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

Submission date 29/04/2008	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 22/05/2008	**Overall study status** Stopped	
Last Edited 05/04/2011	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr Moritz Wente

Contact details
Universitätsklinikum Heidelberg
Abteilung für Allgemeine, Viszerale und Transplantationschirurgie
Im Neuenheimer Feld 110
Heidelberg
Germany
69120
Moritz.wente@med.uni-heidelberg.de

Additional identifiers

Clinical Trials Information System (CTIS)
2008-000121-19

Protocol serial number
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

Study type(s)
Treatment

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^2/day by continuous intravenous infusion days 1 - 38
2. Second and third cycle 5-FU: 200/mg/m^2/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^2 (capped at body surface area [BSA] = 2 m^2; 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(s)
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).

Key secondary outcome(s))
Secondary objectives are comparison of the treatment groups with respect to safety, overall survival (OS), reccurence-free survival (RFS), quality of life (QoL) and an accompanying immuno-monitoring 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 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.

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^3, platelets greater than 75,000 cells/mm^3
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. Haemogoblin [Hb] greater than 8.0 g/%, white blood cell count [WBC] greater than 3,000 cells/mm^3, platelets greater than 75,000 cells/mm^3
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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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)

ROR
https://ror.org/038t36y30

Funder(s)

Funder type
University/education

Funder Name
Individual funder - Dr. Wild (Germany)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration