Hematopoietic Cell Transplantation for Primary Plasma Cell Leukemia: Results from the Center for International Blood and Marrow Transplant Research

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Abstract

There is limited data on hematopoietic cell transplantation (HCT) in primary plasma cell leukemia (pPCL), an aggressive plasma cell disorder. We report outcomes of 147 patients with pPCL receiving autologous (n=97) or allogeneic (n=50) HCT within 18 months after diagnosis between 1995 and 2006. Median age was 56 years and 48 years for autologous HCT and allogeneic HCT respectively. Progression-free survival (PFS) at 3 years was 34% (95% CI, 23%-46%) in the autologous group and 20% (95% CI, 10%-34%) in the allogeneic group. Cumulative incidence of relapse at 3 years was 61% (95% CI, 48%-72%) in the autologous group and 38% (95% CI, 25%-53%) in the allogeneic group. Overall survival (OS) at 3 years was 64% (95% CI, 52%-75%) in the autologous group and 39% (95% CI, 26%-54%) in the allogeneic group. Non-relapse mortality (NRM) at 3 years was 5% (95% CI, 1-11%) in the autologous group and 41% (95% CI, 28%-56%) in the allogeneic group. The encouraging OS after autologous HCT, establishes the safety and feasibility of this consolidative treatment option after initial induction therapy for pPCL. Allogeneic HCT, although associated with a significantly lower relapse rate, carries a much higher risk of NRM and no overall survival benefit.

Keywords

primary plasma cell leukemia; stem cell transplant; overall survival

Introduction

Plasma cell Leukemia (PCL) is an aggressive plasma cell neoplasm characterized by circulating plasma cells in the peripheral blood, defined as either an absolute (>2×10^9/L) or relative (>20% of blood leukocytes) plasmacytosis (1). It is a rare disorder, accounting for about 1% of all plasma cell disorders. It may present de novo (primary PCL) or may evolve during the course of multiple myeloma (secondary PCL). Primary and secondary PCL are reported to have a poor prognosis with reported survival of 2-11 months (2-5). While both entities share biologic and clinical similarities as aggressive variants of MM, secondary PCL represents a fulminant plasma cell neoplasm with historic survival of only 1-2 months (6). In contrast, pPCL while aggressive, often responds to induction treatment occasionally resulting in durable responses. We restricted our analysis to patients with pPCL.

Although it has been reported that conventional therapies for MM are useful in primary plasma cell leukemia (pPCL)(2), the use of melphalan/prednisone or vincristine/adriamycin/dexamethasone (VAD) chemotherapy offers only a limited benefit in terms of survival. Some authors have reported that intermediate doses of melphalan could improve survival (7). The poor prognosis is likely due the biologically aggressive nature of the disease. Deletions or mutations of p53 that are known to confer adverse prognosis are reported in...
about 10% of patients with MM compared with 56% of patients with pPCL and 83% of patients with secondary PCL (4, 6).

Given the poor prognosis of patients with pPCL, both autologous and allogeneic HCT have been offered to these patients as consolidation to induction therapy similar to the concept of upfront HCT in MM. However, the efficacy of this approach in pPCL is uncertain due to the small number of patients that have been reported in the literature. Given the low incidence of pPCL and the absence of prospective studies with HCT for pPCL, analysis of cumulative registry data remains the best available way to study the safety and efficacy of HCT in this disease.

We present a retrospective analysis of outcomes after upfront autologous or allogeneic HCT for pPCL reported to the Center for International Blood and Marrow Transplant Research (CIBMTR).

**Patients and Methods**

**Data Sources**

The CIBMTR is a research affiliate of the International Bone Marrow Transplant Registry (IBMTR), Autologous Blood and Marrow Transplant Registry (ABMTR), and the National Marrow Donor Program (NMDP) comprising a voluntary working group of more than 450 transplantation centers worldwide. Participating centers are required to report all transplants consecutively. Patients are followed longitudinally, with yearly follow ups. Participating centers are required to report all transplants consecutively; compliance is monitored by on-site audits. Computerized checks for discrepancies, physicians' review of submitted data and on-site audits of participating centers ensure data quality. Observational studies are done with a waiver of informed consent and in compliance with HIPAA regulations, as determined by the Institutional Review Board of the Medical College of Wisconsin.

