Chromosomal Translocations Play a Unique Role in Influencing Prognosis in Childhood Acute Lymphoblastic Leukemia

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Certain types of chromosomal abnormalities have been shown to exert strong independent influence on treatment outcome in acute lymphoblastic leukemia (ALL). To identify the changes most closely associated with prognosis, we analyzed the completely banded blast cell karyotypes of 161 children with this disease. One hundred twenty-five cases had one or more chromosomal abnormalities, with 45 showing translocations. The frequency of translocations was highest (58%) among patients with pseudodiploid karyotypes and lowest (0%) in the hyperdiploid group defined by 51 or more chromosomes. During the maximum 6-year follow-up period, 30 of the 45 patients with a translocation failed therapy, compared with only 27 of the 116 who lacked this feature. Life-table estimates of event-free survival indicate that only 14% of the translocation group will be in complete remission at 3 years. The percentages of failures associated with random and non-random translocations were virtually identical (68% v 65%). When entered in a Cox proportional hazards model with seven other types of chromosomal abnormalities, and then with 11 clinical and laboratory variables of known prognostic value in ALL, translocation emerged as the strongest single predictor of treatment outcome (P < 0.0001). The model indicated that translocation increases the risk of treatment failure six times by comparison with the absence of this feature. These findings offer an explanation for the majority of early treatment failures in childhood ALL, including those previously attributed to ploidy classification.

IDEALLY, prognostic factors should allow unequivocal separation of risk groups at diagnosis so that more effective treatment can be devised for patients likely to fail. Acute lymphoblastic leukemia (ALL) is now curable in more than 50% of children,1,2 making it possible to concentrate on achieving an optimal risk:benefit ratio for modern therapy. Past reliance on clinical, cytologic, and immunologic factors to classify newly diagnosed patients with ALL has led to relatively diverse systems for assignment of risk categories.3 Sharpening the focus of patient selection methods would be advantageous as a means of improving the reliability, efficiency, and interpretability of clinical trials.

Chromosomal abnormalities have attracted much recent attention as important prognostic factors in ALL. Secker-Walker et al4,5 were the first to demonstrate that chromosome number (or ploidy) strongly influences treatment outcome in childhood leukemia patients, a relationship that has subsequently been confirmed by others.6,7 Among 136 children with ALL, we found that those with modal chromosome numbers of 51 or above had the most favorable treatment responses, whereas those with pseudodiploid karyotypes had the poorest responses.7 Patients with apparently normal, hypodiploid, or 47-49 chromosomes had intermediate responses. The data generated at the Third International Workshop on Chromosomes in Leukemia,5 comprising 330 children and adults with ALL, showed that the specific karyotypic patterns provided significant independent prognostic information, both with regard to remission duration and to survival. Bloomfield et al8 have published data indicating that chromosomal translocations, in general, have an adverse effect on prognosis in ALL.

To assess the impact of leukemia cell karyotype and its component parts on disease-free survival, we analyzed an array of chromosomal and other presenting clinical and laboratory features for 161 children with ALL who had complete G-banding of all chromosomes and adequate follow-up. The results demonstrate that the presence or absence of a translocation conveys the most clinically useful information of all prognostic features examined.

MATERIALS AND METHODS

Patients and Treatment

Of 398 consecutive patients with newly diagnosed ALL admitted to St. Jude Children's Research Hospital from July 1, 1978, to January 1, 1983, 301 had adequate bone marrow samples and successful chromosome studies; 161 of these cases had complete G-banding of all chromosomes. The present analysis was restricted to the latter group to avoid possible underrepresentation of clonal abnormalities. The 161 patients were entered in three institutional clinical trials: 17 in Total Therapy Study IX and 137 in Study X (95 in the standard-risk arm and 42 in the high-risk arm).9,7 Of the 8 B-cell ALL patients were treated separately (unpublished results, protocol available on request). Although treatment components differed among the three studies and between subdivisions of Study X,9 times to failure for patients with fully banded chromosomes showed no significant differences by major therapeutic protocol (P = 0.164, data not shown); similarly, the clinical features and times to failure for all censored patients (n = 237) were comparable to those of the 161 patients in the study group. All patients were enrolled in studies (that included a cell profile analysis) approved by the institution's clinical trials committee. All patients were advised of the procedures and attendant risks, in accordance with institutional guidelines, and informed consent was obtained in each instance.

