A randomised phase II study of radio-chemotherapy with or without panitumumab (Vectibix®) in irresectable squamous cell carcinoma or adenocarcinoma of the oesophagus (Panoramic)

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Primary Objective: Description of the 1-year overall survival after chemo-radiation therapy with or without panitumumab in irresectable carcinoma of the oesophagus. The control arm is used to validate whether the historical cohort used for...

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

Summary

ID

NL-OMON34246

Source
ToetsingOnline

Brief title
PANORAMIC

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
cancer of oesophagus

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,AMGEN BV

Intervention

Keyword: chemoradiotherapy, irresectable, oesophagus cancer, panitumumab

Outcome measures

Primary outcome

1-year overall survival

Secondary outcome

* toxicity

* progressie-free-survival and respons rate

* 1-years overall survival in KRAS-wt patients

* pharmacodynamics (PD) of panitumumab (EGFR, K-RAS, B-RAF, downstream

signalling pathways) compared between the biopsy at baseline (standard) and

the biopsy one week after start chemo-radiation therapy

* Quantification of baseline FDG uptake (SUV) with PET, and SUV changes (ΔSUV)

(in 35 patienten per arm)

baseline

7 days after the first panitumumab dose or for start

chemo-radiation therapy.

during treatment with chemoradiation therapy after

three weeks.

2-4 weeks after finishing treatment.

10-12 weeks after finishing treatment

* Correlation PET results with respons rate and PD of panitumumab

* CTCs and CECs at baseline, after 2 weeks during chemo-radiation therapy and

12 weeks after finishing treatment.

Study description

Background summary

A complete response rate of approximately 30% is achieved for standard treatment of irresectable carcinoma of the oesophagus, consisting of concurrent chemoradiation therapy (50.5 Gy + cisplatin/5-FU). Attempts to improve outcome by intensifying conventional cytotoxic drugs or increasing the radiation dose have not been successful. Future improvements will likely require the incorporation of targeted agents that probably will not add significant toxicity, the use of molecular predictors of response and early identification of responders. In both squamous cell carcinoma and adenocarcinoma of the oesophagus expression of EGFR is correlated with poor outcome. Furthermore the addition of cetuximab, a chimaeric EGFR antibody, to radiation therapy in head and neck cancer and non-small cell lung cancer showed a gain in overall survival. In head and neck cancer studies with the addition of panitumumab to chemo-radiation therapy are currently ongoing. Therefore, we propose to perform a randomised phase II study of chemo-radiation therapy with or without the combination of panitumumab (human EGFR antibody) in irresectable squamous cell carcinoma or adenocarcinoma of the oesophagus without distant metastases.

Study objective

Primary Objective:
Description of the 1-year overall survival after chemo-radiation therapy with or without panitumumab in irresectable carcinoma of the oesophagus. The control arm is used to validate whether the historical cohort used for comparison is similar to our success-rate.

Secondary Objective:
Determination of toxicity, quantification of biological markers of response (pharmacodynamics of panitumumab), response monitoring by quantitative FDG positron emission tomography and quantification of circulating tumour and endothelial cells.

Study design

Randomised Controlled Phase II study

Intervention

Experimental arm (arm A): Chemo-radiation therapy (50.4 Gy/1.8 Gy per fraction + i.v. cisplatin 75 mg/m2 (day 1) and i.v. 5-FU 1000 mg/m2 (day 1-4) in treatment week 1 and 5) combined with i.v. panitumumab 9 mg/kg (day -7 , day 15 and day 36).
Control arm (arm B): Chemo-radiation therapy (50.4 Gy/1.8 Gy per fraction + i.v. cisplatin 75 mg/m2 (day 1) and i.v. 5-FU 1000 mg/m2 (day 1-4) in treatment week 1 and 5) without panitumumab

Study burden and risks

Possibility of more side-effects because of addition of panitumumab
Small risk of complications of second biopsy

