Progetto Ematologia Romagna

Quale e quando inviare il paziente al trapianto

Barbara Guiducci

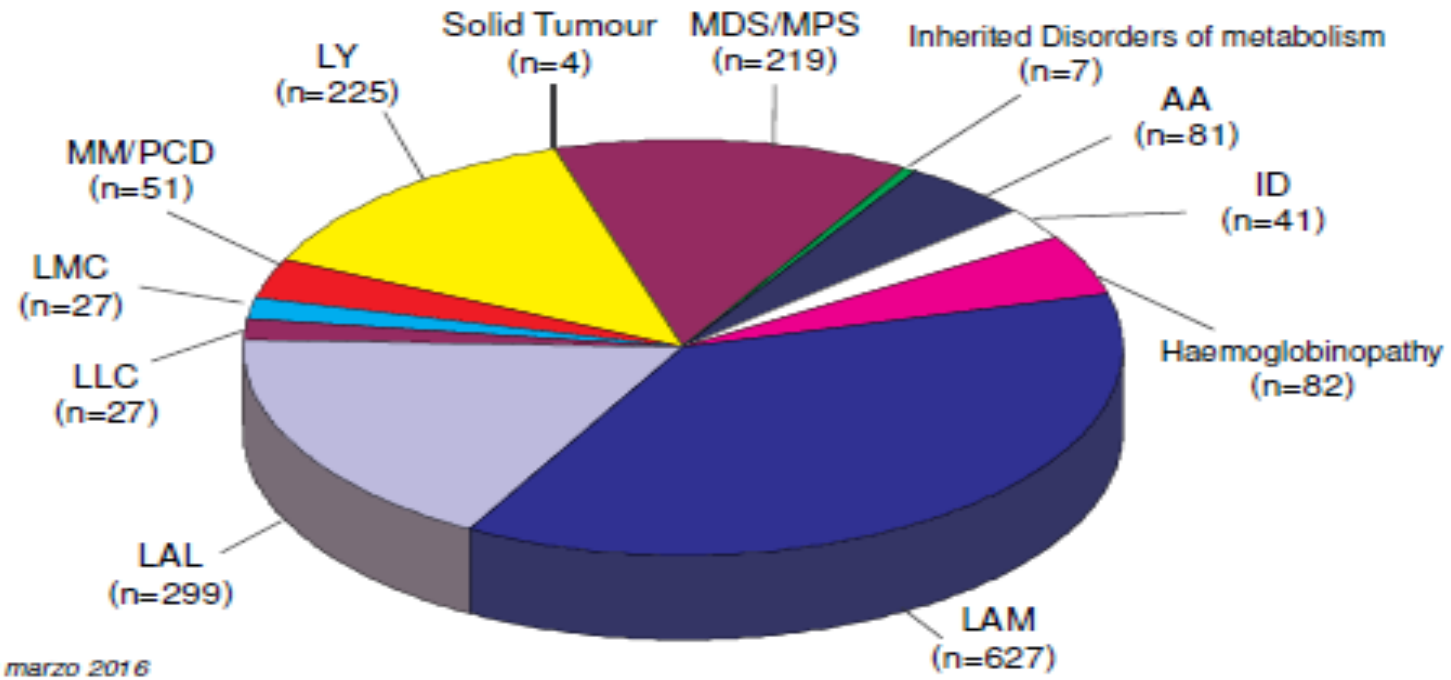
Azienda ospedaliera Ospedali Riuniti Marche Nord

No disclosure to declare

GITMO Trapianto Allogenico

Numero Trapianti per principali Patologie

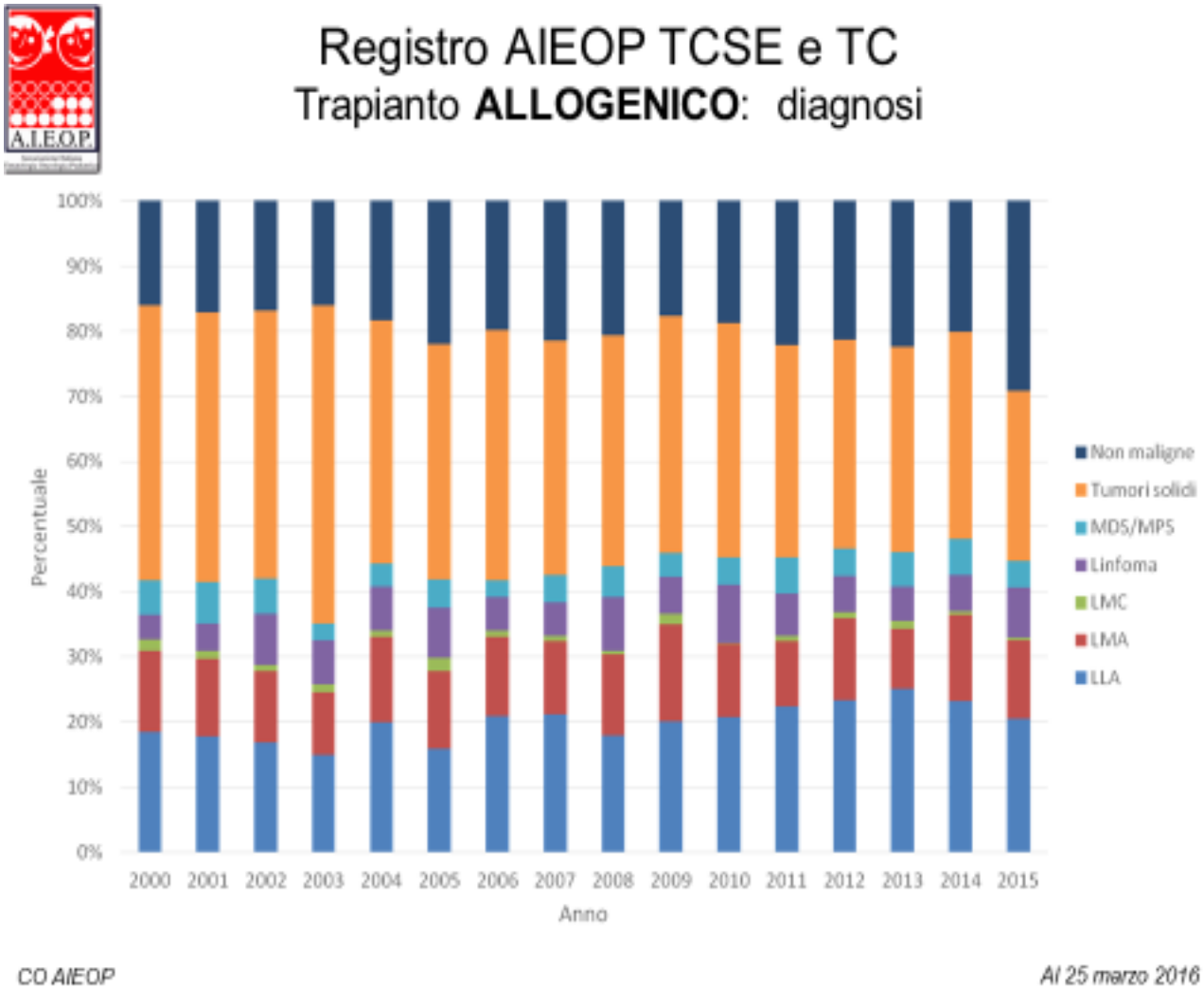
Attività 2015



al 30 marzo 2016

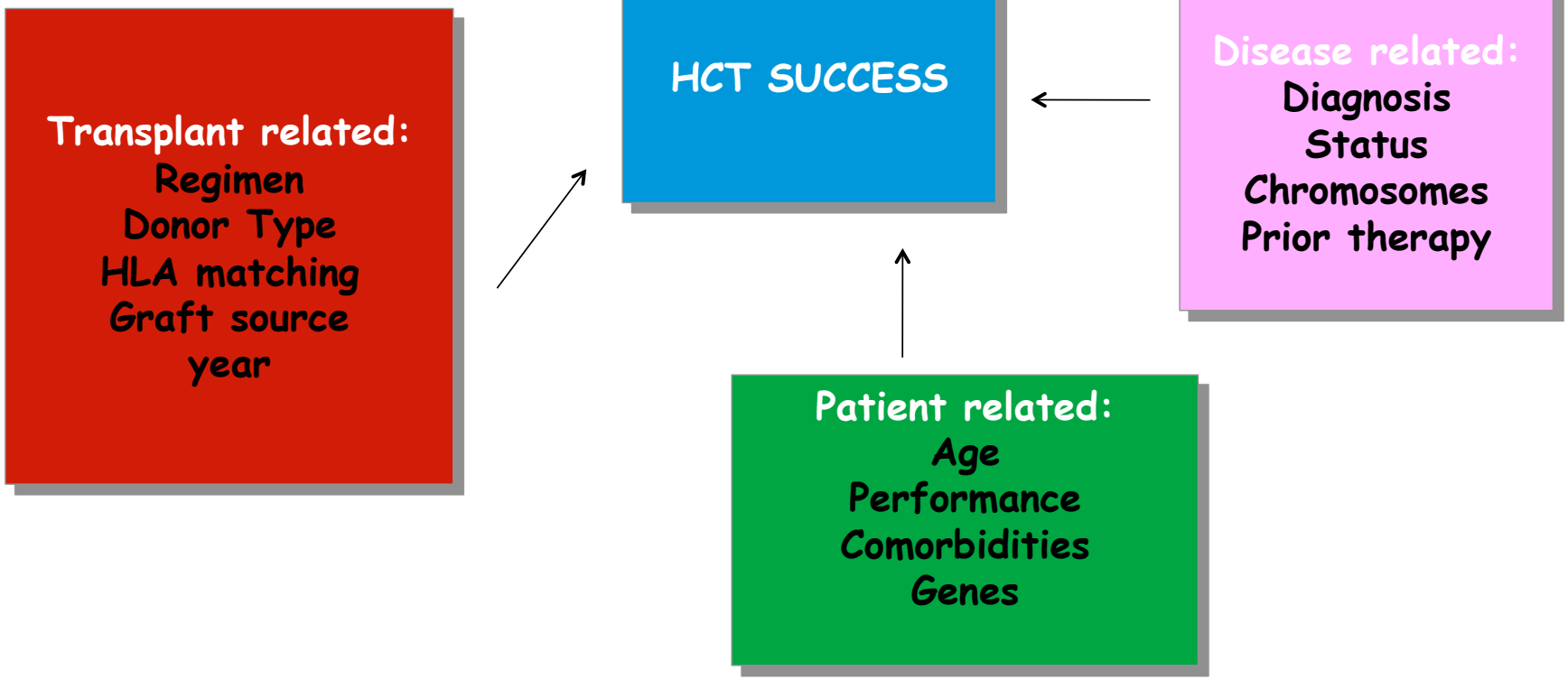
DA VITA NASCE VITA: PROMUOVERE LA DONAZIONE DI CELLULE STAMINALI EMOPOIETICHE IN ITALIA