The percentage of completely banded cases versus the total number of patients admitted to the hospital per year is as follows: 20% (8/41) in 1978, 27% (24/88) in 1979, 34% (30/88) in 1980, 46% (46/100) in 1981, and 58% (53/92) in 1982. These percentages
do not include cases with partial banding or those in which only ploidy classification was obtained.

The distribution of follow-up times for patients with complete banding was as follows: 22 cases for 0 to 2 years, 51 cases for 2 to 3 years, 40 cases for 3 to 4 years, 27 cases for 4 to 5 years, and 21 cases for 5 to 6 years. Follow-up time was defined as the number of years between the date on-study and the analysis date (ie, August 1, 1984).

**Chromosome Analysis**

Chromosomes were prepared by a direct bone marrow technique for ALL developed in our laboratory. Marrow cells were collected in RPMI-1640 medium supplemented with 30% fetal calf serum. Only 0.1 mL of sedimented cells was processed per centrifuge tube. Without delay, the cells were exposed to Colcemid (0.06 μg/mL) for 25 minutes, and then to hypotonic KCL (0.075 mol/L) for a total of 32 minutes (including mixing time, standing time, and centrifuging time). They were then fixed in 3:1 methanol-acetic acid (v/v) and slides were prepared by an edging-flaming technique. Appropriate drying of the slides was achieved by natural aging. G-banding was done by treatment with trypsin and staining with Wright's stain.

For each case, 10–35 metaphases (mean, 20) were studied by direct microscopy to determine the modal number and to identify the malignant stem-line. Karyotypes were prepared from photographic prints. Chromosomal abnormalities were classified according to international conventions. The definition of an abnormal stem line was that proposed by the Second International Workshop on Chromosomes in Leukemia. A case was considered abnormal if it had an abnormal clone, regardless of the proportion of normal metaphases. In 12 of 13 cases with two leukemic lines, the second line derived from the other through clonal evolution; hence, only the primary line was included in this study. For the single case with two independent stem lines, both lines were included. Because some chromosomal abnormalities appeared in only one to three cases, they were not included in the statistical analysis. These included rings, inversions, and tiny DNA fragments; because all of these occurred in cases with multiple abnormalities, no individual case was excluded.

The abnormalities analyzed were whole chromosome gain or loss, translocation, unidentified DNA addition not included in translocation because a duplication could not be ruled out, DNA loss (deletion) not identified in a translocation, DNA duplication, iso-chromosome, and unidentified marker. Translocations were designated as "random" or "nonrandom." The random translocations were those appearing only once, and to our knowledge, not previously reported at the time of this study. The nonrandom translocations were those that appeared two or more times and/or have been reported to cluster.

**Hematologic and Immunophenotypic Studies**

The diagnosis of ALL was based on morphologic criteria of the French-American-British (FAB) group and negative myeloid-associated cytochemical findings. Immunophenotypes, determined by published methods, supported the diagnosis in all instances.

**Statistical Analysis**

Time-to-failure curves were plotted by the method of Kaplan and Meier, and significant differences were determined with the Mantel-Cox statistic. Failure was defined as a lack of response to induction therapy, a relapse during first complete remission, or death due to any cause. Cox regression analysis was used to assess the influence of chromosomal abnormalities and other potentially important prognostic factors on failure rate. This "proportional-hazards" model permits measurement of the contribution of a given covariate to duration of complete remission while simultaneously adjusting for the contributions of other covariates. The prognostic factors studied, in addition to chromosome abnormalities and chromosome number, were log leukocyte count, relapse risk as defined for Total Study X at St. Jude Hospital, mediastinal mass, age, sex, race, cell markers, FAB type, E-rosette formation, and CNS leukemia.

**RESULTS**

**Modal Number of Chromosomes**

The distribution of chromosome numbers was typically bimodal, with the first peak occurring at 46 chromosomes (representing mainly patients with pseudodiploid karyotypes) and the second at 55 chromosomes (Fig 1). Each ploidy group appeared to be adequately represented by comparison with findings from an earlier analysis of 136 cases including both partially and fully banded karyotypes. Although the percentage of cases containing a normal karyotype (22%) is not typical of our more recent studies (6%), this group was included in order to obtain the proper perspective in regard to prognosis.

