Autologous Transplantation of Bone Marrow Purged In Vitro With Anti-CD7-(WT1-) Ricin A Immunotoxin in T-Cell Lymphoblastic Leukemia and Lymphoma


Seven patients with high-risk acute T-cell lymphoblastic leukemia (T-ALL) and six with T-cell lymphoma (T-LL) were treated with autologous bone marrow transplantation (ABMT) after in vitro purging of their bone marrow with WT1 (CD7)-ricin A-chain immunotoxin. CD7 expression on the tumor cells showed large variations between the individual patients and was highly related to the specific cytotoxicity of WT1-ricin A. Incubation of bone marrow with up to 10\(^{-5}\)mol/L WT1-ricin A in the presence of 6 mmol/L NH\(_4\)Cl did not compromise the growth potential of the hematopoietic progenitors CFU-GM, CFU-GEMM, and BFU-E. Hematologic engraftment (>10\(^6\) leukocytes/L) occurred within a normal time period (median, 17 days). Seven patients are alive and in complete remission (CR) at 48+, 44+, 40+, 26+, 11+, 7+, and 6+ months after ABMT. Four patients relapsed within 6 months after ABMT. Two of them had the lowest CD7 expression on their tumor cells, the other two were transplanted in CR2 and CR3. Two patients died from transplantation related infections. The immunologic reconstitution was delayed, although the numbers of T-cells reached normal levels within 1 month. The number of CD7\(^+\) cells remained low up to 1 year after transplantation. The T4/T8-ratio was decreased for at least 6 months. The T-cell response to mitogens recovered to normal levels after 1 year. This study shows that ABMT with WT1-ricin A purged bone marrow in high-risk T-cell malignancies results in a complete hematopoietic and a delayed immunologic reconstitution. The actuarial relapse free survival is 61% at 3 years.

MATERIALS, METHODS, AND PATIENTS

Immunotoxin

Ricin A was kindly provided by Dr. F.K. Jansen, Centre de Recherches Clin Midy, Montpellier, France. The murine anti-human T cell monoclonal antibody (MoAb): WT1, anti-CD7 (kindly provided by Dr. W. Tax) was conjugated to ricin A by means of succinimidyl-3-(2-pyridyldithio) propionate (SPDP; Pharmacia Ltd, Uppsala, Sweden) as described previously.

Antigen Density

WT1 was labeled with \(^{125}\)Iodine (Amersham International, Amersham Bucks, UK) using the chloramine T method. The concentration and specific activity of the \(^{125}\)I-labeled MoAb were determined respectively radioimmunoassay and binding assay with limiting quantities of labeled antibody. The absolute number of binding sites per cell was determined as described previously.

Cytotoxicity of WT1-Ricin A

Fresh or thawed cryopreserved leukemic cells were incubated in Eagle's modified Minimum Essential Medium (EMEM) without leucine (Flow Labs, Irvine, Scotland) supplemented with 5% fetal calf serum (FCS), 2 mmol/L glutamine, 1 mmol/L sodium pyruvate and gentamycin (50 \(\mu\)g/mL). Each well of U-bottomed plates (Costar, Cambridge, MA) was filled with 10\(^5\) cells supplemented with varying concentrations of IT in the absence or presence of 6 mmol/L NH\(_4\)Cl to a final volume of 200 \(\mu\)L. Cells were incubated for 24 hours at 37°C in a humidified incubator with 5% CO\(_2\) in air, followed by 24 hours incubation with 0.5 \(\mu\)Ci \(^{3}H\) leucine (TRK510, Amersham). Cells were harvested and radioactivity was counted. The cytotoxicity was expressed as percentage inhibition of \(^{3}H\) leucine incorporation of untreated cells corrected for the background value determined in the presence of 1 mmol/L cycloheximide.

Cytotoxicity to Bone Marrow Progenitor Cells

Bone marrow was aspirated from patients undergoing cardiac surgery after informed consent was obtained and anti-aggregated
with acid citrate dextrose (ACD). Erythrocytes and mature granulocytes were removed by gradient centrifugation on Ficoll (1.077 g/mL). Cells (10^6/mL) were incubated with ITs (10^-9 mol/L) with or without 6 mmol/L ammonium chloride for 24 hours. Cells were washed and the decrease of bone marrow progenitors was determined in clonogenic assays of granulocyte/macrophage and granulocyte/erythrocyte/macrophage/megakaryocyte colony-forming cells (CFU-GM and CFU-GEMM, respectively), and erythroid burst-forming cells (BFU-E) as described previously.