GITMO


Registro AIEOP TCSE e TC
Trapianto ALLOGENICO: diagnosi
A.I.E.O.P.
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Percentuale
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Anno
Non maligne
Tumori solidi
MDS/MPS
Linfoma
LMC
LMA
LLA
CO AIEOP
Al 25 marzo 2016

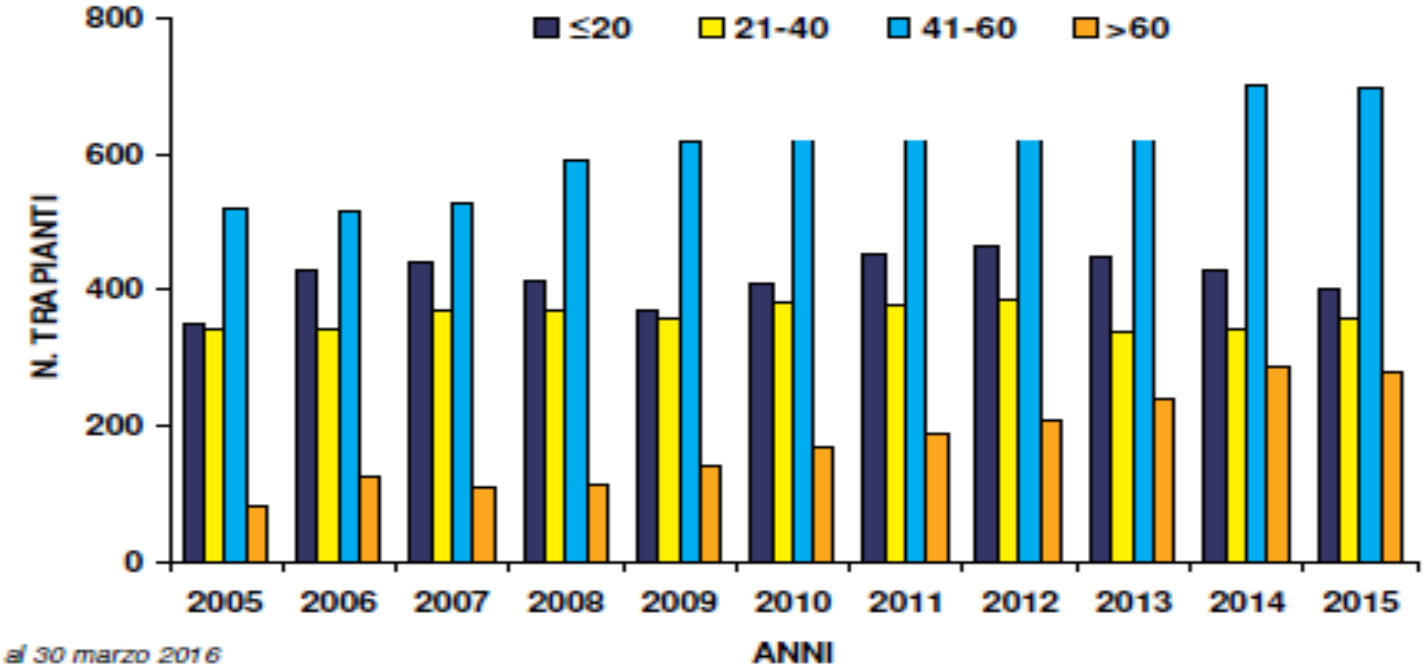
ALLOGENIC HCT
The only potential curative therapy for various hematologic diseases