**Chromosomal Abnormalities By Ploidy Group**

Overall, the most frequent chromosomal abnormalities by case distribution were whole chromosome additions (62 cases), translocations (45 cases), unidentified markers (34 cases), whole chromosome loss (32 cases), and DNA deletions (28 cases). Because of the established relationship between modal chromosome number and prognosis, we next determined the distribution of chromosomal changes according to ploidy group. The results (Fig 2) depict structural and numerical differences as well as specific chromosomes involved in translocations. Findings for the hypodiploid group, which comprised only nine cases, did not permit valid conclusions and were omitted from the figure.

![Figure 1: Distribution of modal numbers among 161 cases of childhood ALL. Note the bimodal distribution pattern, with the first peak occurring at 48 chromosomes (pseudodiploid) and the second at 55 chromosomes. ND = normal diploid; PS = pseudodiploid.](image-url)
Fig 2. Structural and numerical chromosomal abnormalities associated with each ploidy group. The closed blocks represent specific chromosomes involved in translocations. The open blocks represent all other abnormalities not associated with translocations. (A) The pseudodiploid group (55 cases) is characterized by structural abnormalities with a high frequency of translocations (58% of cases) primarily involving chromosomes 1, 8, 9, 11, 14, 19, and 22. (B) The hyperdiploid 47–49 group (31 cases) has nearly equal numbers of structural and whole-chromosome abnormalities, which are randomly distributed. Translocations were found in 26% of patients. (C) The hyperdiploid 51 or above group (30 cases) was characterized primarily by additions of whole chromosomes that most frequently involved chromosomes 4, 6, 10, 14, 17, 18, 20, 21, and X. No translocations were present.

Briefly, this group contained two near-haploid cases (with 26 and 28 chromosomes) and seven cases with 45 chromosomes containing different karyotypes. Five of the latter cases contained translocations (two nonrandom and three random). Each of the nonrandom translocations was identified as the t(1;19) abnormality specifically associated with pre-B-cell ALL.228 Pseudodiploid group. All but one of these 55 cases contained structural abnormalities most frequently involving the long arms (q) of chromosomes 1, 8, 11, 14, and 22 (Fig 2A). Translocations were observed in 32 cases (58%). Twenty nonrandom translocations were identified: seven containing the t(8;14) or 14q+ abnormality, all with B-cell ALL; six the t(9;22) or 22q-; one the t(4;11); four the t(1;19), all with pre-B-cell ALL; and two the t(11;14), both with E+ T-cell ALL.25 Twelve different, apparently random translocations were observed. Structural abnormalities not involving translocations were found in 41 other chromosomes, and there were seven banded but unidentified markers. Numerical changes were much less frequent than structural abnormalities and all were random.

Hyperdiploid group, 47–49. In these 31 cases, numerical and structural abnormalities were distributed nearly equally (Fig 2B). The distribution of abnormal chromosomes was random, and when the six cases of Down’s syndrome with trisomy 21 were excluded, the frequency of an added chromosome 21 (5 cases) was insignificant. Translocations occurred in eight cases (26%), and included three nonrandom [t(9;22), t(1;19), and t(4;11)] and five random translocations. Comparison of karyotypes containing 47, 48, and 49 chromosomes failed to disclose any related patterns of abnormalities, and there were no similarities between this ploidy group and the group with 51 or more chromosomes (see below).

Hyperdiploid group, 51 or above. This group of 30 cases differed markedly from the other abnormal ploidy groups, with most of the abnormalities involving whole chromosome additions (Fig 2C). Extra chromosomes formed trisomies, with numbers 4, 6, 10, 14, 17, 18, 20, 21, and X added most frequently and number 21 added twice in 12 cases. This apparent nonrandom addition of at least nine chromosomes contributed to the secondary peak of 55 chromosomes apparent in Fig 1. Only one patient in this group had Down’s syndrome with trisomy 21, and the leukemic clone contained only that one extra 21 chromosome. Thus, the influence of cases with Down’s syndrome on the observations related to chromosome 21 was negligible. Structural abnormalities were relatively infrequent, most often involving q in a partial
duplication, and included 16 unidentified markers. Translocations were not identified in these 30 cases.

Our most recent studies indicate that translocations do occur in this group, in up to 14% of cases, but this number is still relatively small in comparison to the other ploidy groups. Preliminary results indicate that as in other ploidy groups, the presence of a translocation carries more prognostic import in this setting than does hyperdiploidy. Additional case studies and longer follow-up are needed to confirm this finding.

