Benign Monoclonal B Cell Lymphocytosis—A Benign Variant of CLL: Clinical, Immunologic, Phenotypic, and Cytogenetic Studies in 20 Patients

By Tin Han, H. Ozer, M. Gavigan, R. Gajera, J. Minowada, M.L. Bloom, N. Sadamori, A.A. Sandberg, G.A. Gomez, and E.S. Henderson

From 1951 through 1978, we have seen 20 cases of stage 0 chronic lymphocytic leukemia (CLL) without disease progression for 6.5–24 years. The cohort included 7 males and 13 females, aged 48–77 years at the time of diagnosis. None presented with anemia, thrombocytopenia, or neutropenia nor developed cytopenias during follow-up. Mean total lymphocyte count in these patients was 20,100/µL, with ranges from 10,000 to 43,700 at the time of diagnosis, and was 20,600, with ranges from 1,000 to 47,200, at last follow-up. Of 12 patients studied, 8 and 4 were phenotyped as heavy chain µ- and µ-type, respectively, with 7 κ- and 4 λ-type (no light chain was detectable in one patient). Of 13 patients studied, one had a slightly elevated IgG level and two had slightly depressed serum IgA and IgM levels. All patients had positive delayed hypersensitivity responses to at least one of five skin test antigens. Each of seven patients studied for an in vitro leukocyte thymidine uptake had a low level of [3H]thymidine incorporation. Nine of 12 patients studied had elevated total T cells, and the remaining 3 had normal T cell counts. In vitro unseparated lymphocyte response to phytohemagglutinin showed normal kinetics of DNA synthesis, with a peak response on day 3 or 4 of culture in 4 and slightly or moderately depressed and/or delayed kinetics in 8 patients studied. Cytogenetic analyses by Q- or G-banding techniques of polyclonal B cell mitogen-stimulated lymphocytes in all six patients studied showed normal karyotypes. These data are consistent with a previously undescribed syndrome involving a monoclonal B cell lymphocytosis, a prolonged asymptomatic or benign clinical course, and essentially normal humoral and cellular immunity and normal karyotype. Our observations indicate that these 20 patients with stage 0 CLL have a benign clinical course and that they may also be designated as benign monoclonal B cell lymphocytosis (BMBL), a benign variant of CLL.

CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) has been considered to be a malignancy characterized by the monoclonal proliferation of small lymphocytes of B cell origin in almost all instances.1,2 These leukemic B cells bear surface immunoglobulin either of the µδ- or µ-heavy chain class, as well as κ or λ-light chains in virtually all the cases.3–6 It has long been recognized that some patients with CLL live for many years, while other patients die within a short period following diagnosis. Rai et al,7 in 1975, proposed a staging system for CLL based on a retrospective study of survival data in 125 patients. They found the following median survival times in months from diagnosis: stage 0, 150; stage I, 101; stage II, 71; stage III or IV, 19. Since then, this staging system has generally been accepted as a useful and accurate indicator of survival in CLL by most investigators.8–10 In each and every publication, it has been consistently observed that patients with lymphocytosis alone (stage 0) usually survive more than one decade. However, all reported studies,8–16 with the exception of the series by Rai et al, reported lack of any documentation of disease progression in stage 0 CLL patients. Rai et al7 observed that, of 22 patients with stage 0, 11 remained stage 0 without disease progression for 2½–12 years. We have observed and documented 20 cases of stage 0 CLL without disease progression for 6.5–24 years, requiring no treatment. The present report deals with clinical, immunologic, phenotypic, and cytogenetic studies in these 20 patients.

MATERIALS AND METHODS

From 1951 through 1978, we have seen over 500 cases of CLL (all stages) at Roswell Park Memorial Institute. Of these, approximately 100 cases could have been classified as stage 0 CLL.1 At the time of their referral, the essential criteria for the diagnosis of CLL were (a) a persistently elevated lymphocyte count in the peripheral blood (over 10,000/µL) and (b) a lymphocytosis (≥30%) of all nucleated cells from aspirate smear of bone marrow. In all patients first seen after 1974, the diagnosis of CLL was made by phenotypic analysis at their initial visits, and in some of the patients seen before 1974, the diagnosis of CLL was subsequently established by phenotypic analysis. Patients with stage 0 CLL were followed periodically without treatment, and complete physical findings were recorded for each clinical visit. Adequate follow-up data were available in only 46 patients with stage 0 CLL. Of these 46 patients, 20 did not progress for 6½–24 years, 9 also did not progress for 2–6 years, and the remaining 17 did progress to a higher stage within 5 years from the...
BENIGN MONOCLONAL B CELL LYMPHOCYTOSIS

