

## Immunophenotypic, Cytogenetic and Clinical Features in Chinese Adult Acute Lymphoblastic Leukaemia (ALL) Patients

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### Abstract

**Introduction:** This study sought to investigate the immunophenotypic subtype profiles of 110 Chinese adult patients with acute lymphoblastic leukaemia (ALL) and its association to cytogenetics and the clinical features. **Materials and Methods:** A total of 110 adult patients with ALL were immunophenotyped by CD45/SSC double parameters and 4 colour flow cytometry. Seventy-three cases were also subjected to karyotype analysis by R-banding technology. The clinical and laboratory data of 110 ALL patients were retrospectively analysed. **Results:** Of all the patients, 21.8% were identified as T-ALL, 78.2% as B-ALL. Abnormal karyotypes were detected in 37 out of 73 (50.7%) cases and the most common cytogenetic abnormality was the Philadelphia (Ph) chromosome, which was found in 23.3% (17/73) of the cases. Myeloid antigen (MyAg) expression was documented in 47.3% of the 110 adult ALL cases analysed and CD13 was the most commonly expressed MyAg in ALL patients (32.1 %). No difference was observed in the expression of MyAg between the groups of patients with T-ALL (45.8%) and B-ALL (47.7%). Our data showed that older age, higher CD34 positivity and lower proportion of patients with splenomegaly were found to be correlated with MyAg+ ALL, and that patients with Ph+ B-ALL were older, presented with higher haemoglobin level and higher CD34 expression. No statistical difference was noted in complete remission (CR) rate, relapse rate, induction mortality or total death rate among My+ and My-, Ph+ and Ph-, or B-ALL and T-ALL patients. **Conclusion:** Our results indicate that the distribution of ALL in Chinese adult patients was similar with the general distribution pattern in the other countries, and the expression of MyAg in patients with T-ALL and B-ALL was comparable. Both the expression of MyAg and the presence of Ph chromosome in adult ALL were significantly associated with median age and CD34 expression while not with the response to induction treatment.

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**Key words:** Biological characteristics, Cytogenetics, Immunophenotype

### Introduction

Acute lymphoblastic leukaemia (ALL) is a malignant disease resulting from the accumulation of genetic alterations of B or T lymphoid precursor cells.<sup>1,2</sup> Immunophenotyping, cytogenetic-molecular studies, and more recently, high resolution genome-wide screening are characterising ALL as a heterogeneous disease with distinct manifestations and prognostic and therapeutic implications.<sup>3</sup> Of the many variables that influence prognosis, genetic subsets, initial white blood cell count (WBC), age at diagnosis, and early treatment response are the most important.<sup>4</sup> ALL is the most

common leukaemia in children and accounts for 20% of acute leukaemias in adults, and it remains one of the most challenging adult malignancies, especially with respect to therapy. The 5-year event-free survival is over 80% for children but only approximately 40% for adults with ALL.<sup>1</sup> Though the outcome of patients with ALL has improved with intensification of therapy and complete remission (CR) can now be achieved in majority of adults with ALL, only 30% to 40% of them are cured with varying proportion according to clinical and biological risk factors.<sup>5-9</sup>

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Because leukaemic lymphoblasts lack specific morphologic and cytochemical features, the assessment of immunophenotype by flow cytometry and the identification of distinct cytogenetic-molecular abnormalities have become essential and are part of the World Health Organization classification of neoplastic diseases of hematopoietic and lymphoid tissues.<sup>10</sup> In this study, we have investigated the clinical and biologic features of 110 adult patients with ALL and analysed the correlations between immunophenotype, cytogenetic abnormalities and clinical features of these patients. One of the most important aims of this study was to investigate the prevalence of the expression of the myeloid associated antigens in adult ALL and to relate their presence to the initial clinical and biologic features as well as to early response to therapy. Expression of myeloid antigen (MyAg) was a common aberrancy in ALL and reports vary widely on the degree of MyAg expression.<sup>11-14</sup> Consequently, the clinical significance of MyAg expression is unclear. One potential reason for this variation is differences in the binding characteristics of different monoclonal antibody clones.<sup>15</sup> Different thresholds for antigen positivity and different flow cytometry methods, instruments, and reagents may also have a role. Some scholars indicated that ALL patients with MyAg expression had poor prognosis.<sup>16,17</sup> However, most reports indicate that MyAg expression in ALL patients is not associated with adverse presenting clinical and biological features and prognosis.<sup>14,18</sup> The relatively small numbers of patients in ALL series and differences in the treatment protocols have led to divergent results. Although the presence of MyAg lacks prognostic significance, it can be useful in distinguishing leukaemic cells from normal hematogones and in monitoring patients for minimal residual disease (MRD).<sup>19</sup>

## Materials and Methods

### *Study Population and Treatment Protocols*

A total of 110 adult patients with newly diagnosed ALL were enrolled in this study and their bone marrow (BM) were collected from January 2007 to July 2010 in our hospital. Of these subjects, there are 60 males and 50 females with a median age of 31 years, ranging from 15 to 77 years old. The only inclusion criterion was the availability of a full immunophenotypic profile.

