

Allogeneic transplantation of multiple myeloma patients may allow long-term survival in carefully selected patients with acceptable toxicity and preserved quality of life

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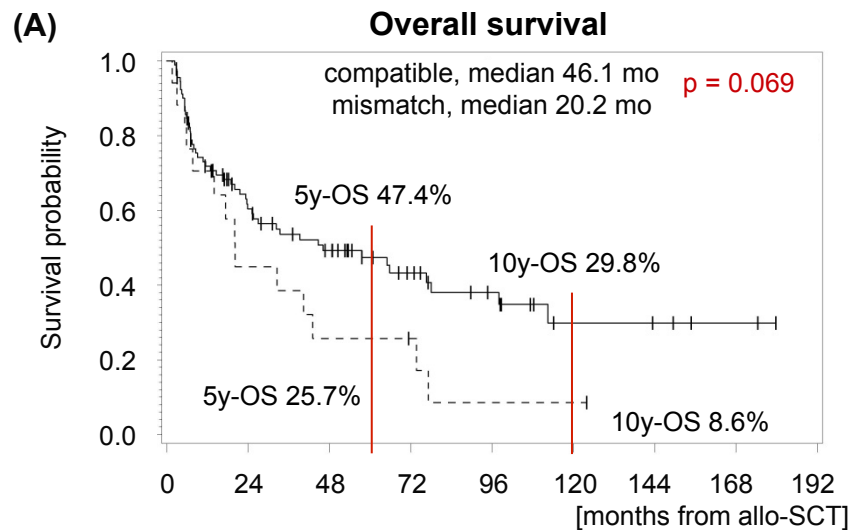
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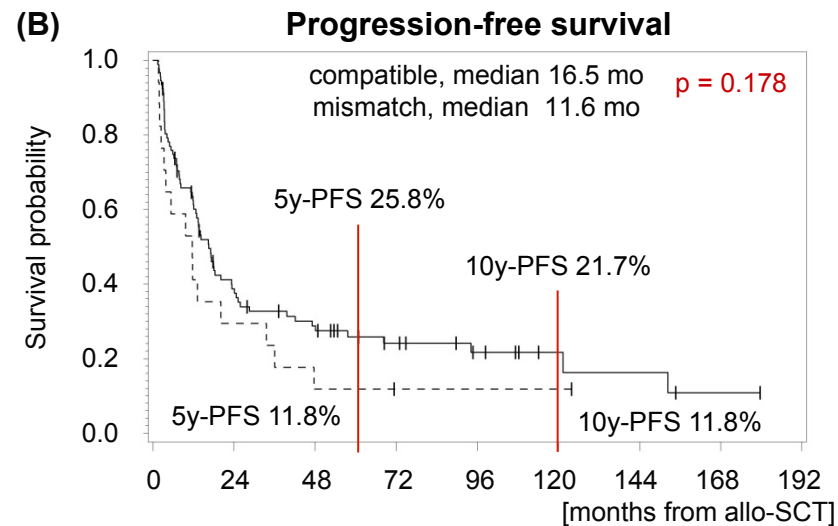
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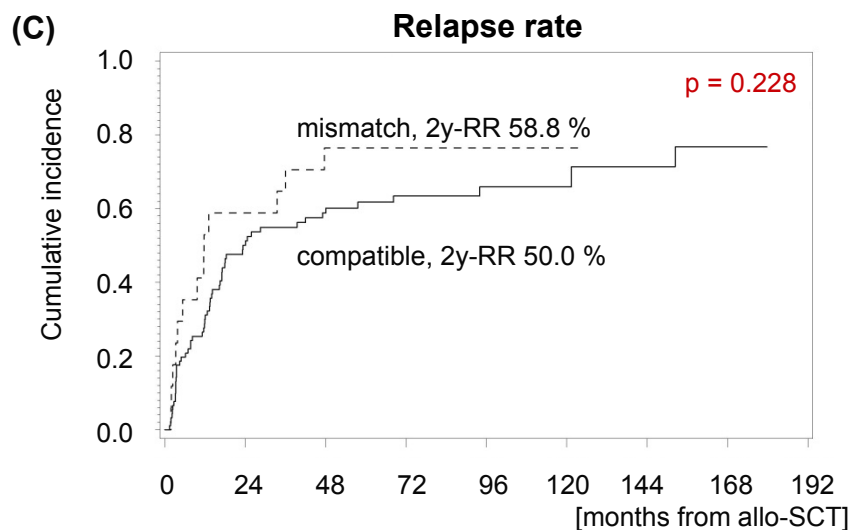
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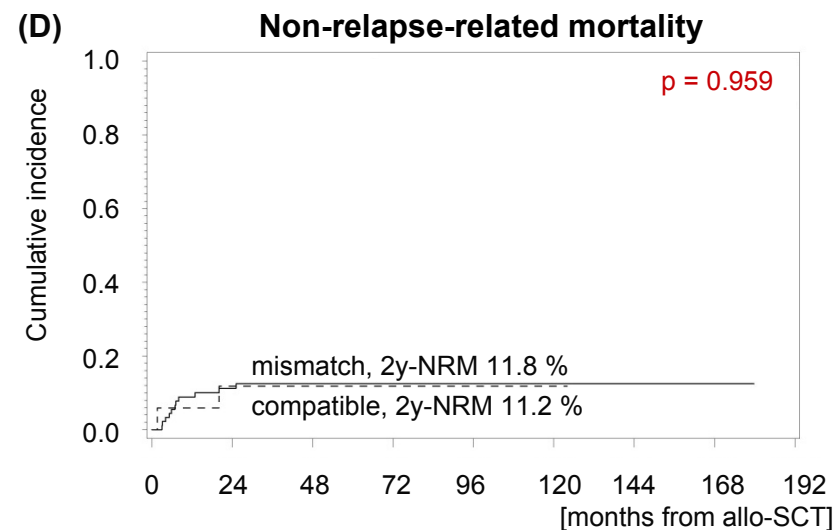
Patients at risk		0	24	48	72	96	120	144	168	192
mismatch	92	46	33	19	12	5	4	2	0	
compatible	17	7	4	3	1	1	0	0	0	



