Extragonadal Germ Cell Tumors Treatment (PDQ®): Treatment - Health Professional Information [NCI]

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General Information About Extragonadal Germ Cell Tumors

Incidence and Mortality
Extragonadal germ cell tumors are rare and account for only a small percentage of all germ cell tumors. However, the true incidence of these tumors may conceivably be higher than originally thought because of failure to diagnose them properly.

Related Summaries

- Ovarian Germ Cell Tumors Treatment
- Testicular Cancer Treatment

Cellular Classification of Extragonadal Germ Cell Tumors
Extragonadal germ cell tumors can be benign (teratoma) or malignant. The latter group can be divided into seminoma and nonseminoma germ cell tumors, which include the following:

- Embryonal carcinomas.
- Malignant teratomas.
- Endodermal sinus tumors.
- Choriocarcinomas.
- Mixed germ cell tumors.

Extragonadal germ cell tumors occur much more commonly in males than in females [1] and are usually seen in young adults. They are aggressive neoplasms and can arise virtually anywhere, but typically the site of origin is in the midline (mediastinum, retroperitoneum, or pineal gland). Gonadal origin should be excluded by careful testicular examination and ultrasound. The diagnosis can be difficult and should be considered in
any patient with a poorly defined epithelial malignancy, particularly young individuals with midline masses.[2,3]

An international germ cell tumor prognostic classification has been developed based on a retrospective analysis of 5,202 patients with metastatic nonseminomatus germ cell tumors and 660 patients with metastatic seminomatous germ cell tumors.[4] All patients received treatment with cisplatin-containing or carboplatin-containing therapy as their first chemotherapy course. The prognostic classification, shown below, was agreed on in early 1997 by all major clinical trial groups worldwide and should be used for the reporting of clinical trials' results of patients with extragonadal germ cell tumors.

**Good Prognosis**

**Nonseminoma**

- Testis/retroperitoneal primary
  - and
- No nonpulmonary visceral metastases
  - and
- Good markers - all of:
  -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 x upper limit of normal

56% of nonseminomas

5-year progression-free survival (PFS) rate of 89%

5-year survival rate of 92%

**Seminoma**

- Any primary site
  - and
- No nonpulmonary visceral metastases
  - and
- Normal AFP, any hCG, any LDH

90% of seminomas

5-year PFS rate of 82%

5-year survival rate of 86%

**Intermediate Prognosis**
Nonseminoma

• Testis/retroperitoneal primary
  and
• No nonpulmonary visceral metastases
  and
• Intermediate markers - any of:
  ◦ AFP 1,000 ng/mL or greater and 10,000 ng/mL or less
  or
  ◦ hCG 5,000 iu/L or greater and 50,000 iu/L or less
  or
  ◦ LDH 1.5 × N or greater and 10 × N or less

28% of nonseminomas
5-year PFS rate of 75%
5-year survival rate of 80%

Seminoma

• Any primary site
  and
• Nonpulmonary visceral metastases
  and
• Normal AFP, any hCG, any LDH
10% of seminomas
5-year PFS rate of 67%
5-year survival rate of 72%

Poor Prognosis

Nonseminoma

• Mediastinal primary
  or
• Nonpulmonary visceral metastases
  or
• Poor markers - any of:
  ◦ AFP greater than 10,000 ng/mL
  or
  ◦ hCG greater than 50,000 iu/L (1,000 ng/mL)
  or
- LDH greater than $10 \times$ upper limit of normal

16% of nonseminomas

5-year PFS rate of 41%

5-year survival rate of 48%

**Seminoma**

No patients are classified as poor prognosis.

**References:**


**Benign Teratoma**

Benign teratomas are treated with surgical excision only. These tumors are frequently very large, and the surgical procedure can be formidable.

**Current Clinical Trials**

Check the list of NCI-supported cancer clinical trials that are now accepting patients with benign teratoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI website.

**Seminoma**

The diagnosis of seminoma requires that the serum alpha fetoprotein (AFP) be normal, and no other germ cells be present. Management decisions in patients presenting with these tumors can sometimes be difficult.

As in testicular seminoma, these tumors are very radiosensitive. About 60% to 80% of patients will remain disease free after treatment with radiation therapy.[1] Craniospinal
radiation therapy for intracranial germinomas (the intracranial counterpart of seminoma) is associated with relapse-free and overall survival rates of 90% to 95% at 5 years, as evidenced in the GER-GPO-MAKEI-86/89 trial, for example.[2][Level of evidence: 3iiiA]

Initial chemotherapy with regimens used in nonseminoma testicular cancer is also very efficacious. Practically speaking, patients with localized relatively small tumors are usually treated initially with radiation, while those with very bulky tumors or nonlocalized tumors are treated with etoposide-based and cisplatin-based chemotherapy regimens.