Patients received remission-induction and consolidation therapy, followed by risk-directed continuation treatment. The main remission-induction programme is VDLP regimen (vincristine 2 mg, day 1; daunomycin 40 mg/day, days 1 to 3; L-asparaginase 10,000 U/day, days 14 to 25 and dexamethasone 10 mg/day, days 1 to 20, then dexamethasone 5 mg/day, days 21 to 25). Once remission was achieved, patients received consolidation therapy and continuation treatment as scheduled: VDLP-EA-high dose

methotrexate-VMLP-EA-high dose methotrexate-VDLP, repeat from VDLP for 5 cycles. EA (etoposide + Ara-C) regimen: etoposide 40 mg/m<sup>2</sup>/day, days 1 to 5; cytosine arabinoside 2g/m<sup>2</sup>/day, days 1 to 5. Methotrexate 3 to 5 g/m<sup>2</sup>, 24 hours. VDLP regimen: vincristine 2 mg, day 1; daunomycin 60 mg/day, days 1 to 3; cyclophosphamide 800 mg/day, days 1, 3 and dexamethasone 10 mg/day, days 1 to 20, then dexamethasone 5 mg/day, days 21 to 25. VMLP regimen: vincristine 2 mg, day 1; mitoxantrone 10 mg/day, days 1 to 3; L-asparaginase 10,000 U/day, days 14 to 25 and dexamethasone 10 mg/day, days 1 to 20, then dexamethasone 5 mg/day, days 21 to 25.

Morphologic CR was defined as less than 5% blast cells in a regenerated BM aspirate, absence of extramedullary leukaemia, and peripheral blood (PB) neutrophil and PLT counts of  $>1.5 \times 10^9$  and  $>100 \times 10^9/L$ , respectively. Clinical relapse was defined as detection of at least 5% blast cells in BM or detection of leukaemic cells extramedullary. The study was approved by the ethics committee in our hospital with written informed consent from the parents or guardians, as well as from the patients.

### *Immunophenotype Detection of Leukaemia Cells*

Immunophenotype was determined for ALL cases using 4 colour flow cytometry profiles with fluorescein isothiocyanate (FITC), phycoerythrin (PE), allophycocyanin (APC) or peridinin chlorophyll-protein (Per-CP) labeled monoclonal antibodies, including CD45, CD34, CD10, CD19, CD2, CD13, HLA-DR, CD33, CD7, CD38, CD20, CD22, CD15, CD9, CD117, CD14, CD3, CD5, CD4, CD8, CyCD3, CyIgM, and CyCD79a. The reagents and 12 × 75 mm Falcon™ capped polystyrene test tubes were provided by Becton-Dickinson Bioscience in the United States. Cells were acquired and analysed with Cell Quest and Paint-A-Gate software in FACS Calibur flow cytometer (BD Bio). Abnormal populations were recognised by CD45/SSC gating, which was the base of calculating the positive rate of leukaemia-related antigens expressed on the abnormal cells. Cell populations were designated as positive for a particular antigen if more than 20% of the leukaemic lymphoblast events stained beyond an appropriate isotypic cutoff (set at 98% of isotypic control staining); otherwise they were designated as negative. We regarded  $\geq 10\%$  of cell expression in a tube as positive for CyIgM, CyCD79a or CyCD3.

### *Cytogenetic Analysis*

BM cells were cultured for 24 hours to prepare for conventional chromosome detection, and karyotype was analysed with R-banding technique. Each karyotype was named according to International Human Chromosomes Nomenclature (ISCN 1995).

### Statistical Methods

Statistical analysis was performed taking into account gender, age, WBC count, haemoglobin (HB) level, PLT count, BM blasts, presence or absence of hepatomegaly, splenomegaly and lymphadenopathy, immunophenotype, cytogenetics and the patients's response to treatment. Data analysis was carried out using SPSS software (version 13.0, SPSS, Chicago, IL, USA). Statistical differences of various clinical and laboratory parameters between groups were analysed by the Kruskal-Wallis H test, Mann-Whitney U test, chi-Square or Fisher's Exact tests. *P* values of less than 0.05 were considered significant.

