Note: Consider Clinical Trials as treatment options for eligible patients.

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**Testicular Cancer**

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**CLINICAL PRESENTATION**

- Suspicious testicular mass

**INITIAL EVALUATION**

- History and physical
- Alpha-fetoprotein (AFP)
- Beta-hCG (quantitative)
- Sodium, potassium, chloride, CO₂, BUN, creatinine, magnesium, total bilirubin, AST, ALT, alkaline phosphatase, albumin, calcium, uric acid, phosphorus and total LDH
- Scrotal ultrasound
- Chest x-ray

**TUMOR HISTOLOGY**

- Solid intratesticular mass on ultrasound?  
  - Yes: Radical inguinal orchiectomy  
  - Evaluate contralateral testicle  
  - Discuss sperm banking
  - Nonseminomatous Germ Cell Tumor or Mixed Histology
  - Pure Seminoma (and normal AFP)
  - Non-germ Cell Testicular Tumors

- No: Consider other etiologies

**Note:** Consider Clinical Trials as treatment options for eligible patients.
**Testicular Cancer**  
Nonseminomatous Germ Cell Tumor (NSGCT): workup and clinical stage

---

**HISTOLOGY**

Mixed or Nonseminomatous Germ Cell Tumor Histology

- Repeat Alpha-fetoprotein (AFP), Beta-hCG, and LDH
- CT abdomen and pelvis
- CT chest if embryonal carcinoma-predominant or abnormal chest x-ray, or abnormal CT of abdomen/pelvis
- Bone scan if clinically indicated
- Brain imaging if clinically indicated

---

**FURTHER WORK-UP**

**Imaging negative for metastasis?**

- Yes
  - Tumor markers normalize with appropriate half-life?
    - Yes
      - Stage IA (no lymphovascular invasion)
    - No, Stage IS
      - **Consider emergency chemotherapy**

- No
  - Symptomatic from metastases (brain, lung, retroperitoneal mass)?
    - Yes
      - Stages: IIA, IIB, IIC, IIIA
    - No
      - Stage IIIB
        - **Intermediate Prognosis**
      - Stage IIIC
        - **Poor Prognosis**

**“Average risk Stage I”:**

- **“High risk Stage I”:** tumor has Lymphovascular invasion or Embryonal predominant or Stage IB

---

1. See Appendix A for International Classifications of Germ Cell Cancer
2. It is acceptable to administer emergency chemotherapy to selected patients with advanced metastatic nonseminomatous germ cell tumor on the basis of clinical presentation before orchectomy, and without a tissue diagnosis.

---

Note: Consider Clinical Trials as treatment options for eligible patients.
Testicular Cancer  Seminoma: workup and clinical stage

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Note: Consider Clinical Trials as treatment options for eligible patients.

HISTOLOGY  FURTHER WORK-UP

Pure Seminoma Histology

- Repeat Alpha-fetoprotein (AFP), Beta-hCG, and LDH
- CT abdomen and pelvis
- CT chest if abnormal chest x-ray or involved lymph nodes on CT of abdomen/pelvis
- Bone scan if clinically indicated
- Brain imaging if clinically indicated

AFP within normal limits?

Yes

Imaging negative for metastasis?

Yes

No

Suspect unrelated source of non-specific AFP?

Yes

No

Post-operative beta-hCG or LDH elevated?

Yes

Consider occult metastasis or consider PET scan

See Page 6

No

Clinical Stage I

See Page 6

“Intermediate Prognosis”\(^1\)

Extra-pulmonary metastases?

- Bone
- Liver
- Brain

Yes

No

Metastases in lymph nodes or lungs only “Good Prognosis”\(^1\)

Follow algorithm for Nonseminomatous Germ Cell Tumor

See Page 11

See Page 10

\(^1\) See Appendix A for International Classifications of Germ Cell Cancer
**Testicular Cancer**

**Clinical Stage I Nonseminoma: post-orchiectomy management**

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

### Tumor Markers

- **Any pT/Tx**
- **N0**
- **M0**
- **S1-3**

**Stage IS:**
- hCG or AFP elevated
- Metastatic workup negative

**High risk features?**

**Any pT/Tx**
- **N0**
- **M0**
- **S0**

**High Risk – probability of recurrence is approximately 50%**
- Consider sperm banking

**Average Risk – probability of recurrence is approximately 30%**
- Consider sperm banking

### Management Options

#### Consider management options:
- **1.** Surveillance (in compliant patients, pT1-2) or
- **2.** Adjuvant chemotherapy (1-2 cycles BEP³)

