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φ Diagnostic Radiology
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▷ Internal medicine
ω Urology
* Writing committee member

NCCN Guidelines Panel Disclosures
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Clinical Trials: The NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

To find clinical trials online at NCCN member institutions, click here: nccn.org/clinical_trials/physician.html

NCCN Categories of Evidence and Consensus: All recommendations are Category 2A unless otherwise specified.

See NCCN Categories of Evidence and Consensus

These guidelines are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The National Comprehensive Cancer Network makes no representations or warranties of any kind, regarding their content use or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2009.
Summary of the Guidelines updates

Summary of changes in the 1.2010 version of the Testicular Cancer Guidelines from the 2.2009 version include:

**Seminoma**
- **TEST-4**
  - Residual mass, positive PET scan, “salvage therapy’ was clarified as “second line chemotherapy”.
  - Follow-up abdominal/pelvic CT interval was clarified as “4 mo post surgery, then as indicated”.

**Nonseminoma**
- **TEST-11**
  - Surveillance after complete response to chemotherapy and/or RPLND and months between abdominal/pelvic CT:
    - For 6 + years, the interval between CT scans was changed from “12- 24 mo” to “as clinically indicated”.
    - Previous footnote was modified as, “CT scans apply only to patients treated with chemotherapy alone. For patients who are post RPLND, a postoperative baseline CT scan is recommended and additional CT scans as clinically indicated” and moved under surveillance for clarification.

- **TEST-12**
  - Second line therapy for favorable prognosis, “high-dose chemotherapy” was added as a treatment option.
  - Second line therapy, incomplete response or relapse, “high-dose chemotherapy” was modified by adding “if not previously given” to preferred.

- **TEST-A:**
  - Nonseminoma, “post-orchiectomy” was added to markers for clarification for each risk status

- **TEST-C**
  - High-dose chemotherapy regimens were added to the page.
WORKUP

Suspicous testicular mass
- H&P
- Alpha-fetoprotein (AFP)
- beta-hCG\(^a\)
- LDH
- Chemistry profile
- Chest x-ray
- Optional:
  - Testicular ultrasound

PRIMARY TREATMENT

- Discuss sperm banking
- Radical inguinal orchietomy
- Consider open inguinal biopsy of contralateral testis if:
  - Suspicious ultrasound for intratesticular abnormalities
  - Cryptorchid testis
  - Marked atrophy

PATHOLOGIC DIAGNOSIS

Seminoma (AFP negative; may have elevated beta-hCG)

Nonseminomatous germ cell tumor\(^b\)

\(^a\)Quantitative analysis of beta subunit.
\(^b\)This includes seminoma histology with elevated AFP.

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### Testicular Cancer

#### Seminoma

<table>
<thead>
<tr>
<th>CLINICAL STAGE</th>
<th>PRIMARY TREATMENT</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA, IB</td>
<td>Surveillance if: (category 1) • Horseshoe or pelvic kidney • Inflammatory bowel disease • Prior RT Consider surveillance if: (category 2B) • T1 or T2 histology in selected patients committed to long-term follow-up or Single agent carboplatin (category 1) (AUC=7 x 1 cycle or AUC=7 x 2 cycles) or RT: Infradiaphragmatic (20-30 Gy) to include para-aortic ± ipsilateral iliac nodes (category 1)</td>
<td>H&amp;P + chest x-ray, AFP, beta-hCG, LDH: every 3-4 mo for year 1, every 6 mo for year 2, then annually Pelvic CT annually for 3 years (for patients status post only para-aortic RT)</td>
</tr>
<tr>
<td>Stage IS</td>
<td>RT: Infradiaphragmatic (25-30 Gy) to include para-aortic ± ipsilateral iliac nodes</td>
<td>H&amp;P + chest x-ray, AFP, beta-hCG, LDH: every 3-4 mo for years 1-3, every 6 mo for years 4-7, then annually Abdominal/pelvic CT at each visit, chest x-ray at alternative visits (up to 10 y)</td>
</tr>
<tr>
<td>Stage IIA, IIB</td>
<td>RT: Infradiaphragmatic (35-40 Gy) to include para-aortic and ipsilateral iliac nodes or Consider primary chemotherapy: EP for 4 cycles for selected stage IIB patients</td>
<td>H&amp;P + chest x-ray, AFP, beta-hCG, LDH: every 3-4 mo for years 1-3, every 6 mo for year 4, then annually Abdominal CT at month 4 of year 1</td>
</tr>
<tr>
<td>Stage IIC, III</td>
<td>Primary chemotherapy: EP for 4 cycles (category 1) or BEP for 3 cycles (category 1)</td>
<td>See Post Chemotherapy Management and Follow-up (TEST-4)</td>
</tr>
<tr>
<td>Stage IIC, III</td>
<td>Intermediate risk f Primary chemotherapy: BEP for 4 cycles (category 1)</td>
<td>See Post Chemotherapy Management and Follow-up (TEST-4)</td>
</tr>
</tbody>
</table>

**Note:** All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

---

**EP = Etoposide/cisplatin**

**BEP = Bleomycin/etoposide/cisplatin**

---

**See Risk Classification (TEST-A).**

**See Primary Chemotherapy Regimens for Germ Cell Tumors (TEST-B).**
STAGE IIB, IIC, III AFTER PRIMARY TREATMENT WITH CHEMOTHERAPY

- Chest, abdominal, pelvic CT scan
- Serum tumor markers

**POST CHEMOTHERAPY MANAGEMENT**

- No residual mass and normal markers
  - Surveillance
  - C183

  - PET scan (preferred)
    - Negative
      - Surveillance
    - Positive
      - Consider surgery with biopsy or biopsy and second line chemotherapy or RT (category 2B)

  - PET scan not feasible
    - Residual mass (nodes > 3 cm on CT)
      - Surveillance or Surgery (category 2B) or RT (category 2B)
    - Residual mass (nodes ≤ 3 cm on CT)
      - Surveillance

  - Progressive disease (growing mass or rising markers)
    - See Second line Therapy for nonseminoma (TEST-12)
  - Residual mass and normal markers
    - Surveillance

**FOLLOW-UP**

- H&P + chest x-ray, AFP, beta-hCG, LDH: every 2 mo for year 1, every 3 mo for year 2, every 4 mo for year 3, every 6 mo for year 4, then annually
- Abdominal/pelvic CT 4 mo post surgery, then as indicated
- PET scan as clinically indicated
- Recurrence, See Second line Therapy (TEST-12)

- For persistent elevated beta-hCG which is not rising, repeat serial markers, testosterone suppression test and consider a PET scan
  - See Second Line or Subsequent Chemotherapy Regimens for Metastatic Germ Cell Tumors (TEST-C).

