CROSSFIRE Trial: Comparing the Efficacy of Irreversible Electroporation With Radiotherapy

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22388

Source
Nationaal Trial Register

Brief title
CROSSFIRE trial

Health condition

Pancreatic cancer

Sponsors and support

Primary sponsor: VU University Medical Center, Amsterdam
Source(s) of monetary or material Support: Adessium Foundation
VU University Medical Center
Angiodynamics

Intervention

Outcome measures

Primary outcome

The primary outcome of the study is efficacy in terms of overall survival.

Secondary outcome

Secondary outcomes are progression free survival, safety/toxicity, immunomodulation, tumor marker CA-19.9, quality of life, and total direct and indirect costs for each treatment arm (cost-effectiveness analysis).

Study description

Background summary

Pancreatic cancer has the highest mortality rate of all major cancers; 94% of pancreatic cancer patients will die within five years of diagnosis, 74% within the first year of diagnosis; only 6% will survive for more than five years. Surgical resection is the only curative option. However, about 40% present with non-metastatic locally advanced pancreatic carcinoma (LAPC; AJCC stage III). These patients are not eligible for surgical resection because the tumor involves major blood vessels such as the superior mesenteric artery, celiac axis, common hepatic artery and/or portal vein. These patients are currently treated with palliative chemotherapy as first line therapy. Focal therapy using external beam radiation therapy (EBRT) may further improve survival, but outcome remains poor. Stereotactic ablative radiotherapy (SABR) is a form of EBRT that has important advantages over conventional radiotherapy such as a more precise and greater biological dose delivery and hence less toxicity and presumably better outcome.

For patients diagnosed with LAPC, a combination of chemotherapy plus local tumor destruction using irreversible electroporation (IRE), a novel tumor ablation technique, has recently shown great promise. IRE is based on permeabilization of the cell membrane through electrical pulses leading to apoptosis. Theoretically, IRE only affects viable tumor tissue, leaving surrounding vital structures relatively intact. It is therefore considered to cause less morbidity than thermal ablative strategies.

The CROSSFIRE-trial is a prospective, randomized controlled phase-II/III trial.The primary aim of this study is to compare the efficacy of chemotherapy and IRE (experimental arm) to the efficacy of chemotherapy and radiation (control arm) in patients with locally advanced, non-resectable, non-metastasized, pancreatic cancer.

In total, 138 patients with histologically proven locally advanced pancreatic adenocarcinoma (AJCC stage III), aged ≥ 18 years will be included. Patients with a specific cardiac history (arrhythmias, pacemaker), pre-existent ECG-abnormalities and/or non-retrievable metallic self-expanding biliary stents are excluded from participation. Patients will be randomly allocated to receive either chemotherapy and radiation (control arm) or chemotherapy and IRE (experimental arm).

Study objective

For patients diagnosed with non-metastatic locally advanced pancreatic cancer, a combination of chemotherapy (FOLFIRINOX) plus local tumor destruction using stereotactic ablative radiotherapy (SABR) or irreversible electroporation (IRE), will result in a prolonged overall survival.

Study design

The follow-up period will be till the date of death from any cause.

Intervention

IRE is based on permeabilization of the cell membrane through electrical pulses leading to apoptosis. Theoretically, IRE only affects viable tumor tissue, leaving surrounding vital structures relatively intact. It is therefore considered to cause less morbidity than thermal ablative strategies.

Stereotactic ablative radiotherapy (SABR) is a form of external beam radiation that has important advantages over conventional radiotherapy such as a more precise and greater biological dose delivery and hence less toxicity and presumably better outcome.

Contacts

Public
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Eligibility criteria

Inclusion criteria

Inclusion Criteria:

- Radiologic confirmation of LAPC by at least ceCT of chest and abdomen (with the upper abdomen scanned according to a dedicated 3mm slice multiphase pancreatic tumor

protocol);

- Maximum tumor diameter ≤ 5 cm;

- Histological or cytological confirmation of pancreatic adenocarcinoma;

- Age > 18 years;

- ASA-classification 0 – 3; World Health Organisation scale (WHO) performance status 0 – 1 ;

- Adequate bile drainage in case of biliary obstruction;

- Written informed consent;

Exclusion criteria

Exclusion Criteria:

- Resectable pancreatic adenocarcinoma as discussed by our multidisciplinary hepatobiliary team;

- The presence of suspect lymph nodes

- Stage IV pancreatic carcinoma;

- Trans-mucosal tumor invasion into surrounding duodenum or stomach;

- History of epilepsy;

- History of cardiac disease:

o Congestive heart failure >NYHA class 2;

o Active Coronary Artery Disease (defined as myocardial infarction within 6 months prior to screening);

o Ventricular cardiac arrhythmias requiring anti-arrhythmic therapy or pacemaker (beta blockers for antihypertensive regimen are permitted; atrial fibrillation is not contra-indicated);

- Uncontrolled hypertension. Blood pressure must be ≤160/95 mmHg at the time of screening on a stable antihypertensive regimen;

- Compromised liver function (e.g. signs of portal hypertension, INR > 1,5 without use of anticoagulants, ascites);

- Uncontrolled infections (> grade 2 NCI-CTC version 3.0);

- Pregnant or breast-feeding subjects. Women of childbearing potential must have a negative pregnancy test performed within 7 days of the start of treatment;

- Immunotherapy prior to the procedure;

- Radiotherapy prior to study enrollment;

- Previous surgical therapy for pancreatic cancer;

- Second primary malignancy, except adequately treated non-melanoma skin cancer, in situ carcinoma of the cervis uteri or other malignancies treated at least 5 years previously without signs of recurrence;

- Allergic to contrast agent.

- Any implanted stimulation device;

- Any condition that is unstable or that could jeopardize the safety of the subject and their compliance in the study;

- Non-removable Self Expanding Metal biliary Stent (SEMS), which cannot be removed during surgery.

- Contra-indications for MRI since no safety data for 0.35 Tesla MRI scanners are available on electronic devices such as pacemakers or implanted defibrillators, deep brain stimulators, cochlear implants, this constitutes an absolute contraindication for this study, even for devices that have been considered safe for MRI scans with higher field strengths.

o Patients who have a metallic foreign body in their eye, or who have an aneurysm clip in their brain, cannot have an MRI scan since the magnetic field may dislodge the metal

o Patients with severe claustrophobia may not be able to tolerate an MRI scan

o Patients with a hip prosthesis will not be eligible for the MRI scan

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-04-2016
Enrollment:	138
Type:	Anticipated

Ethics review

Positive opinion

Date:	27-05-2016
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 50215
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL5722
NTR-old	NTR5875
CCMO	NL55158.029.15
OMON	NL-OMON50215

Study results