THE MOST COMPLICATED PROCEDURE IN MEDICINE



GITMO Trapianto Allogenico

Età al trapianto



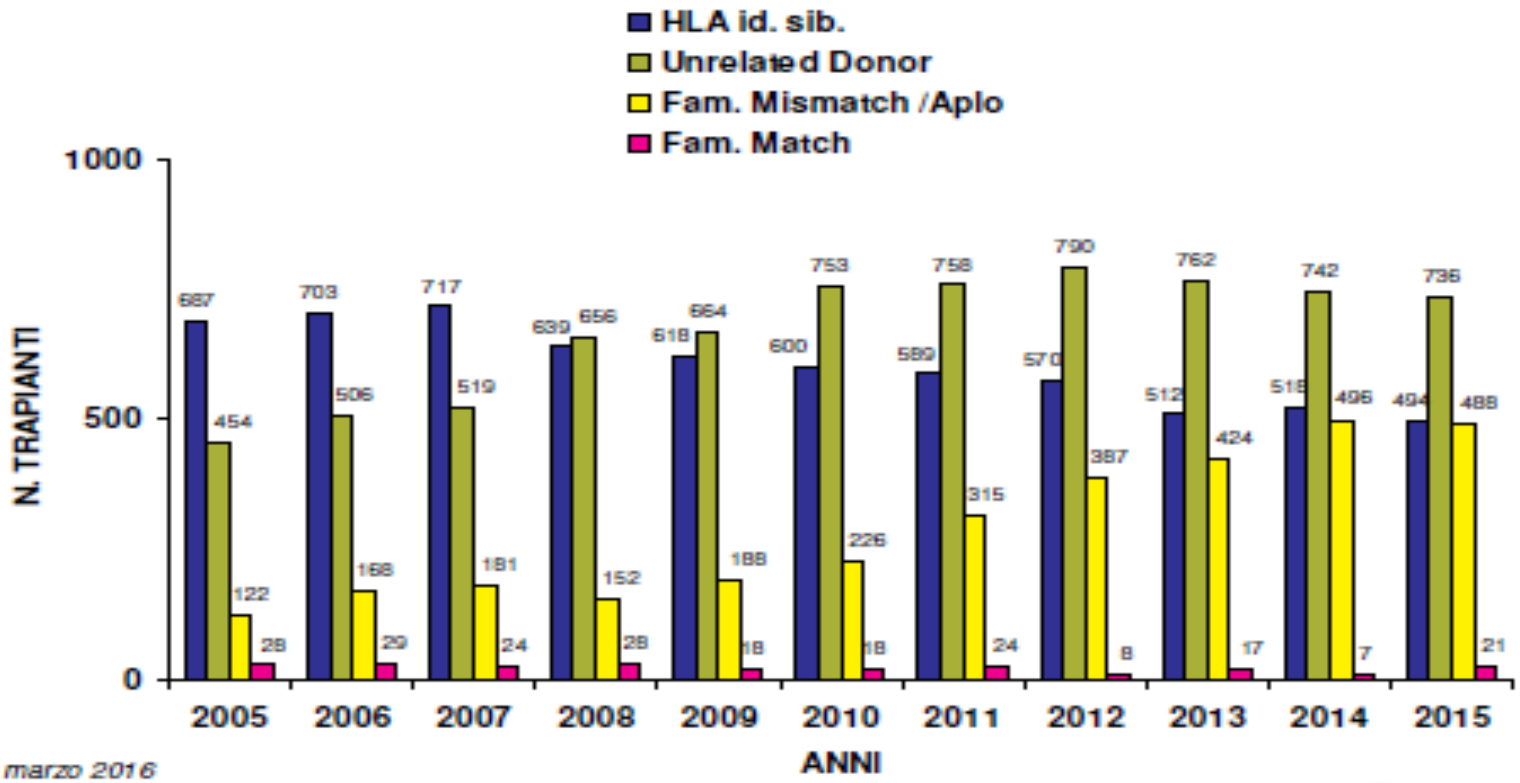
al 30 marzo 2016

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

GITMO

GITMO Trapianto Allogenico

Tipo di trapianto

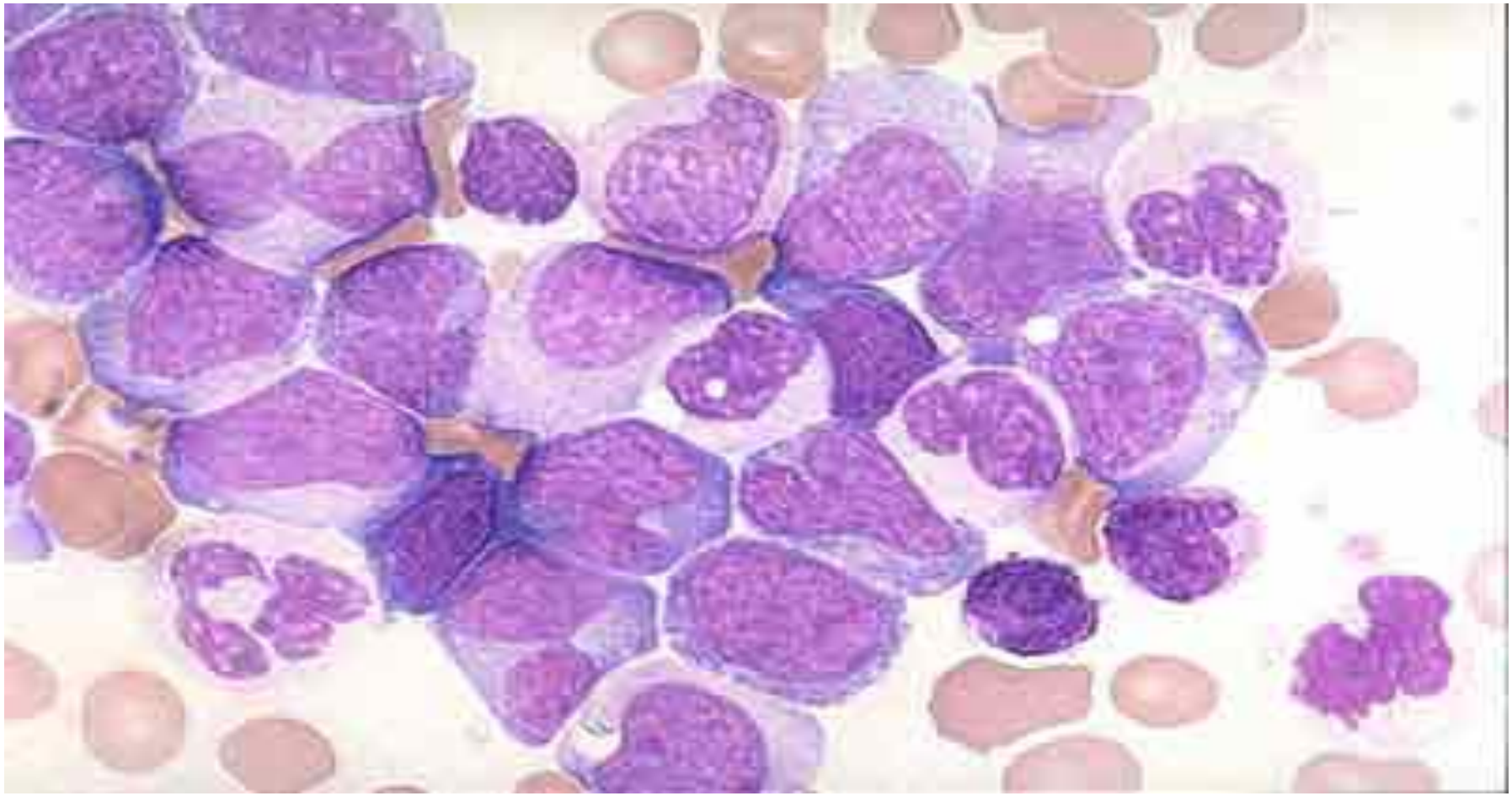


al 30 marzo 2016

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

GITMO

2017



PROGETTO EMATOLOGIA – ROMAGNA Rimini, 8 aprile 2017

blood
JOURNAL OF THE AMERICAN SOCIETY OF HEMATOLOGY

Genetic group	Subsets
Favorable	t(8;21)(q22;q22); *RUNX1-RUNX1T1*
	inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
