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ADULT AND CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: CLINICO-BIOLOGICAL DIFFERENCES BASED ON CD34 ANTIGEN EXPRESSION

NICOLA CASCAVILLA, PELLEGRINO MUSTO, GIOVANNI D'ARENA, SAVERIO LADOGANA, ROSELLA MATERA, MARIO CAROTENUTO

Division of Hematology, IRCCS "Casa Sollievo della Sofferenza" Hospital, San Giovanni Rotondo, Italy

ABSTRACT

Background and Objective. The prognostic significance of CD34 antigen expression in acute lymphoblastic leukemias (ALL), especially in adult patients, is still not well established. In the present report we analyzed a series of biological and clinical findings from 128 ALL patients in order to evaluate the possible clinical significance of this marker.

Methods. The clinical and biological significance of CD34 expression, an early marker of hemopoietic cells, was analyzed by flow cytometry in a series of 128 patients affected by ALL, including 78 adults and 50 children under 15 years old.

Results. Overall, 68.7% of patients showed significant (> 10%) CD34 expression. There was no difference between $CD34^+$ and $CD34^-$ ALL with respect to age, sex, FAB morphology, hepatosplenomegaly, Plt count, Hb level, DNA index, P-170 expression. $CD34^+$ ALL displayed a significantly lower frequency of extramedullary involvement, a lower LDH level and lower WBC count, lower proliferative activity (as evaluated by the Ki67 monoclonal antibody) than $CD34^-$ ALL. CD34 expression was also associated with *early* phenotypes in both B- and T-ALL, co-expression of myeloid antigens, and the presence of the Ph' chromosome. Due to a different distribution of prognostic factors investigated, DFS and OS were both significantly better in $CD34^+$ than in $CD34^-$ childhood ALL, whereas no statistical difference was found in adults. Multivariate analyses confirmed these data in children.

Interpretation and Conclusions. Expression of the CD34 antigen is a positive prognostic factor in childhood ALL. In adult ALL the presence of this marker on leukemic cell does not seem to influence the clinical outcome of these patients.

Key words: acute lymphoblastic leukemia, CD34, prognostic factors

The clinical heterogeneity of acute lymphoblastic leukemia (ALL) is affected considerably by the stage of leukemic expansion along B or T differentiative pathways[1-3] and by the patient's age[4,5] which likely reflect multiple molecular mechanisms.[6] In fact, phenotypic classes may be associated with different clinical characteristics, such as tumoral mass, response to therapy and outcome,[7-10] while age influences unequal distribution and significance of both immunophenotype and karyotype abnormalities. Indeed a distinctive prognosis was reported when ALL patients were stratified for age under or over 15 years.[5] The clinical outcome is also different for childhood and adult ALL, even when similar protocols have been applied.[11]

CD34 antigen is an early marker of hematopoietic progenitors.[12-15] According to the hypothesis that acute leukemia is a clonal expansion with maturation arrest,[16] CD34 expression on leukemic cells might define peculiar characteristics of immaturity, with the possibility of reflecting distinctive clinical features, in both adult and pediatric age. CD34 antigen has been already utilized as a tumor marker in acute myeloid leukemias (AML), where it was found to be associated with poor prognosis.[17-21] However, other authors have not reported any such association.[22-25] In contrast, in childhood B-lineage ALL a strong association has been reported between CD34 expression and some favorable biological and clinical features, such as age between 1 and 10 years, low serum lactate dehydrogenase (LDH) level, rare initial central nervous system (CNS) involvement, hyperdiploidy > 50 chromosomes, and prolonged event free survival (EFS).[26,27]

In a recent report,[28] on the other hand, the presence of CD34 on blast cells of adult ALL was associated with features of poor prognosis (higher WBC count, total or partial monosomy of chromosome 7, presence of Ph' chromosome and absence of hyperdiploidy). Nevertheless, no statistical differences were seen in this study with respect to leukemia-free survival (LFS) and overall survival (OS) between CD34 positive and negative cases. In the present report we analyzed a series of biological and clinical findings from 128 patients affected by ALL in relation to pediatric and adult age and to

Correspondence: Dott. Nicola Cascavilla, Divisione di Ematologia, IRCCS Ospedale "Casa Sollievo della Sofferenza", viale Cappuccini, 71013 San Giovanni Rotondo, Italy. Tel. international +39.882.410295. Fax international +39.882.411705.
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the expression of the CD34 antigen on leukemic blast cells, in order to evaluate the possible clinical significance of this marker.

