Perioperative versus adjuvant FOLFIRINOX for resectable pancreatic cancer: the PREOPANC-3 study.

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Investigate whether perioperative mFOLFIRINOX improves overall survival compared to adjuvant mFOLFIRINOX in resectable pancreatic cancer.

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

Summary

ID

NL-OMON54274

Source
ToetsingOnline

Brief title
PREOPANC-3

Condition

- Exocrine pancreas conditions
- Gastrointestinal neoplasms malignant and unspecified

Synonym
pancreatic cancer, resectable pancreatic cancer

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: mFOLFIRINOX, Pancreatic cancer, Perioperative treatment, Randomized multicenter phase III clinical trial

Outcome measures

Primary outcome

Primary endpoint is overall survival by intention to treat.

Secondary outcome

To compare between the study arms:

• Progression free survival (PFS)

• Distant metastases free survival

• Locoregional progression free survival

• Distant metastases free interval

• Locoregional progression free interval

• Chemotherapy start rate

• Number of chemotherapy cycles received

• Chemotherapy completion rate

• Dose intensity

• Staging laparoscopy rate

• Laparoscopy yield

• Surgical exploration rate

• Resection rate

• Microscopically margin-negative resection rate

• Lymph node-negative resection rate

• Adverse events

• Postoperative complications

• Quality of life

• Serum CA 19-9 and CEA response

To investigate in arm 1 only:

• Clinical response rate

• Pathologic response

Study description

Background summary

Surgical resection followed by adjuvant FOLFIRINOX (a combination of 5-fluorouracil with leucovorin, irinotecan, and oxaliplatin) is the standard of care for resectable pancreatic cancer in the Netherlands. However, 50% of patients never receive chemotherapy due to postoperative complications, clinical deterioration or early recurrence. Neoadjuvant chemotherapy (i.e. before surgery) can identify patients with rapidly progressing disease who can be spared futile surgery, ensure early treatment of micro-metastases, and improve the microscopically complete resection rate.

Study objective

Investigate whether perioperative mFOLFIRINOX improves overall survival compared to adjuvant mFOLFIRINOX in resectable pancreatic cancer.

Study design

Multicenter randomized phase III superiority trial.

Intervention

Patients in the intervention arm receive 8 cycles of neoadjuvant mFOLFIRINOX followed by surgical resection and 4 cycles of adjuvant mFOLFIRINOX. Patients in the comparator arm undergo surgical resection followed by 12 cycles of adjuvant mFOLFIRINOX.

Study burden and risks

All patients undergo a CT scan of the chest and abdomen for staging and a pathological diagnosis is obtained using endoscopic ultrasonography (EUS) with fine needle aspiration or biopsy (FNA/FNB) or a brush of the bile duct.
Patients in the intervention arm start with 8 cycles of neoadjuvant mFOLFIRINOX followed by curative-intent surgery. Patients who discontinue neoadjuvant chemotherapy because of toxicity proceed to surgery. After successful resection, patients will receive 4 cycles of adjuvant mFOLFIRINOX.
Patients in the comparator arm start with curative-intent surgery. After resection patients receive 12 cycles of adjuvant mFOLFIRINOX.
Evaluation with CT and tumor markers is performed in the intervention arm after 4 and 8 cycles of neoadjuvant treatment and after surgery. In the comparator arm, evaluation with CT and tumor markers is performed after surgery and after 4 and 8 cycles of adjuvant mFOLFIRINOX.
After treatment, patients will go into routine follow-up for 5 years. Follow up includes outpatient clinic visits, CT scans, and blood collection. All patients are asked to complete questionnaires about quality of life during follow-up.
Toxicity of the mFOLFIRINOX regimen is well described, because it is already the standard of care in the metastatic, locally advanced, and adjuvant setting. In two large studies no death was attributed to mFOLFIRINOX.

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

• Histologically or cytologically (Bethesda 5 or 6) confirmed pancreatic ductal adenocarcinoma.
• Resectable tumor according to DPCG criteria: no arterial contact and venous contact with the superior mesenteric vein or portal vein of 90 degrees or less
• No evidence for metastatic disease*
• WHO performance status of 0 or 1
• Ability to undergo surgery and mFOLFIRINOX chemotherapy
• Leucocytes (WBC) >= 3.0 X 109/L
• Platelets >= 100X 109/L
• Hemoglobin >= 6.0 mmol/l
• Renal function: eGFR >= 40 ml/min
• Age >= 18 years
• Written informed consent

* Lesions on chest CT that are too small to characterize are not considered metastatic disease.

Exclusion criteria

• Prior radiotherapy, chemotherapy, or surgery for pancreatic cancer.
• Prior chemotherapy precluding mFOLFIRINOX.
• Previous malignancy (excluding non-melanoma skin cancer, pancreatic neuroendocrine tumor (pNET) <2cm, and gastrointestinal stromal tumor (GIST) <2cm), unless no evidence of disease and diagnosed more than 3 years before diagnosis of pancreatic cancer, or with a life expectancy of more than 5 years from date of inclusion.
• Pregnancy or lactation.
• 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 phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-09-2021
Enrollment:	303
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fluorouracil
Generic name:	5-Fluorouracil
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Irinotecan
Generic name:	Irinotecan-HCL trihydrate
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Leucovorin calcium
Generic name:	Folinic acid
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Oxaliplatin
Generic name:	Oxaliplatin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-01-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	10-09-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-10-2022
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:	10-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	30-05-2023
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
EudraCT	EUCTR2020-005141-16-NL
CCMO	NL75539.078.20