	Mutated *NPM1* without *FLT3*-ITD (normal karyotype)
	Mutated *CEBPA* (normal karyotype)
Intermediate-I*	Mutated *NPM1* and *FLT3*-ITD (normal karyotype)
	Wild-type *NPM1* and *FLT3*-ITD (normal karyotype)
	Wild-type *NPM1* without *FLT3*-ITD (normal karyotype)
Intermediate-II	t(9;11)(p22;q23); *MLLT3-MLL*
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	inv(3)(q21q26.2) or t(3;3)(q21;q26.2);*RPN1-EVI1*
	t(6;9)(p23;q34); *DEK-NUP214*
	t(v;11)(v;q23); *MLL* rearranged
	–5 or del(5q); –7; abnl(17p); complex karyotype

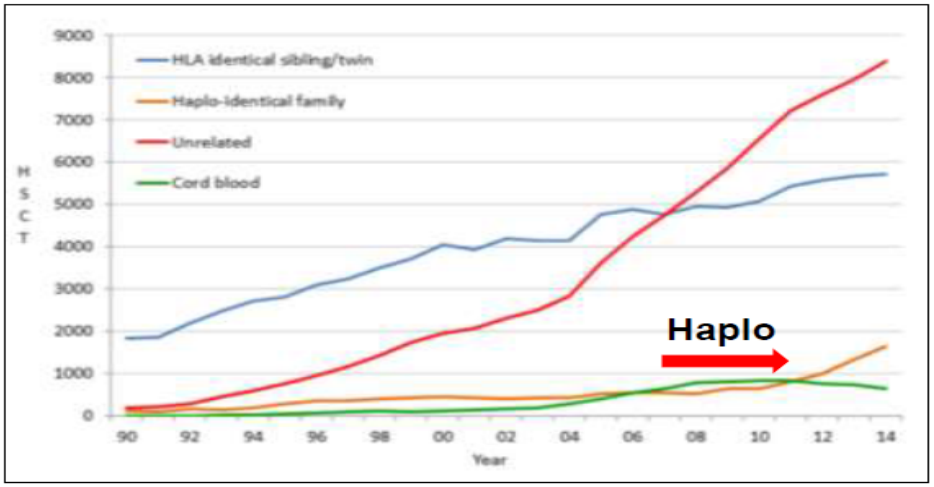
Dohner, H. et al. Blood 2010;115:453-474