**Patients**

Between 1995 and 2006, 147 patients with pPCL who received autologous (n=97) or allogeneic (n=50) HCT were reported to the CIBMTR. All patients met criteria for PCL at initial diagnosis and were reconfirmed by review. The analysis was restricted to those receiving upfront HCT defined as HCT within 18 months of diagnosis.

**Definition of Response and Endpoints**

Responses were defined according to the International Myeloma Working Group (IMWG) criteria for myeloma (1). Notably, the IMWG criteria are formulated for patients with MM and specific response criteria for PCL have not been defined. Primary outcomes studied included non-relapse mortality (NRM), relapse, progression-free survival (PFS) and overall survival (OS). NRM was defined as death from any cause within the first 28 days after transplantation or death thereafter in the absence of relapse or progression. Survival (OS) was defined as the time from transplantation to death from any cause. PFS was defined as time from transplantation to relapse, progressive disease, or death from any cause. Other outcomes examined were the incidence and severity of acute and chronic graft-versus-host
disease (GVHD) after allogeneic HCT and the causes of death (COD). Acute GVHD (aGVHD) was defined and graded using established criteria(8). Chronic GVHD (cGVHD) was determined by clinical criteria in allogeneic recipients surviving more than 90 days (9).

**Statistical Analysis**

Probabilities of OS and PFS were calculated using the Kaplan-Meier product limit estimate. Cumulative incidence of NRM and relapse/progression were calculated using cumulative incidence curves to accommodate competing risks. Associations between patient-, disease-, and transplant-related factors and survival were assessed using multivariate Cox proportional hazards regression in the autologous cohort. The variables considered in the multivariate analysis were: age at transplant (continuous), Karnofsky performance status at transplant (≤80% vs. >80%), Durie-Salmon stage at diagnosis (I vs. II vs. III), immunochemical subtype, disease status at transplant, number of lines of chemotherapy pre-transplant (1 vs. >1), thalidomide or bortezomib as part of therapy (No vs. Yes), time from diagnosis to transplant (<6 vs. 6-12 vs. 12-18 months) and planned upfront transplant (No vs. Yes). Forward stepwise variable selection at a 0.05 significance level was used to identify covariates associated with the main outcome. In the model, the assumption of proportional hazards was tested for each variable using a time-dependent covariate and graphical methods. All variables considered in the multivariate analysis satisfied the proportionality assumption. All computations were made using the statistical package SAS version 9.

**Results**

**Autologous HCT cohort**

Ninety seven patients received an autologous HCT (Table 1). Median follow up of recipients was 38 months. The median age was 56 years (range, 32-74 years). The median time from diagnosis to autologous HCT was 7 months (range 3-18 months). Sixty eight of the ninety seven patients received a single autologous HCT and twenty five patients received a tandem autologous HCT.

Disease status at transplant in the autologous HCT group: 20% were in complete remission, 56% in partial remission and 1% had relapsed/progressive disease. Sixty four of the 97 pts (66%) are alive. Progressive disease accounted for 85% of the deaths (Table 2). At 3 years, PFS was 34% (95% CI, 23%-46%) (Figure 1a) and OS was 64% (95% CI, 52%-75%) (Figure 1b). NRM at 3 years was 5% (95% CI, 1%-11%) (Figure 1c) and the incidence of relapse/progression 61% (95% CI, 48%-72%) (Figure 1d). None of the variables tested in the multivariate analysis were significantly associated with survival. PFS at 3 years was 36% (95% CI, 23%-50%) for the single autologous HCT group and 37% (95% CI, 13%-65%) for the tandem autologous HCT group. OS at 3 years was 56% (95% CI, 42%-70%) for the single autologous HCT group and 84% (95% CI, 64%-97%) for the tandem autologous HCT group with a trend towards superior survival in the tandem cohort. There was no difference in survival between patients receiving autologous HCT within 6 months of diagnosis (N=29) compared with those transplanted greater than 6 months after
diagnosis (N=68). Overall outcomes were similar after HCT for those transplanted after 2000 (Table 3).