Note: All recommendations are category 2A unless otherwise indicated.
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Nonseminomatous germ cell tumor\textsuperscript{b}

\textbf{POSTDIAGNOSTIC WORKUP}

- Abdominal/pelvic CT
- Chest CT if:
  - Abnormal abdominal CT
  - Abnormal chest x-ray
- Repeat beta-hCG, LDH, AFP\textsuperscript{e}
- Brain MRI, if clinically indicated
- Bone scan, if clinically indicated
- Discuss sperm banking

\textbf{STAGING, DISCUSSION, REFERENCES}

\textsuperscript{b}This includes seminoma histology with elevated AFP.

\textsuperscript{e}Elevated values should be followed with repeated determination to allow precise staging.

\textsuperscript{i}Treatment may be initiated prior to histology for patients with rising markers and a deteriorating clinical situation.

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Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
<table>
<thead>
<tr>
<th>CLINICAL STAGE</th>
<th>PRIMARY TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA</td>
<td>Surveillance (in compliant patients) or Open nerve-sparing RPLND&lt;sup&gt;k&lt;/sup&gt; [See Postsurgical Management (TEST-9)]</td>
</tr>
<tr>
<td></td>
<td>See Follow-up for Nonseminoma (TEST-11)</td>
</tr>
<tr>
<td></td>
<td>See Postsurgical Management (TEST-9)</td>
</tr>
<tr>
<td>Stage IB</td>
<td>Persistent marker elevation</td>
</tr>
<tr>
<td></td>
<td>Primary chemotherapy:&lt;sup&gt;g&lt;/sup&gt; EP for 4 cycles or BEP for 3 cycles [See Follow-up for Nonseminoma (TEST-11)]</td>
</tr>
<tr>
<td></td>
<td>See Postchemotherapy Management (TEST-8)</td>
</tr>
<tr>
<td>Stage IS</td>
<td>Persistent marker elevation</td>
</tr>
<tr>
<td></td>
<td>Primary chemotherapy:&lt;sup&gt;g&lt;/sup&gt; EP for 4 cycles or BEP for 3 cycles</td>
</tr>
<tr>
<td></td>
<td>See Postchemotherapy Management (TEST-8)</td>
</tr>
</tbody>
</table>

The EP and BEP chemotherapy regimens have shown survival advantage in randomized clinical trials and may be considered as category 1 compared with other chemotherapy regimens.

EP = Etoposide/cisplatin
BEP = Bleomycin/etoposide/cisplatin

<sup>g</sup> See Primary Chemotherapy Regimens for Germ Cell Tumors (TEST-B).
<sup>k</sup> Retroperitoneal lymph node dissection (RPLND) is recommended within 4 weeks of CT scan and 7-10 days of markers (category 2B).
**CLINICAL STAGE**

**Stage IIA**

- Markers negative
  - Open nerve-sparing RPLND
  - or
  - Primary chemotherapy: EP for 4 cycles or BEP for 3 cycles

- Persistent marker elevation
  - Primary chemotherapy: EP for 4 cycles or BEP for 3 cycles

**Stage IIB**

- Markers negative
  - Lymph node metastases, within lymphatic drainage sites (landing zone positive)
    - Open nerve-sparing RPLND
    - or
    - Primary chemotherapy: EP for 4 cycles or BEP for 3 cycles

- Persistent marker elevation
  - Multifocal symptomatic lymph node metastases with aberrant lymphatic drainage
    - Primary chemotherapy: EP for 4 cycles or BEP for 3 cycles

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*See Primary Chemotherapy Regimens for Germ Cell Tumors (TEST-B).*

*See Postchemotherapy Management (TEST-8).*

*See Postchemotherapy Management (TEST-9).*

The EP and BEP chemotherapy regimens have shown survival advantage in randomized clinical trials and may be considered as category 1 compared with other chemotherapy regimens.

EP = Etoposide/cisplatin
BEP = Bleomycin/etoposide/cisplatin

k Retroperitoneal lymph node dissection (RPLND) is recommended within 4 weeks of CT scan and 7-10 days of markers (category 2B).
Stage IB, IS, IIA, IIB treated with primary chemotherapy

- Negative markers, residual mass
  - Open nerve-sparing RPLND$^k$
    or Surveillance (category 2B)

- Negative markers, Normal CT scan, no mass
  - Open nerve-sparing RPLND$^k$
    (category 2B)
    or Surveillance (category 2B)

See Follow-up for Nonseminoma (TEST-11)

$k$Retroperitoneal lymph node dissection (RPLND) is recommended within 4 weeks of CT scan and 7-10 days of markers (category 2B).

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POSTSURGICAL MANAGEMENT

Stage IA, IB, IIA, IIB treated with open nerve-sparing RPLND

pN0

Surveillance

Surveillance (preferred) or Chemotherapy: EP for 2 cycles or BEP for 2 cycles

Compliant

pN1

Noncompliant

Chemotherapy: EP for 2 cycles or BEP for 2 cycles

pN2

Compliant

Surveillance or Chemotherapy (preferred): EP for 2 cycles or BEP for 2 cycles

Noncompliant

Chemotherapy: EP for 2 cycles or BEP for 2 cycles

pN3

Chemotherapy: EP for 4 cycles or BEP for 3 cycles (preferred)

See Follow-up for Nonseminoma (TEST-11)

EP = Etoposide/cisplatin
BEP = Bleomycin/etoposide/cisplatin

See Primary Chemotherapy Regimens for Germ Cell Tumors (TEST-B).

