De (kosten)effectiviteit van neoadjuvante FOLFIRINOX versus neoadjuvante chemoradiotherapie met gemcitabine en adjuvante gemcitabine voor patiënten met (borderline) resectabel pancreaskanker - PREOPANC-2 studie

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28312

Source
Nationaal Trial Register

Brief title
PREOPANC-2 trial

Health condition

Resectable pancreatic ductal adenocarcinoma, Borderline resectable pancreatic ductal adenocarcinoma

Sponsors and support

Primary sponsor: Erasmus MC University Medical Center, Department of Surgery
Source(s) of monetary or material Support: KWF Kankerbestrijding, ZonMw

Intervention

Outcome measures

Primary outcome

Overall survival

Secondary outcome

To compare between the study arms:

• Chemotherapy rate

• Chemotherapy completion rate

• Staging laparoscopy rate

• Laparoscopy yield

• Exploratory laparotomy rate

• Resection rate

• R0 resection rate

• Progression free survival (PFS)

• Locoregional failure free interval (LFFI)

• Distant metastases free interval (DMFI)

• Disease free survival (DFS)

• Locoregional recurrence free interval (LRFI)

• Postoperative complications

• Toxicity

• Quality of life years (QALYs)

• Indirect and direct medical and nonmedical costs

• Clinical response rate defined according to RECIST criteria

• Serum Cancer Antigen 19-9 (CA 19.9) and Carcino-Embryonal-Antigen (CEA) response

• Pathologic response

Study description

Background summary

Pancreatic cancer has a dismal prognosis. In 2030, pancreatic cancer is expected to be the second leading cause of cancer death. (Rahib et al., Cancer Res 2014;74:2913-21) Upfront resection with adjuvant gemcitabine has long been the standard of care for patients with (borderline) resectable pancreatic cancer in the Netherlands as stated in the Dutch national guideline. However, multiple studies have shown a benefit of neoadjuvant Gemcitabine based chemoradiotherapy treatment, both in overall survival, progression free survival and R0-resection rates. (Versteijne et al., Br J Surg. 2018 Jul;105(8):946-958; Jang et al., Ann Surg. 2018 Feb 16; van Tienhoven et al., ASCO 2018).

Since FOLFIRINOX (a combination of 5-fluorouracil, irinotecan, oxaliplatin, and leucovorin) is a more potent chemotherapy compared to Gemcitabine, this treatment may further improve survival. Moreover, it is already the standard of care in patients with locally advanced and metastatic pancreatic cancer. A patient-level meta-analysis of FOLFIRINOX for patients with (borderline) resectable pancreatic cancer found a median overall survival of 24 months. (Janssen et al., in preparation)

This randomized phase III trial will investigate whether neoadjuvant chemotherapy with FOLFIRINOX (a combination of 5-fluorouracil, irinotecan, oxaliplatin, and leucovorin) improves overall survival compared to neoadjuvant gemcitabine based chemoradiotherapy with adjuvant gemcitabine in patients with (borderline) resectable pancreatic ductal adenocarcinoma.

A total of 252 events (deaths) are need to assess a difference of seven months in overall survival (from 17 months to 24 months).

Study objective

To investigate whether neoadjuvant chemotherapy with FOLFIRINOX (a combination of 5-fluorouracil, irinotecan, oxaliplatin, and leucovorin) improves overall survival compared to neoadjuvant gemcitabine based chemoradiotherapy with adjuvant gemcitabine in patients with (borderline) resectable pancreatic ductal adenocarcinoma.

Study design

Final analysis will take place 1.5 years after full inclusion.

Intervention

Two arm, randomized trial for patients with resectable or borderline resectable pancreatic cancer.

- Standard arm: Neoadjuvant Gemcitabine based chemoradiotherapy followed by an evaluation with a CT-scan and tumor markers. If the tumor remains (borderline) resectable, patients will undergo explorative surgery, if possible resulting in pylorus preserving or classical pancreaticoduodenectomy. If patient is recovered within 12 weeks after surgery, this is followed by the remainder of adjuvant Gemcitabine chemotherapy.

Preoperative treatment (experimental arm) is Gemcitabine 1000 mg/m2 day 1,8, one week rest. Then Gemcitabine 1000 mg/m2 day 1,8,15, concomitant with radiotherapy: 36 Gy, 15 fractions of 2.4 Gy. Then Gemcitabine 1000 mg/m2 day 1,8 one week rest.
After surgery (standard arm) four (remaining) courses of Gemcitabine 1000 mg/m2 day 1,8,15, one week rest.

- Experimental arm:

4 cycles of chemotherapy with FOLFIRINOX, followed by an evaluation CT scan. In case of no disease progression after 4 cycles, the patient will receive an additional 4 cycles of FOLFIRINOX.
After completion of all neoadjuvant treatment evaluation with a CT-scan and tumor markers will be performed. If the tumor remains (borderline) resectable, patients will undergo explorative surgery, if possible resulting in pylorus preserving or classical pancreaticoduodenectomy. No adjuvant treatment will be given.

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Eligibility criteria

Inclusion criteria

• Histologically or cytologically confirmed pancreatic cancer (i.e. pancreatic ductal adenocarcinoma)

• (Borderline) resectable tumor without metastatic disease* (DPCG definitions of resectability)

• WHO performance status 0 or 1

• Ability to undergo surgery, chemoradiotherapy, and chemotherapy**

• Leucocytes (WBC) ≥ 3.0 X 109/l

• Platelets ≥ 100X 109 /l

• Hemoglobin ≥ 6 mmol/l

• Renal function: E-GFR > 50 ml/min

• Age ≥ 18 years

• Written informed consent

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

** In some patients this may require assessment by both a surgical and medical oncologist and radiotherapist prior to study inclusion.

Exclusion criteria

• Prior radiotherapy, chemotherapy, or resection for pancreatic cancer.

• Prior radiotherapy or chemotherapy precluding chemoradiotherapy or FOLFIRINOX.

• 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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2018
Enrollment:	368
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	19-06-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55463
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7094
NTR-old	NTR7292
CCMO	NL61961.078.17
OMON	NL-OMON55463

Study results