Leucemia acuta mieloide
Gruppi di rischio ed indicazione al trapianto (in I RC)

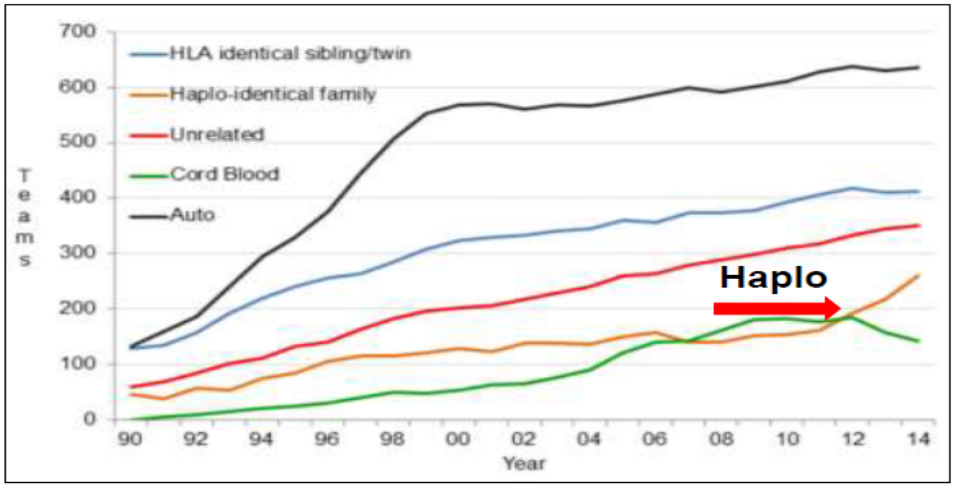
GRUPPO	FATTORI PROGNOSTICI		TMO
FAVOREVOLE BASSO RISCHIO	Citogenetici	t (15;17), t(8,21), inv 16	NO
	Molecolari	Mutazione NPM1 Mutazione CEBPA	
INTERMEDIO		Ne favorevoli Ne sfavorevoli	SI/NO
SFAVOREVOLE ALTO RISCHIO	Clinici	GB esordio >30000-100000 Malattia extramidollare Non RC dopo I ciclo Malattia residua minima LAM secondaria	SI
	Citogenetici	-5,-7,-17, inv 3, t(6,9), t(6,11) Cariotipo complesso	
	Molecolari	FLT3, mutazione MLL, mutazione IDH1	

25% increase in Haplo SCT in 2014 in comparison to 2013

No. of Transplants



No. of Teams

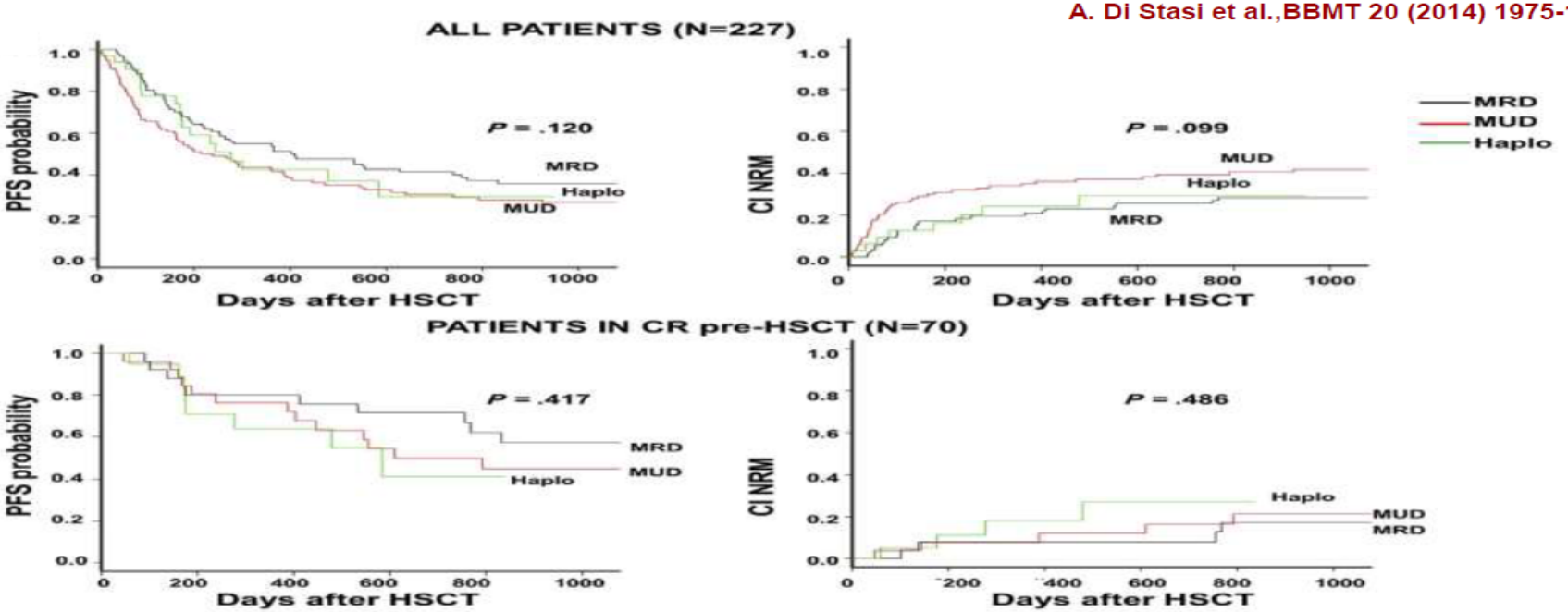


- 40,829 SCT; 15,765 alloSCT (43%); 20,704 autoSCT (57%)
- Compared to 2013 – 13% increase in alloSCT for AML CR1
- Main indication for SCT is Leukemias: 11,853 (33% of total, 96% allo)