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**Testicular Cancer**

**Nonseminoma**

**CLINICAL STAGE**

**Good risk**
- Stage IIC
- Stage IIIA
- Primary chemotherapy:
  - EP for 4 cycles or BEP for 3 cycles
- Complete response, negative markers
- Surveillance (category 2B) or Open nerve-sparing RPLND\(^k\) (category 2B)

**Intermediate risk**
- Stage IIIB
- Primary chemotherapy:
  - BEP for 4 cycles
- Clinical trial (preferred) or BEP for 4 cycles or VIP for 4 cycles in selected patients\(^m\)
- Partial response, residual masses\(^n\) with normal AFP and beta-hCG levels
- Surgical resection of all residual masses
- Teratoma or necrosis
- Residual embryonal, yolk sac, choriocarcinoma, or seminoma elements
- Chemotherapy for 2 cycles (EP\(^g\) or TIP\(^i\) or VIP\(^g\)/VeIP\(^i\))

**Poor risk**
- Stage IIIC
- Primary chemotherapy:
  - BEP for 4 cycles or VIP for 4 cycles in selected patients\(^m\)
- Incomplete response\(^n\)
- See Second Line Therapy (TEST-12)

**Brain metastases**
- Primary chemotherapy\(^g\) + RT ± surgery, if clinically indicated

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The EP and BEP chemotherapy regimens have shown survival advantage in randomized clinical trials and may be considered as category 1 compared with other chemotherapy regimens.

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\(^f\) See Risk Classification (TEST-A).
\(^g\) See Second Line or Subsequent Chemotherapy Regimens for Germ Cell Tumors (TEST-B).
\(^i\) See Second Line or Subsequent Chemotherapy Regimens for Metastatic Germ Cell Tumors (TEST-C).
\(^k\) Retroperitoneal lymph node dissection (RPLND) is recommended within 4 weeks of CT scan and 7-10 days of markers (category 2B).
\(^m\) Patients who may not tolerate bleomycin.
\(^n\) There is limited predictive value for PET scan for residual masses.

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EP = Etoposide/cisplatin
BEP = Bleomycin/etoposide/cisplatin
TIP = Paclitaxel/ifosfamide/cisplatin
VeIP = Vinblastine/ifosfamide/cisplatin
VIP = Etoposide/ifosfamide/cisplatin

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### FOLLOW-UP FOR NONSEMINOMA

#### Surveillance for Stage IA, IB Testicular Cancer

<table>
<thead>
<tr>
<th>Year</th>
<th>Months between visits, markers, chest x-ray</th>
<th>Months between abdominal/pelvic CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1-2</td>
<td>2-3</td>
</tr>
<tr>
<td>2</td>
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<td>3-4</td>
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<tr>
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<td>4</td>
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<tr>
<td>4</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>6+</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

#### Surveillance After Complete Response to Chemotherapy and/or RPLND

<table>
<thead>
<tr>
<th>Year</th>
<th>Months between visits, markers, chest x-ray (category 2B for chest x-ray frequency)</th>
<th>Months between abdominal/pelvic CT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-3</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>2-3</td>
<td>6-12</td>
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<tr>
<td>3</td>
<td>4</td>
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<td>4</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>6+</td>
<td>12</td>
<td>As clinically indicated</td>
</tr>
</tbody>
</table>

*CT scans apply only to patients treated with chemotherapy alone. For patients who are post RPLND, a postoperative baseline CT scan is recommended and additional CT scans as clinically indicated.

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**Recurrence, See Salvage Therapy (TEST-12)**
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See Second Line or Subsequent Chemotherapy Regimens for Germ Cell Tumors (TEST-C).
### RISK CLASSIFICATION

<table>
<thead>
<tr>
<th>Risk Status</th>
<th>Nonseminoma</th>
<th>Seminoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Good Risk</strong></td>
<td>Testicular or retroperitoneal primary tumor and</td>
<td>Any primary site and</td>
</tr>
<tr>
<td></td>
<td>No nonpulmonary visceral metastases</td>
<td>No nonpulmonary visceral metastases and</td>
</tr>
<tr>
<td></td>
<td>Post-orchiectomy markers- all of:</td>
<td>Normal AFP and</td>
</tr>
<tr>
<td></td>
<td>AFP &lt; 1,000 ng/mL</td>
<td>Any HCG</td>
</tr>
<tr>
<td></td>
<td>hCG &lt; 5,000 iu/L</td>
<td>Any LDH</td>
</tr>
<tr>
<td></td>
<td>LDH &lt; 1.5 x upper limit of normal</td>
<td></td>
</tr>
<tr>
<td><strong>Intermediate Risk</strong></td>
<td>Testicular or retroperitoneal primary tumor and</td>
<td>Any primary site and</td>
</tr>
<tr>
<td></td>
<td>No nonpulmonary visceral metastases</td>
<td>No nonpulmonary visceral metastases and</td>
</tr>
<tr>
<td></td>
<td>Post-orchiectomy markers- any of:</td>
<td>Normal AFP and</td>
</tr>
<tr>
<td></td>
<td>AFP 1,000-10,000 ng/mL</td>
<td>Any HCG</td>
</tr>
<tr>
<td></td>
<td>hCG 5,000-50,000 iu/L</td>
<td>Any LDH</td>
</tr>
<tr>
<td></td>
<td>LDH 1.5-10 x upper limit of normal</td>
<td></td>
</tr>
<tr>
<td><strong>Poor Risk</strong></td>
<td>Mediastinal primary tumor or</td>
<td>No patients classified as poor prognosis</td>
</tr>
<tr>
<td></td>
<td>Nonpulmonary visceral metastases or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-orchiectomy markers- any of:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AFP &gt; 10,000 ng/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hCG &gt; 50,000 iu/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>LDH &gt; 10 x upper limit of normal</td>
<td></td>
</tr>
</tbody>
</table>


1 Markers used for risk classification are post-orchiectomy.

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## PRIMARY CHEMOTHERAPY REGIMENS FOR GERM CELL TUMORS

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Etoposide</th>
<th>Cisplatin</th>
<th>Bleomycin</th>
<th>Repeat every 21 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>EP</td>
<td>100 mg/m²</td>
<td>20 mg/m²</td>
<td>30 units</td>
<td></td>
</tr>
<tr>
<td>BEP</td>
<td>100 mg/m²</td>
<td>20 mg/m²</td>
<td>30 units</td>
<td></td>
</tr>
<tr>
<td>VIP</td>
<td>75 mg/m²</td>
<td>20 mg/m²</td>
<td>1200 mg/m²</td>
<td></td>
</tr>
</tbody>
</table>

*Some NCCN Institutions administer bleomycin on a 2, 9, 16 schedule.