Patients at risk		0	24	48	72	96	120	144	168	192
mismatch	92	32	22	13	8	4	3	1	0	
compatible	17	5	2	1	1	1	0	0	0	

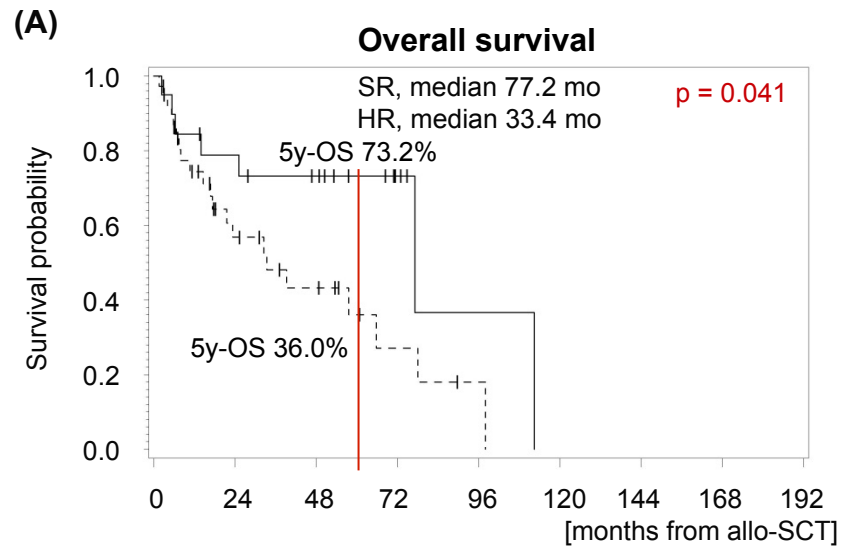


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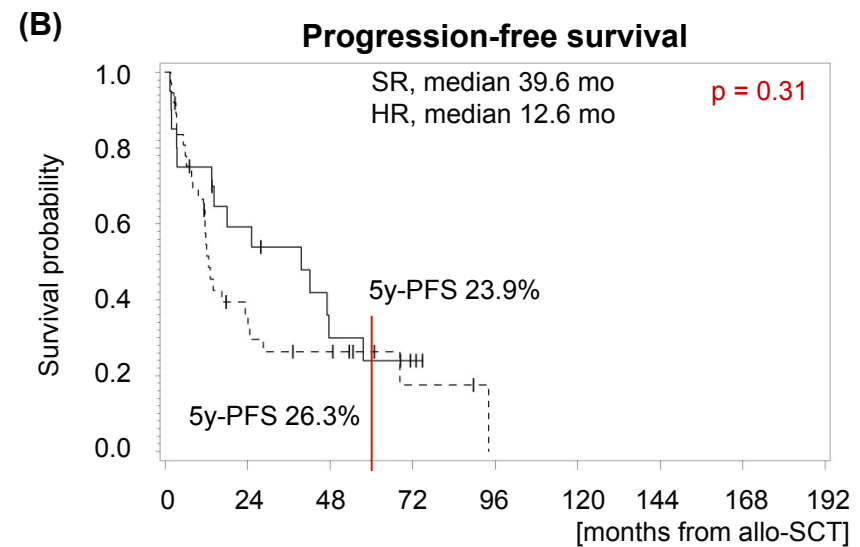
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Suppl. Figure 1. Subgroup analysis in respect of HLA-compatibility of patients with HLA-identical donor (n = 91) vs. those with HLA-mismatch allo-SCT (n = 18). (A) Kaplan-Meier estimates for OS. (B) Kaplan-Meier estimates for PFS. (C) Cumulative incidence of RR. (D) Cumulative incidence of NRM. **Abbreviations.** y: year; HLA: Human Leukocyte Antigen; OS: overall survival; PFS: progression-free survival; RR: relapse rate; NRM: non-relapse mortality; allo-SCT: allogeneic stem cell transplantation.



