IKZF1 DELETIONS PREDICT REFRACTORY DISEASE AND POOR SURVIVAL IN *DE NOVO* PH-NEGATIVE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: DATA FROM THE RALL-2016 STUDY

O.A. Aleshina, E.S. Kotova, G.A. Isinova, B.V. Biderman, Yu. A. Chabaeva, E.N. Parovichnikova[1]
National Medical Research Center for Hematology, Moscow

National Hematology Society

Introduction

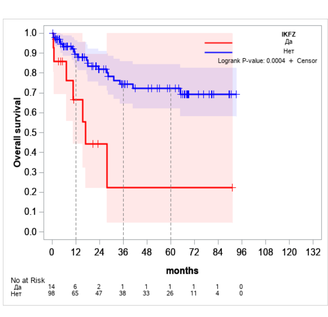
The transcription factor IKAROS is a regulator of lymphocyte development. Deletions within *IKZF1* in B-cell acute lymphoblastic leukemia (B-ALL) lead to a loss of normal IKAROS function, conferring leukemic stem cell properties, including self-renewal and subsequent uncontrolled growth.

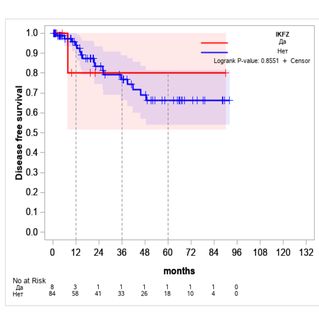
Aim

To analyze the effectiveness of the RALL-2016 protocol (NCT03462095) in B-ALL patients according to *IKZF1* status.

Methods

From December 2016 to February 2025, 112 new Ph-negative B-ALL patients were treated according to the RALL-2016 protocol, and intragenic deletions of *IKZF1* were detected using breakpoint-specific fluorescent multiplex polymerase chain reaction. The median age of patients recruited to RALL-2016 (n=112) was 30 years (range, 18–54 years); 59 were female, and 53 were male. Cytogenetic studies and centralized assessment of minimal residual disease (MRD) by flow cytometry on protocol day +70 (after completion of two induction phases) were performed in all patients. If the patient did not achieve remission on day +70 by protocol (after second phase induction), resistance was diagnosed. Statistical data processing was carried out using SAS.





Results

Complete remission was achieved in 104 (93%) patients. No therapy-related death was detected. Five-year overall survival and disease-free survival were 63% and 59%, respectively. *IKZF1* deletions were detected in 14 (12.5%) of the 112 patients: 10 cases with del 4-7 (72%), 2 with del 2-7 (14%), 1 with del 2-8 (7%), and 1 with all types of deletions (del 4-7, del 4-8, del 2-7, del 2-8). Resistance of disease was detected in 4 (40%) patients with *IKZF1* del (9 of 10 without resistance and with *IKZF1* del were MRD-persistent after induction) and in 4 (4%) patients without *IKZF1* del (*P*=0.0009). The long-term outcomes according to *IKZF1* status were as follows: 5-year overall survival, 22% (*IKZF1* del) vs 72% (*IKZF1* wild) (*P*=0.0004), 5-year disease-free survival, 80% (*IKZF1* del) vs 66% (*IKZF1* wild) (*P*=0.85).

Summary

IKZF1 deletions are associated with treatment resistance and inferior outcomes for patients treated by the RALL-2016 protocol.

The scheme of regime «ALL-2016»