**Treatment Response According to Chromosomal Abnormality**

From the preceding analysis, it was clear that a high frequency of structural abnormalities, particularly translocations, distinguishes pseudodiploid cases. This was in contrast to the high frequency of added intact chromosomes and the relative paucity of structural abnormalities, including translocations, in the 51 or above group. Table 1 tests our impression that the presence or absence of a translocation explains prognostic differences among commonly recognized ploidy groups. Within the pseudodiploid and 47–49 groups, the presence of a translocation had a highly significant influence on the frequency of treatment failure. In the pseudodiploid group, only 56% of patients with a translocation achieved a complete remission (CR). The best overall response was found in the group with 51 or more chromosomes, which contained no translocations. When the analysis included only cases without translocations, failure rates among the three ploidy groups showed no significant differences ($P = 0.4246$). Addition of hypodiploid cases without translocations, as well as cases with normal karyotypes, did not alter this finding ($P = 0.8050$, data not shown).

Overall, patients with translocations had strikingly different times to failure compared with those lacking the abnormality ($P < 0.0001$, Fig 3A). Remission induction failure rates also differed: 20% for the translocation group versus 4% for others ($P = 0.002$). All but 1 of the 30 patients with translocations who failed did so within 2½ years, while receiving combination chemotherapy; whereas those without translocations had a more variable clinical course. A comparison of survival times (Fig 3B) emphasized the aggressiveness of disease in cases with translocations. Only two patients

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**Table 1. Relationship of Translocation Frequency Within Ploidy Groups to Treatment Outcome**

<table>
<thead>
<tr>
<th>Major Abnormal Ploidy Group</th>
<th>With Translocation</th>
<th>Without Translocation</th>
<th>$P$ Value$\dagger$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>CR*</td>
<td>Failures†</td>
<td>Patients</td>
</tr>
<tr>
<td>Pseudodiploid</td>
<td>32/55 (56%)</td>
<td>18/32 (75%)</td>
<td>23/55 (42%)</td>
</tr>
<tr>
<td>Hyperdiploid</td>
<td>8/31 (26%)</td>
<td>7/8 (88%)</td>
<td>23/31 (74%)</td>
</tr>
<tr>
<td>47–49§</td>
<td>0/30 (0%)</td>
<td>—</td>
<td>30/30 (100%)</td>
</tr>
<tr>
<td>Hyperdiploid 51 or above</td>
<td>0/30 (0%)</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

*Complete remission induction.
†No response to induction therapy, relapse during first complete remission, or death due to any cause.
‡From Mantel-Cox comparison of failure rates over time.
§The designation 47–49 is made in this paper because there were no cases with exactly 50 chromosomes.
in this category have lived beyond 3 years from diagnosis despite attempts to secure new remissions.

Table 2 lists all of the translocations identified in the study, categorized as either nonrandom or random. The first group consisted of well-recognized translocations identified without a translocation, and the second comprised 20 different translocations (not previously found in clusters) in 19 patients and involved many different chromosomes. Comparison of failure rates over time, using the Mantel-Cox statistic, disclosed no significant differences between the two groups ($P = 0.9078$, data not shown).

**Multivariate Analysis**

Table 3 shows the relative prognostic importance of the eight major categories of chromosome abnormalities, as determined by Cox regression analysis. When the categories were studied singly, translocation exerted the strongest influence on remission duration ($P < 0.0001$), followed in descending order by whole chromosome gain ($P = 0.0165$) and unidentified marker ($P = 0.0578$). After adjustment for translocation, neither variable retained significance, but translocation lost none of its predictive power in the presence of other covariates.

A number of clinical and laboratory features have been found in the past to have prognostic value in childhood ALL. Prominent among these have been leukocyte count, mediastinal mass, age, sex, race, immunophenotype, FAB type, and CNS leukemia. Table 4 lists the distribution of these features among our population of patients separated as: (1) those without a translocation and (2) those with a translocation. In those with a translocation there is a higher frequency of increased leukocyte counts, black race, B-cell phenotype, L3 FAB type, and CNS leukemia. When the eight features were studied in each of the 45 patients with a translocation individually, results indicated that 37 out of 45 (82%) had at least one high-risk feature.

