Efficacy and feasibility of the combination of everolimus and capecitabine in patients with metastatic or locally advanced pancreatic carcinoma

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The primary objective of this study is to determine the efficacy and feasibility of the combination of everolimus and capecitabine in a group of patients with metastatic or locally advanced pancreatic cancer.

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON31280

Source
ToetsingOnline

Brief title
everolimus and capecitabine in pancreatic cancer

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
pancraetic carcinoma, pancreatic cancer

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: mTOR inhibition, pancreatic cancer

Outcome measures

Primary outcome

The primary endpoint of this study will be six-month survival rate.

Secondary outcome

As secondary endpoints are defined:

- Objective complete and partial response rate

- Time to treatment failure

- Overall survival

- One year survival rate

- Toxicity profile

Study description

Background summary

Pancreatic cancer accounts for only 3% of all malignancies in the western world, but is one of the leading causes of cancer-related mortality. Over the past 30 years many chemotherapeutic drugs have been evaluated as treatment for patients with pancreatic cancer, but tumour control with the current available systemic chemotherapy is disappointing. At present, gemcitabine is widely accepted as the standard chemotherapy for patients with pancreatic cancer, with a modest objective response rate of 11%, but a substantial impact on clinical benefit rate. Despite this advantage, there is need for a different approach to attack this highly aggressive and resistant form of cancer resulting in a prolonged survival of patients with inoperable/ metastatic pancreatic cancer.

The phosphatidylinositol 3*-kinase (PI3K)/Akt pathway is important for cell growth and survival and is often dysregulated in cancer. Akt is activated downstream of PI3K and can activate several effector proteins, including

mammalian target of rapamycin (mTOR). Dysregulation of mTOR signaling occurs in a wide variety of human tumours, including pancreatic cancer. Thus, mTOR might therefore be a promising objective of novel molecular targeting therapy for pancreatic cancer. Indeed, a couple of pre-clinical studies with mTOR inhibitors demonstrated promising results and adding chemotherapy improved the efficacy even more. However, a recently published phase I study demonstrated unacceptable toxicity of the combination everolimus and gemcitabine. Therefore, in our study we have chose to add capecitabine, a chemotherapeutic drug with the same objective response activity in patients with metastatic pancreatic cancere, to the mTOR inhibitor.

Study objective

The primary objective of this study is to determine the efficacy and feasibility of the combination of everolimus and capecitabine in a group of patients with metastatic or locally advanced pancreatic cancer.

Study design

Everolimus seems the most attractive mTOR inhibitor because of the favourable pharmacokinetic profile and possibility of oral administration. Everolimus will be administrated daily at a dose of 9 mg, devided into 2 doses. Capecitabine is an orally administered fluoropirimidine. The dose will be 1000 mg/m2 twice daily for 2 weeks, with one week rest period.

Intervention

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Study burden and risks

Each cycle contains 3 weeks, in which the patients take everolimus daily and capecitabine the first 2 weeks. At day 1 of every cycle the patient will come to the hospital for blood investigations and evaluation of the toxicity profile. After 3 cycles (9 weeks) during the treatment fase a CTscan will be performed to establish response.
The expected adverse events of everolimus are nausea, vomiting, rash, fatigue, anorexia, hyperlipidemia, hyperglycaemia, diarrhoea, elevation of transaminases, headache and stomatitis. During the first 2 weeks of the study patients will be treated with everolimus alone, to monitor everolimus induced toxicity. In case of grade 3 or 4 toxicity patients will be excluded from the trial and there will be no further treatment with everolimus.
The most common reported side effects of capecitabine are: diarrhoea, nausea and vomiting, stomatitis, anorexia, hand-foot syndrome, fatigue, elevated

bilirubine levels and bone marrow suppression.
If the combination of everolimus and capecitabine will result in increased adverse evnets is unknown and will be investigated in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Signed informed content obtained prior to treatment
- Cytological or histological confirmed adenocarcinoma of the pancreas
- Metastatic or non-resectable disease
- Measurable lesion according to RECIST criteria
- ECOG/ WHO performance 0-2
- Age > 18 years
- Life expectancy > 3 months

- Adequate renal function (creatinine < 150 µmol/L)
- Adequate liver function (bilirubin < 1.5 times upper limit of normal, ALAT or ASAT < 5.0 times upper limit of normal in case of liver metastases and < 2.5 the upper limit of normal in absence of liver metastases
- Adequate bone marrow function (WBC > 3.0 x 10 9/L, platelets > 100 x 10 9/L)
- Mentally, physically, and geographically able to undergo treatment and follow up

Exclusion criteria

- Clinical or radiological evidence of CNS metastases
- Pregnancy (positive serum pregnancy test) and lactation
- Serious concomitant systemic disorder that would compromise the safety of the patient, at the discretion of the investigator

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2007
Enrollment:	33
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	certican
Generic name:	everolimus
Registration:	Yes - NL outside intended use

Product type:	Medicine
Brand name:	xeloda
Generic name:	capecitabine
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2007-000857-74-NL
CCMO	NL16639.018.07