# TESTICULAR TUMORS

## Initial Workup

- **Histology:**
  - Diagnosis is based on histology of the testicular mass removed preferably through inguinal orchiectomy approach.
- **Biopsy and/or β-HCG:**
  - In the context of the differential diagnosis in patients presenting with the extra-gonadal tumor.
- **Staging and risk assessment.**
- **Laboratory Investigations:**
  - Full blood count,
  - Serum creatinine,
  - Electrolytes and
  - Liver enzymes.
- **Tumor markers:**
  - Alpha-fetoprotein (AFP)
  - human chorionic gonadotropin (β-HCG)
  - Lactate dehydrogenase (LDH)

  **N.B.** Pure classical seminoma does not secrete AFP, though in some cases elevated levels of B-HCG may be present. So, Seminoma patients having a raised AFP should be managed as for non-seminoma.
- **Imaging:** At baseline, post-therapy, and follow-up intervals.
  - Thoracic imaging: plain chest x-ray; CT scan
  - CT abdomen and pelvis.
  - MRI of the central nervous system in advanced stages, particularly if being symptomatic, extensive lung metastases & high level of β-HCG.
  - Bone scan; 18F-Sodium Fluoride (NAF) scan
  - PET scanning for:
    - Advanced stages;
    - Assessment for the presence of a residual tumor.

  **N.B.** All patients should be advice for pre-operative and pre-chemotherapy determination of total testosterone, LH, FSH semen analysis, and sperm banking.

## Staging

| Primary Tumor (T) | |
|---|---|
| **pT** | Intratubular |
| **pT1** | Testis and epididymis, no vascular/lymphatic invasion |
| **pT2** | Testis and epididymis with vascular/lymphatic invasion or tunica vaginalis |
| **pT3** | Spermatic cord |
| **pT4** | Scrotum |

| Regional Lymph Nodes (N) | |
|---|---|
| **N1** | ≤ 2 cm |
| **N2** | > 2 – 5 cm |
| **N3** | > 5 cm |

| Distant Metastasis (M) | |
|---|---|
| **M1a** | Non-regional lymph node or pulmonary metastasis |
| **M1b** | Non-pulmonary visceral metastasis |

| Serum Tumor Markers (S) | | | |
|---|---|---|---|
| **SX** | Serum marker studies not available or not performed | | |
| **S0** | Serum marker study levels within normal limits | | |
| **S1** | LDH <1.5 x N | β-HCG <5,000 | AFP <1,000 |
| **S2** | LDH 1.5-10 x N | β-HCG 5,000 – 50,000 | AFB 1,000 – 10,000 |
| **S3** | LDH >10 x N | BHCG >50,000 | AFP >10,000 |
| N indicates the upper limit of normal for the LDH assay | | | |

| Cancer stage grouping | | | | |
|---|---|---|---|---|
| **Stage 0** | pT | N0 | M0 | SX |
| **Stage I** | pT1-4 | N0 | M0 | SX |
| **Stage IA** | pT1 | N0 | M0 | S0 |
| **Stage IB** | pT2 | N0 | M0 | S0 |
| | pT3 | N0 | M0 | S0 |

| | | | | |
|---|---|---|---|---|
| | pT4 | N0 | M0 | S0 |
| **Stage IS** | Any pT/TX | N0 | M0 | S1-3 |
| **Stage II** | Any pT/TX | N1-3 | M0 | S0 |
| **Stage IIA** | Any pT/TX | N1 | M0 | S0 |
| | Any pT/TX | N1 | M0 | S1 |
| **Stage IIB** | Any pT/TX | N2 | M0 | S0 |
| | Any pT/TX | N2 | M0 | S1 |
| **Stage IIC** | Any pT/TX | N3 | M0 | S0 |
| | Any pT/TX | Any N | M1, M1a | SX |
| **Stage IIIA** | Any pT/TX | Any N | M1, M1a | S0 |
| | Any pT/TX | Any N | M1, M1a | S1 |
| **Stage IIIB** | Any pT/TX | N1-3 | M0 | S2 |
| | Any pT/TX | Any N | M1, M1a | S2 |
| **Stage IIIC** | Any pT/TX | N1-3 | M0 | S3 |
| | Any pT/TX | Any N | M1, M1a | S3 |
| | Any pT/TX | Any N | M1b | Any S |

## Testicular Seminoma

**Risk categories**

| Good Risk | Intermediate risk | Poor Risk |
|---|---|---|
| Any primary site | Any primary site | None |
| Non-pulmonary/visceral metastases ABSENT | Non-pulmonary/visceral metastases PRESENT | |
| Normal AFP | Normal AFP | |
| Any HCG | Any HCG | |
| Any LDH | Any LDH | |

**Treatment of primary tumor** is orchiectomy.

**Post-orchiectomy:**

- Surveillance
- Single-agent one or two cycles of adjuvant carboplatin AUC 7.