Table 1. Dates of Diagnosis, Referral, and Last Visit to RPMI and the Fate of Each of 20 Patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (Years) at Diagnosis</th>
<th>Sex</th>
<th>Date of Diagnosis</th>
<th>Date of Referral</th>
<th>Date of Last Follow-up</th>
<th>Fate</th>
<th>Survival (in Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T.F.</td>
<td>M</td>
<td>4/51</td>
<td>10/51</td>
<td>5/75</td>
<td>Died of pneumonia</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>R.S.</td>
<td>F</td>
<td>9/55</td>
<td>9/55</td>
<td>12/79</td>
<td>Died of heart failure</td>
<td>24</td>
</tr>
<tr>
<td>3</td>
<td>E.S.</td>
<td>M</td>
<td>3/66</td>
<td>3/65</td>
<td>5/78</td>
<td>Lost</td>
<td>23</td>
</tr>
<tr>
<td>5</td>
<td>J.P.</td>
<td>M</td>
<td>6/60</td>
<td>6/60</td>
<td>6/75</td>
<td>Died of bilateral bronchopneumonia</td>
<td>15</td>
</tr>
<tr>
<td>7</td>
<td>H.C.</td>
<td>F</td>
<td>9/55</td>
<td>9/57</td>
<td>2/70</td>
<td>Died of heart failure</td>
<td>14</td>
</tr>
<tr>
<td>8</td>
<td>R.M.</td>
<td>M</td>
<td>5/71</td>
<td>5/71</td>
<td>1/83</td>
<td>Alive</td>
<td>11</td>
</tr>
<tr>
<td>9</td>
<td>G.M.</td>
<td>M</td>
<td>7/63</td>
<td>12/63</td>
<td>9/73</td>
<td>Lost</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>R.H.</td>
<td>F</td>
<td>7/71</td>
<td>2/73</td>
<td>3/81</td>
<td>Died of heart failure</td>
<td>9.5</td>
</tr>
<tr>
<td>11</td>
<td>M.M.</td>
<td>M</td>
<td>9/65</td>
<td>9/65</td>
<td>7/75</td>
<td>Lost</td>
<td>9.5+</td>
</tr>
<tr>
<td>12</td>
<td>R.V.</td>
<td>M</td>
<td>3/72</td>
<td>5/75</td>
<td>1/82</td>
<td>Alive</td>
<td>9.5</td>
</tr>
<tr>
<td>13</td>
<td>N.H.</td>
<td>M</td>
<td>2/64</td>
<td>2/64</td>
<td>2/73</td>
<td>Died of cardiac arrhythmia</td>
<td>9</td>
</tr>
<tr>
<td>14</td>
<td>L.M.</td>
<td>M</td>
<td>1/63</td>
<td>1/63</td>
<td>7/71</td>
<td>Died of esophageal cancer</td>
<td>8.5</td>
</tr>
<tr>
<td>15</td>
<td>I.D.</td>
<td>F</td>
<td>6/73</td>
<td>11/78</td>
<td>8/81</td>
<td>Alive</td>
<td>8</td>
</tr>
<tr>
<td>16</td>
<td>F.B.</td>
<td>M</td>
<td>4/74</td>
<td>1/75</td>
<td>4/82</td>
<td>Alive</td>
<td>8</td>
</tr>
<tr>
<td>17</td>
<td>J.K.</td>
<td>F</td>
<td>10/74</td>
<td>11/77</td>
<td>9/82</td>
<td>Alive</td>
<td>8</td>
</tr>
<tr>
<td>18</td>
<td>C.P.</td>
<td>M</td>
<td>4/69</td>
<td>4/69</td>
<td>2/76</td>
<td>Died of lung cancer</td>
<td>7</td>
</tr>
<tr>
<td>19</td>
<td>L.G.</td>
<td>F</td>
<td>11/75</td>
<td>3/77</td>
<td>8/82</td>
<td>Alive</td>
<td>6.5</td>
</tr>
<tr>
<td>20</td>
<td>J.G.</td>
<td>F</td>
<td>6/76</td>
<td>7/76</td>
<td>12/82</td>
<td>Alive</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Table 2. Hematologic Data at the Time of Diagnosis and at Last Follow-up Visit in 20 Patients

