

what is called Richter syndrome or Richter transformation (74,75,76). 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 (77).

## e. Lymphoid Neoplasms

### 1. *Acute Lymphocytic Leukemia*

In the United States, there are over 5000 new cases of ALL per year (78). 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 diagnosis in children under 15 years of age (79). Appelbaum et al. (80) reviewed the endpoints used in clinical trials on ALL.

ALL can be treated by administering the enzyme, asparaginase (81,82). Asparaginase catalyzes the breakdown of extracellular asparagine into aspartic acid and ammonia. Depletion of extracellular asparagine inhibits the growth of lymphocytic leukemic cells. Unlike normal cells, lymphoblasts lack the enzyme that biosynthesizes asparagine, and thus require an exogenous source of this amino acid.

Imatinib (Gleevec®), shown below, is a small molecule that inhibits tyrosine kinase. Specifically, this drug inhibits the tyrosine kinase activity of the fusion protein, BCR-ABL (83). The drug is used for treating hematological disorders where cells contain the Philadelphia chromosome (or express BCR-ABL) (84). These disorders include CML and a subset of cases of AML. Regarding this subset

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<sup>76</sup>Omoti CE, Omoti AE. Richter syndrome: a review of clinical, ocular, neurological and other manifestations. *Br. J. Haematol.* 2008;142:709–16.

<sup>77</sup>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;48:513–20.

<sup>78</sup>National Cancer Institute. What you need to know about leukemia. NIH publication no.08-3775; 2008 (55 pp.).

<sup>79</sup>Deschler B, Lübbert M. Acute myeloid leukemia: epidemiology and etiology. *Cancer* 2006;107:2099–107.

<sup>80</sup>Appelbaum FR, Rosenblum D, Arceci RJ, et al. End points to establish the efficacy of new agents in the treatment of acute leukemia. *Blood* 2007;109:1810–6.

<sup>81</sup>Asselin B, Rizzari C. Asparaginase pharmacokinetics and implications of therapeutic drug monitoring. *Leuk. Lymphoma* 2015;11:1–8.

<sup>82</sup>Masetti R, Pession A. First-line treatment of acute lymphoblastic leukemia with pegasparaginase. *Biologics* 2009;3:359–68.

<sup>83</sup>Woyach JA, Furman RR, Liu TM, et al. Resistance mechanisms for the Bruton's tyrosine kinase inhibitor ibrutinib. *New Engl. J. Med.* 2014;370:2286–94.

<sup>84</sup>Kantarjian H, O'Brien S, Cortes J, et al. Therapeutic advances in leukemia and myelodysplastic syndrome over the past 40 years. *Cancer* 2008;113(7 Suppl.):1933–52.