**Allogeneic HCT Cohort**

Fifty patients received an allogeneic HCT. Thirty four patients (68%) received myeloablative conditioning regimens and sixteen patients (32%) received non-myeloablative/reduced-intensity (NMA/RIC) conditioning. Recipients of allogeneic transplants were younger with a median age of 48 years (range, 24-62 years) and the median time from diagnosis to transplant was 6 months (range 2-16 months). Disease status at transplant included 18% in complete remission, 46% in partial remission and 8% with relapsed/progressive disease. Incidence of acute GVHD (Grade II-IV) was 28% (95% CI, 17%-41%) while chronic GVHD at 3 years was 26% (95% CI, 14%-41%) [18% with extensive, 8% with limited cGVHD]. At a median follow-up of 52 months, 11 of the 34 patients (32%) are alive in the myeloablative HCT group and 8 of the 16 patients (50%) are alive in the NMA/RIC group. Progressive/relapsed disease accounted for 22% of the deaths in the allogeneic recipients (Table 2). At 3 years, PFS was 21% (95% CI, 8%-37%) in the myeloablative group and 18% (95% CI, 2%-44%) in the nonmyeloablative group; OS was 32% (95% CI, 17%-50%) in the myeloablative group and 56% (95% CI, 31%-79%) in the NMA/RIC group. Non-relapse mortality and relapse were similar in the myeloablative and NMA/RIC cohorts. NRM at 3 years was 41% (95% CI, 25%-58%) and relapse/progression was 38% (95% CI, 22%-56%) in the myeloablative group. In the NMA/RIC cohort, NRM at 3 years was 42% (95% CI, 19%-68%) and the incidence of relapse/progression was 39% (95% CI, 15%-66%). In the allogeneic HCT group, OS was not different between those transplanted within 6 months of diagnosis (N = 20) vs. those transplanted beyond 6 months (N=29). However in the early allogeneic HCT cohort, relapse risk was lower (3 year incidence of relapse 22% (7- 44) vs. 50% (31-69), p = 0.04) and PFS was superior (3 year PFS; 36% (95% CI 16-59) vs. 8% (95% CI 1-23), p = 0.02). For patients receiving allogeneic HCT after 2000, long term outcomes were inferior compared with MM patients receiving allografts in a similar time period (Table 4).

Cytogenetic information was available in 68 patients of whom 18 had abnormal cytogenetics at diagnosis. The most common abnormalities among those with abnormal cytogenetics were hypodiploidy (50%) and abnormalities of chromosome 13 (33%). Among the 10 autologous HCT recipients with abnormal cytogenetics, hypodiploidy was seen in 4 patients, hyperdiploidy in 2 patients, abnormalities of chromosome 13q in 2 patients, abnormalities of chromosome 1 in 2 patients and t(11;14) in 2 patients. Among the 8 allogeneic HCT recipients with abnormal cytogenetics, hypodiploidy was seen in 5 patients, hyperdiploidy in 1 patients, abnormalities of chromosome 13q in 4 patients, abnormalities of chromosome 1 in 2 patients and t(11;14) in 2 patients.

The use of novel anti-myeloma agents was relatively rare during this time period. Twenty-five percent of the patients receiving autologous HCT, 25% of the patients non myeloablative HCT recipients and 6% of those receiving myeloablative HCT received thalidomide as part of their induction regimen. Bortezomib was rarer and used pre-transplant in 5% of the autologous cohort, 6% of the myeloablative cohort and none of the NMA/RIC
group. None of the patients were reported to have received lenalidomide as part of the induction regimen.

