Immunophenotype of MRD-cells as an additional prognostic marker in ALL

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Abstract

Measurable residual disease (MRD) is an independent prognostic factor in acute lymphoblastic leukemia (ALL). However, the impact of the immunophenotype of MRD-cells on survival had not been studied.

In present study we divide B-ALL as well as T-ALL patients into 3 clusters according to immunophenotype of residual leukemia cells in bone marrow (BM) and show different relapse free survival (RFS) probability of patients in these clusters.

Objective

To determine the significance of the immunophenotype of MRD-cells detected at the end of induction in ALL patients.

Study design

This study included data from 2016 to 2022 years of 267 patients enrolled in Russian multicenter study RALL-2016 (NCT03462095). The MRD was assessed on 70th day of therapy (after 2nd induction course) in patients with complete remission.

Materials & Methods

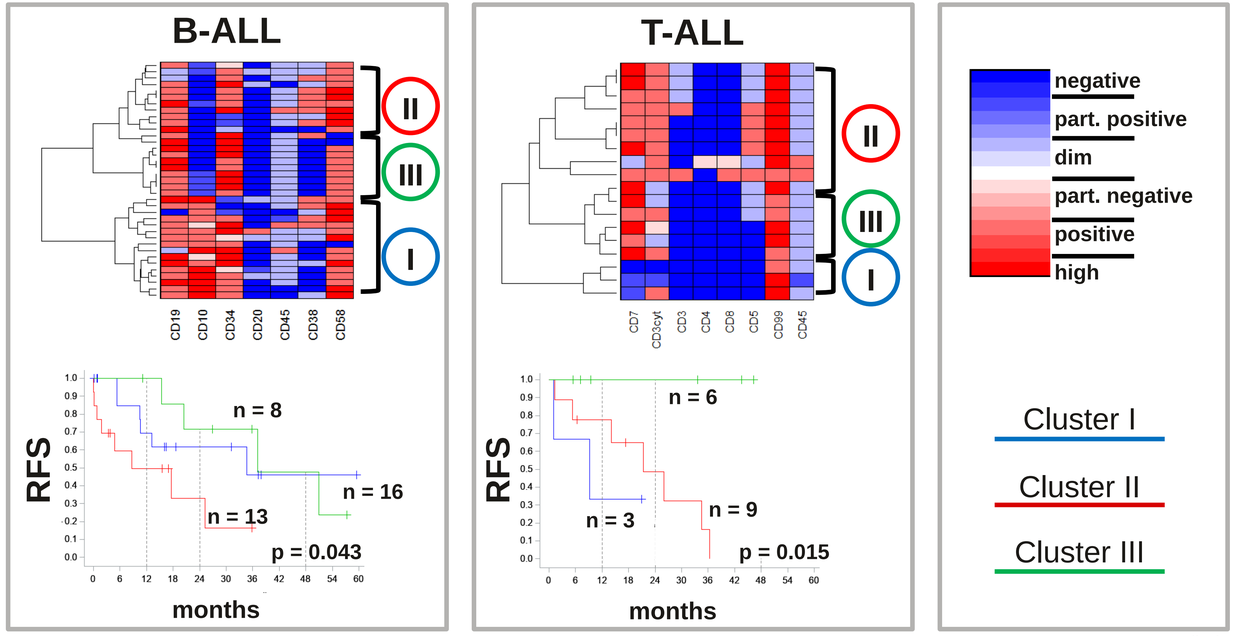
The MRD was assessed in 94 B-ALL, and 77 T-ALL patients. Analysis of MRD was performed by 6-11-color flow cytometry (BD FACSCanto II or BC CytoFLEX cytometers). CD19, CD34, CD10, CD20, CD38, CD45, and CD58 were analyzed to detect MRD in all B-ALL patients. CD7, CD3^{sur}, CD3^{cyt}, CD4, CD8, CD5, CD99, CD45 were analyzed to detect MRD in T-ALL patients. The expression of these antigens was assessed relative to normal BM cells and transformed into a numeric score. The dendrogram was constructed using the “ward.D” method in R 3.4.4. The RFS was estimated with the Kaplan–Meier method, and comparisons were assessed using the log-rank test.

Results

MRD was revealed in 37 (39%) B-ALL and 18 (23.4%) T-ALL patients. The RFS was lower in MRD-positive patients (54% vs 90% ($p < 0.0001$) in B-ALL and 59% vs 83% ($p < 0.0025$) in T-ALL).

In B-ALL 3 clusters of MRD-cells were detected. Cluster I (n = 16) included cases of CD10^{+} MRD, while clusters II (n = 13) and III (n = 8) - CD10^{-} MRD. Expression of CD38 and CD58 was higher in cluster II than in cluster III. RFS were 62%, 33%, and 71% ($p = 0.043$) in clusters I,II, and III respectively.

Results



In T-ALL also 3 clusters were found. Cluster I included 3 CD7^{-} cases, cluster II – 9 CD7^{+}CD5^{+}CD3$^{dim/+}$ cases, and cluster III – 6 CD7^{high}CD5$^{-/dim}$CD3^{-} cases. RFS were 33%, 49%, and 100% ($p = 0.015$) respectively.

Conclusion

MRD at the end of induction impairs RFS of patients in RALL-2016 study. The immunophenotype of MRD-cells is associated with RFS, and could be an additional prognostic factor.

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