**Patients**

ABMT was performed in 13 patients with high-risk T-cell malignancies: seven T-ALL and six T-LL. Reasons for assignment to transplantation included one or more of the following risk factors: for T-ALL age of 30 years or older, leukocyte counts at diagnosis >30 x 10^9/L, hepato/splenomegaly, CNS involvement and status of disease; for T-LL stage 4 of disease with CNS involvement or with lactic dehydrogenase (LDH) >300 U/L and hepato/splenomegaly. Patients no. 8, 9, 11, and 13 with T-LL had no CNS localization but bone marrow involvement and either splenomegaly or LDH >300 U/L. Before ABMT nine patients were in CR1, one in CR2, and three in CR3 (Table 1). None of these patients had an HLA-identical sibling donor. The mean age was 21 years (range, 10 to 35 years). Data of phenotype of the malignant T cells and clinical status of the individual patients at time of diagnosis and before ABMT are given in Table 1. Antigen density and cytotoxicity of WT1-ricin A to the malignant cells were determined before the marrow harvest.

**Bone marrow processing**

Bone marrow was aspirated from the posterior iliac crests under general anesthesia and anticoagulated with heparin. Hematopoietic progenitor cells were enriched by density floatation separation in Percoll gradients. The low density fraction (d ≤ 1.070 g/mL; 10^6 cells/mL) was incubated with 10^-9 mol/L WT1-ricin A in the presence of 6 mmol/L ammonium chloride in RPMI 1640 supplemented with 5% FCS, 2 mmol/L glutamine and 50 μg/mL gentamycin at 37°C in a humidified incubator with 5% CO2 for 16 hours. After incubation cells were washed, cryopreserved, and stored until the day of reinfusion (designated day 0). The recovery of hematopoietic progenitors CFU-GM and BFU-E before and after IT treatment, and after cryopreservation was determined to check the procedure. Cell recovery and morphology were assessed in each fraction.

**Transplantation procedure**

Patients were conditioned with cyclophosphamide 60 mg/kg under protection of 12 mg/kg 2-mercaptopurinethesulfonate (Mesna) to prevent hemorrhagic cistitis on days -6 and -5 and total body irradiation (TBI: total dose 800 cGy given in a single fraction) or HD-melphalan 180 mg/m^2 (patient no. 5) on day -1. All patients received CNS prophylaxis with methotrexate intrathecally. On day 0 purged bone marrow was thawed rapidly and reinfused immediately. Daily blood counts were performed during hypoplasia to define the day of engraftment (leukocyte count >1 x 10^9/L). Platelet levels were maintained above 20 x 10^9/L with irradiated (20 Gy) platelet transfusions.

**Follow-up of T-cell recovery**

Heparinized venous blood and bone marrow aspirates (sternum) were obtained from every patient 1, 3, 6, and 12 months posttransplantation. Hematologic reconstitution and cell numbers were determined in blood count analysis and morphology of blood and bone marrow smears.

The reconstitution of lymphocyte subpopulations was determined by flow cytometry of the lymphocyte scatter area in relation to indirect immunofluorescence of bound MoAbs. The following anti-T-cell MoAbs were used: WT32 (CD3), WT1 (CD7), and WT82 (CD8) provided by Dr. W. Tax; OKT6 (CD1), OKT4 (CD4), OKT8 (CD8) from ORTHO Diagnostic Systems Inc (Raritan, NJ). Additionally the following were used: OKB2, identifying B-cells, pre-B cells, and granulocytes; OKB7, identifying B cells expressing the 175 Kd antigen; OKM1 (CD11a) and OKM5,
recognizing monocytes and platelets expressing the 88 Kd antigen. After the initial incubation with MoAbs, cells were incubated with FITC-labelled goat anti-mouse IgG (Fab) 2 fragment (GAM-FITC; American Qualex International Inc, La Mirada, CA).