A comparison of the outcomes of pPCL patients with an unselected cohort of patients with multiple myeloma who underwent autologous or allogeneic HCT after 2000 (chosen to reflect novel therapy) is presented in Tables 3 and 4.

**Discussion**

Plasma cell leukemia is a rare malignancy with an aggressive clinical course and grave prognosis. Limited data on therapeutic outcomes and the absence of randomized data makes treatment decisions difficult in this disorder. This study of 147 patients is among the largest series of patients with pPCL and defines the outcomes after HCT in this disease.

In a recent study, 291 patients with PCL were identified in the Surveillance, Epidemiology, and End Results (SEER) database from 1973-2004 (10). The study did not distinguish between primary and secondary PCL. The median OS was 4 months and the median disease-specific survival was 6 months for patients with PCL; the 1-year, 2-year, and 5-year OS rates were 27.8%, 14.1%, and 6.4%, respectively. The median age was 67 years (range, 19-98 years) which is older than the median age of patients in our series. There is an inherent selection bias in a retrospective transplant series such as ours reflecting selection of patients who are younger, with better performance status and those surviving induction therapy, clinically improving on initial induction treatment and thus able to proceed to HCT.

In view of the aggressive course of plasma cell leukemia, the need for treatment with a relatively early and sustained response is desirable. The use of high dose melphalan in multiple myeloma was followed soon after with its use in plasma cell leukemia (11). Allogeneic HCT has also been explored in this disease given the potential of a graft versus tumor effect. However, there is paucity of data reflecting the benefit of either approach in this disease (12). Even with the caveat of patient selection bias, our data represent the highest quality evidence available regarding the role of HCT in pPCL. These data indicate that there is a significant subset patients for whom autologous HCT results in significant disease control and survival.

An analysis of the European Group for Blood and Marrow Transplantation (EBMT) reported outcomes after autologous HCT for patients with pPCL (13). The EBMT study included patients reported to the registry with limited report forms regardless of complete data from 1980 onwards and excluded those receiving allogeneic HCT. In contrast to our results, the EBMT study demonstrated inferior post HCT survival in pPCL compared with MM. The limited data and the differing years of HCT for the EBMT cohort make direct comparisons difficult. Our analysis was restricted to those receiving HCT after 1995 (with >60% transplanted after 2000) and HCT early in the disease course making it more applicable to current practices. This may account for the relatively superior results for this cohort compared to the EBMT data.

In our analysis, for those patients with pPCL able to receive a consolidative autologous HCT within 18 mo of diagnosis, the PFS and OS were broadly similar to a cohort of MM patients.
receiving autologous HCT during the same time frame. However, during the same time period, 8% of patients with MM reported to the CIBMTR underwent an allogeneic HCT compared with 32% patients in our series with pPCL. This likely reflects a practice bias favoring the use of allogeneic HCT in pPCL based on its predicted aggressive biologic behavior. The median time from diagnosis to transplant was similar in the autologous and allogeneic HCT group. Our data indicates that although relapse rates are lower, allogeneic HCT carries a much higher risk of NRM and lower OS and PFS. The advent of NMA/RIC has not significantly changed overall outcomes compared with myeloablative conditioning in our cohort of allogeneic HCT recipients.

Despite a significant number of patients in our series undergoing HCT after 2000, few patients received novel agents (thalidomide, lenalidomide or bortezomib) as part of their induction regimen. Introduction of novel agents have been associated with an improvement in outcomes in multiple myeloma and in case reports of patients with PCL (14-17). Emerging data in MM indicates improved PFS in patients who receive maintenance treatment post autologous HCT (18). It is unclear from our database if patients received planned maintenance treatment and if so the nature of the treatment. Median PFS and OS was similar in the patients who underwent autologous HCT prior to and after 2000.

