Published in final edited form as:
Biol Blood Marrow Transplant. 2013 August ; 19(8): 1227–1232. doi:10.1016/j.bbmt.2013.05.017.

Impact Of t(11;14)(q13;q32) On The Outcome Of Autologous Hematopoietic Cell Transplantation In Multiple Myeloma

Koji Sasaki, MD[1], **Gary Lu, MD**[2], **Rima M. Saliba, PhD**[3], **Qaiser Bashir, MD**[3], **Chitra Hosing, MD**[3], **Uday Popat, MD**[3], **Nina Shah, MD**[3], **Simrit Parmar, MD**[3], **Yvonne Dinh**[3], **Sairah Ahmed, MD**[3], **Elizabeth J. Shpall, MD**[3], **Partow Kebriaei, MD**[3], **Jatin J. Shah, MD**[4], **Robert Z Orlowski, MD, PhD**[4], **Richard Champlin, MD**[3], and **Muzaffar H. Qazilbash, MD**[3]

[1]Department of Medicine, Beth Israel Medical Center, New York, NY

[2]Department of Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, TX

[3]Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX

[4]Department of Lymphoma and Myeloma, The University of Texas MD Anderson Cancer Center, Houston, TX

Abstract

Backgrounds—The t(11;14)(q13;q32) is seen in 15–20% patients with multiple myeloma (MM). In general, it is not associated with worse outcome. We studied the impact of t(11;14)(q13;q32) on the outcome of patients with MM who received high-dose chemotherapy followed by an autologous hematopoietic stem cell transplantation (auto-HCT).

Method—Eligible patients underwent high-dose chemotherapy followed by auto-HCT at the M.D. Anderson Cancer Center between February 2000 and August 2010, and had conventional cytogenetic (CC) or fluorescent *in situ* hybridization (FISH) results available prior to auto-HCT. The cohort is divided into three groups of patients: (1) normal (diploid by CC, and negative by FISH); (2) t(11;14)(q13;q32) by CC or FISH; and (3) high-risk (HR) abnormalities by CC or FISH. The primary objective was to compare the outcome of patients with t(11;14)(q13;q32) to patients with diploid or HR markers by CC or FISH studies.

Results—CC or FISH studies were available for 993 patients in the 3 groups described above. Eight-hundred and sixty-nine patients had normal, 27 patients had t(11;14)(q13;q32) and 97 patients HR markers by CC or FISH studies. Of the 27 patients with t(11;14)(q13;q32), 18 had isolated t(11;14)(q13;q32) while 9 patients had concurrent HR abnormalities. We compared the outcome of patients with t(11;14)(q13;q32) to patients with normal or HR markers. Median follow up in surviving patients was 37 months. 3-year PFS for normal, t(11;14)(q13;q32) and HR groups were 47%, 27% and 13%, respectively (p=<0.00001). 3-year OS for normal, t(11;14)(q13;q32) and HR groups were 83%, 63% and 34%, respectively (p=<0.00001). On multivariate analyses, t(11;14)(q13;q32) and HR abnormalities by CC or FISH, and relapsed disease at auto-HCT were associated with shorter PFS, while t(11;14)(q13;q32) and HR abnormalities by CC or FISH, β_2 microglobulin of >3.5 and relapsed disease at auto-HCT were associated with shorter OS.

Conclusions—Patients with t(11;14)(q13;q32) had worse outcome than patients with normal CC or FISH, but better than patients with HR markers by CC or FISH studies.

Introduction

Multiple myeloma (MM) accounts for approximately one percent of all cancers and approximately 10 percent of hematologic malignancies in the United States [1, 2]. Routine conventional cytogenetic (CC) analyses and interphase fluorescence *in situ* hybridization (FISH) are helpful in stratifying patients with MM into high or standard-risk disease categories [3–5]. Deletion of 13q or monosomy 13 and hypoploidy by CC, and t(4;14)(p16.3;q32), t(14;16)(q32;q23), t(14;20)(q32;q11.2) and del17p13 by CC or FISH are considered HR abnormalities [5–8]. Approximately 15% of patients with symptomatic myeloma have HR disease and their median overall survival despite optimal therapy is about 2–3 years [7, 8]. Recent trials incorporating bortezomib as part of induction regimen have shown significant improvement in the outcome of patients with t(4;14), which is now considered an intermediate-risk abnormality by some investigators [9–11]. In the HOVON study, use of bortezomib before and after an auto-HCT was associated with a longer PFS and OS in a subset of patients with del 17p [10]. Based on these preliminary results, bortezomib-based induction and maintenance is now the preferred therapy for patients with HR myeloma.

The t(11;14)(q13;q32) abnormality involving *IgH* and *CCND1-XT* genes can be seen in approximately 15 to 20% of patients with newly diagnosed MM [12–14]. Previous studies have shown that t(11;14)(q13;q32) is associated with non-secretory myeloma, IgM or IgE monoclonal protein [14,15], lymphoplasmacytic or small mature plasma cell morphology, and CD20 expression [15–19]. In general, the presence of t(11;14)(q13;q32) is not associated with a worse outcome in MM [13, 20–22]. However, there are limited data about the prognostic significance of t(11;14)(q13;q32) in the context of autologous stem cell transplant (auto-HCT) [21]. In this study, we report the impact of t(11;14)(q13;q32) on the outcome of patients with MM who underwent auto-HCT at our institution, and compared their outcome to patients with diploid CC or negative FISH, and patients with HR markers by CC or FISH.

Materials and Methods

Patients

We performed a retrospective chart review on patients with symptomatic MM who underwent high-dose chemotherapy followed by auto-HCT at the M.D. Anderson Cancer Center between February 2000 and August 2010. Patients who had CC or FISH results available at any point before auto-HCT were eligible for the study. The t(11;14)(q13;q32) was defined as an abnormal signal pattern in at least 2 metaphases by CC or *IgH/CCND1-XT* rearrangement using 7% as a cutoff by interphase FISH. HR cytogenetic abnormalities were defined as del(13q)/−13 or hypoploidy by CC studies only, or t(4;14)(p16.3;q32), t(14;16)(q32;q23), t(14;20)(q32;q11.2) or del(17p13) by CC or FISH studies [5–7]. Normal was defined as diploid by CC and negative FISH studies at every time point before auto-HCT.

Response and Outcome

Response criteria were as defined by the International Myeloma Working Group (IMWG) uniform response criteria [23]. PFS was defined as the time from the day of auto-HCT to the date of disease progression or death [24], whereas OS was defined as the time from the day of auto-HCT to the date of death from any cause.

Statistical Analysis

The primary objective of the study was to compare the rate of progression free survival (PFS) and overall survival (OS) in patients with t(11;14)(q13;q32) to those with normal or HR CC or FISH studies. PFS was defined as the time from transplant to either disease progression or death, and OS as the time form transplant to death of any cause. Patients who were alive at the time of analysis were censored on the last date of the last follow-up. Actuarial estimates of PFS and OS were calculated by the Kaplan-Meier method [25]. Cox's proportional hazards regression analysis was used to evaluate the impact of a number of risk factors, including t(11;14)(q13;q32), on the rate of PFS and OS. Factors considered included age, sex, year of auto-HCT, interval between diagnosis and auto-HCT, CC or FISH abnormalities, β_2 microglobulin level at diagnosis and at auto-HCT, disease status at auto-HCT, response to induction, prior autologous transplant, and prior use of novel agents. Statistical significance was defined at the 0.05 level and factors significant in univariate analysis were considered in multivariate analyses. Statistical analyses were performed using STATA 9.0.

Results

Patient Characteristics

We identified 993 patients with MM and CC and FISH as described above, who underwent auto-HCT between February 2000 and August 2010. Patient characteristics are summarized in Table 1. Among 993 patients, 869 patients had normal CC or FISH results, 27 patients had t(11;14)(q13;q32) and 97 patients had HR abnormalities by CC or FISH. Patients in 3 groups were fairly evenly matched. Overall, 15% patients had relapsed disease at auto-HCT, with 13%, 37% and 7%, in normal, HR and t(11;14)(q13;q32) groups.

In 27 patients with t(11;14)(q13;q32), CC studies were available for all 27 patients, while FISH studies were performed on 19 patients only. In 19 patients with *IgH/CCND1-XT* rearrangement, t(11;14)(q13;q32) by CC was detected in only 13 (68%) patients, reinforcing the greater sensitivity of FISH studies in detecting this abnormality. Overall, 21 of 27 patients had t(11;14)(q13;q32) on CC studies. Out of these 21 patients with this abnormality, 5 (24%) patients had a hyperdiploid clone, 9 (43%) a hypodiploid and 7 (33%) a pseudodiploid clone. Eighteen of 27(67%) patients with t(11;14)(q13;q32) had either isolated t(11;14)(q13;q32) abnormality or associated with other non-HR abnormalities. Nine patients (33%) had at least one HR abnormality: t(11;14)(q13;q32) plus del(13q) in 7 patients and t(11;14)(q13;q32) plus del(13q) and del(17p13) in 2 patients (7%). Bone marrow flow cytometric analyses showed CD20 expression on plasma cells in 3 (11%) patients, and absence of CD20 expression on plasma cells in 24 (89%) patients with t(11;14)(q13;q32).

Eighty-nine (92%) of the 97 patients with HR abnormalities had del(13q) alone or in combination with other HR abnormalities, 4 (4%) patients had del(17p13) alone and 4 (4%) had t(4;14)(p16.3;q32), t(14;16)(q32;q23) or t(14;20)(q32;q11.2).

Induction Therapy and Preparative Regimen

Disease status and responses to prior induction therapy are summarized in Table 1. Novel agents including thalidomide, lenalidomide or bortezomib were used for induction or salvage before auto-HCT in 573 (66%) patients with normal CC or FISH, 21 (78%) patients with t(11;14)(q13;q32) and 74 (76%) patients with HR CC or FISH (Table 1). Melphalan alone was used as preparative regimen for 720 (83%) in normal, 24 (89%) in t(11;14)(q13;q32) and 80 (82%) in HR patients.