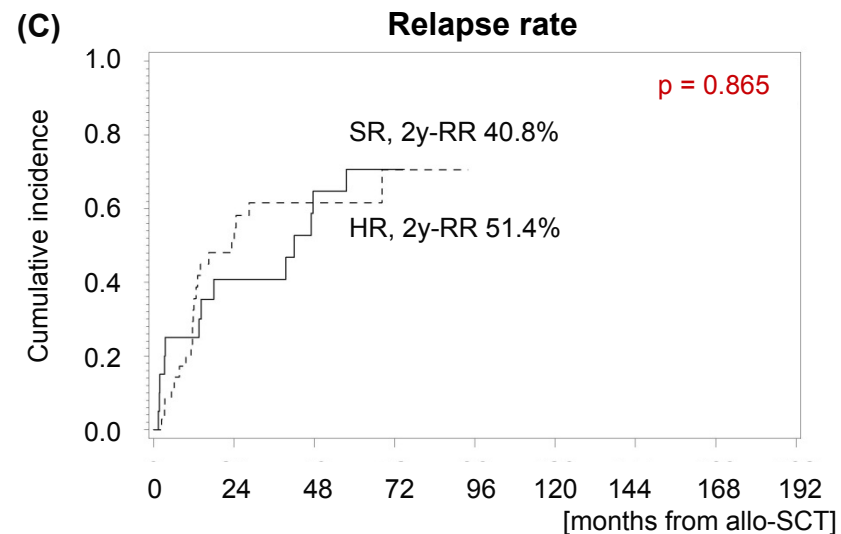
Patients at risk

SR	20	14	11	4	1	0	0	0	0
HR	37	15	9	3	1	0	0	0	0



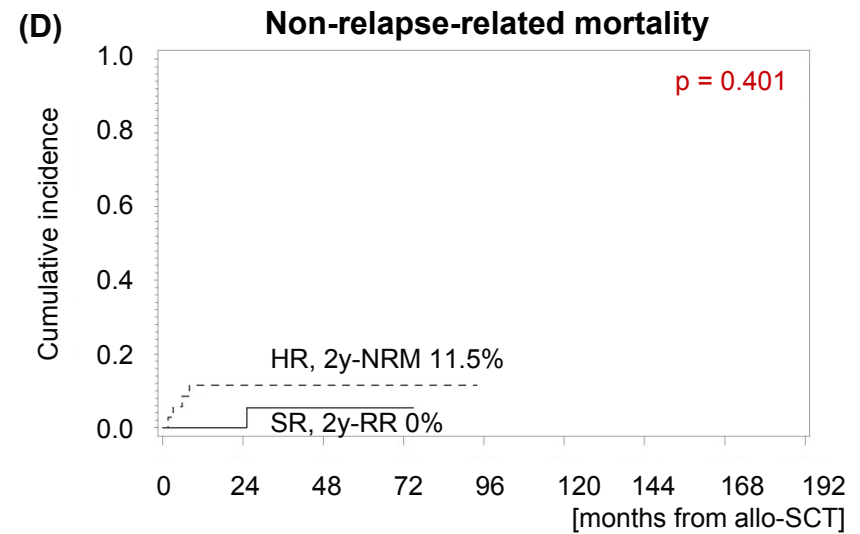
Patients at risk

SR	20	11	5	2	0	0	0	0	0
HR	37	11	7	2	0	0	0	0	0



