

# NEOPA: Sequential NEOadjuvant chemoradiotherapy (CRT) followed by curative surgery vs. primary surgery alone for resectable, non-metastasized Pancreatic Adenocarcinoma

<b>Submission date</b> 02/01/2014	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 11/02/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 20/05/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

We are carrying out a study in people with pancreatic cancer in the head of the pancreas in which the tumour can be surgically removed. This study is comparing an intervention consisting of a preoperative combined chemoradiotherapy (CRT) and surgery with surgery alone without pre-treatment.

Our goal is to prove the effectiveness of the combined pre-treatment and surgery over surgery alone. The results of the study have the potential to considerably change the treatment regimen of patients with pancreatic cancer and help improve their treatment.

### Who can participate?

Men and women over 17 years of age diagnosed with pancreatic cancer.

### What does the study involve?

Patients are randomly allocated to either receive chemoradiotherapy (CRT) followed by surgical resection or receive surgery alone without any treatment before the surgery. Patients allocated to undergo CRT will receive Gemcitabine for 6 weeks combined with radiotherapy followed by surgical resection. Patients allocated to the reference group undergo primary surgery in curative intent. Irrespective of whether or not CRT has been performed, all patients undergo adjuvant chemotherapy, preferentially with Gemcitabine.

### What are the possible benefits and risks of participating?

All patients will receive an established treatment for pancreatic cancer in the head of the pancreas. Expected effects of the chemoradiotherapy treatment before surgery are a prolongation of 3-year survival and time to tumour recurrence, a higher rate of complete surgical resection and fewer postoperative complications. Potential risks of the CRT are a reduction of white blood cell count, which reduces the immune defence, resulting in infections,

and reduction of red blood cells and blood platelets. Other side effects are nausea, vomiting, diarrhoea, flu symptoms, respiratory problems, liver function disorders, allergic reactions and dysfunction of the kidneys.

Where is the study run from?

The organizing trial centre is the Department of General, Visceral and Thoracic Surgery at the University Hospital Hamburg, Eppendorf, Germany. Over 15 study centres across Germany are participating.

When is the study starting and how long is it expected to run for?

The study started in January 2014 and will run for a minimum of 6 years (3 years recruiting, 3 years follow-up).

Who is funding the study?

The study is funded by the Bundesministerium für Bildung und Forschung der Bundesrepublik Deutschland (Federal Ministry of Education and Research of the Federal Republic of Germany).

Who is the main contact?

Prof. Dr Jakob R. Izbicki  
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## Contact information

### Type(s)

Scientific

### Contact name

Prof Jakob R. Izbicki

### Contact details

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## Additional identifiers

### EudraCT/CTIS number

2012-003669-17

### IRAS number

### ClinicalTrials.gov number

NCT01900327

### Secondary identifying numbers

N/A

# Study information

## Scientific Title

Sequential NEOadjuvant chemoradiotherapy (CRT) followed by curative surgery vs. primary surgery alone for resectable, non-metastasized Pancreatic Adenocarcinoma: NEOPA- a randomized multicenter phase III study

## Acronym

NEOPA

## Study objectives

Efficacy of neoadjuvant CRT in improving 3-year survival probability from 30% in the control arm undergoing upfront surgery without neoadjuvant CRT to 42% (relative increase of 40%) in the study arm undergoing CRT. The underlying guess of a 30% 3-year survival probability in the control group derives from an assumed median overall survival (MOS) of 20.7 months which corresponds with a MOS of 17.9 months to 23.6 months reported in several randomized trials.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

Ethics Committee, Medical Association of Hamburg (Ethik-Kommission der Ärztekammer Hamburg), 17/12/2013, ref: PVN4472

## Study design

Randomized multicenter phase III study

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## Health condition(s) or problem(s) studied

Biopsy-proven, non-metastasized, adenocarcinoma of the pancreatic head/uncinate process larger than 2 cm in size ( $\geq$ cT2) and/or in close contact with the mesenterico-portal axis and superior mesenteric artery (SMA) (less than 3 mm).

## Interventions

Group 1: Experimental intervention: Neoadjuvant CRT with weekly Gemcitabine 300 mg/m<sup>2</sup> for 6 weeks combined with external beam radiotherapy (EBRT) delivering a total dose of 50.4 Gy over 28 days in 1.8 Gy fractions will be followed by classical or pylorus-preserving partial pancreateoduodenectomy (PD) and adjuvant chemotherapy (CTx), preferentially using Gemcitabine (1000 mg/m<sup>2</sup>, six cycles at day 1, 8, 15 of each 28-day cycle).

Group 2: Control intervention: Upfront PD followed by adjuvant CTx, preferentially with Gemcitabine (1000 mg/m<sup>2</sup>, six cycles at day 1, 8, 15 of each 28-day cycle).

Follow-up per patient: 36 to 72 months, depending on day of recruitment.

Duration of intervention per patient: 5 weeks CRT preceding surgery, which is scheduled 3 to 6 weeks after completion of CRT.