Survival

Median follow up in surviving patients was 37 months (range 1 to 130 months). Accordingly, outcomes were compared within 3 years following transplant. Median PFS for normal, t(11;14)(q13;q32) and HR groups were 33 months, 23 and 9.7 months, respectively (Figure 1A). 3-year PFS for normal, t(11;14)(q13;q32) and HR groups were 47%, 27% and 13% (normal vs. t(11;14)(q13;q32): p=0.02, t(11;14)(q13;q32) vs. HR: p= 0.05), respectively (Fig. 1A). Median OS for normal, t(11;14)(q13;q32) and HR groups were 87, 51 and 21 months, respectively (Fig. 1B). 3-year OS for normal, t(11;14)(q13;q32) and HR groups were 82%, 63% and 34% (normal vs. t(11;14)(q13;q32): p=0.01, t(11;14)(q13;q32) vs. HR: p= 0.04), respectively (Fig. 1B). Median PFS and OS showed similar trends when patients with relapsed disease at auto-HCT were excluded from the survival anlyses (p <0.0001 for both PFS and OS).

On univariate analyses, t(11;14)(q13;q32), HR abnormalities by CC or FISH, β_2 microglobulin of >3.5 either at diagnosis or at auto-HCT, relapsed disease at auto-HCT, <PR at auto-HCT and induction therapy without novel agents were associated with significantly shorter PFS and OS (Table 2). Because of the large proportion of unknown values of β_2 microglobulin at diagnosis, this variable was not considered in multivariate analysis despite reaching statistical significance on univariate analysis. On multivariate analyses, t(11;14)(q13;q32) and HR abnormalities by CC or FISH and relapsed disease at auto-HCT were independently associated with shorter PFS. On multivariate analyses for OS, t(11;14)(q13;q32) and HR abnormalities by CC or FISH, β_2 microglobulin of >3.5 and relapsed disease at auto-HCT were independently associated with shorter OS (Tables 3 and 4).

Discussion

This retrospective analysis shows that myeloma patients carrying t(11;14)(q13;q32) by CC or FISH had intermediate PFS and OS when compared to patients with normal or HR CC or FISH studies before auto-HCT. This translocation is frequently seen in myeloma patients; however there are conflicting data about its clinical implications. Several studies have studied the impact of t(11;14)(q13;q32) on the outcome of patients with MM [4–7,12–21].

Fonseca et al. reported on 336 patients with newly diagnosed myeloma that were enrolled into the Eastern Cooperative Oncology Group (ECOG) trial, E9486. They identified 53 (16%) patients with t(11;14)(q13;q32) detected by FISH. Patients with the t(11;14)(q13;q32) appeared to have better survival and response to treatment, although this did not reach statistical significance. The patients in this study did not receive auto-HCT and novel agents [4–7, 13].

Dewald et al. compared the clinical efficacy of metaphase CC and FISH with interphase FISH in 154 patients with newly diagnosed myeloma. They found increased detection of chromosomal abnormalities with interphase FISH (86%) vs. metaphase CC or FISH (40%). In this study, presence of t(11;14)(q13;q32) by CC was associated with intermediate outcome in terms of OS between normal CC and HR CC. However, detection of t(11;14)(q13;q32) by interphase FISH was not associated with an adverse outcome [20].

Moreau et al. reported the impact of recurrent 14q32 translocations on the outcome of 168 newly diagnosed patients with multiple myeloma enrolled between January 1995 and December 2000 with the median follow-up of 27 months. All patients received at least one auto-HCT while 10 patients received allogeneic HCT. They identified 26 patients (15.5%) with t(11;14)(q13;q32) by interphase FISH. Patients with t(11;14)(q13;q32) had longer survival compared to those without this abnormality [21].

Gertz et al. evaluated the clinical implications of t(11;14)(q13;q32) in myeloma patients treated with high-dose therapy. No survival difference was found in patients with and without t(11;14)(q13;32) [26]. In another report, 1064 patients with newly diagnosed myeloma enrolled into the Intergroupe Francophone du Myélome (IFM) 99 trials were screened for chromosomal aberrations frequently seen in MM: t(11;14)(q13;q32) was seen in 21% of patients. Majority of the patients received auto-HCT while 65 underwent allogeneic HCT. The presence of t(11;14)(q13;q32) did not adversely impact the survival [27].

In our study, patients with t(11;14)(q13;q32) had an intermediate outcome between patients with normal or HR CC or FISH abnormalities. We also compared patients with t(11;14)(q13;q32) only (18/27) and t(11;14)(q13;q32) plus other HR abnormalities (9/27) to patients with normal or HR CC or FISH studies in a multivariate model. When analyzed separately, both t(11;14)(q13;q32) alone and t(11;14)(q13;q32) with other HR abnormalities were predictive of significantly shorter PFS, while t(11;14)(q13;q32) only showed a trend strong trend towards a shorter OS.