Patients at risk

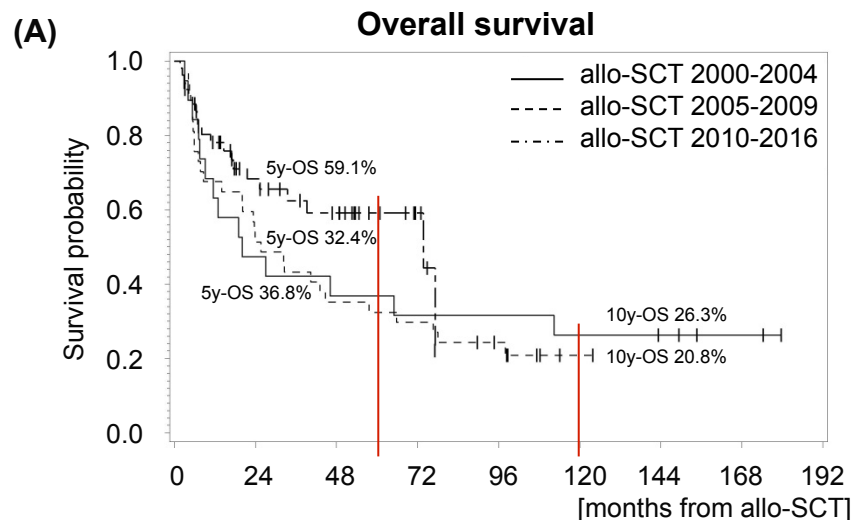
SR	20	11	5	2	0	0	0	0	0
HR	36	11	7	2	0	0	0	0	0



Patients at risk

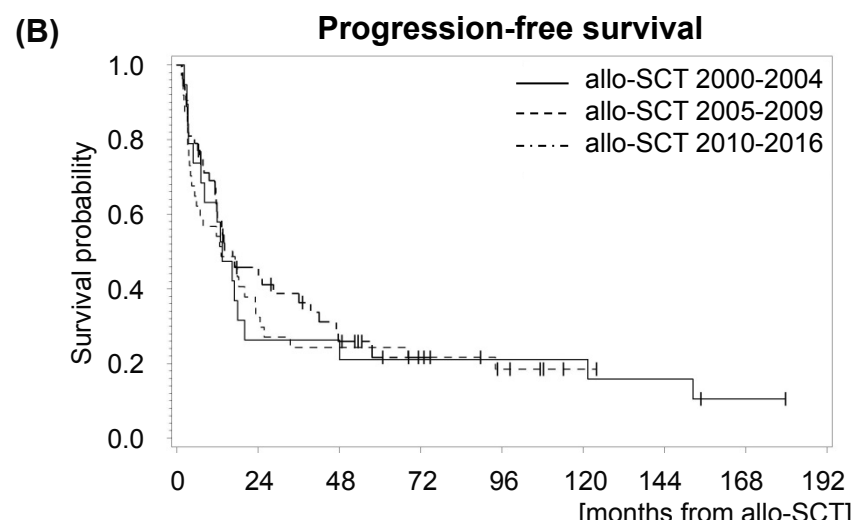
SR	20	11	5	2	0	0	0	0	0
HR	36	11	7	2	0	0	0	0	0