Materials and Methods

Patient characteristics

This study included 128 ALL patients (78 adults and 50 children under 15 years old; 75 males, 53 females) admitted at our Institution from 1986 to 1994. Diagnosis of ALL was made according to morphological and immunological criteria.[29] L3 FAB/SmIg+ cases were excluded due to their biological and clinical peculiarities. The median follow-up was 45 months (range 1 to 101).

Immunologic analysis

Immunophenotypic classification was performed by a large panel of monoclonal antibodies: CD7 (Leu9), CD5 (OKT1), CD2 (OKT11), CD1 (OKT6), CD4 (OKT4), CD8 (OKT8), CD3 (OKT3), CD24 (OKB2), HLA-DR class II (OKDR), CD10 (OKB-calla), CD19 (B4), CD20 (B1), CD22 (B2), CD14 (My4), CD13 (My7), CD33 (My9), CD15 (Leum1), CD41 (GpIIb/IIIa), CD38 (OKT10), CD71 (OKT9), CD34 (HPCA-1 until 1991, then HPCA-2). Direct and indirect immunofluorescence methods in flow cytometry (SPECTRUM III or FACScan) using bone marrow cells have already been reported.[30] Negative controls with isotype matched irrelevant IgG1, IgG2a and IgM monoclonal antibodies were performed in all cases. CD34 positivity was defined as antigenic expression greater than 10% on leukemic blasts, as suggested by the distribution of CD34 values (see Figure 1).[17,26,27] We corrected for contaminating normal hematopoietic cells as follows: first, on the basis of side and forward scattering properties, we gated the mononuclear cell fraction; then, in B-lineage ALL we corrected the results by subtracting the CD7- or CD3-positive cells from the measured CD34 value. In T-lineage ALL no subtraction was made because all marrow samples contained more than 85% blasts. In 24 ALL the two anti-CD34 monoclonal antibodies (HPCA-1 and HPCA-2) were both used; in these cases the observed differences didn't change the distribution below or above the 10% cutoff. Surface immunoglobulins, cytoplasmic mu chains, CD3 and CD22 and nuclear TdT were evaluated by microscope fluorescence or immunocytochemical techniques, as previously reported.[31] The growth fraction (percent of leukemic cells with nuclear positivity for the Ki67 monoclonal antibody) and membrane expression of the multidrug resistance (MDR) marker P-170 glycoprotein (at least 1% of leukemic cells positive for C-219 monoclonal antibody, comparable to that of the MDR-positive control CEM VLB 100 cell line) were also evaluated immunocytochemically in 90 cases (48 adults and 42 children).[32] On the basis of the immunologic study, we classified B-lineage ALL into three groups: early pre-B-ALL ($CD19^+/CD10^-$), common ALL ($CD19^+/CD10^+/CD20^\pm$) and pre-B-ALL ($CyIgM^+$). According to personal experience,[33] T-lineage ALL were divided instead into two groups: *early T-ALL* ($CyCD3^+/CD7^+/CD5^\pm/CD2^\pm$) and *late T-ALL* ($CD7^+/CD5^+/CD2^+/CD1^\pm/CD3^\pm$).

