

# Comparison of three different therapies (radio-, chemo- and immunotherapy) in patients with resected pancreatic adenocarcinoma

<b>Submission date</b> 29/04/2008	<b>Recruitment status</b> Stopped	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 22/05/2008	<b>Overall study status</b> Stopped	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 05/04/2011	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**  
2008-000121-19

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

N/A

## Study information

### Scientific Title

A randomised multicentre phase II trial comparing adjuvant therapy in patients with resected pancreatic adenocarcinoma treated with interferon alpha-2b and 5-fluorouracil (5-FU) alone or in combination with either external radiation treatment and cisplatin (CapRI) or radiation alone regarding event-free survival

### Acronym

CapRI II

### Study objectives

Only 10 - 20% of patients with pancreatic cancer can be resected with curative intent at the time of diagnosis. Unfortunately, loco-regional recurrence and/or metastatic disease develop in the majority of patients who undergo pancreatic resection. Most patients typically relapse within 9 - 15 months from initial presentation and have median life expectancies of only 12 - 15 months without adjuvant therapy. The 5-year survival of patients with resected pancreatic adenocarcinoma is approximately 10% for patients without adjuvant therapy.

In this clinical trial a de-escalation of CapRI-regime (cisplatin, 5-fluorouracil, interferon alpha-2b [INTRON A®] and external beam radiation) is investigated. We hypothesise that removal of cisplatin and radiotherapy will have no significant effect or only a minor impact on the clinical response but result in lower toxicity.

Please note that this is a follow-up study to a previously registered trial (see ISRCTN62866759 - <http://www.controlled-trials.com/ISRCTN62866759>).

Please also note that as of 02/10/2008 the initial inclusion and exclusion criteria of this trial were updated with the approval of the national competent authority. All changes to this trial record can be found in the relevant field under the above update date. Please also note that this update resulted in a change of the anticipated start and end dates of this trial. The initial anticipated start and end dates were as following:

Initial anticipated start date: 01/01/2009

Initial anticipated end date: 01/03/2012

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Ethics approval received from the Ethics Board of the Medical Faculty at the University of Heidelberg on the 16th May 2008 (ref: Afmu-071/2008; EudraCT no.: 2008-000121-19).

### Study design

A controlled, open, prospective, randomised, multicentre trial

### 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**

Resected pancreatic adenocarcinoma

### **Interventions**

The clinical trial CapRI II is subdivided into three different interventional study arms:

1. Arm A: cisplatin, 5-fluorouracil, INTRON A® and external beam radiation (CapRI)
2. Arm B: 5-fluorouracil, INTRON A® and external beam radiation (CapRI light)
3. Arm C: 5-fluorouracil and INTRON A® (CapRI ultra light)

In all arms, patients will be treated for 23 weeks. All patients will be treated with 5-fluorouracil and INTRON A®. Patients randomised to arms A or B will additionally receive external beam radiation; patients in arm A receive additional cisplatin.

Dosage, frequency:

1. First cycle of 5-FU: 200 mg/m<sup>2</sup>/day by continuous intravenous infusion days 1 - 38
2. Second and third cycle 5-FU: 200/mg/m<sup>2</sup>/day by continuous intravenous infusion days 64 - 101 and 120 - 161
3. Interferon alpha-2b: 3 million units subcutaneously on Monday, Wednesday and Friday (SQ MWF) days 1 - 38 (17 total doses) plus one injection prior to treatment start given during week -1 (approx. day -6)
4. Cisplatin (arm A): 30 mg/m<sup>2</sup> (capped at body surface area [BSA] = 2 m<sup>2</sup>; maximum single cisplatin dose of 60 mg) intravenously (IV) over 60 minutes on days 1, 8, 15, 22, 29, 36 (6 doses). Two to three hours before and after cisplatin dose the patients will receive hydration of at least 2 litres. Patients will be taught to drink at least 1 litre during the day.
5. Radiotherapy (arm A and B): the pancreatic bed will be covered with a minimum margin of 2 cm. The porta hepatis, origins of the celiac axis and superior mesenteric artery will be included. The anteroposterior/posteroanterior (AP/PA) fields must include the entire duodenal C-loop as seen on pre-operative computed tomography (CT) scan. Total dose will be 50.4 Gy in 28 fractions over 5.5 weeks (1.8 Gy/day). The dose contribution from the lateral fields should be restricted to 20 Gy.

Total duration of follow-up for all treatment arms:

The duration of the trial for each patient is expected to be 6 months. The duration of the overall trial is expected to be approximately 3 years. Recruitment of patients will start in I/2009. The actual overall duration or recruitment may vary. Patients will be tracked by quarterly phone follow-up for recurrence and/or death.

### **Intervention Type**

Drug

## **Phase**

Phase II

## **Drug/device/biological/vaccine name(s)**

Cisplatin, 5-fluorouracil, interferon alpha-2b [INTRON A®], external beam radiation

## **Primary outcome measure**

Primary objective is the comparison of the treatment groups with respect to event-free survival.

Primary endpoint:

Event-free survival (EFS) - EFS is defined as time from resection to objective tumour recurrence, grade 3 or grade 4 toxicity (according to Common Toxicity Criteria version three [CTC 3.0]), or death (whichever occurs first).

