

# TESTICULAR GERM CELL TUMOURS

Date Developed: April, 2005

Date Revised: May, 2009

The recommendations contained in this guideline are a consensus of the Alberta Provincial Genitourinary Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

## GUIDELINE GOALS AND OBJECTIVES

To outline management decisions for seminomas and nonseminoma germ cell tumors of the testicle.

## GUIDELINE QUESTIONS

- What are the appropriate management and follow up strategies for: seminomas?
- What are the appropriate management and follow up strategies for: non-seminomas?

## DEVELOPMENT PANEL

This **guideline** was reviewed and endorsed by the Alberta Provincial Genitourinary Tumour Team. Members of the Alberta Provincial Genitourinary Tumour Team include medical oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists. **Evidence** was selected and reviewed by a working group comprised of members from the Alberta Provincial Genitourinary Tumour Team and a Knowledge Management Specialist from the Guideline Utilization Resource Unit.

## SEARCH STRATEGY

Entries to Medline (April 2005 to February 2009) and clinical practice guideline databases were searched for updated evidence relevant to this topic.

## RECOMMENDATIONS

### Seminomas

#### *T1-4, N0, M0*

Indications	<ul style="list-style-type: none"> <li>• Patients staged as disease localized to testicle only post-radical orchidectomy</li> </ul>	
Staging <sup>1</sup>	<ul style="list-style-type: none"> <li>• CT thorax, abdomen, pelvis</li> <li>• Chest x-ray</li> </ul>	<ul style="list-style-type: none"> <li>• CBC</li> <li>• Creatinine</li> <li>• LDH</li> <li>• αFP</li> <li>• HCG</li> </ul>
Management	<ul style="list-style-type: none"> <li>• Therapeutic options include surveillance, radiotherapy, or adjuvant chemotherapy</li> <li>• Surveillance is indicated for the individual who will comply with surveillance.</li> <li>• Patients with a higher risk for recurrence (e.g. presence of a tumor &gt;4cm and/or rete testes involvement) should discuss risk factors with oncologist; these patients could be offered radiotherapy. However, even patients in the high risk group have a greater than 65% chance of being relapse free without adjuvant treatment, surveillance remains an excellent option.</li> <li>• Radiotherapy: 2000-2500 cGy/10-20 fractions, to para-aortic ± ipsilateral pelvis lymph nodes.</li> <li>• Chemotherapy can be considered in select cases (carboplatin AUC 7 x 2 courses)</li> <li>• Possibility of sperm banking</li> </ul>	

	<p><b>** Surveillance protocol:</b>          Years 1-2: P/E, tumor markers, CT abdomen/pelvis, CXR q 4 months.          Years 3-5: P/E, tumor markers, CXR, CT abdomen/pelvis q 6 months.          Years 6-10 follow-up annually: P/E, tumor markers, CXR, CT abdomen/pelvis</p>
F/U post –RT	<ul style="list-style-type: none"> <li>Evaluation post-radiotherapy or chemotherapy (re-staging), then              Years 1-5: P/E, tumor markers, CXR, CT abdomen/pelvis q 6 months.              Years 6-10: P/E, tumor markers, CXR, CT abdomen/pelvis q 12 months</li> </ul>
Duration of F/U	<ul style="list-style-type: none"> <li>F/U up to 10 years.</li> </ul> <p><i>Consideration of years 3-10 follow-up by family physician, clinical associate, or NP</i></p>