- Adjuvant radiotherapy
  - Treatment of other stages will be as for Non-seminoma, based on chemotherapy, would be 3-4 cycles of:
    - BEP (bleomycin, etoposide, and platinum) or
    - EP (etoposide and cisplatin).
  - The decision will be based on each patient after discussion with the tumor board.
  - In case of potentially increased risk for bleomycin-induced lung toxicity, bleomycin should be omitted.

## Testicular Non-Seminoma

**Treatment of primary tumor** is Radical orchiectomy through an inguinal incision.

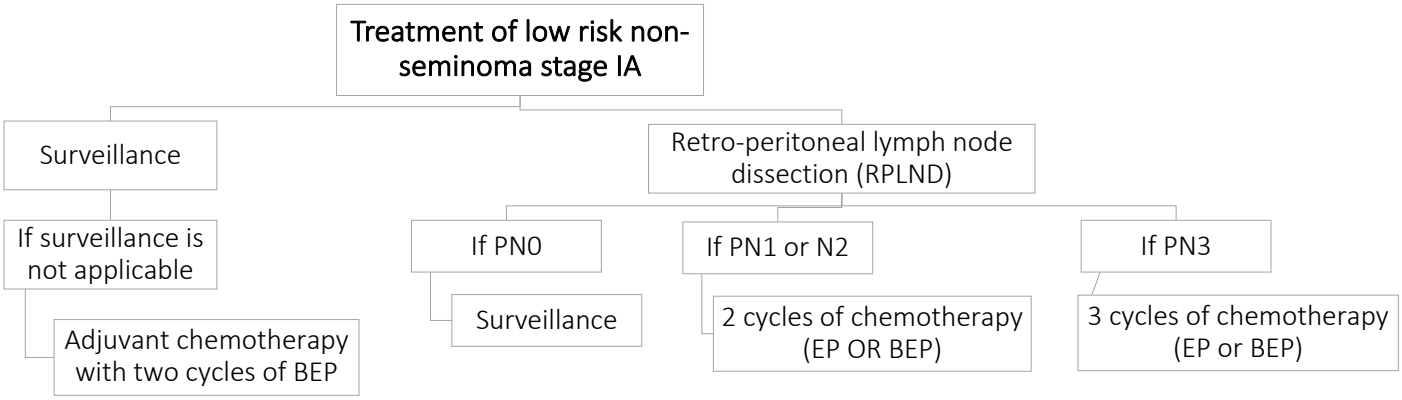
**Risk assessment:**

| Good Risk | Intermediate risk | Poor Risk |
|---|---|---|
| Testis/retroperitoneal primary | Testis /retroperitoneal primary | Mediastinal primary |
| No liver/bone/CNS metastases | Non-regional nodes and/or pulmonary metastases | Liver/bone/CNS or other visceral metastases ± pulmonary metastases |
| Good markers | Intermediate markers | Poor markers |
| LDH <1.5 N | LDH: 1.5 – 10 N | LDH >10 N |
| β-HCG <5000 | β-HCG: 5000 – 50000 | β-HCG >50000 |
| AFP <1000 | AFP: 1000 – 10000 | AFP >10000 |

### Treatment of non-seminoma stage I

**Stage I patients are divided into**

- Low risk (20% relapse rate)
- High risk (40%–50% relapse rate) related to the presence of lymphatic and /or vascular invasion



**Treatment of high-risk non-seminoma stage IB:**

| Treatment option | Relapse Rate |
|---|---|
| Surveillance on the selected patient with T2 or T3 disease (category 2B) | 40 – 50% |
| Adjuvant chemotherapy; two cycles of BEP | 3-4% |
| Retro-peritoneal lymph node dissection (RPLND) | |