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SECOND LINE OR SUBSEQUENT CHEMOTHERAPY REGIMENS FOR
METASTATIC GERM CELL TUMORS

Conventional dose chemotherapy regimens

VeIP
Vinblastine 0.11 mg/kg IV Push on Days 1 - 2
Mesna 400 mg/m² IV every 8 hours on Days 1 - 5
Ifosfamide 1200 mg/m² IV on Days 1 - 5
Cisplatin 20 mg/m² IV on Days 1 - 5
Repeat every 21 days¹

TIP
Paclitaxel 250 mg/m² IV on Day 1
Ifosfamide 1500 mg/m² IV on Days 2 - 5
Mesna 500 mg/m² IV before ifosfamide, and then 4 and 8 hours after each ifosfamide dose on Days 2 - 5
Cisplatin 25 mg/m² IV on Days 2 - 5
Repeat every 21 days²

High-dose chemotherapy regimens

Carboplatin 700 mg/m² (Body Surface Area) IV
Etoposide 750 mg/m² IV
Administer 5, 4, and 3 days before peripheral blood stem cell infusion for 2 cycles⁶

Paclitaxel 200 mg/m² IV over 24 hours
Ifosfamide 2000 mg/m² over 4 hours with mesna protection
Repeat every 14 days for 2 cycles followed by
Carboplatin AUC 7 - 8 IV over 60 minutes Days 1 - 3
Etoposide 400 mg/m² IV Days 1 - 3
Administer with peripheral blood stem cell support at 14 - 21 day intervals for 3 cycles⁷

Palliative chemotherapy regimen

GEMOX
Gemcitabine 1000 mg/m² IV on Days 1 and 8 followed by
Oxaliplatin 130 mg/m² IV on Day 1
Repeat every 21 days³,⁴

or

Gemcitabine 1250 mg/m² IV on Days 1 and 8 followed by
Oxaliplatin 130 mg/m² IV on Day 1
Repeat every 21 days⁵

See Chemotherapy References (TEST-C 2 of 2)
SECOND LINE OR SUBSEQUENT CHEMOTHERAPY REGIMENS FOR METASTATIC GERM CELL TUMORS

CHEMOTHERAPY REFERENCES

## Staging

### Table 1

**AJCC Staging of Testis Tumors**

#### Primary Tumor (pT)

The extent of primary tumor is usually classified after radical orchiectomy, and for this reason, a *pathologic* stage is assigned.

<table>
<thead>
<tr>
<th>pTX</th>
<th>Primary tumor cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT0</td>
<td>No evidence of primary tumor (e.g. histologic scar in testis)</td>
</tr>
<tr>
<td>pTis</td>
<td>Intratubular germ-cell neoplasia (carcinoma in situ)</td>
</tr>
<tr>
<td>pT1</td>
<td>Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis</td>
</tr>
<tr>
<td>pT2</td>
<td>Tumor limited to the testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis</td>
</tr>
<tr>
<td>pT3</td>
<td>Tumor invades the spermatic cord with or without vascular/lymphatic invasion</td>
</tr>
<tr>
<td>pT4</td>
<td>Tumor invades the scrotum with or without vascular/lymphatic invasion</td>
</tr>
</tbody>
</table>

*pNote:* Except for pTis and pT4, extent of primary tumor is classified by radical orchiectomy. TX may be used for other categories in the absence of radical orchiectomy.

#### Regional Lymph Nodes (N)

<table>
<thead>
<tr>
<th>NX</th>
<th>Regional lymph nodes cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>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</td>
</tr>
<tr>
<td>N2</td>
<td>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 greater than 2 cm but not more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis with a lymph node mass more than 5 cm in greatest dimension</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>pNX</th>
<th>Regional lymph nodes cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>pN1</td>
<td>Metastasis with a lymph node mass, 2 cm or less in greatest dimension and less than or equal to 5 nodes positive, none more than 2 cm in greatest dimension</td>
</tr>
<tr>
<td>pN2</td>
<td>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 tumor</td>
</tr>
<tr>
<td>pN3</td>
<td>Metastasis with a lymph node mass more than 5 cm in greatest dimension</td>
</tr>
</tbody>
</table>

#### Distant Metastasis (M)

<table>
<thead>
<tr>
<th>MX</th>
<th>Distant metastasis cannot be assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>M1a</td>
<td>Non-regional nodal or pulmonary metastasis</td>
</tr>
<tr>
<td>M1b</td>
<td>Distant metastasis other than to non-regional lymph nodes and lungs</td>
</tr>
</tbody>
</table>

*Continued...*
<table>
<thead>
<tr>
<th>Serum Tumor Markers (S)</th>
<th>Stage Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>SX</td>
<td>Stage 0 pTis</td>
</tr>
<tr>
<td></td>
<td>N0  M0  S0</td>
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<tr>
<td>SO</td>
<td>Stage I pT1-4</td>
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<td>N0  M0  SX</td>
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<tr>
<td>S1</td>
<td>Stage IA pT1</td>
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<td></td>
<td>N0  M0  S0</td>
</tr>
<tr>
<td></td>
<td>Stage IB pT2</td>
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<td></td>
<td>Stage II pT3</td>
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<tr>
<td></td>
<td>N0  M0  S0</td>
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<tr>
<td></td>
<td>Stage II A pT4</td>
</tr>
<tr>
<td></td>
<td>N0  M0  S0</td>
</tr>
<tr>
<td>S2</td>
<td>Stage IS Any pT/TX N0  M0  S1-3</td>
</tr>
<tr>
<td></td>
<td>Stage II A Any pT/TX N1  M0  S0</td>
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<td></td>
<td>Stage II B Any pT/TX N2  M0  S0</td>
</tr>
<tr>
<td></td>
<td>Stage II C Any pT/TX N3  M0  S0</td>
</tr>
<tr>
<td></td>
<td>Stage III Any pT/TX N3  M0  S1</td>
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<tr>
<td></td>
<td>Stage III A Any pT/TX N1  M1  S0</td>
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<tr>
<td></td>
<td>Stage III B Any pT/TX N1  M1  S2</td>
</tr>
<tr>
<td></td>
<td>Stage III C Any pT/TX N1  M1  S3</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* N indicates the upper limit of normal for the LDH assay.