**T1-4, N1-2, M0**

Indications	<ul style="list-style-type: none"> <li>Patients with retroperitoneal lymph node disease &lt;5 cm in diameter</li> <li>Stage T1-4, N1, M0 (enlarged node &lt;2 cm)</li> <li>Stage T1-4, N2, M0 (enlarged node(s) 2 cm-5 cm)</li> </ul>
Staging <sup>1</sup>	<p><b>Staging</b></p> <ul style="list-style-type: none"> <li>Tumor markers (B-HCG, αFP, LDH)</li> <li>CT thorax, abdomen and pelvis</li> <li>Bone scan, if clinically indicated</li> </ul> <p><b>Preparation for Therapy</b></p> <ul style="list-style-type: none"> <li>Baseline CBC, Cr</li> <li>Discuss sperm banking</li> </ul>
Management	<p><b><u>External-beam radiotherapy</u></b><sup>2,3</sup></p> <ul style="list-style-type: none"> <li>Treatment volume should include PA nodes and ipsilateral pelvic nodes to 20-30 Gy.</li> <li>Boost grossly involved nodes by 10 Gy.</li> </ul> <p><b><u>Chemotherapy</u></b><sup>4,5,6</sup></p> <ul style="list-style-type: none"> <li>Consider BEP × 3 cycles when optimal radiotherapy not possible. EP x 4 cycles may be considered in patients with contraindication to bleomycin.</li> <li>Consider BEP × 3 cycles, in extensive stage IIB disease (same as stage IIC). EP x 4 cycles may be considered in patients with contraindication to bleomycin.</li> </ul> <p><b><u>Management of Residual Disease</u></b></p> <ul style="list-style-type: none"> <li>If the residual mass &gt; 3cm, consider PET scan. PET 4-12 weeks after d 21 of last cycle</li> <li>If PET scan is positive, decisions should be made using a multi-disciplinary approach. Due to the difficulty of surgical resection and radio-sensitivity of seminoma, consider biopsy and/or radiotherapy. If required, surgery can still be performed</li> </ul>

F/U	<p><u>Post-Therapy Evaluation</u></p> <ul style="list-style-type: none"> <li>• P/E tumor markers, and CXR (or CT Thorax)</li> <li>• CT Abdomen and Pelvis</li> </ul> <p><u>Management of Residual Disease</u></p> <ul style="list-style-type: none"> <li>• PET scan for evaluation of residual disease<sup>7,8,9,10</sup></li> <li>• Negative: Evaluation post completion of therapy with CT abdomen and pelvis</li> </ul> <p><u>Post-Therapy Surveillance</u></p> <ul style="list-style-type: none"> <li>▪ Year 1: P/E, markers, q 2-3 months. CXR, CT scan of area of known disease q 4-6 months; CT Abdomen and Pelvis q 6-12 months</li> <li>▪ Perform visits q 3-6 months for years 1-3, then annually thereafter Year 2: P/E, markers, q 3-4 months. CXR, CT scan of area of known disease q 6 months</li> <li>▪ Year 3: P/E, markers, CXR q 6 months. CT scan of area of known disease q 6 month</li> <li>▪ Year 4&amp;5: P/E, markers, CXR q 6-12 months. CT if clinically indicated</li> <li>▪ Year 6-10: P/E, markers, CXR q 12 months. CT if clinically indicated</li> </ul>
Duration of F/U	<ul style="list-style-type: none"> <li>• F/U up to 10 years.</li> </ul> <p><i>Consideration of years 3-10 follow-up by family physician, clinical associate, or NP</i></p>

**T1-4, N3, M0, T1-4, Nx, M1**

Indications	<ul style="list-style-type: none"> <li>• Patients with retro-peritoneal lymph node disease &gt;5 cm in diameter, or distant metastases</li> </ul>
Staging	<p><u>Staging</u></p> <ul style="list-style-type: none"> <li>• Tumor markers (B-HCG, αFP, LDH)</li> <li>• CT chest, abdomen, pelvis</li> <li>• CT head (if symptomatic)</li> <li>• Bone scan, CT brain, if clinically indicated</li> </ul> <p><u>Preparation for Therapy</u></p> <ul style="list-style-type: none"> <li>• Baseline CBC, biochemistry, LFTs, Alkaline phosphatase</li> <li>• Discuss sperm banking</li> </ul>
Management	<ul style="list-style-type: none"> <li>• Cisplatin-based combination chemotherapy:<sup>5,6,11</sup> <ul style="list-style-type: none"> <li>▪ Good risk as per IGCCC: BEP x 3. EP may be considered if bleomycin is contraindicated. Intermediate risk as per IGCCC: PEB x 4</li> </ul> </li> </ul> <p><u>Management of Residual Disease</u></p> <ul style="list-style-type: none"> <li>• If residual mass &gt; 3 cm, consider PET scan 4-12 weeks after d 21 of last cycle</li> <li>• If PET scan is positive, decisions should be made using a multi-disciplinary approach due to the difficulty of surgical resection and radio-sensitivity of seminoma, consider biopsy and/or radiotherapy. If required, surgery can still be performed in the future.<sup>12</sup></li> </ul>