These results are consistent with earlier observations that patients with any CC abnormality, regardless of risk category, had worse outcome than patients with normal karyotype [5, 20, 28]. This may be a function of higher proliferation in the cells where a karyotypic abnormality is detected [21]. Furthermore, the relatively worse outcome for patients with t(11;14)(q13;q32) in our study could be due to the inclusion of a number of patients with relapsed disease at auto-HCT (15%) or with concurrent HR abnormalities in 9/27 (33%) patients. Using gene expression profiling, Nair et al. categorized patients with t(11;14)(q13;q32) into two subsets [29]. The subset with CD20 expression was associated with a

durable remission while the subset lacking CD20 expression had shorter duration of remission. Since almost 90% of patients with t(11;14)(q13;q32) in our study lacked CD20 expression, it may have been partly responsible for their worse outcome.

Other significant prognostic markers were a high β_2 microglobulin level at auto-HCT and patients with relapsed disease at auto-HCT. Both of these are known risk factors for worse outcome for myeloma [30–33]. High β_2 microglobulin level either at diagnosis or at auto-HCT has been shown to be associated with worse outcome in several prior studies and retrospective analyses. Similarly, it is well known that patients transplanted after a relapse have significantly shortened PFS and OS after an auto-HCT.

There are several potential limitations to consider in interpreting the results of our study. They included the retrospective nature of the study, heterogeneous patient population in terms of disease status and non-transplant therapy, relatively small number of patients with t(11;14)(q13;q32), and concurrent HR CC or FISH abnormalities in about a third of patients with t(11;14)(q13;q32).

In summary, our study showed that patients with t(11;14)(q13;q32) had intermediate outcome compared to patients with normal and HR abnormalities by CC or FISH studies. This finding may be used to stratify patients into risk categories and may predict the outcome.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. 2012; 62:10–29. [PubMed: 22237781]
2. Rajkumar SV, Gahrton G, Bergsagel PL. Approach to the treatment of multiple myeloma: a clash of philosophies. Blood. 2011; 118:3205–3211. [PubMed: 21791430]
3. Dispenzieri A, Rajkumar SV, Gertz MA, et al. Treatment of newly diagnosed multiple myeloma based on Mayo Stratification of Myeloma and Risk-adapted Therapy (mSMART): consensus statement. Mayo Clin Proc. 2007; 82:323–341. [PubMed: 17352369]
4. Fonseca R, Barlogie B, Bataille R, et al. Genetics and cytogenetics of multiple myeloma: a workshop report. Cancer Res. 2004; 64:1546–1558. [PubMed: 14989251]
5. Munshi NC, Anderson KC, Berqsagel PL, et al. Consensus recommendations for risk stratification in multiple myeloma: report of the International Myeloma Workshop Consensus Panel 2. Blood. 2011; 117:4696–4700. [PubMed: 21292777]
6. Kumar SK, Mikhael JR, Buadi FK, et al. Management of newly diagnosed symptomatic multiple myeloma: updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) consensus guidelines. Mayo Clin Proc. 2009; 84:1095–1110. [PubMed: 19955246]
7. Stewart AK, Bergsagel PL, Greipp PR, et al. A practical guide to defining high-risk myeloma for clinical trials, patient counseling and choice of therapy. Leukemia. 2007; 21:529–534. [PubMed: 17230230]
8. Rajkumar SV. Multiple myeloma, 2012 update on diagnosis, risk-stratification, and management. Am J Hematol. 2012; 87:78–88. [PubMed: 22180161]
9. San Miguel JF, Schlag R, Khuageva NK, et al. Bortezomib plus melphalan and prednisone for initial treatment of multiple myeloma. N Engl J Med. 2008; 359:906–917. [PubMed: 18753647]
10. Neben K, Lokhorst HM, Jauch A, et al. Administration of bortezomib before and after autologous stem cell transplantation improves outcome in multiple myeloma patients with deletion 17p. Blood. 2012; 119:940–948. [PubMed: 22160383]

