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Adult Acute Lymphoblastic Leukemia: A Genetic Overview and Application to Clinical Practice

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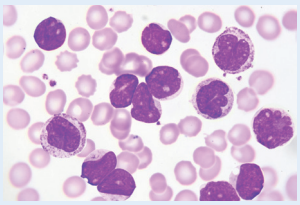

Background: Cytogenetic and molecular features of diseases, such as B-cell precursor acute lymphoblastic leukemia (BCP-ALL), are increasingly used for diagnostic, prognostic, and treatment decisions in health care.

Objectives: This review provides information on the current recommendations for evaluating genetic aberrations in patients with BCP-ALL and details how the results are incorporated to determine risk stratification. It also offers a brief overview of developing research on newly found genetic features that may play a role in prognostic and treatment decisions.

Methods: Databases were reviewed using search terms relevant to BCP-ALL genetics, as well as to the prognostic significance of genetic changes commonly seen in BCP-ALL. Because of the scope of this review, studies identified as having outcomes with implications for clinical practice were included.

Findings: Cytogenetic and molecular aberrations in BCP-ALL are important not only for risk stratification but also for treatment decisions. To provide efficient and effective care for patients with BCP-ALL, clinical practitioners need to be aware of current recommendations and the state of prevailing research.

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According to the National Comprehensive Cancer Network ([NCCN], 2016), 6,590 new cases of acute lymphoblastic leukemia (ALL) were estimated to occur in 2016, along with 1,430 deaths. ALL is the most common cancer seen in children (Mullighan, 2012). Among ALL classifications, lymphoblasts derived from B-cell lineages (B-cell precursor ALL [BCP-ALL]) represent the majority of these instances, with 88% of childhood ALL and 75% of adult ALL cases identified as B cell (NCCN, 2016). Risk factors for the development of ALL can be found in Figure 1. Childhood ALL has relatively good outcomes associated with diagnosis; about 80% of those diagnosed in childhood achieve long-term event-free survival (EFS), whereas adults with ALL typically have much poorer outcomes (National Cancer Institute [NCI], 2016b).

In addition to clinical factors, such as age and white blood cell count, cytogenetic and molecular techniques have been used to provide prognostic information regarding risk stratification and treatment response in patients with BCP-ALL. In addition, the NCCN (2016) has made treatment recommendations, including whether a patient should proceed with hematopoietic stem cell transplantation (HSCT) based on these cytogenetic and molecular risk classifications.

Various cytogenetic techniques (e.g., karyotyping, fluorescence in situ hybridization [FISH]) have identified several recurrent genetic aberrations in this population shown to correspond with poor outcome. These poor risk aberrations include *BCR-ABL* translocation (chromosome abnormality in which parts of separate chromosomes become rearranged), *MLL* rearrangements, hypodiploidy, and a complex karyotype (greater than five genetic abnormalities) (Moorman, 2012). Patients harboring one or more of these alterations are identified as being in a high-risk group (NCCN, 2016). In contrast, patients with BCP-ALL found to have hyperdiploidy