BONE CANCER CHEMOTHERAPY REGIMENS Part 1 of 2

The selection, dosing, and administration of anti-cancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anti-cancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The chemotherapy regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

GENERAL TREATMENT NOTES[1]

- Chemotherapy for Ewing's sarcoma and osteosarcoma should include growth factor support
- Conventional chrondosarcoma has no known standard chemotherapy options
- Mesenchymal chrondrosarcoma: Follow Ewing's sarcoma regimens
- Malignant fibrous histiocytoma (MFH) of bone: follow osteosarcoma regimens

REGIMEN	DOSING
EWING'S SARCOMA AND MESENCHYMAL CHONDROSARCOMA	
FIRST-LINE (Primary/Neoadjuvant/Adjuvant) OR PRIMARY THERAPY FOR METASTATIC DISEASE AT INITIAL PRESENTATION	
VAC/IE (vincristine [Oncovin] + doxorubicin [Adriamycin] + cyclophosphamide [Cytoxan] alternating with ifosfamide [Ifex] + etoposide [Toposar, VePesid, Etopophos VP-16][1,2]	Alternating VAC and IE cycles; repeat each cycle every 21 days for 17 cycles *VAC cycles* **Day 1:** Vincristine 2mg/m^2 (max 2mg) IV + doxorubicin 75mg/m^2 IV bolus + cyclophosphamide 1,200mg/m^2 IV. Actinomycin D can be substituted for doxorubicin if there are concerns regarding cardiotoxicity[2]; actinomycin D 1.25mg/m^2 IV can be substituted for doxorubicin when a total doxorubicin dose of 375mg/m^2 is reached. *IE cycles* **Days 1-5:** Ifosfamide 1,800mg/m^2 IV + etoposide 100mg/m^2 IV
VAI (vincristine + ifosfamide + actinomycin D [dactinomycin; Cosmegen] + doxorubicin)[1,3]	**Day 1:** Vincristine 1.5mg/m^2 IV, plus **Days 1–3:** Ifosfamide 2,000mg/m^2 IV, plus **Days 1,3, and 5:** Actinomycin 0.5mg/m^2 IV, plus **Days 2, 4:** Doxorubicin 30mg/m^2 IV Repeat cycle every 21 days
VIDE (vincristine + ifosfamide + doxorubicin + etoposide)[1,4]	**Day 1:** Vincristine 1.4mg/m^2 (max 2mg), plus **Days 1–3:** Doxorubicin 20mg/m^2 IV + ifosfamide 3mg/m^2 IV + mesna 3g/m^2 continuous IV infusion + etoposide 150mg/m^2 IV Repeat cycle every 21 days for up to 6 cycles
CVD (cyclophosphamide [Cytoxan] + vincristine + doxorubicin or actinomycin D)[1,5]	**Day 1:** Vincristine 2mg/m2 IV + cyclophosphamide 1,200mg/m^2 + doxorubicin 75mg/m^2 (the first 5 cycles) or actinomycin D 1.25mg/m^2 IV (subsequent cycles) Repeat cycle every 21 days for 17 cycles
SECOND-LINE THERAPY (Relapsed or Refractory Disease)	
Cyclophosphamide + topotecan (Hycamtin)[1,6]	**Days 1–5:** Cyclophosphamide 250mg/m^2/day IV + topotecan 0.75mg/m^2/day IV Repeat cycle every 21 days for 12–14 cycles
Irinotecan (CPT-11; Camptosar) and temozolomide (Temodar)[1,7]	**Days 1–5:** Temozolomide 100mg/m^2/day orally, plus **Days 1–5 and 8–12:** Irinotecan 10–20mg/m^2/day IV at least one hour after temozolomide Repeat cycle every 21 or 28 days for 6 or 3 cycles, respectively
Carboplatin (Paraplatin) + ifosfamide + etoposide[1,8]	**Days 1 and 2:** Carboplatin 400mg/m^2/day IV, plus **Days 1–5:** Ifosfamide 1,800mg/m^2/day IV + etoposide 100mg/m^2/day IV Repeat cycle every 21 days for up to 12 cycles (median 1 cycle)

(continued)

BONE CANCER CHEMOTHERAPY REGIMENS Part 2 of 2

REGIMEN	DOSING
EWING'S SARCOMA AND MESENCHYMAL CHONDROSARCOMA (continued)	
SECOND-LINE THERAPY (Relapsed or Refractory Disease) (continued)	
Gemcitabine (Gemzar) + docetaxel (Taxotere)[1,9]	**Days 1 and 8:** Gemcitabine 675mg/m^2 IV, plus **Day 8:** Docetaxel 75–100 mg/m^2 IV Repeat cycle every 21 days for up to 13 cycles (median 4 cycles)
OSTEOSARCOMA	
FIRST-LINE (Primary/Neoadjuvant/Adjuvant) OR PRIMARY THERAPY FOR METASTATIC DISEASE AT INITIAL PRESENTATION[1]	
Cisplatin (CDDP; Platinol) + doxorubicin (Adriamycin)[1,10]	**Days 1–3:** Doxorubicin 25mg/m^2/day IV, plus **Day 1:** Cisplatin 100mg/m^2 IV continuous IV infusion Repeat cycle every 21 days for 6 cycles
MAP (high-dose methotrexate [MTX] + cisplatin + doxorubicin)[1,11]	**Day 1:** Methotrexate 8g/m^2 IV (with leucovorin rescue 15mg every 6 hrs for 11 doses, starting 24 hrs after beginning methotrexate), then **Days 7–9:** Cisplatin 120mg/m^2/day intra-arterially, then **Day 9:** Doxorubicin 60mg/m^2 IV (48 hrs after start of cisplatin infusion) Repeat cycle once after 28 days
SECOND-LINE THERAPY (Relapsed or Refractory Disease)	
Carboplatin + ifosfamide + etoposide[1,8]	**Days 1 and 2:** Carboplatin 400mg/m^2/day IV, plus **Days 1–5:** Ifosfamide 1,800mg/m^2/day IV + etoposide 100mg/m^2/day IV Repeat cycle every 21 days for up to 12 cycles (median 1 cycles)
Gemcitabine (Gemzar) + docetaxel (Taxotere)[1,9]	**Days 1 and 8:** Gemcitabine 675mg/m^2 IV, plus **Day 8:** Docetaxel 75–100 mg/m^2 IV. Repeat cycle every 21 days for up to 13 cycles (median 4 cycles)

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