#### Consider management options:
- **1.** Surveillance (in compliant patients, pT1-2) or
- **2.** Prophylactic RPLND³
- **3.** Adjuvant chemotherapy (1-2 cycles BEP³)

#### Consider management options:
- **1.** Surveillance (in compliant patients) or
- **2.** Prophylactic RPLND³

---

1. High Risk Features (in the primary tumor):
   - a. Lymphovascular invasion
   - b. Invasion of tunica vaginalis
   - c. Invasion of spermatic cord or scrotum (pT3-4)
   - d. Embryonal carcinoma predominant

2. BEP = Bleomycin, Etoposide, and Cisplatin
3. RPLND = Retroperitoneal Lymph Node Dissection

---

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**Testicular Cancer**

**Clinical Stage I Pure Seminoma: post-orchiectomy management**

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

### TUMOR MARKERS

- Any pT/Tx
  - N0
  - M0
  - S1-3

- Stage IS: hCG or LDH elevated
  - Metastatic workup negative

- Primary tumor greater than 4 cm or pT3-4?
  - Yes
    - Consider sperm banking
  - No
    - Consider sperm banking

### MANAGEMENT OPTIONS

**Stage IS:**
- hCG or LDH elevated
- Metastatic workup negative
- Consider sperm banking

**Any of the following?**
- Horseshoe or pelvic kidney
- Inflammatory bowel disease
- Prior radiotherapy

- Yes
  - Consider combination chemotherapy for Stage IS; surveillance or single-dose carboplatin for all others
- No
  - See appropriate surveillance schedule based on treatment

**Primary tumor greater than 4 cm or pT3-4?**
- Yes
  - Radiotherapy to para-aortic with or without ipsilateral iliac lymph nodes or surveillance
- No
  - Consider sperm banking

**Most patients with clinical stage IA pure seminoma can be offered three options:**
- Surveillance in compliant patients who are committed to long term follow-up or
- Radiotherapy to para-aortic with or without ipsilateral iliac lymph nodes or
- Adjuvant carboplatin single dose, AUC = 7

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Testicular Cancer  
Stage IIA, IIB, IIC Nonseminoma: post-orchiectomy management

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

### TNM STAGE

- Any pT/Tx
- N1-3
- M0
- S0-1

### PRETREATMENT WORKUP

- Baseline pulmonary function testing
- Consider baseline audiometry testing
- Consider sperm banking

- Total LDH less than 1.5 times upper limit of normal AND
- hCG less than 5,000 mIU/mL AND
- AFP less than 1,000 ng/mL?

- Stage IIA AND
  - N0 (Markers not elevated) AND
  - Teratoma component in primary tumor
  - Not embryonal carcinoma predominant tumor?

  Yes
  - See Page 12 for post-chemotherapy management

  No
  - Intermediate Prognosis:
    - Total LDH 1.5-10 times upper limit of normal OR
    - hCG 5000-50,000 mIU/mL OR
    - AFP 1000-10,000 ng/mL

  - Poor Prognosis:
    - Total LDH greater than 10 times upper limit of normal OR
    - hCG greater than 50,000 mIU/mL OR
    - AFP greater than 10,000 ng/mL

- Bleomycin, etoposide, and cisplatin for 3 cycles OR
- Etoposide and cisplatin for 4 cycles

### TREATMENT

- Consider retroperitoneal lymph node dissection OR
- Bleomycin, etoposide, and cisplatin for 3 cycles OR
- Etoposide and cisplatin for 4 cycles

- Good Prognosis

- Baseline pulmonary function testing
- Consider baseline audiometry testing
- Consider sperm banking
Testicular Cancer  
Stage IIIA, IIIB Nonseminoma: post-orchiectomy management

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Note: Consider Clinical Trials as treatment options for eligible patients.