Since the majority of patients with a translocation had one or more “classic” high-risk features, it was important to account for their competing effects on treatment outcome. Thus, the same proportional hazards model was used to determine the influence of translocation on failure rates relative to these well-recognized prognostic factors in ALL (Table 5). In the univariate analysis, translocation, and ploidy emerged as the strongest variables ($P < 0.0001$). Log leukocyte count ($P = 0.0021$) also made a significant contribution, as did cell markers ($P = 0.0378$). When the individual variables were adjusted by translocation, only chromosome number retained significance but at a greatly reduced level. Again, as in Table 3, no covariate added prognostic information to translocation, even when the four next most important factors (log leukocyte count, chromo-
some number, relapse risk, and cell markers) were considered as a group (data not shown).

From results of the Cox regression analysis, it was possible to calculate the relative risk of treatment failure associated with each covariate. Patients with a translocation were six times more likely to fail treatment than those without the abnormality. The probability of treatment failure before the end of the first year was much greater for patients with translocations: 0.57 v 0.10 for patients lacking the abnormality. Similarly, those with translocations had a much greater probability of dying (0.39 v 0.05).

**DISCUSSION**

In this analysis of fully banded chromosomes from a large series of childhood leukemia patients, we were able to identify translocation as the abnormality most frequently associated with treatment failure. These observations confirm and extend some of the work of the Third International Workshop6 and of Bloomfield et al.9 The unusual distribution of translocations, predominantly among the pseudodiploid group, offers an explanation for the prognostic strength assigned to chromosome number in previous studies.4,9 The relatively small number of translocations in the 51 or above group, first observed by the Third International Workshop on Chromosomes in Leukemia, is consistent with the low failure rate observed in this study (Table 1) and the paucity of other high-risk features previously observed among patients in this category. Moreover, these hyperdiploid ALL cases had an apparent nonrandom pattern of whole chromosome additions, forming trisomies, that was not seen in the 47–49 or other ploidy groups; cases with exactly 50 chromosomes have not been observed by us at diagnosis. These facts provide compelling evidence that the 51 or above group is

<table>
<thead>
<tr>
<th>Feature</th>
<th>Total Cases</th>
<th>Distribution of Subgroups</th>
<th>Univariate Analysis</th>
<th>Covariates Adjusted for Translocation</th>
<th>Translocation Adjusted for Other Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Translocation</td>
<td>161</td>
<td>45 (yes)</td>
<td>36.11 &lt;.0001</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Log leukocyte count†</td>
<td>161</td>
<td>55 (pseudo)</td>
<td>22.24 &lt;.0001</td>
<td>3.35 .0472</td>
<td>29.95 &lt;.0001</td>
</tr>
<tr>
<td>Chromosome no.‡</td>
<td>161</td>
<td>116 (standard)</td>
<td>0.86 .2933</td>
<td>0.59 .2049</td>
<td>0.29 .6113</td>
</tr>
<tr>
<td>Relapse risk§</td>
<td>161</td>
<td>116 (standard)</td>
<td>3.46 .0250</td>
<td>0.62 .6293</td>
<td>0.4302 .0000</td>
</tr>
<tr>
<td>Mediastinal mass</td>
<td>161</td>
<td>16 (yes)</td>
<td>0.63 .2893</td>
<td>1.87 .1717</td>
<td>36.85 &lt;.0001</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>161</td>
<td>116 (yes)</td>
<td>1.12 .2893</td>
<td>1.59 .2072</td>
<td>35.15 &lt;.0001</td>
</tr>
<tr>
<td>Sex</td>
<td>161</td>
<td>55 (male)</td>
<td>2.55 .1103</td>
<td>0.26 .6069</td>
<td>0.39 .0001</td>
</tr>
<tr>
<td>Race</td>
<td>161</td>
<td>147 (white)</td>
<td>0.86 .2933</td>
<td>0.59 .2049</td>
<td>0.29 .6113</td>
</tr>
<tr>
<td>Cell markers</td>
<td>157</td>
<td>26 (T)</td>
<td>4.32 .0478</td>
<td>0.2 .1407</td>
<td>0.39 .0001</td>
</tr>
<tr>
<td>FAB type</td>
<td>160</td>
<td>122 (L1)</td>
<td>1.09 .2967</td>
<td>0.63 .2861</td>
<td>0.63 .2861</td>
</tr>
<tr>
<td>E-rosette formation</td>
<td>160</td>
<td>17 (yes)</td>
<td>1.14 .2861</td>
<td>0.63 .2861</td>
<td>0.63 .2861</td>
</tr>
<tr>
<td>CNS leukemia</td>
<td>160</td>
<td>17 (yes)</td>
<td>1.14 .2861</td>
<td>0.63 .2861</td>
<td>0.63 .2861</td>
</tr>
</tbody>
</table>