Suppl. Figure 2. Subgroup analysis in respect of cytogenetic risk group of patients with SR (n = 20) vs. those with high, poor and ultra-high risk (summarized as HR; n = 36). (A) Kaplan-Meier estimates for OS. (B) Kaplan-Meier estimates for PFS. (C) Cumulative incidence of RR. (D) Cumulative incidence of NRM. **Abbreviations.** y: year; OS: overall survival; PFS: progression-free survival; RR: relapse rate; NRM: non-relapse mortality; SR/HR: standard/high risk.



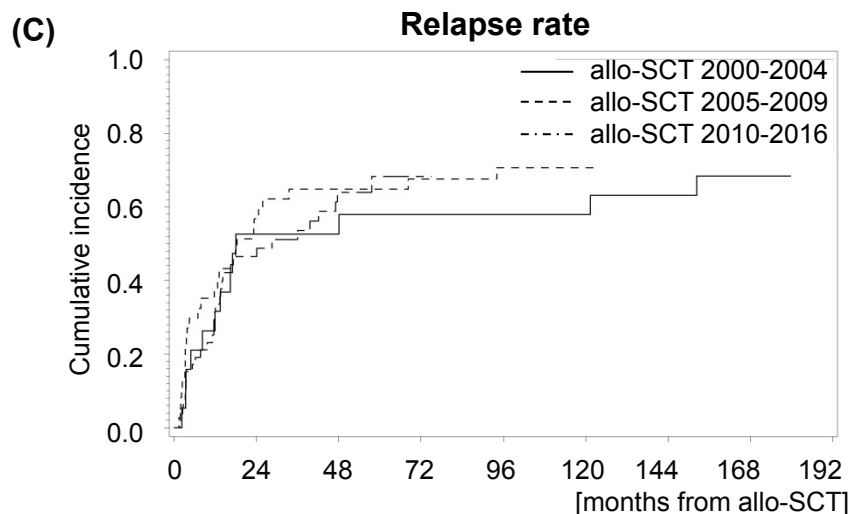
Patients at risk

2000-2004	19	9	7	6	6	5	4	2	0
2005-2009	37	19	13	11	7	1	0	0	0
2010-2016	53	25	17	5	0	0	0	0	0



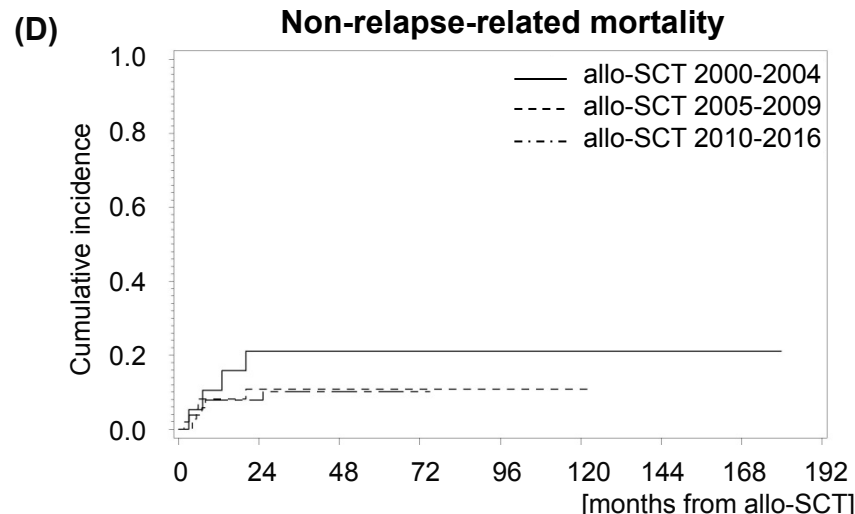
Patients at risk

2000-2004	19	5	5	4	4	4	3	1	0
2005-2009	37	12	9	8	5	1	0	0	0
2010-2016	53	20	10	2	0	0	0	0	0



