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Testicular Germ Cell Tumors

The American Society of Clinical Oncology offers the following clinical guidance on treatment alternatives during shortages of antineoplastic agents. Decisions should be based on specific goals of the therapy where evidence-based medicine has shown survival outcomes and life-extending benefits in both early and advanced stages. For more information on ASCO's general principles during drug shortages, please visit ASCO's Clinical Guidance page. For further consideration of ethical guidance, please visit ASCO's Ethical Principles and Implementation Strategies page.

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General Principle for Testicular Germ Cell Cancers

1. Regardless of disease stage or line of therapy, **curative intent is the goal of treatment for germ cell tumors (GCTs)**. For testicular GCTs, there are **no alternatives to cisplatin in the first-line setting.**
2. There are several settings in which there are no platinum alternatives. While non-platinum-containing regimens exist, based upon inferior outcomes with older regimens, the preference is for the patient to travel to an area where platinum is available or to obtain the drug for the individual patient.

1. Early-Stage Disease

A. SEMINOMA GERM CELL TUMOR (SGCT)

Recommended post-operative treatment after radical orchiectomy:

- For patients with stage IA or IB disease, active surveillance is the standard of care and is the preferred approach.
- For patients with stage IIA disease, radiotherapy is a standard of care but etoposide plus cisplatin (EP) can be given as an alternative.
- For stage IIB, radiotherapy or bleomycin, etoposide, and cisplatin (BEP) or EP are both considered standard options. For stage IIC, BEP, or EP are standard.

ALTERNATIVES:

- For patients with high-risk stage I disease who are not appropriate for active surveillance, adjuvant radiation or single-agent carboplatin (AUC 7) is an option.
- When platinum is not available for patients for whom active surveillance is a viable option, adjuvant radiation should be utilized.

- For patients with stage IIA disease, radiotherapy is standard of care, and the cisplatin shortage should not significantly impact care for most patients.
- For patients with stage IIB disease, because radiotherapy and chemotherapy are both considered standard options, patients without access to cisplatin should be offered radiotherapy especially those with non-bulky (≤ 3cm) disease.
- For patients with stage IIC disease without access to cisplatin, radiotherapy is an option. Radiotherapy can successfully treat some patients with stage IIC disease, but the incidence of relapse makes chemotherapy the preferred treatment option.

B. NONSEMINOMATOUS GERM CELL TUMOR (NSGCT)

Stage I

Recommended post-operative treatment after radical orchiectomy:

- Patients with low-risk stage I can be monitored using active surveillance. Patients with high-risk stage I disease should be treated with BEP or EP or surgery with retroperitoneal lymph node dissection (RPLND).
- Stage II patients should be treated with BEP or EP following RPLND.

ALTERNATIVES:

- Patients with high-risk Stage I disease can be monitored using active surveillance if cisplatin and RPLND is not available. There are no platinum alternatives for patients with stage IIB and IIC disease.

Relapsed low volume cisplatin-naïve disease

- RPLND (possibly followed by chemotherapy based upon pathologic results as per treatment of stage II disease above)

Relapsed low volume disease after one prior cycle of BEP with good-risk disease at relapse

Recommended systemic treatment:

- BEP (3 cycles)
- EP (4 cycles)

ALTERNATIVES

- There are no platinum alternatives for this setting (see General Principle #2).

Comment:

- During drug shortages, BEP x3 is preferred, except for patients with compromised pulmonary function, males with compromised renal function, and those over the age of 50 years.

Relapsed low volume disease after two prior cycles of BEP with good-risk disease at relapse

Recommended systemic treatment:

- EP (4 cycles)

ALTERNATIVES:

- There are no platinum alternatives for this setting (see General Principle #2).

Late-relapsing disease

- Recommended systemic treatments are the same as in those with early relapse disease described above.

ALTERNATIVES:

- Surgery is an alternative for patients whose relapsed disease is limited and who have normal serum tumor markers.

2. Metastatic Chemotherapy-Naïve Disease (stage III, seminomatous and nonseminomatous germ cell tumors)

Risk stratification should be performed based upon the International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification.

A. Good Risk Disease

Recommended treatment:

- For patients with metastatic disease, BEP or EP are recommended. BEP is preferred for those without significant lung disease, which requires only 3 cycles for patients with good-risk metastatic germ cell tumors (as opposed to 4 cycles of cisplatin with EP).

ALTERNATIVES:

- There are no platinum alternatives in this setting (see General Principle #2).

B. Intermediate- or poor-risk disease

Recommended systemic treatment:

- BEP (4 cycles)

ALTERNATIVES:

- For selected patients with poor-risk disease and significant pulmonary involvement or compromise, an alternative is VIP (4 cycles)
- There are no platinum alternatives for this setting (see General Principle #2).

3. Relapsed or Refractory Disease

Cisplatin-naïve disease

Recommended cisplatin-based chemotherapy as above based upon the International Germ Cell Cancer Collaborative Group (IGCCCG) risk classification.

Prior first-line chemotherapy

Recommended treatment:

- Clinical trial
- Vinblastine, ifosfamide and cisplatin (VeIP) (standard dose for 4 cycles)
- Paclitaxel, ifosfamide, and cisplatin (TIP) (standard dose for 4 cycles)

ALTERNATIVES:

- If carboplatin is available, high-dose chemotherapy with etoposide and carboplatin (EC) or paclitaxel/ifosfamide/carboplatin/etoposide. If neither cisplatin nor carboplatin are available, see General Principle #2.

Prior second-line chemotherapy

Recommended treatment:

- Clinical trial
- High-dose chemotherapy with carboplatin/etoposide or paclitaxel/ifosfamide/carboplatin/etoposide.

ALTERNATIVES:

- If carboplatin is not available and cisplatin was not used previously, conventional dose salvage chemotherapy (VeIP or TIP)
- If neither cisplatin nor carboplatin are available, see General Principle #2.

Prior high-dose chemotherapy

Recommended treatment:

- Clinical trial
- Conventional dose salvage chemotherapy (VeIP or TIP)

ALTERNATIVES:

- Best supportive care

4. Late-relapsing Disease

- Recommended systemic treatment are the same as in those with early relapse disease described above in a-d.
- High-dose chemotherapy with EC or paclitaxel/ifosfamide/carboplatin/etoposide plus autologous hematopoietic cell transplantation (HCT)

ALTERNATIVES:

- When carboplatin is not available, but cisplatin is available, standard dose cisplatin-based chemotherapy with a regimen such as TIP is preferred.
- When cisplatin is not available, but carboplatin is available, high dose chemotherapy (EC or paclitaxel/ifosfamide/carboplatin/etoposide) with autologous HCT is preferred at centers able to administer this approach.

Platinum-refractory disease

Recommended systemic treatment:

- High-dose chemotherapy plus autologous HCT
- TIP (standard dose) in those who have no previous exposure to paclitaxel or ifosfamide.

ALTERNATIVES:

- When carboplatin is not available, but cisplatin is available, standard dose cisplatin-based chemotherapy with a regimen such as TIP is preferred.
- When cisplatin is not available, but carboplatin is available, high dose chemotherapy (EC) with autologous HCT is preferred at centers able to administer this approach.
- If neither cisplatin nor carboplatin are available, see General Principle #2.

Treatment after progression on high-dose chemotherapy and HCT

Recommended treatment:

- Referral to center of excellence for an individualized and comprehensive care plan
- Clinical trial

ALTERNATIVES:

- Gemcitabine plus oxaliplatin
- Gemcitabine plus paclitaxel
- Paclitaxel, gemcitabine, and oxaliplatin
- Oral etoposide