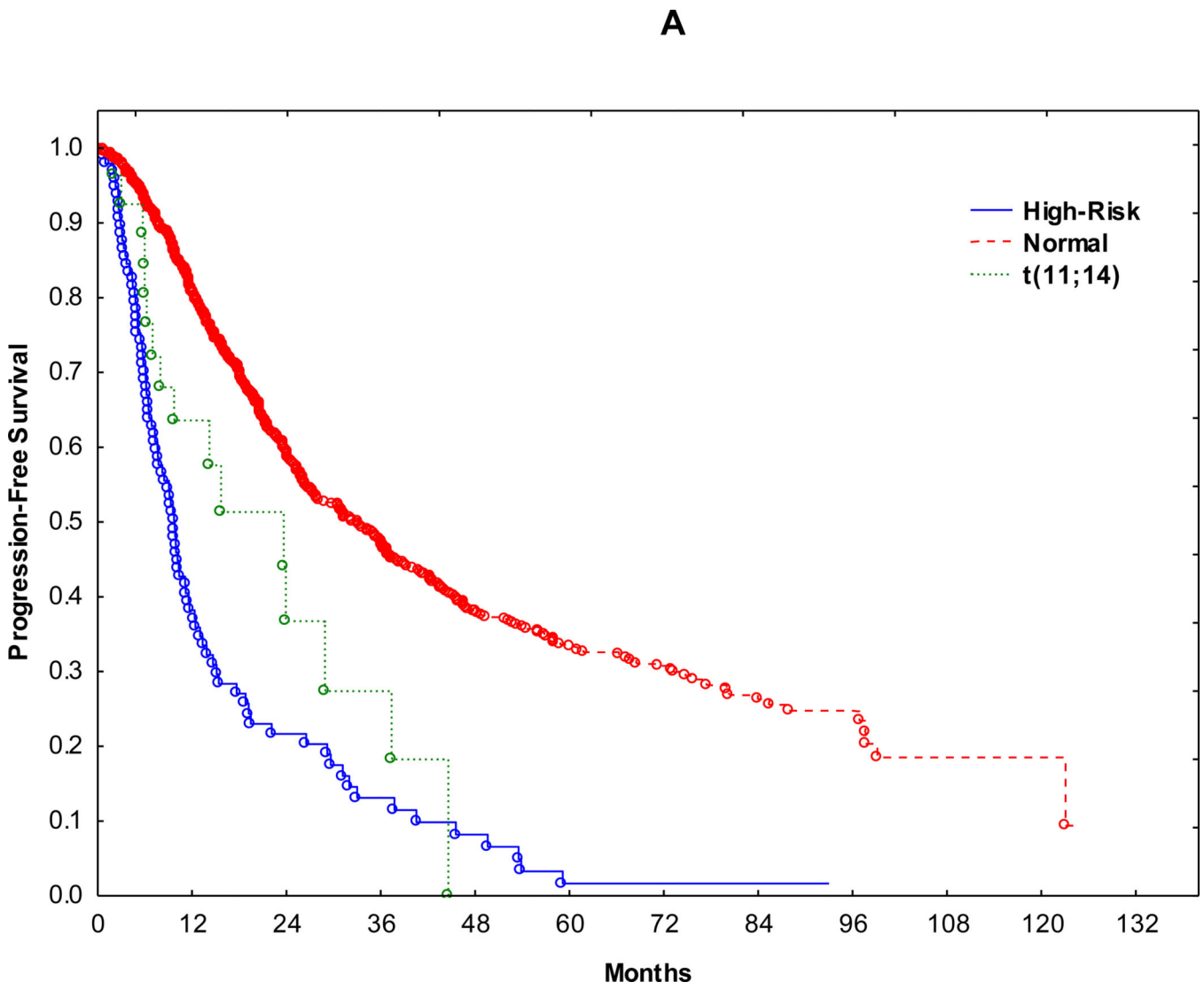
11. Avet-Loiseau H, Leleu X, Roussel M, et al. Bortezomib plus dexamethasone induction improves outcome of patients with t(4;14) myeloma but not outcome of patients with del(17p). J Clin Oncol. 2010; 28:4630–4634. [PubMed: 20644101]
12. Avet-Loiseau H, Li JY, Facon T, et al. High incidence of translocations t(11;14)(q13;q32) and t(4;14)(p16;q32) in patients with plasma cell malignancies. Cancer Res. 1998; 58:5640–5645. [PubMed: 9865713]
13. Fonseca R, Blood EA, Oken MM, et al. Myeloma and the t(11;14)(q13;q32); evidence for a biologically defined unique subset of patients. Blood. 2002; 99:3735–3741. [PubMed: 11986230]
14. Königsberg R, Zojer N, Ackermann J, et al. Predictive role of interphase cytogenetics for survival of patients with multiple myeloma. J Clin Oncol. 2000; 18:804–812. [PubMed: 10673522]
15. Avet-Loiseau H, Garand R, Lodé L, et al. Translocation t(11;14)(q13;q32) is the hallmark of IgM, IgE, and nonsecretory multiple myeloma variants. Blood. 2003; 101:1570–1571. [PubMed: 12393502]
16. Feyler S, O'Connor SJ, Rawstron AC, et al. IgM myeloma: a rare entity characterized by a CD20-CD56-CD117- immunophenotype and the t(11;14). Br J Haematol. 2008; 140:547–551. [PubMed: 18275432]
17. Garand R, Avet-Loiseau H, Accard F, Moreau P, Harousseau JL, Bataille R. t(11;14) and t(4;14) translocations correlated with mature lymphoplasmacytoid and immature morphology, respectively, in multiple myeloma. Leukemia. 2003; 17:2032–2035. [PubMed: 14513054]
18. Hoyer JD, Hanson CA, Fonseca R, Greipp PR, Dewald GW, Kurtin PJ. The (11;14)(q13;q32) translocation in multiple myeloma. A morphologic and immunohistochemical study. Am J Clin Pathol. 2000; 113:831–837. [PubMed: 10874884]
19. Robillard N, Avet-Loiseau H, Garand R, et al. CD20 is associated with a small mature plasma cell morphology and t(11;14) in multiple myeloma. Blood. 2003; 102:1070–1071. [PubMed: 12702507]
20. Dewald GW, Therneau T, Larson D, et al. Relationship of patient survival and chromosome anomalies detected in metaphase and/or interphase cells at diagnosis of myeloma. Blood. 2005; 106:3553–3558. [PubMed: 16030187]
