Original Study

# Alemtuzumab-Based Reduced-Intensity Conditioning Allogeneic Transplantation for Myeloma and Plasma Cell Leukemia – A Single-Institution Experience

Karthik Ramasamy,[1,2] Shameem Mahmood,[1] ZiYi Lim,[1,2] Sophie Corderoy,[1] Stephen Devereux,[1,2] Ghulam J. Mufti,[1,2] Antonio Pagliuca,[1,2] Stephen Schey[1,2]

## Abstract

**Background:** Reduced-intensity conditioning allogeneic transplantation for myeloma is associated with lower non-relapse mortality and higher relapse rates in comparison with myeloablative conditioning transplants. **Patients and Methods:** We have retrospectively audited 19 patients with myeloma or primary plasma cell leukemia who received allogeneic transplantation with a uniform alemtuzumab-based reduced-intensity conditioning protocol. These patients had not been treated with bortezomib or lenalidomide before transplantation. **Results:** The treatment-related mortality at 1 year was (4/19) 21% with low incidence of graft-versus-host disease (6%) and 2-year progression-free survival and overall survival rates of 35% and 42%, respectively. **Conclusion:** Progression-free survival in this cohort of patients is comparable to previously published data of reduced-intensity conditioning allogeneic transplantation in myeloma. However, there is no plateau observed on the survival curves with a significant transplant-related mortality of 21%. Therefore, alemtuzumab-based allogeneic transplantation cannot be recommended as standard practice outside of clinical trials for treatment of myeloma.

*Clinical Lymphoma, Myeloma & Leukemia,* Vol. 11, No. 2, 242-5 
**Keywords:** Myeloma, Alemtuzumab, Reduced-intensity conditioning, Allogeneic transplantation, Donor lymphocyte infusion, Primary plasma cell leukemia

## Introduction

Myeloablative conditioning regimens are associated with a high transplant-related mortality (TRM) in myeloma patients with less than half of the treated patients achieving long-term disease-free survival.[1] Reduced-intensity conditioning (RIC) regimens are associated with a lower TRM and have facilitated the expansion of allogeneic hematopoietic stem cell transplantation (HSCT) for myeloma. In vivo T-cell depletion (antithymocyte globulin or alemtuzumab) has been used to further reduce the incidence of graft-versus-host disease (GVHD), although this approach may be offset by a higher rate of disease progression.[2] In view of these concerns, we report herein a retrospective audit of 19 patients treated with alemtuzumab-based uniform RIC allogeneic stem cell transplantation (SCT) for myeloma or primary plasma cell leukemia.

[1]Kings College Hospital NHS Foundation Trust, London, England
[2]Kings College, London, England

Submitted: Jul 27, 2010; Revised: Oct 25, 2010; Accepted: Nov 3, 2010

Address for correspondence: Karthik Ramasamy, MD, Kings College Hospital NHS Foundation Trust & Kings College London, Haematological Medicine, Denmark Hill, Camberwell, London SE5 9RS, UK
Fax: 20-329-93-514; e-mail contact: karthik.ramasamy@kcl.ac.uk

## Patients and Methods

Nineteen consecutive patients with myeloma or primary plasma cell leukemia were transplanted using an RIC conditioning protocol at Kings College Hospital from 1999 to 2009. Patients were offered an allogeneic transplant for one of the following reasons: primary plasma cell leukemia (PCL), relapsed disease, younger than 60 years old with fully matched sibling donor, failed stem cell mobilization and therefore cannot be consolidated, or high-risk cytogenetics.[3] Patients received 100 mg of alemtuzumab intravenously (IV) in divided doses over 5 days (day -8 to day -4) along with fludarabine 150 mg/m$^2$ (IV) in divided doses over 5 days (day -7 to day -3) and melphalan 140 mg/m$^2$ (IV) on day -2 as pretransplant conditioning with GVHD prophylaxis using cyclosporin A. Sequential chimerism was performed posttransplant as described previously.[4] Patient characteristics are summarized in Table 1. There were 9 females and 10