The functional reconstitution of the T lymphocytes was determined in stimulation assays carried out in 96-well U-bottom plates. Each well was filled with 10^5 cells in culture medium in the absence or the presence of 40 μg/mL phytohaemagglutinin (PHA) or 15 μg/mL concanavalin A (Con A) to a final volume of 200 μL and incubated at 37°C in a humidified atmosphere with 5% CO₂ in air for 48 hours, followed by a labeling with 0.5 μCi ³H thymidine (TRK 61, Amersham) for 24 hours. Thereafter cells were harvested and radioactivity was counted. Stimulation was expressed as percentage ³H thymidine incorporation by PHA or Con A stimulated lymphocytes of normal individuals, all corrected for background incorporation of unstimulated cells.

Statistical analysis. Differences in leukocyte number and hematopoietic progenitors before and after IT treatment were analyzed by the matched-pair r test.

After ABMT patients with no evidence of relapse were classified as being in CR. The overall survival and the probability of relapse posttransplant were evaluated by the Kaplan-Meier method.

RESULTS

Cytotoxicity of WT1-Ricin A to Malignant T Cells
In Vitro in Relation to Antigen Density

The cytotoxic potency of WT1-ricin A in the presence of 6 mmol/L NH₄Cl was tested on the malignant cells of 12 of 13 patients and expressed as dose required for 50% reduction of protein synthesis (ID₅₀) (Table 2). Malignant cells before initial therapy of patient no. 4 were not available for cytotoxicity studies. Protein synthesis was inhibited mainly depending on antigen density of CD7 on the cell surface. The average antigen density varied individually from 9,000 to 250,000 molecules per cell. As described previously, a strong correlation was found between cytotoxicity and antigen density of CD7. Malignant cells from patients with C-ALL and B-ALL without CD7 expression were used as controls.

Effect of WT1-Ricin A on Hematopoietic Progenitors

The cytotoxicity of WT1-ricin A with or without NH₄Cl to hematopoietic progenitors was determined by means of clonogenic assays. Cells were incubated with 10⁻⁸ mol/L WT1-ricin A, the dose used to treat large amounts of bone marrow. In comparison with untreated cells no influence of IT treatment in the presence of 6 mmol/L NH₄Cl was found on the plating efficiency of CFU-GM (97 ± 11%), CFUGEMM (101 ± 11%), and BFU-E (94 ± 10%) as determined in five independent experiments.

Purging of Bone Marrow

Average 5.4 x 10⁶ (range, 2.8 to 9.8 x 10⁶) low density marrow cells (d < 1.070 g/mL) were incubated with 10⁻⁸ mol/L WT1-ricin A in the presence of 6 mmol/L NH₄Cl. This resulted in a 10% reduction of nucleated cells, and 26% reduction of CFU-GM and BFU-E, that was probably not caused by cytotoxicity of the IT but largely due to the procedure itself. Patients received a mean cell dose per kg of 7.3 ± 2.7 x 10⁹ (range, 4.5 to 13.4 x 10⁹) nucleated cells, 10.5 ± 9.5 x 10⁶ (range, 1.9 to 37.6 x 10⁶) CFU-GM, and 17.2 ± 11.2 x 10⁶ (range, 3.7 to 42.9 x 10⁶) BFU-E.

Hematologic Engraftment

All patients engrafted after reinfusion of WT1-ricin A purged bone marrow. The mean day of recovery of leukocyte count to >10⁹/L was day 17.3 ± 5.0 (median, 17; range, 9 to 25 days) (Table 3). After recovery of leukocytes to >10⁹/L patient no. 6 was treated with ganciclovir, fluconazole, and flucytosine because of the suspicion of cytomegalovirus (CMV) infection and a proven Candidemia. Subsequently leukocyte count dropped and the patient died in aplasia. Platelet recovery (>50 x 10⁹/L) was delayed in three patients (patients nos. 8, 10, and 11) and was not evaluable in two (patients no. 6 and 9). The median recovery occurred on day 40 (range, days 14 through 270). No relation was found between the state of disease, the number of reinfused hematopoietic progenitor cells (CFU-GM and BFU-E), or the day of engraftment.

