CHEMOTHERAPY REGIMENS

Leukemias, Lymphomas, and Other Hematologic Cancers

Leukemia

The selection, dosing, and administration of anticancer 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 anticancer 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.

NOTE: Grey shaded boxes contain updated regimens.

LEUKEMIA (Part 1 of 2)	
REGIMEN	**DOSING**
Acute Myeloid Leukemia (AML)[1]	
Induction Therapy	
Cytarabine (Cytosar-U; ARA-C) **+ an anthracycline** (daunorubicin [Cerubidine], idarubicin [Idamycin], mitoxantrone [Novantrone])[2,3]	**Days 1–3:** An anthracycline (eg, daunorubicin at least 60mg/m²/day IV, idarubicin 10–12mg/m²/day IV, or mitoxantrone 10–12mg/m²/day IV), **plus** **Days 1–7:** Cytarabine 100–200mg/m²/day continuous IV infusion. **OR** **Days 1–3:** An anthracycline (eg, daunorubicin 45mg/m²/day IV, idarubicin 12mg/m²/day IV, or mitoxantrone 12mg/m²/day IV), **plus** **Days 1–7:** Cytarabine 100mg/m²/day continuous IV infusion.
Intermediate-dose cytarabine[4]	Cycle 1 **Days 1–7:** Cytarabine 200mg/m²/day continuous IV infusion, **plus** **Days 5–6:** Idarubicin 12mg/m²/day IV. Cycle 2 **Days 1–6:** Cytarabine 1,000mg/m² continuous IV infusion for 3 hrs twice daily, **plus** **Days 3, 5 and 7:** Amsacrine 120mg/m²/day.
Consolidation Therapy	
Cytarabine + idarubicin[5]	**Days 1:** Idarubicin 9mg/m² IV, **plus** **Days 1–5:** Cytarabine 60mg/m² SQ every 12 hrs. Repeat cycle monthly for 6 cycles.
Cytarabine + daunorubicin[5]	**Days 1:** Daunorubicin 45mg/m² IV, **plus** **Days 1–5:** Cytarabine 60mg/m² SQ every 12 hrs. Repeat cycle monthly for 6 cycles.
Relapsed/Refractory AML	
ADE (cytarabine + daunorubicin + etoposide [Toposar, VePesid, Etopophos; VP-16])[6]	Course 1 **Days 1–10:** Cytarabine 100mg/m² IV every 12 hrs, **plus** **Days 1, 3 and 5:** Daunorubicin 50mg/m²/day IV, **plus** **Days 1–5:** Etoposide 100mg/m²/day IV. Course 2 **Days 1–8:** Cytarabine 100mg/m² IV every 12 hrs, **plus** **Days 1, 3 and 5:** Daunorubicin 50mg/m²/day IV, **plus** **Days 1–5:** Etoposide 100mg/m²/day IV.
CLAG-M (cladribine [Leustatin] + cytarabine + mitoxantrone)[7]	Induction therapy **Days 1–5:** Cladribine 5mg/m²/day IV followed by cytarabine 2g/m²/day IV, **plus** **Days 1–3:** Mitoxantrone 10mg/m²/day IV. Repeat cycle if partial response. Proceed with consolidation chemotherapy once complete response is achieved. Consolidation therapy—Course 1 **Days 1–3:** Cytarabine 1.5g/m²/day IV, **plus** **Days 3–5:** Mitoxantrone 10mg/m²/day IV. Consolidation therapy—Course 2 **Days 1, 3 and 5:** Cytarabine 2g/m² IV every 12 hrs ± cladribine 5mg/m²/day.
Azacitidine (Vidaza)[8]	**Days 1–7:** Azacitidine 75mg/m²/day SQ. Repeat cycle every 28 days for at least 4 cycles.
Tipifarnib (Zarnestra)[9]	**Days 1–21:** Tipifarnib 600mg orally twice a day. Repeat cycle every 28 days. After 3 cycles, may increase dose to tipifarnib 900mg orally twice daily if no significant drug-related toxicity.
Lenalidomide (Revlimid)[10]	Cycle 1 **Days 1–14:** Lenalidomide 50mg/day orally once daily; **followed by** 30 days off therapy. Cycle 2 **Days 1–21:** Lenalidomide 35mg/day orally once daily; **followed by** 30 days off therapy. No therapy Cycle 3. Subsequent cycles Days 1–28: Lenalidomide 5mg/day orally once daily for 5 cycles.

continued

LEUKEMIA (Part 2 of 2)

REGIMEN	DOSING
Acute Promyelocytic Leukemia	
Arsenic trioxide (Trisenox)[11]	Induction therapy Arsenic trioxide 0.15mg/kg IV daily until bone marrow remission; max 60 doses. Consolidation therapy Initiate 3–6 weeks after completion of induction therapy. Arsenic trioxide 0.15mg/kg IV daily for 25 doses over a period of up to 5 weeks.
Chronic Myelogenous Leukemia (CML)[12]	
Imatinib (Gleevec)[13–15]	Imatinib 400mg orally once daily. May increase to imatinib 600–800mg orally once daily if complete response not achieved within 3 months.
Dasatinib (Spyrcel)[16, 17]	Newly diagnosed Philadelphia chromosome-positive chronic phase myeloid leukemia (Ph+ CML-CP) Dasatinib 100mg orally once daily; up to 140mg once daily. Resistant or intolerant accelerated phase Ph+ CML, myeloid or lymphoid blast CML, Ph+ acute lymphoblastic leukemia (ALL) Dasatinib 140mg orally once daily; up to 180mg once daily.
Nilotinib (Tasigna)[18–20]	Newly diagnosed Ph+ CML-CP Nilotinib 300mg orally twice daily. Resistant or intolerant chronic and accelerated phase Ph+ CML Nilotinib 400mg orally twice daily.

