Invasive bladder cancer: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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incidence
The crude incidence of invasive bladder cancer in the European Union is 19.5/100 000/year, the mortality is 7.9/100 000/year; 70% of patients with bladder cancer are >65 years of age.

diagnosis
Pathological diagnosis should be made according to the WHO classification (Table 1) from a biopsy obtained by transurethral resection (TUR) of primary tumor. Ninety percent of bladder carcinomas are transitional cell carcinomas.

staging and risk assessment
Complete history and physical examination, blood counts, creatinine, chest X-ray (or CT), CT scan of the abdomen and pelvis and urine cytology. Additional diagnostic tests, such as bone scan, should be performed if clinically indicated.

Cystoscopic examination and TUR with a bimanual examination under anesthesia (EUA), with biopsy and determination of size, and the presence of extravesical extension or invasion of adjacent organs.

Management of bladder cancer is based on the pathologic findings of the biopsy, with attention to histology, grade and depth of invasion. Patients with invasive bladder cancer should be staged according to the TNM system and be grouped into the categories shown in Table 2.

treatment of stage I disease
• TUR is the treatment of choice followed by intravesical therapy or by careful surveillance in patients with low-risk disease.

• Patients with high-risk disease (recurrent, large, deeply invasive, multifocal, poorly differentiated or with carcinoma in situ) can be treated with intravesical Bacillus Calmette-Guérin (BCG) therapy after initial TUR [I, A] or radical cystectomy.
• If there is no response to BCG, cystectomy should be considered due to the high risk of progression.

treatment of stage II and III disease
• Radical cystectomy is the standard treatment for patients with muscle-invasive bladder cancer.
• Bladder-preserving approaches, with a complete TUR and radiotherapy alone or with concomitant chemotherapy, are reasonable alternatives to cystectomy for patients who are medically unfit for surgery and for patients who seek an alternative [II, A].

Two large randomized trials and a meta-analysis support the use of neo-adjuvant chemotherapy before cystectomy for T2 and T3 disease. The demonstrated survival benefit encourages the use of platinum-based combination chemotherapy for

Table 1. WHO/ISUP 1998 Consensus WHO, 2004

<table>
<thead>
<tr>
<th>WHO, World Health Organization</th>
<th>ISUP, International Society of Urologic Pathology</th>
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<tbody>
<tr>
<td>Papilloma</td>
<td>Papillary urothelial neoplasm of low malignant potential</td>
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<tr>
<td>Urothelial carcinoma low grade</td>
<td>Urothelial carcinoma high grade</td>
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<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
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<tbody>
<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2a–T2b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3a–T3b, T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
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<tr>
<td></td>
<td>Any T</td>
<td>N1–N3</td>
<td>M0</td>
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<td></td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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patients with invasive bladder cancer before radical cystectomy or definitive radiotherapy [II, A]. Although there appears to be a difference in favor of adjuvant chemotherapy in muscle-invasive bladder cancer, available trials provide insufficient evidence for the routine use of adjuvant chemotherapy in clinical practice.

**treatment of stage IV disease**

- Platinum-based combination chemotherapy with methotrexate–vinblastine–doxorubicin–cisplatinum or gemcitabine–cisplatinum prolongs survival [I, A].
- Patients unfit for cisplatin-based chemotherapy may be palliated with carboplatin-based regimen or single-agent taxane or gemcitabine.
- Selected patients with locally advanced disease (T4b N1) may be candidates for cystectomy and lymph node dissection or definitive radiotherapy following systemic therapy.
- Palliative radiotherapy may be used to reduce symptoms.

**response evaluation**

- Response evaluation with cystoscopy and cytology is mandatory following BCG treatment and in patients after bladder preservation strategy.
- Response evaluation during chemotherapy with the initial radiographic tests is necessary.

**follow-up**

There is no generally accepted follow-up protocol and therefore the possible alternatives could be as follows:

- Patients treated with a bladder-preservation strategy, cystoscopy and urinary cytology every 3 months during the first 2 years, and every 6 months thereafter.
- After cystectomy clinical control every 3 months during the first 2 years and subsequently every 6 months for 5 years.

**note**

Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

**literature**