As in testicular seminoma, many patients will be left with a residual mass posttreatment. If the residual mass is smaller than 3.0 cm, the majority of experts agree that observation is appropriate. In those with larger residual masses, some experts favor surgical excision while others favor observation.[3,4]

**Current Clinical Trials**

Check the list of NCI-supported cancer clinical trials that are now accepting patients with extragonadal seminoma. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI website.

**References:**


**Nonseminoma**

Patients with nonseminomas should receive chemotherapy at diagnosis. These patients tend to have a very large tumor volume at diagnosis and are usually symptomatic. Initial debulking surgery is rarely useful. Many high-risk patients qualify for clinical trials. Standard therapy would generally be considered to be four courses of BEP (bleomycin, etoposide, and cisplatin).[1,2]

A randomized study comparing four courses of BEP with four courses of VIP (etoposide, ifosfamide, and cisplatin) showed similar overall survival (OS) and time-to-treatment
failure for the two regimens in patients with advanced disseminated germ cell tumors who had not received previous chemotherapy.[3,4][Level of evidence: 1iiA] Of the 304 patients on this study, 66 patients had extragonadal primary tumors, and in this subset of patients, responses were similar on the two regimens. Hematologic toxic effects in OS were substantially worse with the VIP regimen than with the BEP regimen.

Patients with a residual mass after chemotherapy may achieve long-term disease-free survival after postchemotherapy surgery with resection of all residual disease.[5][Level of evidence: 3iiiDii] Patients with nonseminomatous extragonadal germ cell tumors who relapse after front-line chemotherapy generally have poor prognoses with poor responses to salvage chemotherapy regimens, including autologous bone marrow transplantation, that have had success for recurrent testicular cancer.[6,7,8] Such patients, therefore, are candidates for studies of new approaches.

**Mediastinal Nonseminoma**

Mediastinal nonsemionomas have certain unique aspects. The tumors are more frequent in individuals with Klinefelter syndrome and are associated with a risk of subsequent development of hematologic neoplasia that is not treatment related.[9,10] Approximately 50% of patients with mediastinal nonsemionomas will survive with appropriate management.[11] High risk is partially related to tumor bulk, to chemotherapy resistance, and to a predisposition to develop hematologic neoplasia and other nongerm cell malignancies. In an uncontrolled study, some patients with a postchemotherapy residual mediastinal mass achieved long-term disease-free survival after complete resection, even when serum tumor markers were elevated.[5][Level of evidence: 3iiiDii] Patient selection factors may play a role in these favorable outcomes.

**Retroperitoneal Nonseminoma**

The prognosis of retroperitoneal nonsemionoma is reasonably good and, similar to the situation with nodal metastasis from a testicular primary, is related to tumor volume.

**Current Clinical Trials**

Check the list of NCI-supported cancer clinical trials that are now accepting patients with malignant extragonadal non-seminomatous germ cell tumor. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI website.

**References:**

Recurrent or Refractory Extragonadal Germ Cell Tumors

A randomized, controlled trial compared conventional doses of salvage chemotherapy to high-dose chemotherapy with autologous marrow rescue in 263 patients with recurrent or refractory germ cell tumors. Of the 263 patients, 43 of whom had extragonadal primary tumors, more toxic effects and treatment-related deaths were seen in the high-dose arm without any improvement in response rate or overall survival.[1][Level of evidence: 1iiA]

Current Clinical Trials

Check the list of NCI-supported cancer clinical trials that are now accepting patients with recurrent extragonadal germ cell tumor. The list of clinical trials can be further narrowed by location, drug, intervention, and other criteria.

General information about clinical trials is also available from the NCI website.

References:


Changes to This Summary (02 / 25 / 2015)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

General Information About Extragonadal Germ Cell Tumors

Editorial changes were made to this section.

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About This PDQ Summary

Purpose of This Summary

This PDQ cancer information summary for health professionals provides comprehensive, peer-reviewed, evidence-based information about the treatment of extragonadal germ cell tumors. It is intended as a resource to inform and assist clinicians who care for cancer patients. It does not provide formal guidelines or recommendations for making health care decisions.

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The lead reviewer for Extragonadal Germ Cell Tumors Treatment is:

- Timothy Gilligan, MD (Cleveland Clinic Taussig Cancer Institute)

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