### Results

#### Immunophenotype and MyAg Expression in ALL Patients

CD45 staining and side scatter (SS) properties were used to isolate the leukaemic cell populations, referred to as the bulk of the leukaemia and usually defined by a weak CD45 expression (CD45dim) and low SS (SSlow) (Figs. 1 to 3). B-lineage markers: CyCD79a, CD19, CD10, and CD22 were expressed in the vast majority of B-ALL samples. No more than a single T-cell antigen was expressed in any 1 case, and expression of CD3 was not observed. Thus, T-cell/B-cell biphenotypic leukaemias were not observed in this patient cohort. Of 24 T-ALL cases, CD7 was the only surface T-cell

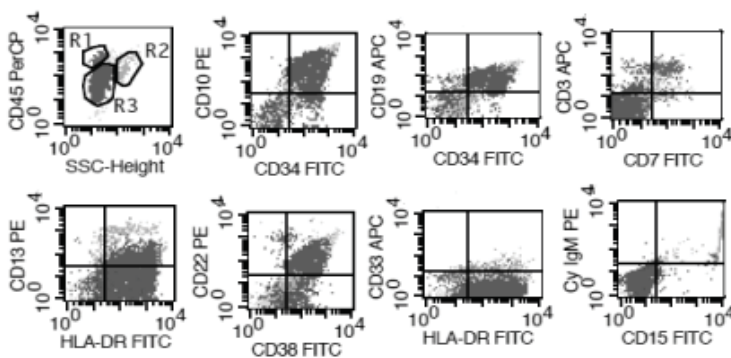


Fig. 1. Com-B ALL. The abnormal blasts (R3) are positive for CD34, CD10, CD19, CD13, HLA-DR, CD38 and CD22.

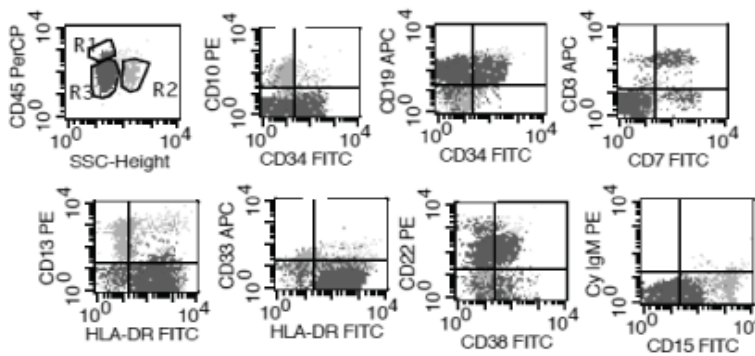


Fig. 2. Pro-B ALL. The abnormal blasts (R3) are positive for CD34, CD19, CD38, HLA-DR, CD22 and CD15.

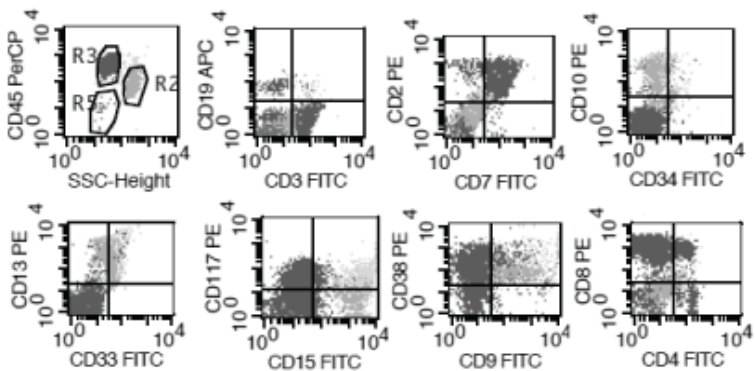


Fig. 3. T-ALL. The abnormal blasts (R3) are positive for CD3, CD2, CD7, CD38, CD8 and CD117.

antigen expressed by all T-ALL cases (100%), followed by CD5 (65.2%), CD2 (65.2%), CD3 (54.2%), CD8 (47.8%) and CD4 (26.1%). The positive rates of CD34 and HLA-DR were much lower in T-ALL than those in B-ALL (25% vs 74.4%, 41.7% vs 100%,  $P = 0.000$ ).