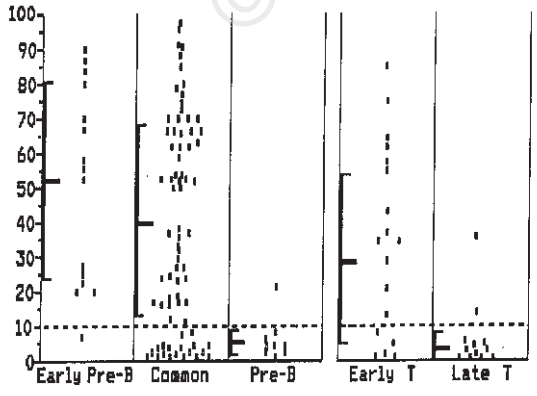

Figure 1. Percentages of CD34+ cells in ALL, according to the phenotypic degree of differentiation. Means and standard deviations are indicated in every group.

Karyotypic and DNA content analysis

Routine karyotypic studies were carried out on bone marrow cells of all cases. Bone marrow leukemic cells were also stained with propidium iodide and analyzed for cellular DNA content by flow cytometry according to conventional techniques in 85 cases (43 adults and 42 children).

Chemotherapy

Therapeutic approaches applied during the nine-year period of the study included the Italian Cooperative Study Groups GIMEMA 0183 and 0288 protocols for adult patients and 82, 87, 88 and 91 AIEOP generation protocols for children.

Statistical analysis

All patients were stratified for adult or pediatric age (above or below 15 years) and for CD34 expression (more or less than 10%). In each group, sex, age, FAB cytotype, lymphadenomegaly, hepatosplenomegaly, mediastinal and CNS involvement, LDH serum level, WBC, Plt and Hb count, immunophenotypic class, myeloid (CD33 and/or CD13 and/or CD15 and/or CD14) antigen co-expression, Ph' chromosome incidence, growth fraction, MDR phenotype, cytofluorimetric DNA index, achievement of complete remission (CR), disease free survival (DFS) and overall survival were evaluated. The differences between $CD34^+$ and $CD34^-$ groups were examined using chi-square or Fisher's exact tests.[34] DFS and OS curves were drawn according to the Kaplan and Meier method[35] and differences were compared by the log-rank test.[36] The correlation between CD34 and CD20 among B-lineage ALL and between CD34 and CD3 among T-lineage ALL was tested by calculating Pearson's correlation coefficient. Since CD34 was found to influence the clinical course of the disease significantly only in children (see *Results*), multivariate analysis with the Cox model[37] was limited to childhood ALL, where all analyzed parameters were available.

Results

All cases

Table 1 reports detailed characteristics of all $CD34^+$ and $CD34^-$ ALL. On the whole, CD34 expression greater than 10% occurred in 68.7% of the patients. No differences emerged between $CD34^+$ and $CD34^-$ groups with respect to age, sex, FAB morphology, incidence of hepatosplenomegaly, Plt count or Hb level. The frequency of lymphadenomegaly, mediastinal or CNS involvement during the course of the disease, and high LDH serum levels was, on the other hand, significantly higher in $CD34^-$ than in $CD34^+$ ALL, where significantly lower mean WBC levels were also observed. The CD34 antigen was more frequently expressed in B-lineage (74.5%) than in T-lineage ALL (50.0%), resulting in a B/T lineage ratio which was significantly higher within $CD34^+$ ALL. CD34 expression decreased, according to phenotype maturation, in both T- and B-lineage ALL (Figure 1).

Table 1. Clinical and laboratory characteristics in CD34+ and CD34– ALL. DNA index was evaluated in 85 patients. Ki67 and MDR phenotype were evaluated in 90 patients.