F/U	<ul style="list-style-type: none"> <li>Evaluation post completion of therapy (restaging) and then: <ul style="list-style-type: none"> <li>Year 1: P/E, markers q 2-3 months. CXR, CT scan of area of known disease q 4-6 month based on IGCCC risk group</li> <li>Year 2: P/E, markers, months. CXR, CT scan of area of known disease q 6 months</li> <li>Year 3: P/E, markers, CXR q 6 months. CT scan of area of known disease q 6 months</li> <li>Year 4&amp;5: P/E, markers, CXR q 6-12 months. CT if clinically indicated</li> <li>Year 6-10: P/E, markers, CXR q 12 months. CT if clinically indicated</li> </ul> </li> </ul>
Duration of F/U	<ul style="list-style-type: none"> <li>Distant relapses occur in up to 50% of patients initially treated with RT for bulky stage II disease</li> <li>If relapses occur, they are more likely to happen early; therefore, close follow-up for 2 years, then as above for 6-10 years. F/U up to 10 years.</li> </ul> <p><i>Consideration of years 3-10 follow-up by family physician, clinical associate, or NP</i></p>

### Non-seminomas

#### T1-4, N0, M0, (S0)

Indications	<ul style="list-style-type: none"> <li>Patients staged as disease localized to testicle only and normalization of markers post radical orchidectomy (t ½ = 24-48 hours for HCG, 5-7 days for αFP)</li> </ul>		
Staging <sup>1</sup>	<table border="0"> <tr> <td> <ul style="list-style-type: none"> <li>Clinical history and physical</li> <li>CT abdomen/pelvis</li> <li>CXR or CT chest</li> </ul> </td> <td> <ul style="list-style-type: none"> <li>CBC</li> <li>LDH</li> <li>αFP</li> <li>HCG</li> </ul> </td> </tr> </table>	<ul style="list-style-type: none"> <li>Clinical history and physical</li> <li>CT abdomen/pelvis</li> <li>CXR or CT chest</li> </ul>	<ul style="list-style-type: none"> <li>CBC</li> <li>LDH</li> <li>αFP</li> <li>HCG</li> </ul>
<ul style="list-style-type: none"> <li>Clinical history and physical</li> <li>CT abdomen/pelvis</li> <li>CXR or CT chest</li> </ul>	<ul style="list-style-type: none"> <li>CBC</li> <li>LDH</li> <li>αFP</li> <li>HCG</li> </ul>		
Management	<ul style="list-style-type: none"> <li>Surveillance (see below) or template retroperitoneal lymph node dissection.</li> </ul> <p><i>The decision for surveillance should consider the higher risk of metastatic disease in patients with pure embryonal histology and lymph-vascular invasion</i></p> <p><i>RPLND (nerve sparing) as primary treatment for selected CS IIA patients with normal markers, ipsilateral LN within landing zone, and patient's preference or refusal of chemotherapy</i></p>		
F/U	<ul style="list-style-type: none"> <li>Surveillance protocol <ol style="list-style-type: none"> <li>Year 1: P/E, αFP, HCG; q 2-3 months, CXR, CT abdomen/pelvis q 4 months</li> <li>Year 2: P/E, αFP, HCG, q 4-6 months; CXR q 3 months; , CT abdomen/pelvis q 6 months</li> <li>Year 3: P/E, αFP, HCG, CXR q 4-6 months; repeat CT as clinically indicated</li> <li>Years 4-5: P/E, αFP, HCG, CXR q 12 months, repeat CT as clinically indicated</li> </ol> </li> <li>If pathologically node negative post lymph node dissection, the risk of relapse in the abdomen is very low. CT of the abdomen may be done at decreased frequency at physician's discretion</li> <li>If lymph node metastases are present and completely excised, adjuvant chemotherapy may be considered.</li> </ul>		