Survival

Clinical data of survival after ABMT are shown in Table 3. Nine of the 13 patients are alive; two of them (patients no. 5 and 7) relapsed within 5 months after ABMT in CR2 and CR3. Seven patients are still in CR (6+, 7+, 11+, 26+, 40+, 44+, 48+ months). Four patients have died; two patients died 1 month after recurrence of leukemia, one patient died by a Candida and CMV infection (patient no. 6), and one patient by Streptococcus viridans and CMV infection (patient no. 9).

The calculated overall survival at 3 years is 66.6% and the probability of relapse-free survival is 61.3% (Fig 1). The four relapses were found in patients treated for T-ALL: two of these patients (nos. 1 and 4) had a low CD7 expression on their malignant cells and the other two patients were transplanted in CR2 and CR3, respectively. In the group of T-LL patients, five of the six patients are alive and disease free 6, 7,
to 0.8

Fig 1. Kaplan-Meier estimate of the probability of actuarial relapse rate (—) and overall survival (—) of 13 patients with T-ALL or T-LL after autologous transplantation with WT1-ricin A purged bone marrow. Tick marks represent censored patients. (CI: 95% confidence interval limits).

Table 3. Clinical Data After ABMT

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Diagnosis Before ABMT</th>
<th>Engraftment* (days)</th>
<th>Status After ABMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T-ALL; CR1</td>
<td>WBC: 14, PLT: 22</td>
<td>Died after 7 mo in relapse (6 mo post-ABMT).</td>
</tr>
<tr>
<td>2</td>
<td>T-ALL; CR1</td>
<td>WBC: 17, PLT: 32</td>
<td>Alive and CR, &gt;48 mo</td>
</tr>
<tr>
<td>3</td>
<td>T-ALL; CR1</td>
<td>WBC: 14, PLT: 38</td>
<td>Alive and CR, &gt;40 mo</td>
</tr>
<tr>
<td>4</td>
<td>T-ALL; CR1</td>
<td>WBC: 9, PLT: 14</td>
<td>Died after 7 mo in relapse (6 mo post-ABMT).</td>
</tr>
<tr>
<td>5</td>
<td>T-ALL; CR2</td>
<td>WBC: 21, PLT: 38</td>
<td>Alive and relapse (5 mo post-ABMT), &gt;15 mo</td>
</tr>
<tr>
<td>6</td>
<td>T-ALL; CR1</td>
<td>WBC: 13, PLT: NE</td>
<td>Died after 51 days by Candida and CMV.</td>
</tr>
<tr>
<td>7</td>
<td>T-ALL; CR3</td>
<td>WBC: 14, PLT: 40</td>
<td>Alive and relapse (5 mo post-ABMT), &gt;12 mo</td>
</tr>
<tr>
<td>8</td>
<td>T-LL 4A; CR1</td>
<td>WBC: 13, PLT: 180</td>
<td>Alive and CR, &gt;44 mo</td>
</tr>
<tr>
<td>9</td>
<td>T-LL 4A; CR3</td>
<td>WBC: 20, PLT: NE</td>
<td>Died after 61 days by Streptococcus viridans and CMV.</td>
</tr>
<tr>
<td>10</td>
<td>T-LL 4A; CR3</td>
<td>WBC: 25, PLT: 270</td>
<td>Alive and CR, &gt;26 mo</td>
</tr>
<tr>
<td>11</td>
<td>T-LL 4A; CR1</td>
<td>WBC: 21, PLT: &gt;210</td>
<td>Alive and CR, &gt;11 mo</td>
</tr>
<tr>
<td>12</td>
<td>T-LL 4A; CR1</td>
<td>WBC: 25, PLT: 60</td>
<td>Alive and CR, &gt;7 mo</td>
</tr>
<tr>
<td>13</td>
<td>T-LL 4A; CR1</td>
<td>WBC: 19, PLT: 57</td>
<td>Alive and CR, &gt;6 mo</td>
</tr>
</tbody>
</table>

Abbreviations: ABMT, autologous bone marrow transplantation; CR, complete remission; T-ALL, acute T-cell lymphoblastic leukemia; T-LL, T-cell lymphoblastic lymphoma; NE, not evaluable.

*Recovery of leukocyte (WBC) counts to >10^9/L and platelet counts to >50 x 10^9/L in days after ABMT.

11, 26, and 44 months after ABMT, whereas one patient died due to infections (patient no. 9).