Patients at risk

2000-2004	19	5	5	4	4	4	3	1	0
2005-2009	37	12	9	8	5	1	0	0	0
2010-2016	53	20	10	2	0	0	0	0	0



Patients at risk

2000-2004	19	5	5	4	4	4	3	1	0
2005-2009	37	12	9	8	5	1	0	0	0
2010-2016	53	20	10	2	0	0	0	0	0

Suppl. Figure 3. Subgroup analysis in respect of the time point of allo-SCT of patients transplanted between 2000-2004 (n = 19), 2005-2009 (n = 37) and 2010-2016 (n = 53), respectively. (A) Kaplan-Meier estimates for OS. (B) Kaplan-Meier estimates for PFS. (C) Cumulative incidence of RR. (D) Cumulative incidence of NRM. **Abbreviations.** y: year; OS: overall survival; PFS: progression-free survival; RR: relapse rate; NRM: non-relapse mortality; allo-SCT: allogeneic stem cell transplantation.

Suppl. Table 1. Conditioning regimen and GvHD prophylaxis.

Conditioning regimen (%)		GvHD prophylaxis (%)	
FluTT	34 (31)		
FLU/Mel	21 (19)		
TBF	18 (17)	CyA/Alemtuzumab	40 (37)
FluTre	14 (13)	CyA/MMF/ATG	36 (33)
FBM	10 (9)	CyA/MMF	19 (17)
TFTreo	4 (4)	CyA/MTX/ATG	9 (8)
FTM	3 (3)	CyA/MTX	3 (3)
BuFlu	3 (3)	CyA	2 (2)
TBI/FLU	1 (1)		
Mel	1 (1)		

Abbreviations. **FluTT:** fludarabine 30mg/m² day -6 to -4, thiotepa 5mg/kg day -6 to -4; **FluMel:** fludarabine 30mg/m² day -6 to -2, melphalan 140mg/m² d -2; **TBF:** thiotepa 5mg/kg day -7 to -6, busulfan 3.2mg/kg day -5 to -3, fludarabine 30mg/m² day -5 to -3; **FluTre:** fludarabine 30mg/m² day -6 to -2, treosulfan 14mg/m² day -6 to -4; **FBM:** fludarabin 30mg/m² d -7 to -4, carmustin 150mg/m² d -7 to -6, melphalan 140mg/m² d -4; **FTM:** fludarabine 30mg/m² day -7 to -4, thiotepa 5mg/kg day -7 to -6, melphalan 140mg/m² day -4; **BuFlu:** busulfan 3.2mg/kg day -7 to -4, fludarabine 30mg/m² day-7 to -4; **TBI/FLU:** total body irradiation 2x2Gy day -8 to -7, fludarabine 30mg/m² day -6 to -3; **Mel:** melphalan 200mg/m² day -5 to -4; CyA: cyclosporin A; MMF: mycophenolate mofetil; ATG: antithymocyte globulin; MTX: methotrexate.

Suppl. Table 2. Overall and progression-free survival.