Duration of F/U	<ul style="list-style-type: none"> <li>As relapses are likely to occur early; close follow-up required for 2 years.</li> <li>Total duration of follow-up is 5 years.</li> </ul> <p><i>Consideration of follow-up in years 3 to 5 by family physician, clinical associate or NP</i></p>
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**T1-4, N0, M0 (S+), T1-4, N+, M0**

Indications	<ul style="list-style-type: none"> <li>cT1-4, N0, M0, (S+): failed marker normalization post radical orchidectomy for CS I disease</li> <li>cT1-4, N+, M0:             <ol style="list-style-type: none"> <li>relapsed disease in the retroperitoneal lymph nodes (RPLN) on surveillance post RIO</li> <li>cN+: RPLN+ on staging CT at presentation</li> <li>pT1-4, N+, M0: pN + post RPLND (see below)</li> </ol> </li> </ul>
Staging <sup>1</sup>	<p><i>Staging</i></p> <ul style="list-style-type: none"> <li>Tumor markers (B-HCG, αFP, LDH)</li> <li>CT Abdomen and Pelvis</li> <li>CT Thorax</li> <li>Bone scan, CT brain, if clinically indicated</li> </ul> <p><i>Preparation for Therapy</i></p> <ul style="list-style-type: none"> <li>Baseline CBC, biochemistry, LFTs, Alkaline phosphatase</li> <li>Discuss sperm banking</li> </ul>
Management	<ul style="list-style-type: none"> <li>Cisplatin-based combination chemotherapy.<sup>13,14,15</sup> <ul style="list-style-type: none"> <li>Good risk as per IGCCC: BEP x 3</li> <li>Intermediate/poor risk as per IGCCC: BEP x 4. VIP may be considered if there is contraindication to bleomycin or in patients at increased risk to bleomycin induced pulmonary toxicity</li> </ul> </li> <li>Consider complete bilateral RPLND if post chemotherapy RP masses &gt; 1.0 cm</li> <li>Role of consolidation chemotherapy is unclear. Post resection treatment depends on histology:             <ul style="list-style-type: none"> <li>Necrosis/fibrosis: 40-50% - observe</li> <li>Teratoma: 30-40% - observe</li> <li>Residual embryonal, yolk sac, chorio, or seminomatous elements: 15-20% - adjuvant chemotherapy with EPx2, TIPx2, or VIPx 2</li> </ul> </li> </ul> <p><i>**RPLND as primary treatment for selected CS IIA patients with normal markers, ipsilateral LN within landing zone, patient's preference or refusal of chemotherapy</i></p> <ul style="list-style-type: none"> <li>Treatment options following RPLND based on pathological staging (also include PSII following RPLND for CSI):             <ol style="list-style-type: none"> <li>PN0 or mature teratoma: observe</li> <li>PS IIA: observation preferred, may use adjuvant EP x 2 or BEP x 2</li> <li>PS IIB: adjuvant EP x 2 or BEP x 2</li> <li>PS IIC: primary chemotherapy as for good risk disease</li> </ol> </li> </ul>

F/U	<ul style="list-style-type: none"> <li>Evaluation post chemotherapy (restaging) and then:             <ol style="list-style-type: none"> <li>Year 1: P/E, markers q2-3 months, CXR, CT scan q 3-4 months of area of known disease based on IGCCC risk group</li> <li>Year 2: P/E, markers q 4-6 months, CXR, CT scan q 4-6 months of area of known disease based on IGCCC risk group</li> <li>Year 3: P/E, markers, CXR; q 6 months, CT if clinically indicated based on IGCCC risk group</li> <li>Years 4 &amp; 5: P/E, markers, CXR q 6-12 months with <math>\alpha</math>FP, HCG, CXR; CT if clinically indicated</li> </ol> </li> </ul>
Duration of F/U	<ul style="list-style-type: none"> <li>If relapses occur, they are likely to happen early, therefore, close follow-up for 2 years, then as above for a total of 5 years.</li> </ul> <p><i>Consideration of years 3-5 follow-up by family physician, clinical associate or NP.</i></p>