	CD34⁺ ALL	*CD34⁻ ALL*	*p*
No.	88 (68.7%)	40 (31.3%)	
Males/Females	51/37	24/16	ns
Mean age (range)	26.1 (2-82)	26.8 (3-78)	ns
Adults/Children	55/33	23/17	ns
L1/L2 FAB	34/54	12/28	ns
Mediastinal mass	7 (7.9%)	10 (25.0%)	< 0.02
Lymphadenomegaly	29 (32.9%)	23 (57.5%)	< 0.007
Hepatomegaly	35 (39.8%)	16 (40.0%)	ns
Splenomegaly	39 (44.3%)	24 (60.0%)	ns
CNS involvement*	3 (3.4%)	6 (15.0%)	< 0.03
Mean WBC (range) x10⁹/L	31.2 (1-216)	65.5 (1-540)	< 0.004
Mean Plt (range) x10⁹/L	95 (1-667)	103 (4-542)	ns
Mean Hb (range) g/dL	9.2 (4.2-16.0)	10.0 (4.7-16.6)	ns
LDH > 400 u/L	50 (56.8%)	30 (75.0%)	< 0.04
B/T lineage	73/15	25/15	< 0.02
Early pre-B	15 (20.5%)	1 (4.0%)	< 0.05
Common	57 (78.1%)	18 (72.0%)	ns
Pre-B	1 (1.4%)	6 (24.0%)	< 0.0009
Early T	13 (86.7%)	5 (33.3%)	< 0.003
Late T	2 (13.3%)	10 (66.7%)	< 0.003
My+ antigens	34 (38.6%)	5 (12.5%)	< 0.001
My+ antigens > 1	12 (13.6%)	—	< 0.008
DNA index > 1.16	29/60 (48.3%)	9/25 (36.0%)	ns
Mean Ki67 (range)	15.7 (0.2-58%)	33.6 (0.3-84%)	< 0.002
MDR phenotype	17/61 (27.9%)	8/29 (27.6%)	ns
Ph' chromosome	8 (9.1%)	—	< 0.05

**during the course of the disease.*

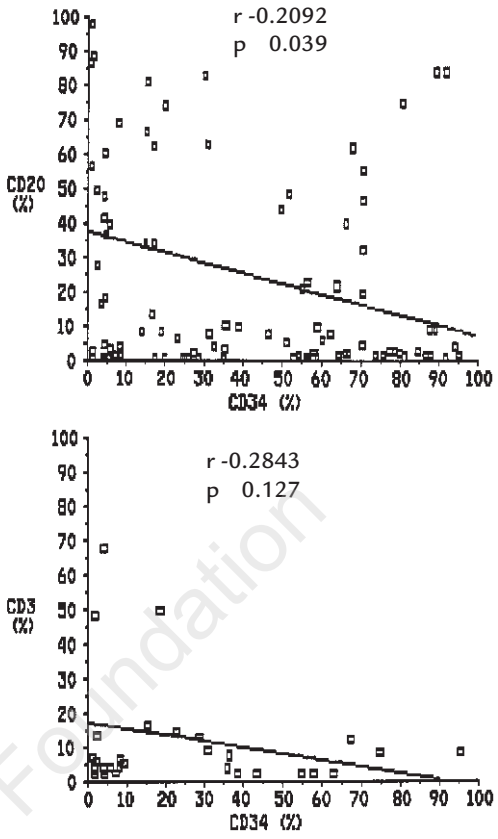

Figure 2. Relationship between expression of CD34 and two markers of B (CD20) and T (CD3) differentiation in ALL.

The ontogenetic hierarchy of CD34 and CD20 expression (for B-lineage ALL) and of CD34 and CD3 expression (for T-lineage ALL), as examined by Pearson's correlation coefficient analysis, was substantially respected, though the inverse expression was significant only for the CD34 and CD20 antigens (Figure 2). The frequency of myeloid antigens was significantly higher in CD34⁺ than CD34⁻ ALL. Furthermore, more than one myeloid antigen and Ph' chromosome were found exclusively in CD34⁺ ALL. Cytofluorymetric hyperdiploidy (DNA index greater than 1.16) and MDR phenotype expression were not statistically different between the two groups, whereas the growth fraction, as evaluated by nuclear positivity for the Ki67 monoclonal antibody, was significantly higher in CD34- ALL.

