IKZF1 status as a prognostic feature in BCR-ABL1-positive childhood ALL.

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Abstract

Childhood BCR-ABL1-positive B-cell precursor acute lymphoblastic leukemia (BCP-ALL) has an unfavorable outcome and shows high frequency of IKZF1 deletions. The prognostic value of IKZF1 deletions was evaluated in 2 cohorts of BCR-ABL1-positive BCP-ALL patients, before tyrosine kinase inhibitors (pre-TKI) and after introduction of imatinib (in the European Study for Philadelphia-Acute Lymphoblastic Leukemia [EsPhALL]). In 126/191 (66%) cases an IKZF1 deletion was detected. In the pre-TKI cohort, IKZF1-deleted patients had an unfavorable outcome compared with wild-type patients (4-year disease-free survival [DFS] of 30.0 ± 6.8% vs 57.5 ± 9.4%; P = .01). In the EsPhALL cohort, the IKZF1 deletions were associated with an unfavorable prognosis in patients stratified in the good-risk arm based on early clinical response (4-year DFS of 51.9 ± 8.8% for IKZF1-deleted vs 78.6 ± 13.9% for IKZF1 wild-type; P = .03), even when treated with imatinib (4-year DFS of 55.5 ± 9.5% for IKZF1-deleted vs 75.0 ± 21.7% for IKZF1 wild-type; P = .05). In conclusion, the highly unfavorable outcome for childhood
BCR-ABL1-positive BCP-ALL with IKZF1 deletions, irrespective of imatinib exposure, underscores the need for alternative therapies. In contrast, good-risk patients with IKZF1 wild-type responded remarkably well to imatinib-containing regimens, providing a rationale to potentially avoid hematopoietic stem-cell transplantation in this subset of patients.

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