	Subgroup	Median [months]	p-value
OS [months]	All [95%-CI]	39.2 [23.4 - 73.7]	
	Disease activity prior to allo-SCT [95%-CI]	CR, vgPR, PR, SD or MR (n = 79) PD (n = 30)	65.0 [32.3 - 78.1] 11.5 [5.3 - 33.4] <i>0.003</i>
	Therapeutical concept [95%-CI]	first-line therapy (n = 46) relapsed/refractory MM (n = 63)	n.r. [65.8 - n.r.] 21.6 [11.5 - 39.3] <i>< 0.001</i>
	HLA-compatibility [95%-CI]	HLA-identical donor (n = 92) HLA-mismatch donor (n = 17)	46.1 [23.9 - 78.1] 20.2 [5.8 - 43.1] <i>0.069</i>
	Cytogenetic risk group, n = 57 [95%-CI]	standard risk (n = 20) (ultra) high / poor risk (n = 36)	77.2 [25.2 - 112.5] 33.4 [16.9 - 65.8] <i>0.041</i>
	Cytogenetic risk group in first-line therapy, n = 20	standard risk (n = 8) (ultra) high / poor risk (n = 12)	77.2 65.8 <i>0.256</i>
	PFS [months]	All [95%-CI]	14.2 [11.9 - 20.1]
Disease activity prior to allo-SCT [95%-CI]		CR, vgPR, PR, SD or MR (n = 79) PD (n = 30)	18.4 [13.5 - 33.5] 5.1 [3.2 - 12.6] <i>< 0.001</i>
Therapeutical concept [95%-CI]		first-line therapy (n = 46) relapsed/refractory MM (n = 63)	47.7 [20.1 - 152.4] 9.6 [5.3 - 14.0] <i>< 0.001</i>
HLA-compatibility [95%-CI]		HLA-identical donor (n = 92) HLA-mismatch donor (n = 17)	16.5 [12.0 - 23.3] 11.6 [2.4 - 33.5] <i>0.178</i>
Cytogenetic risk group, n = 57 [95%-CI]		standard risk (n = 20) (ultra) high / poor risk (n = 36)	39.6 [3.5 - 57.7] 12.6 [9.6 - 24.1] <i>0.31</i>
Cytogenetic risk group in first-line therapy, n = 20		standard risk (n = 8) (ultra) high / poor risk (n = 12)	47.7 68.3 <i>0.874</i>

Abbreviations. OS: overall survival; PFS: progression free survival; CI: confidence intervall; CR: complete remission; (vg)PR: (very good) partial remission; SD: stable disease; MR: minimal response; PD: progressive disease; allo-SCT: allogeneic stem cell transplantation; MM: multiple myeloma; HLA: Human Leukocyte Antigen; n.r.: not reached.

Cytogenetics.

ultra-high risk: ≥ 3 chromosomal aberrations

high risk: nonhyperdiploid karyotyp, t(4;14), t(14;16), t(14;20), del 17p

poor risk: gain 1q, del 1p

Suppl. Table 3. Cumulative incidence of relapse and non-relapse mortality.

Cumulative incidence	Month after allo-SCT	All	Disease activity prior to allo-SCT		HLA-compatibility		Therapeutical concept		Cytogenetic risk group, n = 57	
			CR, vgPR, PR, SD, MR	PD	HLA-identical donor	HLA-mismatch donor	first-line therapy	relapsed/refractory MM	standard risk	(ultra) high/poor risk
RR [%] [95%-CI]	6	22.2 [15.6-16.6]	15.3 [9.1-25.8]	40.0 [25.8-62.0]	19.7 [13.0-29.8]	35.3 [18.5-67.2]	6.5 [2.2-19.5]	33.7 [23.8-47.8]	25 [11.7-53.4]	13.8 [6.1-31.1]
	12	33.6 [25.7-43.9]	26.0 [17.8-38.0]	53.3 [38.2-74.5]	29.9 [21.8-41.1]	52.9 [33.8-82.9]	11.0 [4.8-25.3]	50.3 [39.2-64.5]	25 [11.7-53.4]	34.3 [21.6-54.4]
	24	51.4 [42.6-61.9]	45.4 [35.4-58.3]	66.7 [51.8-85.9]	50.0 [40.5-61.7]	58.8 [39.5-87.6]	24.8 [14.8-41.4]	71.4 [60.7-83.9]	40.8 [23.9-69.7]	52.7 [38.3-72.6]
	60	64.2 [55.4-74.3]	60.2 [49.9-72.8]	73.3 [59.1-91.0]	61.7 [52.1-73.2]	64.7 [45.6-91.9]	36.8 [18.6-46.4]	77.0 [66.9-88.6]	70.7 [52.3-95.4]	62.6 [48.0-81.5]
	120	67.6 [58.6-77.9]	65.3 [54.4-78.4]	73.3 [59.1-91.0]	65.9 [55.9-77.6]	76.5 [58.8-99.5]	40.1 [27.6-58.4]	-	-	-
p-value		-	0.087		0.228		< 0.0001		0.779	
NRM [%] [95%-CI]	6	5.6 [2.6-12.1]	2.6 [0.65-10.1]	13.3 [5.4-33.2]	5.5 [2.4-12.9]	5.9 [0.9-39.4]	4.4 [1.1-16.9]	6.4 [2.5-16.6]	-	8.3 [2.8-24.5]
	12	8.4 [4.5-15.7]	6.5 [2.8-15.2]	13.3 [5.4-33.2]	8.9 [4.6-17.2]	5.9 [0.9-39.4]	8.8 [3.5-22.5]	8.1 [3.5-18.8]	-	11.2 [4.4-28.1]
	24	11.4 [6.7-19.4]	9.3 [4.6-18.8]	16.7 [7.5-37.1]	11.2 [6.3-20.2]	11.8 [3.2-43.3]	13.4 [6.4-28.2]	10.0 [4.7-21.3]	-	11.2 [4.4-28.1]
	60	12.4 [7.4-20.6]	10.7 [5.5-20.6]	16.7 [7.5-37.1]	12.4 [7.2-21.7]	11.8 [3.2-43.3]	13.4 [6.4-28.2]	11.8 [5.9-23.8]	5.4 [0.8-36.2]	11.2 [4.4-28.1]
	120	12.4 [7.4-20.6]	10.7 [5.5-20.6]	16.7 [7.5-37.1]	12.4 [7.2-21.7]	11.8 [3.2-43.3]	13.4 [6.4-28.2]	-	-	-
p-value		-	0.332		0.959		0.793		0.417	

