Testicular seminoma: ESMO Clinical Recommendations for diagnosis, treatment and follow-up

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incidence

- The crude incidence rate of testicular cancer in Europe is 6.3, the death rate 0.38 cases/100 000 males/year. About 40% of these testicular cancers are pure seminoma; 2–3% present as bilateral tumors during lifetime.

diagnosis

- Diagnosis should be based on histology of testis mass removed by inguinal orchiectomy [IV, B].
- Biopsy (trucut or by mediastinoscopy) in patients presenting with retroperitoneal or mediastinal primary [IV, B].
- In rapidly progressive tumors and need for urgent chemotherapy diagnosis may be made on typical clinical picture and marker evaluation.

staging and risk assessment

- All patients should have full blood count, urea, creatinine, electrolytes and liver function tests.
- Tumor markers (zFP, bHCG, LDH) are to be taken before orchiectomy for confirmation of pure seminoma and for risk assessment according to the IGCCCG prognostic index.
- CT scan including chest, abdomen and pelvis are mandatory [III, B]. A chest X-ray, especially if used as a follow up examination.
- A bone scan should be carried out in patients with metastatic disease if bone-related symptoms and/or elevated alkaline phosphatase [IV, B].
- Contralateral testis biopsy is recommended especially in patients with testicular atrophy (<16 ml) [III, B].
- Staging should be done according to the TNM system and for patients with metastatic disease, establishment of the prognostic group according to the International Germ Cell Consensus Classification (see Table 1 below).

treatment plan for localized disease (stage I)

For patients intended for chemotherapy or testicular radiotherapy sperm cryopreservation should be considered.

- Tumor size <4 cm and absence of rete testis involvement identify a group with low relapse risk (12%). Tumors >4 cm with rete testis invasion have a 32% risk of relapse. Patients with one risk factor have a 15% risk of relapse.
- Adjuvant radiotherapy to para-aortic strip and adjuvant carboplatin [area under the curve (AUC) 7] for one cycle result in similar relapse risk and long-term survival. Initial surveillance achieves similar survival results and is a feasible alternative especially in low-risk patients. Radiotherapy carries long-term risk of second malignancy [III, A]. Carboplatin or surveillance are preferred especially in low-/intermediate-risk patients.
- Surveillance in stage I seminoma should be undertaken in defined protocols, for at least 5 years with regular abdominal imaging [III, B].
- Patients with carcinoma in situ of the testis should be treated by radiotherapy to the affected testis (20 Gy/10 fractions in 2 weeks) [I, A]. If previous inguinal/scrotal surgery extend to 'Dogleg' radiotherapy (to include ipsilateral iliac and inguinal lymph nodes), dose 20 Gy/10 fractions/2 weeks [III, B].

follow-up after localized disease (stage I)

- Chest X-ray and clinical examination at 1 month, 3-monthly for 2 years, then 6-monthly to 5 years.
- Pelvic CT may be indicated in patients treated by para-aortic strip at years 1, 2 and 5 [V, D].
### Table 1.

<table>
<thead>
<tr>
<th>Stage grouping</th>
<th>TNM grouping</th>
<th>TNM</th>
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<tbody>
<tr>
<td>I</td>
<td>Any T N0 M0 S0</td>
<td>T1 testis and epididymis, no vascular/lymphatic invasion</td>
</tr>
<tr>
<td>I</td>
<td>S1–3</td>
<td>T2 testis and epididymis, vascular/lymphatic invasion or tunica vaginalis</td>
</tr>
<tr>
<td>IIA</td>
<td>Any T N1 M0 S0–1</td>
<td>N1 ≤ 2 cm</td>
</tr>
<tr>
<td>IIB</td>
<td>Any T N2 M0 S0–1</td>
<td>N2 ≥ 2–5 cm</td>
</tr>
<tr>
<td>IIC</td>
<td>Any T N3 M0 S0–1</td>
<td>N3 &gt; 5 cm</td>
</tr>
<tr>
<td>IIIA</td>
<td>Any T N0–3 M1a S0–1</td>
<td>M1a, non-regional lymph nodes</td>
</tr>
<tr>
<td>IIIB</td>
<td>Any T N1–3 or M1a S2</td>
<td>M1b, distant metastasis at other sites</td>
</tr>
<tr>
<td>IIIC</td>
<td>Any T N1–3 or M1a S3 or any T, any N, M1b any S</td>
<td></td>
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</table>

Good prognosis: all of: normal AFP, any HCG, any LDH and no non-pulmonary visceral metastases present.
Intermediate prognosis: normal AFP, any HCG, any LDH and non-pulmonary visceral metastases present.
S0, no raised markers.
S1, AFP 1000–10,000 ng/ml and βHCG <5000 IU/l (<1000 ng/l) and LDH <1.5 × upper limit of normal (ULN).
S2, AFP 1000–10,000 ng/ml, or βHCG 5000–50,000 IU/l or LDH 1.5–10 × ULN.
S3, AFP >10,000 ng/ml or βHCG >50,000 IU/l or LDH >10 × ULN.

### treatment plan for metastatic disease

For stage IIA–B.
- Dogleg radiotherapy to 30–36 Gy in 15–18 fractions to involved site [IIIA, B].
- Chemotherapy as for stage IIIC (see below) is an active alternative [IIIB–IIIC, B].

For stage IIB–III
- Chemotherapy with three cycles (four cycles for stage IIIC) of etoposide 100 mg/m² on days 1–5, cisplatin 50 mg/m² on days 1–2 or 20 mg/m² on days 1–5 ± bleomycin 30,000 IU on days 1, 8 and 15 [I, A]. The need for bleomycin has not been clearly demonstrated so consideration may be given to omitting it (good prognosis patients only), especially in older patients (>40 years), or patients with poor lung function as they may have higher risk of pneumonitis [IV, B].

For patients relapsing after ‘dogleg’ radiotherapy
- Chemotherapy with four cycles of BEP with lower dose etoposide (360 g/m²/cycle) is recommended [V, D].

### response evaluation for metastatic disease

Chest-X-ray, CT scan and tumor markers at 1 month after treatment [IV, B].

### follow up after metastatic disease

- If normal post-treatment CT scan: follow up as for stage I [IV, D].
- If abnormal post-treatment CT scan: repeat CT scan every 6 months until normal or abnormalities stabilized. A PET scan may help to identify patients who have residual active cancer [III B].
- Consider biopsy or resection for large residual or growing masses [III, B].

### 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