Passweg JR et al, submitted

Similar Transplantation Outcomes for Acute Myeloid Leukemia and Myelodysplastic Syndrome Patients with Haploidentical versus 10/10 Human Leukocyte Antigen-Matched Unrelatedand Related Donors

A. Di Stasi et al.,BBMT 20 (2014) 1975-1981

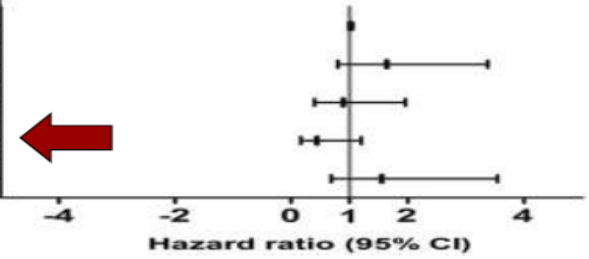


PATIENTS IN CR pre-HSCT (N=70)

Multivariable analysis for Progression free Survival

Effect	Hazard Ratio	*95% CI*	p-value
Age[a]	1.02	*0.99, 1.05*	.301
Cytogenetic (Poor vs. good+intermediate)	1.64	*0.80, 3.38*	.179
Melfalan dose (140 vs. 100)	0.89	*0.40, 1.96*	.771
Donor type (Matched vs. Haplo)	0.44	*0.16, 1.20*	.109
HCT-CI (> 3 vs. ≤ 3)	1.55	*0.68, 3.54*	.303

[a] age is continuous in the model



Haploidentical transplant with posttransplant cyclophosphamide vs matched unrelated donor transplant for acute myeloid leukemia

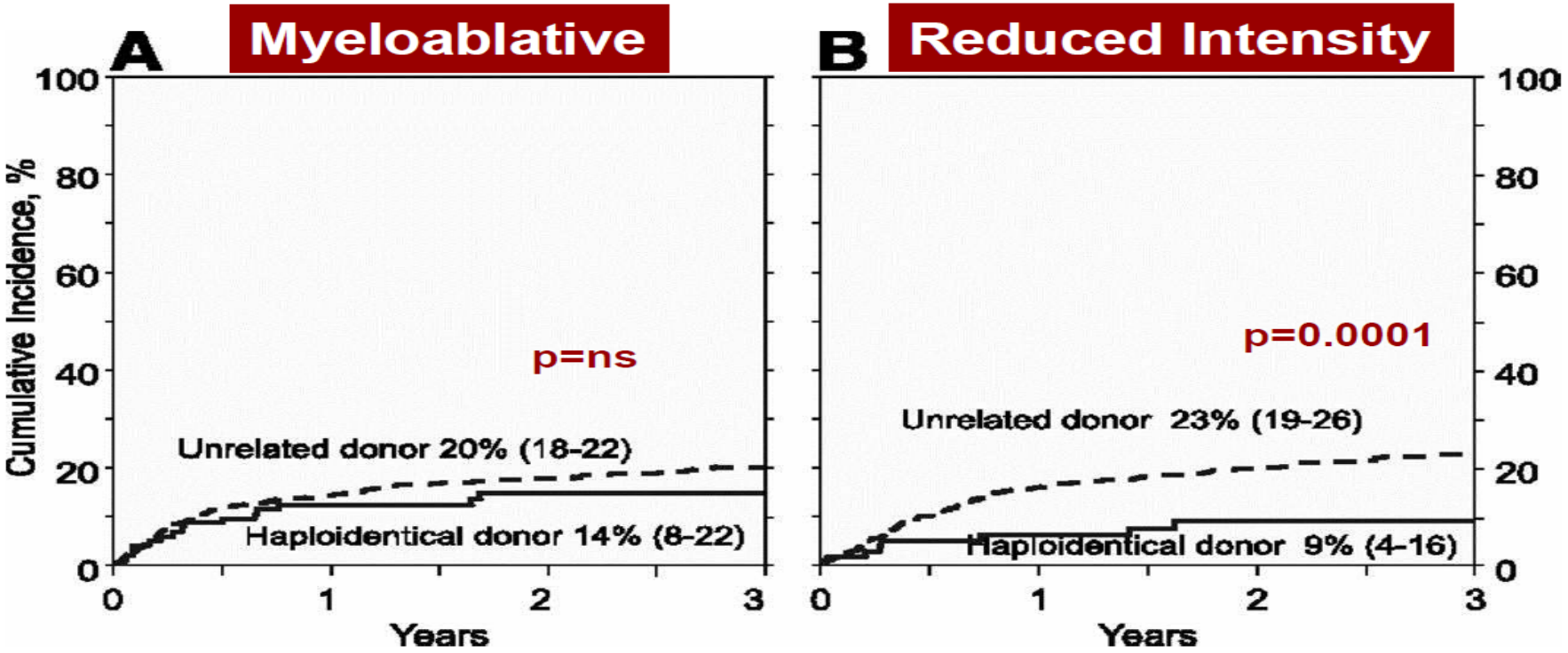
by Stefan O. Ciurea, Mei-Jie Zhang, Andrea A. Bacigalupo, Asad Bashey, Frederick R. Appelbaum, Omar S. Aljitawi, Philippe Armand, Joseph H. Antin, Junfang Chen, Steven M. Devine, Daniel H. Fowler, Leo Luznik, Ryotaro Nakamura, Paul V. O'Donnell, Miguel-Angel Perales, Sai Ravi Pingali, David L. Porter, Marcie R. Riches, Olle T. H. Ringdén, Vanderson Rocha, Ravi Vij, Daniel J. Weisdorf, Richard E. Champlin, Mary M. Horowitz, Ephraim J. Fuchs, and Mary Eapen