Abbreviations. RR: relapse rate; NRM: non-relapse mortality; CI: confidence interval; allo-SCT: allogeneic stem cell transplantation; MM: multiple myeloma; HLA:= Human Leukocyte Antigen.

Suppl. Table 4. Subgroup analyses and timepoint of allo-SCT: The prognostic factors displayed were adjusted in separate multivariate models for the timepoint of allo-SCT (2000 - 2004 vs. 2005 - 2009 vs. 2010 - 2016).

Prognostic factor	OS		PFS		Cumulative incidence of			
	HR [95%-CI]	<i>p-value</i>	HR [95%-CI]	<i>p-value</i>	RR		NRM	
					SHR [95%-CI]	<i>p-value</i>	SHR [95%-CI]	<i>p-value</i>
Disease activity prior to allo-SCT PD vs. CR, vgPR, PR, SD or MR	2.15 [1.3 - 3.6]	<i>0.004</i>	2.20 [1.4 - 3.5]	<i>0.001</i>	1.68 [1.0 - 2.9]	<i>0.071</i>	1.64 [0.5 - 5.4]	<i>0.415</i>
Therapeutical concept relapsed/refractory MM vs. first-line therapy	3.46 [2.0 - 6.1]	<i>< 0.0001</i>	4.27 [2.6 - 7.1]	<i>< 0.0001</i>	3.98 [2.4 - 6.7]	<i>< 0.0001</i>	0.91 [0.3 - 2.6]	<i>0.860</i>
HLA-compatibility HLA-mismatch vs. HLA-identical donor	1.73 [0.9 - 3.2]	<i>0.086</i>	1.49 [0.8 - 2.7]	<i>0.176</i>	1.44 [0.8 - 2.7]	<i>0.271</i>	1.18 [0.2 - 6.2]	<i>0.844</i>
Cytogenetic risk group, n = 57 (ultra) high / poor vs. standard risk	2.48 [0.9 - 6.9]	<i>0.081</i>	1.56 [0.8 - 3.2]	<i>0.229</i>	1.17 [0.5 - 2.7]	<i>0.717</i>	2.35 [0.3 - 18.8]	<i>0.420</i>

Abbreviations. allo-SCT: allogeneic stem cell transplantation; OS: overall survival; PFS: progression free survival; RR: relapse rate; NRM: non-relapse mortality; HR: hazard ratio; SHR: subdistribution hazard ratio; CI: confidence intervall; CR: complete remission; (vg)PR: (very good) partial remission; SD: stable disease; MR: minimal response; PD: progressive disease; MM: multiple myeloma; HLA: Human Leukocyte Antigen.

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