Influence of Clonal Plasma Cell Contamination of Peripheral Blood Stem Cell Autografts on Progression and Survival in Multiple Myeloma Patients After Autologous Peripheral Blood Stem Cell Transplantation in Long-term Observation

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ABSTRACT

Background. High-dose chemotherapy followed by autologous peripheral blood stem cell transplantation (auto-PBSCT) remains the mainstay of treatment of eligible patients diagnosed multiple myeloma. The role of clonal plasma cell (CPC) contamination was found as a reason for relapse, but results in terms of survival, progression, and purging were ambiguous. Therefore, the aim of the study was to explore the influence of CPC contamination in the autograft on survival and progression after auto-PBSCT.

Study Design. The study included 59 patients diagnosed and treated for multiple myeloma in 1998–2004. Cells with coexpression of $CD38^{+++}CD138^{++}CD56^{+}$ and lacking the expression of CD45, CD19, CD10, CD20, and CD23 were considered CPC in flow cytometry.

Results. The risk of death and progression after auto-PBSCT increased significantly by 10% ($P < .021$) and 8% ($P < .034$) per 1×10^6/kg of the CPC number, respectively. For CPC number above 2.96×10^6/kg overall survival achieved clinical significance. Two years after auto-PBSCT, the risk of death was independent of CPC number among the patients who survived ($P = .70$). Analogous conclusions concerned results of progression-free survival at 1 year after auto-PBSCT.

Conclusions. High clonal plasma cell contamination (>2.96 ×1 0^6/kg; 90th percentile of CPC number) is associated with the worst progression-free survival and overall survival. Therefore purging *in vitro* might be considered for the patients with the highest CPC contamination. Negative consequences of CPC contamination on the risk of death are observed for only 2 years after auto-PBSCT. Thereafter only those patients who had lower CPC contamination survived.

HIGH-DOSE chemotherapy followed by autologous peripheral blood stem cell transplantation (auto-PBSCT) remains the mainstay of treatment of eligible multiple myeloma (MM) patients [1–3]. The autografts from patients with MM may contain detectable clonal plasma cell (CPC) contamination. It seems reliable that contamination of the autograft may contribute to MM relapse and progression [1]. To optimize the results of auto-PBSCT, it seems reasonable to take into account factors that are responsible for early progression or relapse and shorten survival, which could help to individualize treatment. The issue of personalized medicine is becoming more

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Table 1. Patient Characteristics

	N	n	% or X ± SD	Median (IQR)	Range
Sex (female)	59	28	47.5%		
Age, years	59		54.5 ± 8.6	55.5 (48.7–62.3)	32–69
Type of monoclonal protein	59				
IgG		19	32.2%		
IgG kappa		10	17.0%		
IgG lambda		8	13.6%		
Lambda light chain		7	11.9%		
IgA		5	8.5%		
Kappa light chain		4	6.8%		
IgA kappa		3	5.1%		
IgA lambda		2	3.4%		
Nonsecretory		1	1.7%		
Clonal plasma cells in bone marrow $\geq$ 60%	59	5	8.5%		
Bone lytic changes (present)	59	39	66.1%		
Anemia <10 g/dL (women), <12 g/dL (men)	59	35	59.3%		
Hypercalcemia (Ca > 2.65 mmol/L)	59	9	15.3%		
Creatinine concentration > 2 mg/dL	59	12	20.3%		
LDH activity > ULN (423 U/L)	59	26	44.1%		
Beta-2-microglobulin > 3 mg/L	43	29	67.4%		
Albumine concentration < 3 g/dL	59	9	15.3%		
Unfavorable result of cytogenetic examination	38	8	20.5%		
International Staging System					
Stage 1	43	11	25.6%		
Stage 2	43	15	34.9%		
Stage 3	43	17	39.5%		
Stage according to Durie Salmon Classification	59				
IA		3	5.1%		
IB		0	0.0%		
IIA		16	27.1%		
IIB		4	6.8%		
IIIA		27	45.8%		
IIIB		9	15.3%		
Chemomobilization regimen					
1st procedure	59				
Cyclophosphamide + G-CSF		48	81.4%		
Cyclophosphamide + GM-CSF		11	18.6%		
2nd procedure	21				
Vepeside + G-CSF		10	47.6%		
Cyclophosphamide + G-CSF		6	28.6%		
Cyclophosphamide + GM-CSF		4	19.0%		
Cyclophosphamide + Vepeside + G-CSF		1	4.8%		
No. of leukaphereses during 1st procedure					
0 leukaphereses		6	10.2%		
1–2 leukaphereses		2	3.4%		
3–4 leukaphereses		34	57.6%		
5–7 leukaphereses		17	28.8%		
No. of leukaphereses during 2nd procedure					
0 leukaphereses		3	14.3%		
1–2 leukaphereses		2	9.5%		
3–4 leukaphereses		11	52.4%		
5–8 leukaphereses		5	23.8%		
No. of $CD34^+$ collected cells, mln/kg					
1st procedure			5.6 ± 3.7	5.0 (0–2.4)	0–14.9
2nd procedure			2.1 ± 4.2	0.0 (0–2.4)	0–18.3
Conditioning before auto-PBSCT	59				
Melphalan 200 mg/m^2		30	50.8%		
Melphalan 140 mg/m^2		3	5.1%		
Melphalan 100 mg/m^2		24	40.7%		
Melphalan 75 mg/m^2		2	3.4%		

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