

Early relapse after autologous transplant for myeloma is associated with poor survival regardless of cytogenetic risk

Jill Corre,^{1,2*} Lydia Montes,^{3*} Elodie Martin,⁴ Aurore Perrot,⁵ Denis Caillot,⁶ Xavier Leleu,⁷ Karim Belhadj,⁸ Thierry Facon,⁹ Cyrille Hulin,¹⁰ Mohamad Mohty,¹¹ Jean Fontan,¹² Margaret Macro,¹³ Sabine Brechignac,¹⁴ Arnaud Jaccard,¹⁵ Anne-Marie Stoppa,¹⁶ Frederique Orsini-Pio-celle,¹⁷ Didier Adiko,¹⁸ Laurent Voillat,¹⁹ Faiza Keddar,²⁰ Marly Barry,²¹ Helene Demarquette,²² Marie-Noelle Certain,²³ Isabelle Plantier,²⁴ Murielle Roussel,²⁵ Benjamin Hébraud,²⁵ Thomas Filleron,⁴ Michel Attal^{2,25} and Hervé Avet-Loiseau^{1,2}

*JC and LM contributed equally as co-first authors

¹Unit for Genomics in Myeloma, Institut Universitaire du Cancer de Toulouse-Onco-pole, University Hospital, Toulouse; ²Centre de Recherche en Cancérologie de Toulouse, Institut National de la Santé et de la Recherche Médicale U1037, Toulouse; ³Hematology Department, University Hospital, Amiens; ⁴Biostatistics Department, Institut Claudius Regaud, IUCT-O, Toulouse; ⁵Hematology Department, University Hospital, Nancy; ⁶Hematology Department, University Hospital, Dijon; ⁷Hematology Department, University Hospital, Poitiers; ⁸Hematology Department, University Hospital, Créteil; ⁹Hematology Department, University Hospital, Lille; ¹⁰Hematology Department, University Hospital, Bordeaux; ¹¹Hematology Department, University Hospital, Paris; ¹²Hematology Department, University Hospital, Besançon; ¹³Hematology Department, University Hospital, Caen; ¹⁴Hematology Department, University Hospital, Bobigny; ¹⁵Hematology Department, University Hospital, Limoges; ¹⁶Hematology Department, Institut Paoli Calmettes, Marseille; ¹⁷Hematology Department, Department Hospital, Annecy; ¹⁸Hematology Department, Department Hospital, Libourne; ¹⁹Hematology Department, Department Hospital, Chalon-sur-Saône; ²⁰Hematology Department, Department Hospital, Valenciennes; ²¹Hematology Department, Department Hospital, Boulogne-Sur-Mer; ²²Hematology Department, Department Hospital, Dunkerque; ²³Hematology Department, Department Hospital, Mâcon; ²⁴Hematology Department, Department Hospital, Roubaix and ²⁵Hematology Department, Institut Universitaire du Cancer de Toulouse-Onco-pole, University Hospital, Toulouse, France

Correspondence: JILL CORRE corre.jill@iuct-oncopole.fr

doi:10.3324/haematol.2019.236588

Supplemental Table 1: Univariable analysis of overall survival (landmark analysis at 18 months)

