

## SHORT COMMUNICATION

## Allogeneic Haematopoietic Stem Cell Transplantation for Patients with Cutaneous T-cell Lymphoma

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Cutaneous T-cell lymphomas (CTCL) are rare non-Hodgkin's lymphomas with homing preference to the skin. The most common type of CTCL is mycosis fungoides (MF) (1). The clinical course of MF is mostly indolent, but approximately 25% may progress to advanced disease, with a median survival below 4 years. Some subtypes of MF, such as folliculotropic MF, can be very therapy-resistant and present with a progressive disease course. Sézary syndrome (SS) and primary skin peripheral T-cell lymphoma, unclassified (PCTCL) are less common variants of CTCL with an aggressive course. SS was previously considered a leukaemic variant of CTCL, but it is today understood to be a subtype of its own, originating primarily from central memory T cells (2). In SS, 5-year survival is 18–20% (3). Also, for advanced stages of MF there are few treatment options.

Allogeneic haematopoietic stem cell transplantation (allo-SCT) is a treatment modality for patients with malignant or non-malignant haematological disease. Conditioning regimens may be either myeloablative or non-myeloablative. Patients treated with allo-SCT may experience life-threatening acute or chronic graft-versus-host disease (GVHD) or serious infectious complications. Allo-SCT has been used to treat advanced-stage MF and SS (4, 5) but the experience is limited and treatment protocols vary to a great extent. However, long-term follow-up data of the European Group for Blood and Marrow Transplantation show that patients with CTCL may benefit from allo-SCT (6).

We report here 3 patients with CTCL who received allo-SCT, one of whom achieved complete remission.

## PATIENTS AND METHODS

We describe here 3 patients with CTCL (2 males and 1 female) who were transplanted in our stem cell transplantation unit during the years 2013 to 2014. The first patient had primary cutaneous PCTCL (case 1), the second SS (case 2), and the third folliculotropic MF (case 3). Age at diagnosis ranged from 39 to 52 years.

All patients had experienced several modes of CTCL treatments according to the current guidelines (7). The demographic data and previous treatments are shown in Table I. Case 1 had undergone autologous stem cell transplantation (auto-SCT) with BEAM conditioning one year before allo-SCT. However, the PTCL had relapsed within 6 months after the auto-SCT.

All 3 patients had active disease involvement at the time of allo-SCT. The median age of the patients at the time of allo-SCT was 46 years (range 44–55 years).

Each of the 3 patients was transplanted with a graft from an unrelated registry donor with 11/12 match. Both male patients (cases 1 and 2) received a graft from a male donor. Reduced intensity conditioning with treosulfan, 30 mg/m<sup>2</sup>, and fludarabine, 150 mg/m<sup>2</sup>, were given to all patients. All 3 patients received ATG-Fresenius (Neovii Biotech, Munich, Germany), 30 mg/kg. Cyclosporin A (CsA) and a short course of methotrexate were used for prophylaxis of GVHD. All patients received stem cell grafts collected from peripheral blood, with a median CD34<sup>+</sup> cell dose of 8.56 × 10<sup>6</sup>/kg (range 4.9–9.6 × 10<sup>6</sup>/kg).

## RESULTS

Neutrophil engraftment was achieved on day 18 (range 17–21 days). The patients were discharged at 17, 18 and 23 days post-transplant. Full donor chimerism could be detected in all patients at 8 weeks post-transplant.

All patients experienced acute GVHD of grades I–II. The involved organs were skin in 2 patients (cases 2 and 3) and gut in one patient (case 1). All patients were treated with methylprednisolone (MP) with initial doses of 5–10 mg/kg daily. In addition, case 2 received mycophenolate mofetil and 6 extracorporeal photopheresis treatments. Acute GVHD resolved in all patients completely. Cytomegalovirus viraemia was detected in all patients and polyoma virus cystitis in 1 patient (case 3).

The median follow-up time is 16 months (range 10–25 months) at time of writing. The SS patient (case 2) was clinically and radiologically assessed as in complete remission at 14 months post-transplant (Fig. 1 a, b). The patient with PTCL (case 1) relapsed 6 months after allo-SCT. His immunosuppressive treatment with CsA

Table I. Demographic data and previous treatments

Pat. No/Sex	Diagnosis	Age at		Previous therapies	Follow-up	Outcome
		allo-SCT	allo-SCT			
1/M	PTCL	55		PUVA, narrowband ultraviolet B, cyclosporine, alemtuzumab, CHOP, BEAM, bendamustine	25	Deceased
2/M	SS	44		Narrowband ultraviolet B, PUVA, acitretin, CHOP, doxorubicin, interferon, ECP, bexarotene	14	Alive, remission
3/F	fMF	46		Acitretin, narrowband ultraviolet B, bexarotene, interferon, PUVA, doxorubicin, gemcitabine, CHOP, total skin electron beam	10	Alive, remission (graft-versus-host)

PCTCL: peripheral T-cell lymphoma; SS: Sézary syndrome; fMF: follicular mycosis fungoides; allo-SCT: allogeneic haematopoietic stem cell transplantation; PUVA: psoralen+ultraviolet A; CHOP: cyclophosphamide, doxorubicin, vincristine; BEAM: carmustine, etoposide, melphalan; ECP: extracorporeal photopheresis.



Fig. 1. Patient with Sézary syndrome (case 2) (a) before and (b) one month after allogeneic haematopoietic stem cell transplantation (allo-SCT). Patient with folliculotropic mycosis fungoides (case 3) with (c) tumorous infiltrates and (d) chronic graft-versus-host disease (GVHD) (6 months after allo-SCT).

was tapered down, leading to the appearance of chronic GVHD of the skin 2 weeks later. The GVHD resolved with the start of MP treatment, 0.5 mg/kg daily, and the tumorous skin infiltrations also resolved. However, lymphoma relapsed in skin and lymph nodes, leading to the death of the patient 25 months after allo-SCT.

The MF of case 3 relapsed as a plaque on the forehead without folliculotropic features 9 weeks after the transplant. CsA treatment was stopped and the dose of MP was reduced to enhance the graft-versus-lymphoma effect. Because of tumorous skin infiltrations treatment with brentuximab vedotin was started at 4 months post-transplant. After the first course of treatment all tumorous skin infiltrates resolved, and after 5 treatments with brentuximab vedotin, only signs of chronic GVHD of the skin were seen (Fig. 1c, d). The patient is still on low-dose MP, 8 mg daily, and has returned to work.

## DISCUSSION

For patients with advanced-stage CTCL, several consecutive systemic therapies are often used. These treatments can result in a high overall response, but the duration of the response is short. Stem cell transplantation is an option to cope with this challenge. With the advent of reduced intensity conditioning, allo-SCT treatment of heavily pre-treated, but otherwise fit, lymphoma patients has become possible. Until recently, only case reports of CTCL patients treated with allo-SCT have been published. Very recently, 5 studies with 129, 60, 47, 37 and 9 patients with CTCL treated with allo-SCT were published (4–6, 8, 9). In the largest study, approximately one-third of patients were alive 5 years post-transplantation and, of those, half remained disease-free.

Indeed, according to our experience, allo-SCT can be considered as an option for the treatment of young CTCL patients with relapsing disease progressing through several lines of chemotherapy. However, achievement of complete remission or very good partial remission prior to the allo-SCT is critical. A persistent graft-versus-lymphoma effect

could be beneficial in controlling the disease, as was the case in one of our patients.

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