### **Intervention Type**

Other

### **Phase**

Not Applicable

### **Primary outcome measure**

Survival time (3-year survival)

### **Secondary outcome measures**

1. Histology-proven R0 resection rate based on a standardized histopathological handling of the surgical specimen.
2. Frequency of moderate and severe toxicity events and drop-out rate due to therapy-related toxicity (NCI Common Toxicity Criteria v2.0)
3. Resectability rate (Note: includes both R0 and R1 resection status)
4. Rate of unexpected intraoperative irregularities, operative time, blood transfusion requirement, postoperative morbidity rate, especially that of pancreatic fistula, and mortality rate
5. Rate of patients with severe postoperative complications (postop. recovery > 8 weeks) rendering adjuvant treatment worthless
6. Disease progression during neoadjuvant therapy
7. Quality of life analysis before neoadjuvant, before and 3, 6, 9, 12, 15, 18, 24, 30 and 36 months after surgery (EORTC QLQ C30 questionnaire)
8. Median disease-free survival (DFS, local and distant), overall survival (OS)
9. First site of tumor recurrence

### **Overall study start date**

17/01/2014

### **Completion date**

16/01/2020

## **Eligibility**

### **Key inclusion criteria**

1. Male and female, age 18 years and older
2. Histology-proven, resectable adenocarcinoma of the pancreatic head/uncinate process with a

tumor size greater than 2 cm ( $\geq$ cT2) and/or close contact to the superior mesenteric vessels ( $\leq$ 3 mm in preoperative staging).

3. No evidence of metastasis to distant organs (liver, peritoneum, lung, others).

4. Serum creatinine level  $\leq$  3.0 mg/dl

5. Serum total bilirubin level  $\leq$  3.0 mg/dl in the absence of biliary obstruction. In the event of biliary obstruction, patients allocated to the CRT group must undergo interventional endoscopy or percutaneous drainage for biliary decompression. Post-interventionally, bilirubin levels should be  $\leq$  3.0 mg/dl before patients are subjected to CRT. In control patients undergoing upfront surgery, serum total bilirubin levels  $\leq$  10.0 mg/dl are tolerated, unless there are clinical and laboratory signs of severe cholangitis. Patients with serum total bilirubin level  $>$  10.0 mg/dl undergo preoperative biliary decompression, preferentially by interventional endoscopy)

6. White blood cell count  $\geq$   $3.5 \times 10^9$ /ml, platelet count  $\geq$   $100 \times 10^9$ /ml

7. Ability to understand and willingness to consent to formal requirements for study participation

8. Written informed consent

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

410

### **Key exclusion criteria**

1. Age  $\leq$  18 years

2. Recurrent disease

3. Infiltration of extrapancreatic organs (except duodenum and transverse colon)

4. Persistent cholestasis/cholangitis despite adequate biliary stenting

5. Gastric outlet obstruction, especially in the event of endoscopically evidenced tumor invasion into the gastroduodenal mucosa.

6. Tumor-specific pre-treatment

7. History of gastrointestinal perforation, e.g. perforated colonic diverticulitis, abdominal abscess or intestinal fistula within 6 months prior to potential study participation

8. Radiographic evidence of severe portal hypertension/cavernomatous transformation that may, at the discretion of the participating investigators, hamper surgery

9. Other concurrent malignancies except for basal cell cancer of the skin and in-situ cervical cancer, premalignant hematologic disorders, e.g. myelodysplastic syndrome

10. Severe organ dysfunctions (e.g., liver cirrhosis  $\geq$  Child B; Cardio-pulmonary diseases (NYHA  $\geq$  III, arrhythmia Lown III/IV, global respiratory insufficiency); ascites; acute pancreatitis; bleeding diathesis, coagulopathy, need for full-dose anticoagulation or INR  $>$  1.5; other severe diseases that might prevent completion of the treatment regimen)

11. Chronic infectious diseases, especially immune deficiency syndromes, e.g. HIV infection, active tuberculosis within 12 months prior to potential study participation

12. History of severe neurologic disorders, e.g. cerebrovascular ischemia
13. History of prior deep venous thrombosis or pulmonary embolism
14. Pregnant or nursing women are ineligible and patients of reproductive potential must agree to use an effective contraceptive method during participation in this trial and for 6 months following the trial
15. Serious medical, psychological, familial, sociological or geographical conditions or circumstances potentially hampering compliance with the study protocol and follow-up
16. Participation in other clinical trials during the last 6 months before allocation to trial

**Date of first enrolment**

17/01/2014

**Date of final enrolment**

16/01/2020

## **Locations**

**Countries of recruitment**

Germany

**Study participating centre**

Martinistr. 52

Hamburg

Germany

20246

## **Sponsor information**

**Organisation**

University Hospital Hamburg-Eppendorf (Germany)

**Sponsor details**

Martinistr. 52

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info@uke.de

**Sponsor type**

Hospital/treatment centre

**ROR**

<https://ror.org/01zgy1s35>

# Funder(s)

## Funder type

Government

## Funder Name

Bundesministerium für Bildung und Forschung der Bundesrepublik Deutschland (Federal Ministry of Education and Research of the Federal Republic of Germany (Germany) ref: 01KG1208

# Results and Publications

## Publication and dissemination plan

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

Not provided at time of registration

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	07/06/2014	09/08/2019	Yes	No
<a href="#">Basic results</a>		25/04/2021	20/05/2022	No	No