Phase I trial evaluating combined radiotherapy with Panitumumab (Vectibix®) in patients with muscle invasive transitional cell carcinoma of the bladder

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This study is a phase I trial. Primary objective is to evaluate the safety of combined radiotherapy with Panitumumab in bladder preservation in invasive bladder cancer. Secondary objectives are to investigate the efficacy of combined radiotherapy...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bladder and bladder neck disorders (excl calculi)
Study type	Interventional

Summary

ID

NL-OMON34833

Source
ToetsingOnline

Brief title
Bladder preservation with Panitumumab and radiotherapy

Condition

- Bladder and bladder neck disorders (excl calculi)

Synonym
bladder cancer, Bladder carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Amgen,donatie vanuit de industrie

Intervention

Keyword: Bladder carinoma, Panitumumab, preservation, radiotherapy

Outcome measures

Primary outcome

Acute Toxicity rate during radiotherapy with Panitumumab treatment (defined in

protocol section 4.4)

Secondary outcome

Secondary endpoints

Complete response rate at 3 months

Local control rate at 6, 12, and 18 months, and at 2 years

Bladder preservation rate

Any grade 3 or 4 adverse event during and within one month after completion

of therapy

Exploratory endpoints

% EGFR expression

RAS mutational status

Response rate in correlation with EGFR and RAS status

Response rate in relation to treatment path

Study description

Background summary

There is renewed interest to explore new organ preserving strategies for invasive bladder cancer. Our goal is to develop an effective treatment strategy for bladder preservation combing radiotherapy with EGFR targeting after induction chemotherapy. This new bladder preserving strategy should eventually be tested against cystectomy in a randomized Phase III trial.
Although radiotherapy is an effective bladder preserving treatment modality for invasive bladder cancer, the results leave substantial room for improvement. Several studies have evaluated the efficacy of radiotherapy in combination with chemotherapy. However, current chemo-radiation schedules are quite toxic and approximately 1/3 of the patients need a salvage cystectomy as a result of insufficient response to the treatment. Therefore, new, more effective, approaches to combined modality treatments of bladder cancer are needed.
As EGFR status seems to be linked to the response to radiotherapy, its inhibition might enhance the radio-responsiveness of bladder tumors. The first fully human monoclonal antibody directed against the EGFR receptor Panitumumab has a high affinity for the EGFR receptor and is characterized by a low incidence of dose-limiting toxicity. Therefore, the combination of radiotherapy with Panitumumab is attractive to explore. The purpose of this study is to evaluate the efficacy and safety of radiotherapy with Panitumumab in bladder cancer treatment.

Study objective

This study is a phase I trial. Primary objective is to evaluate the safety of combined radiotherapy with Panitumumab in bladder preservation in invasive bladder cancer. Secondary objectives are to investigate the efficacy of combined radiotherapy with Panitumumab in bladder preservation in invasive bladder cancer.

Study design

Phase I

Intervention

Patients with a T1 to a T4a bladder carcinoma might be eligible for this study (see protocol section 4.5). Baseline investigations, prior to treatment, will include history, concomitant drug use, blood analysis, cystoscopy (resections or biopsies are optional), EGFR and RAS status and a CT of thorax and abdomen. Patients with N0 disease will have a lymph node dissection (pN0-1 allowed) followed by 2-4 courses of platinum based chemotherapy, while N1-2 patients

will be treated with 2-4 courses of platinum based chemotherapy followed by a lymph node dissection (pN0-1 allowed). During chemotherapy treatment patients will visit their physician at least prior to every course of treatment where history and concomitant drug use will be taken and blood analysis will be performed.
After completion of chemotherapeutic treatment and lymph node dissection, and prior to concomitant radiotherapy and Panitumumab treatment, a CT of thorax and abdomen will be made and a cystoscopy will be performed Within four weeks after completion of chemotherapy or lymph node dissection (N+ disease), radiotherapeutic treatment in combination with Panitumumab treatment will start. A six-week course of radiotherapy with curative intent will be administered to the patients (30-33 fractions of 2 Gy). Panitumumab treatment will be initiated one week before radiotherapy and administered every 2 weeks during radiotherapy to a total of four courses of 6 mg/kg. Visits during combined radiotherapy/Panitumumab treatment will be every two weeks with recording history, concomitant drug use and acute toxicity and blood analysis. After completion of treatment follow-up will start with visits every three months with a total of two years. During follow-up visits history, drug use and toxicity will be recorded and blood analysis will be performed. At 6, 12 , 18 and 24 months after completion of treatment a CT of the pelvis will be made, while a cystoscopy (resections or biopsies are optional) will be performed every three months.

Study burden and risks

It is not clear if this treatment is save and efficient. One expects that this stduy will give a good indication after which one can start a larger trail.

There is always a chance that the patient suffers from adverse events of the chemotherapy, radiation and/or Panitumumab.

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 written informed consent.
Histologically confirmed bladder carcinoma stage (including previous treatment):
T2 N0 M0, refusing surgery and not eligible for brachytherapy
T3-4a N0 M0
T1-4a pN1 M0: with no evidence of lymphnode disease as assessed by CT-scan and pN1 before neoadjuvant chemotherapy as assessed by lymphadenectomy. CR or PR following neoadjuvant chemotherapy as assessed by CT-scan.
T1-4a N1-2 M0 with evidence of lymphnode disease prior to chemotherapy as assessed by CT scan and pN0-1 after neoadjuvant chemotherapy as assessed by lymphadenectomy.
Karnofsky performance of * 70 prior to chemotherapy and prior to combined Panitumumab/radiotherapy treatment.
Hematopoietic function: Neutrophils >= 1.5 x 109/L, platelets >= 100 x 109/L, leucocytes> 3,000/mm3 and hemoglobin >= 9 g/dL.
Hepatic function: Total bilirubin <= 1.5 times the upper normal limit (UNL), ASAT <= 2.5 x UNL and
ALAT <= 2.5 x UNL.
Renal function: Creatinin clearance >= 50 mL/min (calculated clearance).
Metabolic function: Magnesium >= lower limit of normal and Calcium >= lower limit of normal.
Adequate follow-up possibilities for at least two years.

Exclusion criteria

Evidence of M+ (all patients will undergo a pelvic lymphadenectomy prior to chemoradiation).

Prior chemotherapy or radiotherapy to the pelvis.
Prior treatment with anti EGFr and/or anti VEGF treatment.
Previous malignancy except skin carcinoma (basal cell and squamous cell carcinoma).
Candidate for brachytherapy.
No adequate bladder function (functional capacity < 100 cc, frequency > 1/h).
Clinically significant cardiovascular disease (including myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) * 1 year before
enrollment/randomization.
History of interstitial lung disease e.g. pneumonitis or pulmonary fibrosis or evidence of interstitial lung disease on baseline chest CT scan.
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.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2011
Enrollment:	31
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Vectibix
Generic name:	Panitumumab

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-06-2010
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	23-12-2010
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	16-05-2013
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	12-06-2014
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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	EUCTR2009-018246-38-NL
CCMO	NL31148.031.10