## CD20 has no prognostic significance in children with precursor B-cell acute lymphoblastic leukemia

Acute lymphoblastic leukemia (ALL) is the most common leukemia in children. Survival outcomes have greatly improved with combination chemotherapy and the intensification of treatment.[1] Recent improvements in ALL management have largely been due to optimizing treatment according to various risk stratification schema and evaluation of minimal residual disease (MRD) at the end of induction treatment has proved valuable.[2] However, up to half of relapse events occur in patients who are MRD negative at end-induction.[3] We read with interest the article by Mannelli *et al.*[4] and examined whether CD 20 was an adverse prognostic marker in children with precursor B-ALL.

We carried out a retrospective analysis of children (aged 1-18 years) diagnosed with precursor B-ALL over six years between 1st January 2004 to 31st December 2009. The study was approved by the local institutional review board. We considered 20% to be the threshold for positivity (CD20+). Standard risk patients were treated with either POG 9904, POG 9905 or AALL0331, and high-risk patients were treated with either POG 9906 or AALL0232. MRD analysis was made using flow cytometry. MRD values of more than 0.1% were considered positive. Data were analyzed using SPSS software version 11.5. Survival outcomes were assessed by the Kaplan-Meier method and log rank test.[5] Data analysis was censored on 31st December 2010.

**Table 1.** Patients' characteristics.

| Variable | | N. patients |
|---|---|---|
| Gender | Male | 146 (56%) |
| | Female | 113 (44%) |
| CD20 | Positive | 133 (51%) |
| | Negative | 126 (49%) |
| Risk group | Standard risk | 184 (71%) |
| | High risk | 75 (29%) |
| MRD (n=138) | Negative | 130 |
| | Positive | 8 |
| Events (n=14) | Relapse | 13 |
| | Death | 4 |

*MRD: minimal residual disease.*

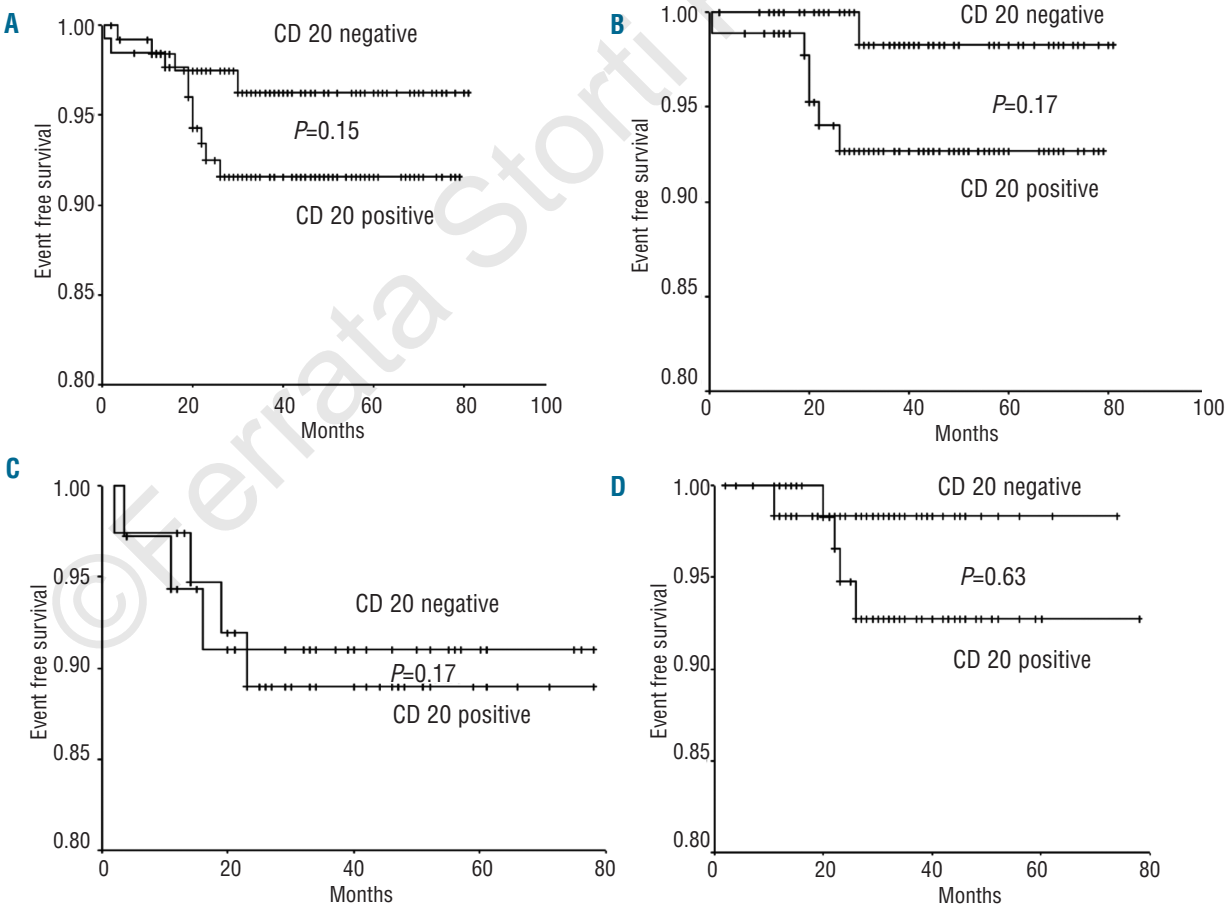


**Figure 1.** (A) Event free survival in all children according to CD 20 status. (B) Event free survival in standard risk group according to CD20 status. (C) Event free survival in high-risk group according to CD20 status. (D) Event free survival in minimal residual negative group according to CD 20 status.

A total of 326 children were diagnosed with ALL over the 6-year period including 259 children treated for precursor B-ALL. Patients' characteristics are shown in Table 1. Mean age of the study cohort was 5.2±4.0 years and median presenting WBC count was 9.1x10$^9$/L (1-841x10$^9$/L). Six patients had end of induction MRD between 0.1 to 1% and 2 had more than 1%. Fourteen patients had an event (13 relapses, 4 deaths). Mean follow up was 41 months ±20 months (median 41 months). There were 2 deaths in each of the CD 20 positive and negative groups.

Overall survival was 98% and this was similar in both groups. Event free survival (EFS) of the standard and the high-risk groups according to CD 20 status is shown in Figure 1A-C. Altogether, CD 20 did not indiate poor prognosis in this population. Results were similar when children with positive CD 20 were divided into those with more than 20% or those with more than 40% positivity. MRD at Day 29 was the strongest predictor of both death ($P$=0.00) and relapse ($P$=0.034). Figure 1D shows event free survival in the MRD negative group according to CD 20 status.

Half of the children in our study group were positive for CD 20. MRD at Day 29 was able to predict outcomes in our patient cohort in agreement with previous reports.[3] We did not notice any effect of CD 20 on event free survival of either standard risk ALL or high-risk ALL. CD 20 positivity did not differentiate EFS among MRD negative patients in our study. Pediatric ALL has a good outcome with modern day combination chemotherapy regimens. Our study is limited by a very small number of events in these patients. Also, MRD was positive in only 8 of 139 patients. Despite these limitations, and similar to the report by Mannelli *et al.*,[4] we conclude that CD 20 has no prognostic significance in children with precursor B-ALL and MRD remains the most powerful predictor of outcome.

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