Recurrent disease detection after resection of pancreatic ductal adenocarcinoma using a standardized surveillance strategy - an international randomized controlled trial by the Dutch Pancreatic Cancer Group

Published: 21-01-2021
Last updated: 12-04-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON56087

Source
ToetsingOnline

Brief title
RADAR-PANC

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
pancreatic cancer, pancreatic ductal adenocarcinoma

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Pancreasresearch UMC Utrecht (I.Q. Molenaar)

Intervention

Keyword: Pancreatic ductal adenocarcinoma recurrence, Postoperative surveillance, Quality of life, Trials within cohorts design

Outcome measures

Primary outcome

The main study endpoint is overall survival after primary resection of PDAC,

designated as the time from the date of surgery until either death from any

cause or last follow-up.

Secondary outcome

The secondary objectives of this study are:

• Quality of Life

• Compliance to a standardized surveillance strategy

• Recurrence-free interval

• Clinical and radiological patterns of PDAC recurrence

• Prognostic factors for PDAC recurrence

• Role of serum tumor marker testing in detecting recurrent PDAC

• Eligibility for additional (experimental) treatment at time of recurrence

diagnosis

• Reasons to abandon treatment for recurrence (i.e. eligibility, deteriorated

condition, patient*s wish, doctors* advice etc.)

• Tolerance of additional treatment for recurrent PDAC

• Morbidity associated with diagnostic testing

• Costs

Study description

Background summary

Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer related mortality in Europe for both men and women. For patients with resectable localized disease, radical resection combined with (neo)adjuvant chemotherapy offers the best chances for long-term survival. However, even after radical resection, almost all patients will experience local and/or distant disease recurrence after sufficient follow-up, mostly within 2 years. Therefore, PDAC continues to be associated with a 5-year survival rate of only 12-27% postoperatively.

Optimal management of recurrent PDAC is less well established as it is for other primary PDAC and exists of either palliative chemotherapy or best supportive care in the Netherlands. The lack of evidence-based effective therapeutic options for the significant group of patients with pancreatic cancer recurrence, in terms of improved quality of life and/or survival, has led to a hesitant attitude towards postoperative recurrence-focused follow-up. In most European countries, including the Netherlands, a standardized approach to follow-up after surgery for PDAC is lacking. Furthermore, current PDAC guidelines regarding follow-up are based on expert opinion and other low-level evidence, and a global controversy about surveillance strategies exists.

According to the current literature, a selected group of patients with recurrent PDAC might benefit from additional therapy. Moreover, the emergence of more potent treatments for PDAC, such as new chemotherapy (e.g. FOLFIRINOX) and stereotactic body radiotherapy (SBRT), has led to a rising interest in diagnosis of recurrent PDAC. Consequently, a standardized surveillance strategy is increasingly recommended. To determine whether early detection of recurrence can lead to improved survival and quality of life, further studies are warranted.

Study objective

The RADAR-PANC trial is designed to investigate whether a standardized surveillance strategy with serial tumor marker testing and routine imaging improves the overall survival in patients after radical resection for

pancreatic ductal adenocarcinoma (PDAC) in the Netherlands, compared to current non-standardized follow-up. Furthermore, the consequences of a standardized surveillance strategy on quality of life and additional (experimental) treatment will be assessed within this study.

We hypothesize that patients in the standardized surveillance arm will be diagnosed with PDAC recurrence at an earlier stage (i.e. localized disease and a good performance status). Consequently, this will lead to a higher number of patients eligible for additional (experimental) treatment for recurrence. The eventual goal of standardized surveillance will therefore be to improve survival.

Study design

The RADAR-PANC is a randomized controlled trial nested within the PACAP and PACOPS-projects according to the Trials within Cohorts (TwiCs) design, in all hospitals affiliated to the Dutch Pancreatic Cancer Group (DPCG) and the UK. The TwiCs design has already gained positive experience within other national cohorts as the Prospective Dutch colorectal cancer cohort (PLCRC, www.plcrc.nl, registered at Clinicaltrials.gov under NCT02070146).

