



High CD38 and CD58 expression on leukemia cells, forming MRD population, dramatically decreases relapse-free survival in B-ALL patients enrolled in RALL-2016 study

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CONTEXT

It is well known that measurable residual disease (MRD) has a significant prognostic impact in patients with acute leukemia. However, the effect of the immunophenotype of MRD cells has not been studied yet.

OBJECTIVE

The aim of the study was to assess a significance of CD38 and CD58 expression on relapse-free survival (RFS) in B-ALL patients.

DESIGN

This study included data from 2016 to 2020 years of patients enrolled in Russian multicenter study RALL-2016 (NCT03462095). The MRD was assessed in the bone marrow at the end of induction (day +70) in patients who achieved a complete remission.

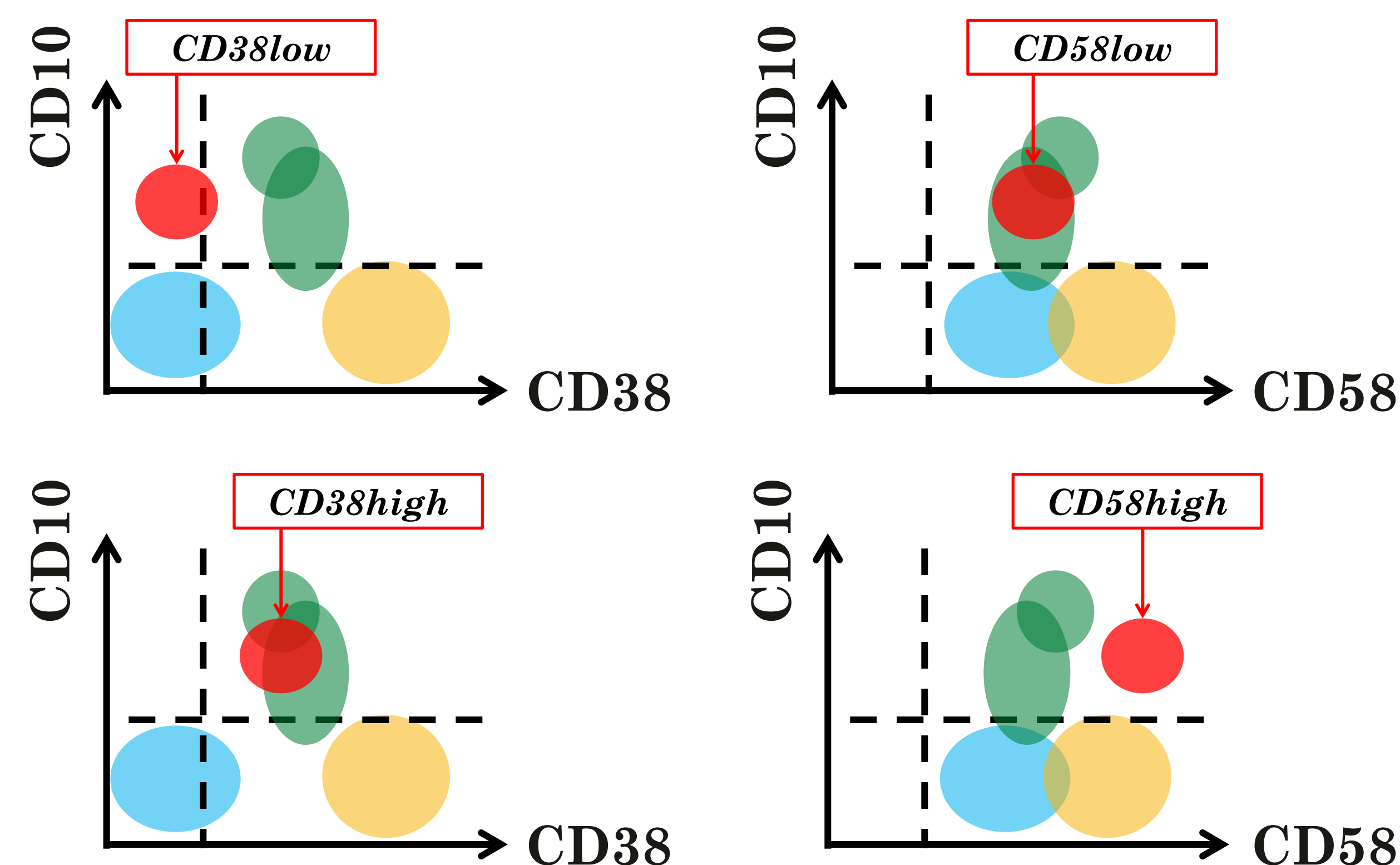
PATIENTS and METHODS

The RALL-2016 study included 207 adult patients. The MRD was assessed in 150 patients (80 B-ALL patients and 70 T-ALL patients). Analysis of MRD was performed by 6- or 10-color flow cytometry. The sensitivity was at least 0.01%. CD19, CD34, CD10, CD20, CD38, CD45, and CD58 were analyzed to detect MRD in B-ALL. The main immunophenotypic features of B-ALL blasts are low CD38 expression and high CD58 expression.

