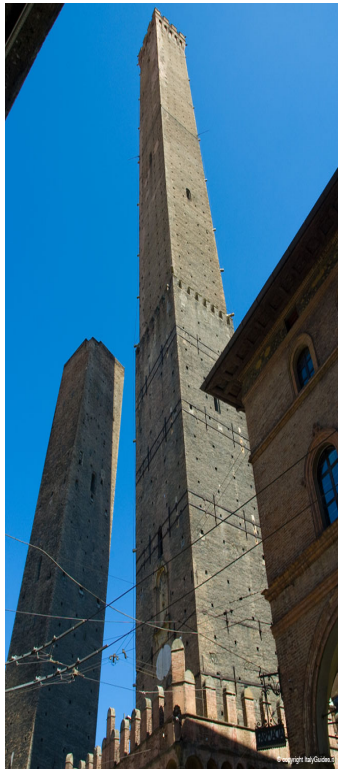


PROGETTO EMATOLOGIA-ROMAGNA

IDONEITA' AL TRAPIANTO OGGI

FOCUS SULL'ETA'



FRANCESCA BONIFAZI

PRESIDENTE



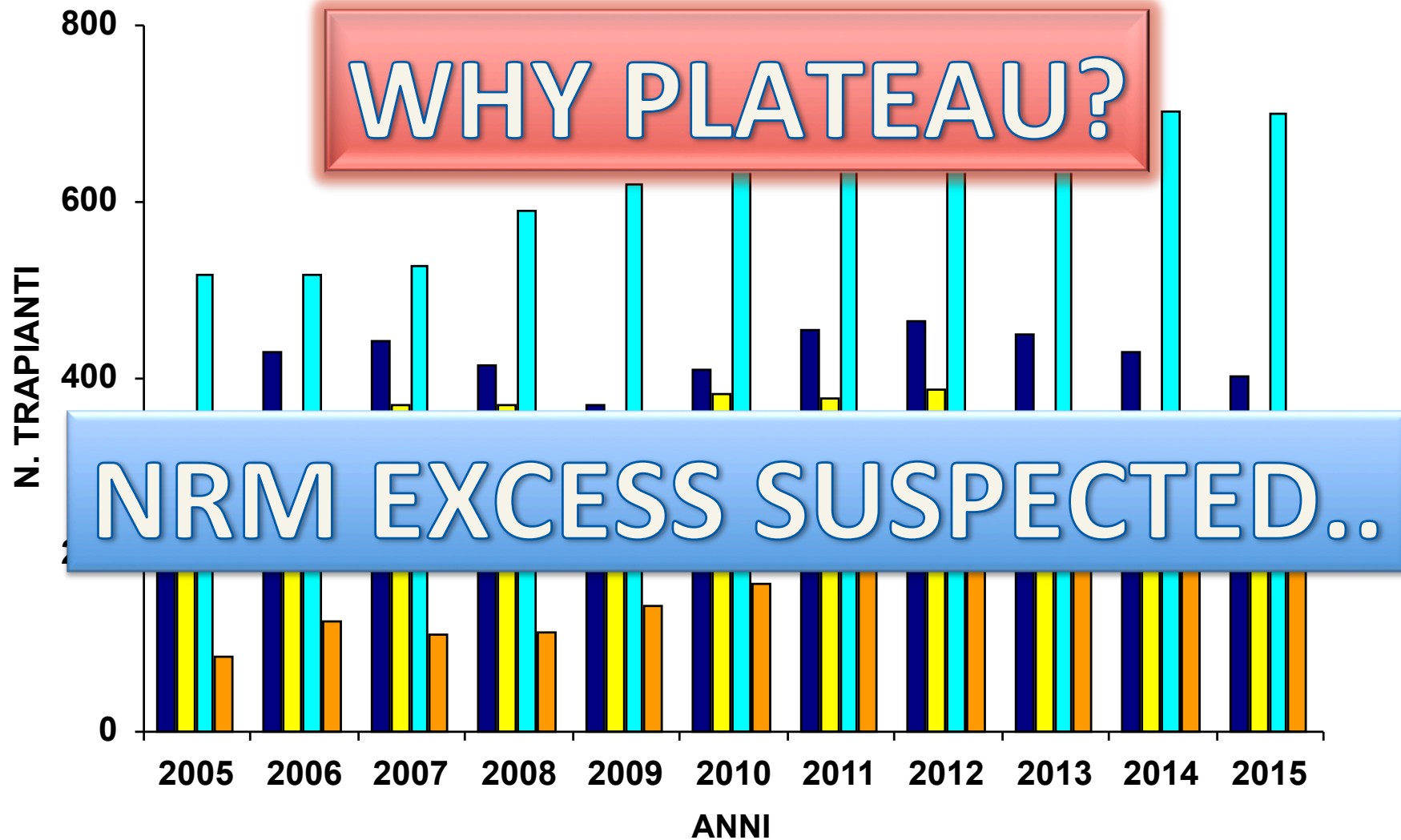
Hematology Dept.

**University Hospital S. Orsola-Malpighi,
Bologna**



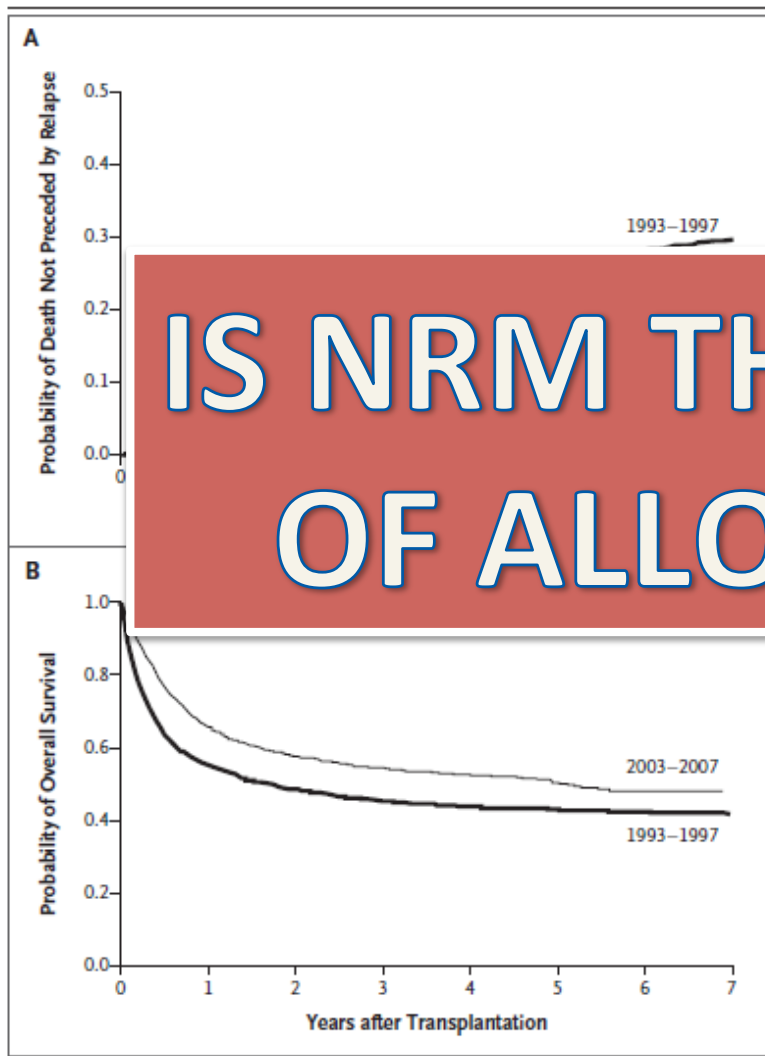
RIMINI , 8 APRILE 2017

GITMO Trapianto Allogeneico



al 30 marzo 2016

DA VITA NASCE VITA: PROMUOVERE LA DONAZIONE DI CELLULE STAMINALI EMOPOIETICHE IN ITALIA



Reduced Mortality after Allogeneic Hematopoietic-Cell

IS NRM THE ACTUAL LIMIT OF ALLO TRANSPLANT?

.D., M.P.H.,
M.D.,
d, M.D.

MIGLIORAMENTO DEL SUPPORTIVE CARE

RIDUZIONE DELLA INTENSITA' DI CONDIZIONAMENTO

UTILIZZO DI SCORES PER PREDIRE LA MORTALITA'

EBMT score

EBMT-AL score

HCI

Gooley N Engl J Med 2010

UTILIZZO DI SCORES PER PREDIRE LA MORTALITA'

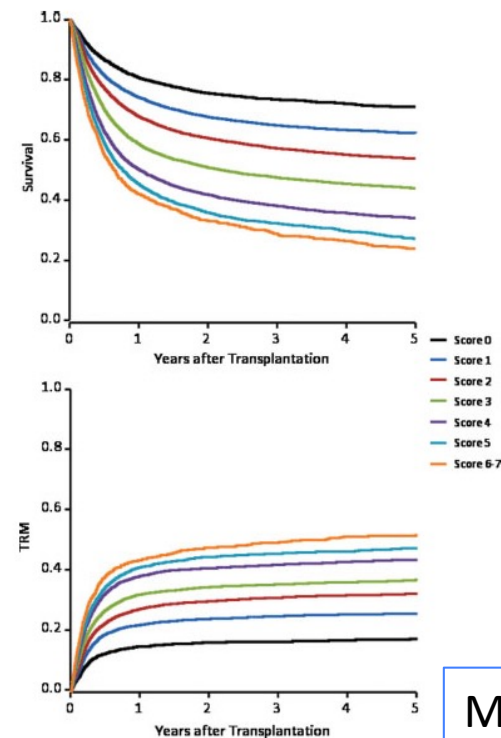
Risk Score for Outcome After Allogeneic Hematopoietic Stem Cell Transplantation