MyAg expression was documented in 47.3% of the 110 adult patients analysed. CD13 was the most commonly expressed MyAg (32.1%) (Fig. 1), followed by CD15 (15.1%) (Fig. 2), CD33 (6.4%) and CD117 (5.7%). CD14 was negative in all ALL patients, and CD117 was negative in all B-ALL patients but positive in 30% T-ALL patients (Fig. 3). CD13 expression was found most commonly in Com B-ALL (42.6%) than CD15 (13.5%) and CD33 (8.5%) ( $P = 0.004$ ,  $P = 0.000$ ), and CD15 expression was found most frequently in ProB-ALL (60%) than that in Com B-ALL (13.5%) and Pre B (3.7%) ( $P = 0.008$ ,  $P = 0.001$ ). The myeloid antigens were detected and seen in the same population as the leukaemic blasts (Figs. 1 to 3). Furthermore, no difference was observed in the expression of MyAg between the groups of patients with T-ALL (45.8%) and B-ALL (47.7%) ( $P = 0.873$ ). MyAg expression was also compared in the subtypes of B-ALL, and MyAg positivity in Com B-ALL (53.2%), Pro B-ALL (58.3%) and Pre B-ALL (50.0%) was comparable.

### Cytogenetics

A total of 73 cases were subjected to karyotype analysis, including 59 cases of B-ALL and 14 cases of T-ALL, and the karyotype studies showed that a total of 37 (50.7%) had an abnormal karyotype. Numerical abnormality of chromosome was found in 12 cases, including 7 cases of hyperdiploid and 5 cases of hypodiploid. Structural abnormality of chromosome was found in 25 cases, and 17 cases of  $t(9;22)(q34;q11)$  were found in Com-B and Pre-B, 1 case of  $t(4;11)(q21;q23)$  were found in Pro-B, and 1 case of  $t(10;14)(q24;q11)$ , 2 cases of  $del(6q)$  were found in T-ALL.

### Clinical and Biological Features in ALL Patients

On the basis of the positivity for at least one myeloid marker, we stratified the patients into 2 groups: MyAg+ and MyAg-. The clinical and biological characteristics of the patients were presented in Table 1. No differences were found between the MyAg+ and MyAg- groups with regard to proportion of females/males, median WBC count, haemoglobin level and PLT count, percentage of patients with high WBC count ( $>50 \times 10^9/L$ ), percentage of BM blasts, proportion of B/T-lineage ALL patients and cytogenetic abnormalities. However, the median age in MyAg+ was older than that in MyAg- ALL ( $P = 0.016$ ), and CD34 expression was found in 75.0% of MyAg+ and in 53.4%

of MyAg- cases ( $P = 0.019$ ). In addition, the percentage of patients with splenomegaly in MyAg+ group was much lower than that in MyAg- group (25.5% vs 55.6%,  $P = 0.002$ ), but there was no significant difference between the 2 groups with regard to cases with hepatomegaly or lymphadenomegaly ( $P = 0.108$ ,  $P = 0.937$ ).

Twenty-five ALL patients stopped treatment after diagnosis while the remaining 85 ALL patients received treatment. Seven patients died during remission-induction therapy. We failed to observe any statistical difference between the 2 groups in induction mortality (10.3% vs 6.5%,  $P = 0.819$ ) and total death rate (25.6% vs 21.7%,  $P = 0.673$ ). Seventy-eight ALL patients who received