### TNM STAGE

- IIA and IIIB:
  - Any pT/Tx
  - Any N, M1a, S0-2, or N1-3, M0, S2 (May be good or intermediate prognosis by tumor markers)

### PRETREATMENT WORKUP

- Baseline pulmonary function testing
- Consider baseline audiometry testing
- Consider sperm banking
- Total LDH less than 1.5 times upper limit of normal AND
- hCG less than 5,000 mlu/mL AND
- AFP less than 1,000 ng/mL?

### TREATMENT

- Yes
  - Bleomycin, etoposide, and cisplatin for 3 cycles OR
  - Etoposide and cisplatin for 4 cycles

- No
  - Intermediate Prognosis:
    - Total LDH 1.5-10 times upper limit of normal OR
    - hCG 5000-50,000 mlu/mL OR
    - AFP 1000-10,000 ng/mL

- Clinical trial

See Page 12 for post-chemotherapy management

NOTE: See Page 9 for treatment of Stage IIIC

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Testicular Cancer

Stage IIIC (poor prognosis) Nonseminoma: Initial Management

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Note: Consider Clinical Trials as treatment options for eligible patients.

### TNM STAGE

#### IIIC, Poor Prognosis:
- Any pT/Tx, Any N, M1b\(^1\), Any S
- Total LDH greater than 10 times upper limit of normal OR
- hCG greater than 50,000 mIU/mL OR
- AFP greater than 10,000 ng/mL

---

#### TREATMENT

**Respiratory distress or symptomatic brain metastases?**

- **Yes**
  - Patient with respiratory distress
  - **Etoposide and Cisplatin (limit to 3 days in unstable patient)**
  - **Primary chemotherapy with or without surgery if clinically indicated**

- **No**
  - Patient with symptomatic brain metastases
  - **Clinical trial preferred OR**
  - Bleomycin, etoposide, and cisplatin OR
  - Etoposide, ifosfamide, and cisplatin OR
  - Paclitaxel, ifosfamide, and cisplatin

---

**Patient with respiratory distress or symptomatic brain metastases?**

- **Yes**
  - Baseline pulmonary function testing
  - Consider baseline audiometry testing
  - Consider sperm banking

- **No**
  - **Tumor markers normalized or plateau?**

---

**Tumor markers normalized or plateau?**

- **Yes**
  - Clinical trial preferred OR
  - Bleomycin, etoposide, cisplatin for 4 cycles

- **No**
  - Additional chemotherapy

---

\(^1\) M1b = Distant metastases other than to non-regional lymph nodes and lungs.

\(^2\) Plateau: The observed rate of decline in tumor markers should be compared to the expected serum half-lives of 5-7 days (AFP) and 2-3 days (beta-hCG). It is common to see a slower rate of decline after the second cycle of chemotherapy. A continued rate of decline that is much less than the expected half life and does not normalize should be interpreted as a plateau. The decision to stop chemotherapy should be based on clinical judgement, taking into consideration the clinical status of the patient, which of the markers are elevated, how elevated, and after ruling out potential sources of spurious elevation.

---

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Note: Consider Clinical Trials as treatment options for eligible patients.

**Testicular Cancer**  
**Seminoma: Treatment and Follow-up**

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### CLINICAL STAGE/TREATMENT

- **IA or IB**
  - Single-dose carboplatin
  - No adjuvant therapy
  - Radiotherapy

- **IS**
  - Radiotherapy

- **IIA or IIB**
  - Radiotherapy

- **IIC or III**
  - See management for advanced seminoma on Page 11

### FOLLOW-UP

- **IA or IB**
  - **History and physical, tumor markers (AFP, hCG, LDH), every 3 months for years 1 and 2, then every 4 months for year 3, then every 6 months for years 4-7, then annually for up to 10 years**
  - **CT abdomen/pelvis annually for years 1-3**
  - **Chest x-ray at alternate visits**

- **IS**
  - **History and physical, tumor markers (AFP, hCG, LDH), every 3 months for years 1 and 2, then every 4 months for year 3, then every 6 months for years 4-7, then annually for up to 10 years**
  - **CT abdomen/pelvis every 6 months for years 1-3, then annually for up to 10 years**
  - **Chest x-ray at alternate visits**