<table>
<thead>
<tr>
<th>Hematologic Data</th>
<th>Mean ± SD at Time of Diagnosis</th>
<th>Mean ± SD at Last Follow-up Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>14.3 ± 1.2</td>
<td>13.6 ± 1.5</td>
</tr>
<tr>
<td>Platelets (x 10^11/L)</td>
<td>225.9 ± 69.0</td>
<td>195.4 ± 53.0</td>
</tr>
<tr>
<td>Lymphocytes (x 10^3/L)</td>
<td>20.1 ± 8.1</td>
<td>20.6 ± 14.4</td>
</tr>
<tr>
<td>Lymphocytes (% peripheral blood)</td>
<td>74.6 ± 12.0</td>
<td>70.3 ± 20.4</td>
</tr>
<tr>
<td>Lymphocytes (% bone marrow)</td>
<td>55.0 ± 15.0</td>
<td>—</td>
</tr>
<tr>
<td>Neutrophils (x 10^3/L)</td>
<td>6.5 ± 3.4</td>
<td>5.5 ± 2.4</td>
</tr>
</tbody>
</table>

Clinical and immunobiologic data of these 20 stage 0 CLL patients without disease progression were compared with that of 17 stage 0 CLL patients in whom disease progression to a higher stage was well documented within 5 years from the time of diagnosis.

RESULTS

The cohort with apparently benign disease included 7 males and 13 females, ranging from 48 to 77 years in age at the time of discovery of persistent lymphocytosis. Nine of these 20 patients had general weakness or fatigue at the time of diagnosis. In two patients, the diagnosis was made by a hematologic work-up for infectious complications. Lymphocytosis was noted on routine blood tests during medical check-up in the remaining nine patients.

Hematologic data at the time of diagnosis and at last follow-up visit in 20 patients are shown in Table 2. None presented with anemia, thrombocytopenia, or neutropenia. Lymphocytosis ranged from >10,000 to
43,700/μL and the percentage of lymphocytes in the peripheral blood ranged from 51% to 93%. None developed cytopenias during follow-up. Hemoglobin levels, platelet counts, lymphocyte counts, and neutrophil counts from the time of referral to the time of last clinic visit in case Nos. 1, 2, and 3 are depicted in Figs 1, 2, and 3, respectively. In Fig 4, detailed hematologic data of case Nos. 4, 5, and 7 are presented to show that the lymphocyte counts gradually and spontaneously decreased. The lymphocytosis fluctuated in some cases, and a doubling of the initial lymphocyte count was observed in five cases (Nos. 3, 6, 9, 13, and 20), although the lymphocytosis usually remained below 50,000/μL. Mean values of hemoglobin levels, platelet counts, lymphocyte counts, neutrophil counts, and percentages in peripheral blood lymphocytes of these 20 patients at the time of diagnosis and at the time of last follow-up visit were comparable.

Eight of 20 patients died of causes unrelated to CLL 7–24 years after the time of diagnosis (Table 1). A complete autopsy was carried out on case No. 5 (J.P.), and no microscopic evidence of leukemia was observed. This patient's lymphocytosis spontaneously and gradually decreased, and the total lymphocyte count, as well as lymphocyte proportions, were within normal limits prior to his demise (Fig 4). No autopsies were performed on the other seven cases. In three patients, we lost follow-up after 9.5 years, 10 years, and 23 years, respectively.

Bone marrow aspirations were performed in 19 of the 20 patients. Mean percentage of lymphocytes in the bone marrow was 55%, with ranges from 31% to 88%. In one patient, bone marrow aspiration was not carried out inadvertently. Bone marrow biopsies were performed in 6 of the 20 patients. The results of patterns of bone marrow biopsy infiltration by leu-
The results are presented in Table 4. Of 14 patients studied at the time of diagnosis or at the time of referral, 10 had normal IgG, IgA, and IgM levels and 4 had a slightly elevated level or a slightly depressed level of immunoglobulins. None had panhypogammaglobulinemia. Monoclonal-free light chains in urine or serum were absent in all five patients studied (case Nos. 4, 8, 16, 17, and 19). LDH and AP were within normal limits in all patients, except one who had LDH levels of 250 IU/L, just above the normal upper limit.

