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Efficacy and Outcome of Allogeneic Transplantation in IgD and Nonsecretory Myeloma. A Report on Behalf of the Myeloma Subcommittee of the Chronic Malignancies Working Party of the European Group for Blood and Marrow Transplantation

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A B S T R A C T

We have recently reported on the outcome of autologous transplantation in the rare myelomas (IgD, IgE, IgM, and nonsecretory [NS]) but there is no real information on the outcome of these conditions after allogeneic transplantation. We used the European Group for Blood and Marrow Transplantation myeloma database to compare the outcomes after allogeneic transplantation of 1354 common myelomas (IgG, IgA, and light chain myeloma) with the outcome in 26 IgD myelomas and 52 NS myelomas. There was little difference between common and the IgD and NS myeloma patients with respect to prognostic factors although the IgD group had a higher beta 2 microglobulin at diagnosis, shorter time to transplantation, and more T cell depletion. IgD and NS patients had a significantly greater achievement of complete remission at conditioning but this did not translate into equivalent progression-free survival and overall survival for the IgD patients although the NS outcome was very similar to that of common myeloma. The PFS and OS of IgD, common, and NS myelomas appear similar after allogeneic transplantation, despite a tendency for higher early relapse rate in IgD myeloma. Allogeneic transplantation may, therefore, be an option to investigate in prospective observational studies.

INTRODUCTION

There have been a number of recent reports of the outcome of autologous transplantation for the rare myelomas (IgD, IgE, IgM, and nonsecretory myeloma [NS]) [1-4]. In the largest report [1], we have suggested that IgD, IgE, and IgM myelomas have a worse outcome after autologous transplantation than common myelomas (IgG, IgA, and light

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Table 1
Patient Characteristics at Diagnosis, Transplantation Characteristics, and Outcome Data

Characteristic	Common Myelomas (n = 1354)	% Data Available	IgD Myelomas (n = 31)	% Data Available	NS Myelomas (n = 52)	% Data Available
Patient Characteristics	IgG 794 (55%) IgA 275 (19%) BJ 285 (20%)	100	IgD 26 (1.8%)	100	NS 52 (3.6%)	100
Gender						
Male, %	810 (59.8%)	100	544 (71.0%)	100	33 (63.5%)	100
Age at Tx, Yr	47.0	100	44.8*	100	45.7*	100
β_2m						
mg/L	2.8	30.6	6.7†	38.7	2.6	30.8
Stage at diagnosis						
Salmon Durie I	11.3	84.0	3.7	87.1	7.5	76.9
II	19.8		14.8		17.5	
III	69.0		81.5		75.0	
Graft source						
BM, %	45.2	100	51.6	100	34.6	100
PB, %	54.8		48.4		65.4	
Conditioning						
MAC	70.1	100	67.7	100	63.5	100
RIC	29.9		32.3		36.5	
Time to transplantation, mo	11.7	100	10.9	100	11.6	100
T cell depletion						
No	69.1	91	51.9†	91	65.2	88
Yes – in vivo	7.8		25.9		10.9	
Yes – ex vivo	14.3		11.1		21.7	
Yes – both	8.8		11.1		2.2	
Gender mismatch female -> male						
% of all transplantations	24.4	100	29.0	100	23.1%	100
Disease response at conditioning						
CR	16.3	82	28.0‡	78	42.5	77
PR	62.3		52.0		45.0	
No change	16.1		12.0		7.5	
Relapse/progression	5.3		8.0		5.0	
Use of TBI	60.3	98	61.3	100	42.0§	96
Outcome Data						
CR after transplantation at 12 months						
Cumulative incidence	.32	92	.33	100	.34	100
Median OS, mo (95% CI)	30.6 (25.2-36.7)		16.2 (13.9-NA)		45.0 (13.2-NA)	
Survival at 36 months (95% CI)						
Survival	.47 (.44-.50)	442 patients	38 (.24-0.61)	9 patients	54 (.41-.71)	19 patients
Median PFS, mo (95% CI)	13.6 (11.9-15.1)		16.2 (5.6-NA)		14.9 (8.0-41.4)	
PFS at 36 months (95% CI)	.30 (.28-.33)	296 patients	.38 (.24-.61)	9 patients	.34 (.23-.52)	12 patients

Tx indicates treatment; β_2m, beta 2 microglobulin; BM, bone marrow; PB, peripheral blood; PR, partial response; NA, not available.
* $P = .020$.
† $P = .017$.
‡ $P = .001$.
§ $P = .34$.

chain only) in keeping with their responses to conventional chemotherapy (with NS having an outcome similar to the common myelomas), although 2 other reports suggest an outcome similar to the common myelomas for all rare myelomas. As allogeneic transplantation in myeloma is only about 8.6% of all transplantations in the European Group for Blood and Marrow Transplantation (EBMT) registry of 1997 to 2009 and rare myeloma constitutes <6% of all myeloma, there is little information published on the outcome of allogeneic transplantation in rare myeloma. In this study, we used the myeloma database of the EBMT to study the outcome of allogeneic transplantation in IgD and NS myeloma and have compared the result with that of 1354 common myelomas.

MATERIALS AND METHODS

A retrospective study of 1437 patients with multiple myeloma who underwent first allogeneic transplantation from HLA-identical sibling donors between 1985 and 2009 with complete data for age, sex, and type of myeloma was undertaken. Patients with no follow-up, missing type of conditioning regimen, missing male-female match (<1%), and missing or combined source of cells (<2%) were also excluded. One half of the patients underwent transplantation after 1999. The number of patients with each type of myeloma is shown in Table 1. Five IgM patients were identified but not included in the analysis. Patients with IgG, IgA, and Bence Jones (BJ) myeloma were collectively described as common myeloma. Patients with plasma cell leukemia were analyzed in a concurrent analysis. Solitary plasmacytoma and amyloidosis were also excluded. All patients were reported to the EBMT registry using MED A (limited data set) or MED B (for extensive data set) forms. All 1432 allografted patients (IgM excluded) were included in the study regardless of availability of complete MED A or MED B data. The number of patients who could be evaluated for each parameter was noted and the proportions of evaluable patients are included in the results. Factors known to affect transplantation outcomes from previous EBMT studies were also analyzed [5]. Response criteria were those used by the centers that were in current use at the time of reporting. On account of differences in follow-up, the analysis of outcomes is restricted (artificial censoring) to the first 4 years after transplantation, a figure equivalent to the lowest median follow-up for the 3 groups.

Statistical Methods

Overall survival (OS) and *progression-free survival* (PFS) were defined, respectively, as time from transplantation to death and to the first event among relapse, progression, or death; observations were censored at the time of last follow-up in case of no failure. OS and PFS curves were produced using the Kaplan-Meier estimator. PFS curves were compared by the log-rank test, whereas for OS that presented crossing curves, we tested the