

regardless of their HLA type.
Recently we found that in a pancreatic cancer mouse model both autologous dendritic cells loaded with pancreatic cancer lysate as well as autologous dendritic cells loaded with MM lysate were able to induce a specific immune response as well as resulting in a significant reduction in tumor growth. Interestingly there was no significant difference found between both treatment groups indicating that treating pancreatic cancer patients with autologous dendritic cells loaded with MM lysate should be feasible.

Therefore, in this study we will primarily investigate whether it is feasible to use an allogeneic source of tumor antigens from MM cell lines in pancreatic cancer patients. Our secondary objective is to assess the safety and toxicity of the treatment as well as the occurrence of anti-tumor/immune responses within individual pancreatic cancer patients.

Study objective

The aim of this research is to investigate whether it is feasible and safe to treat operated pancreatic cancer patients who have completed standard of care treatment with dendritic cell immunotherapy using dendritic cells loaded with autologous material or peptides. In addition we will investigate efficacy.

Study design

single center open label phase II study.

Intervention

Leukapheresis is performed of which the monocytes are used for differentiation to dendritic cells using specific cytokines.

Pulsed autologous dendritic cells (MesoPher) are re-injected three times every two weeks. After the third injection with MesoPher, revaccinations to boost the immune system are given after 3 and 6 months.

Furthermore 3 CT scans will be performed to assess treatment response and bloodsamples will be collected to monitor the immune system before, during and after treatment.

Study burden and risks

Patients participating in this study undergo additional outpatient visits and extra invasive actions in the context of the study. The puncture of a blood vessel is necessary for leukopheresis, blood sampling and for injection with the dendritic cells. These invasive actions involve little extra risk.

Leukopheresis is a standard procedure that is performed by qualified personnel according to a standard protocol. There is a small risk of a short-term decrease in blood platelets and white blood cells. The leukapheresis can cause patients to experience transient palpitations, an accelerated heartbeat, a drop in blood pressure and dizziness. All these complaints are, however, transient. In addition, there is a very small risk of calcium reduction. If patients experience these complaints, additional calcium can be given.

The administration of autologous cells that are loaded outside the body with allogeneic human tumor material poses a potential risk, which is why this risk is being investigated in this study. Because the lysate itself is not directly administered to the patient but only when it is processed by the autologous dendritic cells, we expect that this involves a low risk. Previous clinical studies showed that injections of tumor lysate-loaded autologous dendritic cells were generally well tolerated by patients without systemic toxicity. Exceptions to this were flu symptoms such as fever and shivering.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Surgically resected pancreatic cancer.
• Completed post-operative standard treatment. Patients who did not complete standard of care due to toxicity or who are not able to start standard of care due to specific reasons are allowed to participate in the study after approval of the coordinating investigator.
• Patients who received standard of care post-operative treatment must be included within six months after completion of treatment. Patients who did not receive standard of care post-operative treatment must be included within six months after resection.
• No disease activity as assessed by radiological imaging.
• Patients must be at least 18 years old and must be able to give written informed consent.
• Patients must be ambulatory (WHO-ECOG performance status 0,1 or 2) and in stable medical condition.
• Patients must have normal organ function and adequate bone marrow reserve: absolute neutrophil count >1.0 x 10E9/l, platelet count > 100 x 10E9/l, and Hb > 6.0 mmol/l (as determined during screening).
• Women of childbearing potential must have a negative serum pregnancy test at screening and a negative urine pregnancy test just prior to the first study drug administration on Day 1, and must be willing to use an effective contraceptive method (intrauterine devices, hormonal contraceptives, contraceptive pill, implants, transdermal patches, hormonal vaginal devices, infusions with prolonged release) or true abstinence (when this is in line with the preferred and usual lifestyle)* during the study and for at least 12 months after the last study drug administration.
*True abstinence is acceptable when this is in line with the preferred and usual lifestyle of the subject. Periodic abstinence (such as calendar, ovulation, symptothermal, post-ovulation methods) and withdrawal are not acceptable methods of contraception.
• Men must be willing to use an effective contraceptive method (e.g. condom, vasectomy) during the study and for at least 12 months after the last study drug administration.
• Positive DTH skin test (induration > 2mm after 48 hrs) against at least one positive control antigen tetanus toxoid (see section 8.3 for DTH skin test procedure).
• Ability to return to the hospital for adequate follow-up as required by this protocol.
• Written informed consent according to ICH-GCP.

Exclusion criteria

• Medical or psychological impediment to probable compliance with the protocol.
• Current or previous treatment with immunotherapeutic agents.
• Current use of steroids (or other immunosuppressive agents). Patients must have had 6 weeks of discontinuation and must stop any such treatment during the time of the study. Prophylactic usage of dexamethasone during chemotherapy is excluded from this 6 weeks interval.
• Prior malignancy except adequately treated basal cell or squamous cell skin cancer, superficial or in-situ cancer of the bladder or other cancer for which the patient has been disease-free for five years.
• Serious concomitant disease, or active infections.
• History of autoimmune disease or organ allografts (or with active acute or chronic infection, including HIV and viral hepatitis).
• Serious intercurrent chronic or acute illness such as pulmonary disease (asthma or COPD), cardiac disease (NYHA class III or IV), hepatic disease or other illness considered by the study coordinator to constitute an unwarranted high risk for investigational DC treatment.
• Known allergy to shell fish (may contain keyhole limpet hemocyanin (KLH).
• Pregnant or lactating women.
• Inadequate vein access to perform leukapheresis.
• Concomitant participation in another clinical trial (except participation in a biobank study).
• An organic brain syndrome or other significant psychiatric abnormality which would compromise the ability to give informed consent, and preclude participation in the full protocol and follow-up.
• Absence of assurance of compliance with the protocol. Lack of availability for follow-up assessment.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-02-2019
Enrollment:	38
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cells autologous

Ethics review

Approved WMO Date:	31-08-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-11-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-12-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-01-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	19-10-2020
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-06-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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: 28791
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-003222-92-NL
CCMO	NL67169.000.18
Other	NTR NL7674
OMON	NL-OMON28791