REduce BlAdder CAncer REcurrence in patients treated for upper urinary tract urothelial carcinoma (REBACARE Trial)

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

Summary

ID

NL-OMON50424

Source
ToetsingOnline

Brief title
REBACARE TRIAL

Condition

- Renal and urinary tract neoplasms malignant and unspecified
- Ureteric disorders

Synonym
urothelial cancer of the upper urinary tract, Urothelial carcinoma of the upper urinary tract

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: - Preoperative intravesical instillation Mitomycin., - Reduction bladder cancer recurrence., - Upper urinary tract urothelial carcinoma.

Outcome measures

Primary outcome

The primary end point is the bladder recurrence rate (histologically proven urothelial carcinoma) at two years after surgery for an UUT urothelial carcinoma.

Secondary outcome

1) To show a >80% compliance rate and accurate and consistent protocol performance of treating physicians.

2) The overall, cancer-specific, and recurrence-free survival at two years after surgery.

3) The toxicity of the regimen at three months (CTCAE version 4.0).

4) The quality of life of the subjects will be assessed at inclusion (T0, before surgery and neo-adjuvant treatment), at two weeks (T2) and three months (T3) after surgery. The EQ5D-5L and the EORTC QLQ-C30 will be used.

5) Costs from a societal perspective using a time horizon of two years. The costs consist of direct costs (e.g., personnel costs of health professionals involved, disorder related medication, disorder related innervations, time duration of hospital, informal care) and indirect costs (productivity loss) associated with each regimen.

6) Incremental cost-effectiveness ratios. The economic evaluation will be a cost-utility analysis and a cost-effectiveness analysis performed from a

societal perspective.

7) At inclusion, patients will be asked to provide consent on the use of their tumor tissue for molecular analysis. Whole genome sequencing will be performed to investigate tumor-specific somatic mutations and copy number variations to compare the molecular profile of the primary UUT tumor and subsequent bladder tumor.

Study description

Background summary

Following radical nephro-ureterectomy for an upper urinary tract (UUT) urothelial carcinoma, the reported recurrence rate of a urothelial carcinoma in the bladder is 22-47%. A meta-analysis showed that a single intravesical instillation of chemotherapy <10 days after nephro-ureterectomy decreased the risk of a bladder recurrence by 52%; the absolute risk reduction was 13%; no serious adverse events were observed. Despite level I evidence, a recent Dutch survey showed that <10% of treating physicians actually administers an intravesical instillation of chemotherapy following nephro-ureterectomy. This reluctance is due to the fact that a fresh wound is present in the bladder after nephro-ureterectomy, so there is a potential risk of extravasation of chemotherapy. Extravasation of chemotherapy outside the bladder can lead to life-threatening complications for the patient. Therefore, we propose a study of administering a single intravesical instillation of chemotherapy immediately (<3 hours) before surgery. This will circumvent the risk of extravasation of chemotherapy making this approach clinically more applicable, which will improve the compliance of treating physicians.

Study objective

Primary, to show that a single intravesical instillation of chemotherapy immediately before radical surgery for an upper urinary tract (UUT) urothelial carcinoma leads to a 40% reduction in the risk of a subsequent bladder recurrence (urothelial carcinoma) up to two years after surgery compared with historical controls who received no perioperative intravesical instillation. Secondly, to show a >80% compliance rate and accurate and consistent protocol performance of treating physicians. Thirdly, to assess the overall, cancer-specific, and recurrence-free survival, systematic toxicities, the quality of life, and the costs of an intravesical instillation with Mitomycin

compared with no perioperative instillation.

Study design

Multicenter, prospective cohort study in a clinical setting.

Intervention

A single intravesical instillation of Mitomycin within three hours before surgery.

Study burden and risks

Participants will receive a single intravesical instillation of Mitomycin within three hours before surgery. All participants will complete two questionnaires (EQ5D-5L and EORTC QLQ-C30) at three different time points. Investigations during follow-up include cystoscopy and CT-urography, which is in line with the standardized care and will not include additional investigations.

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

- Patients with histologically proven urothelial carcinoma of the UUT with or without concurrent carcinoma in situ (CIS only is also allowed) or patients with a suspicion of a urothelial carcinoma of the UUT on CTscan with or without a urinary cytology sample suspicious of the presence of high-grade urothelial carcinoma. In case urinary cytology shows no abnormality and no diagnostic URS is done, conclusive results of the CT-urography are sufficient for inclusion and the coordinating
investigator will evaluate the eligibility of the subject in consultation with the local investigator.
- Patients treated either by partial ureterectomy or by a radical nephro-ureterectomy (open or laparoscopic) including a bladder cuff.
- Age >= 18 years.
- WHO performance status 0,1, or 2.
- Negative pregnancy test in women with childbearing potential.
- Written informed consent.

Exclusion criteria

- If pre-operative histology obtained by biopsy: aberrant histology of the UUT tumor of >50% (adenocarcinoma, small cell carcinoma, squamous cell carcinoma).
- Postoperative pathological report shows absence of tumor (pT0) or >50% of the UUT tumor shows aberrant histology.
- History or presence of a malignant tumor or carcinoma in situ of the bladder.
- History of UUT urothelial carcinoma on the contralateral side or presence of bilateral UUT urothelial carcinoma.
- Known allergy against Mitomycin.
- Anticipated adjuvant intravesical treatment with chemo- or immunotherapy.
- Anticipated adjuvant intravesical treatment with chemo- or immunotherapy following a diagnostic URS.
- Acute urinary tract infection at the time of inclusion as assessed by urinary culturing.
- Lymphadenopathy or distant metastases as assessed by preoperative CT-scan of thorax and abdomen.
- Any other concurrent severe or uncontrolled disease preventing the safe

administration of intravesical Mitomycin.
- Breastfeeding women.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-11-2017
Enrollment:	190
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Mitomycin
Generic name:	Mytomicin
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	12-04-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	16-06-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-08-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-09-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-10-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-11-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-01-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-01-2018

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-11-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	17-01-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-02-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	06-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 24959
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-000949-53-NL
CCMO	NL60919.078.17
Other	NL6361 (NTR6545)
OMON	NL-OMON24959