

features, LND was performed at the time of nephrectomy, and the numbers and sites of regional lymph node metastasis were recorded for each patient.

**Results and Limitations:** Of the 169 high-risk patients, 64 (38%) had lymph node metastases. All patients with nodal metastases had nodal involvement within the primary lymphatic sites of each kidney prior to involvement of the nodes overlying the contralateral great vessel. A limitation of the study is the lack of a standardized LND performed throughout the study period.

**Conclusions:** Pathologic features of renal tumors are associated with the risk of regional lymph node metastases and lymph node metastases that appear to progress through the primary lymphatic drainage of each kidney. Based on these findings we recommend that when performing LND the lymph nodes from the ipsilateral great vessel and the interaortocaval region be removed from the crus of the diaphragm to the common iliac artery.

### Editorial Comment

The landing zone of lymph node metastasis and hence the extent of lymph node dissection in renal cancer is not very well defined. The authors report on a historical cohort of patients with high-risk renal cancer and demonstrate the extent of lymph node metastases. Several clinically important conclusions can be drawn from these data. First, in 66% of patients with metastases these were unsuspected meaning that roughly one third of lymph node metastases were unsuspected. So clearly, lymphadenectomy (LND) should be performed in all high-risk patients. But to which extent? Interestingly, 45% of metastatic patients had no peri-hilar lymph node involvement. Furthermore, no patient with a right-sided tumor had para-aortic metastases without other retroperitoneal involvement, and no patient with a left-sided tumor had paracaval involvement without involvement of para-aortic or inter-aortocaval lymph nodes.

Thus, the surgical recommendation in high-risk tumors is that in patients with right-sided tumors LND should involve all para-caval and inter-aortocaval nodes, whereas in left-sided tumors para-aortic and inter-aortocaval lymph nodes should be removed.

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### **Sequential intravesical chemoimmunotherapy with mitomycin C and bacillus Calmette-Guérin and with bacillus Calmette-Guérin alone in patients with carcinoma in situ of the urinary bladder: results of an EORTC genito-urinary group randomized phase 2 trial (30993)**

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**Background:** Bacillus Calmette-Guérin (BCG) is the intravesical treatment of choice for carcinoma in situ (CIS).

**Objective:** Our aim was to assess if sequential mitomycin C (MMC) plus BCG after transurethral resection (TUR) is worthy of further study in non-muscle-invasive bladder cancer patients with CIS.

**Design, Setting, and Participants:** In a noncomparative phase 2 study, 96 patients with primary/secondary/concurrent CIS of the urinary bladder were randomized to sequential MMC plus BCG or to BCG alone after TUR.

**Intervention:** Patients received six weekly instillations of MMC followed by six weekly instillations of BCG or six weekly instillations of BCG, 3 wk rest, and three further weekly instillations of BCG. Complete responders received three weekly maintenance instillations at 6, 12, 18, 24, 30, and 36 mo in accordance with the initial randomization.

**Measurements:** End points were complete response (CR) rate at the first control cystoscopy 16-18 wk after start of treatment, disease-free interval, overall survival, and side effects.

**Results and Limitations:** Ninety-six patients were randomized, 48 to each treatment group. Ten patients were ineligible, and three did not start treatment. In all randomized patients, CR rates on MMC plus BCG and BCG alone were 70.8% and 66.7%, respectively. In 83 eligible patients who started treatment, CR rates were 75.6% and 73.8%, respectively. Based on a median follow-up of 4.7 yr, 25 patients (52.1%) on MMC plus BCG and 22 patients (45.8%) on BCG alone were disease free. Twelve patients stopped treatment due to toxicity: three during induction (two MMC plus BCG, one BCG) and nine during maintenance (three MMC plus BCG, six BCG).

**Conclusions:** In the treatment of patients with CIS, sequential chemoimmunotherapy with MMC plus BCG had acceptable toxicity. CR and disease-free rates were similar to those on BCG alone and to previous publications on sequential chemoimmunotherapy.

**Trial Registration:** This study was registered with the US National Cancer Institute clinical trials database (protocol ID: EORTC-30993). <http://www.cancer.gov/search/ViewClinicalTrials.aspx?cdrid=68869&version=HealthProfessional&protocolsearchid=7920643>.

### Editorial Comment

Carcinoma in situ (CIS) of the bladder is relatively rare, still an aggressive disease and treatment options are scarce. Intravesical BCG has proven to be better than chemotherapy in several trials. The authors sought to clarify if a combination of both would improve the outcome. Interestingly, they used an unusual statistical method and claimed their study a phase 2 noncomparative trial in which randomization was not done for the purpose of making a treatment comparison but to provide a simultaneous screening of the two treatments. Thus, no p values were given for the end points.

The differences between both treatment arms were small, if any. Side effects were mostly local and not severe. 48.6% of patients had recurred after 5 years on mitomycin C + BCG versus 56.4% on BCG alone. The authors conclude correctly that the present study and data from the literature do not support the use of sequential intravesical chemotherapy and BCG of CIS.

Furthermore, this study design and conduct shows that if applied carefully, interesting alternatives for large-scale randomized trials do exist.

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### Effect of dutasteride on prostate biopsy rates and the diagnosis of prostate cancer in men with lower urinary tract symptoms and enlarged prostates in the combination of avodart and tamsulosin trial

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