Table 1. Clinical and Biological Features in MyAg+ and MyAg- ALL Patients

| Features                              | MyAg+           | MyAg-           | P values |
|---------------------------------------|-----------------|-----------------|----------|
| Gender (male/female)                  | 27/25           | 33/25           | 0.601    |
| Age (years)                           | 37.0            | 28.5            | 0.016    |
| (range)                               | (24.0 to 49.0)  | (17.3 to 42.0)  |          |
| WBC count ( $\times 10^9/L$ )         | 16.8            | 19.9            | 0.834    |
| (range)                               | (6.2 to 57.5)   | (4.2 to 52.1)   |          |
| Haemoglobin (g/L)                     | 84.0            | 84.5            | 0.867    |
| (range)                               | (62.0 to 108.0) | (58.8 to 113.8) |          |
| PLT count ( $\times 10^9/L$ )         | 41.0            | 38.0            | 0.623    |
| (range)                               | (21.0 to 94.0)  | (17.5 to 72.5)  |          |
| BM blasts (%)                         | 78.1            | 84.5            | 0.544    |
| (range)                               | (66.8 to 89.9)  | (67.4 to 90.6)  |          |
| WBC count ( $\times 10^9/L$ )         |                 |                 |          |
| (>50 / <50)                           | 17/35           | 18/40           | 0.852    |
| CD34 ( $\pm$ )                        | 39/13           | 31/27           | 0.019    |
| Cytogenetics (normal/abnormal)        | 18/21           | 18/16           | 0.563    |
| Ph ( $\pm$ )                          | 10/29           | 7/27            | 0.610    |
| B-ALL/T-ALL                           | 41/11           | 45/13           | 0.873    |
| Hepatomegaly (%)                      | 9/47 (19.1)     | 18/54 (33.3)    | 0.108    |
| Splenomegaly (%)                      | 12/47 (25.5)    | 30/54 (55.6)    | 0.002    |
| Lymphadenomegaly (%)                  | 24/47 (51.1)    | 28/54 (51.9)    | 0.937    |
| CR rate after the first induction (%) | 23/35 (65.7)    | 33/43 (76.7)    | 0.282    |
| Overall CR rate (%)                   | 29/35 (82.9)    | 38/43 (88.4)    | 0.486    |
| Relapse rate (%)                      | 13/29 (44.8)    | 16/38 (42.1)    | 0.824    |
| Induction mortality (%)               | 4/39 (10.3)     | 3/46 (6.5)      | 0.819    |
| Total death rate (%)                  | 10/39 (25.6)    | 10/46 (21.7)    | 0.673    |

BM: Bone marrow; CR: Complete remission; MyAg: Myeloid antigen; Ph: Philadelphia; PLT: Platelet; WBC: White blood count

remission-induction therapy were evaluated for response. No differences were found between the 2 groups in terms of CR rate after the first induction (65.7% vs 76.7%,  $P = 0.282$ ) and overall CR rate (82.9% vs 88.4%,  $P = 0.486$ ). The presence of aberrant MyAg did not affect the cumulative incidence of relapse (44.8% vs 42.1%,  $P = 0.824$ ) and the median relapse (4.8 vs 7.5 months,  $P = 0.221$ ). We separately analysed the presence of MyAg in T and B lineage ALL cases, and failed to find any difference in CR achievement, relapse or death rate between MyAg+ and MyAg− cases in the different ALL subgroups (data not shown).

Analysis of the clinical and laboratory findings in different B-ALL subtypes and T-ALL failed to establish significant association for mean age, mean PLT count, cytogenetic abnormalities, MyAg positivity and percentage of BM blasts, as well as hepatomegaly and splenomegaly (Table 2). However, among different B-ALL subtypes, the proportion

of male patients in Com B-ALL was higher than that in Pre B-ALL ( $P = 0.008$ ). Higher percentage of patients with WBC count ( $>50 \times 10^9/L$ ) and higher median WBC count were both found in Pro B-ALL than those in Com B or Pre B-ALL ( $P = 0.030$ ,  $P = 0.004$ ,  $P = 0.029$ ,  $P = 0.001$ ). Higher CD34 positivity was found in Com B -ALL than that in Pre B -ALL ( $P = 0.025$ ). The total death rate in Pro B-ALL was higher than that in Com B or Pre B-ALL ( $P = 0.003$ ,  $P = 0.032$ ). Besides, compared with B-ALL, higher percentage of male patients ( $P = 0.003$ ), higher percentage of patients with WBC count ( $>50 \times 10^9/L$ ) ( $P = 0.002$ ) and lymphadenomegaly ( $P = 0.030$ ), higher median WBC count ( $P = 0.017$ ) and haemoglobin level ( $P = 0.010$ ), lower CD34 positivity ( $P = 0.000$ ) seem to be the typical features of T-cell ALL subtype. No statistical differences were noted between the 2 groups with regard to CR rate, relapse rate, induction mortality and total death rate.