Adult vs childhood ALL

By stratifying all cases on the basis of age below or above 15 years, we observed that CD34 antigen expression correlated with different findings in childhood and adult ALL (Table 2). In fact, with respect to childhood CD34⁺ ALL, adult CD34⁺ ALL showed: a) higher WBC and lower Plt count; b) increased incidence of L2 FAB cytotype, *early Pre-B* and *early T* ALL; c) lower incidence of *common* and *late T* ALL; d) higher expression of MDR phenotype; e) lower frequency of cytofluorymetric hyperdiploidy; g) strong association between CD34 expression and Ph' chromosome. In contrast, adult CD34⁻ ALL, compared to childhood CD34⁻ ALL, were characterized by: a) lower WBC count; b) low frequency of *pre-B* and *late T* ALL (Table 3). Finally, statistically significant differences between CD34⁺ and CD34⁻ ALL, within homogeneous childhood and adult subgroups, are summarized in Table 4. In particular, childhood CD34⁺ ALL were characterized by lower age, WBC count, growth fraction, CNS involvement and P-170 glycoprotein expression, and by a higher frequency of hyperdiploidy and *favorable* B-phenotypes than childhood CD34⁻ ALL. Adult CD34⁺ ALL were more frequently associated with *early* T phenotype, expression of myeloid antigens, presence of the Ph' chromosome and lower growth fraction and extramedullary tumor mass than adult CD34⁻ ALL.

Clinical outcome

Overall, 113 patients (88.3%) achieved CR: 45 adult CD34⁺ ALL (81.8%) and 19 adult CD34- ALL

Table 2. Clinical and laboratory characteristics in CD34+, subdivided according to adult or childhood age. DNA index was evaluated in 60 patients. Ki67 and MDR phenotype were evaluated in 61 patients.

CD34⁺ ALL	*Adult ALL*	*Childhood ALL*	*p*
No.	55 (70.5%)	33 (66.0%)	ns
Males/Females	32/23	19/14	ns
L1/L2 FAB	13/42	21/12	< 0.003
Mediastinal mass	3 (5.4%)	4 (12.1%)	ns
Lymphadenomegaly	18 (32.7%)	11 (33.3%)	ns
Hepatomegaly	22 (40.0%)	13 (39.4%)	ns
Splenomegaly	23 (41.8%)	16 (48.5%)	ns
CNS involvement	2 (3.6%)	1 (3.0%)	ns
LDH > 400 U/L	31 (56.4%)	19 (57.6%)	ns
Mean WBC (range) x10⁹/L	36.4 (1-216)	23.6 (2-149)	< 0.05
Mean Plt (Range) x10⁹/L	78 (8-358)	120.1 (3-667)	< 0.04
Mean Hb (Range) g/dL	9.6 (4.7-15.0)	8.5 (4.2-15-2)	ns
B/T lineage	44/11	29/4	ns
Early pre-B	13 (29.5%)	2 (7.1%)	< 0.02
Common	30 (68.2%)	27 (85.8%)	< 0.01
Pre-B	1 (2.3%)	-	ns
Early T	11 (100%)	2 (50.0%)	< 0.03
Late T	-	2 (50.0%)	< 0.03
My+ antigens	24 (43.6%)	10 (30.3%)	ns
My+ antigens > 1	9 (16.4%)	3 (9.1%)	ns
Dna index > 1.16	11/31 (35.5%)	18/29 (62.1)	< 0.04
Mean Ki67 (range)	17.2 (0.2-58%)	14.1 (0.5-38%)	ns
MDR phenotype	13/35 (37.1%)	4/26 (15.4%)	< 0.05
Ph' Chromosome	8 (14.5%)	—	< 0.02

Table 3. Clinical and laboratory characteristics in CD34⁻, subdivided according to adult or childhood age. DNA index was evaluated in 25 patients. Ki67 and MDR phenotype were evaluated in 29 patients.

