

### Recurrence during or after intravesical chemotherapy

Patients with non-muscle-invasive bladder cancer (NMIBC) recurrence during or after a chemotherapy regimen can benefit from BCG instillations. Prior intravesical chemotherapy has no impact on the effect of BCG instillations.

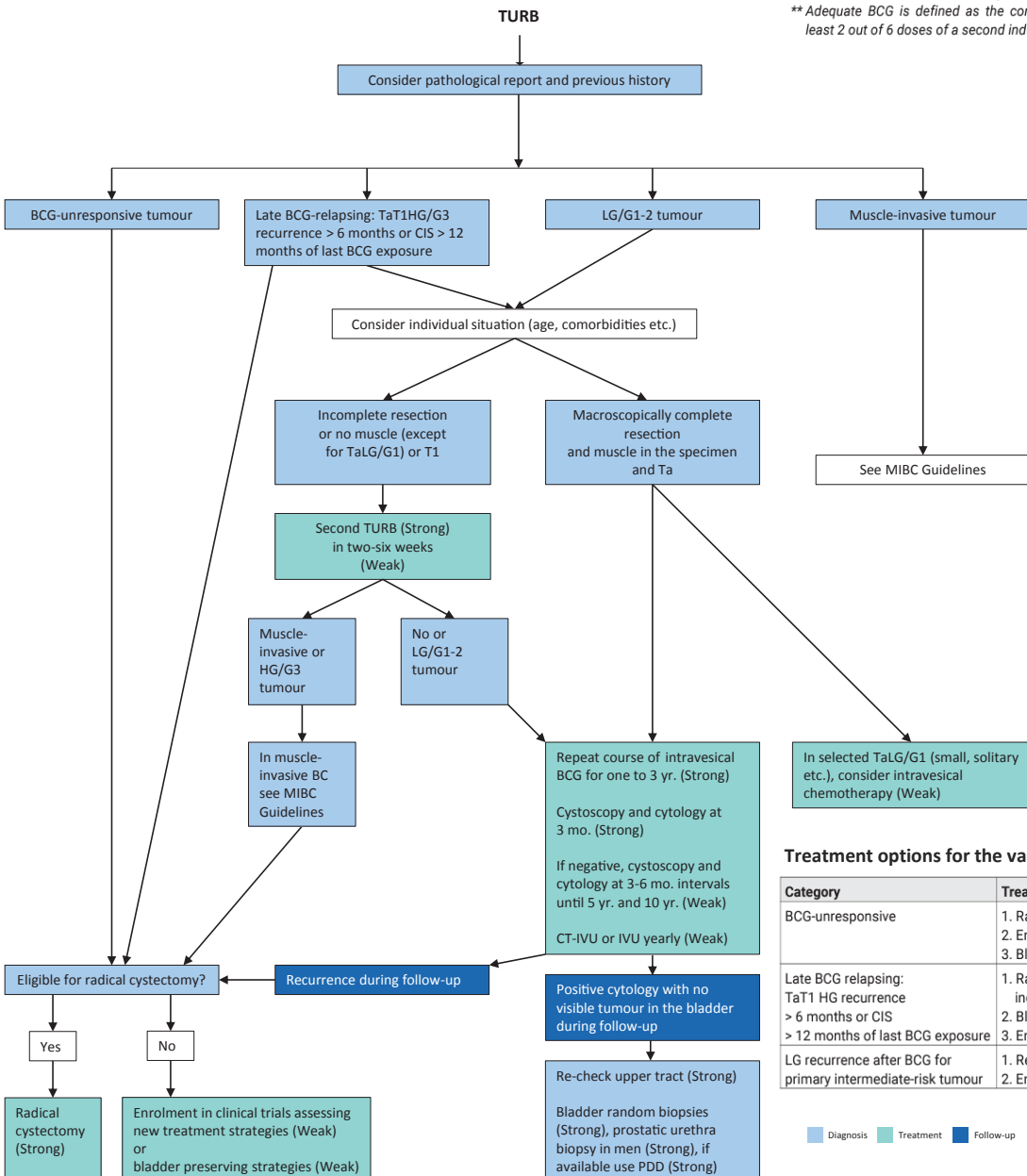
### Treatment failure after intravesical BCG immunotherapy

Several categories of BCG failures, broadly defined as any high grade (HG) disease occurring during or after BCG therapy, have been proposed.

Non-muscle-invasive bladder cancer (BC) may not respond at all (BCG refractory) or may relapse after initial response (BCG relapsing). Some evidence suggests that patients with BCG relapse have better outcomes than BCG refractory patients. The category of BCG-unresponsive tumours comprises BCG-refractory and some of BCG-relapsing tumours

Patients who experience recurrence with HG NMIBC after BCG without meeting BCG-unresponsive criteria may benefit from additional BCG therapy.

### Treatment strategy in recurrence during or after intravesical BCG



### Categories of high-grade recurrence during or after BCG

Whenever a MIBC is detected during follow-up.
<b>BCG-refractory tumour</b>
1. If T1 HG/G3 tumour is present at 3 months [236, 395, 400]. 2. If Ta HG/G3 tumour is present after 3 months and/or at 6 months, after either re-induction or first course of maintenance [368]. 3. If CIS (without concomitant papillary tumour) is present at 3 months and persists at 6 months after either re-induction or first course of maintenance. If patients with CIS present at 3 months, an additional BCG course can achieve a complete response in > 50% of cases [65, 364, 368]. 4. If HG tumour appears during BCG maintenance therapy*.
<b>BCG-relapsing tumour</b>
Recurrence of HG/G3 tumour after completion of BCG maintenance, despite an initial response [401].
<b>BCG-unresponsive tumour</b>
BCG-unresponsive tumours include all BCG refractory tumours and those who develop T1/Ta HG recurrence within 6 months of completion of adequate BCG exposure** or develop CIS within 12 months of completion of adequate BCG exposure [396].
<b>BCG-exposed tumour [398, 399]</b>
1. If Ta HG/G3 or CIS is present at three months evaluation after induction BCG only 2. Delayed relapse after adequate or inadequate BCG
<b>BCG intolerance</b>
Severe side effects that prevent further BCG instillation before completing treatment [337].

\* Patients with LG recurrence during or after BCG treatment are not considered to be a BCG failure.

\*\* Adequate BCG is defined as the completion of at least 5 of 6 doses of an initial induction course plus at least 2 out of 6 doses of a second induction course or 2 out of 3 doses of maintenance therapy.

### Treatment options for the various categories of BCG failure

Category	Treatment options
BCG-unresponsive	1. Radical cystectomy (RC). 2. Enrolment in clinical trials assessing new treatment strategies. 3. Bladder-preserving strategies in patients unsuitable or refusing RC.
Late BCG relapsing: TaT1 HG recurrence > 6 months or CIS > 12 months of last BCG exposure	1. Radical cystectomy or repeat BCG course according to a patient's individual situation. 2. Bladder-preserving strategies. 3. Enrolment in clinical trials assessing new treatment strategies.
LG recurrence after BCG for primary intermediate-risk tumour	1. Repeat BCG or intravesical chemotherapy. 2. Enrolment in clinical trials assessing new treatment strategies.

■ Diagnosis ■ Treatment ■ Follow-up