21. Moreau P, Facon T, Leleu X, et al. Recurrent 14q32 translocations determine the prognosis of multiple myeloma, especially in patients receiving intensive chemotherapy. Blood. 2002; 100:1579–1583. [PubMed: 12176874]
22. Oken MM, Leong T, Lenhard Jr RE, et al. The addition of interferon or high dose cyclophosphamide to standard chemotherapy in the treatment of patients with multiple myeloma: phase III Eastern Cooperative Oncology Group Clinical Trial EST 9486. Cancer. 1999; 86:957–968. [PubMed: 10491521]
23. Durie BG, Harousseau JL, Miguel JS, et al. International uniform response criteria for multiple myeloma. Leukemia. 2006; 20:1467–1473. [PubMed: 16855634]
24. Rajkumar SV, Harousseau JL, Durie B, et al. Consensus recommendations for the uniform reporting of clinical trials: report of the International Myeloma Workshop Consensus Panel 1. Blood. 2011; 117:4691–4695. [PubMed: 21292775]
25. Kaplan EL, Meler P. Nonparametric estimation from incomplete observations. J. Amer. Statist. Assn. 1958; 53:457–481.
26. Gertz MA, Lacy MQ, Dispenzieri A, et al. Clinical implications of t(11;14)(q13;q32), t(4;14)(p16.3;q32), and -17p13 in myeloma patients treated with high-dose therapy. Blood. 2005; 106:2837–2840. [PubMed: 15976175]
27. Avet-Loiseau H, Attal M, Moreau P, et al. Genetic abnormalities and survival in multiple myeloma: the experience of the Intergroupe Francophone du Myelome. Blood. 2007; 109:3489–3495. [PubMed: 17209057]
28. Ahmed S, Lin H, Baladandayuthapani V, et al. Impact of Non High-Risk Chromosomal Abnormalities on the Outcome of Autologous Hematopoietic Stem Cell Transplantation in Multiple Myeloma [abstract]. Blood. 2011 Nov.118:333. (ASH Annual Meeting Abstracts).
29. Nair B, van Rhee F, Shauqhnessy JD, et al. Superior results of Total Therapy 3 (2003-33) in gene expression profiling-defined low-risk multiple myeloma confirmed in subsequent trial 2006-66 with VRD maintenance. Blood. 2010; 115:4168–4173. [PubMed: 20124509]

