# APpendix derived PAncreatic cancer Reactive T-lymphocytes

Published: 10-12-2018
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To evaluate anti-tumor activity of T-cells in the GALT of patients with PDAC.

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

## Summary

### ID

NL-OMON55377

**Source**
ToetsingOnline

**Brief title**
APPART

### 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

### Intervention

**Keyword:** appendix, Cytotoxic T cells, immunotherapy, pancreatic cancer

## Outcome measures

### Primary outcome

To identify tumour specific oncolytic activity of VA-GALT derived T cells in patients with pancreatic cancer.

### Secondary outcome

• To compare tumour specific antigens in plasma and tumor tissue of patients with PDAC.

DNA sequencing will be used to identify mutant antigens, using the Accel-Amplicon 56G Oncology Panel v2 (Swift Biosciences), compatible with the Illumina HiSeq. If the tumor specific antigens in both plasma and tumor of the same patient are comparable we could use the plasma results in the future for peptide production.

• To identify the distinct immune gene expression signature in VAs from patients with LAPC and (borderline) resectable PDAC compared to benign controls.

To define the immune gene expression, we will use whole transcriptome RNA sequencing, or the nCounter PanCancer Immune Profiling Panel (nanoString) that includes 770 human genes. To validate abundance and location of the tumor specific genes on the protein level, identified genes will be validated by immunohistochemical staining of proteins in FFPE VA.. Proteins of interest are selected based on differentially expressed genes from the RNA analyses..

• To compare peripheral blood T-cell and B cell receptor repertoires versus lymphocytes of the VA in patients with PDAC.

Using the ImmunoSEQ Assay (Adaptive Biotechnologies) T cells and B cell

receptors will be sequenced using DNA from both PBMCs and from the of the VA

lymphocytes.

• To assess the VA microbiome we will collect fecal material of the resected

appendix and perform metagenomics shotgun sequencing (Illumina).

# Study description

### Background summary

The majority of pancreatic ductal adenocarcinoma (PDAC) patients are diagnosed with advanced disease stage, for which surgical tumor removal has no impact on survival. Development of novel therapeutic strategies is crucial to improve the clinical outcome of patients with this devastating disease. PDAC is notorious for an immune-suppressive tumor microenvironment, low numbers of intratumoral cytotoxic T-cells which are often functionally exhausted and poor immune checkpoint inhibitor response. We hypothesize that tumor antigens are presented to naïve T-lymphocytes in lymph nodes and gut associated lymphoid tissue (GALT) to induce differentiation to cytotoxic T cells (CTLs). Preclinical studies performed in immune competent PDAC mouse models have shown that murine GALT may be a potential source for pancreatic cancer specific CTLs. This study is designed to investigate the molecular properties and anti-tumor cytolytic function of T-cells isolated from the vermiform appendix (VA) of PDAC patients. If the results of this study reveal that tumor reactive T-cells are present in the GALT and capable of inducing PDAC cancer cell death, this research will open up doors for therapeutic T cell transfer therapy and improvement of immune therapy for PDAC.

### Study objective

To evaluate anti-tumor activity of T-cells in the GALT of patients with PDAC.

### Study design

Single center translational pilot study.

### Intervention

Appendectomy during standard diagnostic laparoscopy or surgical resection in all included patients. In addition, extra peripheral blood will be collected

for isolation of T cells and dendritic cells to be used in several laboratory assays.

### Study burden and risks

There are no extra benefits for the patients involved. The risks associated with laparoscopic appendectomies (LA) for appendix sana are negligible. The risk of complications from anesthesia or the introduction of laparoscopic instrumentations in the abdomen will be shared, and thus not increase by the LA procedure. The diagnostic laparoscopy will take 15 minutes longer, when the LA is performed in addition to the diagnostic laparoscopy.

## 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

• Age between 35 and 80 years.
• Histological or cytological confirmed pancreatic cancer (i.e. pancreatic ductal adenocarcinoma).
• Planned diagnostic laparoscopy for LAPC or planned resection for (borderline) resectable PDAC.
• Ability to undergo diagnostic laparoscopy and appendectomy.
• Written informed consent.

### Exclusion criteria

• Previous appendectomy.
• Previous malignancy (excluding non-melanoma skin cancer), unless no evidence of disease and diagnosed more than 5 years before diagnosis of pancreatic cancer.
• Pregnancy.
• 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.
• Use of immune suppressive medication in the past 3 months ( including TNF-α antibody, azathioprine, mercaptopurine, methotrexaat, ciclosporin, adalimumab, infliximab, or vedolizumab therapy).

## Study design

### Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

### Recruitment

NL
Recruitment status: Completed

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|---|---|
| Start date (anticipated): | 15-01-2019 |
| Enrollment: | 50 |
| Type: | Actual |

## Ethics review

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|---|---|
| Approved WMO Date: | 10-12-2018 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 22-12-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 08-12-2021 |
| 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

No registrations found.

### In other registers

| Register | ID |
| --- | --- |
| CCMO | NL67371.078.18 |

# Study results

Date completed: 01-02-2024

**Summary results**
Trial ended prematurely