CD34⁻ ALL	*Adult ALL*	*Childhood ALL*	*p*
No.	23 (29.5%)	17 (34.0%)	ns
Males/Females	14/9	10/7	ns
L1/L2 Fab	5/18	7/10	ns
Mediastinal mass	4 (17.4%)	6 (35.3%)	ns
Lymphadenomegaly	14 (60.9%)	9 (52.9%)	ns
Hepatomegaly	8 (34.8%)	8 (47.0%)	ns
Splenomegaly	12 (52.2%)	12 (70.6%)	ns
CNS involvement	2 (8.7%)	4 (23.5%)	ns
LDH > 400 U/L	18 (78.3%)	12 (70.6%)	ns
Mean WBC (range) x10⁹/L	37.1 (1-233)	104.2 (1-540)	< 0.008
Mean Plt (range) x10⁹/L	99.6 (4-449)	103.2 (10-452)	ns
Mean Hb (range) g/dL	10.6 (6.0-16.6)	9.3 (4.7-15.1)	ns
B/T lineage	14/9	11/6	ns
Early pre-B	1 (7.1%)	—	ns
Common	12 (85.8%)	6 (54.5%)	ns
Pre-B	1 (7.1%)	5 (45.4%)	< 0.04
Early T	5 (55.5%)	—	< 0.05
Late T	4 (44.5%)	6 (100%)	< 0.05
My+ antigens	3 (13.0%)	2 (11.8%)	ns
My+ antigens > 1	—	—	—
DNA index > 1.16	6/12 (50.0%)	3/13 (23.1%)	ns
Mean Ki67 (range)	30.1 (0.3-81%)	30.7 (3-84%)	ns
MDR phenotype	3/13 (23.1%)	5/16 (31.2%)	ns
Ph' chromosome	—	—	—

Table 4. Clinical and laboratory parameters which proved to be significantly different between CD34⁺ and CD34⁻ ALL, according to adult and childhood age.

	CD34⁺ ALL	*CD34⁻ ALL*	*p*
Childhood ALL			
No.	33(66.0%)	17(34.0%)	
Mean age (range)	7.0 (2-14)	8.5 (3-15)	< 0.04
Age > 10 years	10(30.3%)	10 (58.8%)	< 0.05
CNS involvement	1 (3.0%)	4 (23.5%)	< 0.04
Mean WBC (range)	23.6 (2-149)	104.2 (1-540)	< 0.003
WBC > 100x10⁹/L	2 (6.1%)	5 (29.4%)	< 0.04
Common	27 (93.1%)	6 (54.5%)	< 0.01
Pre-B	—	5 (45.4%)	< 0.0007
DNA index > 1.16	18/29 (62.0%)	3/13 (23.1%)	< 0.03
Mean Ki67 (range)	14.1 (0.5-38%)	30.7 (3-84%)	< 0.02
Adult ALL			
No.	55 (70.5%)	23(29.5%)	
Lymphadenomegaly	18 (32.7%)	14(60.9%)	< 0.02
Early T	11 (100%)	5 (55.5%)	< 0.03
Late T	—	4 (44.5%)	< 0.03
My+ antigens	24 (43.6%)	3 (13.0%)	< 0.007
My+ antigens > 1	9 (16.4%)	—	< 0.04
Ph' chromosome	8(14.5%)	—	< 0.05
Mean Ki67 (range)	17.2 (0.2-58%)	30.1 (0.3-81%)	< 0.01

(82.6%) (p=NS); 33 childhood CD34+ (100%) and 16 childhood CD34⁻ (94.1%) (p=NS). In childhood, both DFS (median not reached at 92 months vs 14 months) and OS (77 vs 31 months) were significantly better in patients expressing the CD34⁺ antigen (Figure 3). No significant difference was found, however, between CD34⁺ and CD34⁻ adult ALL (Figure 4). Multivariate analysis in childhood ALL confirmed the independent positive prognostic weight of CD34 expression at diagnosis, along with *common* phenotype and high WBC count (Table 5).