*By Cox regression analysis.
†Used as a continuous variable in the Cox regression analysis.
‡Pseudodiploid v hyperdiploid ≥ 51 v all others.
§High risk = leukocyte count > 100 × 10⁹/L; mediastinal mass, CNS involvement at diagnosis or E⁺ blasts; standard risk = absence of high-risk features.
ROLE OF TRANSLOCATIONS IN ALL

chromosomally distinct, as first suggested by Kaneko et al., and should be regarded as a unique subset of patients with a better prognosis, except for patients whose karyotypes contain a translocation.

The time-to-failure comparisons in this study indicate that in childhood ALL, translocations as a group convey a poor prognosis. This includes many of the so-called random translocations, which may prove to have a nonrandom (or specific) distribution when larger numbers of cases are studied, as suggested by the finding that the t(1;14) and the t(1;19) correlate with T-cell and pre-B-cell ALL, respectively. Although at least two translocations in other malignancies have been shown to convey a relatively good prognosis [the t(14;18) in follicular small cleaved cell lymphoma and the t(8;21) in ANLL], there has been no similar subgroup identified for ALL in the studies of the Third International Workshop, or in those of Bloomfield, or in our studies. Future studies however, may reveal some heterogeneity of response among translocations as additional new studies. Future studies however, may reveal some heterogeneity of response among translocations as additional new subgroups are identified. Likewise new therapies may partially or completely alter the correlation between translocation and prognosis.

It now seems likely that the recognized consistent translocations affect chromosome segments involved in malignant transformation. In the present study, the high rate of early failure and poor overall survival of patients with translocations suggest an additional effect, ie, one in which translocations are associated with clinical drug resistance. How this might occur is unclear. One attractive possibility is that translocations increase the proliferative rate of malignant cells, leading to more aggressive disease. Patients with B-cell ALL, characterized by the t(8;14) abnormality or one of the variant forms, have a very poor prognosis and a high leukemic cell proliferative rate. Yet, data reported by us for other immunophenotypes of ALL do not support a proliferative advantage for all leukemic cells with a translocation. To the contrary, in that study, T-cell ALL cases with the 11;14 translocation had a significantly lower percentage of cells in S phase than did those without the translocation. Alternatively, drastic genetic reassembly, typified by translocations, could alter gene expression in ways that might decrease the penetration of drugs into cells or perturb their metabolic fate once they are inside cells.

This study indicates that a translocation is the element within the total karyotype that would be most useful to include in the pretreatment risk assignment for the design of clinical trials in ALL. Chromosome number, or ploidy, appears to be the second strongest feature. It is now possible, in ALL, to obtain analyzable chromosomes and identify abnormal leukemic clones in nearly all cases. Several techniques for the study of bone marrow cells are providing good results. In addition, an improved direct technique designed especially for chromosome preparation in ALL is now available, and this method provides a high yield of successfully banded cases, if carefully performed. In our recent experience, it has also allowed identification of chromosomally abnormal lines in a very high percentage of cases analyzed (94%). Recognition of the 51 or above group, especially, may also be achieved by flow cytometric methods and these studies may be used together to confirm and complement each other. However, the identification of a translocation depends upon chromosome analysis. Since it may not be possible in every case to obtain complete banding and thus recognize or rule out a translocation, the use of either translocation or ploidy may in some situations provide a practical assessment of risk of treatment failure in ALL. We suggest that the presence of any translocation can be used routinely to define high-risk cases. At our institution this karyotypic feature is included with the flow cytometrically determined DNA index, white blood cell count, age, and race for allocation of patients to discrete treatment groups.

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REFERENCES

Chromosomal translocations play a unique role in influencing prognosis in childhood acute lymphoblastic leukemia

DL Williams, J Harber, SB Murphy, AT Look, DK Kalwinsky, G Rivera, SL Melvin, S Stass and GV Dahl