Skin tests with five different antigens were carried out in these patients during their follow-up clinic visits, and the results are presented in Table 5. PPD, mumps, Varidase, or monilia skin tests were positive in 71% of the patients tested, whereas Trichophyton skin test results indicate that all patients tested had a low level of [3H]thymidine incorporation (Table 6). T cell counts were calculated by multiplying the total lymphocyte count by the proportion of E rosette-positive cells. Of 12 patients studied, 3 had normal T cell counts, whereas 9 had elevated levels (Table 7). In vitro T cell responses to PHA in 12 patients showed that 4 had normal kinetics and 8 had abnormal kinetics (delayed and/or slightly or moderately depressed responses) of DNA synthesis (Table 7).

In vitro PWM-induced B cell differentiation assays were performed in seven cases at the time of diagnosis, and the results indicate that all patients tested had a low level of [3H]thymidine incorporation (Table 6). T cell counts were calculated by multiplying the total lymphocyte count by the proportion of E rosette-positive cells. Of 12 patients studied, 3 had normal T cell counts, whereas 9 had elevated levels (Table 7). In vitro T cell responses to PHA in 12 patients showed that 4 had normal kinetics and 8 had abnormal kinetics (delayed and/or slightly or moderately depressed responses) of DNA synthesis (Table 7).

In vitro PWM-induced B cell differentiation assays were performed in two cases, and the results are shown in Table 8. Very little or no immunoglobulin-secreting cells were seen in cocultures containing B cells from patient No. 4 and irradiated autologous T cells or allogeneic normal T cells. An insignificant number of immunoglobulin-secreting cells were seen in cocultures containing B cells from patient No. 16 and irradiated autologous T cells. However, over 800 immunoglobulin-secreting cells were found in cocultures containing B cells from patient No. 20 and irradiated autologous T cells.
lin-secreting cells were identified after coculturing B cells from patient No. 16 and irradiated allogenic normal T cells, indicating a low, but significant, degree of B cell differentiation. T cells from both patients were found to be capable of inducing normal B cells to differentiate in the presence of PWM, although the helper activity of their irradiated T cells was less than that of irradiated normal T cells.

Of 12 patients studied, 4 had a \( \mu \alpha \)-phenotype (case Nos. 2, 4, 8, and 16), 3 had a \( \mu \alpha \lambda \)-phenotype (case Nos. 6, 12, and 19), 4 had a \( \mu \lambda \alpha \)-phenotype (case Nos. 10, 15, 17, and 20), and 1 had a \( \mu \lambda \)-phenotype (case No. 3, no light chain was detectable). Surface marker analysis of peripheral blood lymphocytes from case No. 4 was performed utilizing conventional reagents as well as murine monoclonal antibodies, and the results are shown in Table 9. Approximately half of the lymphocytes either rosetted with unsensitized sheep erythrocytes or reacted with OKT11 antibody (specific for the E-receptor), whereas none of the cells reacted with OKT6 antibody (thymus cell or immature T lymphocytes). The majority of peripheral blood lymphocytes also reacted with other monoclonal anti-T antibodies (pan-T as well as T subsets), monoclonal OKT9 antibody (transferrin receptor), and monoclonal OKT10 antibody (activated lymphocytes).

Cytogenetic analyses by Q or G-bandning techniques of polyclonal B cell mitogen-stimulated lymphocytes were carried out in six cases (Nos. 3, 4, 8, 16, 17 and 20). Normal diploid karyotypes were seen in all cases.

