PROSPECTIVE FASE-II TRIAL EVALUATING THE OUTCOME OF INDUCTION CHEMOTHERAPY FOLLOWED BY EXTENDED LYMPH NODE DISSECTION AND CHEMORADIATION FOR HIGH RISK INVASIVE BLADDER CANCER

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- To evaluate the bladder-preservation rate after chemoradiation - To evaluate the toxicity and complications of treatment with induction chemotherapy followed by ePLND and chemoradiation

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON43780

Source
ToetsingOnline

Brief title
CHEMORAD-TRIAL

Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Bladder and bladder neck disorders (excl calculi)
- Renal and urinary tract therapeutic procedures

Synonym
'bladder cancer' and 'high-risk muscle invasive bladder cancer'

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W,Er wordt een subsidie aanvraag ingediend bij KWF

Intervention

Keyword: Bladder Cancer, Bladderpreservation, Chemoradiation

Outcome measures

Primary outcome

-To evaluate the bladder-preservation rate after chemoradiation

-To evaluate the recurrence of disease after 12 months followup, following

chemoradiation

Secondary outcome

- Recurrence rates (local and distant)

- Toxicity rates following induction chemotherapy

- Complication rates following ePLND

- Toxicity rates following chemoradiation

- Quality of Life (EuroQol EQ-5D-3L; SF-12)

- Disease specific survival

- Recurrence free survival

- Genetic biomarkers

Study description

Background summary

Systemic treatment with cisplatin-based combination chemotherapy has been shown to improve the outcome of patients presenting with locally advanced muscle-invasive bladder cancer and patients with lymph node positive disease, albeit at best an absolute 6.5% increase in overall survival at 5-years follow-up. Aims of the present study are: to evaluate the bladder preservation rate after chemoradiation, and furthermore assessment of the toxicity and complications of induction cisplatin-based combination chemotherapy followed by pelvic lymph node dissection (ePLND) and chemoradiation.

Study objective

- To evaluate the bladder-preservation rate after chemoradiation
- To evaluate the toxicity and complications of treatment with induction chemotherapy followed by ePLND and chemoradiation

Study design

Prospective single arm, multicenter fase-II trial

Intervention

After initial staging and informed consent, patients will receive induction chemotherapy followed by ePLND and chemoradiation.

Induction chemotherapy consists primarily of a cisplatin-based regimen, being either high dose intensity MVAC or gemcitabine with cisplatin (Gem/Cis). In case of severe toxicity the schedule may be adjusted to a regimen containing gemcitabine with carboplatin.

Extended pelvic lymph node dissection (ePLND) consists of removal of all pathological lymph nodes together with standard PLND consisting of the removal of all nodes in the region between: the genito-femoral nerve, the obturator fossa, along the internal iliac artery and along the common iliac artery up to the crossing of the ureter or the bifurcation of the aorta. In supraregional spread, also a full RPLND is done. Generally, surgery will be performed within 4-6 weeks after the final course of chemotherapy.

The chemoradiation will start 2-6 weeks following ePLND. There is a wide spread in treatment techniques and availabilities of different techniques among the different institutions. Each institution is free to choose their own treatment technique and margins, but has to define beforehand which technique and margins will be used. The use of adaptive radiotherapy is strongly encouraged but not mandatory.
In case of a solitary bladder tumor on cystoscopy, the patients will be treated with radiotherapy to a dose of 45 Gy to the bladder and 60 Gy to the Gross Tumour volume (GTV), both in 25 fractions. In case of multiple bladder tumors

(>= 2) the whole bladder will be treated to a dose of 60 Gy (whole bladder irradiation).

Patients will receive concomitant chemotherapy during the radiotherapy treatment. Capecitabine 750 mg/m2 twice daily on weekdays and Mitomycine (12 mg/m2 intravenous bolus dose on day 1).

Study burden and risks

The complication-risks of the current 'standard-therapy' consisting of neoadjuvant chemotherapy followed by total cystectomy with urinary diversion are considerable (35-50%). The current study-protocol will offer patients the possibility of bladderpreservation and potentially a decreased complication-risk.

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

All patients with locally advanced (T3-4) and/or node positive bladder cancer (>=N1), who are fit to receive cisplatin-based combination chemotherapy and who are eligible for surgery, may be included in this study. ;Inclusion criteria:
- Signed written informed consent
- Locally advanced urothelial carcinoma of the bladder (cT3-T4) or any cT-stage with cytologically or histologically proven node positive urothelial carcinoma (or positive FDG/PET-CT-scan with suspect lymph nodes, including supraregional retroperitoneal lymph nodes below the diaphragm.
- Renal function: Creatinin clearance >= 50 mL/min (calculated) and serum creatinin <=1.5 x UNL.
- In case of hydronefrosis: relative function of the hydronefrotic kidney should be at least 30%.
- Karnofsky performance >=70

Exclusion criteria

Exclusion criteria:
-Distant metastases (M+)
-Severe bladder symptoms (necessitating cystectomy).
-Bilateral hydronefrosis.
-Persisting hydronephrosis after induction chemotherapy (necessitating cystectomy). A temporary nefrostomy is indicated during chemotherapy.
-Previous radiation therapy on pelvic region

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2015
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	25-09-2015
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Approved WMO Date:	25-03-2016
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
CCMO	NL51464.031.15