Voorbehandeling met bestraling en chemotherapie gevolgd door operatie versus alleen operatie voor operatief verwijderbare of mogelijk verwijderbare alvleesklierkanker. Een gerandomiseerd fase III onderzoek.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22251

Source
Nationaal Trial Register

Brief title
PREOPANC

Health condition

resectable pancreatic carcinoma or borderline resectable pancreatic carcinoma

resectabel of borderline resectabel pancreascarcinoom.

Sponsors and support

Primary sponsor: Academic Medical Center
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Source(s) of monetary or material Support: KWF Nederlandse KankerBestrijding
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Intervention

Outcome measures

Primary outcome

Overall survival.

Secondary outcome

To compare between the study arms:

1. The resection rate;

2. The microscopically complete (R0) resection rate;

3. The disease free survival;

4. The time to locoregional failure;

5. The time to distant metastases;

6. The postoperative complications and morbidity.

To assess in the experimental arm:

1. The radiological response rates after preoperative radiochemotherapy (RECIST criteria);

2. The pathological response rates after preoperative radiochemotherapy;

3. The toxicity of preoperative radiochemotherapy according to Common Terminology Criteria for Adverse Events 4 (CTC-AE 4).

Study description

Background summary

Pancreatic cancer has a dismal prognosis. Pancreaticoduodenectomy may offer cure but only a small percentage of patients can undergo a resection, and also in this cohort the survival is poor. Adjuvant chemotherapy offers a modest survival improvement [Oettle 2008]. From multiple single arm phase two studies and a SEER database observational study, there is a suggestion that preoperative radiochemotherapy may offer an improvement by increasing the resection rate, increasing the R0 resection rate hence improving overall survival in borderline resectable and resectable pancreatic cancer [Stessin 2008, Gillen 2010, van Tienhoven 2011]. A major difficulty in the interpretation of the literature is that most studies are single arm studies, with a selected group of patients that only report on the subset of patients actually undergoing a resection. This hampers comparison of study results and disables proper analysis of a potential increase in resection rate. The only way to evaluate the role of preoperative radiochemotherapy concerning resection rate, R0 resection rate and thus overall survival is to perform a randomized study, analyzing the results by intent to treat [van Laethem 2011].

To investigate whether preoperative radiochemotherapy can indeed improve overall survival in resectable and borderline resectable pancreatic cancer, the Dutch Pancreatic Cancer Group initiates a prospective randomized phase III study: PREOPANC.

In the experimental arm, biliary drainage and laparoscopy to rule out small metastases should be performed before the start of radiochemotherapy. A well tested radiochemotherapy schedule, based on three courses of full dose gemcitabine chemotherapy, was adopted [Talamonti 2006, Small 2008,2011].

A total of 244 patients (176 events) are needed to assess a difference of six months in median survival by intent to treat (from 11-17 months).

Study objective

To investigate whether the addition of preoperative radiochemotherapy to the standard treatment, consisting of explorative laparotomy, pancreaticoduodenectomy if possible, followed by adjuvant chemotherapy, improves the overall survival (analyzed by intent to treat) of patients with resectable or borderline resectable pancreatic cancer.

Study design

Final analysis will take place one year after full inclusion.

Intervention

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

cancer.

Standard arm: Explorative surgery, if possible resulting in pylorus preserving or classical pancreaticoduodenectomy, followed by standard adjuvant chemotherapy.

Standard adjuvant chemotherapy is Gemcitabine 1000 mg/m2 day 1,8 and 15, one week rest, for six courses.

Experimental arm: Preoperative chemoradiotherapy followed by explorative surgery, if possible resulting in pylorus preserving or classical pancreaticoduodenectomy, followed by the remainder of adjuvant 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 (experimental arm) four (remaining) courses of Gemcitabine 1000 mg/m2 day 1,8,15, one week rest. This is to make sure that the total amount of Gemcitabine gifts is barely different in the experimental arm compared to the standard arm.

In the experimental arm, pretreatment evaluation including laparoscopy is necessary, as well as treatment of eventual jaundice. Also post radiochemotherapy evaluation needs to be performed.

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Eligibility criteria

Inclusion criteria

1. Histologically or cytologically confirmed adenocarcinoma of the pancreas;

2. Primarily resectable tumours or Borderline resectable tumours (see table 1, p7 and hereunder) (exception, T1 centrally located tumours with no vascular involvement at all);

3. WHO performance status ≤ 1;

4. Ability to undergo surgery and radiochemotherapy;

5. Leucocytes ≥ 3.5 X 109/l;

6. Platelets ≥ 100X 109 /l;

7. Haemoglobin ≥ 6 mmol/l;

8. Renal function: E-GFR > 50 ml/min;

9. Age ≥ 18 years;

10. Written informed consent;

11. Patients with reproductive potential must use effective contraception.

Exclusion criteria

1. T1 resectable tumours, centrally located with no connection to the SMA, Celiac axis, CHA or SMV/PV;

2. Clearly locally advanced, irresectable, tumours (see table 1, p7 and hereabove);

3. Carcinoma of the Papilla Vateri;

4. Co morbidity precluding surgery or radiochemotherapy;

5. Previous radiotherapy or chemotherapy precluding radiochemotherapy;

6. Distant metastases, including cytologically proven N2 lymph node metastases (base of the celiac trunk or between inferior vena cava and aorta);

7. Pregnancy;

8. Imminent bowel obstruction;

9. Active bleeding;

10. Uncontrolled infection;

11. Anamnestically known positive status for HIV or hepatitis B or C.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2013
Enrollment:	244
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL3525
NTR-old	NTR3709
Other	EUDRACT / KWF datamanagement subsidie : 2010-019225-33 / UVA2012-5696
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
Van Tienhoven G, Gouma, DJ, Richel DJ. Neoadjuvant chemoradiotherapy has a potential role in pancreatic carcinoma Therapeutic Advances in Medical Oncology, 2011;3:27-33