Non Muscle Invasive Bladder Cancer

Option: The recommendation comprises different procedures as the outcome, the interventions and the preferences of patients and doctors are not sufficiently well known.

The recommendations of the working party apply to patients with papillary tumours stages Ta and T1, as well as to carcinoma in situ (CIS), a flat neoplasm. The classification of non-muscle invasive tumors (Ta, T1 and CIS) is according to the TNM classification 2002, table 1.

Table 1: TNM classification 2002

<table>
<thead>
<tr>
<th>Urinary Bladder</th>
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<tbody>
<tr>
<td>Ta Noninvasive papillary</td>
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<tr>
<td>Tis In situ: “flat tumour”</td>
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<tr>
<td>T1 Subepithelial connective tissue</td>
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<tr>
<td>T2 Muscularis</td>
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<tr>
<td>T2a Inner half</td>
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<tr>
<td>T2b Outer half</td>
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<tr>
<td>T3 Beyond muscularis</td>
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<tr>
<td>T3a Microscopically</td>
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<tr>
<td>T3b Extravesical mass</td>
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<td>T4 Tumour invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall</td>
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<tr>
<td>T4a Prostate, uterus, vagina</td>
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<tr>
<td>T4b Pelvic wall, abdominal wall</td>
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<tr>
<td>N1 Single ≤ 2 cm</td>
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<td>N2 Single &gt; 2 to 5 cm, multiple ≤ 5 cm</td>
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<tr>
<td>N3 &gt; 5 cm</td>
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</table>

Characteristics of Stages Ta, T1 and CIS

Stage Ta tumours are confined to the urothelium, have a papil-
lary configuration of their exophytic part and do not penetrate
the urothelium towards the lamina propria or detrusor muscle.

Stage T1 tumours generate from the urothelium but penetrate
the basement membrane which separates the urothelium from
the deeper layers. T1 tumours invade into the lamina propria,
but not so deep that they reach the detrusor muscle.

Carcinoma in situ (CIS) is a high-grade (anaplastic) carcinoma
confined to the urothelium, but with flat non-papillary config-
urations. CIS can be local or diffuse and it can be concomitant
with papillary tumours. Unlike a papillary tumour, CIS
appears as reddened, velvety mucosa is slightly elevated but
sometimes not visible at all.

Characteristics of grade (WHO classification)
Apart from the architecture the individual cells show different
degrees of anaplasia:
Grade 1: well differentiated tumour
Grade 2: moderately differentiated tumour
Grade 3: poorly differentiated tumour

The prognosis of patients is correlated with stage and grade
being excellent for TaG1 and less favourable for T1G3 or CIS.

Therapy and Histological diagnosis
The standard therapy for Ta and T1 papillary bladder tumours
is complete macroscopic eradication by transurethral resection
(TUR) including the underlying muscle. The technique of
transurethral resection is described in the EAU guidelines on
Superficial Bladder Cancer.

CIS cannot be eradicated by transurethral resection. The diag-
nosis of CIS is made by multiple biopsies from the bladder
wall, in conjunction with urine cytology. Since there is consid-
erable risk for recurrences and/or progression of tumours after
transurethral resection, adjuvant intravesical therapy for all
stages (Ta, T1 and CIS) is recommended.

The choice of intravesical adjuvant therapy depends on the
risk of recurrence and/or progression. Patients with non-mus-
cle invasive bladder cancer can be divided into 3 risk groups:
low, intermediate and high risk.

Prognostic Factors
Low risk tumours: single, TaG1, ≤ 3 cm diameter.
High risk tumours: T1G3, multifocal or highly recurrent,
CIS.
Intermediate risk: all other tumours, Ta-1, G1-2, multifocal,
> 3 cm diameter.

- The optimal treatment for low risk, solitary TaG1 lesions is
  complete TUR (standard) plus one instillation of a
  chemotherapeutic drug (mitomycin C, epirubicin or do-
 xorubicine) within 6 hours after transurethral resection.
  The immediate instillation is considered as standard, the
  choice of therapeutic drug is optional.
- The treatment for intermediate Ta-T1, G1-2, multifocal
tumours consists of complete TUR (standard) followed by
  a second TUR after 4 - 6 week(s), if there is any doubt
  regarding the completeness of the initial TUR (optional).
- Adjuvant intravesical therapy is necessary but no consen-
sus exists regarding the optimal drug and the optimal
Recommendations for High risk tumours
The treatment for high risk Ta-T1, G3 with or without carcinoma in situ or for carcinoma in situ (alone) consists of:

1. Complete TUR of papillary tumours (standard)
2. re-TUR after 4 - 6 weeks (recommended)
3A Adjuvant intravesical immunotherapy
drug: BCG (full dose or reduced dose in case of side-effects).
   Maintenance schedule: at least 1 year - optionally up to 3 years
   Or
3B Radical cystectomy plus urinary diversion up front (optional) or if no response to BCG therapy is achieved (standard)

Diagnostic procedures and follow-up are described in the short and long versions of the EAU guidelines on Superficial Bladder Cancer.

This short booklet is based on the more comprehensive EAU guidelines (ISBN 90-806179-8-9), available to all members of the European Association of Urology at their website - www.uroweb.org

Recommendations for Intermediate risk tumours

1. Complete TUR (standard)
2. re-TUR if complete resection is not achieved (optional)
3A Adjuvant intravesical chemotherapy (drug - optional), schedule - optional although the schedule used should not exceed 1 year.
   Or
3B Adjuvant intravesical immunotherapy: drug BCG (full dose or reduced dose in case of side effects).
   Schedule: maintenance: at least 1 year, optionally up to 3 years.

Recommendations for Low risk tumours

1. Complete TUR (standard)
2. An immediate single instillation with a chemotherapeutic drug (standard, drug optional)

Recommendations for Intermediate risk tumours

1. Complete TUR (standard)
2. re-TUR if complete resection is not achieved (optional)
3A Adjuvant intravesical chemotherapy (drug - optional), schedule - optional although the schedule used should not exceed 1 year.
   Or
3B Adjuvant intravesical immunotherapy: drug BCG (full dose or reduced dose in case of side effects).
   Schedule: maintenance: at least 1 year, optionally up to 3 years.