

c. Locations of leukemic cells in the body

Leukemia generally arises from bone marrow. Leukemic cells circulate via blood vessels to organs and tissues throughout the body. Sometimes, leukemia can arise from outside of bone marrow, for example from cells residing in lymph nodes or in a mediastinal mass (41). When the leukemia recurs, recurrence usually arises from a quiescence leukemic cell that was not eradicated by treatment. Depending on the site where the quiescence leukemic cell resides, relapse can occur in any part of the body, generally bone marrow, central nervous system (42) and occasionally in the testes. Brain and testes are sanctuary sites (protected from chemotherapy by the blood–brain barrier or by the P-glycoprotein, which pumps drugs out of the cells) (43). While relapse can occur in any tissue or organ, oncologists rarely refer to leukemic relapse as “recurrence in a metastatic site” (44). While the leukemias can metastasize to various parts of the body, that is, the liver, spleen, testes, or skin, the leukemia causes a diffuse infiltration, rather than a mass (45). Regarding patients with CLL, from 3 to 10% of CLL patients develop what is called Richter syndrome or Richter transformation (46,47,48). This syndrome involves transformation of a leukemic cell to a lymphoma, where the neoplasm can occur in the lymph nodes, central nervous system, gastrointestinal tract, or eye. Lymphomas can be quantitated by a modified form of the RECIST criteria (49).

d. Lymphoid neoplasms

1. Acute lymphocytic leukemia

In the United States, there are over 5,000 new cases of acute lymphocytic leukemia (ALL) per year (50). The terms lymphocyte and lymphoblast refer to the cells that are involved. When normal, the cells are lymphocytes, but in ALL these cells are in a relatively immature state, and are therefore called blasts. For children under 15 years of age, ALL is approximately five times more common than AML, accounting for approximately 76% of all childhood leukemia diagnoses. Leukemia is the most common cancer

⁴¹ Pui CH. E-mail of January 2, 2011.

⁴² Pui CH, Campana D, Pei D, et al. Treating childhood acute lymphoblastic leukemia without cranial irradiation. *New Engl J Med.* 2009;360:2730–2741.

⁴³ Lee CA, Cook JA, Reyner EL, Smith DA. P-glycoprotein related drug interactions: clinical importance and a consideration of disease states. *Expert Opin Drug Metab Toxicol.* 2010;6:603–619.

⁴⁴ Pui CH. E-mail of January 2, 2011.

⁴⁵ Berg SL. E-Mail of January 6, 2011.

⁴⁶ Hartmann T. E-Mail of January 28, 2011.

⁴⁷ Tsimberidou AM, Keating MJ. Richter syndrome: biology, incidence, and therapeutic strategies. *Cancer.* 2005;103:216–228.

⁴⁸ Omoti CE, Omoti AE. Richter syndrome: a review of clinical, ocular, neurological and other manifestations. *Br J Haematol.* 2008;142:709–716.

⁴⁹ Assouline S, Meyer RM, Infante-Rivard C, et al. Development of adapted RECIST criteria to assess response in lymphoma and their comparison to the International Workshop Criteria. *Leuk Lymphoma.* 2007;48:513–520.

⁵⁰ National Cancer Institute. What you need to know about leukemia. NIH publication no. 08–3775, 2008 [55 pages].