TESTICULAR CANCER TREATMENT REGIMENS (Part 1 of 2)

Clinical Trials: The National Comprehensive Cancer Network recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Primary Chemotherapy for Germ Cell Tumors¹

Note: All recommendations are category 2A unless otherwise indicated.

REGIMEN	DOSING
Etoposide + cisplatin (EP) ^{2,a}	Days 1-5: Etoposide 100mg/m ² IV + cisplatin 20mg/m ² IV. Repeat cycle every 21 days.
Bleomycin + etoposide + cisplatin (BEP) ³	Days 1–5: Cisplatin 20mg/m ² IV + etoposide 100mg/m ² IV Days 1, 8, and 15 OR Days 2, 9, and 16: Bleomycin 30 units IV weekly. Repeat cycle every 21 days.
Etoposide + ifosfamide + cisplatin + mesna (VIP) ^{4,b,c}	Day 1 (before ifosfamide): Mesna 120mg/m ² by slow IV push Days 1–5: Etoposide 75mg/m ² IV + mesna 1,200mg/m ² continuous IV infusion + ifosfamide 1,200mg/m ² IV + cisplatin 20mg/m ² . Repeat cycle every 21 days.

Second-Line Chemotherapy For Metastatic Germ Cell Tumors¹

Conventional-dose Chemotherapy Regimens

Vinblastine + ifosfamide + cisplatin + mesna (VeIP) ^{5,c}	Days 1–2: Vinblastine 0.11mg/kg IV push; plus Days 1–5: Ifosfamide 1,200mg/m ² IV + cisplatin 20mg/m ² IV + mesna 240mg/m ² IV over 15 minutes before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose. Repeat cycle every 3 weeks.
Paclitaxel + ifosfamide + mesna + cisplatin (TIP) ^{6,c}	Day 1: Paclitaxel 250mg/m ² IV Days 2-5: Ifosfamide 1,500mg/m ² IV + cisplatin 25mg/m ² IV + mesna 300mg/m ² IV over 15 minutes before ifosfamide, then at 4 and 8 hours from the start of each ifosfamide dose. Repeat cycle every 3 weeks.
High-dose Chemotherapy Regimens	
Carboplatin + etoposide ⁷	Carboplatin 700mg/m ² (body surface area) IV + etoposide 750mg/m ² IV. Administer 5, 4, and 3 days before peripheral blood stem cell infusion for 2 cycles.
Paclitaxel + ifosfamide + mesna + carboplatin + etoposide ⁸	Day 1: Paclitaxel 200mg/m ² IV over 24 hours Days 2-4: Ifosfamide 2,000mg/m ² over 4 hours with mesna protection Repeat every 14 days for 2 cycles; <u>followed by</u> Days 1-3: Carboplatin AUC 7-8mg • min/mL IV over 60 minutes + etoposide 400mg/m ² IV.

Administer with peripheral blood stem cell support at 14- to 21-day intervals for 3 cycles.

Third-line Chemotherapy For Metastatic Germ Cell Tumors¹

Palliative Chemotherapy Regimens

Gemcitabine + oxaliplatin ⁹⁻¹¹	Days 1 and 8: Gemcitabine 1,000mg/m ² IV, <u>plus</u> Day 1: Oxaliplatin 130mg/m ² IV Repeat cycle every 3 weeks. OR Days 1 and 8: Gemcitabine 1,250mg/m ² IV, <u>plus</u> Day 1: Oxaliplatin 130mg/m ² IV. Repeat cycle every 3 weeks.
Gemcitabine + paclitaxel ^{12,13}	Days 1, 8, and 15: Gemcitabine 1,000mg/m ² IV over 30 minutes + paclitaxel 100mg/m ² IV over 1 hour. Repeat every 4 weeks for a maximum of 6 cycles.
Gemcitabine + paclitaxel + oxaliplatin ¹⁴	Days 1 and 8: Gemcitabine 800mg/m ² IV + paclitaxel 80mg/m ² IV Day 1: Oxaliplatin 130mg/m ² IV. Repeat every 3 weeks for at least 2 cycles.
Etoposide ¹⁵	Etoposlde 50mg/m ² orally daily until progression or toxicity.
Pembrolizumab (for MSI-H/dMMR tumors) ^{16,17}	Day 1: Pembrolizumab 10mg/kg IV. Repeat cycle every 2 weeks.

continued

TESTICULAR CANCER TREATMENT REGIMENS (Part 2 of 2)

Notes

- ^a Option only for good-risk patients, patients with pathologic stage II disease, and patients with viable germ cell tumors (GCT) at surgery following first-line chemotherapy.
- ^b Option only for intermediate or poor-risk patients or patients with viable GCT at surgery following first-line chemotherapy.
- ^c These regimens are high risk for febrile neutropenia and granulocyte colony-stimulating factors (G-CSFs) should be used.