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NCCN Categories of Evidence and Consensus

Category 1: The recommendation is based on high-level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus.

Category 2A: The recommendation is based on lower-level evidence and there is uniform NCCN consensus.

Category 2B: The recommendation is based on lower-level evidence and there is nonuniform NCCN consensus (but no major disagreement).

Category 3: The recommendation is based on any level of evidence but reflects major disagreement.

All recommendations are category 2A unless otherwise noted.

Overview

An estimated 8,090 new cases of testicular cancer will be diagnosed in the United States in 2008. Germ cell tumors (GCTs) comprise 95% of malignant tumors arising in the testes. These tumors also occur occasionally in extragonadal primary sites, but they are still managed the same as testicular GCTs. Although GCTs are relatively uncommon tumors that comprise only 2% of all human malignancies, they constitute the most common solid tumor in men between the ages of 15 and 34 years. In addition, the worldwide incidence of these tumors has more than doubled in the past 40 years.

Several risk factors for GCT development have been identified, including prior history of a GCT, positive family history, cryptorchidism, testicular dysgenesis, and Klinefelter’s syndrome. GCTs are classified as seminoma or nonseminoma. Nonseminomatous tumors often include multiple cell types, including embryonal cell carcinoma, choriocarcinoma, yolk sac tumor, and teratoma. Teratomas are considered to be either mature or immature depending on whether adult-type differential cell types or partial somatic differentiation, similar to that present in the fetus, is found. Rarely, a teratoma histologically resembles a somatic cancer, such as sarcoma or adenocarcinoma, and is then referred to as a teratoma with malignant transformation.

The serum tumor markers alpha-fetoprotein (AFP), lactate dehydrogenase (LDH), and human chorionic gonadotropin (hCG) are critical in diagnosing the presence of tumors, determining prognosis, and assessing treatment outcome. These should be determined before, during, and after treatment and throughout the follow-up period. AFP is a serum tumor marker produced by nonseminomatous cells (embryonal carcinoma, yolk sac tumor) and may be seen at any stage. The approximate half-life of AFP is 5 to 7 days. A nonseminoma, therefore, is associated with elevated serum concentrations of AFP. An elevated serum concentration of hCG, which has a half-life of approximately 1–3 days, may also be present with seminomatous and nonseminomatous tumors. Seminomas are occasionally associated with an elevated serum concentration of hCG but not an elevated concentration of AFP.

Nonseminoma is the more clinically aggressive tumor. When both a seminoma and elements of a nonseminoma are present, management follows that for a nonseminoma. Therefore, the diagnosis of a seminoma is restricted to pure seminoma histology and a normal serum concentration of AFP.

More than 90% of patients diagnosed with GCTs are cured, including 70% to 80% of patients with advanced tumors who are treated with chemotherapy. A delay in diagnosis correlates with a higher stage at presentation. Standard therapy has been established at essentially all stages of management and must be closely followed to ensure the potential for cure.
Clinical Presentation
A painless solid testicular mass is pathognomonic for testicular tumor. More often, patients present with testicular discomfort or swelling suggestive of epididymitis or orchitis. A trial of antibiotics may be given in this circumstance, but persistent tenderness, swelling, or any palpable abnormality warrants further evaluation using testicular ultrasound. Although testicular ultrasound is optional if the diagnosis is obvious from the physical examination, it is performed in most instances to define the lesion.

If an intratesticular mass is identified, further evaluation includes measurement of the serum concentrations of alpha-fetoprotein (AFP), lactate dehydrogenase (LDH), and beta-human chorionic gonadotropin (beta-hCG) and a chest radiograph. Elevated values of beta-hCG, LDH, or AFP should be followed up with repeated tests to allow precise staging. Inguinal orchiectomy is considered the primary treatment for most patients who present with a suspicious testicular mass. If a GCT is found, an abdominopelvic computed tomographic (CT) scan is performed. Serum concentrations of hCG and LDH may be elevated in patients with seminoma. An elevated AFP level indicates nonseminoma, and the patient should be managed accordingly. A chest CT may be indicated if the abdominopelvic CT shows retroperitoneal adenopathy or the chest radiograph shows abnormal results. An open inguinal biopsy of the contralateral testis is not routinely performed, but can be considered when a cryptorchid testis or marked atrophy is present. Biopsy may also be considered if a suspicious intratesticular abnormality, such as a hypoechoic mass or macrocalcifications, is identified on ultrasound. In contrast, if microcalcifications without any other abnormality can be observed, testicular biopsy is not necessary. These studies, and others as clinically indicated, determine the clinical stage and direct patient management. If clinical signs of metastases are present, magnetic resonance imaging (MRI) of the brain and bone scanning are indicated.

Further management is dictated by histology, a diagnosis of seminoma or nonseminoma, and stage (ST-1). Patients should consider sperm banking before undergoing any therapeutic intervention that may compromise fertility, including radiation therapy, surgery, and chemotherapy.

Seminoma
The risk classification for seminoma is defined in TEST-A.

Stages IA and IB
Patients with disease in stages IA and IB are treated with radiation (20–30 Gy) to the infradiaphragmatic area, including para-aortic lymph nodes with or without radiation to the ipsilateral ileoinguinal nodes. Prophylaxis to the mediastinum is not provided, because relapse rarely occurs at this site. A single dose of carboplatin has also been investigated as an alternative to radiation therapy. Oliver et al reported on the results of a trial that randomized 1477 patients with stage 1 testicular cancer to undergo either radiotherapy or one injection of carboplatin. In the study, carboplatin was administered at a dose of AUC X 7 (AUC=area under the dose-time concentration curve). The doses were given intravenously and calculated by a formula based on the AUC estimate of drug disappearance from the body. The dose was calculated by the formula 7 X (glomerular filtration rate [GFR, mL/min] + 25) mg. With a median follow-up of 4 years, the relapse-free survivals for both groups were similar. Because late relapses and secondary germ cell tumors can occur beyond 5 and 10 years, the authors continued follow-up of these patients. The updated follow-up results of 1,148 patients were reported at the 2008 ASCO Annual Meeting. In an intent-to-treat analysis, the relapse free rates at 5 years were 94.7% for the carboplatin arm and 96% for the radiotherapy arm (hazard ratio, 1.25; P = .37). There was a significant difference in the rate of new germ cell tumors (2 on carboplatin versus 15 on radiation therapy), giving a hazard ratio (HR) of 0.22 (95% CI 0.05, 0.95 p=0.03). The
authors conclude that a single dose of carboplatin is less toxic and just as effective in preventing disease recurrence as adjuvant radiotherapy in men with stage I seminoma after orchiectomy. The NCCN panel now recommends single dose of carboplatin (category 1) as an alternative to radiation therapy for patients with stages IA and IB disease. Between 15% and 20% of patients with seminoma, experience relapse during surveillance if they do not undergo adjuvant radiation therapy after orchiectomy. The median time to relapse is approximately 12 months, but relapses can occur more than 5 years after orchiectomy.

Because both radiation and chemotherapy can potentially lead to late morbidity, surveillance for stage I seminoma is an option for management of stage I seminoma (category 1). In particular, observation may be offered to selected patients with T1 or T2 disease (category 2B) who are committed to long-term follow-up. Relapse occurring after observation essentially represents a prolongation in the lead time of treatment. Therefore, these patients are treated according to the stage at relapse. Patients for whom radiation therapy is generally not given include those with patients at higher risk for morbidity from radiation therapy. These patients include those with stages IA and IB with a horseshoe or pelvic kidney, with inflammatory bowel disease, and who underwent prior radiation therapy.

Follow up includes a history and physical, with measurement of serum tumor markers, performed every 3 to 4 months for the first year, and 6 months for the second year and annually thereafter. More intense follow-up is recommended for patients not undergoing radiation therapy - a history and physical, with measurement of serum tumor markers, should be performed every 3 to 4 months for the first 3 years, and 6 months for the next 3 years and annually thereafter. Annual pelvic CT is recommended for 3 years for patients who underwent para-aortic RT, whereas an abdominal/pelvic CT scan is recommended at each visit and chest x-ray at alternate visit for up to 10 years for those treated with a single dose of carboplatin or those under surveillance.

**Stage 1S**

Patients with stage IS are treated with radiation (25-30 Gy) to the infradiaphragmatic area, including para-aortic lymph nodes with or without radiation to the ipsilateral ilio inguinal nodes. Follow-up recommendations are similar to that of patients with stages 1A and 1B. If advanced, disseminated disease is suspected, than full course chemotherapy is administered according to guidelines for good risk GCT.

**Stages IIA and IIB**

Stage IIA is defined as disease measuring less than 2 cm in diameter on CT scan, and stage IIB as disease measuring 2 to 5 cm in maximum diameter. For patients with stage IIA or IIB disease, 35 to 40 Gy is administered to the infradiaphragmatic area, including para-aortic and ipsilateral iliac lymph nodes. As in the management of stage I disease, prophylactic mediastinal radiation therapy is not indicated. Surveillance is not an option for patients with stage IIA or IIB disease with relative contraindications for radiation. Instead, 4 courses of etoposide and cisplatin (EP) are recommended.

Follow-up for patients with stage IIA or IIB disease includes a history and physical, with measurement of serum tumor markers, should be performed every 3 to 4 months for the first 3 years, and 6 months for the fourth year and annually thereafter. Abdominal CT is recommended after 4 months during the first year.

**Stages IIC and III**

Patients with stage IIC or III disease are those considered at good or intermediate risk. All stage IIC and stage III disease is considered good risk except for stage III disease with non-pulmonary visceral
metastases, which is considered intermediate risk. Standard chemotherapy is used for both groups of patients, but for patients with good risk, either 4 cycles of EP are recommended or 3 cycles of bleomycin, etoposide, and cisplatin (BEP). In contrast, 4 cycles of BEP are recommended for those with intermediate risk disease. These options are all considered category 1 recommendations.\textsuperscript{9-12}

After initial chemotherapy, patients with stage IIC and III are evaluated with serum tumor markers and a CT scan of the chest abdomen and pelvis. Patients are then classified according to the presence or absence of a residual mass and the status of serum tumor markers. Patients with no residual mass and normal markers need no further treatment and undergo surveillance. In patients with a residual mass with normal markers, a positron emission tomography (PET) scan is recommended to assess for residual viable tumor.\textsuperscript{13} To reduce the incidence of false-positive results, the PET scan is typically performed no less than 6 weeks after completion of chemotherapy. Notably, granulomatous disease, such as sarcoid, is a frequent source of false-positive results. If the PET scan is negative, no further treatment is needed however, the patient should be observed closely for recurrence. If it is positive, then biopsy should be considered followed by surgical excision (category 2B), or salvage therapy. Alternatively, the patient can be treated with radiation therapy (category 2B).