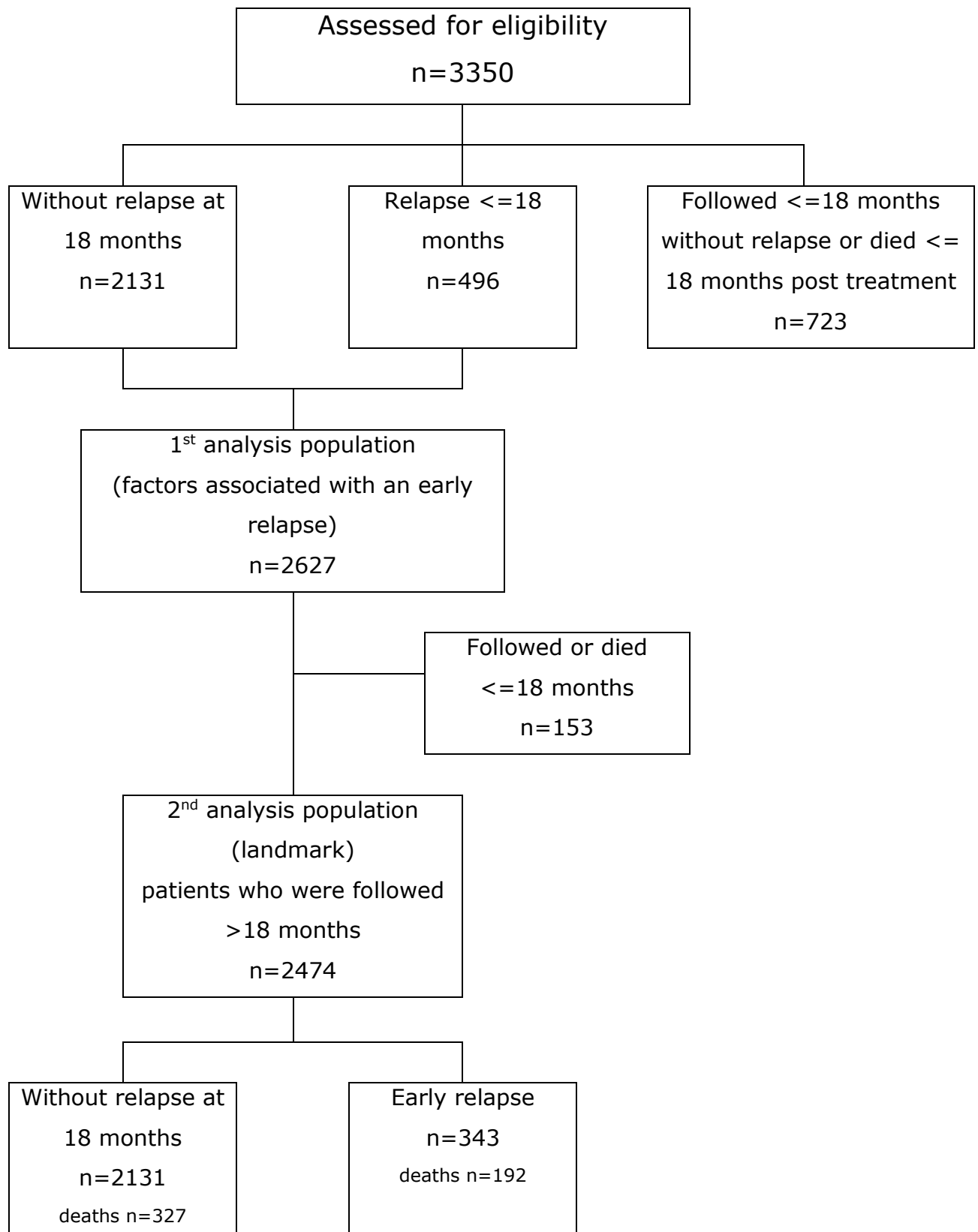
	Death / N	Hazard Ratio [IC95%]	
Sex :			p = 0.0976
Male	309 / 1396	1.00	
Female	207 / 1025	0.86 [0.72; 1.03]	
Age :			p = 0.0055
<60y	284 / 1405	1.00	
>=60y	235 / 1069	1.28 [1.07; 1.52]	
ISS :			p < 0.0001
1	91 / 690	1.00	
2	194 / 882	1.76 [1.37; 2.26]	
3	153 / 481	2.39 [1.84; 3.09]	
Del 17p and/or t4;14) :			p < 0.0001
No	319 / 1782	1.00	
Yes	141 / 359	2.63 [2.16; 3.21]	
Early relapse (<18 months) :			p < 0.0001
No	327 / 2131	1.00	
Yes	192 / 343	5.96 [4.98; 7.14]	
Maintenance :			p = 0.2298
No	467 / 2179	1.00	
Yes	52 / 295	0.84 [0.63; 1.12]	
Best response:			p = 0.0036
VGPR/CR	222 / 1224	1.00	
SD/RP	94 / 299	1.43 [1.12; 1.82]	
Treatment :			p = 0.0002
Triplet	198 / 1552	1.00	
Doublet	321 / 922	1.41 [1.17; 1.69]	

Supplemental Table 2: Multivariable analysis of overall survival (landmark analysis at 18 months)