Immunologic Recovery

The patients who survived more than 1 year were followed for their hematologic and immunologic recovery (Table 4). Leukocyte counts normalized more than 6 months after ABMT, partly due to a longlasting granulocytopenia, whereas lymphocytes and monocytes achieved normal levels within 1 month. The immunologic recovery was delayed for at least 1 year as determined by flow cytometric analysis of the lymphocyte phenotypes. CD3^+ and CD5^+ cells returned to normal levels within 1 month after ABMT. However, the T4/T8-ratio was reversed for more than 6 months and did not return to normal levels for at least 1 year. This decreased T4/T8-ratio was due to a low number of CD4^+ cells, whereas CD8^+ cells returned to normal levels within 1 month. The number of CD7^+ cells did not reach normal values for at least 1 year. The functional recovery was tested by responsiveness to mitogens compared with normal individuals (Table 5). T cells hardly responded to mitogens in the first 3 months, but returned to normal within 1 year after ABMT.

DISCUSSION

Bad risk criteria in patients with ALL and lymphoma are not precisely defined. Age of 30 years or older, leukocytosis of 30 x 10^9/L, hepato/splenomegaly, CNS involvement, and LDH level of >300 U/L can be considered bad prognostic signs at time of presentation according to Hoelzer et al.,16 Herzig et al.,17 and Coleman et al.18 Therefore these patients and patients with more advanced disease can be considered as candidates for ABMT with or without in vitro purging. MoAbs with complement lysis are most commonly used for purging; however, ITs often appear more efficient in cell killing.30,31 The cytotoxicity of WT1-ricin A is highly related to the CD7 density on malignant T cells.15 Previously we demonstrated that WT1-ricin A in the presence of 6 mmol/L ammonium chloride induces more than 6-logs kill of the malignant T cell line CEM.15 CEM expresses intermediate amounts of CD7 comparable with malignant T cells of most patients, which may imply effective reduction of the residual leukemic cells in the bone marrow.

A prolonged purging procedure of bone marrow with IT may be harmful to the hematopoietic stem cells. We have chosen an incubation period of 16 hours based on kinetics of cytotoxicity and internalization of cell bound IT.15 We showed that WT1-ricin A is continuously internalized coinciding with increasing cytotoxicity. In the present and in other studies,19 no cytotoxicity of IT to hematopoietic precur-
The delayed immunologic recovery appeared not to be occurs rapidly compared with reports after purging with ITs was found even after 24 hours incubation. This contrasts with the effects of cytostatic drugs. The slight reduction of hematopoietic precursors after purging with ITs was probably caused by intensive manipulation of the marrow. All patients in this study showed a fast engraftment of bone marrow (median, day 17). The marrow recoveries occurred rapidly compared with reports about nonpurged and otherwise purged autologous bone marrow, and were comparable with syngeneic marrow engraftment. These results provide evidence that sufficient hematopoietic precursor cells survived the WT1-ricin A purging. In contrast the platelet recovery to $50 \times 10^9$/L was strongly delayed in three patients. The same phenomenon was observed in other studies.

Although the number of T lymphocytes attained normal levels within 1 month, the immunologic recovery was delayed for almost 1 year. CD7$^+$ cells remained low for at least 6 months. Data of de Gast et al., suggesting that the recovery of T-cell subsets is mainly due to the proliferation of mature T cells in the graft, may be an explanation for this observation. No T cells with an immature phenotype (CD1) were detected after 1 month. Functional recovery, as measured with response to mitogens, remained low for almost 1 year. This may be due to a defective T-helper function as observed by Armitage et al resulting in a decreased T4/T8-ratio. The delayed immunologic recovery appeared not to be induced by WT1-ricin A because other investigators have found similar results in ABMT with other purging procedures or even without purging and in allogeneic BMT.

Relapse is at date only seen in a group of patients with T-ALL. Whether the recurrence of leukemia was caused by residual leukemic cells in the patient or in the bone marrow graft cannot be determined. It may be of interest that two of the relapsed patients had initially a low CD7 expression on the malignant cells. The susceptibility to WT1-ricin A appeared not to be changed in relapse (data not shown). Our results suggest that only leukemias with high antigen density on the cell surface should be selected for purging with ITs in order to improve the results of ABMT with immunologically purified bone marrow.