30. Qazilbash MH, Saliba RM, Hosing C, et al. Autologous stem cell transplantation is safe and feasible in elderly patients with multiple myeloma. Bone Marrow Transplant. 2007; 39:279–283. [PubMed: 17262062]

31. Sharma M, Khan H, Thall PF, et al. A randomized phase 2 trial of a preparative regimen of bortezomib, high-dose melphalan, arsenic trioxide, and ascorbic acid. Cancer. 2012; 118:2507–2515. [PubMed: 21887685]

32. Greipp PR, Miguel JS, Durie BG, et al. International staging system for multiple myeloma. J Clin Oncol. 2005; 23:3412–3420. [PubMed: 15809451]

33. O'Shea D, Giles C, Terpos E, et al. Predictive factors for survival in myeloma patients who undergo autologous stem cell transplantation: a single-centre experience in 211 patients. Bone Marrow Transplant. 2006; 37:731–737. [PubMed: 16501593]



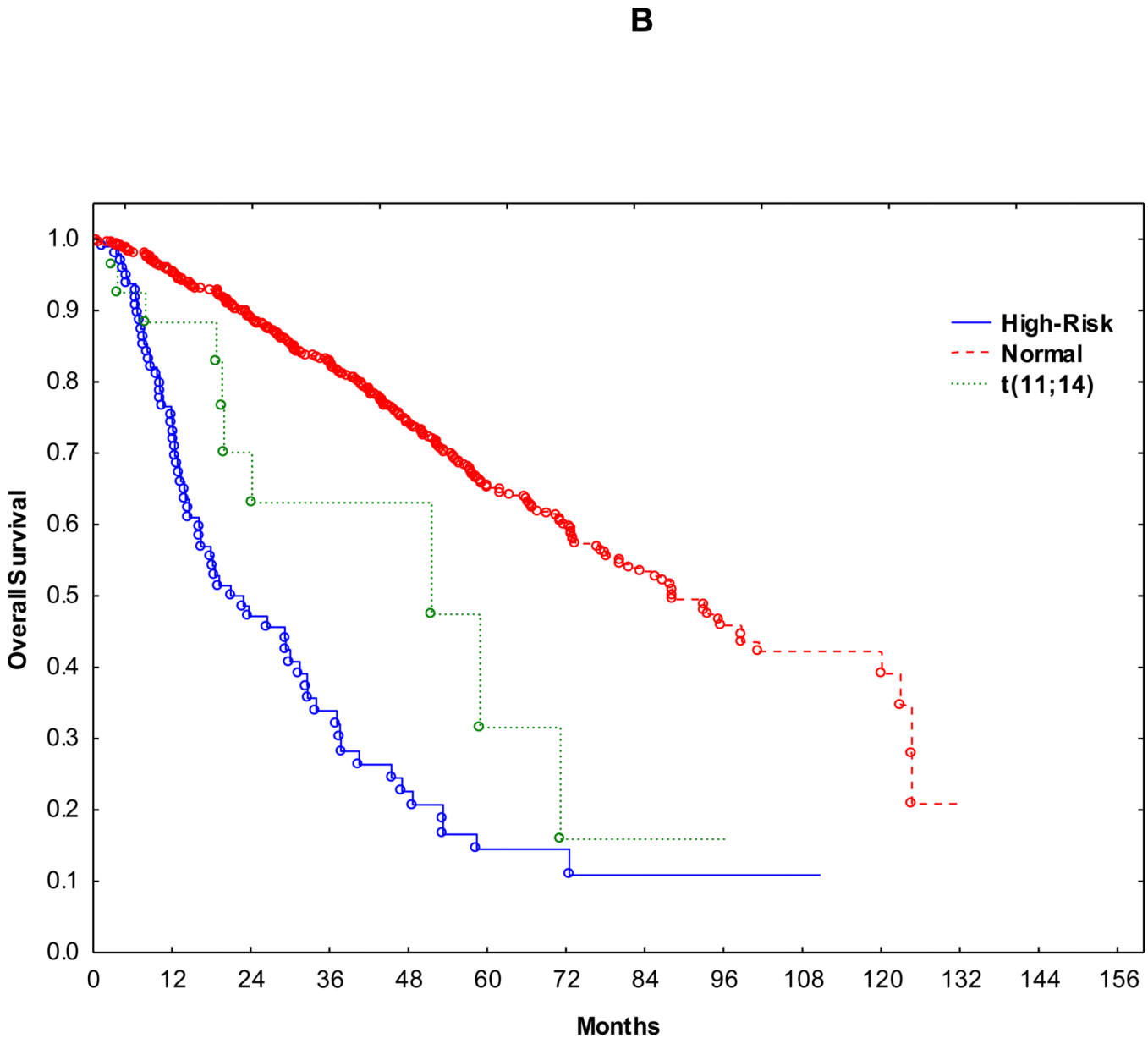


Figure 1.

Table 1

Patient Characteristics

	Overall		**Normal**		**High Risk**		**t=(11;14)**		***P*-value**	
	N=993		**N=869**		**N=97**		**N=27**		***N vs. HR***	***N vs. t(11;14)***
Sex -no. (%)										
M	564	(57)	494	(57)	55	(57)	15	(56)	*0.9*	*0.9*
F	429	(43)	375	(43)	42	(43)	12	(44)		
Age - yr										
Median	58		57		58		59			
(Range)	(29–80)		(29–80)		(31–75)		(44–72)			
Age>65 - no. (%)										
<=65	820	(83)	721	(83)	77	(79)	22	(81)	*0.4*	*0.5*
>65	173	(17)	148	(17)	20	(21)	5	(19)		
Year of Auto-HCT - no. (%)										
<=2005	421	(42)	374	(43)	41	(42)	6	(22)	*0.9*	*0.02*
>2005	572	(58)	495	(57)	56	(58)	21	(78)		
Diagnosis to Auto-HCT - (months)										
Median	7.8		7.9		7.7		6.6			
(Range)	(1.7–262.8)		(1.7–262.8)		(2.1–65.7)		(3.3–60.5)			
<=6 m	330	(33)	287	(33)	34	(35)	9	(33)	*0.7*	*0.6*
>6 m	662	(67)	581	(67)	63	(65)	18	(67)		
Unknown	1		1							
Prior Auto-HCT - no. (%)										
0	950	(96)	832	(96)	92	(95)	26	(96)	*0.4*	*0.7*
1	41	(4)	35	(4)	5	(5)	1	(4)		
2	1	(0)	1	(0)	0	(0)	0	(0)		
Unknown	1		1							
B2 M at diagnosis- no. (%)										
Median	3.3		3.07		4.9		5.1			
(Range)	(0.5–40)		(0.5–40)		(2–33.1)		(1.4–21.2)			