- **IIA or IIB**
  - **History and physical, tumor markers (AFP, hCG, LDH), chest x-ray every 4 months for year 1, then every 6 months for year 2, then annually for up to 10 years**
  - **CT abdomen/pelvis annually for years 1-3**

### RECURRENCE

- **Tumor recurrence**
  - **Treat according to histology and stage (post-orchiectomy management)**

---

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**Testicular Cancer Management for Advanced Seminoma**

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

---

**CLINICAL STAGE/TREATMENT**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIC or III</td>
<td><strong>Good risk</strong>&lt;br&gt;EP¹ for 4 cycles</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td><strong>Intermediate risk</strong>&lt;br&gt;IEP² for 4 cycles</td>
</tr>
</tbody>
</table>

**RESPONSE TO TREATMENT**

- **Complete response**
  - History and physical, tumor markers (AFP, hCG, LDH), abdominal/pelvic CT every 3 months for years 1 and 2, then every 4 months for year 3, then every 6 months for years 4-7, then annually for up to 10 years
  - Chest x-ray at alternate visits
  - PET scan as clinically indicated

- **Partial response**
  - PET
  - PET negative
  - PET positive or not feasible
  - Consider:
    - Radiotherapy
    - Biopsy
    - Surveillance if less than 3 cm

- **Progression**
  - See nonseminoma management of post-chemotherapy tumor recurrence³

---

¹EP = Etoposide and Cisplatin
²IEP = Ifosfamide, Etoposide, and Cisplatin
³Seminoma that is refractory to chemotherapy is rare and should be managed as nonseminoma
Consider Clinical Trials as treatment options for eligible patients.

**Testicular Cancer**  
Nonseminoma: Post-chemotherapy management

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**CILINICAL STAGE**  
**RESPONSE TO CHEMOTHERAPY**  
**FOLLOW-UP**

**IB (or high risk) IS**  
**Markers negative, Complete response**  
See Surveillance on Page 13

**IIA, IIB, IIC**  
**Markers negative, Complete response**  
Orchiectomy if not already done  
See Surveillance on Page 13

**Residual mass, Markers negative, or Plateau**

**Retroperitoneal lymph node dissection**

**Rising markers or Clinical progression**  
Salvage treatment  
See post-chemotherapy recurrence on Page 14

**IIIA, IIIB, IIIC**  
**Markers negative, Complete response**  
Orchiectomy if not already done  
See Surveillance on Page 13

**Partial response**

- Retroperitoneal lymph node dissection  
- Orchiectomy if not already done

**Rising markers, or Clinical progression**  
Salvage treatment  
See post-chemotherapy recurrence on Page 14

---

1 Plateau: The observed rate of decline in tumor markers should be compared to the expected serum half-lives of 5-7 days (AFP) and 2-3 days (beta-hCG). It is common to see a slower rate of decline after the second cycle of chemotherapy. A continued rate of decline that is much less than the expected half life and does not normalize should be interpreted as a plateau. The decision to stop chemotherapy should be based on clinical judgement, taking into consideration the clinical status of the patient, which of the markers are elevated, how elevated, and after ruling out potential sources of spurious elevation.
Table 1: IA, IB NONSEMINOMA SURVEILLANCE

<table>
<thead>
<tr>
<th>Year</th>
<th>Visits, markers, and Chest x-ray</th>
<th>Abdominal/pelvic CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Every 1-2 months</td>
<td>Every 4 months</td>
</tr>
<tr>
<td>2</td>
<td>Every 2-3 months</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>3</td>
<td>Every 3 months</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>4</td>
<td>Every 4 months</td>
<td>Every 8 months</td>
</tr>
<tr>
<td>5</td>
<td>Every 6 months</td>
<td>Annually</td>
</tr>
<tr>
<td>6 and above</td>
<td>Annually</td>
<td>Annually</td>
</tr>
</tbody>
</table>

Table 2: NONSEMINOMA FOLLOW-UP after Complete Response to Chemotherapy and/or Retroperitoneal Lymph Node Dissection (RPLND)