Detailed comparisons of clinical and immunobiologic data between 20 stage 0 CLL patients without disease progression and 17 stage 0 CLL patients with disease progression are shown in Table 10. Of these 17 patients, 5 had general weakness or fatigue and 3 had infection at the time of diagnosis. In nine patients, the diagnosis was made during medical check-up. There were similarities in age distribution, mean hemoglobin level, mean platelet count, mean AP level, elevated T cell count, and hypogammaglobulinemia incidence and bone marrow biopsy infiltration pattern between these two groups. However, there were some differences:

1. Of 20 patients without disease progression, only 7 were males and 13 were females, whereas of 17 patients with disease progression, 9 were males and 8 were females (sex distributions between these 2 groups were not statistically different);
2. Mean total lymphocyte count, mean peripheral blood and bone marrow lymphocyte percentage, and mean LDH level were somewhat higher in those with disease progression than in those without disease progression;
3. [\(^{3}H\)]Thymidine uptake was low in those without disease progression, whereas uptake was high in one of the three patients with disease progression;
4. Three of nine patients with disease progression tested had abnormal karyotypes, whereas none of six patients without disease progression had an abnormal karyotype;
5. The \( \lambda \)-leukemic phenotype was seen in 8 (80%) of 10 patients with disease progression and in only 4 (36%) of 11 patients without disease progression (the differences, however, were not statistically significant).

DISCUSSION

Of interest is the fact that 9 of our patients survived over 10 years without disease progression, 1 patient (case No. 3) is still alive at the time of this report after
23 years, and 2 patients (case Nos. 1 and 3) died of unrelated causes 24 years after the diagnosis of CLL. Richards and Moench described a case of CLL, with lymphocytosis alone, without disease progression and requiring no therapy after 16 years of follow-up. We also found 1 case report by McGavran describing a patient with CLL surviving 25 years. However, it should be pointed out that in McGavran's case with initial stage 0, the disease did progress to stage I and then to stage III, requiring radiation therapy. It should be emphasized that a spontaneous regression of lymphocytosis was observed in 3 of our 20 patients with stage 0 CLL during their follow-up. Though uncommon, spontaneous remission is well recognized in CLL. We have previously observed spontaneous remission in three patients with stage II or III CLL. Some observers might question the diagnosis of CLL in these cases because of the spontaneous remission. It should be pointed out, however, that the phenotypic study carried out in one (case No. 4, W.B.) of these three patients with spontaneous regression of lymphocytosis in this study showed a monoclonal B cell (μ) proliferation.

Age distribution among 20 cases ranged from 50 to 77 years. It is of interest that, of 20 of our cases, only 7 were males and 13 were females. It has uniformly been reported that the male:female ratio in CLL is approximately 2:1. Patterns of bone marrow biopsy infiltration by lymphocytes seen in 6 patients are of interest. In case No. 12, bone marrow biopsy showed normal findings with no evidence of leukemia. Mixed interstitial and nodular or interstitial pattern were seen in 5 cases. These findings suggest that the bone marrow in stage 0 patients is usually focal rather than diffusely involved. It has been reported that diffuse patterns of bone marrow infiltration are frequently associated with advanced stages of CLL. In a preliminary study, we observed that LDH and AP enzyme levels are strongly correlated with the clinical stage of CLL. Our findings in the present study that the LDH and AP levels were within normal ranges in almost all cases may simply be related to the absence of lymphoid organ development. Neither hypogammaglobulinemia nor the presence of urinary free light chains was seen in any of the cases studied.

In the present study, all patients had positive delayed hypersensitivity responsibilities to at least one of five skin test antigens. These observations clearly suggest that these patients have essentially normal in vivo cell-mediated immunity. It should be recognized that 9 of 12 patients studied had elevated total T cells, and the remaining 3 had normal T cell counts, although a majority of peripheral blood lymphocytes were phenotyped as monoclonal B cells. T cell elevations in active and advanced CLL patients have previously been reported. We observed normal kinetics of DNA synthesis by PHA-stimulated T cells in four and slightly or moderately depressed and delayed kinetics in eight patients studied. These observations differ from previously reported findings that showed marked depressed and/or delayed DNA kinetics associated with advances stages of CLL. The finding in the
present study that B cell differentiation was depressed in the two patients tested is in agreement with previously reported observations in CLL patients with various clinical stages.4

Moayeri and Sokal19 recently reported that, among 60 patients with CLL, a higher in vitro uptake of [3H]thymidine by leukocytes in a standard volume of peripheral blood was associated with higher lymphocyte counts, more advanced stages, greater frequency of functional impairment, and shorter survival, whereas a lower in vitro [3H]thymidine uptake was associated with better clinical parameters. Seven patients in the present study with a low [3H]thymidine uptake were included in the study of Moayeri and Sokal.19