When participating in the PACAP or PACOPS-cohort, patients will be followed and treated according to the current, non-standardized practice. To investigate whether an standardized surveillance strategy improves survival rates, subsequent randomization for follow-up method is performed within a subgroup of eligible patients. This subgroup exists of all PACAP and PACOPS-participants with histologically confirmed macroscopic radical resection (R0-R1) of PDAC. Patients who participate in the PREOPANC-2 trial are excluded as these patients are subjected to a study-specific follow-up. Participants are either randomized for follow-up according to the current, non-standardized practice (50%), or routine surveillance according to our study-protocol (50%). Only patients randomized for the investigational arm are approached for participation; patients randomized for the control arm are not further notified. Study-related follow-up will be at 3, 6, 9, 12, 15, 18, 21 and 24 months postoperatively during the first two years after surgery.

The follow-up scheme of this study is based on current surveillance guidelines after resection for PDAC as recommended by the National Comprehensive Cancer Network (NCCN). For the first two years after surgery, clinical evaluation, serum CA 19-9 testing and contrast-enhanced CT imaging of chest and abdomen is performed three-monthly. In case of suspicious findings on CT without elevated tumor markers, a PET-CT scan can additionally be performed. Also, as part of the Dutch Pancreatic Biobank (PancreasParel), extra blood samples are taken each follow-up visit for further scientific research. Quality of Life is assessed during each follow-up appointment, which is already standardly performed by assessing Patient Reported Outcome measures (PROMs) as a part of the current PACAP and PACOPS-projects of the Dutch Pancreatic Cancer Group

(DPCG) and UK.

In case recurrent disease is detected, *best supportive care* or subsequent palliative therapy and type of additional treatment will be administered at the discretion of the treating clinician in both trial arms, which is the current standard practice. According to the concept of the TwiCs studydesign, however, all participants with disease recurrence in the cohort can be offered to participate in new investigational trials on management of recurrent pancreatic cancer. In the Netherlands, within the DPCG, various radiotherapeutic and/or oncologic intervention studies for recurrent pancreatic cancer are being initiated.

Intervention

For the first two years after surgery, clinical evaluation, serum CA 19-9 testing and contrast-enhanced CT imaging of chest and abdomen is performed three-monthly.

Study burden and risks

No side-effects are expected due to the intervention, as the safety protocol of the department of radiology will be followed. CT-scanning is associated with radiation exposure. However, no harm is expected given the short life-expectancy in our study-population. Furthermore, a standardized follow-up carries the potential for harm in terms of decrease in quality of life, since disease progression is diagnosed in the absence of symptoms and the impact on survival is yet unknown. Also, participants could experience stress regarding their follow-up appointments. We will inform patients who are randomized for a standardized surveillance about these issues thoroughly, using a written patient information form, so that they can make a deliberated choice to participate in the intervention arm. This information will be designed in collaboration with the Dutch pancreatic cancer patients* association Living With Hope. Potential benefits may be the possibility to undergo adjuvant (experimental) treatment, a prolonged survival, better symptom directed clinical detection and management, and patient recruitment to investigational studies for innovative diagnostic and treatment modalities of PDAC.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Histologically confirmed macroscopically radical resected (R0-R1) pancreatic adenocarcinoma
- Age >= 18 years
- Written informed consent for being randomized in future studies

Exclusion criteria

- Exclusion criteria for contrast-enhanced CT scan, following the protocol of the department of radiology in each DPCG affiliated hospital
- Mentally or physically incapable of consent
- Participation in other DPCG studies with a study-specific follow-up

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-03-2021
Enrollment:	240
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	21-01-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-03-2023
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	08-11-2023
Application type:	Amendment
Review commission:	METC NedMec

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	NL67115.041.18