Next generation sequencing in patients with pancreatic ductal adenocarcinoma (PAN-NGS).
A nationwide prospective, translational cohort study.

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To determine the prevalence of actionable genetic alterations in PDAC patients

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

Summary

ID

NL-OMON51960

Source
ToetsingOnline

Brief title
PAN-NGS

Condition

- Exocrine pancreas conditions

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,Merus N.V.

Intervention

Keyword: Next generation sequencing, Pancreatic ductal adenocarcinoma, Translational study

Outcome measures

Primary outcome

The main endpoint is determining the percentage of patients with clinically actionable genetic alterations. These alterations are defined as (1) a pathogenic variant that is target of an approved drug in any cancer indication or predicts sensitivity to an approved drug in any cancer indication (e.g. MSI and pembrolizumab), (2) a pathogenic variant that is in the same pathway as a variant that is the target of an approved drug in any cancer indication or (3) a pathogenic variant that has compelling clinical or biological evidence supporting being predictive of response to a drug in PDAC. Clinically actionable mutations are selected using the OncoKB database52 and scientific literature.

Secondary outcome

Feasibility

Feasibility is a composite endpoint of:

• The number of included patients within a one year period. Which is deemed feasible if 200 patients are included within a one-year period.

• The percentage of patients successfully undergoing NGS. Which is deemed feasible if the NGS is successful in 80% of the submitted samples. Including a subgroup analysis of treatment naïve tissue versus tissue after

chemo(radio)therapy.

• Results reported back to the local clinician within relevant time-frame. The relevant time-frame is defined as the molecular tumor profiling report available within 4 weeks after acquisition of tissue and advice of the molecular tumor board within 8 weeks after the acquisition of tissue.

Changes in clinical management

Percentage of patients potentially experiencing a change in clinical management as result of the NGS. This is a change in treatment or referral to the clinical geneticist as a result of the NGS.

Subgroup identification

For the identification of subgroups with more clinically actionable mutations, the incidence will be compared between pre-specified subgroups based on baseline variables, including; age (age < 50 years vs. age 50-60 years), gender, smoking status, disease status (primary, metastatic), tumor biopsy site, metastatic sites, treatment status (treatment naïve, neoadjuvant chemo(radio)therapy), oncologic history and familial history.

Survival outcomes and therapy outcomes

Therapy outcomes and survival data will be obtained from electronic patient records from routine hospital visits, up to 5 years after primary diagnosis.

The following endpoints are included:

• Overall survival, defined as the time interval between the day of primary

diagnosis and the date of the occurrence of death (all causes).

• Cancer-specific survival, defined as the time interval between the day of primary diagnosis and the date of the occurrence of death caused by PDAC.

• Disease-free survival, defined as the length of time between the day of resection with curative intent and the date of local recurrence, regional recurrence, occurrence of distant metastases or death (all causes), whichever occurs first. Date of recurrence or metastasis occurrence is determined by first suspicion on CT scan.

• Local recurrence-free survival, defined as the length of time between the day of resection with curative intent and the date of local recurrence, regional recurrence or death (all causes), whichever occurs first. Date of recurrence is determined by first suspicion by CT.

• Distant metastasis-free survival, defined as the length of time between the day of resection with curative intent and the date of the occurrence of distant metastases or death (all causes), whichever occurs first. Date of occurrence of metastasis is determined by first suspicion by CT.

• Progression-free survival, defined as the length of time between start of systemic treatment and the date of progression of disease or death (all causes), whichever occurs first. Date of progression is determined by first suspicion on CT scan.

Therapy outcomes included response to (systemic) therapy according to RECIST-criteria and treatment toxicity according to CTCAE version 5.0.

Concordance rate

The concordance rate for individual genes and the overall concordance rate (all genes in the ctDNA panel) in ctDNA alterations compared to tumor tissue NGS DNA alterations.

Study description

Background summary

Pancreatic cancer is an aggressive disease that is difficult to treat. Some of the patients undergo surgery to remove the tumor. Unfortunately, in many patients, the pancreatic cancer comes back after it has been removed. The treatment for advanced pancreatic cancer is usually chemotherapy. If the cancer no longer responds to chemotherapy, there are few other treatment options. So there is a need for new and better treatment methods.

Pancreatic cancer is caused by genetic abnormalities in the tissue of the pancreas. Some of these abnormalities can be treated with targeted drugs. Most patients with pancreatic cancer have genetic abnormalities for which unfortunately there is no effective medicine (yet). In this study we try to get a better picture of which genetic abnormalities are present in the tumors of relatively young pancreatic cancer patients. We are particularly interested in genetic abnormalities that could possibly be treated with targeted drugs. These treatments are currently usually only given within a study context to patients who no longer respond to chemotherapy.

Study objective

To determine the prevalence of actionable genetic alterations in PDAC patients <= 60 years old.

Study design

Translational, multicenter cohort study.

Study burden and risks

For NGS, formalin-fixed paraffin embedded (FFPE) tissue is required to yield a sufficient percentage of tumor content (RNA analysis = 10%, DNA analysis = 20%). The tissue of patients that undergo resection of their tumor or a core biopsy during regular diagnostic work-up can be used for next generation

sequencing (NGS). In patients who present with disease recurrence after resection archived FFPE tissue of the resected primary tumor can be used. In case of metastatic PDAC patients with insufficient or no histological tissue available for NGS an additional core biopsy is required. These patients will be offered a core biopsy of the metastasis, which is considered a safe procedure.

At the moment of inclusion the majority of the PDAC patients will have metastatic disease. For these patients there are limited therapeutic options which are mainly based on systemic chemotherapy, offering a median overall survival of 8.5-11 months. In the subgroup of patients identified with an actionable genetic alteration, enrolment in a subsequent basket trial for targeted therapy might offer improved survival. Considering this, the potential benefit of participation in this study outweighs the above mentioned burden and risks.

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

• Cytological or histologically confirmed PDAC, irrespective of treatment status;
• Age > 18 years and <= 60 years at date of primary diagnosis;
• Performance status of ECOG 0-2;
• Estimated life expectancy of at least 12 weeks;
• Written informed consent.

Exclusion criteria

• Unwilling to know if there are any alterations which might be associated with genetic predisposition of cancer;
• Patient with locally-advanced PDAC or local-recurrence of PDAC with no histological tissue available for NGS.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-04-2021
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO

Date:	14-04-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-01-2025
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: 21085
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL75415.078.20