**T1-4, N1-3, M+**

Indications	<ul style="list-style-type: none"> <li>Patients presenting with distant metastatic disease</li> </ul>
Staging <sup>1</sup>	<p><i>Staging</i></p> <ul style="list-style-type: none"> <li>Tumor markers (B-HCG, <math>\alpha</math>FP, LDH)</li> <li>CT Abdomen and Pelvis</li> <li>CT Thorax</li> <li>Bone scan, CT brain, if clinically indicated</li> </ul> <p><i>Preparation for Therapy</i></p> <ul style="list-style-type: none"> <li>Baseline CBC, biochemistry, LFTs, Alkaline phosphatase</li> <li>Discuss sperm banking</li> </ul>
Management	<ul style="list-style-type: none"> <li>Cisplatin-based combination chemotherapy:             <ol style="list-style-type: none"> <li>Good risk as per IGCCC: PEB x 3 EP may be considered if contraindication to bleomycin.</li> <li>Intermediate/poor risk: PEB x 4. VIP may be considered if there is contraindication to bleomycin or in patients at increased risk to bleomycin induced pulmonary toxicity</li> </ol> </li> <li>Consider surgical resection of post chemotherapy RP masses &gt;1.0 cm or &lt;90% volume shrinkage from pre-chemo size with normalization of tumor markers if previously elevated</li> <li>Consider resection of any residual mass in mediastinum/lung. These sites are associated with higher risk of teratoma and viable NSGCT</li> <li>PET remains investigational due to high false negative rate and difficulty in detecting mature teratoma in studies</li> <li>Post resection treatment depends on histology:<sup>16</sup> <ol style="list-style-type: none"> <li>necrosis/fibrosis - observe</li> <li>Teratoma - observe</li> <li>residual embryonal, yolk sac, choriocarcinoma, or seminomatous elements - chemotherapy with EP x 2, TIP x 2, or VIP x 2</li> </ol> </li> </ul>

	d. Patients with brain metastases should be given WBRT (to be given up-front while chemo-therapy is ongoing) ± neurosurgical opinion for isolated disease
F/U	<ul style="list-style-type: none"> <li>Post chemotherapy surveillance (restaging) and then:           <ol style="list-style-type: none"> <li>Year 1: P/E, markers q 2 -3 months, CXR, CT scan q 3-4 months of area of known disease based in IGCCC risk group</li> <li>Year 2: P/E, markers q 4-6 months, CXR, CT scan q 4-6 months of area of known disease based on IGCCC risk group</li> <li>Year 3: P/E, markers, CXR q 4-6 months with αFP, HCG, CXR; CT if clinically indicated based on IGCCC risk group</li> <li>Years 4 &amp; 5: P/E, markers, CXR q 6-12 months with αFP, HCG, CXR; CT if clinically indicated</li> </ol> </li> </ul>
Duration of F/U	<ul style="list-style-type: none"> <li>If relapses occur, they are likely to happen early; therefore, close follow-up for 2 years then as above for a total of five years.</li> </ul> <p><i>Consideration of years 3-5 follow-up by family physician, clinical associate, or NP</i></p>