Table 2. Clinical and Biological Features in Adult Patients with B-ALL and T-ALL

| Features                              | Pro-B           | Com-B           | Pre-B          | Total-B         | T-ALL           |
|---------------------------------------|-----------------|-----------------|----------------|-----------------|-----------------|
| Gender (male/female)                  | 3/9             | 29/18†          | 8/19           | 40/46*          | 20/4            |
| Age (years)                           | 37.0            | 26.5            | 40.0           | 32              | 30.5            |
| (range)                               | (28.3 to 54.0)  | (17.3 to 44.3)  | (22.0 to 55.0) | (20.0 to 46.0)  | (23.0, to 48.8) |
| WBC count ( $\times 10^9/L$ )         | 51.6†           | 17.0†‡          | 7.1            | 11.5*           | 51.2            |
| (range)                               | (14.1 to 190.5) | (6.2 to 49.5)   | (3.8 to 13.5)  | (4.2 to 49.9)   | (16.8 to 123.0) |
| Haemoglobin (g/L)                     | 67.5            | 86.0            | 67.0           | 77.0*           | 108.0           |
| (range)                               | (57.3 to 83.3)  | (61.0 to 120.0) | (57.0 to 91.5) | (58.0 to 100.0) | (76.0 to 125.0) |
| PLT count ( $\times 10^9/L$ )         | 42.0            | 31.0            | 38.0           | 36.0            | 61.5            |
| (range)                               | (9.0 to 94.5)   | (17.0 to 2.0)   | (12.0 to 71.3) | (16.0 to 72.0)  | (21.3 to 110.8) |
| BM blasts (%)                         | 92.6            | 80.1            | 77.0           | 81.2            | 84.5            |
| (range)                               | (71.8 to 94.9)  | (68.0 to 88.4)  | (66.7 to 88.5) | (67.0 to 89.3)  | (69.2 to 95.0)  |
| WBC count ( $\times 10^9/L$ )         |                 |                 |                |                 |                 |
| ( $>50$ / $<50$ )                     | 7/5             | 12/35‡          | 3/24‡          | 22/64*          | 14/10           |
| CD34 ( $\pm$ )                        | 9/3             | 39/8†           | 16/11          | 64/22*          | 6/18            |
| Cytogenetics (normal/ abnormal)       | 7/2             | 14/16           | 9/11           | 30/29           | 6/8             |
| MyAg ( $\pm$ )                        | 7/5             | 25/22           | 9/18           | 41/45           | 11/13           |
| Hepatomegaly (%)                      | 3/10 (30.0)     | 9/44 (20.5)     | 8/23 (34.8)    | 20/77 (26.0)    | 7/24 (29.2)     |
| Splenomegaly (%)                      | 4/10 (40.0)     | 18/44 (40.9)    | 8/23 (34.8)    | 30/77 (39.0)    | 12/24 (50.0)    |
| Lymphadenomegaly (%)                  | 4/10 (40.0)     | 20/44 (45.5)    | 11/23 (47.8)   | 35/77 (45.5)*   | 17/24 (70.8)    |
| CR rate after the first induction (%) | 3/7 (42.9)      | 29/37 (78.4)    | 15/19 (78.9)   | 47/63 (74.6)    | 9/15 (60.0)     |
| Overall CR rate (%)                   | 5/7 (71.4)      | 32/37 (86.5)    | 17/19 (89.5)   | 54/63 (85.7)    | 13/15 (86.7)    |
| Relapse rate (%)                      | 3/5 (60.0)      | 12/32 (37.5)    | 8/17 (47.1)    | 23/54 (42.6)    | 6/13 (46.2)     |
| Induction mortality (%)               | 2/9 (22.2)      | 1/38 (2.6)      | 1/20 (5.0)     | 4/67 (6.0)      | 3/18 (16.7)     |
| Total death rate (%)                  | 6/9 (66.7)      | 5/38 (13.2) ‡   | 4/20 (20.0) ‡  | 15/67 (22.4)    | 5/18 (27.8)     |

BM: Bone marrow; CR: Complete remission; MyAg: Myeloid antigen; PLT: Platelet; WBC: White blood count

\* $P \leq 0.05$ , compared with T-ALL group.

† $P < 0.05$ , compared with Pre-B group.

‡ $P < 0.05$ , compared with Pro-B group.

### Clinical and Biological Features of Ph+ and Ph- Precursor B-cell ALL

The clinical and biological characteristics of the 59 B-ALL patients with Philadelphia (Ph)+ and Ph- are summarised in Table 3. In this study, 28.8% of the adult patients with B-ALL were identified as Ph+. Almost all Ph+ ALL cases have a precursor B-cell phenotype and most expressed CD19, CD10 and CD34 in our patients, which is similar to that reported elsewhere.<sup>20</sup> There was no difference in gender distribution between Ph+ and Ph- patients but the median age was significantly higher in the Ph+ group (35- vs 25-year olds,  $P = 0.025$ ). The Ph+ patients were also characterised by higher median haemoglobin levels (110.5 g/L vs 66.5 g/L,  $P = 0.001$ ). The WBC counts, platelet (PLT) counts and BM blast infiltration were found to be similar in both Ph+ and Ph- patients. Higher CD34 positivity was observed in Ph+ B-ALL than that in Ph- B-ALL (94.1 vs 64.3%,  $P = 0.044$ ). While no statistical significance was observed for expressing of MyAg, organomegaly (lymphadenomegaly, hepatomegaly and splenomegaly), CR rate, death rate, relapse rate and the median relapse among Ph- and Ph+ patients.