	Overall		Normal		High Risk		t=(11;14)		*P*-value	
	N=993		N=869		N=97		N=27		*N vs. HR*	*N vs. t(11;14)*
<=3.5	373	(56)	345	(59)	22	(34)	6	(27)		
3.5–5.5	130	(19)	109	(19)	15	(23)	6	(27)		
>5.5	167	(25)	129	(22)	28	(43)	10	(45)		
Unknown	323		286		32		5			
B2 M at Auto-HCT- no. (%)										
Median	2.6		2.6		3		2.7			
(Range)	(1.2–40)		(1.2–40)		(1.6–23.2)		(1.5–6.9)			
<=3.5	688	(75)	606	(76)	62	(67)	20	(80)	*0.05*	*0.4*
3.5–5.5	141	(15)	124	(16)	14	(15)	3	(12)		
>5.5	86	(9)	67	(8)	17	(18)	2	(8)		
Unknown	78		72		4		2			
Disease Status at Auto-HCT - no. (%)										
Relapse	148	(15)	110	(13)	36	(37)	2	(7)	*<0.001*	*0.3*
Other	845	(85)	759	(87)	61	(63)	25	(93)		
Response prior to Auto-HCT - no. (%)										
CR/VGPR/PR	805	(81)	711	(82)	69	(71)	25	(93)		
MR/SD/PD/NR	181	(18)	151	(17)	28	(29)	2	(7)	*0.007*	*0.1*
NE	7	(1)	7	(1)	0	(0)	0	(0)		
Stem Cell Source- no. (%)										
BM	3	(0)	2	(0)	0	(0)	1	(4)	*0.8*	*0.09*
PB	990	(100)	867	(100)	97	(100)	26	(96)		
Melphalan Alone- no. (%)										
Yes	824	(83)	720	(83)	80	(82)	24	(89)	*0.9*	*0.3*
No	169	(17)	149	(17)	17	(18)	3	(11)		
Novel Agent - no. (%)										
Yes	668	(67)	573	(66)	74	(76)	21	(78)	*0.04*	*0.2*
No	325	(33)	296	(34)	23	(24)	6	(22)		

Biol Blood Marrow Transplant. Author manuscript; available in PMC 2014 September 01.

Table 2

Univariate Analysis

Median f/up in alive (n=670)	**Overall**	**OS**				**PFS**			
Outcomes at 3 yrs	**N=993**	**died**	**HR**	**95% CI**	**p**	**prg/died**	**HR**	**95% CI**	**p**
Normal	869	124	Ref.			388	Ref.		
High-Risk	97	53	5.96	(4.3–8.3)	<0.001	78	3.45	(2.7–4.4)	<0.001
t(11; 14)	27	7	2.7	(1.2–5.7)	0.01	14	1.9	(1.1–3.2)	0.02
Sex									
M	564	109				276			
F	429	75	0.9	(0.7–1.2)	0.6	204	1.02	(0.85–1.2)	0.8
Age>65									
<= 65	820	152				399			
> 65	173	32	1.1	(0.8–1.6)	0.6	81	1.05	(0.8–1.3)	0.7
Year of Auto-HCT									
<=2005	421	89				241			
> 2005	572	95	1.2	(0.9–1.6)	0.2	239	0.99	(0.8–1.2)	0.9
Months DX to Auto-HCT									
<= 6 m	330	47				153			
> 6 m	662	136	1.5	(1.1–2.1)	0.02	326	1.1	(0.9–1.4)	0.2
Unknown	1								
Prior Auto-HCT									
0	950	174	0.7	(0.4–1.4)	0.3	460	1.1	(0.7–1.7)	0.8
1	41	9				18			
2	1	1				1			
Unknown	1								
B2 M at Auto-HCT									
<=3.5	688	102							
3.5–5.5	141	33	1.6	(1.1–2.4)	0.01	320	1.2	(0.9–1.5)	0.2
>5.5	86	31	2.8	(1.9–4.2)	<0.001	72	1.4	(1.04–1.9)	0.02
Unknown	78								

Median f/up in alive (n=670)	Overall	OS				PFS			
Outcomes at 3 yrs	**N=993**	**died**	**HR**	**95% CI**	**p**	**prg/died**	**HR**	**95% CI**	**p**
<=3.5 vs. >3.5			0.5	(0.4–0.7)	<0.001		0.8	(0.6–0.9)	0.035
>5.5 vs. <=5.5							1.4	(1.02–1.9)	0.03
Disease Status at Transplant									
Relapse	148	57	3.2	(2.3–4.4)	<0.001	107	2.5	(2.0–3.11)	<0.001
Other	845	127				373			
Response prior									
CR/VGPR/PR	805	127				373			
MR/SD/PD/NR	181	52	1.8	(1.3–2.5)	<0.001	102	1.3	(1.06–1.6)	0.01
NE	7	5	excld			5	excld		
Melphalan Alone									
Yes	824	143	0.85	(0.6–1.2)	0.4	377	0.8	(0.7–1.01)	0.07
No	169	41				103			

Table 3

Multivariate Analysis for PFS

	Overall	PFS MV		
	N=993	**HR**	**95% CI**	**p**
Normal	869			
High-Risk	97	2.9	2.2	<0.001
t(11; 14)	27	2	1.2	0.01
Disease Status at Transplant				
Relapse	148	1.96	1.5–2.5	<0.001
Other	845			

Table 4

Multivariate Analysis for OS

	Overall	OS MV		
	N=993	**HR**	**95% CI**	**p**
Normal	869			
High-Risk	97	4.6	3.2	<0.001
t(11; 14)	27	3.1	1.4	0.004
B2 M at SE				
<=3.5 vs. >3.5		0.6	0.4–0.8	0.001
>5.5 vs. <=5.5				
Disease Status at Transplant				
Relapse	148	2.2	1.5–3.1	<0.001
Other	845			