<table>
<thead>
<tr>
<th>Year</th>
<th>Visits, markers, and Chest x-ray</th>
<th>Abdominal/pelvic CT$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Every 2-3 months</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>2</td>
<td>Every 2-3 months</td>
<td>Every 6-12 months</td>
</tr>
<tr>
<td>3</td>
<td>Every 4 months</td>
<td>Annually</td>
</tr>
<tr>
<td>4</td>
<td>Every 6 months</td>
<td>Annually</td>
</tr>
<tr>
<td>5</td>
<td>Every 6-12 months</td>
<td>Annually</td>
</tr>
<tr>
<td>6 and above</td>
<td>Annually</td>
<td>Every 12-24 months</td>
</tr>
</tbody>
</table>

$^1$ CT scans for patients treated with chemotherapy. Baseline CT scan for patients status post RPLND.
Testicular Cancer  
Nonseminoma: Post-chemotherapy tumor recurrence

RESPONSE TO TREATMENT

Nonseminoma - Prior Chemotherapy

Incomplete response or first relapse

Salvage chemotherapy¹:
- TIP (preferred)
- VeIP
- POMB-ACE
- Consider HDC

Incomplete response and anatomically resectable

Resect all residual masses

Consider adjuvant chemotherapy if viable malignant tumor

Incomplete response that is unresectable or second relapse

Consider surgery if solitary site
- Second or subsequent salvage chemotherapy:
  - Clinical Trial (preferred)
  - Consider HDC
  - TIP
  - Gemcitabine and Oxaliplatin
  - POMB-ACE

Yes

Response?

Potential for salvage?

No

Palliative chemotherapy or radiotherapy
- Best supportive care

Yes

Third or subsequent relapse

No

Subsequent Treatment

Complete response and normalization of tumor markers

See Surveillance on Page 13

Note: Consider Clinical Trials as treatment options for eligible patients.

¹ TIP = Paclitaxel, Ifosfamide, Cisplatin
VeIP = Vinblastine, Ifosfamide, Cisplatin, Mesna
POMB-ACE = Cisplatin, Vincristine, Methotrexate and Bleomycin alternating with Actinomycin-D, Cyclophosphamide, and Etoposide
HDC = High-dose chemotherapy and autologous stem cell transplant

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### Appraoch:
Consider Clinical Trials as treatment options for eligible patients.

#### APPENDIX A: INTERNATIONAL CLASSIFICATIONS

<table>
<thead>
<tr>
<th></th>
<th>NONSEMINOMA</th>
<th>SEMINOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GOOD PROGNOSIS</strong></td>
<td>Testes/retroperitoneal primary AND No non-pulmonary visceral metastases AND</td>
<td>Any primary site AND No non-pulmonary visceral metastases AND</td>
</tr>
<tr>
<td>FEATURES</td>
<td>All Good Markers: • AFP less than 1,000 ng/mL AND • hCG less than 5,000 iu/L (1,000 ng/mL) AND • LDH less than 1.5 times upper limit of normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Testes/retroperitoneal primary AND No non-pulmonary visceral metastases AND</td>
<td>Any value</td>
</tr>
<tr>
<td><strong>INTERMEDIATE PROGNOSIS</strong></td>
<td>Mediastinal primary OR Non-pulmonary metastases</td>
<td>No patients classified as poor prognosis</td>
</tr>
<tr>
<td>FEATURES</td>
<td>Markers any of: • AFP greater than or equal to 1,000 and less than or equal to 10,000 ng/mL OR • hCG greater than or equal to 5,000 iu/L and less than 50,000 iu/L OR • LDH greater than or equal to 1.5 times normal and less than 10 times normal</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>POOR PROGNOSIS</strong></td>
<td>Mediastinal primary OR Non-pulmonary metastases</td>
<td>No patients classified as poor prognosis</td>
</tr>
<tr>
<td>FEATURES</td>
<td>Markers any of: • AFP greater than 10,000 ng/mL OR • hCG greater than or equal to 50,000 iu/L (10,000 ng/mL) OR • LDH greater than 10 times normal</td>
<td></td>
</tr>
</tbody>
</table>

1 From the International Germ Cell Consensus Classification from the International Germ Cell Cancer Collaborative Group
Testicular Cancer

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Note: Consider Clinical Trials as treatment options for eligible patients.

SUGGESTED READINGS


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DEVELOPMENT CREDITS

This practice consensus algorithm is based on majority expert opinion of the Genitourinary Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical, radiation and surgical oncologists.

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