### Discussion

Of all the adult patients, 21.8% were identified as T-ALL, 78.2% as B-ALL, and comparison of different subtypes of B-ALL in this study has demonstrated a higher frequency of Com-B subtype (54.7%) followed by Pre-B (31.4%) and Pro-B (14.0%) subtype, which was consistent with earlier reports.<sup>21,22</sup> The dissimilarities observed among various studies could largely be due to the small sample size of the patients in many studies and methodological differences in classification of ALL. We confirmed the close association between T-cell phenotype with higher frequency of males, higher median WBC count and haemoglobin level, higher percentage of patients with WBC count ( $>50 \times 10^9/L$ ) and lymphadenomegaly, and lower CD34 positivity, which was also demonstrated by other reports.<sup>23,24</sup> Many groups have confirmed the superior outcome of T-ALL as compared to B-ALL in adults,<sup>24</sup> while others reported that T-cell immunophenotype tended to be associated with a poorer outcome,<sup>25</sup> and adult patients in the B-ALL subgroup did fairly well.<sup>21</sup> It was similar to an early report that CR was achieved in 85.9% patients, with no significant difference in CR rate between B- and T-ALL in our study.<sup>26</sup> Meanwhile, no differences were found between the 2 groups with regard to relapse rate, induction mortality and total death rate.

It has been thought that ALL cells with expression of MyAg originate from initial stem cells earlier than lymph-directional stem cell and progenitor cell. In our study, the overall incidence of MyAg expression in adult ALL patients was 47.3% and CD13 was the most commonly

Table 3. Clinical and Biological Features of Ph+ and Ph- B-ALL

| Features                              | Ph+             | Ph-            | P values |
|---------------------------------------|-----------------|----------------|----------|
| Gender (male/female)                  | 8/9             | 15/27          | 0.418    |
| Age (years)                           | 35.0            | 25.0           | 0.025    |
| (range)                               | (27.5 to 49.5)  | (18.8 to 38.8) |          |
| WBC count ( $\times 10^9/L$ )         | 16.4            | 10.3           | 0.408    |
| (range)                               | (6.1 to 88.0)   | (4.2 to 50.5)  |          |
| Haemoglobin (g/L)                     | 110.5           | 66.5           | 0.001    |
| (range)                               | (72.5 to 126.5) | (54.5 to 84.3) |          |
| PLT count ( $\times 10^9/L$ )         | 39.0            | 39.5           | 0.900    |
| (range)                               | (19.8 to 67.8)  | (19.3 to 72.5) |          |
| BM blasts (%)                         | 83.4            | 84.8           | 0.795    |
| (range)                               | (74.7 to 90.5)  | (66.6 to 90.2) |          |
| WBC count ( $\times 10^9/L$ )         |                 |                |          |
| ( $>50 / <50$ )                       | 4/13            | 12/30          | 0.943    |
| CD34 ( $\pm$ )                        | 16/1            | 27/15          | 0.044    |
| MyAg ( $\pm$ )                        | 10/7            | 20/22          | 0.436    |
| Hepatomegaly (%)                      | 3/17 (17.6)     | 10/35 (28.6)   | 0.609    |
| Splenomegaly (%)                      | 5/17 (29.4)     | 17/35 (48.6)   | 0.190    |
| Lymphadenomegaly (%)                  | 6/17 (35.3)     | 16/35 (45.7)   | 0.476    |
| CR rate after the first induction (%) | 10/13 (76.9)    | 23/31 (74.2)   | 1.000    |
| Overall CR rate (%)                   | 11/13 (84.6)    | 26/31 (83.9)   | 1.000    |
| Relapse rate (%)                      | 5/11 (45.5)     | 10/26 (38.5)   | 0.728    |
| Induction mortality (%)               | 0/13 (0.0)      | 2/33 (6.1)     | 1.000    |
| Total death rate (%)                  | 3/13 (23.1)     | 7/33 (21.2)    | 1.000    |