Discussion

Recent advances in the fields of karyotypic analysis and molecular biology suggest that adult and childhood ALL are probably different diseases and that the detection of a stem cell disorder could be more frequent in adults.[38,39] With the aim of verifying this hypothesis, we compared a series of biological and clinical parameters in childhood and adult ALL, in relation to the differentiative degree of blast cells, based on CD34 antigen expression analysis. We detected the CD34 antigen on at least 10% of leukemic cells in 68.7% of unselected cases, without significant differences, in particular, in sex, age or FAB cytotype. Moreover, CD34 expression was significantly higher in B- than T-lineage ALL. These data are in agreement with previous reports in both childhood[27] and adult series,[28,40] suggesting a more

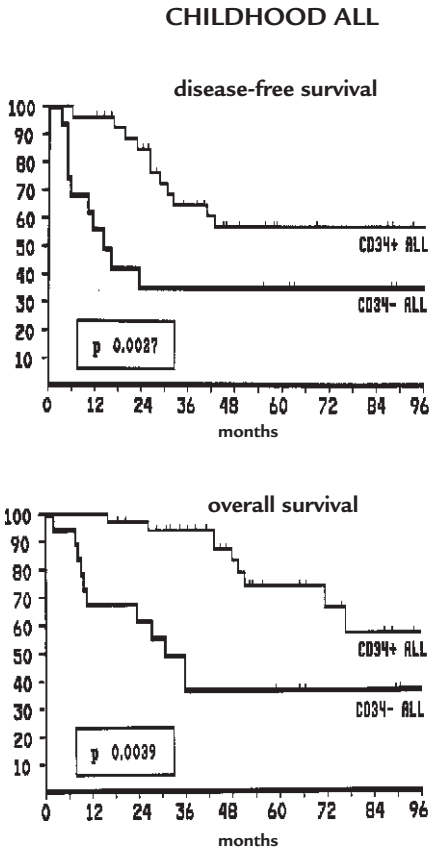

Figure 3. DFS and OS in childhood ALL with or without expression of the CD34 antigen.

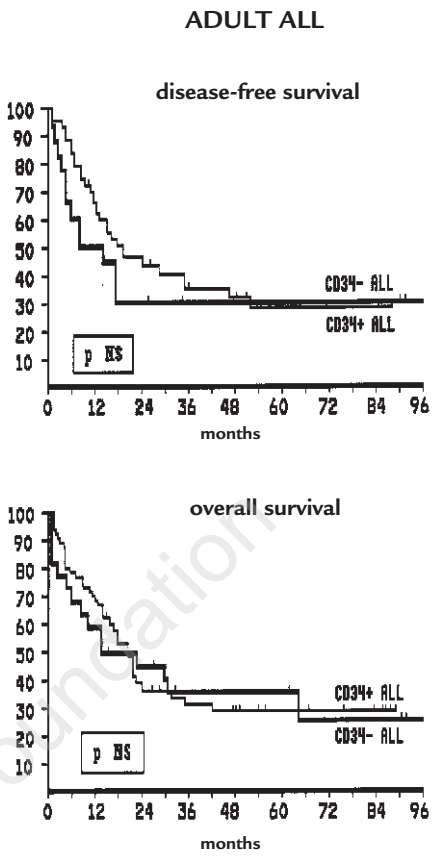

Figure 4. DFS and OS in adult ALL with or without expression of the CD34 antigen.

immature hematopoietic cell involvement in B-lineage ALL. In general, $CD34^+$ ALL were also characterized by reduced leukemic mass, low risk of CNS involvement, *early* B or T phenotype, high incidence of myeloid antigen co-expression and Ph' chromosome, lower growth fraction. Such *crude* results could seem quite intriguing since some of these aspects are known to be parameters of poor prognosis, while others usually correlate with a good clinical outcome.[6,7,9,33,41-49] However, when analyzed

Table 5. Results of multivariate analysis in 39 childhood ALL evaluable for all parameters. The independent prognostic weight of CD34 expression is evident on disease free survival, as well as on overall survival.