## Treatment of non-seminoma stage II

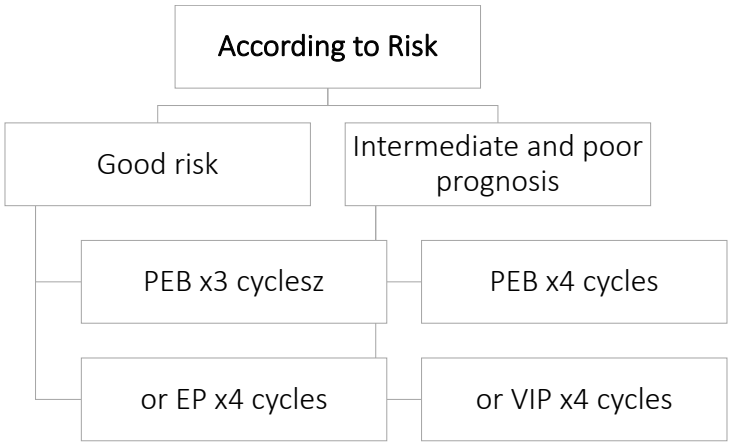
**Stage IIA (marker-negative)**

- Chemotherapy (4 cycles of EP or 3 cycles of BEP)
- Followed by RPLND or surveillance

**Stage IIA (marker-positive) or**
**Stage IIB (marker-positive or negative)**

- The standard treatment is chemotherapy with PEB x 3 cycles or PE x 4 cycles.
- In case of residual tumor (>1 cm lymph node diameter) resection of this residual lesion should be performed, followed by the routine follow-up (independent of the result of the resection).

## Treatment of advanced non-seminoma stage IS/IIC/III



## Management after primary chemotherapy

| Marker normalized with no residual disease |
|---|
| Follow up |

| Marker normalized + respectable residual |
|---|
| Resection |

| If R0-resection with scar tissue only or differentiated teratoma or viable tumor <10% of the resection |
|---|
| Follow-up |

| If >10% viable tumor |
|---|
| Consolidation chemotherapy with two cycles of VIP. |

## Second line therapy for metastatic germ cell tumor:

- Patients who do not have a complete response to first-line chemotherapy or had a recurrence, are divided into favorable or unfavorable prognosis based on prognostic factors.

| Favorable prognostic factors | Unfavorable prognostic factors |
|---|---|
| A complete response to 1st line chemotherapy<br>Low level of post orchiectomy tumor markers<br>Low volume disease. | Incomplete response to first-line chemotherapy<br>High level of serum markers,<br>High volume disease<br>Presence of extra testicular primary site. |
|  |  |
| Conventional-dose chemotherapy (platinum, ifosfamide, combined with vinblastine or paclitaxel) or<br>High dose chemotherapy, | Conventional-dose chemotherapy (VeIP or TIP) and high dose protocol (high dose carboplatin plus etoposide)<br>followed by an autologous stem cell transplant. |

**Palliative therapy:**

- All patients with either resistant or recurrent disease should be considered for palliative:
  - Chemotherapy or
  - Radiotherapy.
- Palliative chemotherapy options include:
  - Gemcitabine/oxaliplatin or
  - Paclitaxel and oral etoposide.

## Follow Up of Non-Seminoma

Table 1 Follow-up for Stage IA, IB on Surveillance *Only*

| Year | Months between H&P, markers, chest x-ray | Months between abdominal CT |
|---|---|---|
| 1 | 1-2 | 3-4 |
| 2 | 2 | 4-6 |
| 3 | 3 | 6-12 |
| 4 | 4 | 6-12 |
| 5 | 6 | 12 |
| 6+ | 12 | 12-24 |

Table 2 Follow-up After Complete Response to Chemotherapy and RPLND

| Year | Months between H&P, markers, chest x-ray (category 2B for chest x-ray frequency) | Months between abdominal/pelvic CT |
|---|---|---|
| 1 | 2-3 | 6 |
| 2 | 2-3 | 6-12 |
| 3 | 3-6 | 12 |
| 4 | 6 | 12 |
| 5 | 6-12 | 12 |
| 6+ | 12 | As clinically indicated |

**Table 3 Follow-up After RPLND Only**

| Year | Months between H&P, markers, chest x-ray (category 2B for chest x-ray frequency) | Months between abdominal/pelvic CT |
|---|---|---|
| 1 | 2-3 | Baseline |
| 2 | 2-3 | As indicated |
| 3 | 3-6 | As indicated |
| 4 | 6 | As indicated |
| 5 | 6-12 | As indicated |
| 6+ | 12 | As indicated |

**References**

1) International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. J Clin Oncol. 1997;15:594-603.
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3) Evidence-based pragmatic guidelines for the follow-up of testicular cancer: optimising the detection of relapse. Br J Cancer. 2008;98:1894-1902.
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5) Siedel C, et al. Efficacy & safety of gemcitabine, oxplatin and paclitaxel in cisplatin-refractory germ cell cancer in routine care. Urol Oncol. 2016;34:167:e121-168.