

# Current Concepts in Treatment of Childhood Acute Lymphoblastic Leukemia

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## **Abstract**

Remarkable progress has been made in the treatment of childhood acute lymphoblastic leukemia (ALL). The 5-year event-free survival rates now exceed 70%, reaching 80% or higher in some studies. Current efforts to improve outcome focus on more precise risk classification to avoid over- or under-treatment. Early treatment response, as defined by measurement of minimal residual disease, reflecting both the drug responsiveness of leukemic cells and host pharmacodynamics and pharmacogenomics, is considered the most reliable indicator for gauging the intensity of treatment. Intensive remission induction may not be necessary for patients with standard- or high-risk ALL, provided that they receive post-induction intensification therapy. Several clinical trials suggested that the use of L-asparaginase in the post-induction period only yielded an excellent remission induction rate and long-term event-free survival with low early morbidity. Increasingly, dexamethasone has replaced prednisone as a glucocorticoid of choice to improve outcome. Extended and stronger double-delayed intensification (or reinduction) improved treatment results even in patients with high-risk ALL and a slow early response. A methotrexate dosage of 2.5 g/m<sup>2</sup> seems adequate for most patients with B-lineage ALL; 5 g/m<sup>2</sup> may be required for those with T-cell ALL. The most successful clinical trials generally feature continuous post-remission therapy; high-dose pulse therapy with long rest period to compensate for myelosuppression was associated with an inferior outcome. Intensity of CNS-directed therapy should be tailored according to the presenting features. Patients with high-risk genetic features, a large leukemic cell burden, T-cell ALL, and the presence of leukemic cells in CSF (even from iatrogenic introduction via traumatic lumbar puncture) require more intensive therapy. In the context of intensive intrathecal and effective systemic therapy, cranial irradiation can now be omitted in over 95% of the patients. Among very high-risk cases, only Philadelphia chromosome-positive ALL cases and perhaps those with T-cell ALL and poor early response benefit from hematopoietic stem cell transplantation with HLA-matched related donor. Ultimately, the curative treatment for very high-risk ALL would depend on the identification and characterization of specific oncoproteins with a pivotal role in leukemogenesis, and the development of molecular-based therapy. Promising agents under evaluation include imatinib mesylate (STI 571) for Ph<sup>+</sup> ALL and FLT3 inhibitors for *MLL*-rearranged leukemia.

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