	Disease free survival			*Overall survival*		
	p	*risk*	*95% C.I.*	*p*	*risk*	*95% C.I.*
Common Vs pre-B	0.0038	6.2	(1.8-21.9)	0.0052	5.3	(1.6-18.2)
CD34 (< Vs > 10%)	0.0168	4.1	(1.3-15.2)	0.0291	3.8	(1.2-13.8)
WBC (< Vs > 100x10⁹/L)	0.4330	3.2	(1.0-9.8)	0.0406	3.4	(1.0-10.2)
MDR phenotype (+ Vs –)	ns	—		ns	—	
Growth fraction (< Vs >20%)	ns	—		ns	—	
DNA index (< Vs > 1.16)	ns	—		ns	—	
FAB (L1 Vs L2)	ns	—		ns	—	
Age (< Vs > 10 yrs)	ns	—		ns	—	
Myeloid antigens (+ Vs –)	ns	—		ns	—	
Phenotype (B Vs T)	ns	—		ns	—	

according to adult and childhood age, CD34$^+$ ALL showed a significant segregation of several prognostic factors. In fact, adult CD34$^+$ ALL were prevalently associated with *negative* parameters (L2 morphology, higher WBC count, lower Plt count, *immature* B- and T-lineage phenotype, less frequent cytofluorimetric hyperdiploidy, presence of Ph' chromosome and higher MDR phenotype), while their *favorable* counterparts characterized CD34$^+$ childhood ALL instead. A high WBC count in childhood was the most consistent difference between CD34$^-$ and CD34$^+$ ALL. The different distribution of various biological and clinical characteristics with relation to CD34 antigen expression was even more evident when we compared CD34$^+$ and CD34$^-$ ALL within the two age groups. Indeed, in children, a series of favorable prognostic factors (lower age, WBC count, growth fraction, P-170 expression and CNS involvement, higher DNA index, higher frequency of *common* and lack of *pre-B* phenotype) clustered within CD34$^+$ with respect to CD34$^-$ ALL. On the other hand, the distribution of prognostic parameters was more heterogeneous in adult ALL, where both potentially negative (*immature* B or T phenotype, co- expression of myeloid antigens, presence of Ph' chromosome) and positive (low growth fraction) findings were represented. This resulted in a clinical outcome which was significantly better, in terms of both DFS and OS, in CD34$^+$ than in CD34$^-$ childhood ALL, while no differences emerged between CD34$^+$ and CD34$^-$ adult ALL. Vaughan *et al*.,[50] in a small series, concluded that very high (> 70%) CD34 expression had no prognostic influence in ALL. More recently, Borowitz *et al*.[26] found that children with B-lineage CD34$^+$ ALL had longer EFS than CD34$^-$ cases, and that CD34 expression had an independent favorable effect on outcome even after exclusion of cases with cytoplasmic Ig and hyperdiploidy. Pui *et al*.[27] also reported that EFS was better for CD34$^+$ childhood ALL. In their study, multivariate analysis showed that the prognostic influence of this antigen was independent of other recognized prognostic factors, suggesting that it would add discriminatory power to current systems of risk assignment. Finally, in a study by Thomas *et al*.[28] on adult ALL, no statistical differences were seen in LFS and OS between CD34$^+$ and CD34$^-$ cases, even though CD34 expression was associated with major adverse prognostic factors. Most of these findings are confirmed and extended in our series. Thus we conclude that: 1) CD34 expression is a frequent event in ALL, without significant differences in incidence between adults and children; 2) CD34 expression is associated with different characteristics in childhood and adult ALL, thus underscoring the profound biological differences between these disorders; 3) detection of CD34 on blast cells has an independent positive prognostic impact in childhood ALL; this does not seem to be the case for adult ALL.

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