

## PREDICTING DISEASE RECURRENCE AND PROGRESSION:

Stratify patients into 4 risk groups to predict progression, according to Table 1. A patient's risk group can be determined using the 2021

EAU risk group calculator available at [www.nmibc.net](http://www.nmibc.net).

Use the 2006 EORTC scoring model to predict the risk of tumour recurrence in individual patients not treated with BCG.	Strong
Use the 2016 EORTC scoring model or the CUETO risk scoring model to predict the risk of tumour recurrence in individual patients treated with BCG intravesical immunotherapy (the 2016 EORTC model is calculated for 1 to 3 years of maintenance, the CUETO model for 5 to 6 months).	Strong

## DISEASE MANAGEMENT:

### General recommendations

In patients with tumours presumed to be at low risk and in those with small papillary recurrences (presumably Ta LG/G1) detected more than one year after previous TURB, offer one immediate single chemotherapy instillation.	Strong
Offer post-operative saline or water continuous irrigation of the bladder to patients who cannot receive a single instillation of chemotherapy.	Strong

Patients with small recurrent low-grade Ta tumours can be effectively and safely offered office fulguration.	Strong
Only offer active surveillance to selected patients with presumed low-grade tumours not amenable to endoscopic ablation.	Strong
In patients with intermediate-risk tumours (with or without immediate instillation), offer one-year full-dose Bacillus Calmette-Guérin (BCG) treatment (induction plus 3-weekly instillations at 3, 6 and 12 months), or instillations of chemotherapy (the optimal schedule is not known) for a maximum of one year. The final choice should be made in a shared decision-making process with the patient, reflecting his/her risk of recurrence and progression, as well as the efficacy and side effects of each treatment modality.	Strong
In patients with high-risk tumours, full-dose intravesical BCG for one to 3 years (induction plus 3-weekly instillations at 3, 6, 12, 18, 24, 30 and 36 months), is indicated. The additional beneficial effect of the second and third years of maintenance should be weighed against its added costs, side effects and access to BCG. Immediate radical cystectomy (RC) may also be discussed with the patient.	Strong
In patients with very high-risk tumours offer immediate RC. Discuss intravesical full-dose BCG instillations for one to 3 years and discuss clinical trials with those who refuse or are unfit for RC.	Strong
Offer transurethral resection of the prostate, followed by intravesical instillation of BCG to patients with CIS in the epithelial lining of the prostatic urethra.	Weak
Cautiously offer quinolones to treat BCG-related side effects*.	Weak
The definition of 'BCG-unresponsive' should be respected as it most precisely defines the patients who are unlikely to respond to further BCG instillations.	Strong
Offer a RC to patients with BCG-unresponsive tumours.	Strong
Offer patients with BCG-unresponsive tumours, who are not candidates for RC due to comorbidities, preservation strategies (intravesical chemotherapy, chemotherapy and microwave-induced hyperthermia, electromotive administration of chemotherapy, intravesical- or systemic immunotherapy; preferably within clinical trials).	Weak
Discuss high-risk and very high-risk patients within a multidisciplinary board, when possible.	Weak

### Technical aspects for intravesical treatment

<b>Intravesical chemotherapy</b>	
If given, administer a single immediate instillation of chemotherapy within 24 hours after TURB.	Weak
Omit a single immediate instillation of chemotherapy in any case of overt or suspected bladder perforation or bleeding requiring bladder irrigation.	Strong
The optimal schedule and duration of further intravesical chemotherapy instillation is not defined; however, it should not exceed one year.	Weak
If intravesical chemotherapy is given, use the drug at its optimal pH and maintain the concentration of the drug by reducing fluid intake before and during instillation.	Strong
The length of individual instillation should be a minimum of one, and up to two hours.	Weak
<b>BCG intravesical immunotherapy</b>	
Absolute contraindications of BCG intravesical instillation are:	Strong
<ul style="list-style-type: none"> <li>during the first two weeks after TURB;</li> <li>in patients with visible haematuria;</li> <li>after traumatic catheterisation;</li> <li>in patients with symptomatic urinary tract infection.</li> </ul>	