References

1. NCCN Clinical Practice Guidelines in Oncology™. Acute Myeloid Leukemia. v 2.2011. Available at: http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed October 16, 2011.
2. Döhner H, Estey EH, Amadori S, et al. European LeukemiaNet. Diagnosis and management of acute myeloid leukemia in adults: recommendations from an international expert panel, on behalf of the European LeukemiaNet. *Blood.* 2010;115:453–474.
3. Rowe JM, Neuberg D, Friedenberg W, et al. Eastern Cooperative Oncology. A phase 3 study of three induction regimens and of priming with GM-CSF in older adults with acute myeloid leukemia: a trial by the Eastern Cooperative Oncology Group. *Blood.* 2004;103:479–485.
4. Löwenberg B, Pabst T, Vellenga E, et al. Dutch-Belgian Cooperative Trial Group for Hemato-Oncology (HOVON) and Swiss Group for Clinical Cancer Research (SAKK) Collaborative Group. Cytarabine dose for acute myeloid leukemia. *N Engl J Med.* 2011;364:1027–1036.
5. Gardin C, Turlure P, Fagot T, et al. for the Acute Leukemia French Association (ALFA). Postremission treatment of elderly patients with acute myeloid leukemia in first complete remission after intensive induction chemotherapy: results of the multicenter randomized Acute Leukemia French Association (ALFA) 9803 trial. *Blood.* 2007;109:5129–5135.
6. Milligan DW, Wheatley K, Littlewood T, Craig JIO, Burnett AK, for the NCRI Haematological Oncology Clinical Studies Group. Fludarabine and cytosine are less effective than standard ADE chemotherapy in high-risk acute myeloid leukemia, and addition of G-CSF and ATRA are not beneficial: results of the MRC AML-HR randomized trial. *Blood.* 2006;107:4614–4622.
7. Wierzbowska A, Robak T, Pluta A, et al. Cladribine combined with high doses of arabinoside cytosine, mitoxantrone, and G-CSF (CLAG-M) is a highly effective salvage regimen in patients with refractory and relapsed acute myeloid leukemia of the poor risk: a final report of the Polish Adult Leukemia Group. *Eur J Haematol.* 2008;80:115–126.
8. Thepot S, Itzykson R, Seegers V, et al. Groupe Francophone des Myelodysplasies (GFM). Treatment of progression of Philadelphia-negative myeloproliferative neoplasms to myelodysplastic syndrome or acute myeloid leukemia by azacitidine: a report on 54 cases on the behalf of the Groupe Francophone des Myelodysplasies (GFM). *Blood.* 2010;116:3735–3742.
9. Harousseau, JL, Lancet, JE, Reiffers, J, et al. A phase 2 study of the oral farnesyltransferase inhibitor tipifarnib in patients with refractory or relapsed acute myeloid leukemia. *Blood.* 2007;109:5151–5156.
10. Fehniger, TA, Byrd, JC, Marcucci, G, et al. Single-agent lenalidomide induces complete remission of acute myeloid leukemia in patients with isolated trisomy 13. *Blood.* 2009;113:1002–1005.
11. Trisenox [prescribing information]. Frazer, PA: Cephalon, Inc.; 2010.
12. NCCN Clinical Practice Guidelines in Oncology™. Chronic Myelogenous Leukemia. v 2.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf. Accessed October 16, 2011.
13. de Lavallade H, Apperley JF, Khorashad JS, et al. Imatinib for newly diagnosed patients with chronic myeloid leukemia: incidence of sustained responses in an intention-to-treat analysis. *J Clin Oncol.* 2008;26:3358–3363.
14. Gleevec [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp., 2011.
15. Hochhaus A, Druker B, Sawyers C, et al. Favorable long-term follow-up results over 6 years for response, survival, and safety with imatinib mesylate therapy in chronic-phase chronic myeloid leukemia after failure of interferon-α treatment. *Blood.* 2008;111:1039–1043.
16. Sprycel [prescribing information]. Princeton, NJ: Bristol-Myers Squibb, 2010.
17. Kantarjian H, Pasquini R, Hamerschlak N, et al. Dasatinib or high-dose imatinib for chronic-phase chronic myeloid leukemia after failure of first-line imatinib: a randomized phase 2 trial. *Blood.* 2007;109:5143–5150.
18. Saglio G, Kim DW, Issaragrisil S, le Coutre P, Etienne G, Lobo C, Pasquini R, Clark RE, Hochhaus A, Hughes TP, Gallagher N, Hoenekopp A, Dong M, Haque A, Larson RA, Kantarjian HM; ENESTnd Investigators. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. *N Engl J Med.* 2010;362:2251–2259.
19. Le Coutre PL, Ottmann OG, Giles F, et al. Nilotinib (formerly AMN107), a highly selective BCR-ABL tyrosine kinase inhibitor, is active in patients with imatinib-resistant or intolerant accelerated-phase chronic myelogenous leukemia. *Blood.* 2008;111:1834–1839.
20. Tasigna [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp., 2011.

(Revised 11/2011)