



# Testicular Cancer Supplement

Classification and treatment

TNM staging classification for testicular cancer (UICC, 2017 8th Edition)

## pT - Primary Tumour\*

pTX	Primary tumour cannot be assessed
pT0	No evidence of primary tumour (e.g. histologic scar in testis)
pTis	Intratubular germ cell neoplasia or ITGCN (sometimes loosely referred to as carcinoma in situ)
pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion: tumour may invade tunica albuginea but not tunica vaginalis
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis
pT3	Tumour invades spermatic cord with or without vascular/lymphatic invasion
pT4	Tumour invades scrotum with or without vascular/lymphatic invasion

## Regional Lymph Nodes Clinical

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node mass 2 cm or less in greatest dimension, or multiple lymph nodes, none more than 2 cm in greatest dimension
N2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension or multiple lymph nodes, any one mass more than 2 cm but not more than 5 cm in greatest dimension
N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension

## Regional Lymph Nodes Pathological

pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension
pN2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour
pN3	Metastasis with a lymph node mass more than 5 cm in greatest dimension

## Distant Metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
- M1a	Non-regional lymph node(s) or lung
- M1b	Other sites

## Serum Markers<sup>†</sup>

Sx	Serum markers not available or cannot be assessed
S0	Serum marker study levels within normal limits
S1	LDH < 1.5 x ULN; hCG < 5000 mIU/mL; AFP < 1000 ng/mL
S2	LDH 1.5-10 x ULN; hCG 5000-50,000 mIU/mL; AFP 1000-10,000 ng/mL
S3	LDH > 10 x ULN; hCG > 50,000 mIU/mL; AFP > 10,000 ng/mL

<sup>†</sup> LDH, lactate dehydrogenase; hCG, human chorionic gonadotrophin; AFP, alpha fetoprotein; ULN, upper limit of normal

\* Except for pTis and pT4, where radical orchidectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchidectomy; see pT. In other circumstances, TX is used if no radical orchidectomy has been performed.

## Treatment options for localised testicular cancer

Following orchidectomy for stage I (localised) disease, metastases can occur in 15-20% of seminoma and 20-30% of NSGCT patients. Adjuvant treatments can decrease this risk, but come at the cost of adverse effects. Surveillance is another management option often used as many patients will not have a recurrence. A risk-adapted approach is now used to determine subsequent management.

### pT1 Seminoma

- Surveillance is recommended (if facilities are available and the patient willing and able to comply)
- Carboplatin-based chemotherapy can be recommended (decreases recurrence rates from 15-20% to 1-3%)
- Adjuvant treatment not recommended for patients at very low risk (<4 cm size, absence of rete testis invasion)
- Radiotherapy is not recommended as adjuvant treatment, although it is a treatment option

### pT1 Non-Seminomatous Germ Cell Tumour (NSGCT)

#### Low risk

(No Lymphovascular invasion, Embryonal component <50%, Proliferative index <70%)

- If the patient is able and willing to comply with a surveillance policy, long-term (at least 5 years) close follow-up should be recommended
- In patients not willing (or unsuitable) to undergo surveillance, adjuvant chemotherapy or nerve-sparing retroperitoneal lymph node dissection (RPLND) are options

#### High risk

(Lymphovascular invasion, pT2-pT4)

- Adjuvant chemotherapy with one or two courses of BEP is recommended
- If the patient is not willing to undergo chemotherapy or if chemotherapy is not feasible, nerve-sparing RPLND or surveillance with treatment at relapse (in about 50% of patients) are options

## Treatment of metastatic disease (pt2-t4)

### The treatment of metastatic germ cell tumours depends on:

- The histology of the primary tumour and
- Prognostic groups as defined by the IGCCCG (International Germ Cell Cancer Collaborative Group)

#### Seminoma

- Radiotherapy (30Gy), or chemotherapy (BEP) can be used with the same schedule as for the corresponding prognostic groups for NSGCT
- Any pT, N3 seminoma is treated as "good prognosis" metastatic tumour with three cycles of BEP or four cycles of EP
- PET scan plays a role in evaluation of post-chemotherapy masses larger than 3 cm

#### NSGCT

B=Bleomycin, E=Etoposide, P=Platinum for BEP or EP combination chemotherapy

- Low volume NSGCT with elevated markers (good or intermediate prognosis), three of four cycles of BEP; if no marker elevation, repeat staging at 6 weeks surveillance to make final decision on treatment
- Metastatic NSGCT with a good prognosis, primary treatment three courses of BEP
- Metastatic NSGCT with intermediate or poor prognosis, four courses of BEP and inclusion in clinical trial recommended
- Surgical resection of residual masses after chemotherapy in NSGCT is indicated in case of visible residual mass and when tumour marker levels are normal or normalising

## IGCCCG Prognostic - based staging system for metastatic germ cell cancer

Prognosis	Seminoma	Non-Seminoma
<b>Good</b> (If ALL criteria are met)	<ul style="list-style-type: none"> <li>• Any primary site</li> <li>• No non-pulmonary metastases</li> <li>• Normal AFP/normal LDH, low hCG</li> </ul>	If all criteria are met: <ul style="list-style-type: none"> <li>• Testis/retroperitoneal primary</li> <li>• No non-pulmonary metastases e.g. liver, brain</li> <li>• Lower levels of tumour markers</li> </ul>
<b>Intermediate</b> (If ALL criteria are met)	If all criteria are met: <ul style="list-style-type: none"> <li>• Any primary site</li> <li>• No non-pulmonary metastases</li> <li>• Normal AFP/normal LDH, medium hCG</li> </ul>	If all criteria are met: <ul style="list-style-type: none"> <li>• Testis/retroperitoneal primary</li> <li>• No non-pulmonary metastases e.g. liver, brain</li> <li>• Medium levels of tumour markers</li> </ul>
<b>Poor</b> (If ANY criteria are met)	No seminoma carries poor prognosis	If any criteria are met: <ul style="list-style-type: none"> <li>• Non-pulmonary metastases e.g. liver, brain</li> <li>• Higher level of tumour markers</li> <li>• Mediastinal primary for NSGCT</li> </ul>

## Additional investigations

### Serum tumour markers

Post-orchidectomy half-life kinetics of serum tumour markers

- The persistence of elevated serum tumour markers 3 weeks after orchidectomy may indicate the presence of metastases, while its normalisation does not necessarily mean an absence of tumour
- Tumour markers should be assessed until they are normal, as long as they follow their half-life kinetics and no metastases are revealed on scans

### Other examinations

Assessment of abdominal and mediastinal nodes and viscera (CT scan) and supraclavicular nodes (physical examination)

- Other examinations such as brain or spinal CT, bone scan or liver ultrasound should be performed if metastases are suspected
- Patients diagnosed with testicular seminoma who have a positive abdominal CT scan are recommended to have a chest CT scan
- A chest CT scan should be routinely performed in patients diagnosed with NSGCT because in 10% of cases small subpleural nodes are present that are not visible radiologically