One possible explanation for the poor outcome of patients with PCL is that many harbor multiple cytogenetic abnormalities that are known to be associated with rapidly progressive disease or high risk multiple myeloma. In one retrospective study, patients with PCL were noted to have deletion of chromosome 13 by FISH in 67 to 85 percent, t(4;14) in 16 percent, t(14;16) in 16 percent and del 17q13 in 50 to 75 percent (3, 4). In our series, data on cytogenetics when available reflected known patterns.

This study is among the largest published experience on HCT for pPCL and confirms that autologous HCT is a safe and reasonable consolidative treatment option. Notably, the vast majority of patients (75%) were in complete or partial remission despite the majority not receiving novel agent induction. It is likely that autologous HCT was offered to patients with chemotherapy sensitive disease thus explaining the excellent outcomes after HCT in this report. Compared to MM, allogeneic HCT seems to be offered at a higher rate in clinical practice but was associated with a higher NRM and inferior outcomes compared with MM patients receiving allografts. In the absence of a defined standard of care, these data indicating similar outcomes and safety for HCT in pPCL sensitive to induction therapy, it is reasonable to consider transplant options similar to high risk MM for this disease. Those with excellent responses to induction therapy may represent a subgroup likely to benefit from autologous HCT.

Progress in the study of a rare disease like pPCL will be facilitated by collaborations between centers with consensus protocols that incorporate appropriate randomization strategies and correlative studies to better understand the biology of the disease. Clinical trials aimed at reducing relapse after autologous HCT, by incorporating the newer agents as part of induction and as maintenance therapy are needed. Ongoing efforts to reduce NRM after allogeneic HCT may result in improved outcomes with this modality in the future.
Acknowledgments

The CIBMTR is supported by Public Health Service Grant/Cooperative Agreement U24-CA76518 from the National Cancer Institute (NCI), the National Heart, Lung and Blood Institute (NHLBI) and the National Institute of Allergy and Infectious Diseases (NIAID); a Grant/Cooperative Agreement SU01HL069294 from NHLBI and NCI; a contract HHSH234200637015C with Health Resources and Services Administration (HRSA/DHHS); two Grants N00014-06-1-0704 and N00014-08-1-0058 from the Office of Naval Research; and grants from AABB; Allos, Inc.; Amgen, Inc.; Anonymous donation to the Medical College of Wisconsin; Astellas Pharma US, Inc.; Be the Match Foundation; BioGen IDEC; BioMarin Pharmaceutical, Inc.; Biovitrum AB; BloodCenter of Wisconsin; Blue Cross and Blue Shield Association; Bone Marrow Foundation; Buchanan Family Foundation; CaridianBCT; Celgene Corporation; CellGenix, GmbH; Children's Leukemia Research Association; ClinImmune Labs; CTT Clinical Trial and Consulting Services; Eisai, Inc.; Genentech, Inc.; Genzyme Corporation; Histogenetics, Inc.; HKS Medical Information Systems; Hospira, Inc.; Kirin Brewery Co., Ltd.; The Leukemia & Lymphoma Society; Merck & Company; The Medical College of Wisconsin; Millennium Pharmaceuticals, Inc.; Miller Pharmacal Group; Milliman USA, Inc.; Miltienyi Biotec, Inc.; National Marrow Donor Program; Nature Publishing Group; Novartis Oncology; Oncology Nursing Society; Osiris Therapeutics, Inc.; Otsuka America Pharmaceutical, Inc.; Pall Life Sciences; Pfizer Inc.; Schering Corporation; Sigma-Tau Pharmaceuticals; Soligenix, Inc.; StemCyte, Inc.; StemSoft Software, Inc.; Sysmex America, Inc.; THERAKOS, Inc.; Vidacare Corporation; ViraCor Laboratories; ViroPharma, Inc.; and Wellpoint, Inc. The views expressed in this article do not reflect the official policy or position of the National Institute of Health, the Department of the Navy, the Department of Defense, or any other agency of the U.S. Government.