For patients who cannot undergo a PET scan, post-chemotherapy management is based on CT scan findings. Controversy exists regarding optimal management when the residual mass is greater than 3 cm, because approximately 25\% of these patients have a viable seminoma or previously unrecognized nonseminoma.\textsuperscript{14} Options include surgery (category 2B), radiation therapy (category 2B), and observation.\textsuperscript{8} If surgery is selected, the procedure consists of resection of the residual mass or multiple biopsies. A full bilateral or modified retroperitoneal lymph node dissection (RPLND) is not performed because of its technical difficulty in patients with seminoma and because of extensive fibrosis, which may be associated with severe morbidity.\textsuperscript{15} If the residual mass is 3 cm or less, patients should undergo observation, which is detailed in TEST-4.

Recurrent disease is initially treated according to the stage at recurrence. Salvage therapy is recommended for patients with rising markers or a growing mass detected on CT scan. Salvage therapy for seminoma and nonseminoma is similar and is discussed further in section on nonseminomas.

Patients with seminoma arising from an extragonadal site, such as the mediastinum, are treated with standard chemotherapy regimens according to risk status.

Approximately 90\% of patients with advanced seminoma are cured with cisplatin-containing chemotherapy.\textsuperscript{16}

Nonseminoma

The risk classification for nonseminoma is defined in TEST-A. Stage-dependent treatment options after inguinal orchietomy include observation, chemotherapy, and RPLND. Although the timing of the RPLND may vary, most patients with nonseminoma will undergo an RPLND for either diagnostic or therapeutic purposes at some point during treatment. The major morbidity associated with bilateral dissection is retrograde ejaculation, resulting in infertility. Nerve-dissection techniques preserve antegrade ejaculation in 90\% of cases.\textsuperscript{17} Template dissections, which avoid the contralateral sympathetic chain, postganglionic sympathetic fibers, and hypogastric plexus, preserve ejaculation in approximately 80\% of patients. In general, an open nerve-sparing RPLND rather than a laparoscopic RPLND is recommended for therapeutic purposes. For example, a concern exists that a laparoscopic RPLND may result in false-negative results caused by inadequate sampling, and no published reports focus
on the therapeutic efficacy of a laparoscopic dissection. Because the recommended number of cycles of chemotherapy is based on the number of positive nodes identified, inadequate sampling may lead to partial treatment.\(^{18}\)

**Stage IA**

Two management options exist for patients with stage IA disease after orchiectomy: (1) surveillance (in compliant patients) or (2) open nerve-sparing RPLND.

The cure rate with either approach exceeds 95%. However, the high cure rate associated with surveillance depends on adherence to periodic follow-up examinations and subsequent chemotherapy for the 20% to 30% of patients who experience relapse. The follow-up examinations in those electing surveillance include an abdominopelvic CT scan every 2 to 3 months for the first year and every 3 to 4 months during the second year. Serum marker determination and the chest radiograph should be performed every 1 to 2 months during the first year and every 2 months during the second year. Noncompliant patients are treated with open RPLND.

The open nerve sparing RPLND is typically performed within 4 weeks of a CT scan and within 7 to 10 days of repeat serum marker testing to ensure accurate presurgical staging. If the dissected lymph nodes are not involved with a tumor (pN0), no adjuvant chemotherapy is given after open nerve sparing RPLND. However, if the resected lymph nodes involve tumor, the decision whether to use adjuvant chemotherapy is based on the degree of nodal involvement and the ability of the patient to comply with surveillance. Chemotherapy is preferred over surveillance in patients with pN2 or pN3 disease. Recommended regimens include either EP or BEP; 2 cycles of either regimen are recommended for patients with pN1 or pN2 disease, with 4 cycles of EP and 3 cycles of BEP (preferred) for patients with pN3 disease.

**Stage IB**

Open nerve sparing RPLND is a treatment option in patients with stage IB disease and the subsequent adjuvant therapy options are similar to those for stage IA. Chemotherapy with 2 cycles of BEP (category 2B) followed by open nerve sparing RPLND or surveillance is another option. Finally, surveillance alone may be offered to compliant patients with T2 disease (category 2B). Vascular invasion is a significant predictor of relapse when orchiectomy is followed by surveillance alone.\(^{2}\) Surveillance is generally not recommended for T2 disease with vascular invasion because of the 50% chance of relapse. Exceptions are made according to individual circumstances in compliant patients. When surveillance is opted in selected patients with T2 disease, both the patient and the physician must be compliant with follow-up recommendations.

**Stage IS**

Patients with stage IS disease exhibit a persistent elevation of markers but no radiographic evidence of disease. These patients are treated with standard chemotherapy with either 4 cycles of EP or 3 cycles of BEP. Either regimen is preferable to initial open nerve sparing RPLND because these patients nearly always have disseminated disease.\(^{19,20}\)

**Stages IIA and IIB**

Treatment for patients with stage IIA nonseminoma depends on serum tumor marker levels. When the levels of tumor markers are persistently elevated, patients are treated with chemotherapy with 4 cycles of EP or 3 cycles of BEP, followed by open nerve sparing RPLND or surveillance.
When the tumor marker levels are negative, 2 treatment options are available. Patients can undergo primary chemotherapy with 4 cycles of EP or 3 cycles of BEP (category 2B), followed by open nerve sparing RPLND or surveillance. This treatment is considered particularly appropriate if the patient has multifocal disease. Alternatively, the patient can undergo open nerve sparing RPLND followed by adjuvant chemotherapy or surveillance, depending on the number of positive lymph nodes identified and patient compliance. For example, surveillance is preferred in compliant patients with pN1 disease, whereas chemotherapy is preferred for pN2 disease and surveillance is not recommended for pN3 disease. Recommended chemotherapy consists of 2 cycles of BEP or EP, resulting in a nearly 100% relapse-free survival rate.

Treatment for patients with stage IIB disease depends on both tumor marker levels and radiographic findings. When tumor markers are negative, the CT findings determine the proper course of treatment. If abnormal radiographic findings are limited to sites within the lymphatic drainage (i.e., the landing zone), 2 management options are available. One option is to perform open nerve sparing RPLND and to consider adjuvant chemotherapy as described for patients with stage II A disease. The second option is to treat with primary chemotherapy with either 4 cycles of EP or 3 cycles of BEP, followed by open nerve sparing RPLND or surveillance. If metastatic disease (based on radiographic findings) is not confined to the lymphatic drainage (i.e., multifocal lymph node metastases outside the lymphatic drainage sites), similar primary chemotherapy is recommended and initial open RPLND is not.