BM: Bone marrow; CR: Complete remission; MyAg: Myeloid antigen; PLT: Platelet; WBC: White blood count

expressed MyAg, which was in line with the data reported in the literature.<sup>23</sup> It was noted by Saxena A et al<sup>27</sup> that precursor B cells co-expressing CD13 showed higher in vitro proliferation compared to that of CD13-CD19+ B cells. By blocking their cell surface CD13 in leukaemic blasts with monoclonal antibody, they were able to inhibit their proliferation, so they hypothesised that CD13 may thus be an important target for novel molecular therapy of early stage acute B-cell leukaemia. It was different from an earlier report that MyAgs were not significantly more frequently associated with B-ALL than with T-ALL.<sup>14,28</sup> The differences observed are probably due to the criteria used to define a “percent positive” cell, the number of antigens tested and the relatively small numbers of T-ALL cases analysed in our study. Our data showed that patients with older age, higher CD34 positivity and lower proportion of patients with splenomegaly were found to be correlated with MyAg+ ALL, but no differences were found with regard to other clinical features, which was different from an earlier

report.<sup>14</sup> It may be due to the relatively small numbers of adult ALL patients in our study. Further analysis of MyAg expression in ALL on the impact of treatment response suggested that no differences were found between the MyAg+ and MyAg- groups with regard to CR rate, relapse rate, induction mortality and total death rate. In conclusion, our findings demonstrated that the presence of MyAg in the surface of blasts from adult ALL patients cannot predict worse outcome, which was consistent with earlier report.<sup>29</sup>

Chromosomal abnormalities in adult ALL had important significance related to diagnosis, management and prognosis. The absence of CD10 expression has been correlated with rearrangements of the MLL gene at 11q23, which is commonly seen in infants and older adults.<sup>30</sup> In our study, CD15 positivity was the highest in Pro B-ALL(60%), and the 1 case with t(4;11)(q21;q23) was an older woman patient with CD10-CD15+, which was consistent with the previous report that 11q23/MLL translocation occurred in CD10-/CD15+ Pro-B ALL.<sup>31</sup> In this study, the most common cytogenetic abnormality was the t(9;22) translocation, resulting in the Ph chromosome and the formation of BCR-ABL fusion transcripts, which was found mainly in B-ALL and none in T-ALL. The karyotype studies showed that 28.8% (17/59) of our B-ALL patients had Ph chromosomes, which was lower than what Bao L et al reported.<sup>32</sup> The difference observed was mainly due to the fact that we analysed the cases only by routine conventional karyotyping but not fluorescence in situ hybridisation and the relatively small numbers of B-ALL cases analysed in our study. Several clinical characteristics observed among Ph+ B-ALL patients in this series, such as older age, higher haemoglobin level, and higher CD34 expression are similar to those reported elsewhere.<sup>32-35</sup> However, unlike their studies, we fail to observe higher white blood cell and blast counts, and higher expression of MyAg in Ph+ B-ALL. No statistically significant differences in initial CR rate, relapse rate and the median relapse were observed between Ph+ and Ph- groups and this was different from a previous study that BCR-ABL positivity is associated with a worse prognosis resulting from a lower initial CR rate and an earlier occurrence of relapse.<sup>20</sup> The presence of Ph chromosome in adults is associated with a very unfavourable prognosis.<sup>9,36,37</sup> Even though CR could be achievable with standard chemotherapy regimens, without an allogeneic stem cell transplant, cures are uncommon. Recent combinations of tyrosine kinase inhibitors (TKIs) with chemotherapy have produced promising results, although the impact on long-term disease-free survival remains unclear.

Our results indicate that the distribution of ALLs in Chinese adult patients was similar with the general distribution pattern in the other countries. Unlike previous studies, we found that the expression of MyAg in patients with T-ALL

and B-ALL was comparable. Our data suggest that MyAg expression is significantly associated with median age, CD34 expression and splenomegaly, but is not associated with adverse presenting clinical and biological features, and that response to treatment and prognosis is comparable in MyAg+ and MyAg- adult ALL patients with regards to CR rate, relapse rate and death rate. In addition, we also found that patients with Ph+ B-ALL were older, presented with higher haemoglobin level and higher CD34 expression, but no differences were observed in other clinical or biological parameters between Ph+ and Ph- groups. In conclusion, ALL is a success story for paediatric cancer therapy but not adult ALL. The poor outcome of chemotherapy in adults with ALL as compared to children relates to multiple factors, including poor tolerance of intensive courses of chemotherapy and a higher incidence of poor prognostic subtypes of ALL such as Ph chromosome-positive ALL. Therapy for adult ALL will remain complex, and progress ultimately depends on effective crossbreeding between drug development, understanding of ALL biology, and sophistication of prognostic systems.

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