**Salvage Chemotherapy for Patients Relapsing Post-BEP Chemotherapy**<sup>17,18,19,20,21,22,23</sup>

Indications	<ul style="list-style-type: none"> <li>Patients with primary cisplatin refractory disease</li> <li>Patients presenting with relapse following cisplatin-based chemotherapy</li> <li>Consider the possibility of growing teratoma syndrome: these patients do not have relapsed viable germ cell tumor</li> </ul>														
Staging <sup>1</sup>	<ul style="list-style-type: none"> <li>CT chest/abdomen/pelvis</li> <li>CBC</li> <li>Chemistry profile including: electrolytes, creatinine, albumin, alkaline phosphatase, ALT, total protein, LDH, αFP, beta HCG</li> <li>CT head and bone scan only if clinically indicated</li> </ul>														
Management	<p>The following discussion is limited to patients who relapse within 2 years of completion of their primary therapy.</p> <ul style="list-style-type: none"> <li>Patients can be divided into good and poor risk based on the following clinical and laboratory parameters at the time of relapse:</li> </ul> <table border="1" data-bbox="409 1501 1425 1843"> <thead> <tr> <th>Good Risk</th> <th>Poor Risk</th> </tr> </thead> <tbody> <tr> <td>Gonadal Primary</td> <td>Non-gonadal primary</td> </tr> <tr> <td>Seminoma</td> <td>Non-seminoma</td> </tr> <tr> <td>CR or PR<sup>TM</sup> as best response to first-line chemotherapy</td> <td>PR/SD/PD as best response to first line chemotherapy</td> </tr> <tr> <td>Relapse &gt; 6 months after completion of first-line chemotherapy</td> <td>Relapse &lt; 6 months after completion of first-line chemotherapy</td> </tr> <tr> <td>αFP &lt; 100</td> <td>αFP &gt; 100</td> </tr> <tr> <td>HCG &lt; 1000</td> <td>HCG &gt; 1000</td> </tr> </tbody> </table>	Good Risk	Poor Risk	Gonadal Primary	Non-gonadal primary	Seminoma	Non-seminoma	CR or PR <sup>TM</sup> as best response to first-line chemotherapy	PR/SD/PD as best response to first line chemotherapy	Relapse > 6 months after completion of first-line chemotherapy	Relapse < 6 months after completion of first-line chemotherapy	αFP < 100	αFP > 100	HCG < 1000	HCG > 1000
Good Risk	Poor Risk														
Gonadal Primary	Non-gonadal primary														
Seminoma	Non-seminoma														
CR or PR <sup>TM</sup> as best response to first-line chemotherapy	PR/SD/PD as best response to first line chemotherapy														
Relapse > 6 months after completion of first-line chemotherapy	Relapse < 6 months after completion of first-line chemotherapy														
αFP < 100	αFP > 100														
HCG < 1000	HCG > 1000														

- There are two approaches to the management of patients relapsing after primary chemotherapy: standard dose salvage chemotherapy or high dose chemotherapy (HDCT) and peripheral blood stem cell transplantation (PBSCT). Given the paucity of randomized, clinical trials in this setting, conclusive evidence in favour of one treatment approach is not available.
- *Good Risk*: standard dose chemotherapy with paclitaxel, ifosfamide, cisplatin, (TIP) or vinblastine, ifosfamide, cisplatin (VIP) x 4 cycles. For VIP/TIP failures or relapses, HDCT and PBSCT can be performed. Patients relapsing after standard dose salvage chemotherapy and HDCT and PBSCT can be considered for palliative chemotherapy. Several agents have modest activity including gemcitabine, oxaliplatin, etoposide, and paclitaxel. Combination regimens such as gemcitabine/ oxaliplatin have activity but responses are short lived.
- *Poor Risk*: standard dose chemotherapy with TIP or VIP x 4 cycles. Patients who are poor risk at relapse should be considered early for HDCT and PBSCT. As these patients often deteriorate quickly, early consideration of HDCT and PBSCT should be considered as they may not be well enough to consider this treatment in the third line setting.
- High Dose Chemotherapy and PBSCT<sup>24,25</sup>
  - It is recommended that prior to HDCT and PBSCT, standard dose chemotherapy be administered to debulk the tumour and facilitate stem cell collection. One or two cycles of chemotherapy may be administered depending on how quickly the stem cell transplantation procedure can be undertaken. Regimens used to debulk may include VIP or TIP. Ifosfamide, carboplatin, and etoposide (ICE) have also been used.
  - The conditioning regimen for the transplant should consist of high dose carboplatin and etoposide. While there are no randomized studies defining the optimal regimen, excess toxicity has been noted when agents such as cyclophosphamide have been included in the conditioning regimen. It appears that the best results for HDCT and PBSCT have been seen when tandem transplants are performed.<sup>26</sup> Therefore, enough stem cells should be collected in order to conduct a tandem transplant.
- Adjunctive Care for All Patients
  - Patients with brain metastases should be given WBRT concurrently while chemotherapy is ongoing. Neurosurgical opinion for isolated metastases may also be considered.
  - After completion of all chemotherapy, resection of any residual masses should be performed.

Unique Clinical Situations:

- Late Relapses
  - A late relapse is defined as relapse occurring > 2 years after completion of primary chemotherapy.