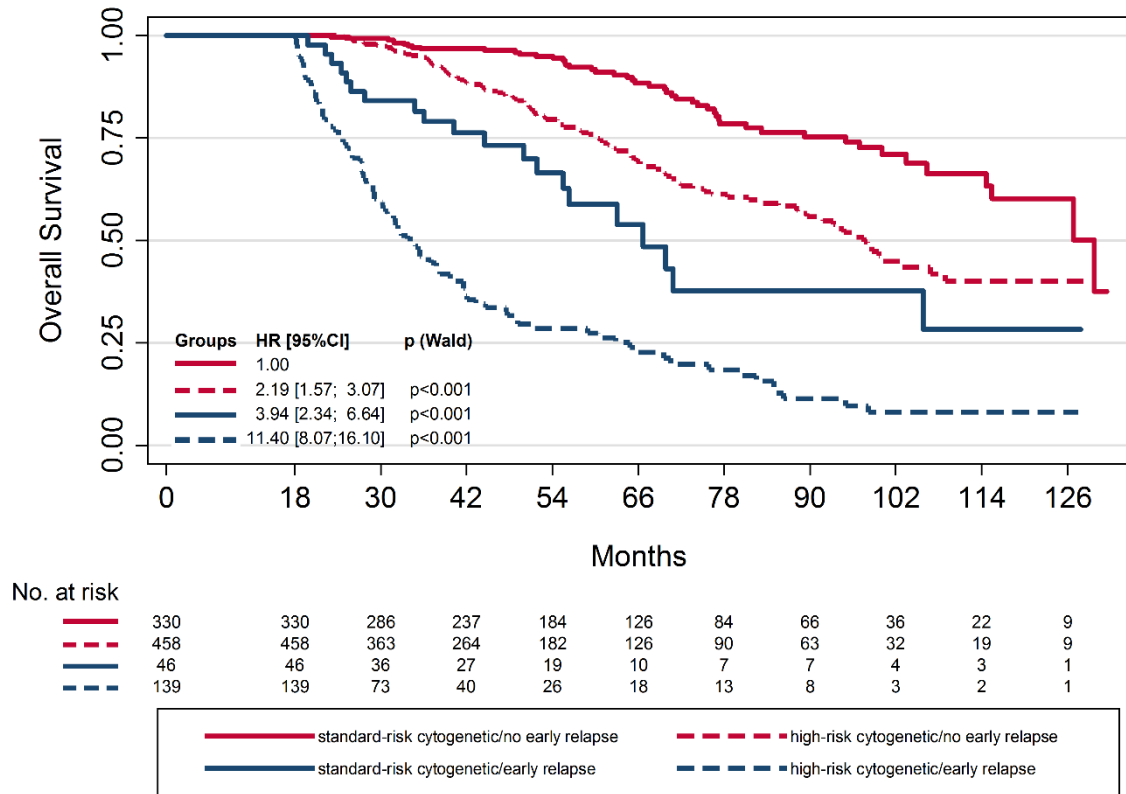
(n=1178, 255 events)	Hazard Ratio	IC95%	p value
ISS			
1	1.00		
2	1.72	[1.24; 2.38]	0.0012
3	1.89	[1.33; 2.68]	0.0003
Early relapse (<18 months)			
No	1.00		
Yes	4.40	[3.34; 5.81]	<0.0001
del17p &/ or t(4;14)			
No	1.00		
Yes	2.05	[1.54; 2.72]	<0.0001
Best response			
VGPR/CR	1.00		
SD/RP	1.15	[0.86; 1.54]	0.3470
Treatment			
Triplet	1.00		
Doublet	1.54	[1.18; 2.00]	0.0015

Supplemental Table 3: Description of patients' cytogenetic factors and their association to early relapse

	No relapse within 18m N = 2131	Early relapse ($\leq 18m$) N = 496	p value
Del(17p) and/or t(4;14) (n = 2273)			p < 0.0001
No	1560 (85.3%)	300 (67.4%)	
Yes	268 (14.7%)	145 (32.6%)	
Missing	303	51	
Trisomy 5 (n = 830)			p = 0.0024
No	363 (57.8%)	141 (69.8%)	
Yes	265 (42.2%)	61 (30.2%)	
Missing	1503	294	
Gain 1q (n = 840)			p < 0.0001
No	420 (66.2%)	99 (48.1%)	
Yes	214 (33.8%)	107 (51.9%)	
Missing	1497	290	
Del(1p32) (n = 820)			p = 0.0007
No	558 (90.6%)	167 (81.9%)	
Yes	58 (9.4%)	37 (18.1%)	
Missing	1515	292	
Del(17p) or t(4;14) or gain 1q or del(1p32) (n = 1061)			p < 0.0001
No	330 (41.9%)	57 (20.9%)	
Yes	458 (58.1%)	216 (79.1%)	
Missing	1343	223	



Supplemental Figure 1: Data flowchart. The flowchart illustrates the selection process of patient data for statistical and model analyses.



Supplemental Figure 2: Kaplan-Meier overall survival curves for patients according to early or no early relapse. Landmark analysis at 18 months. Patients with no early relapse and standard-risk cytogenetic (N=330, red line) vs patients with no early relapse and high-risk cytogenetic (N=458, red dashed line) vs patients with early relapse and standard-risk cytogenetic (N=46, blue line) vs patients with early relapse and high-risk cytogenetic (N=139, blue dashed line). High-risk cytogenetic was defined here by the presence of t(4;14) and/or del(17p) in more than 55% of plasma cells and/or del(1p32) and/or gain 1q.