Contacts

Public
Universitair Medisch Centrum Sint Radboud

postbus 9101
6500 HB Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

postbus 9101
6500 HB Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Age 18 - 70 years
-Histologically proven SCC or adenocarcinoma of the oesophagus
-No proven (distant) metastases (ultrasonography, CT or MRI)
-No prior treatment for carcinoma of the oesophagus
-Karnofsky performance status >=70% (appendix A)
-Irresectable disease as assessed by the multidisciplinary tumour board
-All patients (male and female) must use effective contraception methods according to CPMP/ICH/286/95 if of reproductive potential (e.g. implants, injectables, combined oral contraceptives, IUDs, sexual abstinence or vasectomised partner), for the whole duration of the study and until six months after they received the last treatment dose
-No contraindications for cytotoxic therapy or panitumumab:
-No known hypersensitivity/allergy to any of the compounds used
-Haematology:
*Neutrophil count >= 1.5*109 /L
*Thrombocyte count >= 100*109 /L
*Haemoglobin >= 6.2 mmol/L (100 g/L)
-No known HIV infection or other condition of persistent immunodeficiency
-Renal function:
*Creatinine clearance (MDRD) >= 60 mL/min
-Hepatic function:
*Total bilirubin <= 1.5*ULN
*AST, ALT, AP <= 2.5*ULN
-Electrolyte balance:
*(albumin corrected) calcium <= 2.87 mmol/L (=11.5 mg/dl) but >= lower limit of normal (LLN)
*Magnesium >= LLN
-History of interstitial lung disease e.g. pneumonitis or pulmonary fibrosis or evidence of interstitial lung disease on baseline chest CT scan.
-No known other serious illness or medical condition present at entry in the study including:
* Unstable cardiac disease despite treatment, congestive heart failure NYHA grade 3 and 4
* Clinically significantly abnormal electrocardiogram (ECG) or left ventricular ejection fraction (LVEF) below the institutional ULN
* Clinically significant cardiovascular disease (including myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) <= 1 year before enrolment/randomisation
-Significant neurologic or psychiatric disorders
-Active uncontrolled infection
-Active disseminated intravasal coagulation
-Symptomatic peripheral neuropathy (CTCAE v3.0 term *neuropathy: sensory*) >= grade 2
-Ototoxicity (CTCAE v3.0 any term in *auditory/ear*) >= grade 2 except if due to trauma or

mechanical impairment due to tumour mass
-Other serious underlying medical condition which could impair the ability of the patient to participate in the study
-No or insufficient oral nutrient intake
-No prior exposure to EGFR pathway targeting agents
-No known drug abuse
-Absence of any psychological, familial, sociological (e.g. severe alcohol addiction expected to hamper protocol compliance) or geographical condition potentially hampering compliance with the study protocol and follow-up schedule; those conditions should be discussed with the patient before registration in the trial
-No participation in another interventional clinical trial in the preceding 30 days
-Written informed consent to participate to study must be given according to ICH/GCP, and national/local regulations.

Exclusion criteria

-Prior treatment for this tumour
-Prior treatment with radiation therapy in the area of the oesophagus or other site that will interfere with proposed treatment
-Subject pregnant or breast feeding, or planning to become pregnant within 6 months after the end of treatment.
-Subject (male or female) is not willing to use highly effective methods of contraception (per institutional standard) during treatment and for 6 months (male or female) after the end of treatment.
-History of other prior malignancy in past 5 years, other than basal cell carcinoma, squamous cell carcinoma of the skin, or cervical carcinoma in situ;Exclusion criteria for the PET-scan
-Severe claustrophobia
-Diabetes mellitus (type I and II)
-Serum glucose level >11 mmol/L

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Enrollment:	124
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	5-FU
Generic name:	5-fluorouracil
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vectibix
Generic name:	panitumumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	21-04-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-10-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2010-019595-79-NL
CCMO	NL32031.091.10