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FIGURE 1.
1a. Probability of Progression-free survival after HCT – by transplant type
1b. Probability of Overall Survival after HCT – by transplant type
1c. Cumulative Incidence of Non-relapse Mortality after HCT – by transplant type
1d. Cumulative Incidence of Relapse after HCT – by transplant type
FIGURE 2.
2a. Probability of Progression-free Survival after Auto-HCT, pPCL versus MM
2b. Probability of Progression-free Survival after Allo-HCT, pPCL versus MM
### Table 1
Baseline Characteristics of patients

| Characteristics of patients: | Allogeneic myeloablative N(%) | Allogeneic NMA/RIC N(%) | Autologous N(%) |
|------------------------------|-------------------------------|------------------------|-----------------|
| Number of patients           | 34                            | 16                     | 97              |
| Number of centers            | 24                            | 12                     | 53              |
| Age, median (range), years   | 47 (27-60)                    | 49 (24-62)             | 56 (32-74)      |
| Age at transplant, years     |                               |                        |                 |
| 20-29                        | 1 (3)                         | 1 (6)                  | 0               |
| 30-39                        | 7 (21)                        | 0                      | 8 (8)           |
| 40-49                        | 16 (47)                       | 8 (50)                 | 17 (18)         |
| 50-59                        | 9 (26)                        | 5 (31)                 | 41 (42)         |
| 60-69                        | 1 (3)                         | 2 (13)                 | 28 (29)         |
| >=70                         | 0                             | 0                      | 3 (3)           |
| Male Sex                     | 18 (53)                       | 5 (31)                 | 62 (64)         |
| Karnofsky score>=90%         | 18 (53)                       | 8 (50)                 | 57 (59)         |
| Non Caucasian                | 8 (24)                        | 4 (25)                 | 27 (28)         |
| Immunochemical subtype       |                               |                        |                 |
| IgG                          | 13 (38)                       | 7 (44)                 | 54 (56)         |
| IgA                          | 5 (15)                        | 0                      | 13 (13)         |
| Light chain                  | 8 (24)                        | 6 (38)                 | 16 (16)         |
| Non-secretory/others         | 8 (24)                        | 3 (19)                 | 14 (14)         |
| Albumin<=3.5 at diagnosis, g/dL | 9 (26)                       | 4 (25)                 | 36 (37)         |
| Hemoglobin <10 at diagnosis, mg/dL | 20 (59)                     | 9 (56)                 | 39 (40)         |
| Disease status prior to transplant |                           |                        |                 |
| Complete remission           | 6 (18)                        | 3 (19)                 | 19 (20)         |
| Partial remission            | 16 (47)                       | 7 (44)                 | 54 (56)         |
| Minimal response/Stable disease | 3 (9)                      | 4 (25)                 | 14 (14)         |
| Relapse/Progression          | 3 (9)                         | 1 (6)                  | 1 (1)           |
| Missing                      | 6 (18)                        | 1 (6)                  | 9 (9)           |
| Lines of chemotherapy pretransplant |                     |                        |                 |
| 1                            | 19 (56)                       | 7 (44)                 | 57 (59)         |
| 2                            | 10 (29)                       | 3 (19)                 | 21 (22)         |
| >2                           | 4 (12)                        | 3 (19)                 | 12 (12)         |
| Induction therapy            |                               |                        |                 |
| Melphalan-Prednisone ± others | 4 (12)                       | 3 (19)                 | 2 (2)           |
| VAD                          | 13 (38)                       | 4 (25)                 | 45 (46)         |
| Cyclophosphamide ± others    | 6 (18)                        | 1 (6)                  | 32 (33)         |
| Corticosteroids±others       | 8 (24)                        | 2 (13)                 | 9 (9)           |
| Others                       | 3 (9)                         | 6 (38)                 | 9 (9)           |
| Thalidomide given as part of lines of therapy |                     |                        |                 |
| Yes                          | 2 (6)                         | 4 (25)                 | 24 (25)         |
| Bortezomib given as part of lines of therapy |                 |                        |                 |
### Characteristics of patients:

|                          | Allogeneic myeloablative N(%) | Allogeneic NMA/RIC N(%) | Autologous N(%) |
|--------------------------|-------------------------------|-------------------------|-----------------|
| Yes                      | 2 (6)                         | 0                       | 5 (5)           |
| Conditioning regimen     |                               |                         |                 |
| Melphalan alone          | 6 (18)                        | 4 (25)                  | 54 (56)         |
| Melphalan+TBI+others     | 4 (12)                        | 0                       | 11 (11)         |
| Melphalan based no TBI   | 6 (18)                        | 5 (31)                  | 23 (24)         |
| TBI based- No melphalan  | 11 (32)                       | 3 (19)                  | 0               |
| Busulfan+cyclophosphamide+others | 6 (18) | 0     | 6 (6)           |
| Others                   | 1 (3)                         | 4 (25)                  | 3 (3)           |
| Time from diagnosis to transplant, median (range) | 6 (2-13) | 7 (3-16) | 7 (3-18) |
| Time from diagnosis to transplant |             |                         |                 |
| < 6 months               | 15 (44)                       | 6 (38)                  | 29 (30)         |
| 6 - 12 months            | 17 (50)                       | 8 (50)                  | 58 (60)         |
| 12 - 18 months           | 2 (6)                         | 2 (13)                  | 10 (10)         |
| Second transplant        |                               |                         |                 |
| Auto+auto                | 0                             | 0                       | 25 (26)         |
| Auto+allo                | 0                             | 0                       | 4 (4)           |
| Type of donor            |                               |                         |                 |
| HLA-identical            | 26 (76)                       | 12 (75)                 | NA              |
| Identical twin           | 1 (3)                         | 0                       |                 |
| Other related            | 2 (6)                         | 2 (13)                  |                 |
| Unrelated                | 5 (15)                        | 2 (13)                  |                 |
| Year of transplant       |                               |                         |                 |
| 1995-1996                | 6 (18)                        | 1 (6)                   | 6 (6)           |
| 1997-1998                | 4 (12)                        | 0                       | 13 (13)         |
| 1999-2000                | 3 (9)                         | 1 (6)                   | 16 (16)         |
| 2001-2002                | 11 (32)                       | 7 (44)                  | 10 (10)         |
| 2003-2004                | 3 (9)                         | 6 (38)                  | 16 (16)         |
| 2005-2006                | 7 (21)                        | 1 (6)                   | 36 (37)         |
| Median follow-up of recipients, months | 52 (3 - 81) | 30 (18 - 59) | 38 (3 - 149) |

* Conditioning regimen:

- **Myeloablative:**
  - CY+TBI (TBI dose >= 500 cGy single dose or TBI dose > 800 cGy fractionated) (n=11)
  - TBI dose >=500 cGy single dose or TBI dose >800 cGy fractionated) (n=4)
  - Busulfan+cyclophosphamide (n=10)
  - Busulfan dose > 9 mg/kg (n=1)
  - Melphalan dose > 150 mg/m² (n=8)

- **Non-myeloablative (NMA):**
  - Fludarabine + cyclophosphamide (n=1)
  - TBI=200 cGy (n=1)
  - Fludarabine+TBI=200cGY (n=2)
Reduced-intensity (RIC):

- Melphalan $\leq 150$ mg/m$^2$ (n=8)
- Busulfan $\leq 9$ mg/kg (n=2)
- Not specified (n=2)
## Table 2

### Causes of death

| Characteristics of patients: | MA N (%) | NMA/RIC N (%) | Autologous N(%) |
|------------------------------|----------|---------------|-----------------|
| Number of patients           | 34       | 16            | 97              |
| Number of deaths             | 23       | 8             | 33              |
| Causes of death              |          |               |                 |
| Infection                    | 4 (17)   | 2 (25)        | 1 (3)           |
| Primary disease              | 10 (43)  | 1 (13)        | 28 (85)         |
| Organ failure                | 3 (13)   | 0             | 1 (3)           |
| Secondary malignancy         | 0        | 0             | 1 (3)           |
| Graft failure                | 1 (4)    | 0             | 0               |
| GVHD                         | 2 (9)    | 0             | 0               |
| Other non relapse            | 3 (13)   | 5 (63)        | 2 (6)           |