A Retrospective Analysis

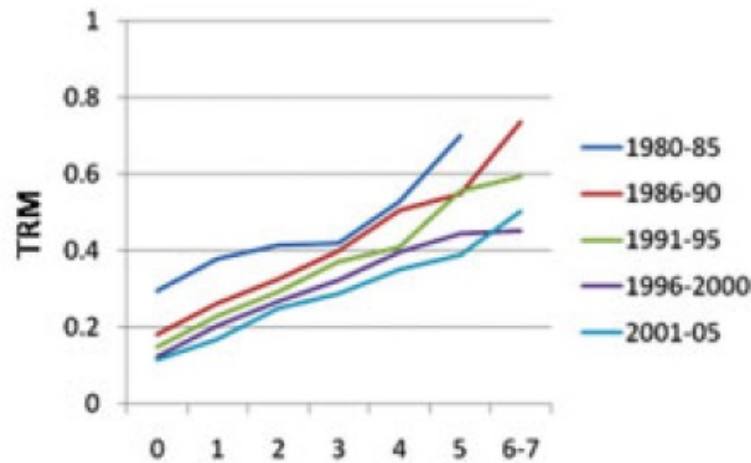
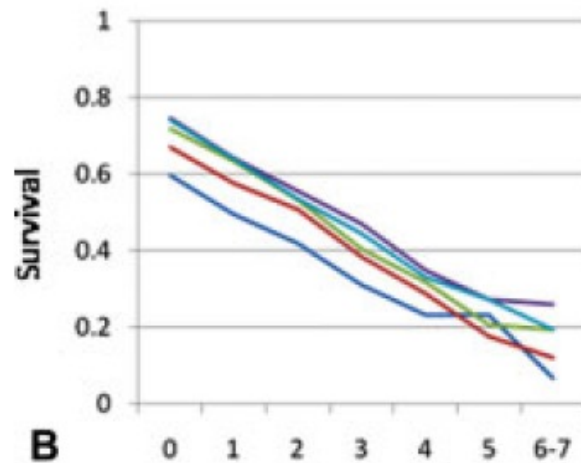
Alois Gratwohl, MD¹; Martin Stern, MD¹; Ronald Brand²; Jane Apperley, MD³; Helen Baldomero¹; Theo de Witte, MD⁴; Giorgio Dini, MD⁵; Vanderson Rocha, MD⁶; Jakob Passweg, MD⁷; Anna Sureda, MD⁸; André Tichelli, MD⁹; and Dietger Niederwieser, MD¹⁰ for the European Group for Blood and Marrow Transplantation and the European Leukemia Net

BACKGROUND: It was investigated whether the European Group for Blood and Marrow Transplantation risk score, previously established for chronic myeloid leukemia, could be used to predict outcome after allogeneic hematopoietic stem cell transplantation (HSCT) for hematological disease in general. **METHODS:** Age of patient, disease stage, time interval from diagnosis to transplant, donor type, and donor-recipient sex combination were used to establish a score from 0 to 7 points. Its validity was tested in 56,505 patients, 33,113 (58%) male, 23,392 female, median age 33 years (range, 0.5-77 years), with an allogeneic HSCT for a hematological disorder between 1980 and 2005. **RESULTS:** Survival probability at 5 years decreased from 71% (95% confidence interval [CI], 69%-73%) for risk score 0 for the whole cohort (75%, 95% CI, 72%-78% for the most recent time cohort) to 24% (95% CI, 21%-27% for risk score 6 and 7; 25%, 95% CI, 22%-29% most recent cohort). Transplant-related mortality increased from 15% (95% CI, 14%-17%) for risk score 0 (11%, 95% CI, 9%-13%, most recent cohort) to 47% with risk score 6 and 7 (95% CI, 44%-50%) for the whole cohort (45%, 95% CI, 42%-48%, most recent cohort). The risk score was predictive in all

Cancer 2009 Oct 15;115(20):4715-26



MUD VS SIB
 Fd/Mr vs all others
 Age <20 20-40 >40
 Dis phase
 Interval dg-tx



Prediction of Allogeneic Hematopoietic Stem-Cell Transplantation Mortality 100 Days After Transplantation Using a Machine Learning Algorithm: A European Group for Blood and Marrow Transplantation Acute Leukemia Working Party Retrospective Data Mining Study

Roni Shouval, Myriam Labopin, Ori Bondi, Hila Mishan-Shamay, Avichai Shimoni, Fabio Ciceri, Jordi Esteve, Sebastian Giebel, Norbert C. Gorin, Christoph Schmid, Emmanuelle Polge, Mahmoud Aljurf, Nicolaus Kroger, Charles Craddock, Andrea Bacivalupo, Ian I. Cornelissen, Frederic Baron, Ron Unver, Arnon Naveh.

Predicting Allo-HSCT Outcomes With a Machine Learning Approach

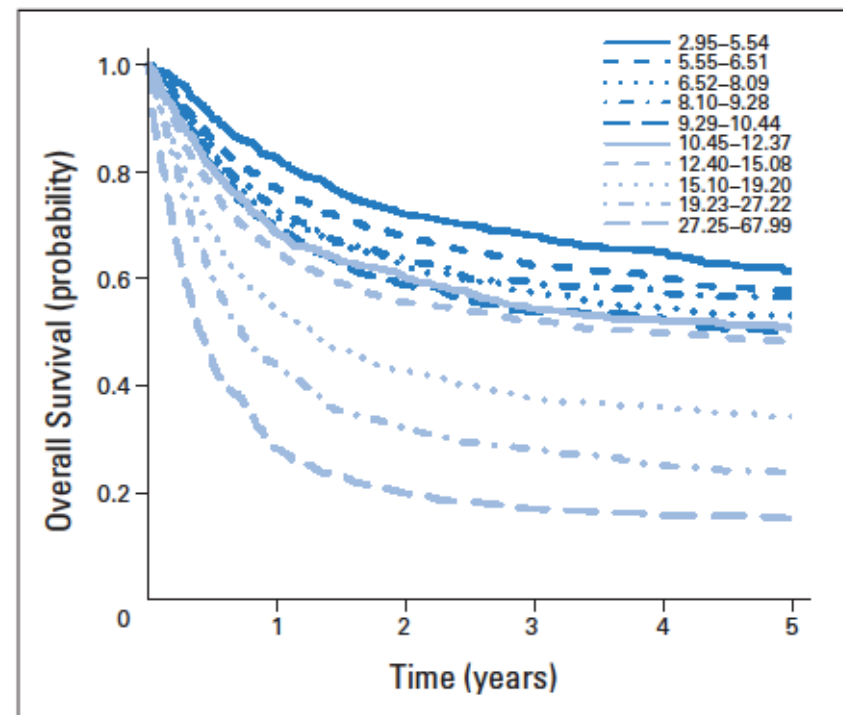
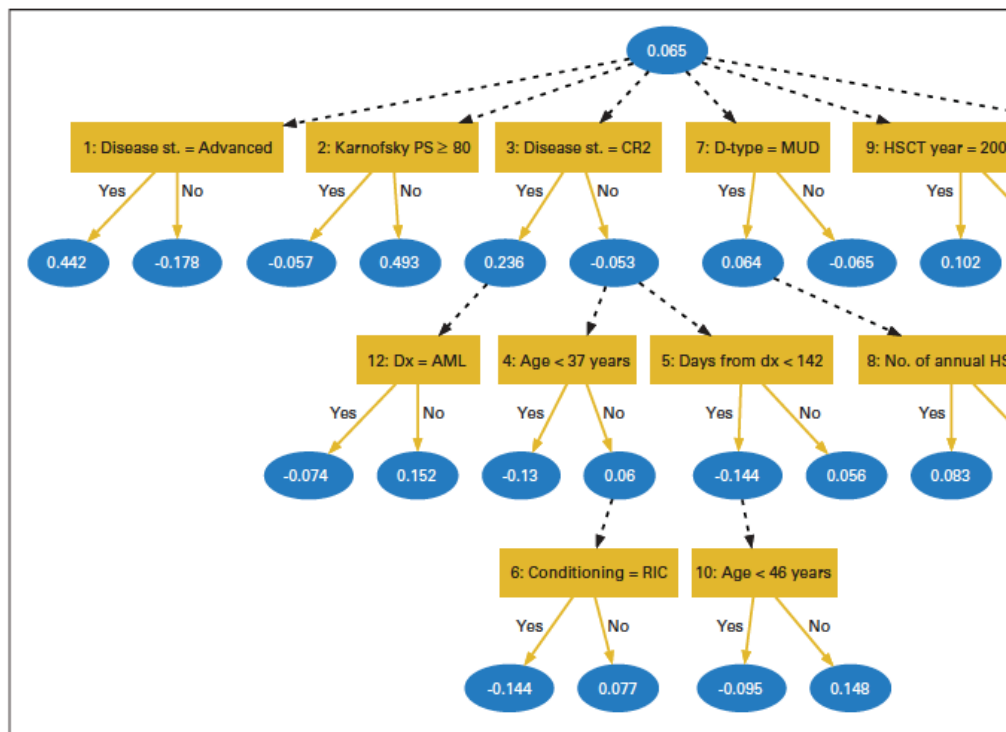


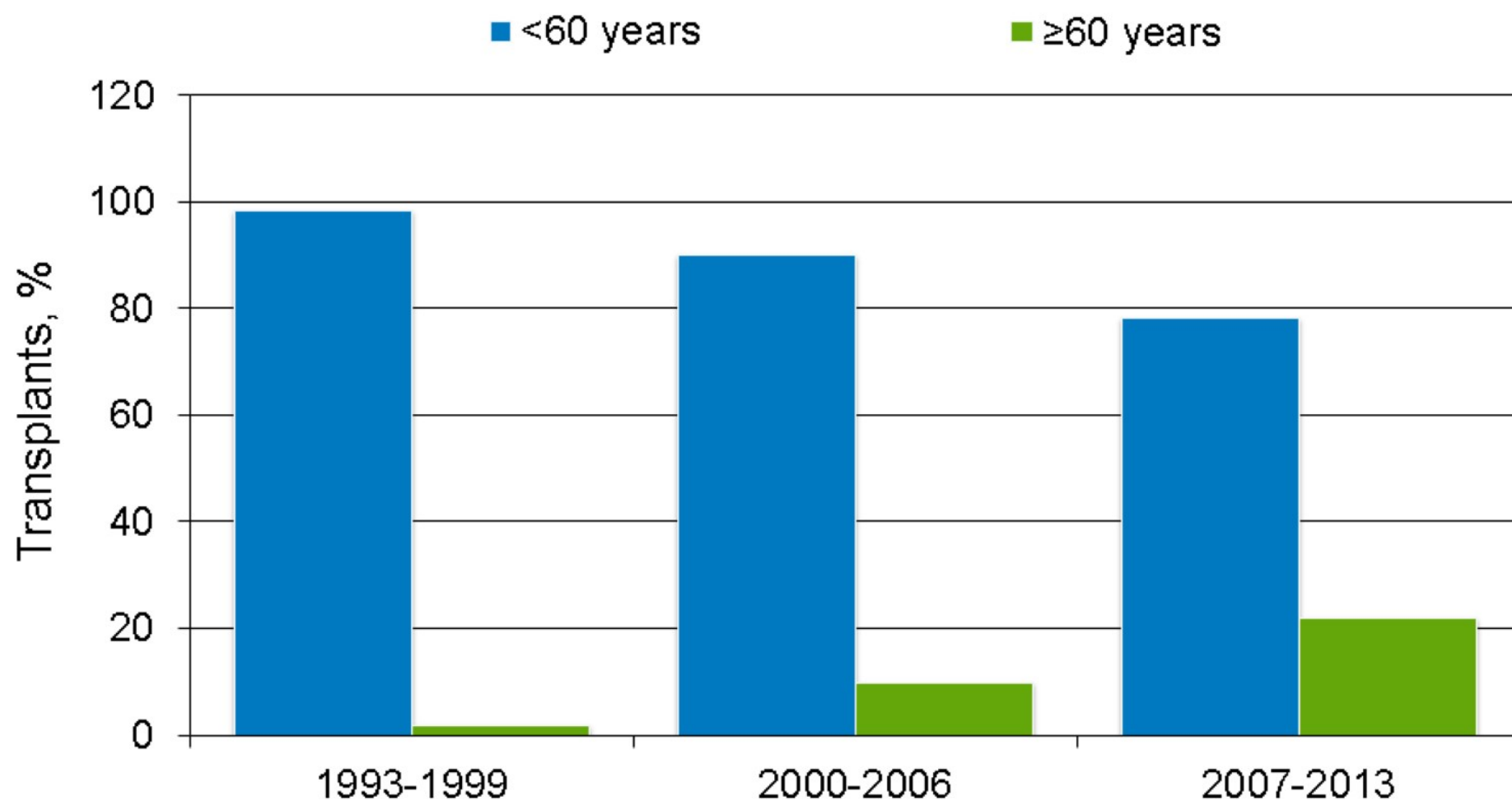
Fig 3. Kaplan-Meier curves of overall survival stratified by the categorized

PREVALENZA DEL TRAPIANTO ALLO IN FUNZIONE DELL'ETA'

DATO AMERICANO

DATO EUROPEO

Trends in Allogeneic Transplants by Recipient Age*





HHS Public Access

Author manuscript

Biol Blood Marrow Transplant. Author manuscript; available in PMC 2016 November 01.

Published in final edited form as:

Biol Blood Marrow Transplant. 2015 November ; 21(11): 1863–1869. doi:10.1016/j.bbmt.2015.07.032.

Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation

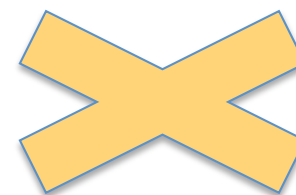
Navneet S Majhail¹, Stephanie H Farnia², Paul A Carpenter³, Richard E Champlin⁴, Stephen Crawford⁵, David I Marks⁶, James L Omel⁷, Paul J Orchard⁸, Jeanne Palmer⁹, Wael Saber^{10,11}, Bipin N Savani¹², Paul A Veys¹³, Christopher N Bredeson, MD, MSc¹⁴, Sergio A Giralt^{#15}, and Charles F LeMaistre^{#16}

Age in Patient Selection for HCT

Age by itself should not be a contraindication to transplantation in patients who may benefit from this procedure. Selected older patients with limited comorbidities and good functional status can safely receive HCT with a relatively low and acceptable risk of non-relapse mortality.³²⁻³⁴ Instead of chronological patient age, evaluations such as functional status, HCT Comorbidity Index (HCT CI) score, EBMT risk score and Pre-transplantation Assessment of Mortality (PAM) risk score can assist in determining risks of non-relapse mortality and transplant candidacy for individual patients.

Allogeneic Hematopoietic Cell Transplantation in Elderly Patients Aged 65 and Older: A Retrospective Analysis By the Complications and Quality of Life Working Party of the EBMT. Basak et al ASH 2016 PO 681

n	6046
Median age	67 (65-84)
Group I	65-69
Group II	≥70
M: F	63: 37
Programs	270
Countries	32
Transplant years	2000: <1% 2014: 6.7%
Source	PBSC 91% BM 7% CB 2%



Donor type	HLA id sib	28%
	VUD	68%
	Haplo	4%
	AL	50%
	MDS	37%
	Lymph	4%
	Chron Leuk	8%
	PC dis	0.6%
	BMF	1%
T-CELL DEPLETION (any)	66%	
GRAFT FAILURE	6%	
GVHD 2-4	28%	
Stage 2-4 skin	50%	
gut	28%	
liver	7%	
VOD	2%	
Median survival	13 months	

AVOID GVHD

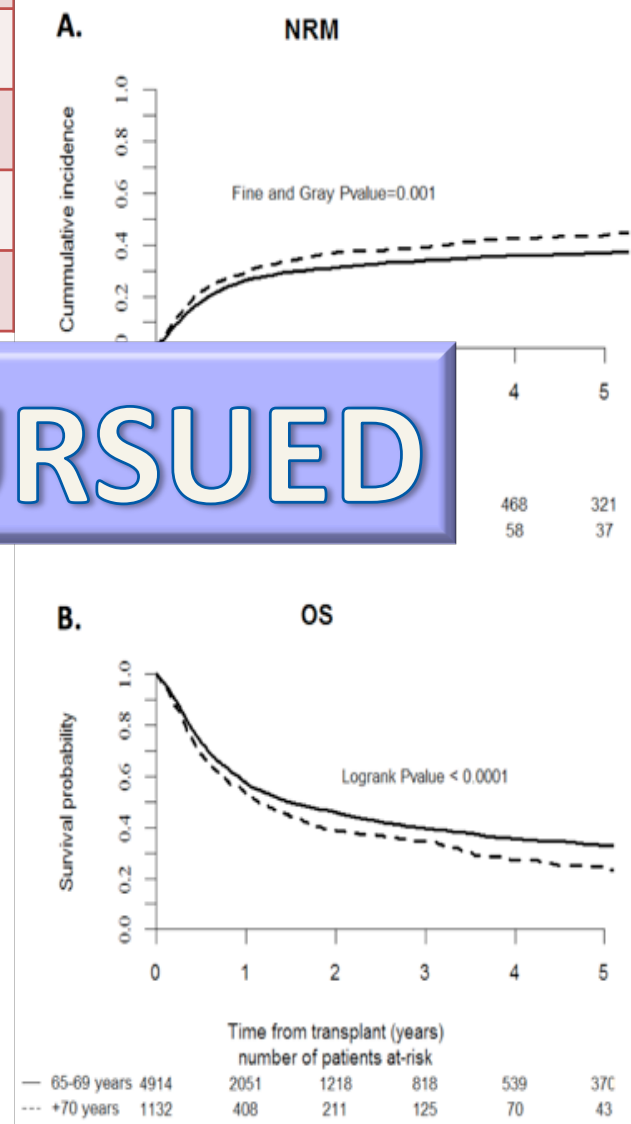
Overall elderly tx population

1-yr NRM	27%
3-yr NRM	39%
1-yr RI	25%
3-yr RI	32%
1-yr OS	56.6%
3-yr OS	38.6%

Younger is better but....



Figure 1. Non-relapse mortality (NRM, A) and overall survival (OS, B) of patients aged 65-69 (solid line) and ≥ 70 (dashed line) after alloHCT.

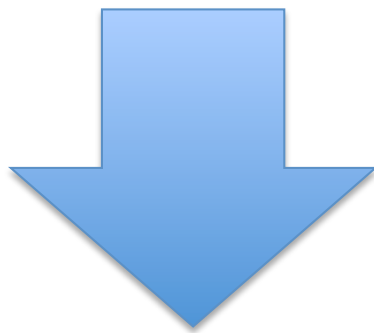


SELECTION (BIAS) PURSUED

1-yr NRM	26%
3-yr NRM	34%
1-yr OS	56%
3-yr OS	38%

Basak et al ASH MEETING 2016

1/3 SUCCESS
2/3 FAILURE

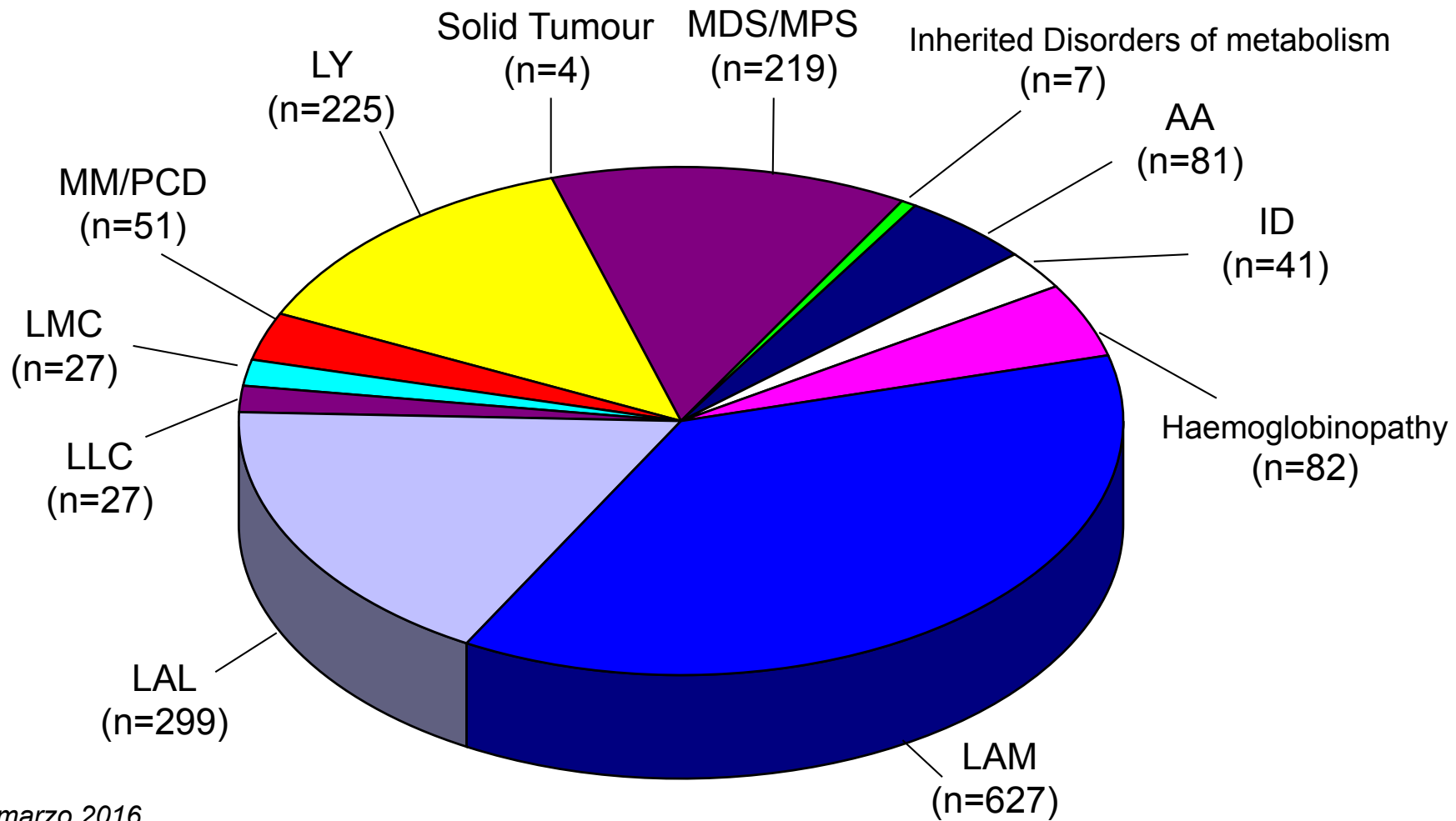


INDICATION

GITMO Trapianto Allogeneico

Numero Trapianti per principali Patologie

Attività 2015



al 30 marzo 2016

DA VITA NASCE VITA: PROMUOVERE LA DONAZIONE DI CELLULE STAMINALI EMPOIETICHE IN ITALIA

Effect of Age on Outcome of Reduced-Intensity Hematopoietic Cell Transplantation for Older Patients With Acute Myeloid Leukemia in First Complete Remission or With Myelodysplastic Syndrome

Brian L. McClune, Daniel J. Weisdorf, Tanya L. Pedersen, Gisela Tunes da Silva, Martin S. Tallman, Jorge Sierra, John DiPersio, Armand Keating, Robert P. Gale, Biju George, Vikas Gupta, Theresa Hahn, Luis Isola, Madan Jagasia, Hillard Lazarus, David Marks, Richard Maziarz, Edmund K. Waller, Chris Bredeson, and Sergio Giralt

A B S T R A C T

Purpose

Acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS) primarily afflict older individuals. Hematopoietic cell transplantation (HCT) is generally not offered because of concerns of excess morbidity and mortality. Reduced-intensity conditioning (RIC) regimens allow increased use of allogeneic HCT for older patients. To define prognostic factors impacting long-term outcomes of RIC regimens in patients older than age 40 years with AML in first complete remission or MDS and to determine the impact of age, we analyzed data from the Center for International Blood and Marrow Transplant Research (CIBMTR).

Patients and Methods

We reviewed data reported to the CIBMTR (1995 to 2005) on 1,080 patients undergoing RIC HCT. Outcomes analyzed included neutrophil recovery, incidence of acute or chronic graft-versus-host disease (GVHD), nonrelapse mortality (NRM), relapse, disease-free survival (DFS), and overall survival (OS).

JCO 2010

Table 1. Demographics and Clinical Characteristics of Patients With AML in First Complete Remission Age \geq 40 Years Receiving Allogeneic HCT From 1995 to 2005

Characteristic	No. of Evaluable Patients	Age								<i>P</i>
		40-54 Years		55-59 Years		60-64 Years		\geq 65 Years		
		No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	
No. of patients	545	201		149		132		63		

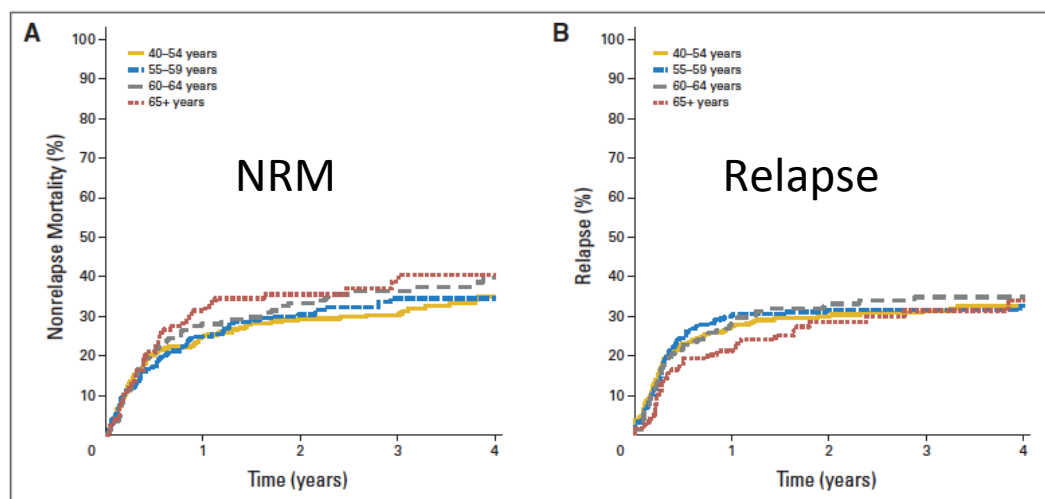


Table 5. Multivariate Analysis of 2-Year Disease-Free Survival and Overall Survival After Allogeneic HCT for Patients With AML in First Complete Remission and MDS

Variable	Disease-Free Survival				Overall Survival			
	No. of Patients	OR	95% CI	<i>P</i>	No. of Patients	OR	95% CI	<i>P</i>
Age, years								
40-54	399	1.00*		.81†‡	401	1.00*		.74†‡
55-59	289	1.03	0.82 to 1.29	.81	291	1.02	0.82 to 1.27	.85
60-64	255	1.12	0.89 to 1.42	.33	255	1.09	0.86 to 1.37	.48
\geq 65	116	1.07	0.79 to 1.45	.68	116	1.16	0.86 to 1.57	.32

We observed that transplantation toxicity, relapse, and survival for older adults are not significantly different than those for younger adults undergoing a similar NMA or RIC allogeneic HCT. Previous nontransplantation studies have shown uniformly poor survival in patients older than age 60 years, with little improvement over the last 30 years.^{4,30} Our data indicate that allogeneic HCT offers a treatment option able to provide long-term disease control in almost one third of patients older than age 40 years, which was similar even in the oldest cohort of patients ≥ 65 years old.

HCT for these older patients did not result in excess NRM, as many clinicians might fear. NRM was similar across all four age co-

NON TRANSPLANT APPROACHES IN OLDER AML PATIENTS SHOWED LITTLE IMPROVEMENTS...

**NRM IS NOT THE FIRST CAUSE OF FAILURE
OF ALLO SCT IN ACUTE LEUKEMIA**

BUT

NRM SHOULD BE MINIMISED, HOPEFULLY

NRM SHOULD BE PREDICTED, FOR SURE

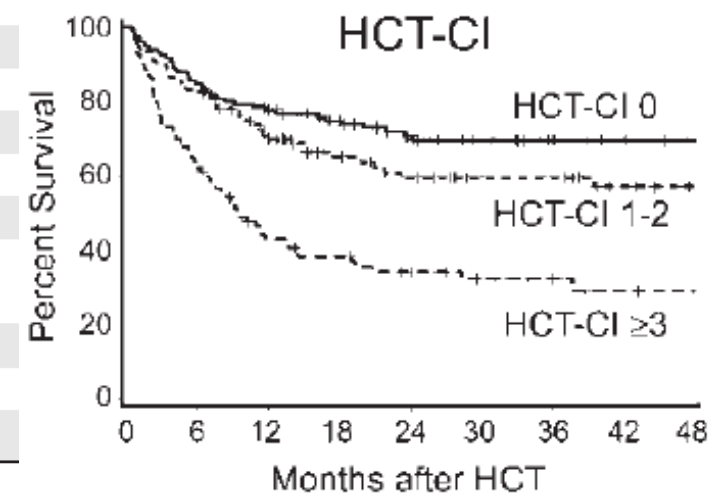
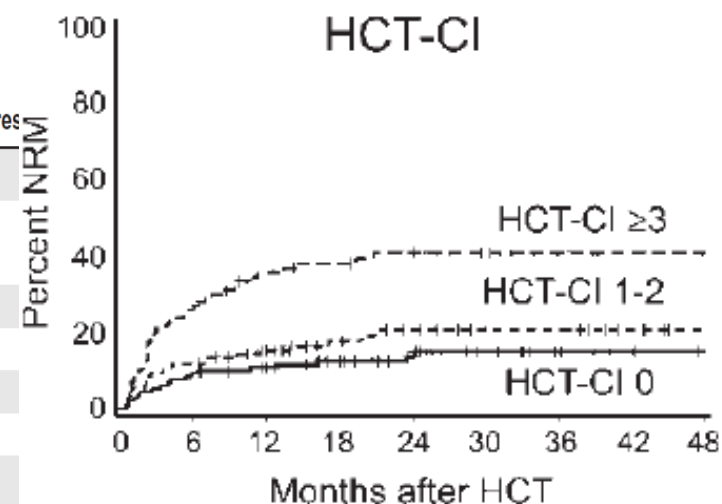
TRANSPLANT AND AGING

- **COMORBIDITY ASSESSMENT**
- GERIATRIC ASSESSMENT
- AGING- ASSOCIATED BIOMARKERS VALIDATION

Hematopoietic cell transplantation (HCT)–specific comorbidity index: a new tool for risk assessment before allogeneic HCT

Mohamed Sorrow, Michael Maris, Rainer Storb, Frederic Baron, Brenda Sandmaier, David Maloney, Barry Storer

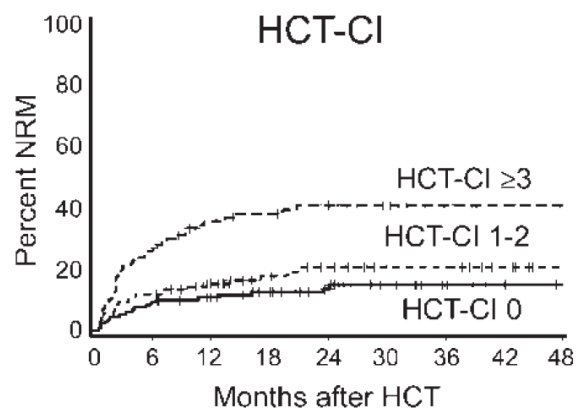
Comorbidity	Definitions of comorbidities included in the new HCT-CI	HCT-CI weighted scores
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias	1
Cardiac‡	Coronary artery disease,§ congestive heart failure, myocardial infarction, or EF ≤ 50%	1
Inflammatory bowel 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 × ULN, or AST/ALT > ULN to 2.5 × 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 ≤ 65% or dyspnea at rest or requiring oxygen	3
Moderate/severe hepatic‡	Liver cirrhosis, bilirubin > 1.5 × ULN, or AST/ALT > 2.5 × ULN	3



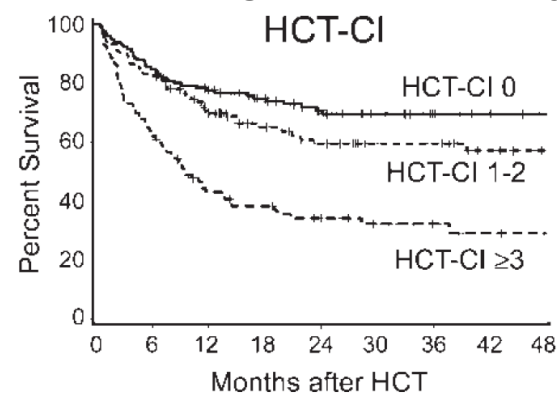
Risultati casistica originale Seattle

		casistica originale Seattle	
HCT-CI score	gruppo di rischio	NRM a 2 anni	OS a 2 anni
0	basso	14%	71%
1 - 2	intermedio	21%	60%
≥ 3	alto	41%	34%

A NRM. Original Sorror study



C OS. Original Sorror study



Validation of the Hematopoietic Cell Transplantation-Specific Comorbidity Index: a prospective, multicenter GITMO study

Roberto Raimondi, Alberto Tosetto, Rosi Oneto, Riccardo Cavazzina, Francesco Rodeghiero, Andrea Bacigalupo, Renato Fanin, Alessandro Rambaldi, and Alberto Bosi

→ Confermata la validità dell' HCT-CI

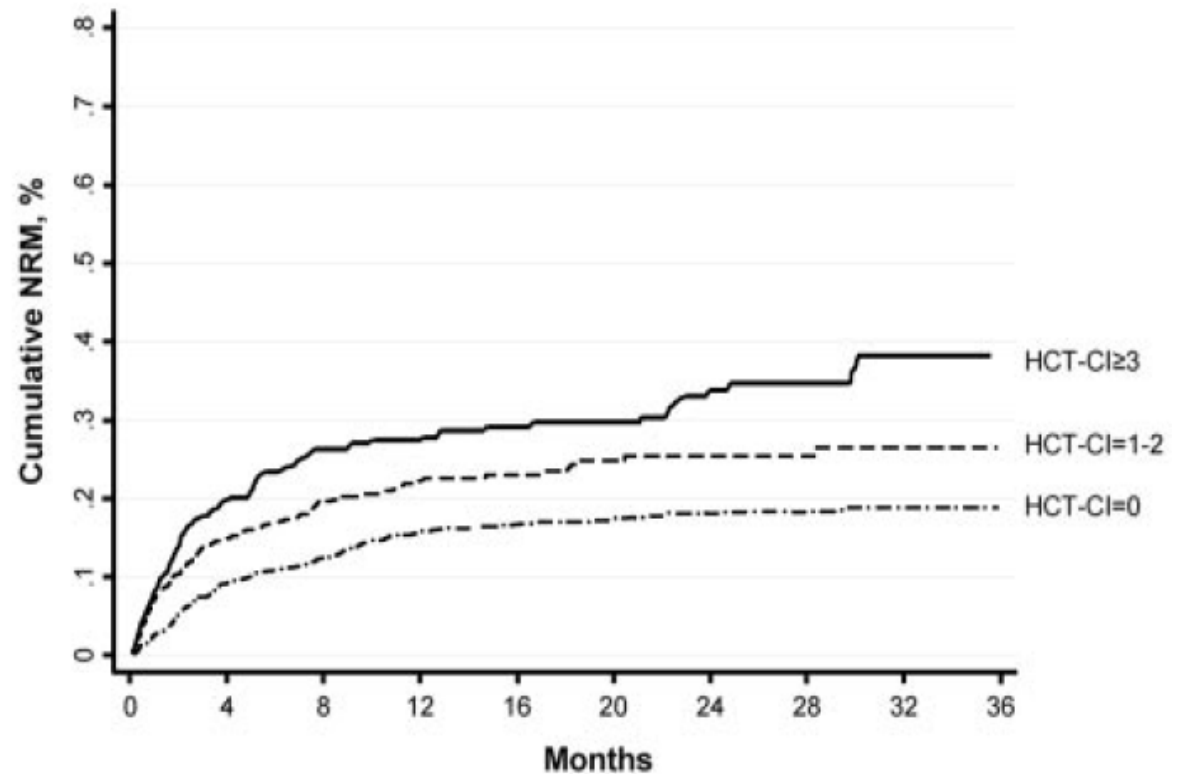


Figure 1. NRM cumulative incidence by HCT-CI score group.

Risultati
valore dello score in analisi multivariata, per NRM e OS a 2 anni

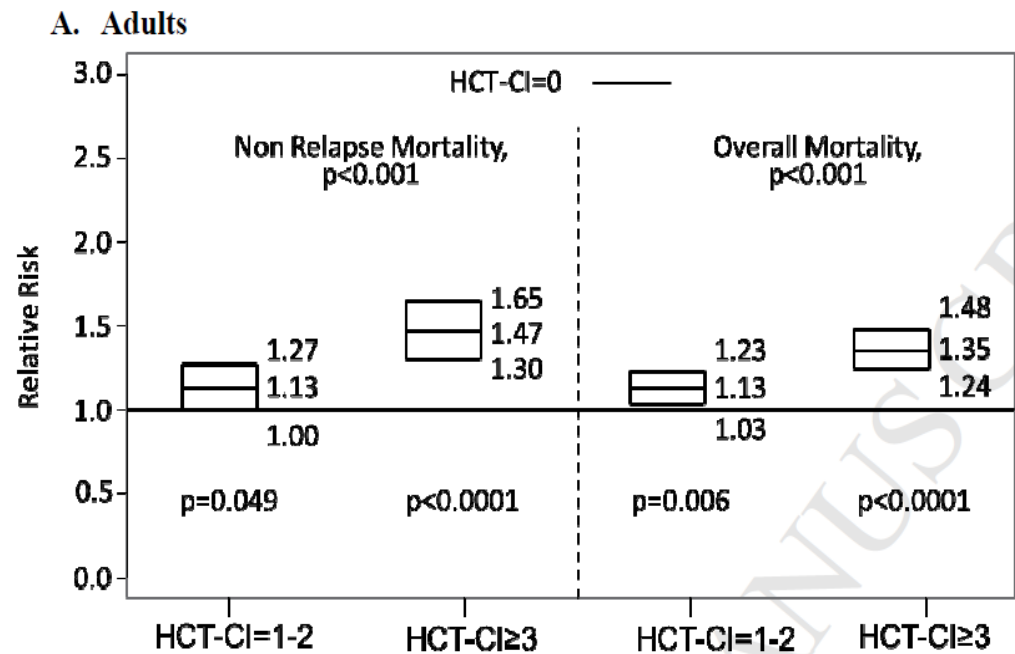
Predictor	Multivariate			
	NRM		OS	
	HR	P-value	HR	P-value
HCT-CI = 0	1		1	
HCT-CI= 1-2	1.54	< 0.001	1.29	0.009
HCT-CI ≥ 3	1.90	< 0.000	1.93	< 0.000
Donor type (unrelated vs. related)	2.01	< 0.000	1.38	< 0.000
Disease group (high vs. low risk)	1.62	< 0.000	1.75	< 0.000
Age (>50 vs ≤50 years)	1.33	0.008	1.25	0.004
Conditioning regimen (MA vs RIC)	1.04	0.675	1.33	0.002
Source (PBSC vs. bone marrow)	1.03	0.813	0.98	0.910
Sex (male vs. female)	0.87	0.234	1.00	0.925
Female donor/male recipient vs. other	1.07	0.571	1.00	0.952
CMV serostatus D neg/R neg vs. other	0.92	0.592	0.86	0.171

Prospective Validation of the Predictive Power of the Hematopoietic Cell Transplantation Comorbidity Index: A CIBMTR® Study

Mohamed Sorrow, Brent Logan, Xiaochun Zhu, J. Douglas Rizzo, Kenneth Cooke, Philip McCarthy, Vincent Ho, Mary Horowitz, Marcelo Pasquini,

→ Confermata, negli USA, la validità dell' HCT-CI (anche per Auto)

Score HCT-CI	Allo			
	NRM %		OS %	
	1 anno	3 anni	1 anno	3 anni
0	17	24	69	54
1-2	21	28	62	47
≥ 3	26	35	56	38



Multi-centre validation of the prognostic value of the haematopoietic cell transplantation - specific comorbidity index among recipient of allogeneic haematopoietic cell transplantation

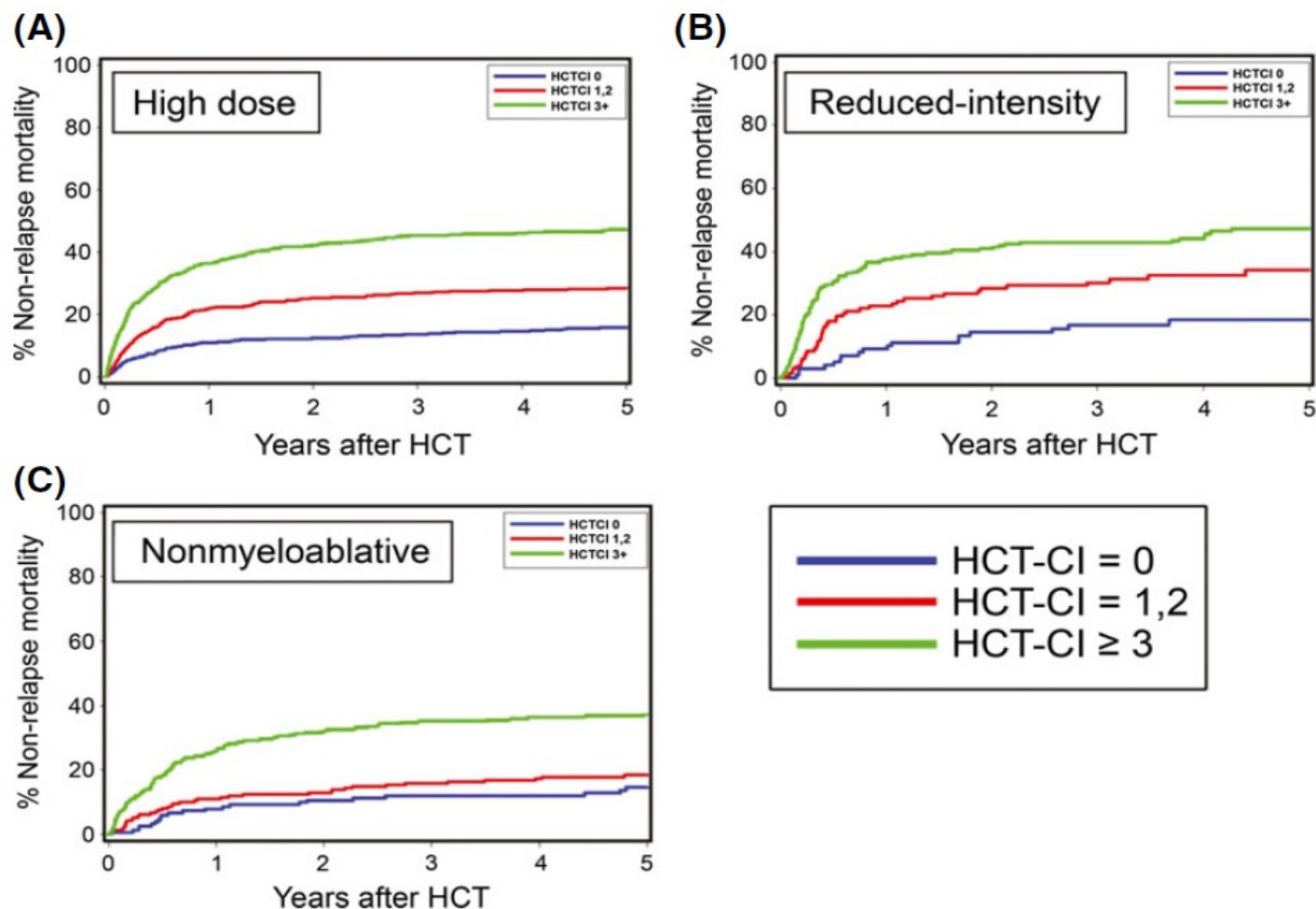
Mahmoud ElSawy, Barry Storer, Michael Pulsipher, Richard Maziarz, Smita Bhatia, Michael Maris, Karen Syrjala, Paul Martin, David Maloney, Brenda Sandmaier, Rainer Storb and Mohamed Sorrow

→ validità in tutti i gruppi di età

	Cumulative percent incidence of NRM (2-year)				Percent overall survival (2-year)			
	HCT-CI scores				HCT-CI scores			
Age groups, years	0	1-2	≥3	<i>P</i>	0	1-2	≥3	<i>P</i>
0-19, malignant diseases	8	26	28	<0.001	73	61	41	<0.001
0-19, non-malignant diseases	NE	NE	NE		84	57	40	<0.001
20-39	11	20	39	<0.001	80	62	33	<0.001
40-49	12	26	43	<0.001	75	56	39	<0.001
50-59	21	31	39	<0.001	60	48	33	<0.001
≥60	7	27	38	<0.001	63	47	27	<0.001

Multi-centre validation of the prognostic value of the haematopoietic cell transplantation-specific comorbidity index among recipient of allogeneic haematopoietic cell transplantation

Mahmoud EISawy, Barry Storer, Michael Pulsipher, Richard Maziarz, Smita Bhatia, Michael Maris, Karen Syrjala, Paul Martin, David Maloney, Brenda Sandmaier, Rainer Storb and Mohamed Sorrow



Comorbidity-Age Index: A Clinical Measure of Biologic Age Before Allogeneic Hematopoietic Cell Transplantation

Mohamed L. Sorrow, Rainer F. Storb, Brenda M. Sandmaier, Richard T. Maziarz, Michael A. Pulsipher, Michael B. Maris, Smita Bhatia, Fabiana Ostronoff, H. Joachim Deeg, Karen L. Syrjala, Elihu Estey, David G. Maloney, Frederick R. Appelbaum, Paul J. Martin, and Barry E. Storer

- L' indice composito (HCT-CI + età) - Comorbidity/Age index:**
- ha buona capacità predittiva per NRM (e OS)
 - incorpora l' età nell' insieme delle altre condizioni inerenti al paziente, senza lasciarla come parametro isolato

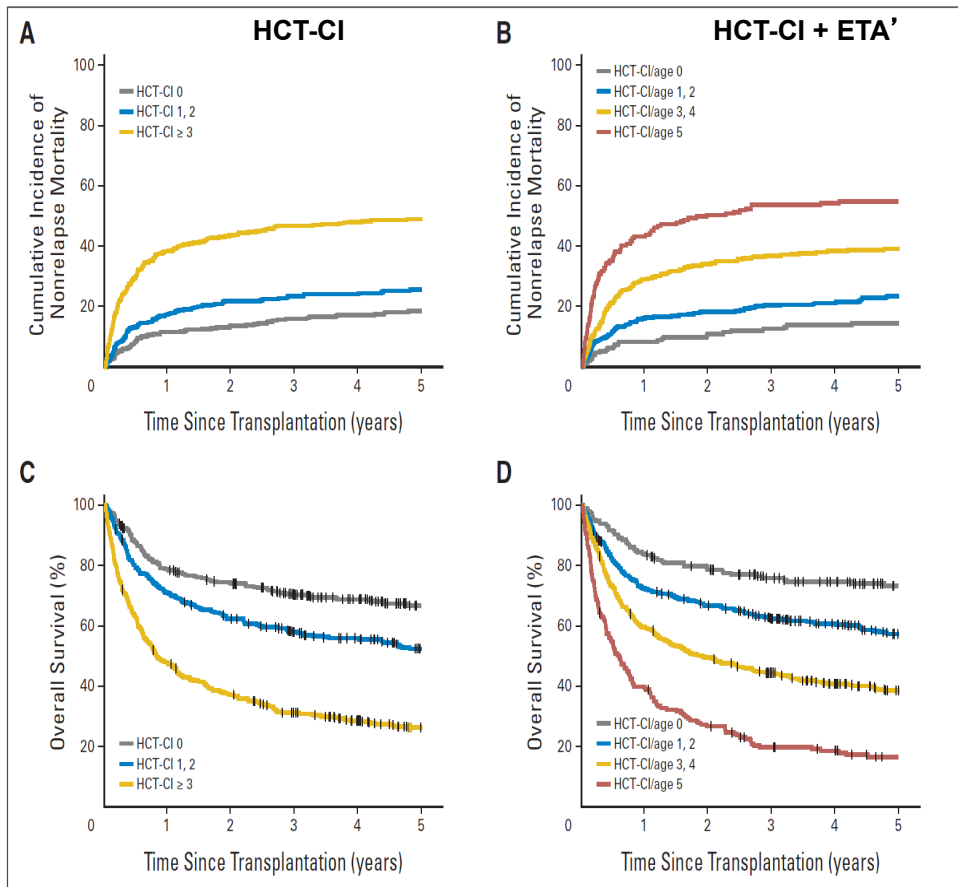


Table 4. Overall Mortality According to Conditioning Intensity Within Each Comorbidity/Age Risk Group

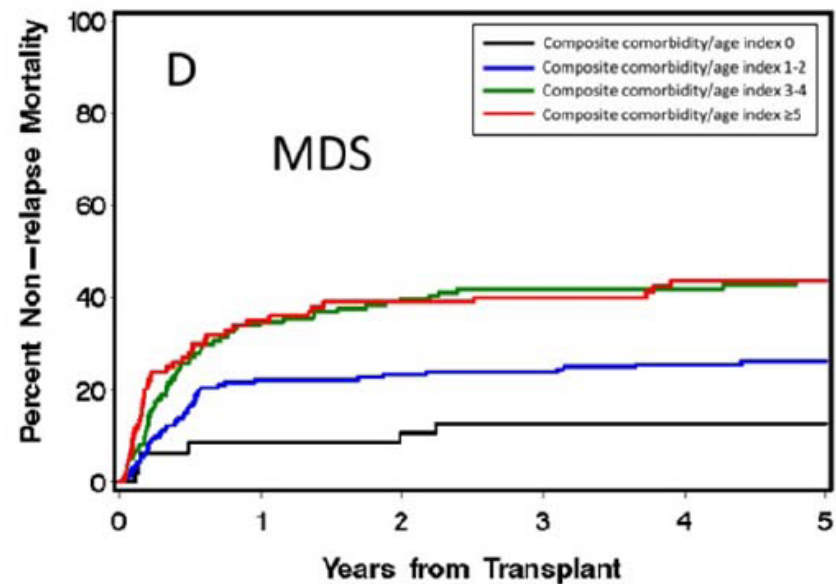
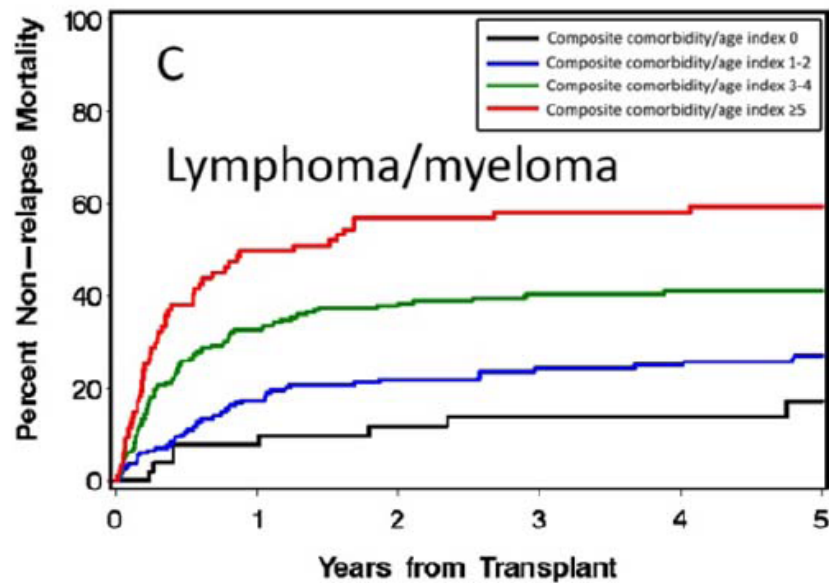
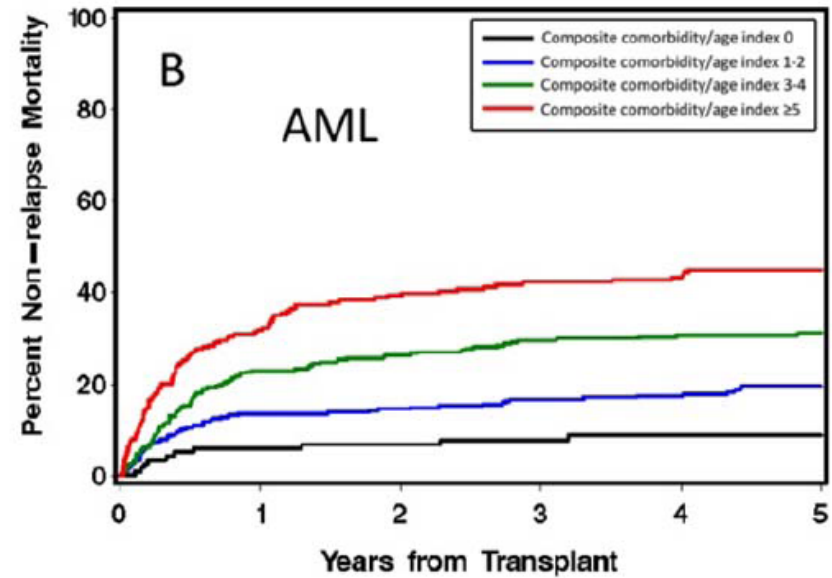
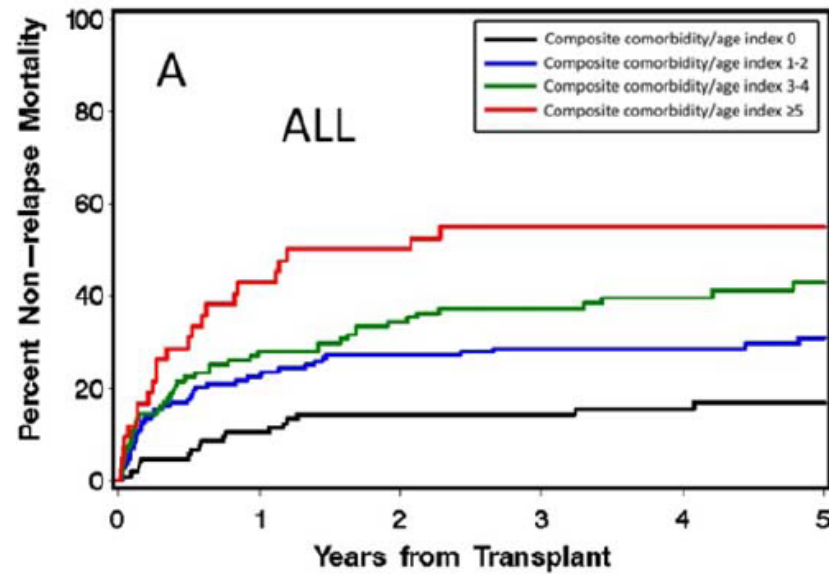
HCT-CI/Age Composite Score	Regimen		Overall 2-Year Survival (%)		Cox Regression Model*		
	Intensity	No. of Patients	Observed	Adjusted†	HR	95% CI	P
0 (n = 495)	High dose	417	79		1.0		
	Reduced intensity	40	87	83	0.76	0.3 to 1.7	.51
	Nonmyeloablative	38	81	85	0.72	0.4 to 1.5	.38
1-2 (n = 1,079)	High dose	737	66		1.0		
	Reduced intensity	130	66	70	0.79	0.6 to 1.1	.15
	Nonmyeloablative	212	67	74	0.89	0.7 to 1.1	.26
3-4 (n = 944)	High dose	499	45		1.0		
	Reduced intensity	178	47	50	0.82	0.8 to 1.3	.95
	Nonmyeloablative	267	54	59	0.72	0.6 to 0.9	.004
≥ 5 (n = 515)	High dose	236	29		1.0		
	Reduced intensity	117	34	35	0.86	0.6 to 1.1	.29
	Nonmyeloablative	162	35	37	0.73	0.6 to 1.0	.02

Abbreviations: ATG, antithymocyte globulin; CMV, cytomegalovirus; HCT-CI, hematopoietic cell transplantation–comorbidity index; HR, hazard ratio; KPS, Karnofsky performance status.

*The Cox regression models were adjusted for diagnosis category, disease risk, HCT-CI risk group, donor type, stem-cell source, KPS percentage, No. of prior regimens, use of ATG, and CMV serology status.

†Adjusted for patient characteristics of recipients of high-dose conditioning.

- **pazienti anche con età > 60 anni possono tollerare bene condizionamenti MA se non hanno altre comorbidity, cioè se hanno score composito 1-2**
- **pazienti con età giovane, anche < 40 anni, ma con comorbidity significative (score composito ≥ 3 e ≥ 5) hanno un alto rischio di NRM**



Stratification of the probabilities of non-relapse mortality (NRM) using the composite comorbidity/age scores among different diagnoses groups

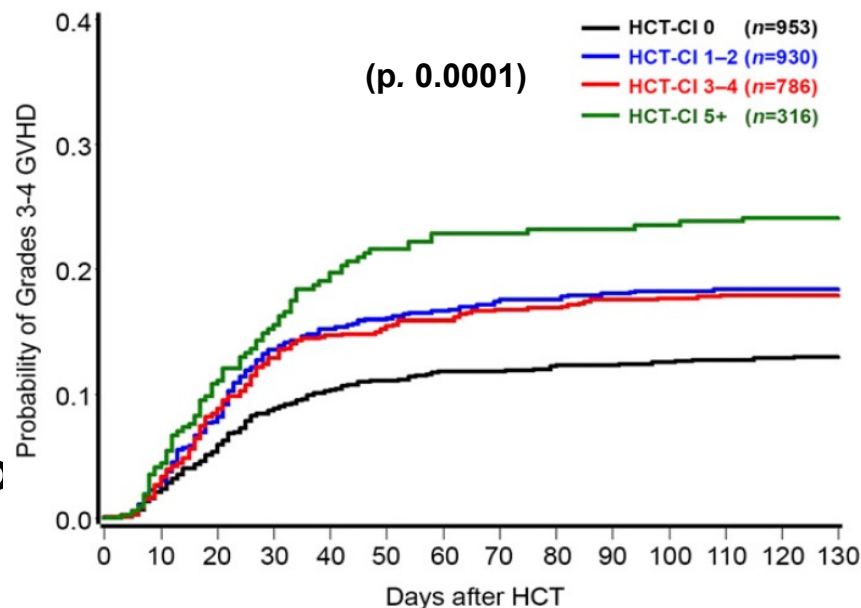
Pretransplant comorbidities predict severity of acute graft-versus-host disease and subsequent mortality

Mohamed Sorrow, Paul Martin, Rainer Storb, Smita Bhatia, Richard Maziarz, Michael Pulsipher, Michael Maris, Christopher Davis, Joachim Deeg, Stephanie Lee, David Maloney, Brenda Sandmaier, Frederick Appelbaum, Theodore Gooley

In sintesi: maggiore HCT-CI score = maggiore grado di GVHD acuta

HCT-CI	aGVHD III-IV %
0	13
1 - 4	18
≥ 5	24

Inoltre l' HCT-CI sembra associato anche alla mortalità da GVHD



- COMORBIDITY ASSESSMENT

- GERIATRIC ASSESSMENT

- AGING- ASSOCIATED BIOMARKERS VALIDATION

Geriatric assessment to predict survival in older allogeneic hematopoietic cell transplantation recipients

Lori S. Muffly,¹ Masha Kocherginsky,² Wendy Stock,¹ Quynh Chu,¹ Michael R. Bishop,¹ Lucy A. Godley,¹ Justin Kline,¹ Hongtao Liu,¹ Olatoyosi M. Odenike,¹ Richard A. Larson,¹ Koen van Besien,³ and Andrew S. Artz¹

Table 1. Patients' demographic and clinical characteristics.

Demographic/Characteristic	N.	%
Total evaluable	203	100
Age, years		
50-59	124	61
60-69	75	37
≥70	4	2
Sex		
Male	130	64
Female	73	36
Primary disease		
AML	87	43
MDS	30	15
NHL	38	19
ALL	12	6
CML	11	5
CLL	10	5
Other	15	7
Disease risk at HCT		
Standard	112	55
High	91	45
Hematopoietic cell donor		
Matched related	92	45
Matched unrelated, 8/8	81	40
Mismatched unrelated, 7/8	2	1
Cord*	28	14
Conditioning regimen intensity		
Ablative	49	24
RIC	154	76
CMV serostatus		
CMV ⁺	123	60
CMV ⁻	40	20
CMV missing	40	20

Two groups:

50-59 yrs

60-73 yrs

AML = acute myeloid leukemia; MDS = myelodysplastic syndrome; NHL = non-Hodgkin lym.

Table 4. Multivariate analyses* of geriatric assessment on overall survival following allogeneic HCT, stratified by age group.

Variable	Total population			50-59 years			60-73 years		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Main model variables									
Age >60	1.83	1.26-2.65	0.001	–	–	–	–	–	–
HCT-CI ≥3	1.56	1.07-2.28	0.02	1.50	0.88-2.53	0.13	1.72	0.99-2.98	0.05
Active disease at HCT	1.31	0.90-1.90	0.16	1.54	0.92-2.58	0.10	1.27	0.71-2.27	0.42
Myeloablative regimen	1.54	1.02-2.31	0.04	2.14	1.24-3.69	0.01	1.07	0.54-2.10	0.85
GA variables									
IADL impairment	2.38	1.59-3.56	<0.001	1.86	1.07-3.24	0.03	3.25	1.75-6.05	<0.001
Slow walk speed	1.80	1.14-2.83	0.01	1.16	0.60-2.28	0.66	3.27	1.68-6.39	0.001
Reduced mental health	1.67	1.13-2.48	0.01	1.55	0.92-2.62	0.10	1.87	1.01-3.49	0.04
Low albumin	1.52	0.94-2.46	0.09	1.23	0.57-2.63	0.60	2.62	1.26-5.47	0.01
High CRP	2.51	1.54-4.09	<0.001	1.89	0.94-3.79	0.07	3.13	1.52-6.46	0.002

HR: hazard ratio; 95% CI: 95% confidence interval; GA: geriatric assessment; HCT-CI: hematopoietic cell transplantation comorbidity index; HCT: hematopoietic cell transplantation.

We further stratified the adjusted survival analyses by the two age cohorts of 50-59 years *versus* 60 years or over (Table 4). HRs for all GA measures were quantitatively higher in the older age cohort, suggesting a greater predictive effect of GA in older transplant recipients. The prognostic effect of the IADL/HCT-CI risk score was similarly amplified in the older cohort (Figure 1B and C). For example, 2-year OS for those patients aged 60 years or over with an IADL/HCT-CI score of 1 was 29% (compared to 53% for 50-59 year olds with a score of 1), and for those aged 60 years or over with a score of 2 was 0%.

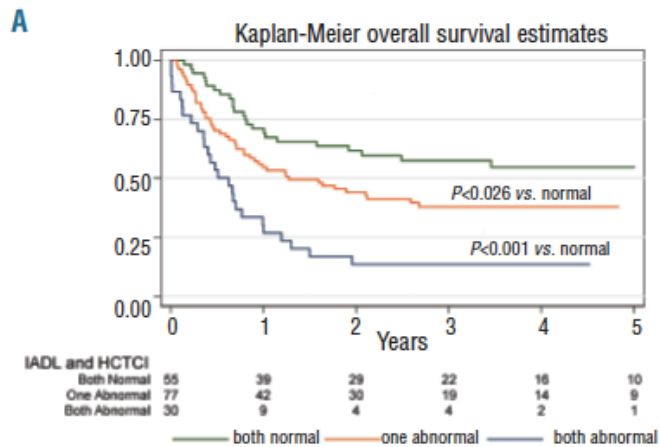
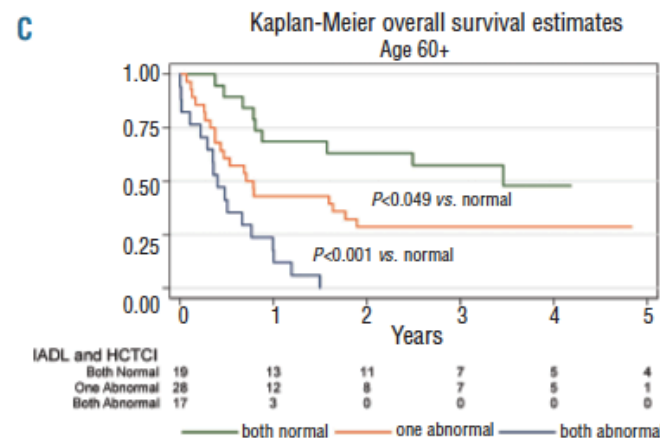
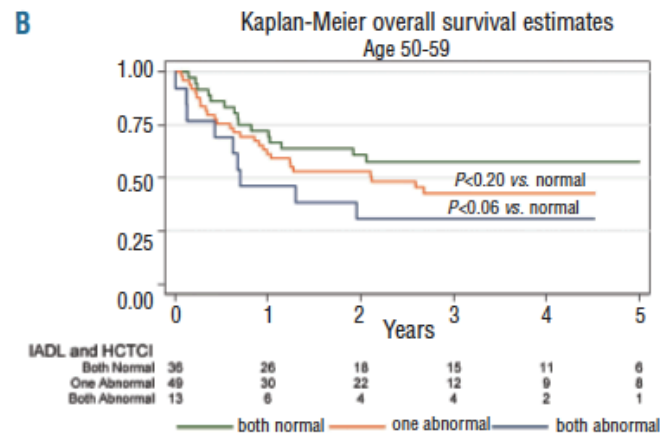


Figure 1. Overall survival by IADL and HCT-CI risk score for total cohort (A), age 50-59 years (B), and age 60-73 years (C). Abnormal IADL required at least one limitation and abnormal HCT-CI required a score of 3 or more.



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Disegno sperimentale

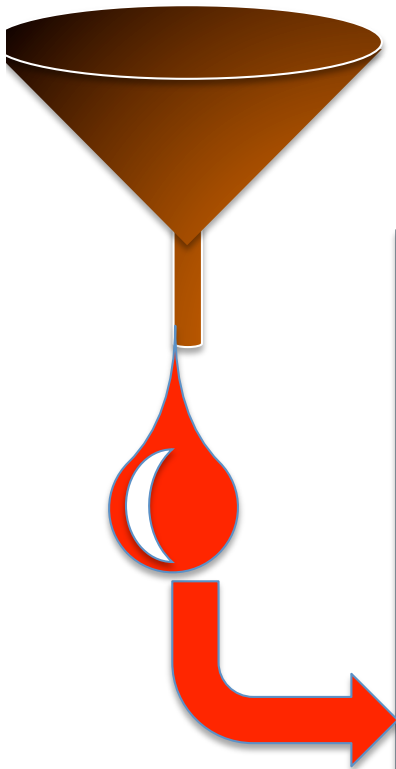
10 CBU (da banca ERCBB)

20 CSE da donatore

10 BM (donatore di midollo) + 10 PB (donatore di periferiche)

20 CSE da Riceventi

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