Pancreatic cancer: validation of circulating predictive biomarkers

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To validate promising circulating predictive biomarkers for FOLFIRINOX response in patients with PDAC, found in our previous pilot cohort (iKnowIT study, NL65025.078.18, MEC-2018-087) and to generate a biobank of blood samples to investigate future...

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

Summary

ID

NL-OMON55991

Source
ToetsingOnline

Brief title
PANCAKE

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: biomarkers, chemotherapy, FOLFIRINOX, pancreatic cancer

Outcome measures

Primary outcome

To validate the predictive value of circulating TP53 tumor mutations before chemotherapy in combination with a homozygote TP53 Pro72arg germline variant AND the predictive value of circulating microRNA 17-3p, 18a-5p, 194-5p, 24-3p, and 27a-3p expression before and after one cycle of chemotherapy for the prediction of progressive disease during FOLFIRINOX treatment in PDAC patients.

Secondary outcome

To collect blood samples of PDAC patients during chemotherapy treatment and create a pancreatic biobank to investigate future predictive or prognostic biomarkers. In addition, we will expand our biomarker research field with fragmentomics for which we work together with the Amsterdam University Medical Centre (Amsterdam UMC).

Finally, we will investigate the correlation between circulating biomarkers and tissue IHC for molecular subtypes in pancreatic cancer.

Study description

Background summary

Pancreatic ductal adenocarcinoma (PDAC) has a very high mortality rate, partially because of diagnosis at late stage of disease. Only 20% of patients present with resectable disease. Nowadays, the standard first-line treatment for locally advanced (LAPC) and metastatic PDAC is FOLFIRINOX chemotherapy, a combination of fluorouracil, leucovorin, irinotecan and oxaliplatin. Despite increased overall survival in FOLFIRINOX-treated patient groups, 20-30% of

patients will already show progressive disease during chemotherapy treatment. In the meantime, 60-70% of patients experiences grade 3-5 toxicity from FOLFIRINOX treatment. Biomarkers, especially those that can be easily measured in the peripheral blood instead of tumor tissue, are necessary to stratify patients for available therapies. Being able to select only patients that will benefit from FOLFIRINOX chemotherapy could prevent non-responding patients from severe FOLFIRINOX-induced toxicity. These non-responders might benefit from other types of (chemo)therapy instead. In a previous pilot study (NL65025.078.18, MEC-2018-087), we found some promising candidate biomarkers, measured in the peripheral blood of PDAC patients, that might predict FOLFIRINOX response. In addition, we will investigate the correlation of circulating biomarkers with tissue immunohistochemistry (IHC) for molecular subtypes of pancreatic cancers. These subtypes have previously been identified and are known to correlate to prognosis, but are also expected to predict response to FOFIRINOX. Correlating the IHC with the biomarkers could give more insight into the disease and understanding of the prognosis and therapy response.

Study objective

To validate promising circulating predictive biomarkers for FOLFIRINOX response in patients with PDAC, found in our previous pilot cohort (iKnowIT study, NL65025.078.18, MEC-2018-087) and to generate a biobank of blood samples to investigate future biomarkers.

Study design

Prospective multicenter cohort study. 240 patients will be included over a period of 2 years (200 in the experimental group and 40 in the control group). Blood samples will be drawn at three time points: before the first cycle and before the second cycle of FOLFIRINOX, and after 4 cycles of FOLFIRINOX. After every 4 cycles of FOLFIRINOX a CT scan will be performed as standard of care to evaluate progression of disease. Additionally, tissue obtained for diagnosis will be investigated for correlation between immunohistochemical subtypes and circulating biomarkers.

Study burden and risks

There is no extra benefit or risks for the patients involved.

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

Experimental group
• Age >= 18 years.
• Diagnosed with (borderline) resectable, locally advanced or metastatic PDAC.
• Treatment with FOLFIRINOX chemotherapy, including neoadjuvant therapy.
• Written informed consent (either for PANCAKE in case of locally advanced PDAC and metastasized PDAC or for the PREOPANC-2/PREOPANC-3 trial in case of (borderline) resectable PDAC).

Control group
• Age >= 18 years.
• Diagnosed with (borderline) resectable, locally advanced or metastatic PDAC.
• Treatment with gemcitabine, with or without nab-paclitaxel, chemotherapy, including neoadjuvant therapy.
• Written informed consent (either for PANCAKE in case of locally advanced PDAC and metastasized PDAC or for the PREOPANC-2 trial in case of (borderline) resectable PDAC).

Exclusion criteria

Experimental group
• Combined treatment with other chemotherapeutics then FOLFIRINOX.
• Previous treatment with FOLFIRINOX chemotherapy.
• 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.

Control group
• Combined treatment with other chemotherapeutics then gemcitabine and nab-paclitaxel.
• Previous treatment with FOLFIRINOX or gemcitabine-based chemotherapy.
• 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.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-06-2021
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	08-04-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-11-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	26-02-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-12-2024
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	NL75936.078.20