

Recovery of polyclonal immunoglobulins one year after autologous stem cell transplantation as a long-term predictor marker of progression and survival in multiple myeloma

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Supplementary Table 1. Autologous stem cell transplantation characteristics (1993-2014).

Characteristics	MM (n=295)
Time from diagnosis to ASCT, median months (range)	8 (3-186)
Age at ASCT, median years (range)	59 (29-71)
Number of previous chemotherapy regimens, median (range)	1 (1-4)
1, no. (%)	235 (80)
2, no. (%)	45 (15)
≥3, no. (%)	15 (5)
Mobilization regimen PBSC, no.	
G-CSF alone (5mcg/kg sc)	231 (79)
Cyclophosphamide + G-CSF	61 (20)
Other	2 (1)
Infused dose CD34+ cells, x10 ⁶ /kg median, (range)	4.0 (0.4-7.7)
Infused dose MNC, x10 ⁸ /kg, median, (range)	2.5 (0.2-26.5)
Conditioning regimen, no (%):	
Melphalan 200 mg/m ²	264 (89)
Melphalan reduced dose	12 (4)
Busulphan + Melphalan	14 (5)
Other	5 (2)
Tandem ASCT, no. (%)	21 (7)
Time to ANC >500/μL, days, median (range)	11 (5-41)
Time to platelets >20,000/μL, days, median (range)	12 (0-67)
Time to platelets >50,000/μL, days, median (range)	15 (7-188)
Graft failure, no. (%)	1(0.4)
Total length of hospitalization during ASCT, median days (range)	19 (14-82)
MRT, no. deaths related to transplant (%)	6 (1.7)

ASCT: autologous stem cell transplantation ; no. : number; PBST: peripheral blood stem cells; G-CSF: granulocyte-colony stimulating factor; MNC: mononuclear cells; ANC: absolute neutrophil count; MRT: mortality related to transplantation.

Supplementary Table 2. Comparison of progression free survival and overall survival from the different landmark points according to Ig recovery after transplantation.

Time after ASCT			Median PFS (mo)			Median OS (yr)		
	Imm group, n	Ig Recovery, n	Imm group	Ig Recovery	P value	Imm group	Ig Recovery	P value
100 days	205	58	28.0	35.8	NS	7.0	8.0	NS
6 months	126	69	31.6	40.9	NS	7.4	8.4	NS
9 months	102	74	31.6	49.2	NS	7.9	11.3	NS
1year	81	88	27.9	60.4	<0.001	7.9	11.3	0.001
18 months	64	76	37.0	69.3	.003	8.3	13.7	.003
2 years	38	68	43.3	87.1	.003	11.1	13.8	NS
3 years	21	54	94.2	95.0	.NS	NR	13.7	NS
5years	7	35	98.9	122.3	NS	NR	17.3	NS

ASCT: autologous stem cell transplantation; PFS: progression free survival; mo: months; OS: overall survival; Imm: immunoparesis; Ig: immunoglobulin; mo: months; yr: years; NR: not reached; NS: not significant.

Supplementary table 3. Univariate and Multivariate analysis of covariates affecting PFS and OS by conditional version of the Cox regression model for 100-days landmark point. 283 patients alive and progression-free at this moment are included.

Covariates	n (%)	PFS after ASCT since 100 days				OS after ASCT since 100 days			
		Median (mo)	Univ.	Multivariate		Median (yr)	Univ.	Multivariate	
			P value	HR (95%)	P value		P value	HR (95%)	P value
ISS									
III	48 (20)	18.4	0.002	1.4 (0.8-2.4)	NS	4.6	0.001	1.6 (0.6-4.1)	NS
I or II	197 (80)	32.4		Ref		8.3		Ref	
NA	38								
Cytogenetic-risk:									
High	43 (21)	19.9	0.001	1.7 (1.1-2.7)	0.03	3.5	0.0001	2.4 (1.2-4.8)	0.01
Standard	161 (79)	35.3		Ref		11.1		Ref	
NA	79								
Renal impairment at diagnosis									
Yes	37 (20)	16.8	0.06	-	-	4.8	0.01	2.3 (1.1-4.8)	0.03
No	152 (80)	29.1				9.3		Ref.	
NA	94								
Induction									
Conventional	156 (55)	31.6	NS	-	-	6.7	0.06	-	-
Novel agents	127 (45)	30.2				NR			
NA	-								
PMN engraftment									
≤10day	32 (13)	60.8	0.004	0.4 (0.2-0.8)	0.02	9.8	NS	-	-
>10day	221 (87)	29.6		Ref		7.1			
NA	30								
Response before ASCT									
<PR	26 (10)	15.9	0.001	1.2 (0.9-1.7)	NS	4.8	NS	-	-
≥PR	257(90)	32.9		Ref		7.4			
NA	-								
Response 100 days									
CR	135 (47)	35.3	0.09	-	-	8.4	NS	-	-
Not CR	146 (53)	27.4				7.3			
NA	-								
Ig recovery 100 days									
Yes	58 (22)	35.9	NS	-	-	8.0	NS	-	-
No	205 (78)	28.1				7.0			
NA	20								
Interferon maintenance									
Yes	112 (45)	33.2	0.05	0.6 (0.4-1.1)	NS	8.4	0.04	0.5 (0.3-0.9)	0.05
No	128 (55)	22.4		Ref		7.1		Ref	
NA	43								

ASCT: autologous stem cell transplantation; PFS: progression free survival; mo: months; univ: univariate analysis; yr: years; HR: hazard ratio; OS: overall survival; ISS: International staging system; PMN: neutrophils; PR: partial response; CR: complete response; Ig: immunoglobulin; NA: not available; NS: not significant; NR: not reached.

Supplementary Table 4. Multivariate analysis with Immunoglobulin recovery as time-varying covariate.

Variable	PFS	
	Multivariate	
	HR (95%)	P value
ISS III I or II	2.2 (1.1-4.3) Ref	0.018
Cytogenetic-risk: High Standard	2.3 (1.4-3.9) Ref	0.0011
Induction Conventional Novel agents	1.7 (1.1-2.8) Ref	0.0236
PMN engraftment >10day ≤10day	1.9 (0.9- 4.0) Ref	NS
Response 100 days Not CR CR	1.3 (0.8-2.0) Ref	NS
Ig recovery No Yes	1.8 (1.1–2.9) Ref	0.0154

This analysis was done incorporating patients with available data belonging to the whole cohort of 295 patients who underwent autologous stem cell transplantation.

PFS: progression-free survival; HR: hazard ratio; ISS: International staging system; PMN: neutrophils; CR: complete response; Ig: immunoglobulin; Ref: reference category; NS: not significant.