## **Secondary outcome measures**

Secondary objectives are comparison of the treatment groups with respect to safety, overall survival (OS), recurrence-free survival (RFS), quality of life (QoL) and an accompanying immunomonitoring to screen for predictive marker and to analyse the mode of action of IFN-alpha.

Secondary endpoints:

1. Overall survival (OS), defined both as time from randomisation and resection to death
2. Recurrence-free survival (RFS) defined both as time from randomisation and resection or death from any cause (whichever occurs first)

Time from resection to OS/RFS is important for comparability with other randomised controlled trials (RCTs) for adjuvant treatment of pancreatic carcinoma

3. Quality of life (QoL): European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for Cancer patients (EORTC QLQ-C30) and EORTC Quality of Life Questionnaire for Pancreatic cancer (QLQ PAN26)

4. Immunological parameters: the translational research will be based on the immunological parameters (vascular endothelial growth factor [VEGF], basic fibroblast growth factor [bFGF], interleukin-2 [IL-2], interferon-alpha [IFN-alpha], tumour necrotising factor [TNF-alpha], interleukin-12 [IL-12], soluble MHC class I chain related molecules [sMIC], inactivated C3b complement [iC3b], etc.). For each parameter, several (longitudinal) measurements will be available. Apart from the parameter values themselves, further parameters will be generated, such as differences, or relative differences, of values after versus before administration of IFN-alpha, or binary variables obtained by applying threshold values.

## **Overall study start date**

01/10/2008

## **Completion date**

01/04/2012

## **Reason abandoned (if study stopped)**

Objectives no longer viable

## **Eligibility**

### **Key inclusion criteria**

As of 02/10/2008, point two of the initial inclusion criteria has been amended as follows:

2. Adequate laboratory parameters:

2.1. Bone marrow, liver and kidney function

2.2. Haemoglobin (Hb) greater than 8.0 g/dl, white blood cell count (WBC) greater than 3,000 cells/mm<sup>3</sup>, platelets greater than 75,000 cells/mm<sup>3</sup>

2.3. Alanine aminotransferase (ALT)/aspartate aminotransferase (AST) less than or equal to 1.5 mg/dL

2.4. Calculated or measured creatinine clearance (CrCl) of greater than or equal to 60 ml/min

All other points have remained the same.

Initial criteria at time of registration:

Patients meeting all of the following criteria will be considered for admission to the trial:

1. R0/R1 resected pancreatic ductal adenocarcinoma

2. Adequate laboratory parameters:

2.1. Bone marrow, liver and kidney function

2.2. Haemoglobin [Hb] greater than 8.0 g/%, white blood cell count [WBC] greater than 3,000 cells/mm<sup>3</sup>, platelets greater than 75,000 cells/mm<sup>3</sup>

2.3. Alanine aminotransferase [ALT]/aspartate aminotransferase [AST] less than or equal to 2 x upper limit of normal [ULN]

2.4. Creatinine less than or equal to 1.5 mg/dL and calculated or measured creatinine clearance (CrCl) of greater than or equal to 60 ml/min

3. Therapy starts within eight weeks after surgery

4. Ability of patient to understand character and individual consequences of clinical trial

5. Written informed consent must be available before enrolment in the trial

6. For women with childbearing potential, adequate contraception

7. Age greater than or equal to 18 years, either sex

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

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

135

### **Key exclusion criteria**

As of 02/10/2008, point five of the initial exclusion criteria has been amended as follows:

5. Patients with severe heart diseases (New York Heart Association [NYHA] stadium three and four) or severe lung disease (chronic obstructive pulmonary disease [COPD] Grade III, Asthma bronchiale Grade IV)

At this time, the following exclusion criteria were also added:

10. General condition worse than Eastern Cooperative Oncology Group (ECOG) grade 2

11. Any contraindication met for any investigational product

12. Serious uncontrolled acute infections at the time of therapy initiation or patients with known HIV infection, other immunodeficiencies or autoimmune diseases

Initial criteria at time of registration:

Patients presenting with any of the following criteria will not be included in the trial:

1. Metastatic disease
2. Previous chemo- or radiotherapy for pancreatic carcinoma
3. Previous radiotherapy in the corresponding region
4. Patients with known severe depression
5. Patients with severe heart or lung disease
6. Pregnancy and lactation
7. History of hypersensitivity to the investigational product or to any drug with similar chemical structure or to any excipient present in the pharmaceutical form of the investigational product
8. Patients with mental diseases (International Classification of Diseases version 10 [ICD-10] code F30, F31, F32.2 ff. or F33.2 ff.)
9. Participation in other clinical trials and observation period of competing trials, respectively

No patient will be allowed to enrol in this trial more than once.

**Date of first enrolment**

01/10/2008

**Date of final enrolment**

01/04/2012

## **Locations**

**Countries of recruitment**

Germany

**Study participating centre**

**Universitätsklinikum Heidelberg**

Heidelberg

Germany

69120

## **Sponsor information**

**Organisation**

University of Heidelberg (Germany)

**Sponsor details**

Im Neuenheimer Feld 672

Heidelberg

Germany

69120

**Sponsor type**

University/education

**Website**

<http://www.uni-heidelberg.de>

**ROR**

<https://ror.org/038t36y30>

**Funder(s)****Funder type**

University/education

**Funder Name**

Individual funder - Dr. Wild (Germany)

**Results and Publications****Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration