Treatment of High Grade Non-Muscle Invasive Urothelial Carcinoma of the Bladder by Standard Number and Dose of Intravesical BCG Instillations Versus Reduced Number of Intravesical Instillations with Standard Dose of BCG. A European Association of Urology Research Foundation Randomised Phase III Clinical Trial

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON19940

Bron
NTR

Verkorte titel
NIMBUS

Aandoening

Non-Muscle Invasive Urothelial Carcinoma of the Bladder.
Niet spierinvasief urothelial carcinoma van de blaas

Ondersteuning

Primaire sponsor: EAU Research Foundation
Arnhem, the Netherlands
Overige ondersteuning: EAU Research Foundation
National Grants: Deutsche Krebshilfe

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Time to first recurrence

Toelichting onderzoek

Achtergrond van het onderzoek

A total of 824 patients with high grade Ta-T1 urothelial carcinoma of the bladder with or without CIS and who did not receive any BCG intravesical instillation therapy are to be recruited from urology departments in European hospitals participating in this study.

The primary objective of this study is to identify if reduced number of BCG instillations are not inferior to standard number and dose intravesical BCG treatment in patients with high grade NMIBC. The primary endpoint for inferiority analysis is time to first recurrence.
The secondary objectives are to identify if number and grade of recurrent tumors, rate of progression to a higher stage (T2 or higher) of the disease and safety, specifically the presence of treatment related toxicity > grade 2 differ between the two study arms.

Doel van het onderzoek

Intravesical instillation of BCG is a widely accepted strategy to prevent recurrence of non muscle invasive bladder cancer. The most accepted treatment schedule is induction of BCG: weeks 1 through 6 plus maintenance (weeks 1,2,3) at months 3,6 and 12, but it is unknown how many administrations are really necessary.
Scientific evidence prones to the hypothesis that after an initial sensitization to BCG antigens has occurred the number of instillations can be reduced for a proper anamnestic immune response resulting in similar clinical efficacy and potentially less side-effects and costs.

Onderzoeksopzet

The timing of measurement of the outcomes are variable and will be done each time a

patient comes into the clinic for A) control of the disease or B) for the instillation of adjuvant BCG treatment (See INTERVENTIONS).

When the patient comes for the instillation of adjuvant BCG treatment, the incidence and severity of side effects will be measured or registered. Also during subsequent follow up visits, side effects that have not resolved will be measured or registered.

When the patient comes for control of the disease which is cystoscopy and cytology and the investigator suspects a recurrent bladder cancer, the patient will be scheduled for transurethral resection of the suspect lesion. If the suspect lesion is pathologically confirmed bladder cancer, the time of first recurrence, number and grade of recurrent tumors and progression to a higher stage can be determined.

Onderzoeksproduct en/of interventie

This is a multicentre prospective, randomized, parallel group, not blinded, trial to compare the efficacy and safety of two different adjuvant treatment schedules:

1) Induction cycle BCG-full dose; weeks 1 through 6 plus maintenance cycles at months 3, 6 and 12 (wks 1,2,3); total 15 full dose BCG instillations;

2) Induction cycle BCG-full dose (reduced frequency); weeks 1,2, and 6 plus maintenance cycles at months 3, 6 and 12 (wks 1,3); total 9 full dose BCG instillations.
BCG intravesical instillation therapy is registered as adjuvant treatment for the prevention of recurrence of NMIBC and can be considered as standard treatment for the type of patients requested in this trial. For each individual centre, one of the three locally available BCG strains in Europe will be used: BCG Tice, BCG Medac or BCG Connaught. After the first transurethral resection (TUR), patient undergoes re-TUR at weeks 4-6 after initial resection. Treatment with the randomised treatment schedule will start 2 weeks after and no later than 6 weeks after the last resection. The first maintenance therapy should be given 3 months after the last instillation of the induction BCG cycle (week 6) and hereafter at months 6 and 12 after the last instillation of the induction BCG cycle. Standard Dose Instillations will take place with 1 vial of BCG.

Follow up cystoscopy and cytology will be done every 3 months the first 2 years; bi-annually until the fifth year and yearly thereafter.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Presence of high grade (Ta-T1) urothelial carcinoma of the bladder with or without CIS

1.a. Tumors can be primary or recurrent;

1.b. Tumors can be single or multiple.

2a. In case of a Ta high grade tumor in the initial resection, a re-TUR can be performed at the discretion of the investigator. Initial resection or re-TUR must include the deep resection or cold cup biopsy (deep enough to obtain muscle tissue) of the (initial) tumor site(s)

2b. In case of a T1 high grade tumor in the initial resection, a re-TUR should be performed at weeks 4-8 after initial resection, which must include the deep resection or cold cup biopsy (deep enough to obtain muscle tissue) of the initial tumor site(s)

3. Re-re-TUR should be performed at weeks 4-8 after re-TUR in case of histological detection of T1 low/high grade tumor in the re-TUR, which must include the deep resection or cold cup biopsy (deep enough to obtain muscle tissue) of the initial tumor site(s)

4. Histopathologically confirmed absence of T1 low/high grade tumor(s) in the re-TUR specimen and/or re-re-TUR specimen

5. All visible papillary tumors must be completely resected

6. If the patient is male, he must use a condom during sexual intercourse during the first week after BCG treatment. If the patient is female, and of childbearing potential, she must practice adequate contraception for 30 days prior to administration of study treatment, have a negative pregnancy test and continue such precautions during all study treatment period and for 3 months after the last BCG treatment.

7. Patient is clinically fit enough to receive BCG bladder instillations.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Any previous intravesical BCG therapy

2. Presence of primary CIS only

3. Presence of histopathologically proven muscle invasive urothelial carcinoma of the bladder at first or (re-)re-TUR surgical specimens

4. Presence of any tumors in upper urinary tract or in the prostatic urethra at any time

5. Presence of any other histological type of resected tumor other than urothelial carcinoma on the first or second resection

6. Presence of another malignancy in the 5 years before randomisation except for basal cell carcinoma of the skin or localised prostate cancer in active surveillance

7. Presence of pregnancy or lactation

8. Presence of active tuberculosis, any form of immunodeficiency (eg HIV + serology, transplant recipients) and/or any other contraindication of BCG therapy

9. Patients who have received any systemic cytostatic agents or multi-instillation intravesical chemotherapy in the 3 months prior to randomisation.

Early postoperative (within 6 hours of resection) single dose chemotherapy is allowed after the first resection. However, it should not be given after (re-)re-TUR if the patient is considered eligible for this study.

10. Patients with uncontrollable UTI.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	24-05-2013
Aantal proefpersonen:	824
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	03-06-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL3829
NTR-old	NTR4011
Ander register	Eudract 2010-019181-91 : EAU RF 2008-01
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten