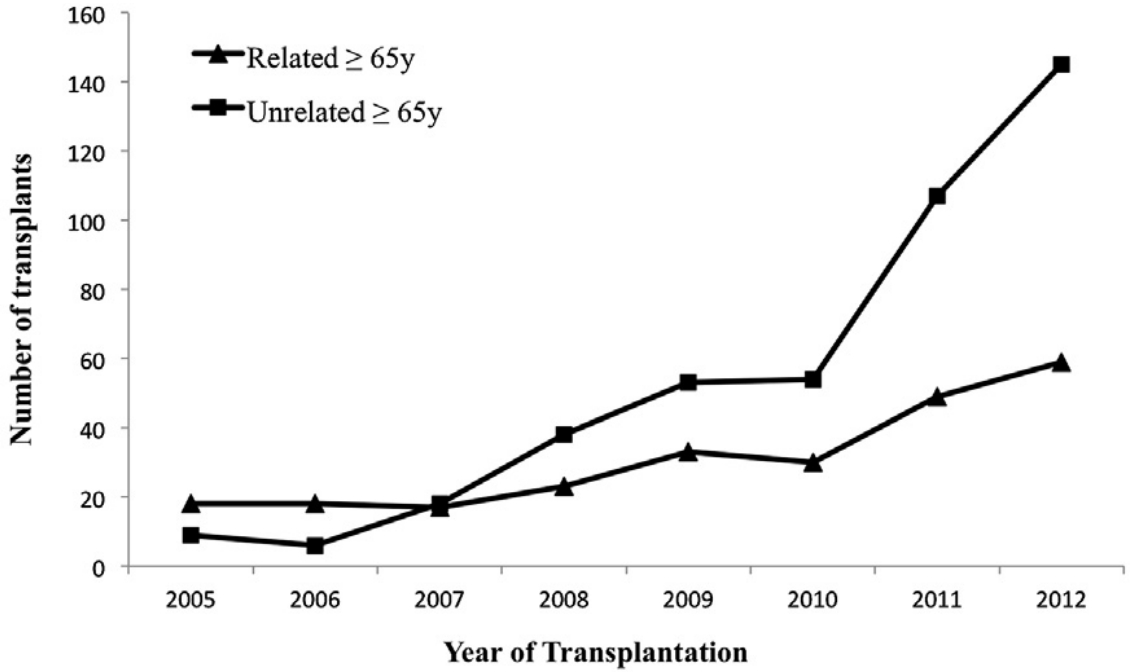
FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

L'attuale approccio clinico al paziente con **Sindrome Mielodisplastica**

Il trapianto allogenico: quando e per chi?

Daniela Cilloni (Torino)

Number of allogeneic HCTs for MDS patients 65 years of age in the United States, 2005-2012.



	2005	2006	2007	2008	2009	2010	2011	2012
Related ≥ 65y	18	18	17	23	33	30	49	59
Unrelated ≥ 65y	9	6	18	38	53	54	107	145

Allogeneic Stem Cell Transplantation for Patients Age ≥ 70 Years with Myelodysplastic Syndrome: A Retrospective Study of the MDS Subcommittee of the Chronic Malignancies Working Party of the EBMT

Silke Heidenreich [1,*], Dimitris Ziagkos [2], Liesbeth C. de Wreede [2,3], Anja van Biezen [4], Jürgen Finke [5], Uwe Platzbecker [6], Dietger Niederwieser [7], Hermann Einsele [8], Wolfgang Bethge [9], Michael Schleuning [10], Dietrich W. Beelen [11], Johanna Tischer [12], Arnon Nagler [13], Bertram Glass [14], Johan Maertens [15], Lucrecia Yáñez [16], Yves Beguin [17], Heinz Sill [18], Christof Scheid [19], Matthias Stelljes [20], Arnold Ganser [21], Pierre Zachée [22], Dominik Selleslag [23], Theo de Witte [24], Marie Robin [25], Nicolaus Kröger [1]

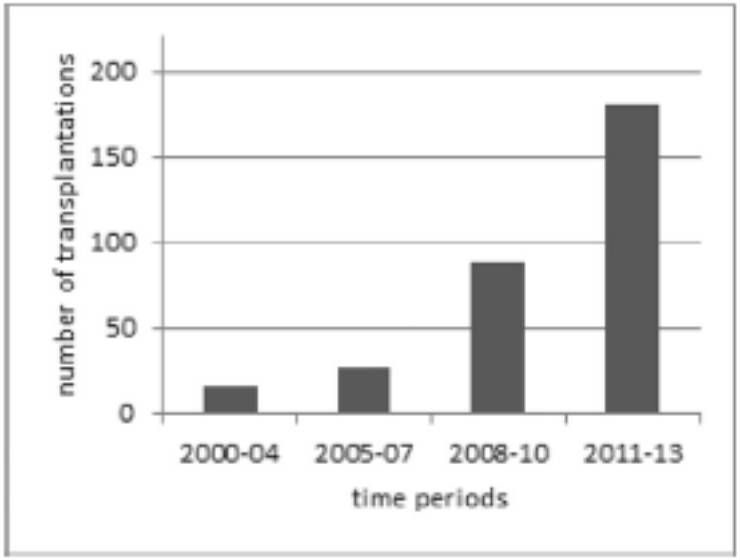


Figure 1. HSCT for MDS/sAML patients ages 70 to 79 years. The number of transplantations per year increased over time: 2000-2004, n = 16; 2005-2007, n = 27; 2008-2010, n = 89; 2011-2013, n = 181.

Biology of blood and marrow transplantation 2017

HSCT in MDS : for whom, when and how?

- Selection of patients
- Type of transplant (HSC source)
- Treatment before transplant
- Induction regimens/intensity
- Timing of transplant

For whom?

- Intermediate 2 and high IPSS risk
- Intermediate, high and very high R-IPSS
- Therapy related MDS
- High transfusion requirement

The Indications for Allogeneic Stem Cell Transplantation in Myeloid Malignancies

Lutz P. Müller, Carsten Müller-Tidow

Indication for allogeneic stem cell transplantation in myelodysplastic syndrome*

Risk (IPSS score)	Indication for allogeneic SCT				
Low (0)	None				
Intermediate-1 (0.5 or 1)	In special cases: high-risk cytogenetics or severe cytopenias				
Intermediate-2 (1.5 or 2)	Standard				
High (2.5 to 3.5)	Standard				
	IPSS				
Variable	Score				
	0	0.5	1	1.5	2
BM blasts	<5	5–10		11–20	21–30
Cytogenetics	Good	Intermediate	Poor		
Cytopenia	0 or 1	2 or 3			
Cytogenetics	Good	Normal, only del(5q), only del(20q), only –Y			
	Intermediate	All others			
	Poor	Complex with >2 aberrations; anomalies of chromosome 7			

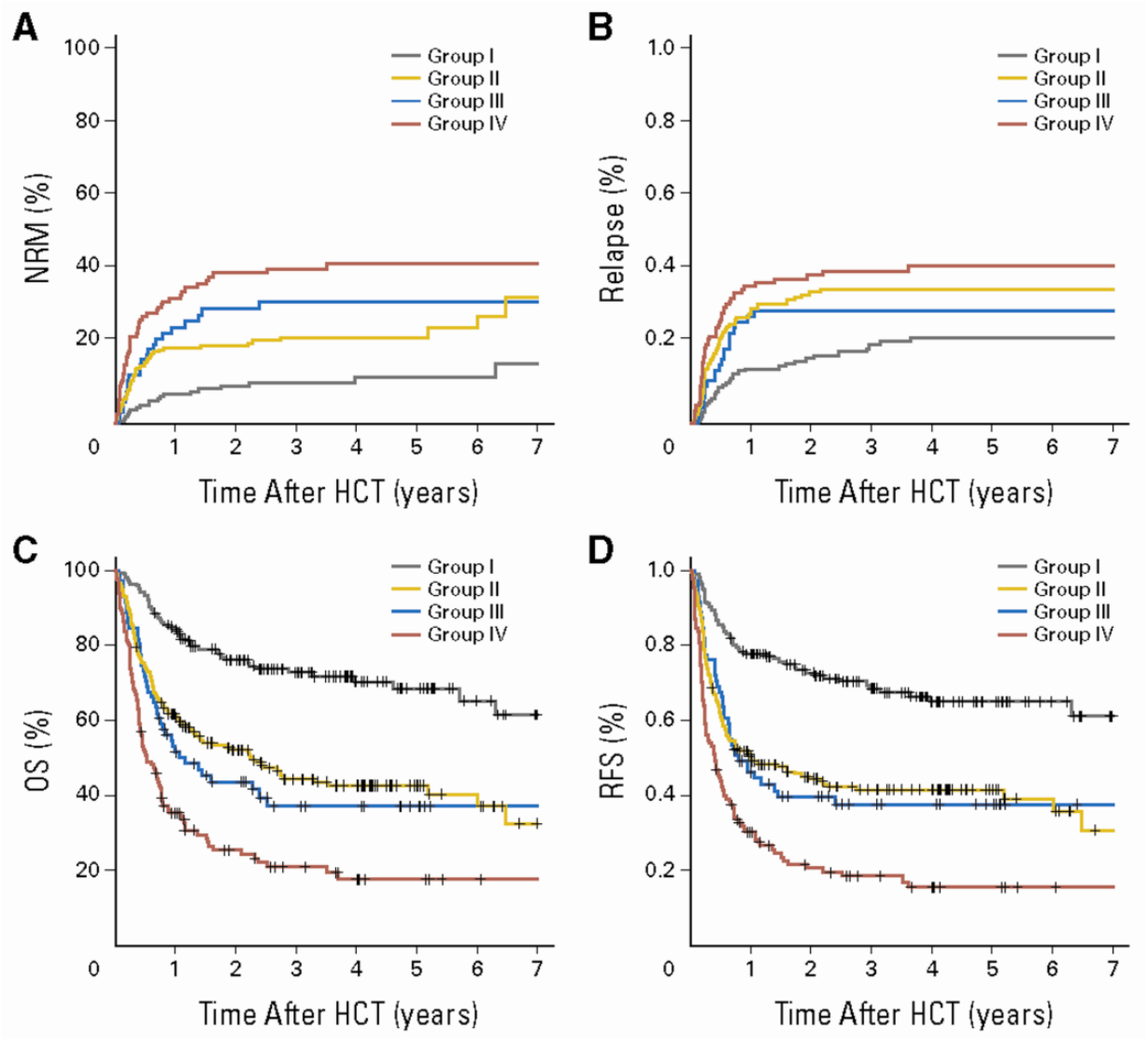
2015

Hematopoietic cell transplantation (HCT)-specific comorbidity index

Blood 2005;106:2912-9

Comorbidity	Definitions of comorbidities included in the new HCT-CI	HCT-CI weighted scores
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias	1
Cardiac‡	Coronary artery disease,§ congestive heart failure, myocardial infarction, or EF $\leq$ 50%	1
Inflammatory bowel disease	Crohn disease or ulcerative colitis	1
Diabetes	Requiring treatment with insulin or oral hypoglycemics but not diet alone	1
Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	1
Psychiatric disturbance†	Depression or anxiety requiring psychiatric consult or treatment	1
Hepatic, mild‡	Chronic hepatitis, bilirubin $>$ ULN to 1.5 $\times$ ULN, or AST/ALT $>$ ULN to 2.5 $\times$ ULN	1
Obesity†	Patients with a body mass index $>$ 35 kg/m^2	1
Infection†	Requiring continuation of antimicrobial treatment after day 0	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, or polymyalgia rheumatica	2
Peptic ulcer	Requiring treatment	2
Moderate/severe renal‡	Serum creatinine $>$ 2 mg/dL, on dialysis, or prior renal transplantation	2
Moderate pulmonary‡	DLco and/or FEV_1 66%-80% or dyspnea on slight activity	2
Prior solid tumor‡	Treated at any time point in the patient's past history, excluding nonmelanoma skin cancer	3
Heart valve disease	Except mitral valve prolapse	3
Severe pulmonary‡	DLco and/or $FEV_1 \leq$ 65% or dyspnea at rest or requiring oxygen	3
Moderate/severe hepatic‡	Liver cirrhosis, bilirubin $>$ 1.5 $\times$ ULN, or AST/ALT $>$ 2.5 $\times$ ULN	3

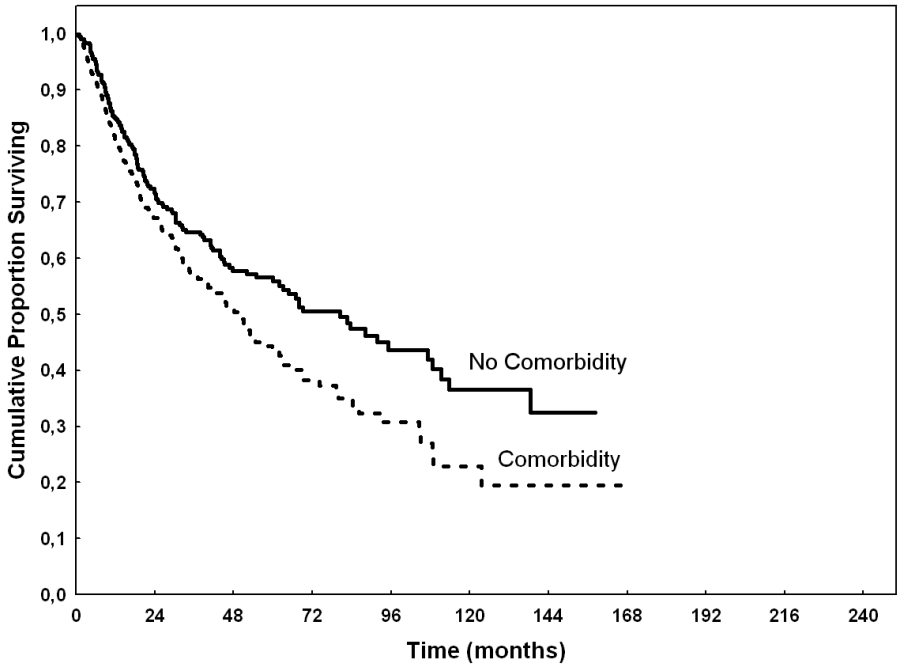
Comorbidity and Disease Status–Based Risk Stratification of Outcomes Among Patients With AML or MDS Receiving Allogeneic Hematopoietic Cell Transplantation



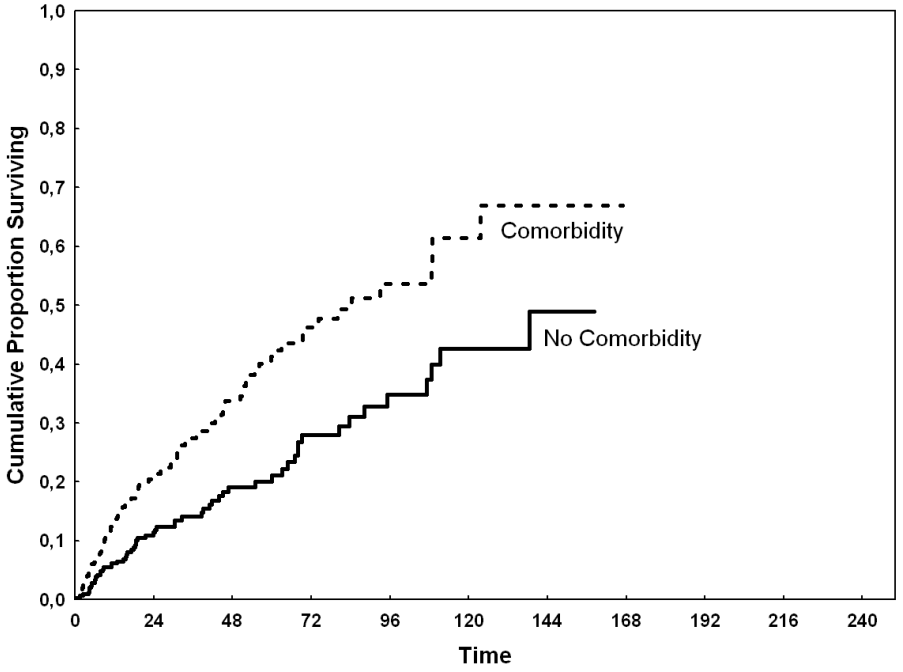
J Clin Oncol 2007;25:4246-54

Effect of comorbidity on survival of MDS patients

Overall Survival



Risk of Non-Leukemic Death

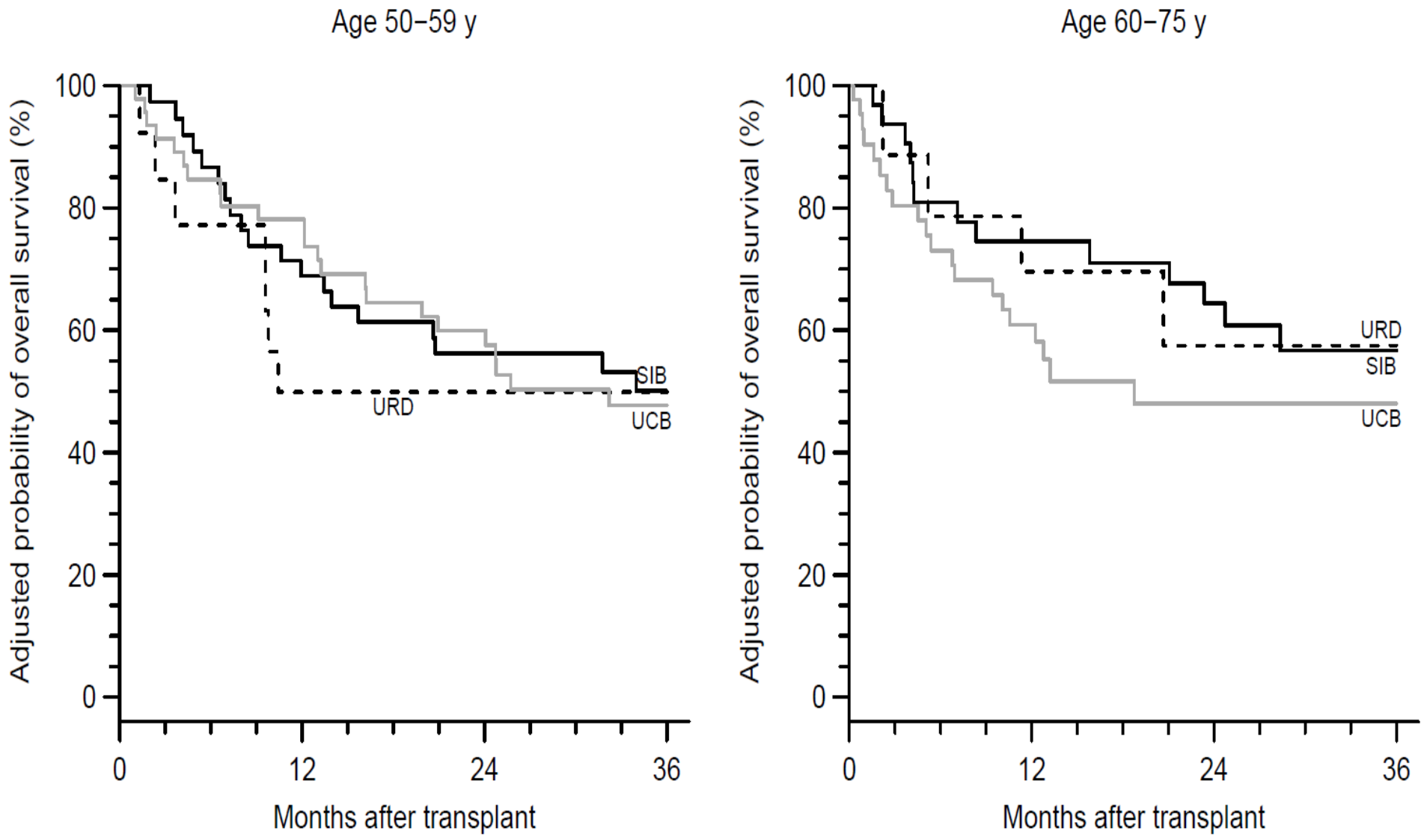


Blood 2007;110:#2453

AML HSCT: URD, Sibling Donor, and UCB Survival

Peffault de la Tour, 2013

Minnesota, Paris, and Nantes



What about low/intermediate-1 IPSS?

- Life expectancy of patients with Intermediate-1 or low IPSS risk at diagnosis was higher when transplanation was delayed but performed before progression to AML.

Cutler et al., Blood 2004; 104:579-585

A decision analysis of allogeneic bone marrow transplantation for the myelodysplastic syndromes: delayed transplantation for low-risk myelodysplasia is associated with improved outcome

Corey S. Cutler, Stephanie J. Lee, Peter Greenberg, H. Joachim Deeg, Waleska S. Pérez, Claudio Anasetti, Brian J. Bolwell, Mitchell S. Cairo, Robert Peter Gale, John P. Klein, Hillard M. Lazarus, Jane L. Liesveld, Philip L. McCarthy, Gustavo A. Milone, J. Douglas Rizzo, Kirk R. Schultz, Michael E. Trigg, Armand Keating, Daniel J. Weisdorf, Joseph H. Antin, and Mary M. Horowitz

Bone marrow transplantation (BMT) can cure myelodysplastic syndrome (MDS), although transplantation carries significant risks of morbidity and mortality. Because the optimal timing of HLA-matched BMT for MDS is unknown, we constructed a Markov model to examine 3 transplantation strategies for newly diagnosed MDS: transplantation at diagnosis, transplantation at leukemic progression, and transplantation at an interval from diagnosis but prior to leukemic progression. Analyses using individual patient risk-assessment data from transplantation and non-transplantation registries were performed for all 4 International Prognostic Scoring System (IPSS) risk groups with adjustments for quality of life (QoL). For low and intermediate-1 IPSS groups, delayed transplantation maximized overall survival. Transplantation prior to leukemic transformation was associated with a greater number of life years than transplantation at the time of leukemic progression. In a cohort of patients under the age of 40 years, an even more marked survival advantage for delayed transplantation was noted. For intermediate-2 and high IPSS groups, transplantation at diagnosis maximized overall survival. No changes in the optimal transplantation strategies were noted when QoL adjustments were incorporated. For low- and intermediate-1–risk MDS, delayed BMT is associated with maximal life expectancy, whereas immediate transplantation for intermediate-2– and high-risk disease is associated with maximal life expectancy. (Blood. 2004;104:579-585)

No SCT

SCT

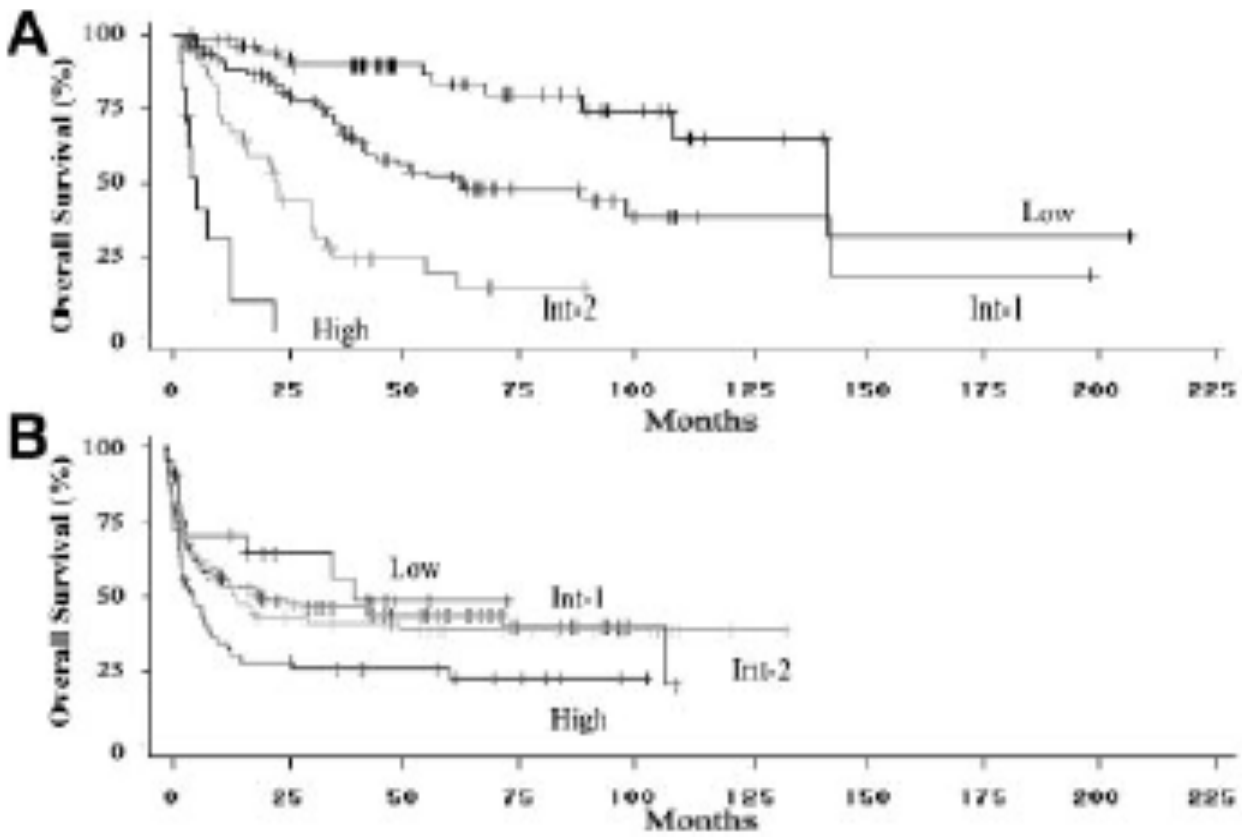


Figure 2. Overall survival of patients included in the analysis. (A) Overall survival of the International MDS Risk Assessment Workshop patients who did not undergo stem cell transplantation, stratified by IPSS score at the time of diagnosis ($P < .001$ for differences in risk groups). (B) Overall survival of the IBMTR/FHCRC bone marrow transplantation cohort of patients, stratified by IPSS risk score at the time of transplantation ($P < .001$ for differences in risk groups).

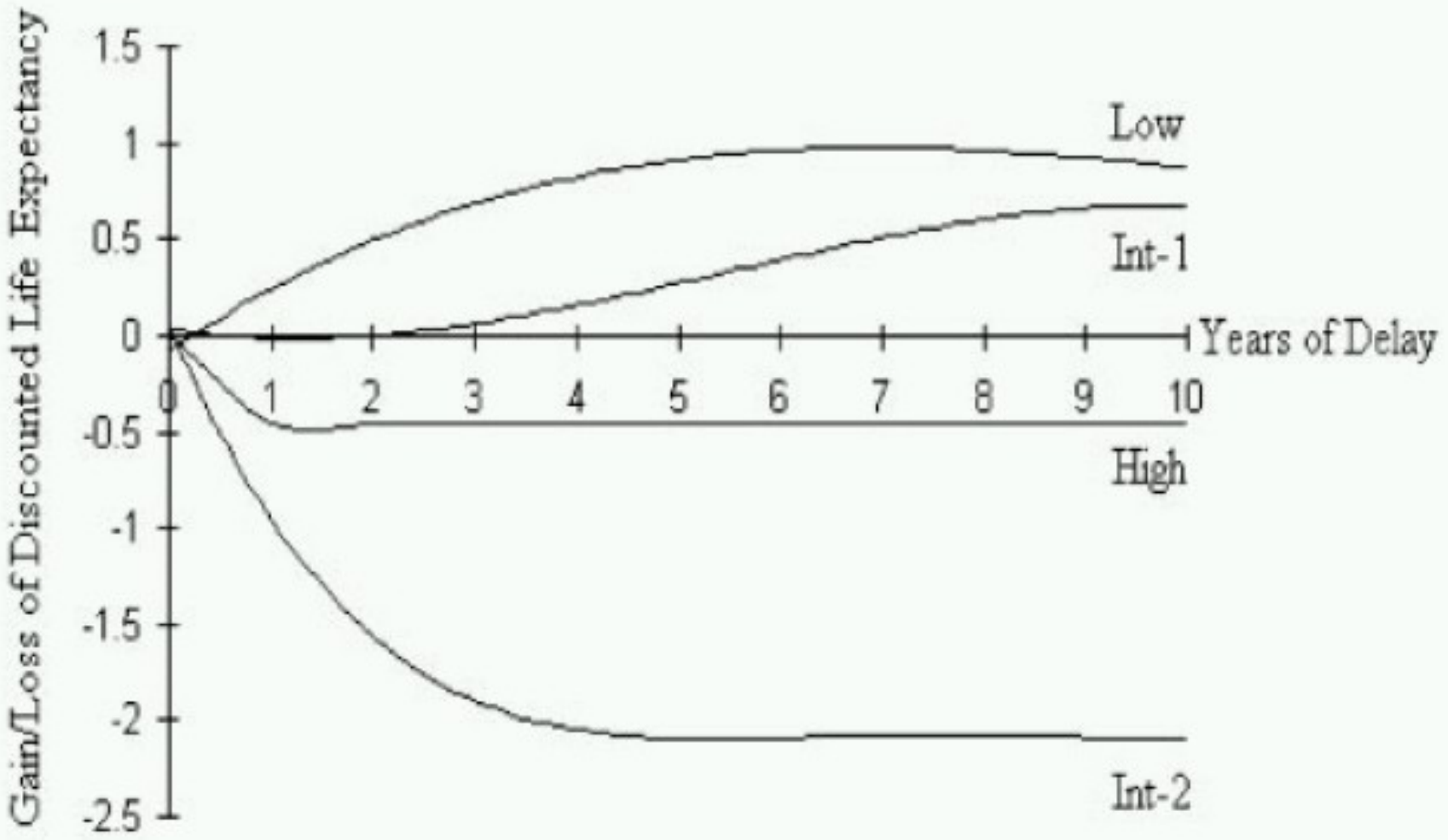
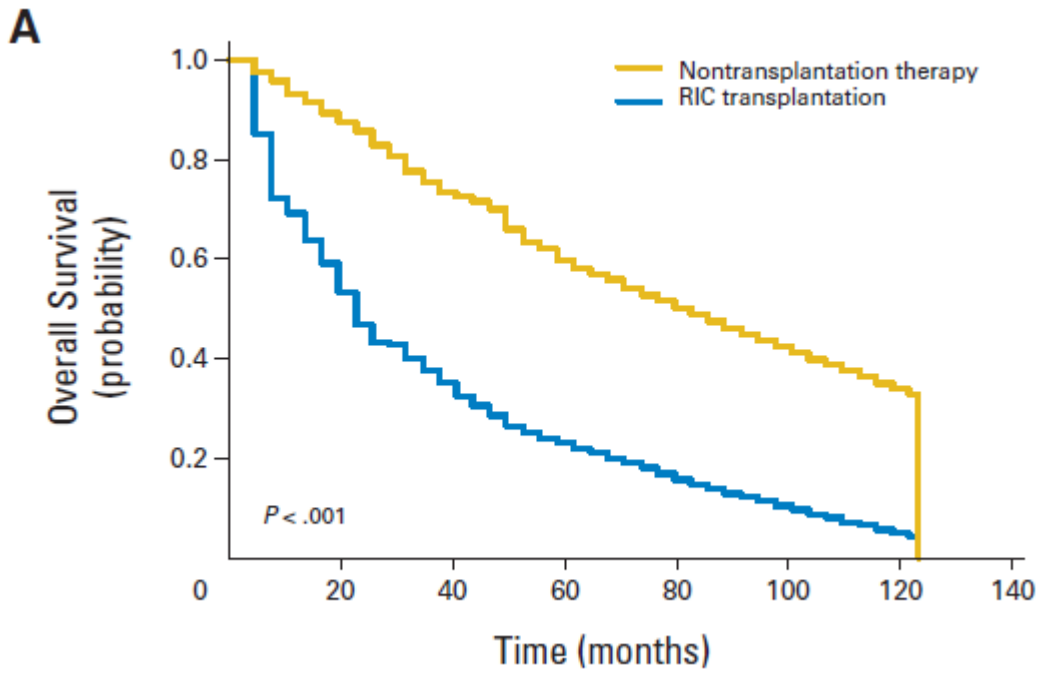


Figure 3. Net benefit or loss of overall discounted life expectancy for the 4 IPSS risk groups are shown above and below the x-axis. A net benefit for delaying transplantation is noted for low and int-1 risk groups, whereas any delay in the time to transplantation is associated with a loss in survivorship in the higher risk groups.

Role of Reduced-Intensity Conditioning Allogeneic Hematopoietic Stem-Cell Transplantation in Older Patients With De Novo Myelodysplastic Syndromes: An International Collaborative Decision Analysis

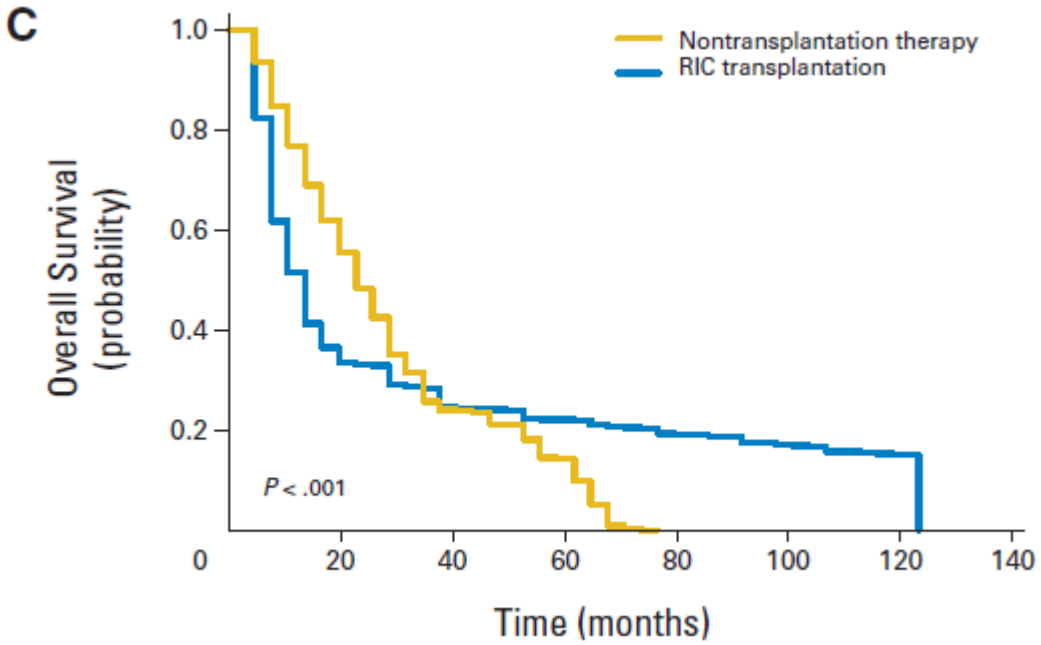


Low and Intermediate-1 risk IPSS patients

survival benefit of the nontransplantation strategy in low/intermediate-1 IPSS MDS

Adapted from Koreth et al. JCO 2013

Role of Reduced-Intensity Conditioning Allogeneic Hematopoietic Stem-Cell Transplantation in Older Patients With De Novo Myelodysplastic Syndromes: An International Collaborative Decision Analysis



Intermediate-2 and high risk IPSS patients

survival benefit of the early RIC transplantation strategy in intermediate-2 and high risk IPSS MDS

Adapted from Koreth et al. JCO 2013

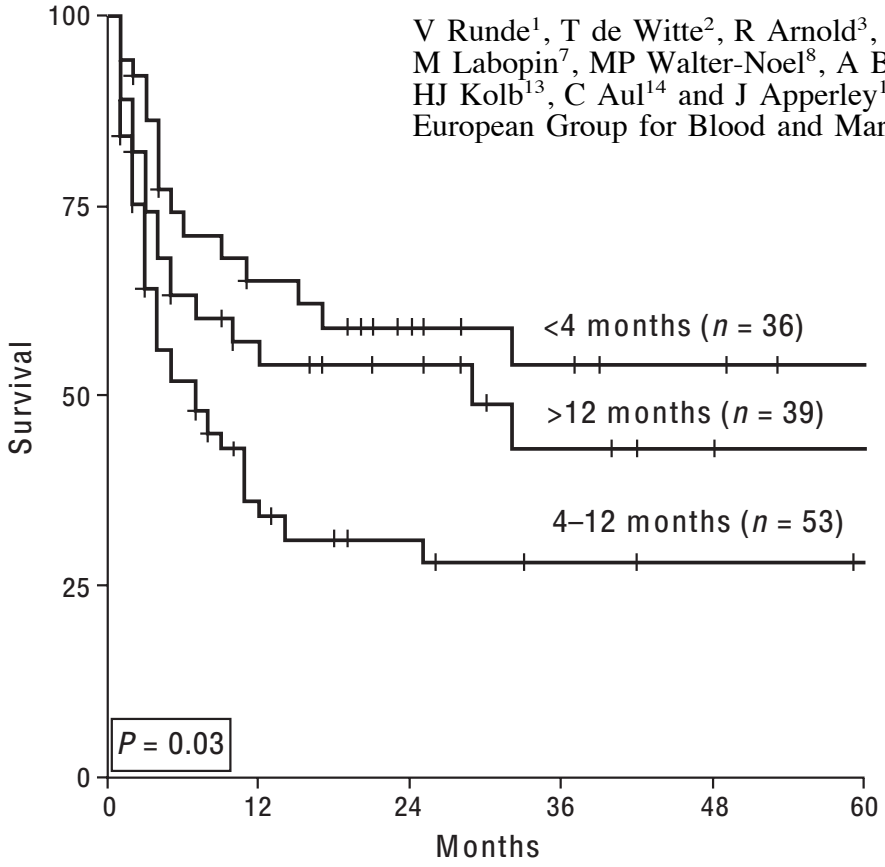
When? Timing of transplantation

- immediate transplantation for Int-2/high-risk pts
- delayed transplantation for Int1/low risk pts until progression (but before transformation to AML)

Early HSCT is associated with improved outcome

Bone marrow transplantation from HLA-identical siblings as first-line treatment in patients with myelodysplastic syndromes: early transplantation is associated with improved outcome

V Runde[1], T de Witte[2], R Arnold[3], A Gratwohl[4], J Hermans[5], A van Biezen[5], D Niederwieser[6], M Labopin[7], MP Walter-Noel[8], A Bacigalupo[9], N Jacobsen[10], P Ljungman[11], E Carreras[12], HJ Kolb[13], C Aul[14] and J Apperley[15] on behalf of the Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation (EBMT)



Bone Marrow Transplantation 1998

HSCT in MDS : for whom, when and how?

- Selection of patients
- Type of transplant (HSC source)
- Treatment before transplant
- Induction regimens/intensity
- Timing of transplant

Stem cell source (PBSC or BM?)

PBSC compared to BM as SC source :

- faster engraftment
- more cGVHD
- lower NRM
- better 2-yrs EFS

Guardiola et al., Blood 2002
Maris et al. Blood 2003
Deeg et al., Blood 2002

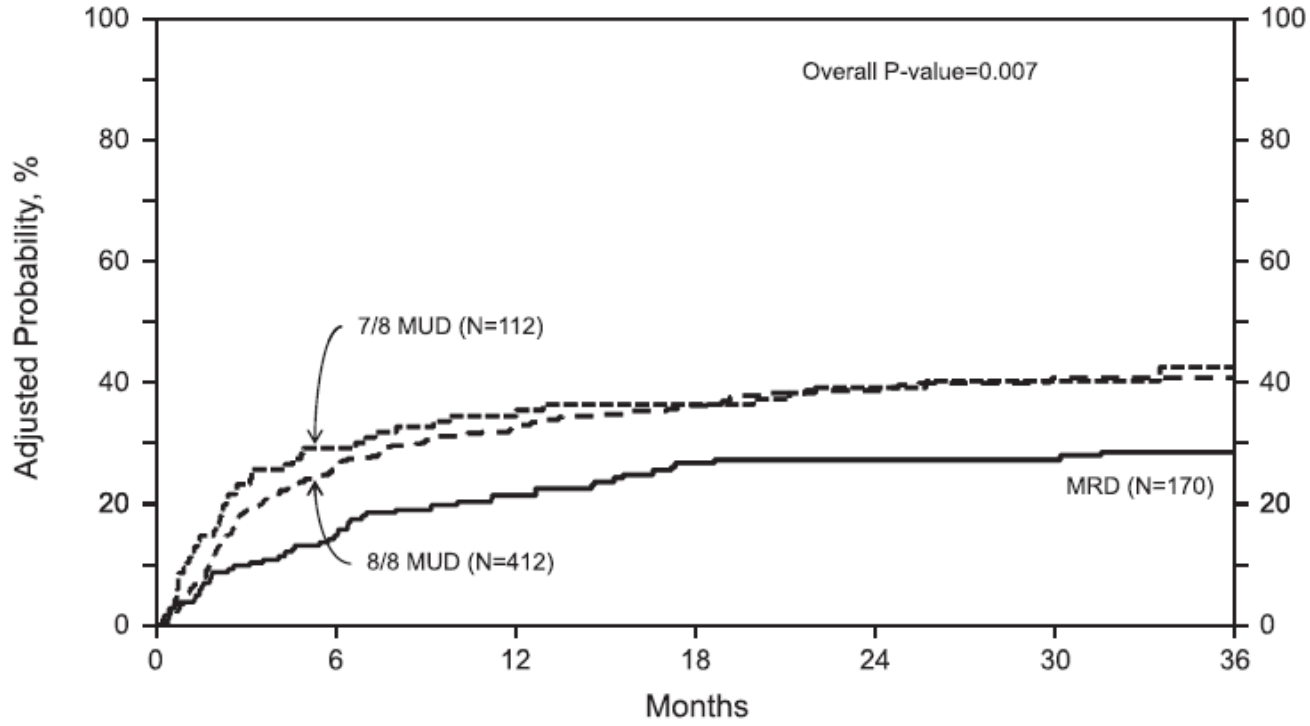
Stem cell donor

- match related donor (MRD)
- match unrelated donor (MUD) 8/8
- match unrelated donor (MUD) 7/8

- **Alternative donors?**
- Cord blood
- Haploidentical donor

Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS)

Wael Saber,[1] Corey S. Cutler,[2] Ryotaro Nakamura,[3] Mei-Jie Zhang,[1] Ehab Atallah,[4] J. Douglas Rizzo,[1] Richard T. Maziarz,[5] Jorge Cortes,[6] Matt E. Kalaycio,[7] and Mary M. Horowitz[1]



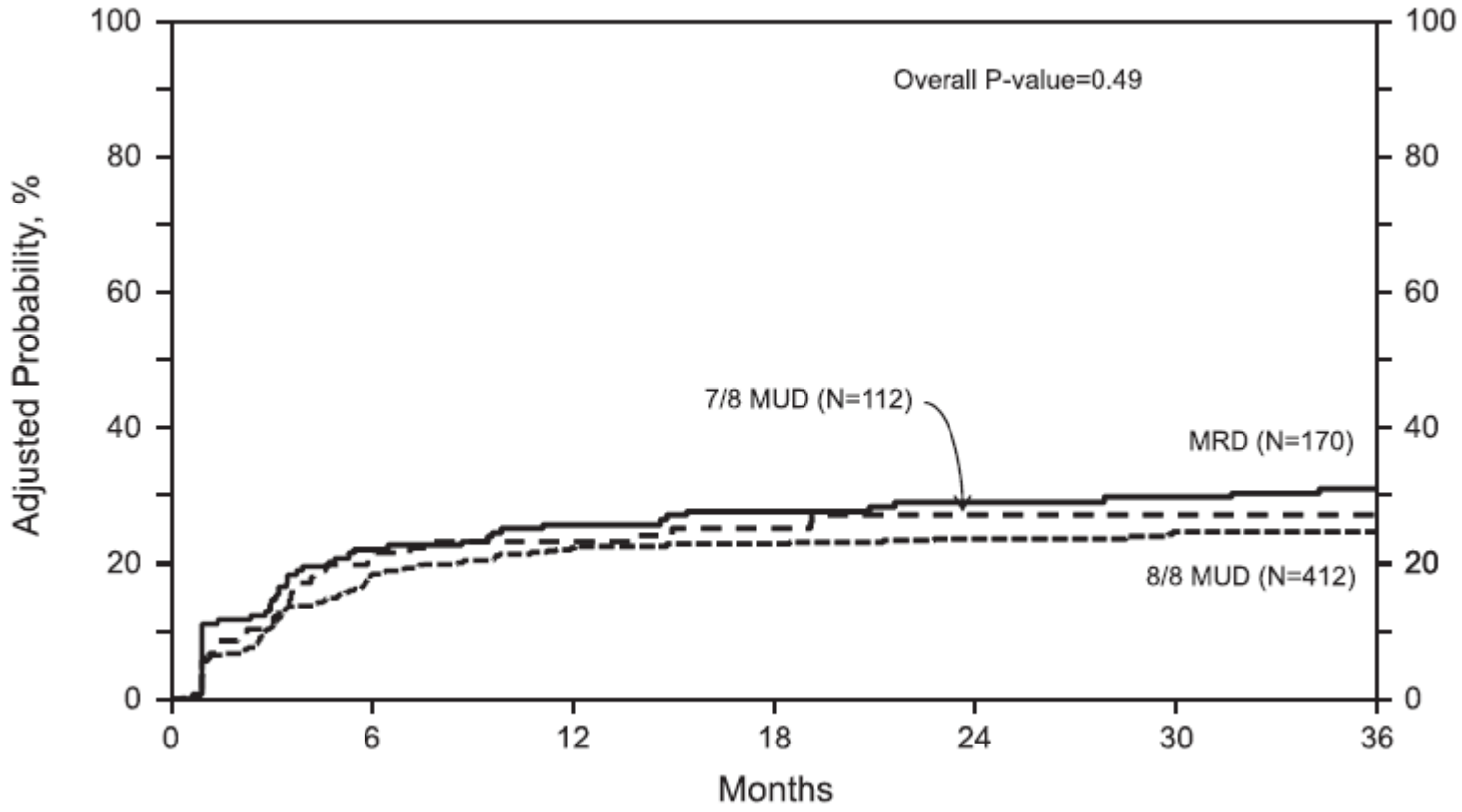
Adjusted probability of **transplant-related mortality** in adult MDS patients by donor source.

MUD= match unrelated donor
MRD= match related donor

Blood 2013;122:1974

Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS)

Wael Saber,[1] Corey S. Cutler,[2] Ryotaro Nakamura,[3] Mei-Jie Zhang,[1] Ehab Atallah,[4] J. Douglas Rizzo,[1] Richard T. Maziarz,[5] Jorge Cortes,[6] Matt E. Kalaycio,[7] and Mary M. Horowitz[1]



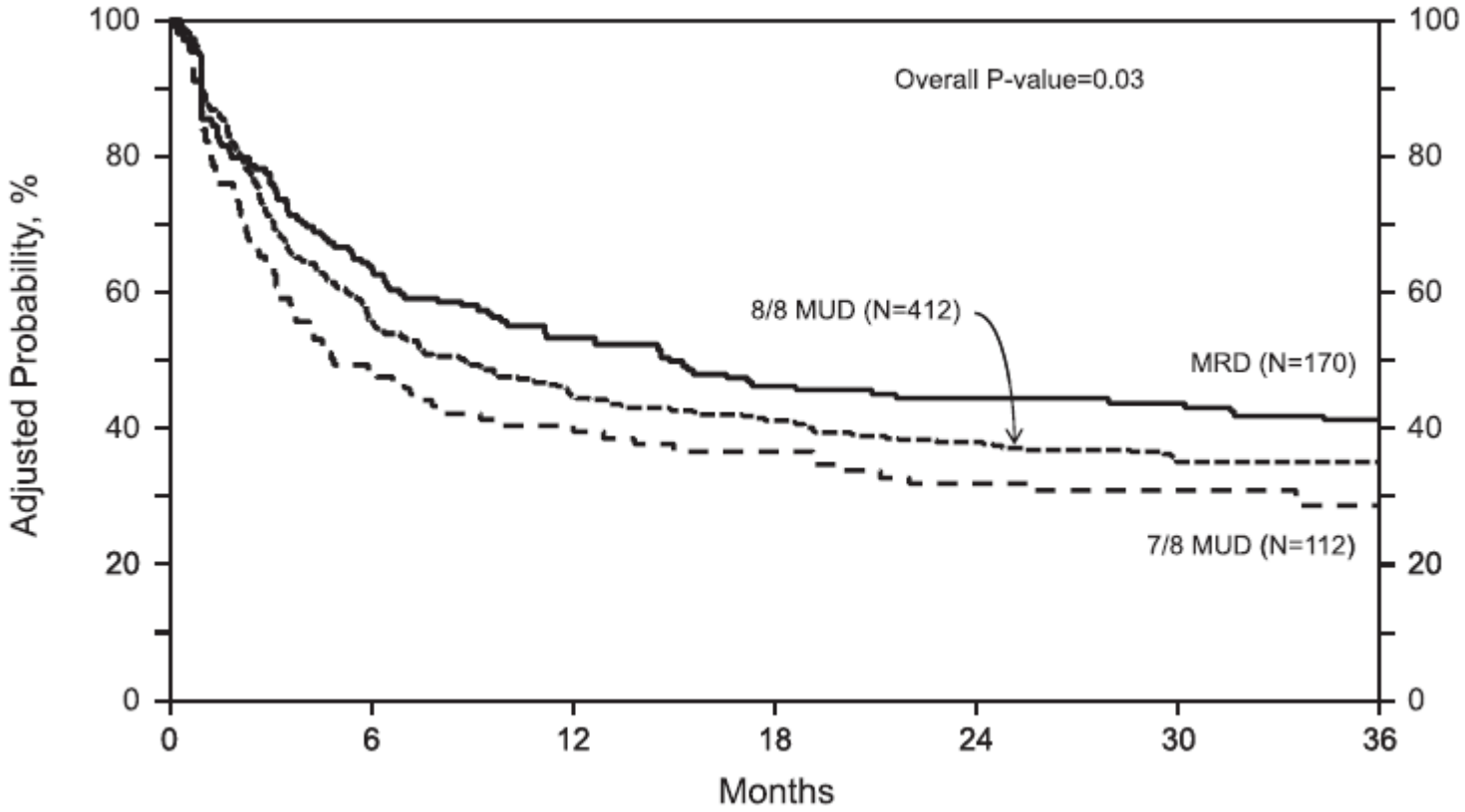
Adjusted probability of **relapse** in adult MDS patients by donor source

MUD= match unrelated donor
MRD= match related donor

Blood 2013;122:1974

Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS)

Wael Saber,[1] Corey S. Cutler,[2] Ryotaro Nakamura,[3] Mei-Jie Zhang,[1] Ehab Atallah,[4] J. Douglas Rizzo,[1] Richard T. Maziarz,[5] Jorge Cortes,[6] Matt E. Kalaycio,[7] and Mary M. Horowitz[1]



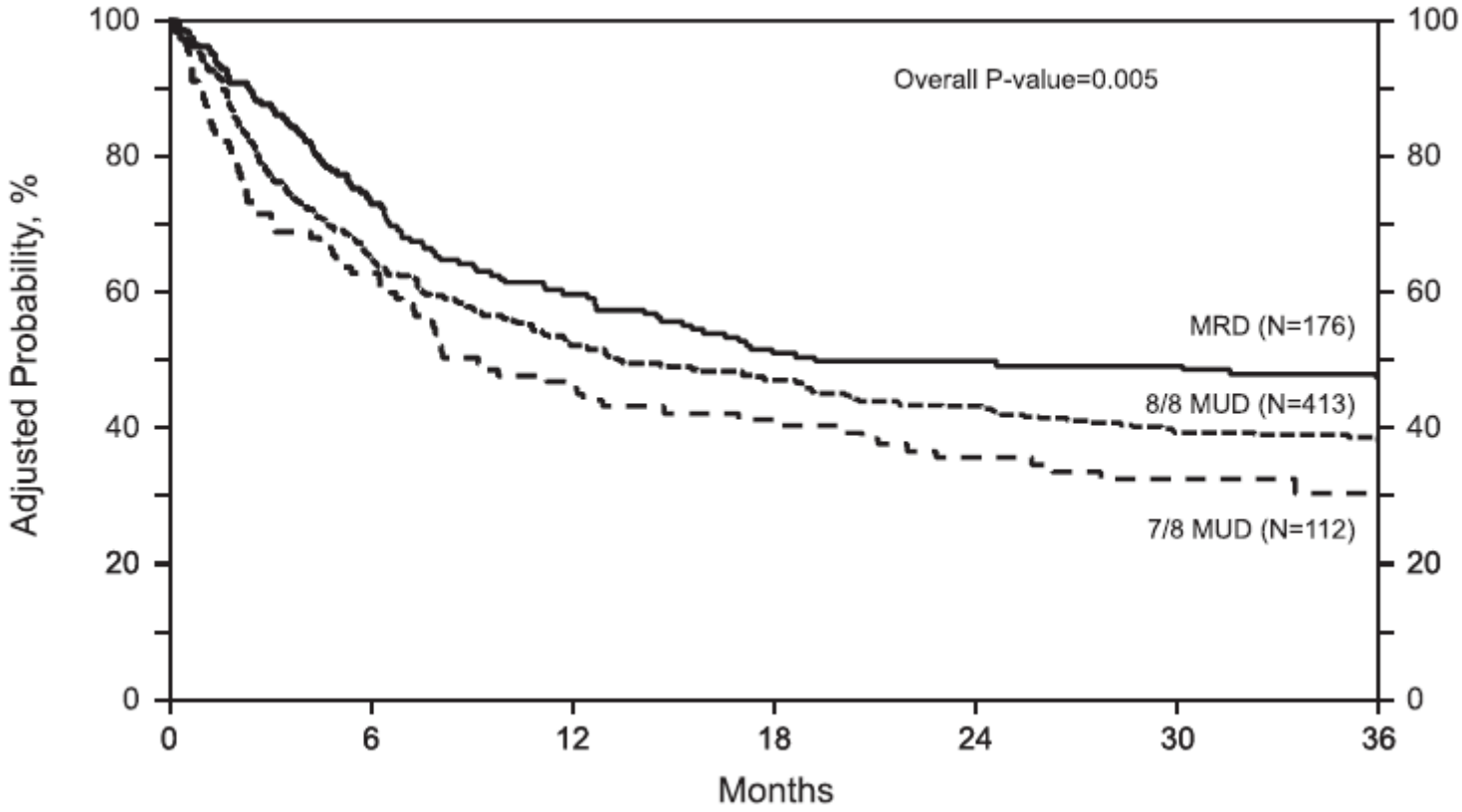
Adjusted probability of **DFS** in 694 adult MDS patients by donor source.

MUD= match unrelated donor
MRD= match related donor

Blood 2013;122:1974

Impact of donor source on hematopoietic cell transplantation outcomes for patients with myelodysplastic syndromes (MDS)

Wael Saber,[1] Corey S. Cutler,[2] Ryotaro Nakamura,[3] Mei-Jie Zhang,[1] Ehab Atallah,[4] J. Douglas Rizzo,[1] Richard T. Maziarz,[5] Jorge Cortes,[6] Matt E. Kalaycio,[7] and Mary M. Horowitz[1]



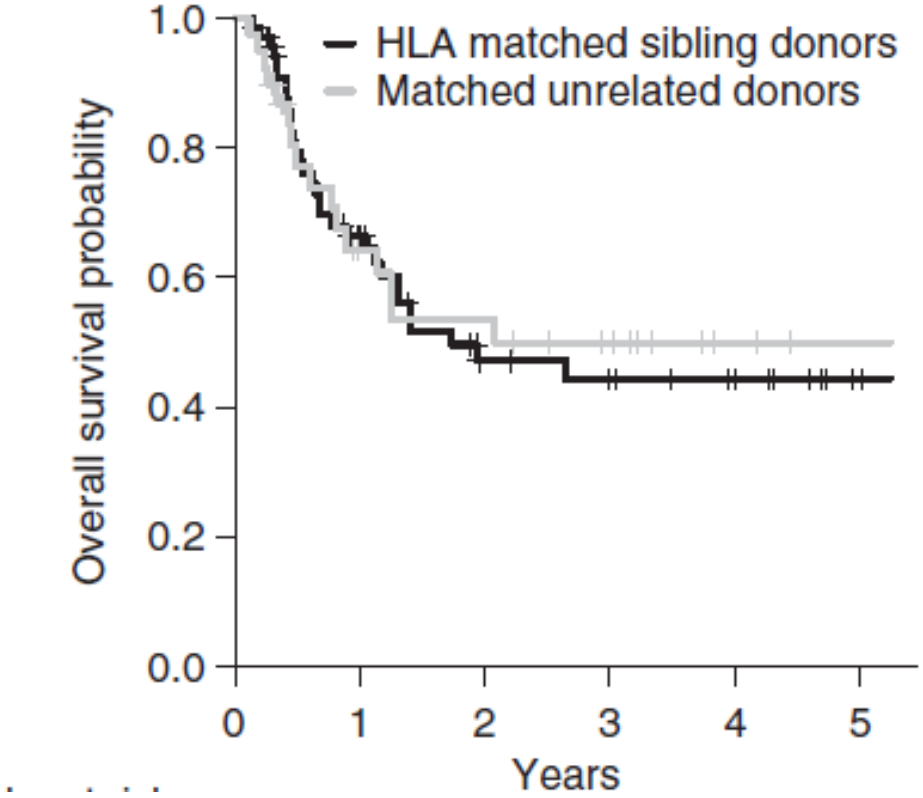
Adjusted probability of **overall survival** in 701 adult MDS patients by donor source.

MUD= match unrelated donor
MRD= match related donor

Blood 2013;122:1974

Matched unrelated or matched sibling donors result in comparable outcomes after non-myeloablative HSCT in patients with AML or MDS

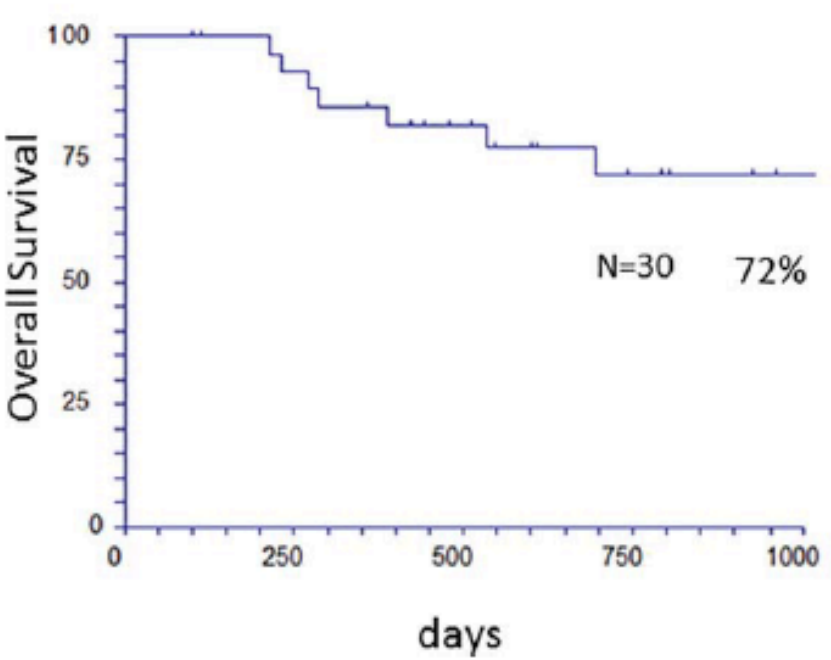
M Robin[1], R Porcher[2], L Adès[3], N Boissel[4], E Raffoux[4], A Xhaard[1], J Larghero[5], C Gardin[3], C Himberlin[6], A Delmer[6], P Fenaux[3], H Dombret[4], G Socié[1,7] and R Peffault de Latour[1,7]

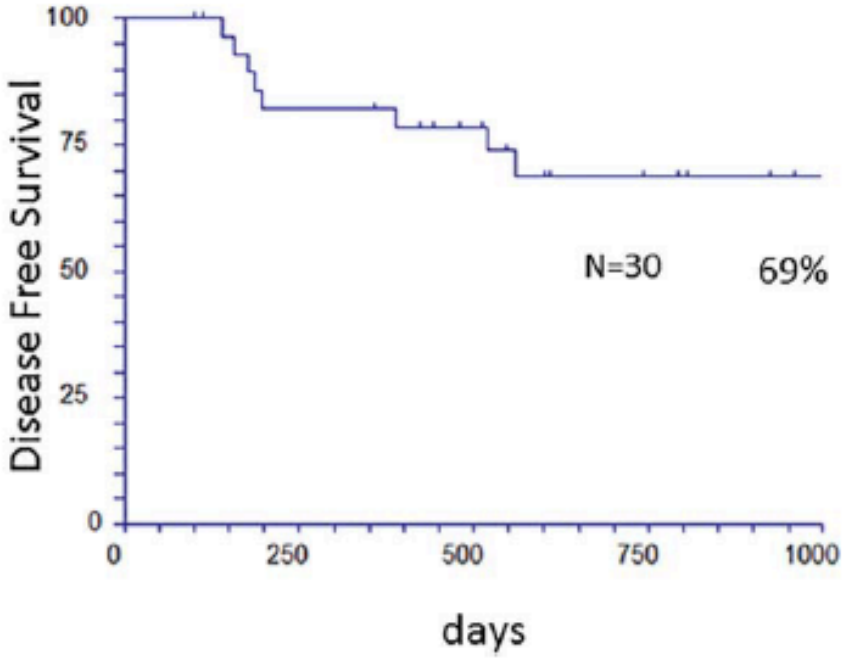


Bone Marrow Transplantation (2013), 1–6

Haploidentical bone marrow transplantation in patients with advanced myelodysplastic syndrome

Varaldo Riccardo[1], Raiola Anna Maria[1], Di Grazia Carmen[1], Aquino Sara[1], Beltrami Germana[1], Bregante Stefania[1], Cruciani Fabio[1], Dominietto Alida[1], Ghiso Anna[1], Giannoni Livia[1], Gualandi Francesca[1], Ibatici Adalberto[1], Lamparelli Teresa[1], Marani Carlo[1], Van Lint Maria Teresa[1], Valeria Santini[2,3], Bacigalupo Andrea[4], Angelucci Emanuele[1,3]





American Journal of Hematology 2017

Pre transplant induction therapy: really needed?

- Chemotherapy for those with high blast count ?(>10%)
- Hypomethylating agents before transplant ?

Hypomethylating agents and transplant

Patients who discontinue 5AC for various reasons have a median survival of only 5.6 months

When 5AC is discontinued because of progressive disease the median survival is 17 months even after HSCT

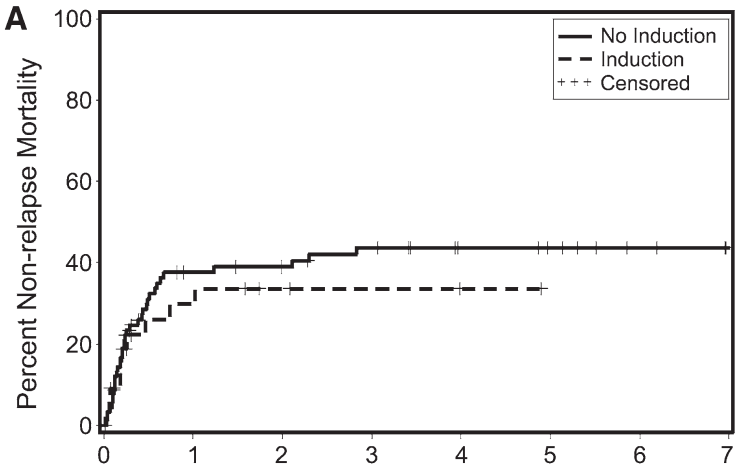
In the study by Prébet et al the median survival was not reached in patients transplanted with stable disease at the time when 5AC was stopped

CONCLUSION: for patients who are transplant candidates HCT should be considered while still responding to hypomethylating therapy

Pretransplantation Induction Chemotherapy and Posttransplantation Relapse in Patients with Advanced Myelodysplastic Syndrome

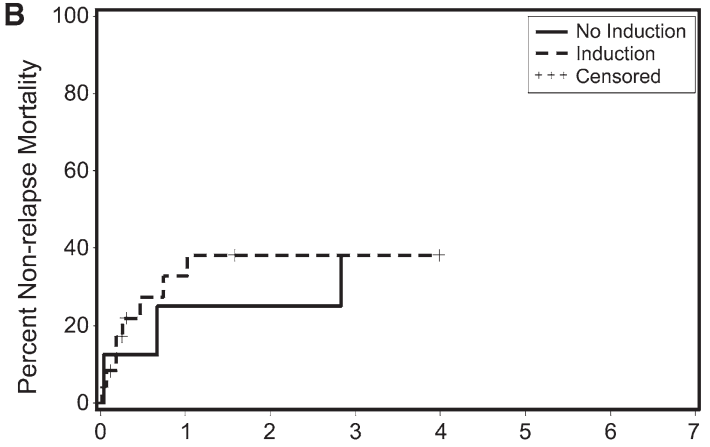
Bart L. Scott,[1,2] Barry Storer,[1,2] Michael R. Loken,[3] Rainer Storb,[1,2] Frederick R. Appelbaum,[1,2] H. Joachim Deeg[1,2]

[1]Fred Hutchinson Cancer Research Center; [2]University of Washington School of Medicine; and [3]Hematologics Inc., Seattle, Washington

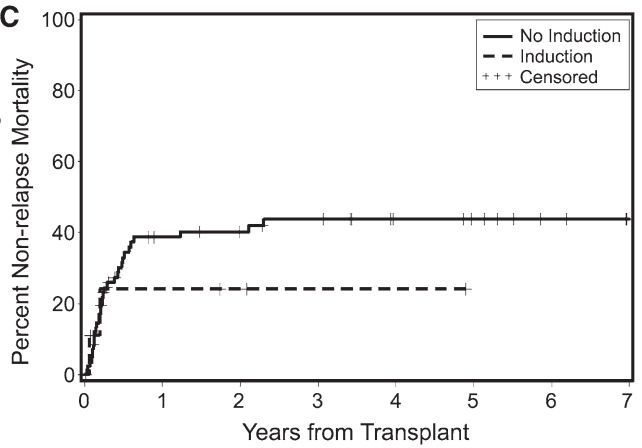


125 MDS patients
33 chemotherapy
92 no chemotherapy

32 S-AML
24 CHT
8 no CHT



93 RAEB/RAEB-T
9 CHT
62 no CHT

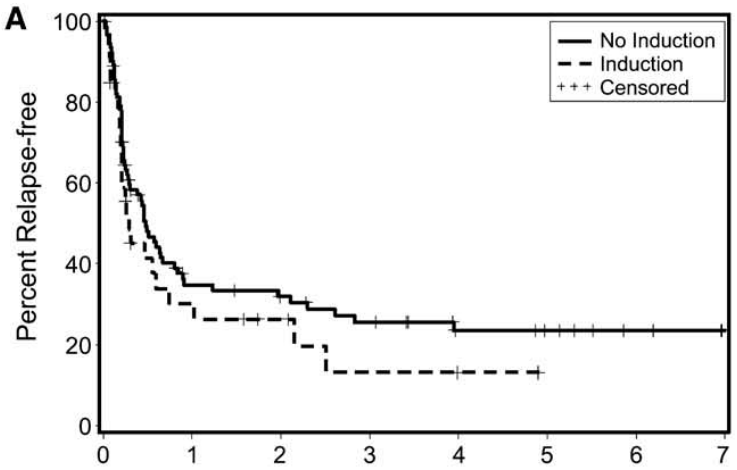


. Biology of Blood and Marrow Transplantation 11:65-73 (2005)

Pretransplantation Induction Chemotherapy and Posttransplantation Relapse in Patients with Advanced Myelodysplastic Syndrome

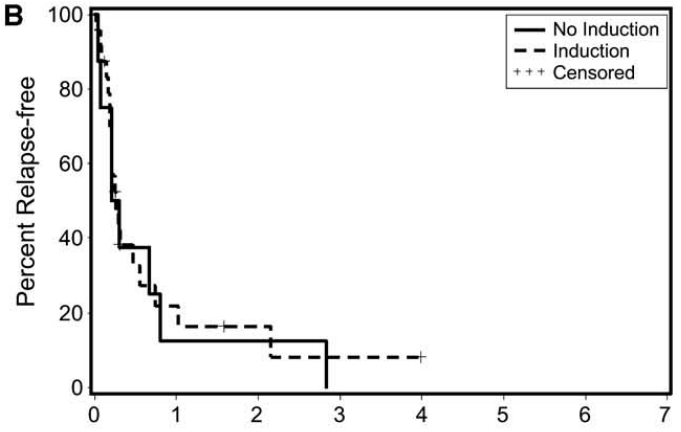
Bart L. Scott,[1,2] Barry Storer,[1,2] Michael R. Loken,[3] Rainer Storb,[1,2] Frederick R. Appelbaum,[1,2] H. Joachim Deeg[1,2]

[1]Fred Hutchinson Cancer Research Center; [2]University of Washington School of Medicine; and [3]Hematologics Inc., Seattle, Washington

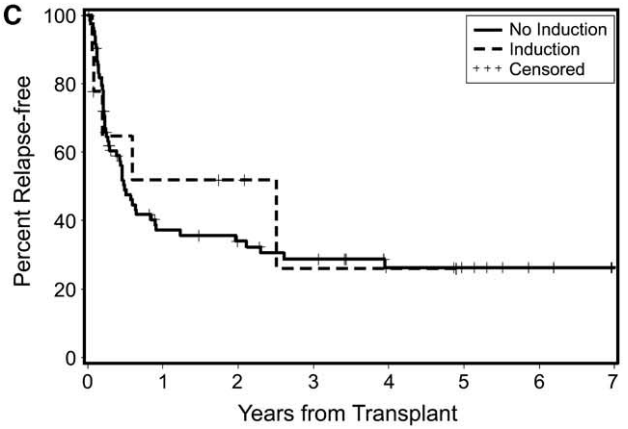


125 MDS patients
33 chemtorapy
92 no chemotherapy

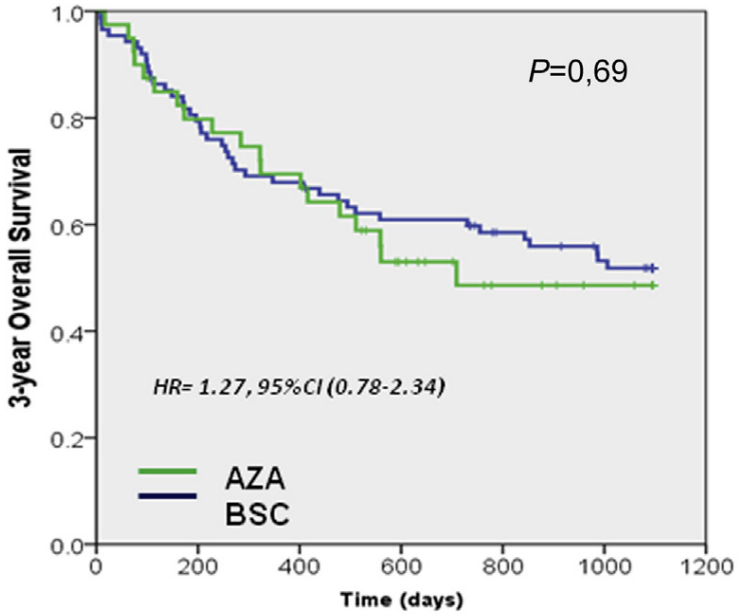
32 S-AML
24 CHT
8 no CHT

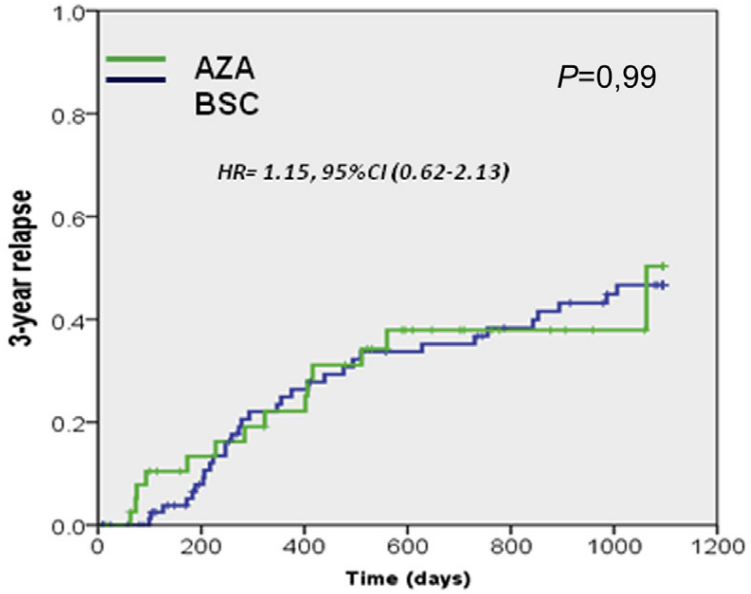


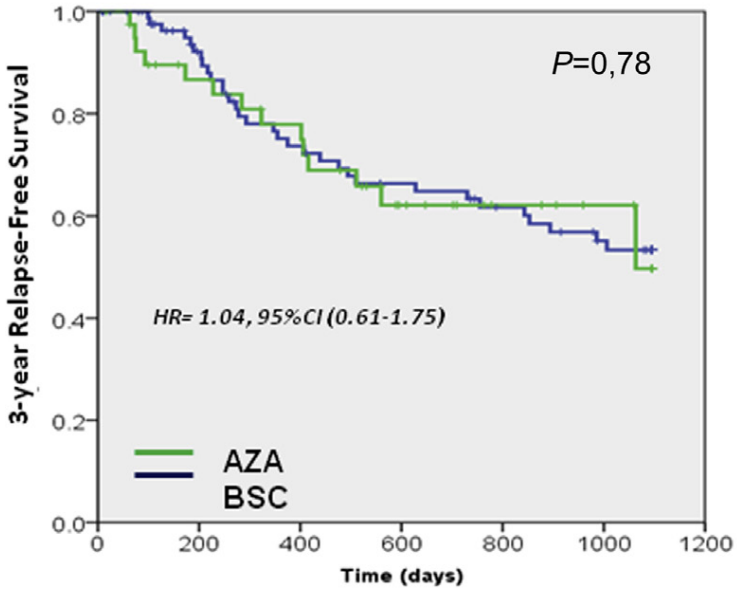
93 RAEB/RAEB-T
9 CHT
62 no CHT

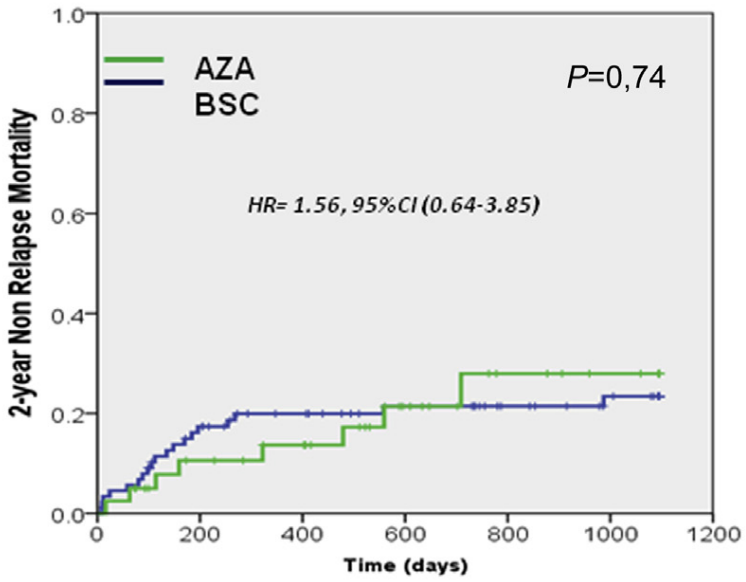


. Biology of Blood and Marrow Transplantation 11:65-73 (2005)





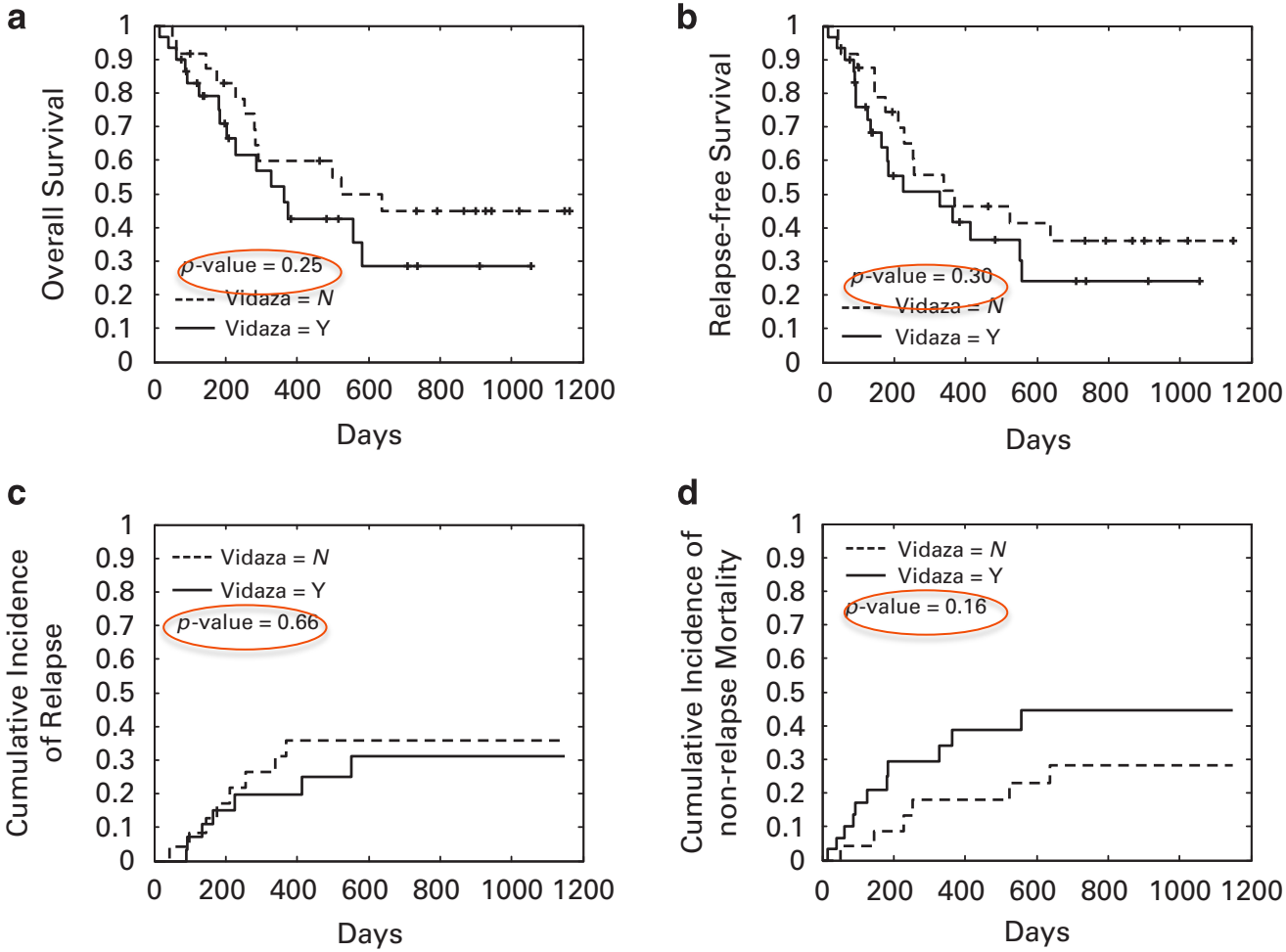




Damaj et al. Biol Blood and Marrow Transpl 2014

5-Azacitidine for myelodysplasia before allogeneic hematopoietic cell transplantation

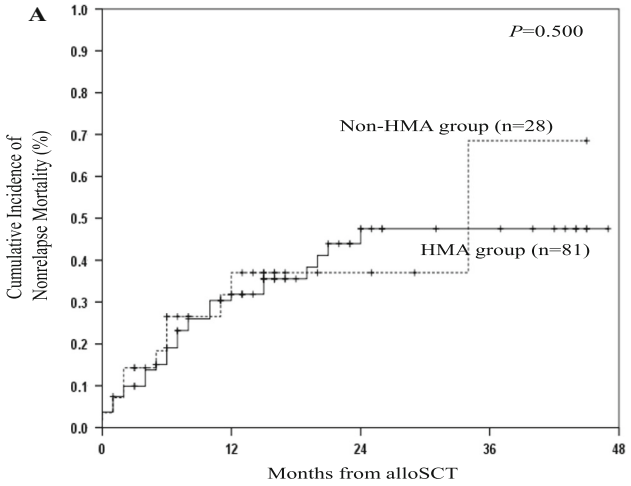
T Field[1], J Perkins[1], Y Huang[2], MA Kharfan-Dabaja[1], M Alsina[1], E Ayala[1], HF Fernandez[1], W Janssen[1], J Lancet[3], L Perez[1], D Sullivan[1], A List[3] and C Anasetti[1]



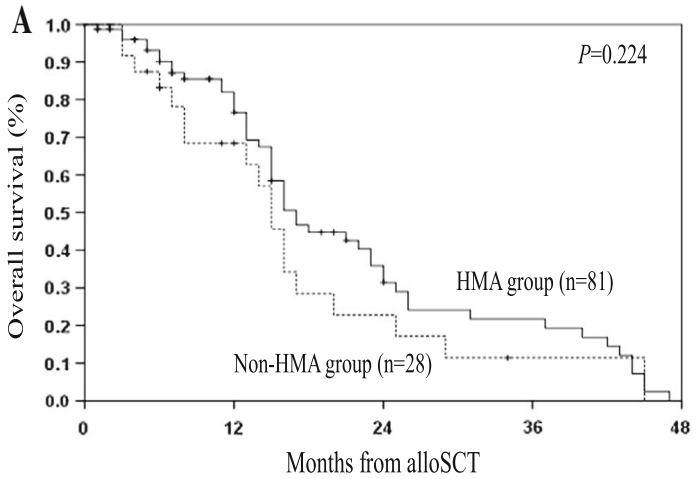
54 patients
30 AZA
24 no AZA

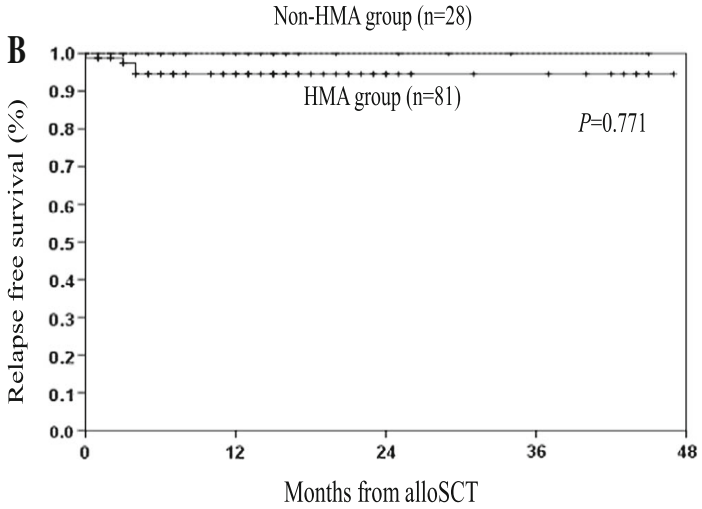
Bone Marrow Transplantation (2010) 45, 255–260

Multicenter study evaluating the impact of hypomethylating agents as bridging therapy to hematopoietic stem cell transplantation in myelodysplastic syndromes



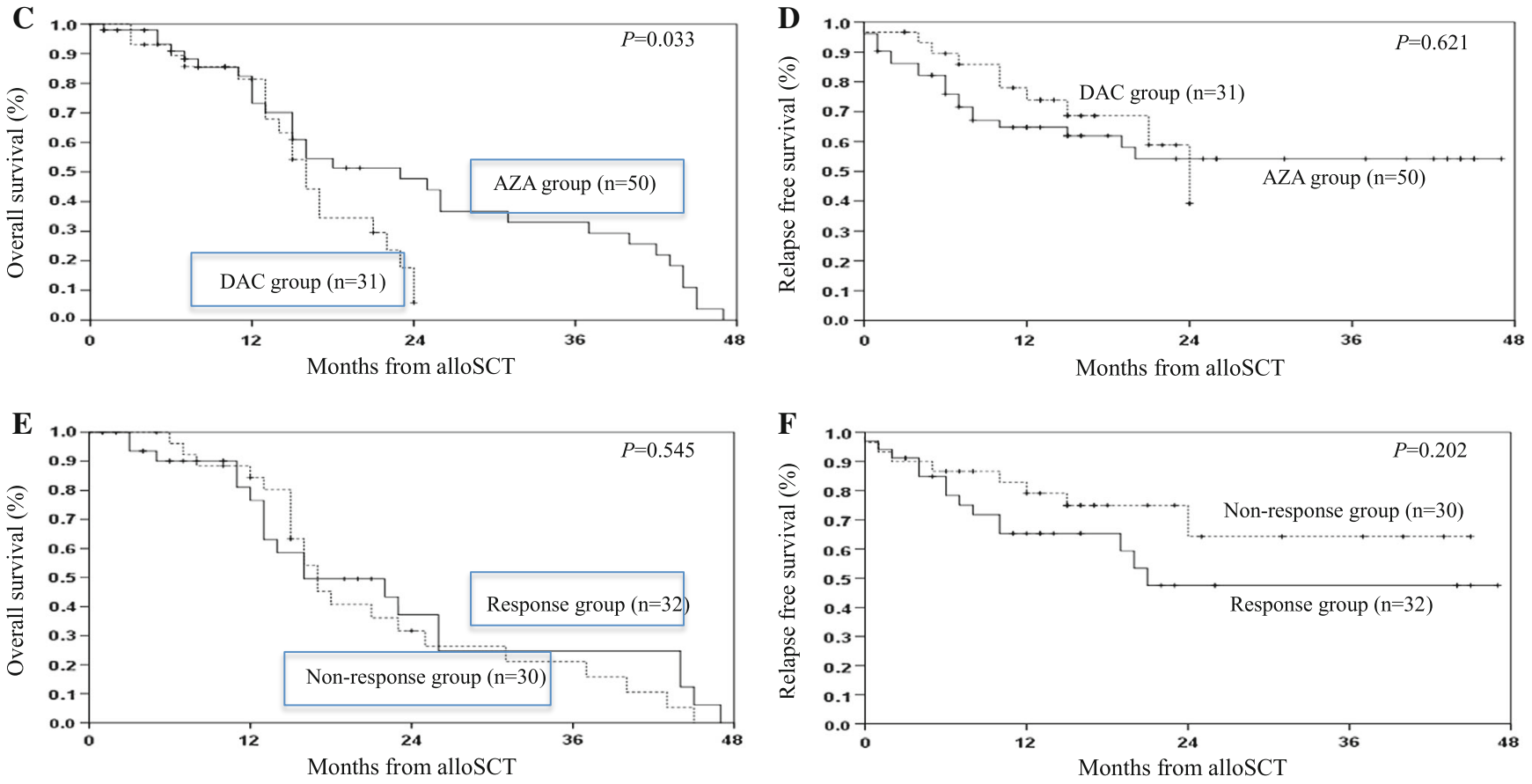
109 patients
81 HMA
28 no HMA





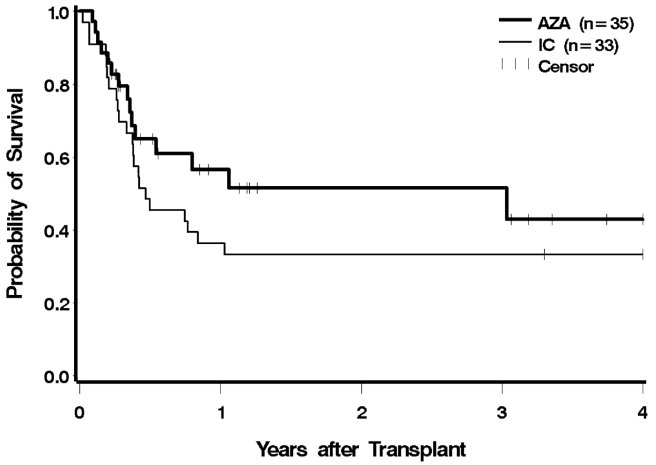
Kim et al . Int J Hemtol 2014

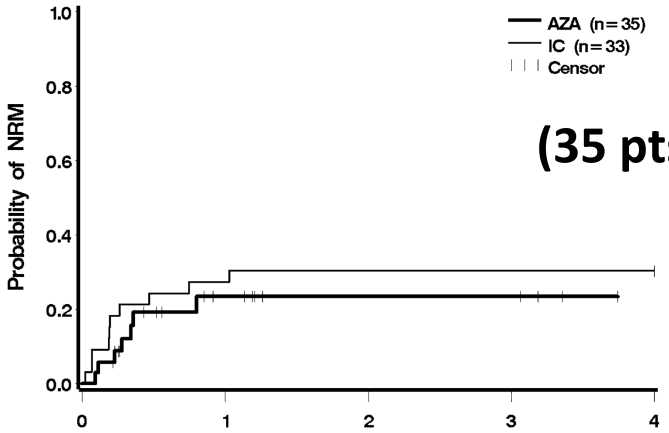
OS and RFS according to HMA treatment group



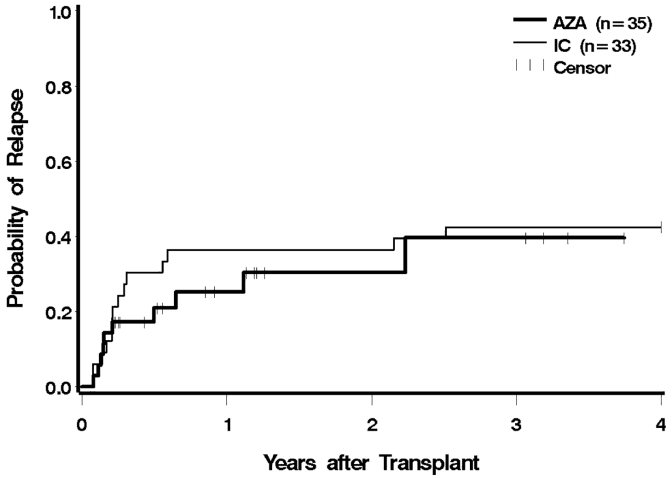
Kim et al . Int J Hemtol 2014

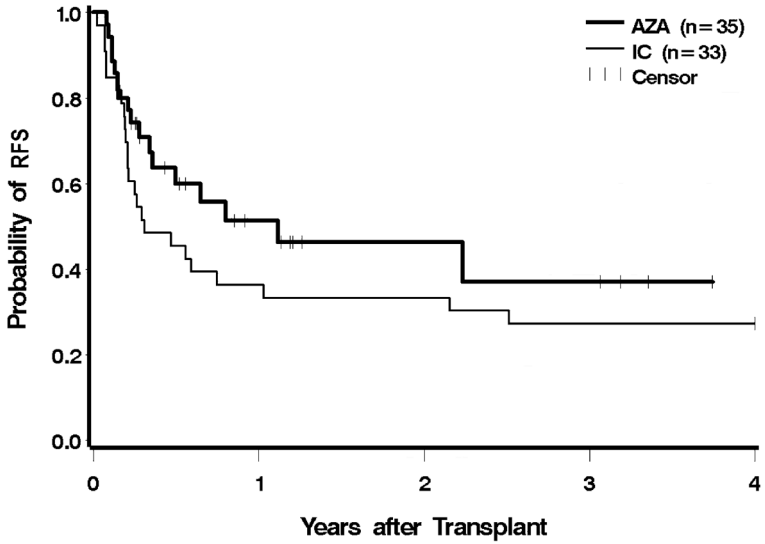
Azacitidine vs induction chemotherapy before HSCT: Seattle retrospective data in 68 patients





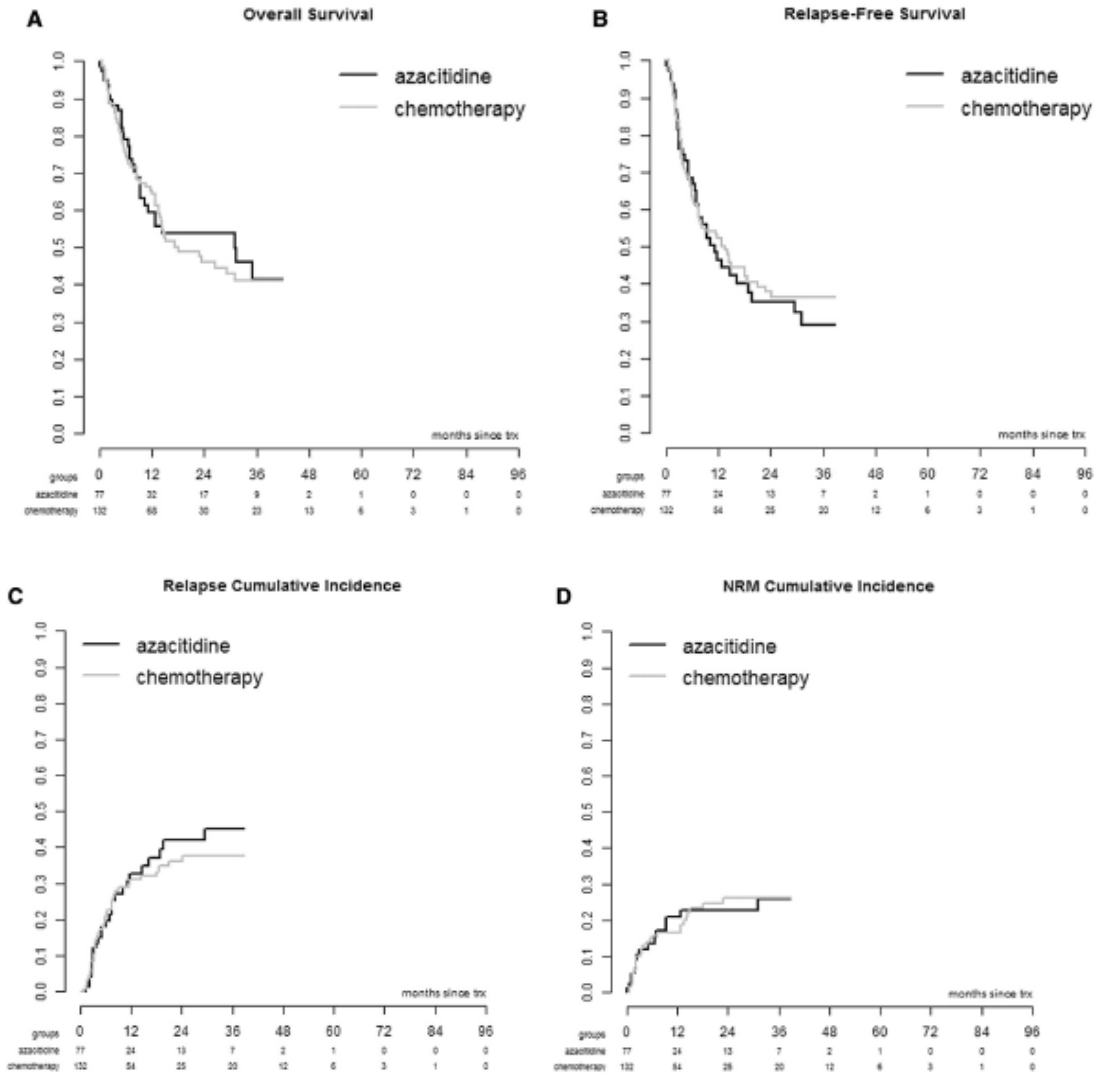
(35 pts AZA, 33 IC)





Gerds A.T.et al. Biol Blood Marrow Transpl. 2012

Comparison of Intensive Chemotherapy and Hypomethylating Agents before Allogeneic Stem Cell Transplantation for Advanced Myelodysplastic Syndromes: A Study of the Myelodysplastic Syndrome Subcommittee of the Chronic Malignancies Working Party of the European Society for Blood and Marrow Transplant Research



Biol Blood Marrow Transplant 22 (2016)

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

2014

Cytogenetics, Donor Type, and Use of Hypomethylating Agents in Myelodysplastic Syndrome with Allogeneic Stem Cell Transplantation

Betul Oran [1,*], Piyanuch Kongtim [1], Uday Popat [1], Marcos de Lima [1], Elias Jabbour [2], Xinyan Lu [3], Julien Chen [1], Gabriella Rondon [1], Partow Kebriaei [1], Sairah Ahmed [1], Borje Andersson [1], Amin Alousi [1], Stefan Ciurea [1], Elizabeth Shpall [1], Richard E. Champlin [1]

256 MDS patients at the **MD Anderson Cancer Centres**

40 (15.6%) chemotherapy

122 (47.7%) HMA

16 (6.2%) Chemo+HMA

Variable	RI		TRM		EFS		OS	
	HR	*P* Value	HR	*P* Value	HR	*P* Value	HR	*P* Value
Age, per 10 yr	1.06	.50	1.4	.002	1.3	.002	1.3	.002
WHO histological subtype								
Low/intermediate	Ref		Ref		Ref		Ref	
High risk	2.0	.02	1.0	.90	1.6	.02	1.5	.05
CMML	1.5	.30	1.4	.40	1.6	.10	1.5	.20
MDS-U	1.0	.90	1.4	.20	1.3	.20	1.3	.20
T-MDS	1.4	.10	1.2	.40	1.5	.02	1.5	.01
Cytogenetics by 5-group risk								
Very good/good	Ref		Ref		Ref		Ref	
Intermediate	1.2	.70	1.4	.40	1.4	.20	1.3	.30
Poor	1.4	.40	1.2	.50	1.4	.20	1.6	.06
Very poor	3.9	<.0001	1.1	.60	3.4	<.0001	3.3	<.0001
MK								
CN	Ref		Ref		Ref		Ref	
MK−	1.2	.50	1.4	.20	1.5	.06	1.6	.03
MK+	4.1	<.0001	1.2	.50	3.7	<.0001	3.7	<.0001
Previous therapy for MDS								
Untreated	Ref		Ref		Ref		Ref	
Chemo only	1.1	.70	1.5	.30	1.4	.20	1.4	.20
HMA only	1.0	.90	1.5	.10	1.3	.20	1.4	.10
Chemo+HMA	.8	.70	1.8	.20	1.2	.50	1.5	.30
Response by IWG at HSCT								
CR	Ref		Ref		Ref		Ref	
AD	.8	.30	1.7	.10	1.1	.50	1.3	.20
Untreated	.8	.50	1.0	.90	.8	.50	.9	.60
Cytogenetic remission								
Yes	Ref		Ref		Ref		Ref	
No	1.2	.60	1.0	.90	1.3	.20	1.5	.10
BM blast at HSCT								
<5%	ref		Ref		Ref		Ref	
≥5%	2.0	.01	.9	.80	1.6	.006	1.6	.006
Ferritin level								
≤1130	Ref		Ref		Ref		Ref	
>1130	1.0	.80	2.0	.009	1.6	.01	2.0	.001
Missing	1.7	.06	1.2	.60	1.5	.05	1.7	.02
Stem cell source								
PB	Ref		Ref		Ref		Ref	
BM	.9	.90	1.4	.20	1.2	.30	1.3	.10
Donor source								
MRD	ref		Ref		ref		Ref	
MUD	.7	.20	1.7	.02	1.2	.30	1.4	.06
Conditioning regimen								
MAC	Ref		Ref		ref			
RIC	.6	.05	2.1	.001	1.2	.20	1.2	.40
Time to transplantation after diagnosis								
≤8 months	Ref		Ref		ref			
>8 months	.6	.03	1.2	.50	.8	.10	.8	.10
Transplantation yr								
Before 2005	Ref		Ref		Ref		Ref	
After 2005	.8	.30	.8	.40	.7	.10	.7	.10

Best conditioning regimens

The ideal regimen would have no associated toxicity and prevent relapse in all patients, but….

- the extent of toxicity correlates with conditioning intensity

- RIC regimens are associated with minimal toxicity, but they carry a higher risk of relapse than high-intensity regimens

Major advantage of RIC: possibility of applying HCT to older patients, who are unlikely to tolerate high dose therapy.

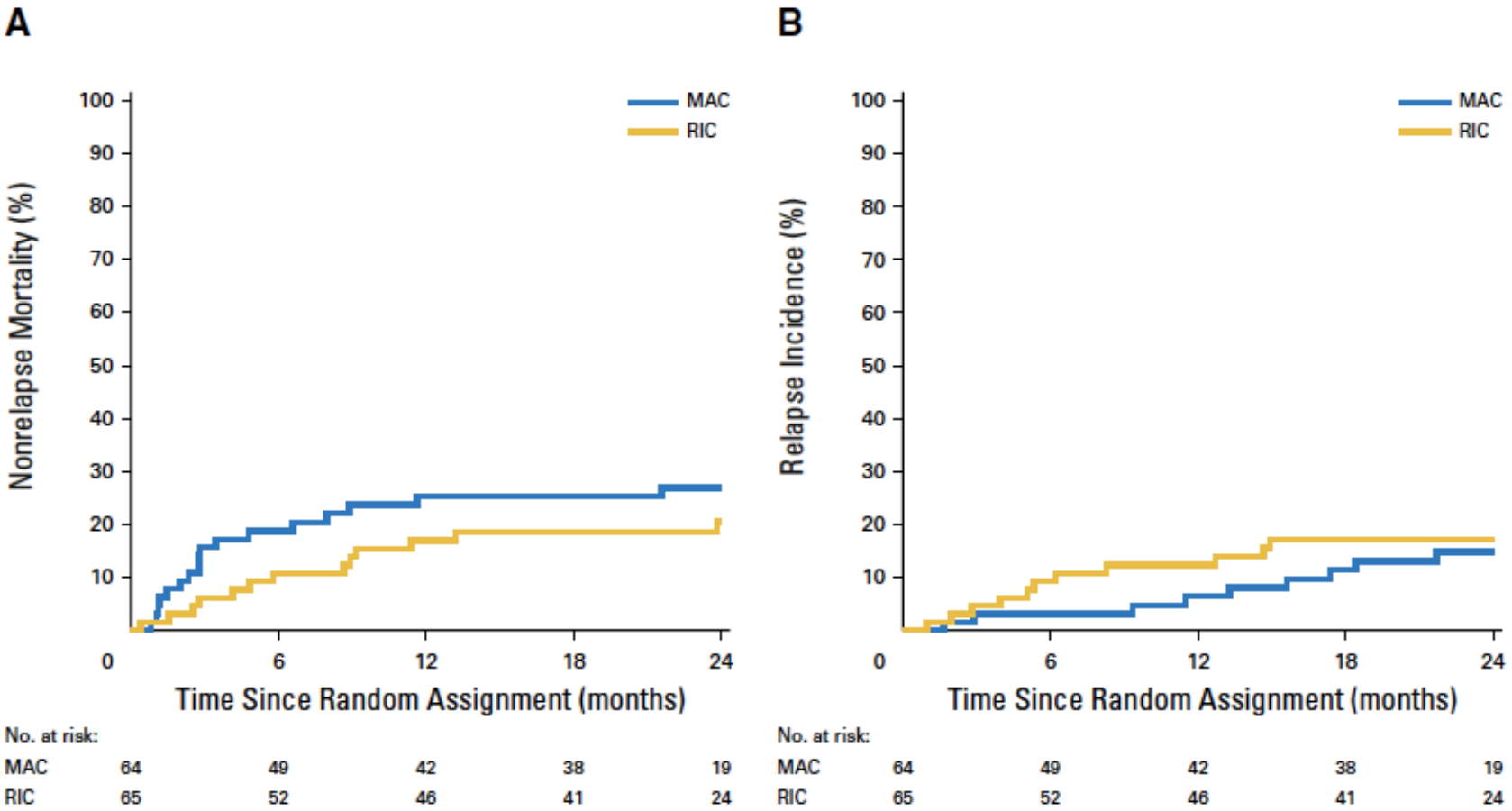
patients more than 60-65 years of age or pts with significant comorbid conditions should receive RIC regimens.

Poor cytogenetyc risk should receive intensification of the conditioning regimen because of the high risk of relapse

Dose-Reduced Versus Standard Conditioning Followed by Allogeneic Stem-Cell Transplantation for Patients With Myelodysplastic Syndrome: A Prospective Randomized Phase III Study of the EBMT (RICMAC Trial)

JCO 2017

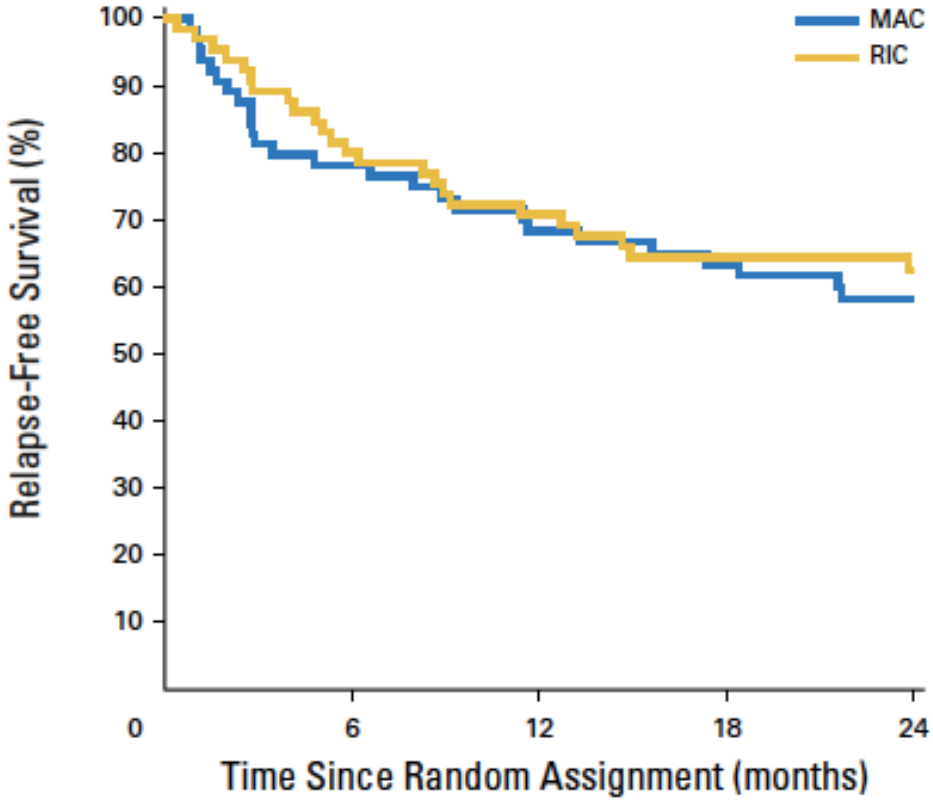
Nicolaus Kröger, Simona Iacobelli, Georg-Nikolaus Franke, Uwe Platzbecker, Ruzena Uddin, Kai Hübel, Christof Scheid, Thomas Weber, Marie Robin, Matthias Stelljes, Boris Afanasyev, Dominik Heim, Giorgio Lambertenghi Deliliers, Francesco Onida, Peter Dreger, Massimo Pini, Stefano Guidi, Liisa Volin, Andreas Günther, Wolfgang Bethge, Xavier Poiré, Guido Kobbe, Marleen van Os, Ronald Brand, and Theo de Witte



Conclusion

This prospective, randomized trial of the European Society of Blood and Marrow Transplantation provides evidence that RIC resulted in at least a 2-year relapse-free survival and overall survival similar to MAC in patients with MDS or secondary acute myeloid leukemia.

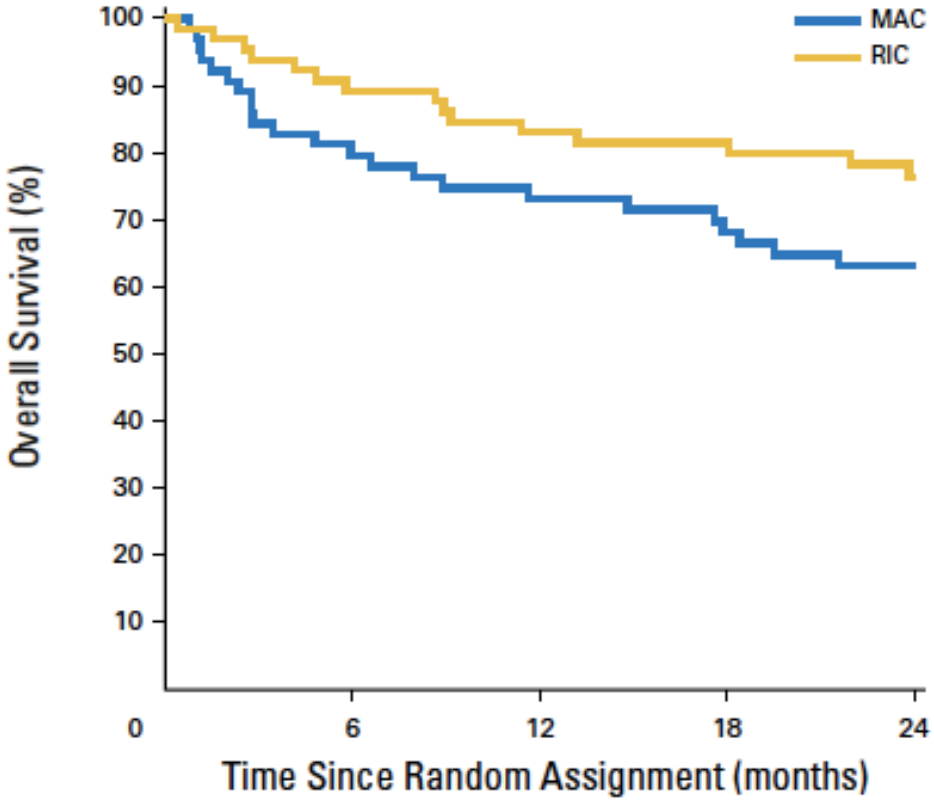
C



No. at risk:

MAC	64	49	42	38	19
RIC	65	52	46	41	24

D



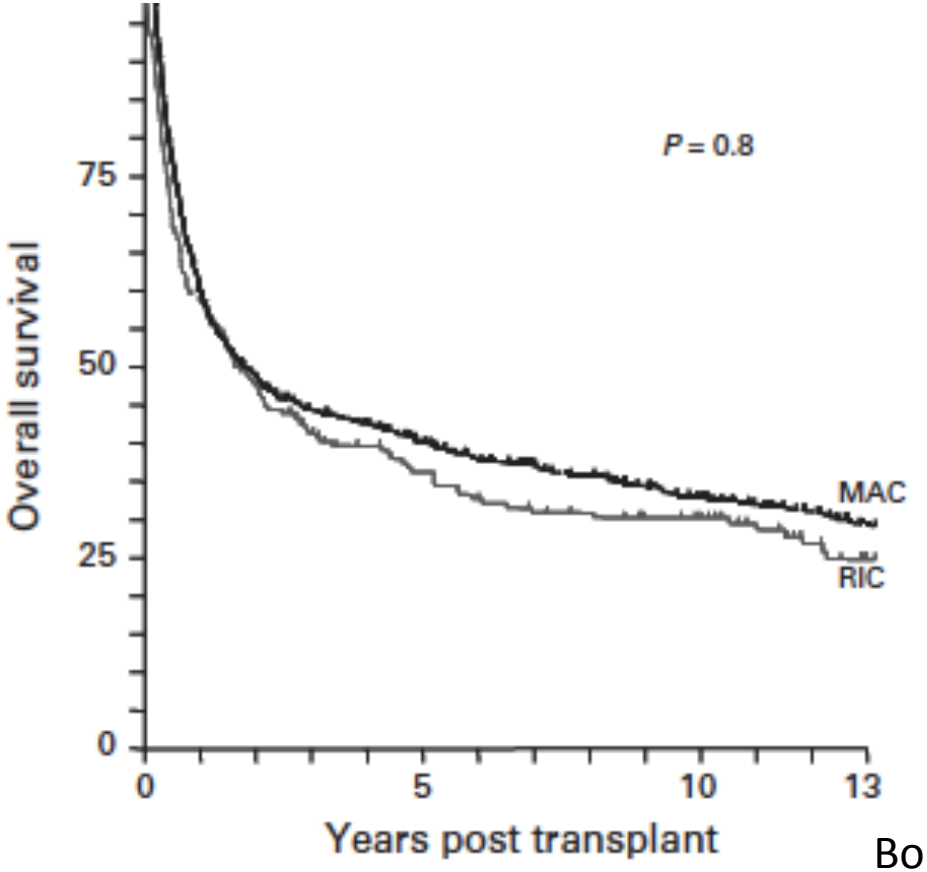
No. at risk:

MAC	64	50	45	41	22
RIC	65	58	54	52	31

Kroger JCO 2017

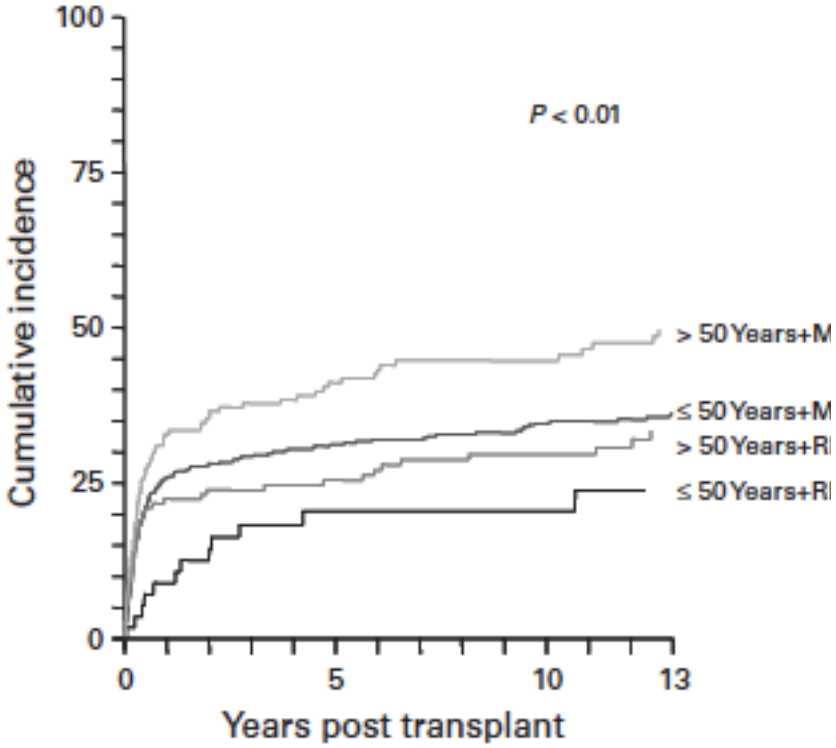
Long-term follow-up of a retrospective comparison of reduced-intensity conditioning and conventional high-dose conditioning for allogeneic transplantation from matched related donors in myelodysplastic syndromes

R Martino[1], A Henseler[2], M van Lint[3], N Schaap[4], J Finke[5], D Beelen[6], S Vigouroux[7], EP Alessandrino[8], GJ Mufti[9], JH Veelken[10], B Bruno[11], I Yakoub-Agha[12], L Volin[13], J Maertens[14], R Or[15], V Leblond[16], M Rovira[17], P Kalhs[18], AF Alvarez[19], A Vitek[20], J Sierra[1], E Wagner[21], M Robin[22], T de Witte[4] and N Kröger[23] for the Myelodysplastic Syndrome subcommittee of the Chronic Malignancies Working Party of the European Blood and Marrow Transplantation Group

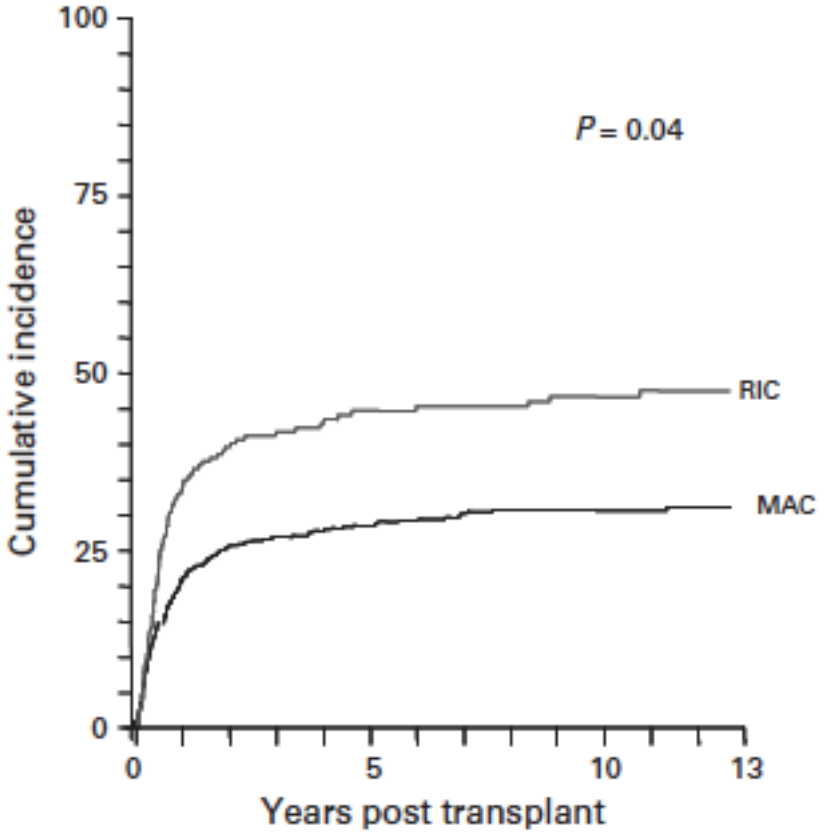


Bone Marrow Transplantation (2017), 1–6

NRM

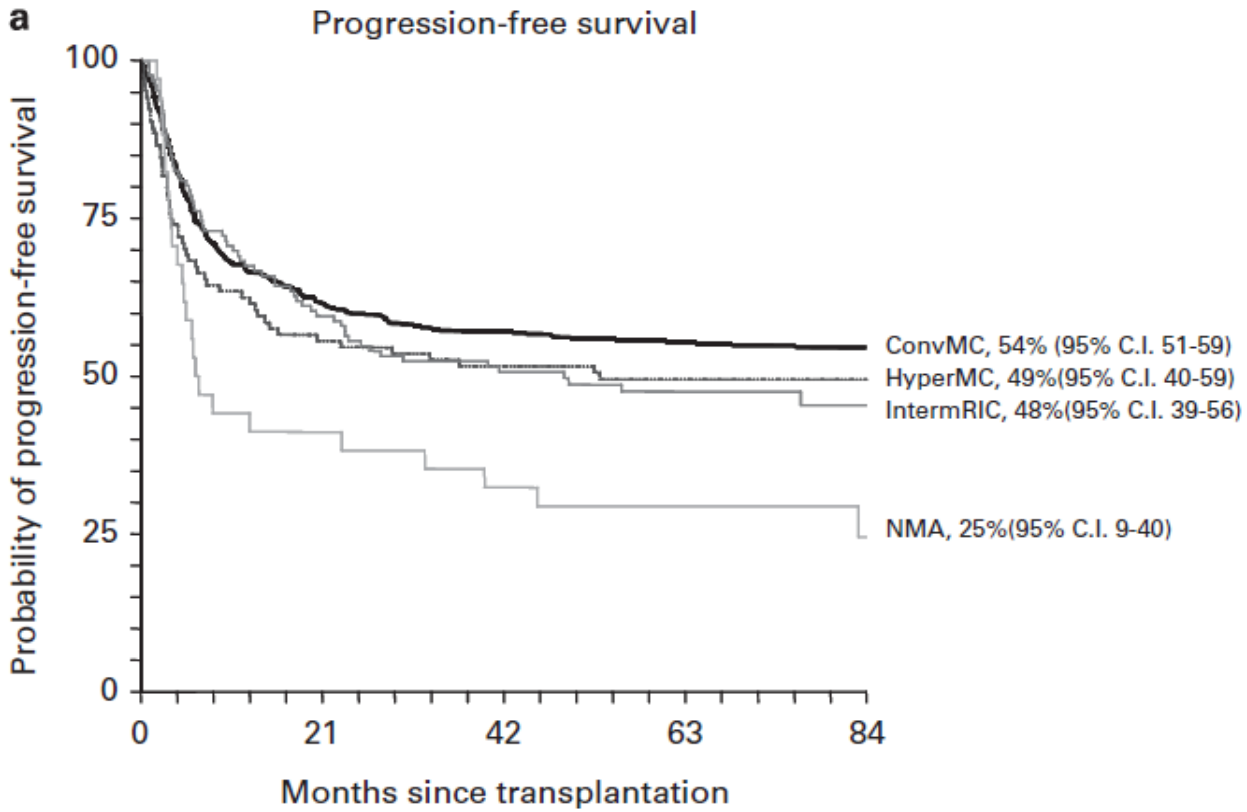


Relapse



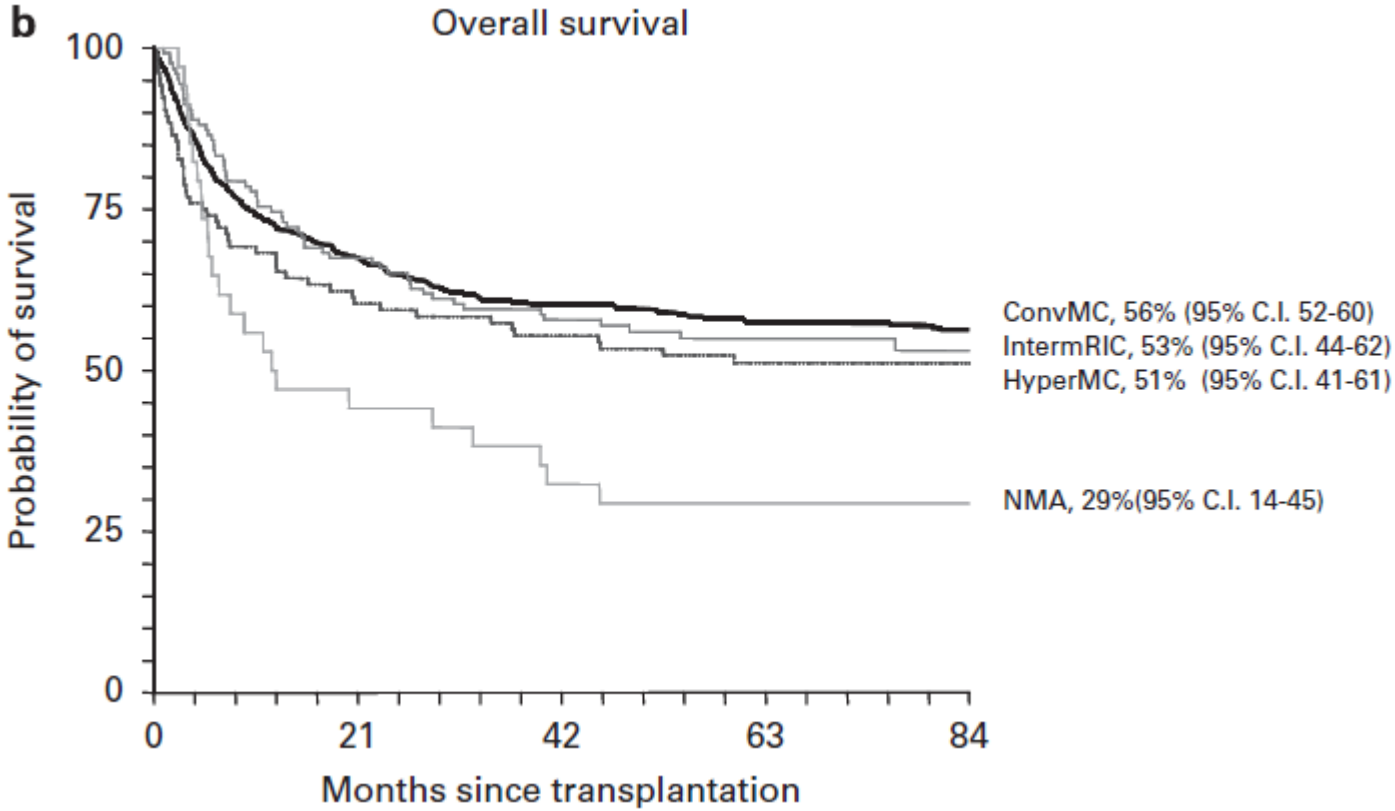
Bone Marrow Transplantation (2017), 1–6

Comparison of conditioning regimens of various intensities for allogeneic hematopoietic SCT using HLA-identical sibling donors in AML and MDS with <10% BM blasts: a report from EBMT



Conv MC=Conventional high-dose myeloablative conditioning regimen
HyperMC =hyperintensive myeloablative conditioning regimen
IntermRIC= intermediate-intensity conditioning
NMA= non-myeloablative or minimal-intensity conditioning

Martino et al. Bone Marrow Transplantation (2013) 48, 761



Conv MC=Conventional high-dose myeloablative conditioning regimen
HyperMC =hyperintensive myeloablative conditioning regimen
IntermRIC= intermediate-intensity conditioning
NMA= non-myeloablative or minimal-intensity conditioning

Martino et al. Bone Marrow Transplantation (2013) 48, 761

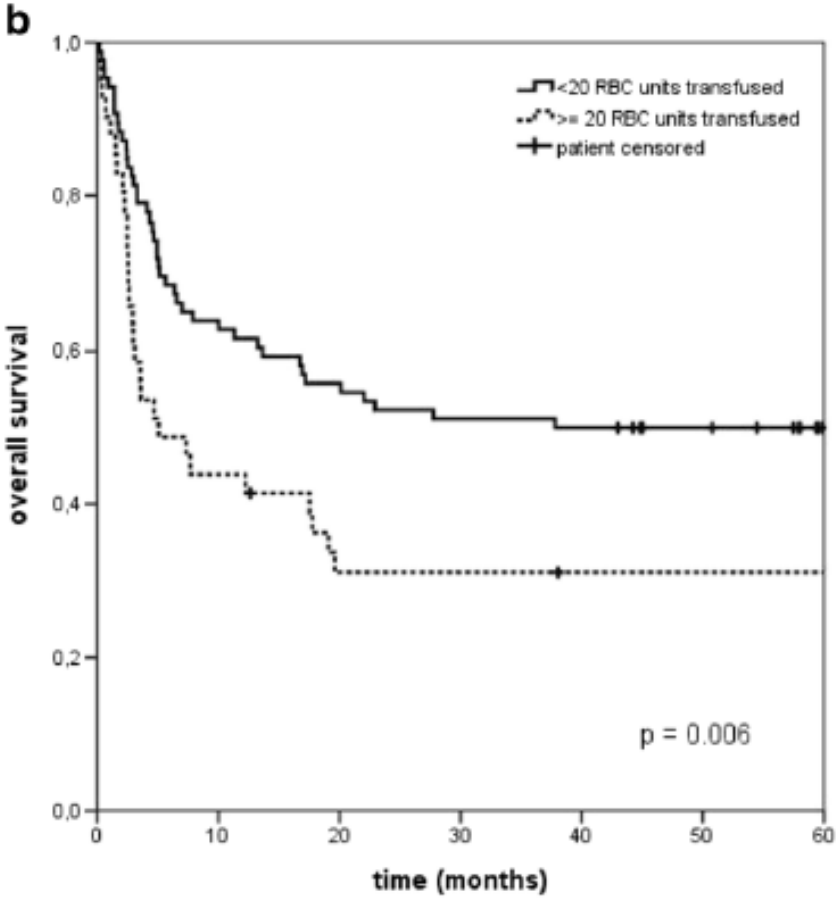
Table 1. Prognostic risk factors relevant for HSCT eligibility and for outcome after HSCT

Prognostic risk factor	Tools to measure risk factors in patients with MDS	Outcome after	
		Nontransplant interventions, including supportive care	HSCT
Patient related			
Age (chronological)	Calendar, IPSS-R[20]	Age influences prognostic impact of disease-related factors[20]	Impact age influenced by other patient-related factors[15]
Performance status (functional ability)	Karnofsky status ≥ 80%		Better survival after HSCT[15]
Frailty (reduced physical fitness)	Specific tools have to be tested in HSCT[117]		Fit patients better outcome[12,16-18]
Comorbidities	HSCT-specific CI (HCT-CI)[14]		Low CI better outcome[13]
Disease related			
Percentage of marrow blasts	IPSS(-R), WPSS, WHO[20,21]	Related to prognosis[20,21]	Only impact if <5% marrow blasts[22]
Cytogenetic risk groups	IPSS(-R), WPSS, CPSS[20,21,44]	5 prognostic groups[19]	Only very-poor-risk[29] and monosomal karyotype[30]
Severity of cytopenias	IPSS(-R), WPSS[41,42]	IPSS-R better prediction of prognosis compared with IPSS[42]	Only very-poor-risk group of IPSS-R prognostic
Marrow fibrosis	WHO criteria[51]	Severity fibrosis prognostic[51]	Severity fibrosis prognostic[52]
Transfusions burden	WPSS[41,63]	WPSS[41]	WPSS[64]
FCM	ELN FCM score[25,27]	ELN FCM score[24]	Not validated yet[27]
Molecular mutations	No specific tools yet[34]	Mutations in RUNX1, U2AF1, ASXL1, TP53, and others: poor prognosis[34]	Mutations in TP53, EZH2, ETV6 poor prognostic[23,35]
Disease status (after nontransplant treatment interventions)			
ESA failure	High Epo levels, high transfusion intensity[6,68]	High Epo levels, high transfusion intensity[6,68]	No direct impact reported
Lenalidomide failure	Absence of 5q−[5]	Absence of 5q−[5]	No direct impact reported
HMA failure	HMA-therapy–specific risk score[71]	HMA-therapy–specific risk score,[71] complex karyotype[118] TET2 and TP53 mutations[72,73]	Best available treatment after HMA failure,[76] but response status prognostic factor
ICT	MDS-specific risk score[4]	MDS-specific risk score[4]	Best available treatment available after failure of first-line ICT,[70] but response status and remission duration prognostic factor[31]

De Witte et al. Blood 2017

Prognostic pre-transplant factors in myelodysplastic syndromes primarily treated by high dose allogeneic hematopoietic stem cell transplantation: a retrospective study of the MDS subcommittee of the CMWP of the EBMT

E. M. P. Cremers[1,13] · A. van Biezen[2] · L. C. de Wreede[2] · M. Scholten[2] · A. Vitek[3] · J. Finke[4] · U. Platzbecker[5] · D. Beelen[6] · R. Schwerdtfeger[7] · L. Volin[8] · N. Harhalakis[9] · N. Blijlevens[10] · A. Nagler[11] · N. Kröger[12] · T. de Witte[10]

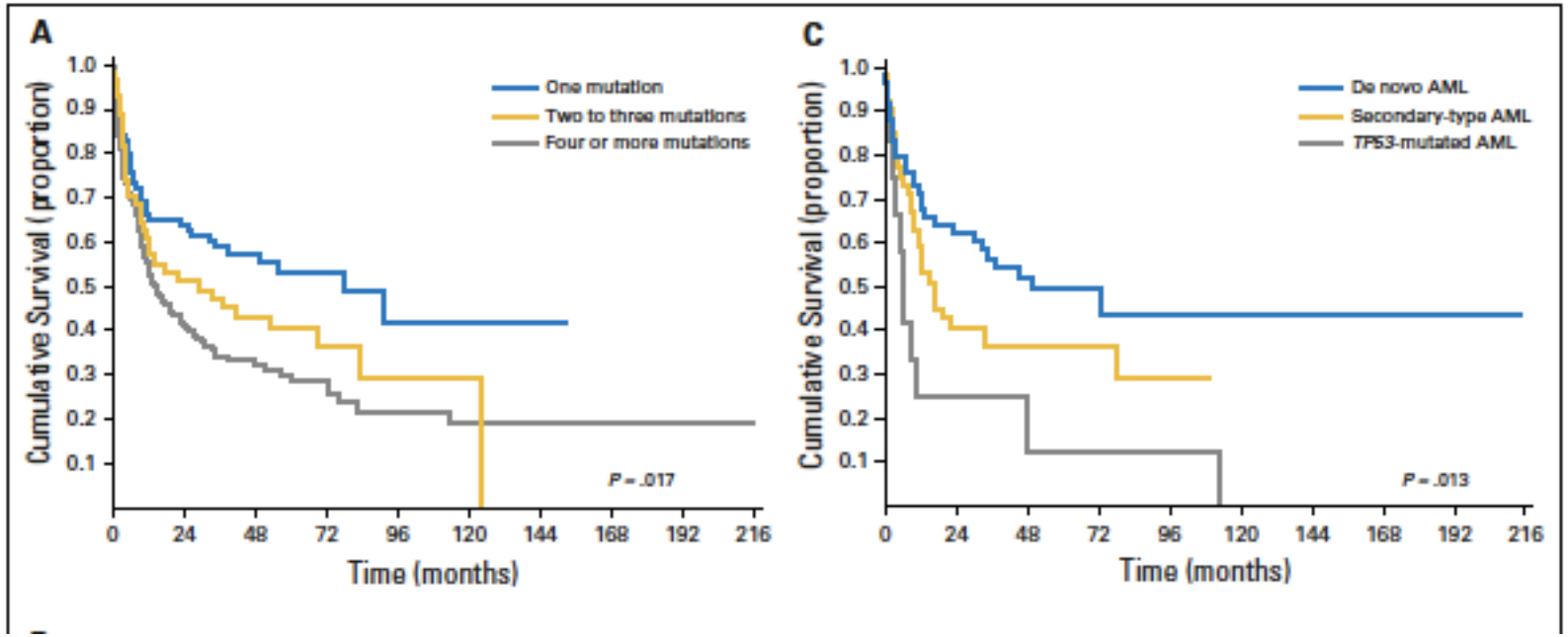


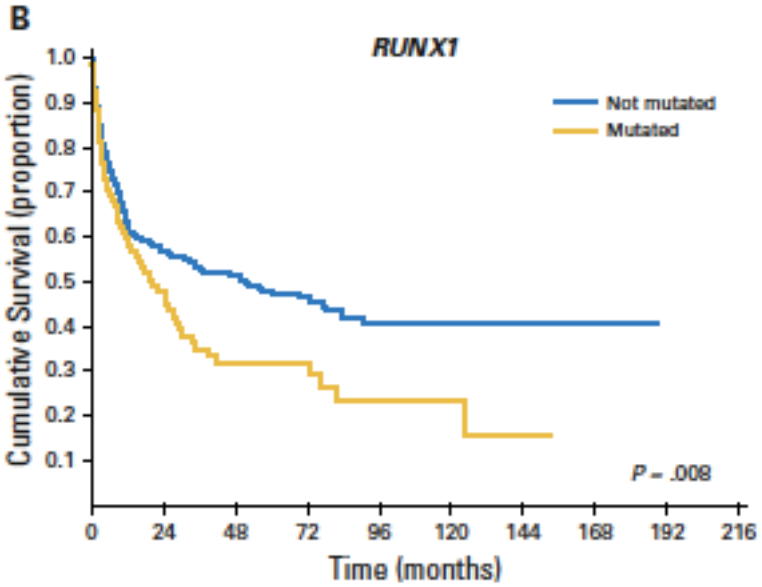
Impact of red blood cell transfusion requirement

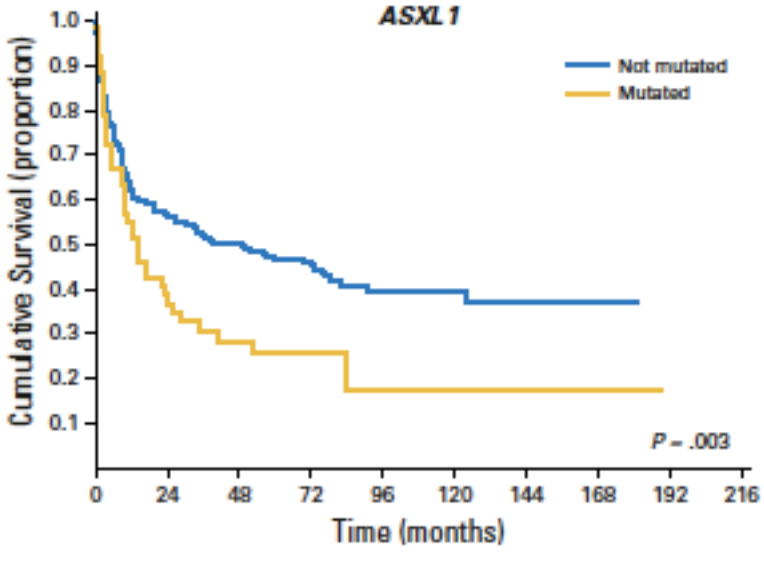
Ann Hematol (2016) 95:1971–1978

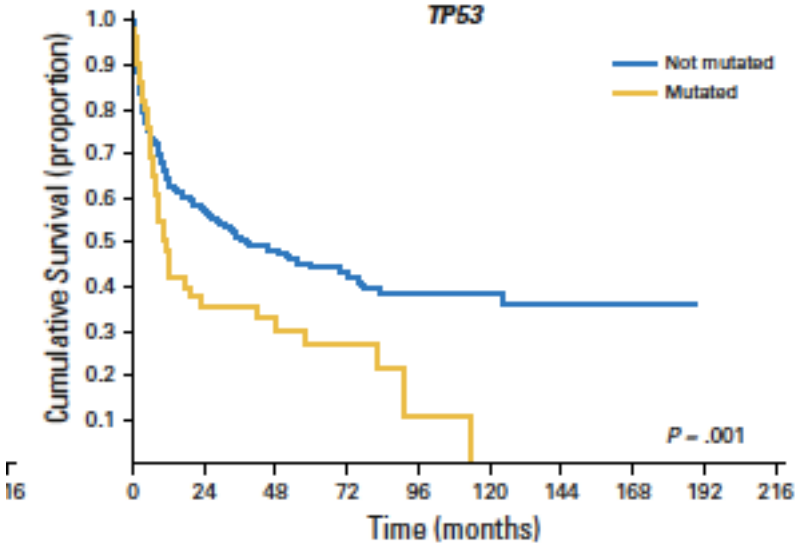
Clinical Effects of Driver Somatic Mutations on the Outcomes of Patients With Myelodysplastic Syndromes Treated With Allogeneic Hematopoietic Stem-Cell Transplantation

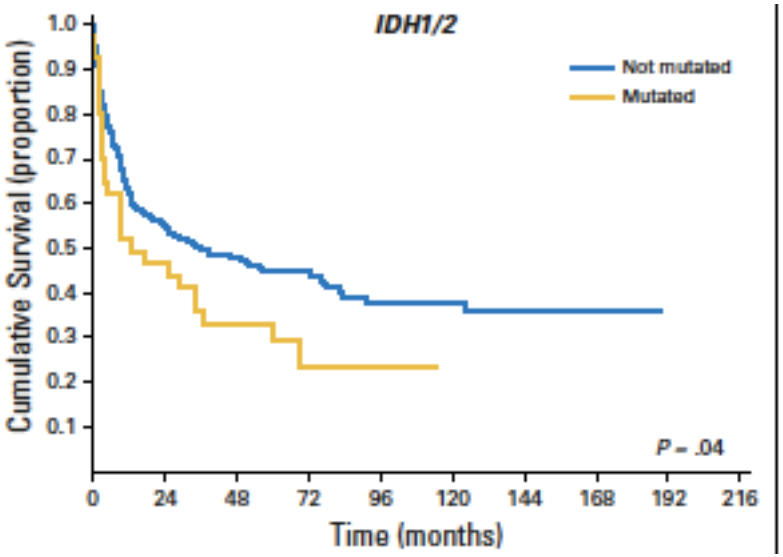
Matteo G. Della Porta, Anna Galli, Andrea Bacigalupo, Silvia Zibellini, Massimo Bernardi, Ettore Rizzo, Bernardino Allione, Maria Teresa van Lint, Pietro Pioltelli, Paola Marenco, Alberto Bosi, Maria Teresa Voso, Simona Sica, Mariella Cuzzola, Emanuele Angelucci, Marianna Rossi, Marta Ubezio, Alberto Malovini, Ivan Limongelli, Virginia V. Ferretti, Orietta Spinelli, Cristina Tresoldi, Sarah Pozzi, Silvia Luchetti, Laura Pezzetti, Silvia Catricalà, Chiara Milanesi, Alberto Riva, Benedetto Bruno, Fabio Ciceri, Francesca Bonifazi, Riccardo Bellazzi, Elli Papaemmanuil, Armando Santoro, Emilio P. Alessandrino, Alessandro Rambaldi, and Mario Cazzola




B
RUNX1
Not mutated
Mutated
Cumulative Survival (proportion)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
P = .008
0
24
48
72
96
120
144
168
192
216
Time (months)


ASXL1
Not mutated
Mutated
Cumulative Survival (proportion)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
P = .003
0
24
48
72
96
120
144
168
192
216
Time (months)


TP53
Not mutated
Mutated
Cumulative Survival (proportion)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
P = .001
0
24
48
72
96
120
144
168
192
216
Time (months)


IDH1/2
Not mutated
Mutated
Cumulative Survival (proportion)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
P = .04
0
24
48
72
96
120
144
168
192
216
Time (months)

Several questions remain to be answered

- How intensive does a conditioning regimen need to be in order to allow for engraftment and prevent relapse?
- What intensity will the patient tolerate?
- Should the conditioning intensity be adjusted to the disease stage (i.e. the risk of relapse)?
- Is it beneficial to give pre-HCT “debulking” therapy?
- Is there a place for post-HCT adjuvant or preemptive therapy?