B-cell ALL with High Risk Features in Adults

Dong Won Baek
Kyungpook National University School of Medicine, Korea

Adult B-cell acute lymphoblastic leukemia (B-ALL) comprises a biologically heterogeneous group of malignancies, among which patients with high-risk features continue to experience inferior outcomes despite advances in therapy. High-risk B-ALL is defined by a constellation of clinical, cytogenetic, and molecular factors, including advanced age, leukocytosis at diagnosis, minimal residual disease (MRD) persistence, and adverse genomic alterations such as BCR::ABL1, KMT2A rearrangements, complex karyotype, hypodiploidy, and Ph-like signatures. Recent progress in genomic profiling has refined risk stratification and enabled more precise prognostication. MRD assessment using multiparameter flow cytometry or next-generation sequencing has emerged as one of the most powerful predictors of relapse and survival, guiding post-remission therapeutic decisions. Patients with persistent MRD or high-risk genetics are often considered for early allogeneic hematopoietic stem cell transplantation (allo-HSCT) in first remission. Therapeutic paradigms have evolved substantially with the incorporation of targeted and immunotherapeutic agents. Tyrosine kinase inhibitors have transformed outcomes in Ph-positive disease, while monoclonal antibodies and T-cell–engaging therapies—such as anti-CD20, anti-CD19, and bispecific antibodies—have improved response depth and MRD negativity rates. Chimeric antigen receptor (CAR) T-cell therapy has further expanded salvage options for relapsed/refractory high-risk patients.