## Risk stratification and disease management

Table 1:

Clinical composition of the new EAU NMIBC prognostic factor risk groups based on the WHO 2004/2016 or the WHO 1973 grading classification

Risk group	
<b>Low Risk</b>	<ul style="list-style-type: none"> <li>A primary, single, TaT1 LG/G1 tumour &lt; 3 cm in diameter without CIS in a patient ≤ 70 years</li> <li>A primary Ta LG/G1 tumour without CIS with at most ONE of the additional clinical risk factors</li> </ul>
<b>Intermediate Risk</b>	Patients without CIS who are not included in either the low-, high-, or very high-risk groups
<b>High Risk</b>	<ul style="list-style-type: none"> <li>All T1 HG/G3 without CIS, EXCEPT those included in the very high-risk group</li> <li>All CIS patients, EXCEPT those included in the very high-risk group</li> </ul> <p><b>Stage, grade with additional clinical risk factors:</b></p> <ul style="list-style-type: none"> <li>Ta LG/G2 or T1G1, no CIS with all 3 risk factors</li> <li>Ta HG/G3 or T1 LG, no CIS with at least 2 risk factors</li> <li>T1G2 no CIS with at least 1 risk factor</li> </ul>
<b>Very High Risk</b>	<p><b>Stage, grade with additional clinical risk factors:</b></p> <ul style="list-style-type: none"> <li>Ta HG/G3 and CIS with all 3 risk factors</li> <li>T1G2 and CIS with at least 2 risk factors</li> <li>T1 HG/G3 and CIS with at least 1 risk factor</li> <li>T1 HG/G3 no CIS with all 3 risk factors</li> </ul>

### Guidelines for the treatment of TaT1 tumours and carcinoma in situ according to risk stratification

#### EAU risk group: Low

- Offer one immediate instillation of intravesical chemotherapy after transurethral resection of the bladder (TURB).

#### EAU Risk Group: Intermediate

- In all patients either one-year full-dose Bacillus Calmette-Guérin (BCG) treatment (induction plus 3-weekly instillations at 3, 6 and 12 months), or instillations of chemotherapy (the optimal schedule is not known) for a maximum of one year is recommended. The final choice should reflect the individual patient's risk of recurrence and progression as well as the efficacy and side effects of each treatment modality.

- Offer one immediate chemotherapy instillation to patients with small papillary recurrences detected more than one year after previous TURB.

#### EAU risk group: High

- Offer intravesical full-dose BCG instillations for one to 3 years but discuss immediate radical cystectomy (RC).

Prior intravesical chemotherapy has no impact on the effect of BCG instillation.

#### EAU risk group: Very High

- Offer RC or intravesical full-dose BCG instillations for one to 3 years to those who refuse or are unfit for RC.

### Treatment options for the various categories of BCG failure (Table 2)

Treatments other than RC must be considered oncologically inferior in patients with BCG-unresponsive tumours

Table 2:

Category	Treatment options
BCG-unresponsive	<ol style="list-style-type: none"> <li>Radical cystectomy (RC).</li> <li>Enrolment in clinical trials assessing new treatment strategies.</li> <li>Bladder-preserving strategies in patients unsuitable or refusing RC.</li> </ol>
Late BCG relapsing: TaT1 HG recurrence > 6 months or CIS > 12 months of last BCG exposure	<ol style="list-style-type: none"> <li>Radical cystectomy or repeat BCG course according to a patient's individual situation.</li> <li>Bladder-preserving strategies.</li> </ol>
LG recurrence after BCG for primary intermediate-risk tumour	<ol style="list-style-type: none"> <li>Repeat BCG or intravesical chemotherapy.</li> <li>Radical cystectomy.</li> </ol>