**Stages IIC and III**

Patients with stage IIC and stage III disease are treated with primary chemotherapy regimens based on risk status. Also, patients with an extragonadal primary site, whether retroperitoneal or mediastinal, are treated with initial chemotherapy. Classifications of risk status emerged from chemotherapy research designed to decrease the toxicity of the regimens while maintaining maximal efficacy.

Initial chemotherapy combinations studied in the 1970s contained cisplatin, vinblastine, and bleomycin and achieved a complete response in 70% to 80% of patients with metastatic GCTs. These regimens were associated with serious adverse effects, including neuromuscular toxic effects, death from myelosuppression or bleomycin-induced pulmonary fibrosis, and Raynaud’s phenomenon.

The high cure rate and toxicity associated with cisplatin, vinblastine, and bleomycin regimens resulted in efforts to stratify patients and tailor therapy according to risk. Extent of disease and serum tumor markers were identified as important prognostic features, and models were developed to stratify patients into good- and poor-risk categories.

The International Germ Cell Cancer Consensus Classification was developed and incorporated the risk groups into the American Joint Committee on Cancer staging for GCTs (ST-1). This classification categorized patients as good-, intermediate-, or poor-risk.

**Good-Risk (Stages IIC and IIIA) Nonseminoma**

Treatment programs for good-risk GCTs were designed to decrease toxicity while maintaining maximal efficacy. Randomized clinical trials showed that this was achieved by substituting etoposide for vinblastine, and either eliminating or reducing the dose of bleomycin. Presently, 2 regimens are considered standard treatment programs in the United States for good-risk GCTs: 4 cycles of EP or 3 cycles of BEP. Either regimen is well tolerated and cures approximately 90% of patients with good risk.
Intermediate- (Stage IIIB) and Poor-Risk (Stage IIIC) Nonseminoma

Between 20% and 30% of all patients with metastatic GCTs are not cured with conventional cisplatin therapy. Poor prognostic features at diagnosis that can be used to identify these patients include nonpulmonary visceral metastases and high serum tumor marker concentrations or mediastinal primary site in patients with nonseminoma. After patients are rendered disease-free, standard observation is initiated. Patients who experience an incomplete response to first-line therapy or unresectable disease at surgery are treated with salvage therapy.

For patients with intermediate risk, the cure rate is approximately 70% for standard therapy with 4 cycles of BEP. In patients with poor-risk GCTs (stage IIIC), less than one half experience a durable complete response to 4 cycles of BEP, and therefore treatment in a clinical trial is preferred. The panel recommends 4 cycles of etoposide, ifosphamide, and cisplatin (VIP regimen) for patients who may not tolerate bleomycin.

Primary chemotherapy plus radiotherapy is indicated for patients in whom brain metastases are detected. If clinically indicated, surgery should also be performed.

Postchemotherapy Management for Stages IIC and IIIA–IIIC Nonseminoma

At the conclusion of induction chemotherapy, CT scans of the abdomen and pelvis are indicated, along with serum tumor marker assays. PET scans for residual disease have limited predictive value. If a complete response is found and the tumor markers are negative, 2 management options exist: surveillance (category 2B) or an open nerve sparing RPLND (category 2B).

If residual disease is found and the serum tumor markers have normalized, then all sites of residual disease are resected. If only necrotic debris or mature teratoma is encountered, no further therapy is necessary and standard observation is initiated. In the 15% of patients who have viable residual cancer, 2 cycles of chemotherapy (EP, VelP [paclitaxel/ifosphamide/cisplatin], or TIP [vinblastine/ifosphamide/cisplatin]) are administered.

Salvage Therapy

Patients who do not experience a complete response to first-line therapy are divided into those with a favorable or unfavorable prognosis. Favorable prognostic factors include a testicular primary site, prior complete response to first-line therapy, low levels of serum markers, and low-volume disease. Standard therapy for patients with these features is 4 cycles of cisplatin and ifosphamide combined with vinblastine or paclitaxel. Approximately 50% of patients treated with the vinblastine regimen experience a complete response, and 25% experience durable complete remission. If the patient experiences an incomplete response or relapses after salvage chemotherapy, high-dose chemotherapy with autologous stem cell support is the preferred option. Surgical salvage should be considered if a single site of metastasis is present and resectable. Other options are participation in a clinical trial or best supportive care. Third-line therapy with 2 cycles of high-dose carboplatin plus etoposide, with or without cyclophosphamide (or...
ifosfamide), results in a durable complete response in 15% to 20% of patients.33

For patients being considered for treatment with a high-dose program, prognostic factors are used in deciding treatment. Patients with a testicular primary site and rising markers during first-line therapy are considered for high-dose programs as second-line therapy. Predictors of poor outcome to high-dose carboplatin-containing chemotherapy include a high serum hCG concentration, mediastinal primary site, and insensitivity to cisplatin (absolute refractory disease).34 Patients with these features are generally spared the morbidity of this therapy and are considered for investigational therapy or surgical resection—particularly patients with a mediastinal primary or single site of metastasis.

For patients who do not experience complete response to high-dose therapy, the disease is nearly always incurable; the only exception is the rare patient with elevated serum tumor markers and a solitary site of metastasis (usually retroperitoneal) that undergoes surgical resection.35 All other patients should be considered for palliative outpatient chemotherapy or radiation therapy. A recommended palliative second line salvage therapy for patients with intensively pretreated, cisplatin-resistant, or refractory germ cell tumor is combination of gemcitabine with oxaliplatin (category 2A recommendation). This recommendation is based on data from phase II studies.36-38 These studies investigated the efficacy and the toxicity of gemcitabine and oxaliplatin (GEMOX) in patients with relapsed or cisplatin-refractory GCTs. Toxicity was found to be primarily hematological and generally manageable. The results showed that oxaliplatin-gemcitabine combination is a safe for patients with cisplatin-refractory testicular GCTs and may offer a chance of long-term survival.36-38
References