MA – myeloablative transplant; NMA – nonmyeloablative transplant; GVHD – graft versus host disease

*Leukemia. Author manuscript; available in PMC 2012 November 01.*
Table 3
Comparison of outcomes after autologous HCT for pPCL between 2000 and 2006 (vs. MM patients during the same time period).

| Outcomes                  | PPCL N=68 | MM N=1380 | P-value |
|---------------------------|-----------|-----------|---------|
| Non-relapse mortality     |           |           |         |
| @ 1 year                  | 1 (0-6)   | 4 (3-6)   | 0.06*   |
| @ 3 years                 | 4 (0-12)  | 7 (5-8)   | 0.443*  |
| @ 5 years                 | 4 (0-12)  | 8 (7-10)  | 0.178*  |
| Relapse/Progression       |           |           |         |
| @ 1 year                  | 29 (18-42)| 28 (25-30)| 0.854*  |
| @ 3 years                 | 64 (48-79)| 59 (57-62)| 0.57*   |
| @ 5 years                 | 77 (60-91)| 74 (71-77)| 0.703*  |
| Progression free survival |           |           |         |
| @ 1 year                  | 70 (57-81)| 68 (65-70)| 0.783*  |
| @ 3 years                 | 32 (18-48)| 34 (31-37)| 0.777*  |
| @ 5 years                 | 19 (6-36) | 17 (15-20)| 0.891*  |
| Overall survival          |           |           |         |
| @ 1 year                  | 86 (76-93)| 89 (87-91)| 0.439*  |
| @ 3 years                 | 68 (52-81)| 67 (64-69)| 0.913*  |
| @ 5 years                 | 51 (32-71)| 49 (46-53)| 0.848*  |

* Pointwise
Table 4
Comparison of outcomes after Allogeneic HCT for pPCL between 2000 and 2006 (vs. MM patients during the same time period).

| Outcomes                  | PPCL N-36 | MM N-580 | P-value |
|---------------------------|-----------|----------|---------|
|                           | 27 (13-43)| 24 (21-28)| 0.773*  |
| Non-relapse mortality     | 44 (27-62)| 29 (25-33)| 0.094*  |
| @ 1 year                  | 52 (35-70)| 29 (26-34)| 0.015*  |
| @ 3 years                 | 44 (27-62)| 29 (25-33)| 0.094*  |
| @ 5 years                 | 52 (35-70)| 29 (26-34)| 0.015*  |
| Relapse/Progression       | 24 (11-40)| 33 (29-36)| 0.291*  |
| @ 1 year                  | 48 (30-65)| 47 (43-52)| 0.948*  |
| @ 3 years                 | 48 (30-65)| 55 (50-61)| 0.413*  |
| @ 5 years                 | 48 (30-65)| 55 (50-61)| 0.413*  |
| Progression free survival | 49 (32-66)| 43 (39-47)| 0.512*  |
| @ 1 year                  | 8 (1-22)  | 24 (20-28)| 0.006*  |
| @ 3 years                 | 8 (1-22)  | 15 (11-20)| <0.001* |
| @ 5 years                 | 8 (1-22)  | 15 (11-20)| <0.001* |
| Overall survival          | 59 (42-75)| 60 (56-64)| 0.922*  |
| @ 1 year                  | 39 (23-56)| 39 (35-44)| 0.988*  |
| @ 3 years                 | 39 (23-56)| 39 (35-44)| 0.988*  |
| @ 5 years                 | 20 (1-53) | 29 (24-34)| 0.517*  |

* Pointwise