METHODS

CD38 expression in MRD-cells was considered as low if it was lower than on normal B-cell progenitors. CD58 expression was considered as high if it was equal to or higher than on plasma cells (**Fig. 1**).

The relapse-free survival (RFS) was estimated with the Kaplan-Meier method, and comparisons were assessed using the log-rank test.



Legend: Mature B-cells B-cell precursors Plasma cells MRD

Fig. 1. Examples of CD38 and CD58 expression in MRD. CD19⁺ cells are shown.

RESULTS

Among B-ALL patients 48 (60%) patients were MRD-negative, and 32 (40%) patients remained MRD-positive at the end of induction. The duration of RFS was lower in MRD-positive patients (median 29.5 months vs median undefined, $p=0.004$) (**Fig. 2**). High CD38 expression was found on MRD-cells in 8 patients and 7 (87.5%) out of them relapsed or died.

RFS was shorter in CD38high-MRD patients than in CD38low-MRD (median 5.2 months vs median undefined, $p<0.001$). RFS in CD58high-MRD was also shorter (medians 9.7 vs 34.7 months, $p<0.001$) (**Fig. 3**).

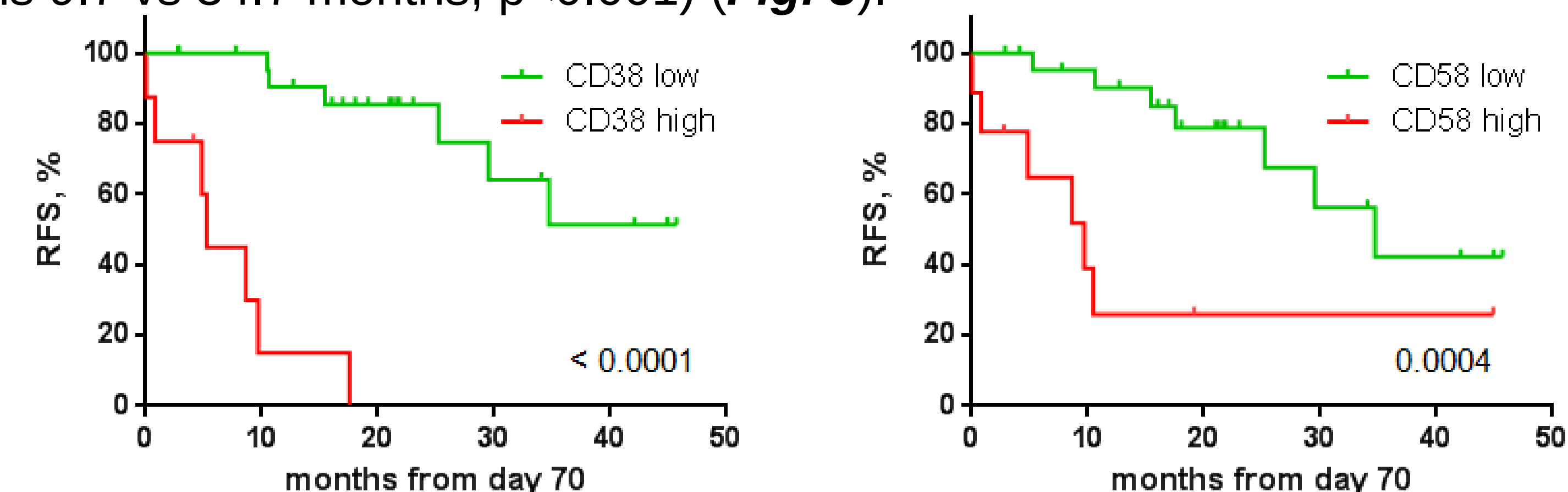


Fig. 3. RFS in B-ALL MRD-positive patients according to CD38, and CD58 expression.

CONCLUSION

MRD at the end of induction was confirmed as an important prognostic factor in RALL-2016 study. However, immunophenotype of residual blasts could improve the prognostic impact of MRD. High expression of CD58 and CD38 on MRD cells dramatically decreases the duration of RFS in B-ALL patients.