Outcomes of Autologous Stem Cell Transplantation in Patients with Relapsed or Refractory HIV-associated Lymphoma

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The Origins of ASCT

Jacobsen’s radiation protection experiments:

- 1000 rads
- Shield hind limb
- Inject spleen cells
- Died
- Protected
- Protected
Stem Cell Transplant, Simplified

1. Bone marrow removed or blood is drawn
2. Stem cells are collected
3. Stem cells stored or frozen
4. Chemotherapy destroys bone marrow
5. Stem cells returned to bloodstream

Autologous bone marrow transplant
High-dose therapy and autologous haematopoietic stem-cell transplantation for HIV-1-associated lymphoma

Jean Gabarre, Nabil Azar, Brigitte Autran, Christine Katlama, Véronique Leblond

We describe the results of autologous haematopoietic stem-cell transplantation in eight patients with HIV-1-associated lymphoma. Collection and grafting of stem cells is feasible and this treatment seems appropriate in chemotherapy-sensitive HIV-1-associated lymphoma.

High-dose chemotherapy followed by autologous haematopoietic stem-cell transplantation is the first-choice salvage treatment for patients with relapsed chemotherapy-sensitive non-Hodgkin lymphoma (NHL). Despite the improvement of immunological status in HIV-1-infected patients as a result of new antiretroviral combinations, lymphomas are still seen in this setting. Few patients with HIV-1-associated lymphoma treated with high-dose chemotherapy followed by autologous haematopoietic stem-cell transplantation have been described and the efficacy of such treatment is unknown in terms of the efficiency of stem-cell collection and engraftment, and the impact of intensive therapy on the course of HIV-1 lymphoma and immune disease (table 1). All patients, except one (patient 1) who was grafted in 1994, had received highly-active antiretroviral therapy (HAART) for a median of 24 months (12–30) before stem-cell transplantation; this therapy was maintained during graft collection, transplantation, and after transplantation. The median CD4-cell count before high-dose chemotherapy was 122 cells/μL and viral load was undetectable in the seven patients receiving HAART (table 2). Bone marrow was harvested from patient 1, and peripheral-blood stem cells were collected from the other seven patients after chemotherapy and treatment with granulocyte colony-stimulating factor. The mean CD34-cell count in the grafts was 7.17×10⁹/kg (range 4.5–17.6), and patients had a median of one apheresis session (1–3).

Pre-graft conditioning consisted of high-dose chemotherapy alone in three patients and high-dose chemotherapy plus total-body irradiation in the other five patients. Five patients (patients 1, 2, 3, 6, and 7) received myeloablative salvage chemotherapy before grafting with cell
# Histological Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Relapse n=113</th>
<th>Intention to Transplant (ITT) n=44</th>
<th>ASCT n=18</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic B cell</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>DLBCL</td>
<td>61 (54%)</td>
<td>15 (34%)</td>
<td>6 (35%)</td>
</tr>
<tr>
<td>BL</td>
<td>24 (21%)</td>
<td>7 (16%)</td>
<td>3 (18%)</td>
</tr>
<tr>
<td>PEL</td>
<td>2 (2%)</td>
<td>2 (5%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Hodgkin's</td>
<td>19 (54%)</td>
<td>16 (36%)</td>
<td>7 (41%)</td>
</tr>
<tr>
<td>Plasmoblastic</td>
<td>4 (4%)</td>
<td>2 (5%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>T-cell</td>
<td>3 (3%)</td>
<td>2 (5%)</td>
<td>1 (6%)</td>
</tr>
</tbody>
</table>
## Chemotherapy and Assessment

<table>
<thead>
<tr>
<th>Response prior to ASCT</th>
<th>ITT underwent ASCT N=18</th>
<th>ITT did not proceed to ASCT N=26</th>
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</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>8 (44%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>5 (28%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>2 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>0 (0%)</td>
<td>12 (46%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (17%)</td>
<td>10 (38%)</td>
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</table>

<table>
<thead>
<tr>
<th>Response following ASCT</th>
<th>ITT underwent ASCT N=18</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Response</td>
<td>13 (72%)</td>
<td></td>
</tr>
<tr>
<td>Partial Response</td>
<td>1 (6%)</td>
<td></td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>4 (22%)</td>
<td></td>
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</tbody>
</table>

**Flowchart:**
- Diagnosis of r-HIV+Ly
  - Salvage Chemotherapy
  - Imaging
  - ASCT
  - Imaging
CD4 Count Changes

CD4+ Lymphocyte Count

Diagnosis, Relapse, Salvage Chemotherapy, ASCT, Post-ASCT, 6 months, 1 year, 3 years, 5 years
Long-Term Control of HIV by CCR5 Delta32/Delta32 Stem-Cell-Cell Transplantation

Gero Hütter, M.D., Daniel Nowak, M.D., Maximilian Mossner, B.S., Susanne Ganepola, M.D., Arne Müßig, M.D., Kristina Allers, Ph.D., Thomas Schneider, M.D., Ph.D., Jörg Hofmann, Ph.D., Claudia Kücherer, M.D., Olga Blau, M.D., Igor W. Blau, M.D., Wolf K. Hofmann, M.D., and Eckhard Thiel, M.D.

SUMMARY

Infection with the human immunodeficiency virus type 1 (HIV-1) requires the presence of a CD4 receptor and a chemokine receptor, principally chemokine receptor 5 (CCR5). Homozygosity for a 32-bp deletion in the CCR5 allele provides resistance against HIV-1 acquisition. We transplanted stem cells from a donor who was homozygous for CCR5 delta32 in a patient with acute myeloid leukemia and HIV-1 infection. The patient remained without viral rebound 20 months after transplantation and discontinuation of antiretroviral therapy. This outcome demonstrates the critical role CCR5 plays in maintaining HIV-1 infection.
Conclusions

Outcomes comparable to other results.

Treatment appears to be efficacious, feasible and safe.

People living with HIV should receive the same cancer therapy as the general population.
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