References

- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology[™]. Testicular Cancer. v 1.2018. Available at: http://www.nccn.org/professionals/physician_gls/ pdf/testicular.pdf. Accessed January 18, 2018.
- Xiao H, Mazumdar M, Bajorin DF, et al. Long-term follow-up of patients with good-risk germ cell tumors treated with etoposide and cisplatin. J Clin Oncol. 1997;15(7):2553–2558.
- Saxman SB, Finch D, Gonin R, Einhorn LH. Long-term follow-up of a phase III study of three versus four cycles of bleomycin, etoposide, and cisplatin in favorable-prognosis germ-cell tumors: the Indiana University experience. J Clin Oncol. 1998;16(2):702–706.
- Nichols CR, Catalano PJ, Crawford ED, et al. Randomized comparison of cisplatin and etoposide and either bleomycin or ifosfamide in treatment of advanced disseminated germ cell tumors: an Eastern Cooperative Oncology Group, Southwest Oncology Group, and Cancer and Leukemia Group B Study. J Clin Oncol. 1998;16(4):1287-1293.
- Loehrer PJ Sr, Lauer R, Roth BJ, et al. Salvage therapy in recurrent germ cell cancer: ifosfamide and cisplatin plus either vinblastine or etoposide. *Ann Intern Med.* 1988;109(7): 540–546. Erratum in: *Ann Intern Med.* 1988;109(10):846.
- Kondagunta GV, Bacik J, Donadio A, et al. Combination of paclitaxel, ifosfamide, and cisplatin is an effective second-line therapy for patients with relapsed testicular germ cell tumors. *J Clin Oncol.* 2005;23(27):6549–6555.
- Einhorn LH, Williams SD, Chamness A, et al. High-dose chemotherapy and stem-cell rescue for metastatic germ-cell tumors. *N Engl J Med.* 2007;357(4):340–348.
- Feldman DR, Sheinfeld J, Bajorin DF, et al. TI-CE high-dose chemotherapy for patients with previously treated germ cell tumors: results and prognostic factor analysis. J Clin Oncol. 2010; 28(10):1706–1713. Erratum in: J Clin Oncol. 2010; 28(34):5126.

- Pectasides D, Pectasides M, Farmakis D, et al. Gemcitabine and oxaliplatin (GEMOX) in patients with cisplatin-refractory germ cell tumors: a phase II study. Ann Oncol. 2004;15(3):493–497.
- Kollmannsberger C, Beyer J, Liersch R, et al. Combination chemotherapy with gemcitabine plus oxaliplatin in patients with intensively pretreated or refractory germ cell cancer: a study of the German Testicular Cancer Study Group. J Clin Oncol. 2004;22(1):108–114.
- De Giorgi U, Rosti G, Aieta M, et al. Phase II study of oxaliplatin and gemcitabine salvage chemotherapy in patients with cisplatin-refractory nonseminomatous germ cell tumor. *Eur Urol.* 2006;50(5):1032–1039.
- Einhorn LH, Brames MJ, Juliar B, Williams SD. Phase II study of paclitaxel plus gemcitabine salvage chemotherapy for germ cell tumors after progression following high-dose chemotherapy with tandem transplant. J Clin Oncol. 2007; 25(5):513–516.
- Mulherin B, Brames MJ, Einhorn L. Long-term survival with paclitaxel and gemcitabine for germ cell tumors after progression following high-dose chemotherapy with tandem transplants. J Clin Oncol. 2011;29(Suppl):Abstract 4562.
- Bokemeyer C, Oechsle K, Honecker F, et al. Combination chemotherapy with gemcitabine, oxaliplatin, and paclitaxel in patients with cisplatin-refractory or multiply relapsed germ-cell tumors: a study of the German Testicular Cancer Study Group. Ann Oncol. 2008;19(3):448-453.
- Miller JC, Einhorn LH. Phase II study of daily oral etoposide in refractory germ cell tumors. Semin Oncol. 1990;17 (1 Supp 2):36–39.
- Le DT, Durham JN, Smith KN, et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade. Science. 2017;357:409–413.
- Le DT, Uram JN, Wang H, et al. PD-1 blockade in tumors with mismatch-repair deficiency. N Engl J Med. 2015;372:2509–2520.

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