Phenotypic studies in all 12 patients demonstrated monoclonality of B cell lymphocytosis by light and heavy chain analysis. Peripheral blood mononuclear cells from one patient tested were reactive with monoclonal pan-T antibodies. Reactivity of leukemic B cells from a majority of patients with various stages of CLL with monoclonal pan-T antibodies has recently been described.30-32

Cytogenetic abnormalities in polyclonal B cell mitogen-stimulated peripheral blood lymphocytes in patients with CLL have recently been reported.33-36 Trisomy 12, alone or in combination with other changes, was the most frequent chromosome abnormality in CLL.33-36 We have further demonstrated that trisomy 12 as a sole abnormality is more frequently associated with the early stages (0, I, and II) of CLL.37 The finding in the present study that each of six patients analyzed had normal diploid karyotypes is of particular interest. It should be pointed out that an abnormal karyotype (trisomy 12) was seen in 4 of our 17 recently diagnosed and untreated patients.38

CLL is a disease known to have a variable course; some patients die within a few years after diagnosis, while others live more than a decade. In view of the fact that we have studied over 500 patients with CLL, it may be that these 20 stage 0 CLL patients are simply the tail end of those with the most benign course. It should be emphasized that, in detail comparisons of clinical and immunobiologic data between 20 stage 0 CLL patients without disease progression and 17 stage 0 CLL patients with disease progression, we found several striking differences between these 2 groups. About two thirds of nonprogression group patients and only 8 of 17 progression group patients were females. Several poor prognostic factors, such as marked lymphocytosis,10 high LDH level,28 high [3H]thymidine uptake of peripheral blood leukocytes,19 and abnormal karyotype,37 were associated with some stage 0 CLL patients with disease progression. Of particular interest is the fact that, of 10 patients with disease progression, 8 had λ-leukemic phenotypes and only 2 had κ-leukemic phenotypes, whereas of 11 patients without disease progression, 7 had κ-phenotypes and only 4 had λ-phenotypes. These observations suggest that stage 0 CLL patients with λ-phenotypes may have a more likely chance of disease progression than those with κ-phenotypes. It has been reported that CLL patients with lymphocytes expressing κ-light chains may have a more benign disease than λ-CLL39 and that most of the CLL patients with benign clinical course had κ-phenotypes.40 It should be pointed out that the numbers of stage 0 CLL patients in our study, as well as reported studies,39,40 were rather small. These observations, nevertheless, deserve further investigation in a larger number of patients with stage 0 CLL.

To our knowledge, this is the first report describing the documentation of lack of progression in patients with stage 0 CLL, phenotypically characterized as monoclonal B cell leukemia. Very recently, Gordon et al41 reported three women with a newly described disorder termed persistent polyclonal lymphocytosis of B lymphocytes (PPBL). The benign clinical course of these three patients followed for 8–15 years was similar, but other clinical and laboratory parameters differed. Three patients with PPBL were 41–54 years old, whereas our patients were 50–77 years old, suggesting that PPBL may be more frequently associated with somewhat younger individuals than typical CLL. Total lymphocyte counts in PPBL patients were only slightly elevated (5,900–7,700/μL), and bimucleated lymphocytes were observed in all PPBL cases. Polyclonal serum IgM elevation was also present in these cases, whereas none of our patients presented with an IgM elevation. In vitro PWM-induced B cell differentiation in PPBL was normal, whereas such B cell differentiation was markedly depressed in both patients tested in the present study. The most striking difference between these two studies is that each of 12 patients tested in the present study showed monoclonal lymphocytosis of B cell origin, while each of 3 PPBL patients showed polyclonal lymphocytosis of B cell origin.

The data in the present study indicate that these 20 patients with stage 0 CLL have a benign clinical course and that they may also be designated as benign monoclonal B cell lymphocytosis (BMBL)—a benign variant of CLL.

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REFERENCES

30. Royston I, Majda JA, Baird SM, Reserve BL, Griffiths JC: Human T cell antigens defined by monoclonal antibodies: The 65,000 dalton antigen of T cells (T-65) is also found on CLL leukemic cells bearing surface immunoglobulins. J Immunol 125:725, 1980
38. Sadamori N, Han T, Minowada J, Sandberg AA: Clinical


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