2152-2650/$ - see frontmatter 
doi: 10.1016/j.clml.2011.03.004

**Table 1 Patient Characteristics and Transplant Outcomes**

| Patient | Age at Transplant | Isotype | SD Stage | Metaphase Cytogenetics | Lines of Therapy Including Auto | Donor | Status Pre-Allo | GVHD | Response Post-Allo |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 50 | IgG | II | N/A | 1 | MRD | PR | No | PR |
| **2** | 54 | PCL | II | Failed | 3 | MUD | PR | No | CR |
| **3** | 45 | IgG | II | N/A | 2 | MRD | PR | No | PR |
| **4** | 53 | PCL | II | Failed | 2 | MRD | PR | No | CR |
| **5** | 44 | IgG | II | Normal | 4* | MRD | SD | No | PR |
| **6** | 62 | PCL | II | N/A | 2 | MRD | CR | Yes | CR |
| **7** | 56 | IgG | II | Inv 9 | 2 | MRD | VGPR | No | VGPR |
| **8** | 59 | IgA | III | Del 13 | 4 | MUD | PD | No | PR |
| **9** | 50 | κ LC | II | Normal | 2* | MRD | CR | No | CR |
| **10** | 40 | IgG | II | N/A | 4 | MUD | VGPR | No | VGPR |
| **11** | 59 | IgA | III | Normal | 3 | MRD | CR | No | CR |
| **12** | 59 | IgA | II | Normal | 2* | MRD | CR | No | CR |
| **13** | 60 | Non secretory | II | Normal | 2 | MRD | CR | No | CR |
| **14** | 52 | IgG Λ + amyloidosis | III | N/A | 2 | MRD | PD | No | SD |
| **15** | 59 | IgG κ | II | Del 13 | 2 | MRD | CR | No | CR |
| **16** | 57 | IgA κ | II | Normal | 2* | MRD | VGPR | Yes | VGPR |
| **17** | 59 | IgG κ | II | N/A | 2* | MRD | VGPR | No | CR |
| **18** | 41 | PCL | III | Normal | 2* | MRD | CR | No | CR |
| **19** | 36 | IgG κ | III | Normal | 3* | MRD | CR | No | CR |

* Auto/Allo.
Abbreviations: Allo = allogeneic transplantation; CR = complete remission; Del 13 = deletion chromosome 13; GVHD = graft-versus-host disease; Ig = immunoglobulin; Inv 9 = inversion chromosome 9; MRD = matched related donor; MUD = matched unrelated donor; N/A = not available; PCL = plasma cell leukemia; PR = partial response; SD = stable disease; VGPR = very good partial response.

males with a median age at transplantation of 53 years (range, 40 to 62 years). Four patients had PCL and 15 patients had myeloma. Disease stage at the time of transplant and response following transplantation is summarized in Table 1. The median lines of previous therapy were 2 (range, 1-4). Although some patients received thalidomide-based therapy at induction or salvage, these patients were not exposed to lenalidomide or bortezomib. Fifteen patients (79%) had a previous autograft, which was part of a planned tandem autograft/allograft procedure in 7 patients. Autograft was performed as a consolidation strategy after first induction in 5 patients, and the remaining 3 patients had autograft at relapse.

Sixteen patients were transplanted with matched related donors (10 of 10 loci) and 3 with a matched unrelated donor (10 of 10 loci). Human leukocyte antigen (HLA) matching was performed by serology and polymerase chain reaction – sequence specific oligonucleotide methods. Donor gender was male in 10 transplants and female in the remaining 9 patients; with a median age of 42 years (range, 30 to 67years). All patients received peripheral blood progenitor stem cells, with a median cell dose of $4.0 \times 10^6$ CD34/kg (range, 1.8 to 12.3 CD34/kg).

Escalating doses of pre-emptive donor lymphocyte infusion (pDLI) were administered after day 100 in patients with declining donor T-cell chimerism (<50%) without GVHD or disease progression. All patients were off immunosuppression by day +100 in the absence of GVHD. Patients who had morphologic relapse posttransplant were salvaged with combination therapy. Disease response was assessed by international uniform response criteria.[5] TRM was defined as death unrelated to refractory or progressive disease. Overall survival (OS) was measured from day 0 to death from any cause or last follow-up; progression-free survival (PFS) was measured from day 0 to the first indicator of relapse, death of any cause, or last follow-up. Survival curves were estimated using Kaplan-Meier methodology, and a log-rank test was used to assess differences between groups. Univariate analysis was performed on the following variables: recipient age, presence of GVHD, disease status at transplant, disease response posttransplant, and median lines of previous therapy.

## Results

The median follow-up period of all patients was 24 months (rang,: 4 to 105 months). One patient with progressive disease had primary graft failure at day 100. TRM for this small cohort of patients at 2 years was 21% (4/19). One patient died of respiratory failure and cytomegalovirus viral reactivation 4 months posttransplant. One patient developed unexplained liver failure and subsequent respiratory failure 11 months after transplant. One patient succumbed to thrombotic thrombocytopenic purpura 12 months posttransplant complicated by a probable fungal pneumonia. One patient was admitted to his local hospital and died of respiratory failure; cause of