- These patients have disease that is more chemotherapy resistant and immediate surgical resection of recurrent disease should be undertaken if feasible, irrespective of the level of tumour markers.
- Whether or not to offer chemotherapy post surgical resection in this setting is controversial but could be considered.
- TIP has been used in late relapsers who are not surgical candidates, with modest success.
- Non-Testicular Germ Cell Tumours(GCT)
  - Germ cell neoplasms may arise in a non-gonadal location. These include the retroperitoneum, mediastinum, and CNS (e.g. germinomas).
  - Patients presenting with masses in these anatomic locations should have a biopsy to confirm histology. Tumour marker assessment and staging investigations as per the guidelines for gonadal primaries should also be performed.
  - After appropriate work-up, patients should be classified into the appropriate risk category as per the IGCCC guidelines and treated as per the guidelines for their level of risk. All patients will require cisplatin-based chemotherapy.
- Retroperitoneal Primary GCT
  - Patients should be classified as good, intermediate or poor risk based on histology and clinical parameters as per IGCCC criteria and appropriate primary chemotherapy given.
  - After completion of chemotherapy, strong consideration for RPLND should be given.
  - If patients relapse after primary therapy, they should be treated as per the guidelines for relapsing patients presented earlier in this document
- Mediastinal Primary GCT
  - Patients should be classified as good, intermediate, or poor risk based on histology and clinical parameters as per IGCCC criteria and appropriate primary chemotherapy given.
  - After completion of chemotherapy, surgery to resect any residual mediastinal masses should be strongly considered.
  - Patients with mediastinal primary GCT who relapse have a poor prognosis. In transplant series, very few if any of these patients have successfully been salvaged with a transplant. Therefore, as a general rule, transplant should not be offered to patients with relapsed mediastinal primary GCT. However, depending on the results from salvage chemotherapy, patient performance status, individual factors, and the desire of the patient to pursue transplant, it may be considered but only after an honest discussion between the clinician and the patient such that the patient realizes that the chance of long term remission or cure are very low.
- CNS Germ Cell Neoplasms
  - Please refer to the CNS tumour guidelines.

**GLOSSARY OF ABBREVIATIONS**

<b>Acronym</b>	<b>Description</b>
áFP	alpha fetal protein
AFP	alpha fetal protein
ALT	alanine transaminase
AUC	area under the curve
BEP	bleomycin, etoposide, cisplatin
CBC	complete blood count
CBCD	CBC, differential
CNS	central nervous system
CS	clinical stage
CT	computed tomography
CXR	chest x-ray
EP	etoposide, cisplatin
GCT	germ cell tumors
Gy	unit of radiation dosage
HCG	human chorionic gonadotropin
HDCT	high dose chemotherapy
ICE	ifosamide, carboplatin, etoposide
IGCCC	International Germ Cell Consensus Classification
LDH	lactate dehydrogenase
LN	lymph node
NCCN	National Comprehensive Cancer Network
PBSCT	peripheral blood stem cell transplantation
P/E	physical evaluation
PE	cisplatin, etoposide
PEB	cisplatin, etoposide, bleomycin
PET	positron emission tomography
PR	partial response
PR/SD/PD	partial response, stable disease, progressive disease
RIO	Reviewers International Organization
RP	retroperitoneal
RPLN	retroperitoneal lymph node
RT	radiation therapy
TIP	paclitaxel, ifosfamide, cisplatin
VIP	vindesine, ifosfamide, platinum
WBRT	whole brain radiation therapy

## IMPLEMENTATION STRATEGY

- Present the guideline in the tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services website.

## EVALUATION STRATEGY

A formal review will be conducted in 2010, however if new evidence is brought forward before that time, the guideline will be changed accordingly.

## DECLARATION OF CONFLICT OF INTEREST

None of the authors of this guideline had any conflict of interest related to evidence or recommendations in this guideline.

## REFERENCES

- <sup>1</sup> IGCCCG. International Germ Cell Consensus Classification: A Prognostic Factor-Based Staging System for Metastatic Germ Cell Cancers. *JCO* 1997; 15(2):594-603.
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