Statistical evaluation of survival after ABMT is virtually impossible because of the low number of patients and the heterogeneous group of diseases. Though the results of survival are preliminary, 43% of patients transplanted for T-ALL (seven patients) remained in CR, which is comparable with data of Gorin et al. In the group of T-LL none of the patients relapsed. Although this group is too small for statistical analysis our results seem in accordance with those of others obtained in lymphoblastic lymphoma.

The advantage of bone marrow purging is difficult to assess due to the various methods used for marrow purging and the small number of patients studied. Gorin et al demonstrated by analysis of 125 patients with ALL in first CR that, although no statistically significant advantage for purging exists, patients who received purged bone marrow had a higher percentage of disease-free survival in 3 years (58%) than patients with nonpurged bone marrow (30%).

We conclude that purging of bone marrow with WT1-ricin A before ABMT is a safe therapeutic option. It may be the treatment of choice for patients with high risk T-cell malignancies.

### Table 4. Hematologic and Immunologic Recovery in Patients Who Survived More Than 1 Year After ABMT

<table>
<thead>
<tr>
<th></th>
<th>Months After ABMT</th>
<th>1</th>
<th>3</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte</td>
<td></td>
<td>1.8 ± 1.0</td>
<td>2.5 ± 1.3</td>
<td>3.8 ± 1.4</td>
<td>4.8 ± 1.4</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td></td>
<td>0.73 ± 0.30</td>
<td>0.96 ± 0.56</td>
<td>0.95 ± 0.57</td>
<td>1.37 ± 0.68</td>
</tr>
<tr>
<td>CD1</td>
<td></td>
<td>0.02 ± 0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CD3</td>
<td></td>
<td>0.68 ± 0.35</td>
<td>0.52 ± 0.30</td>
<td>0.64 ± 0.38</td>
<td>0.88 ± 0.50</td>
</tr>
<tr>
<td>CD4</td>
<td></td>
<td>0.28 ± 0.09</td>
<td>0.18 ± 0.06</td>
<td>0.21 ± 0.04</td>
<td>0.45 ± 0.23</td>
</tr>
<tr>
<td>CD5</td>
<td></td>
<td>0.52 ± 0.29</td>
<td>0.41 ± 0.25</td>
<td>0.64 ± 0.38</td>
<td>0.85 ± 0.50</td>
</tr>
<tr>
<td>CD7</td>
<td></td>
<td>0.12 ± 0.01</td>
<td>0.23 ± 0.12</td>
<td>0.29 ± 0.19</td>
<td>0.67 ± 0.70</td>
</tr>
<tr>
<td>CD8</td>
<td></td>
<td>0.43 ± 0.28</td>
<td>0.35 ± 0.21</td>
<td>0.34 ± 0.21</td>
<td>0.42 ± 0.25</td>
</tr>
<tr>
<td>Anti-B cell</td>
<td></td>
<td>0.08 ± 0.06</td>
<td>0.05 ± 0.03</td>
<td>0.09 ± 0.06</td>
<td>0.15 ± 0.08</td>
</tr>
</tbody>
</table>

Values are expressed as mean absolute number of cells $\times 10^{10}$/L ± SD. Percentage of cells is given in parentheses.

### Table 5. Functional Recovery of Lymphocytes in Patients After ABMT

<table>
<thead>
<tr>
<th></th>
<th>Months After ABMT</th>
<th>1</th>
<th>3</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHA</td>
<td></td>
<td>3 ± 3</td>
<td>14 ± 2</td>
<td>42 ± 10</td>
<td>101 ± 11</td>
</tr>
<tr>
<td>Con A</td>
<td></td>
<td>2 ± 3</td>
<td>8 ± 6</td>
<td>41 ± 27</td>
<td>97 ± 9</td>
</tr>
</tbody>
</table>

Values are expressed as mean percentage of $^3$H thymidine incorporation by cells of normal individuals ± SD of five measurements. Average incorporation by lymphocytes of five normal individuals was 37,104 ± 1,441 cpm after PHA stimulation and 26,691 ± 2,608 cpm after Con A stimulation.

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Autologous transplantation of bone marrow purged in vitro with anti-CD7-
(WT1-) ricin A immunotoxin in T-cell lymphoblastic leukemia and
lymphoma

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