Conditioning	Haploidentical	MUD	Total
Myeloablative	104	1245	1349
Reduced Intensity	88	737	825
Total	192	1982	2174

Blood Volume 126(8):1033-1040, August 20, 2015

blood

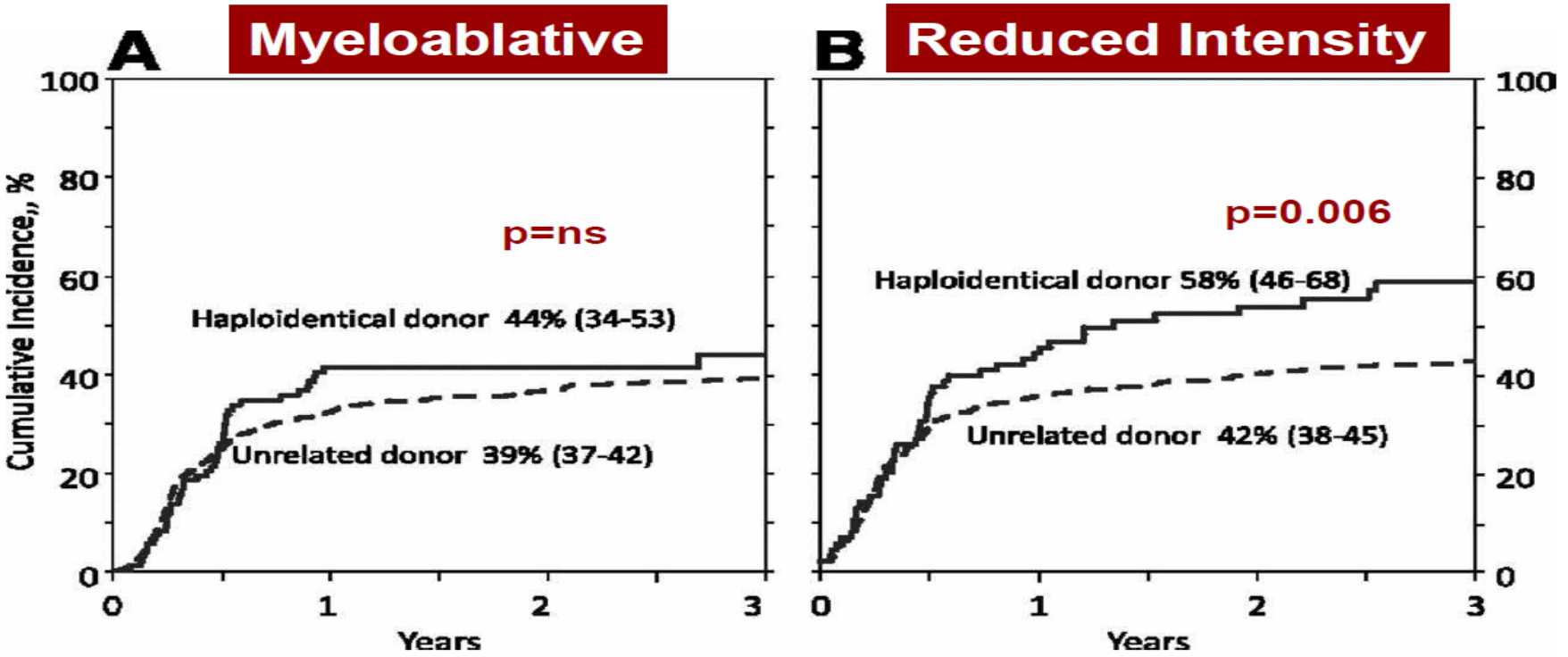
Non relapse mortality.



Stefan O. Ciurea et al. Blood 2015;126:1033-1040

blood

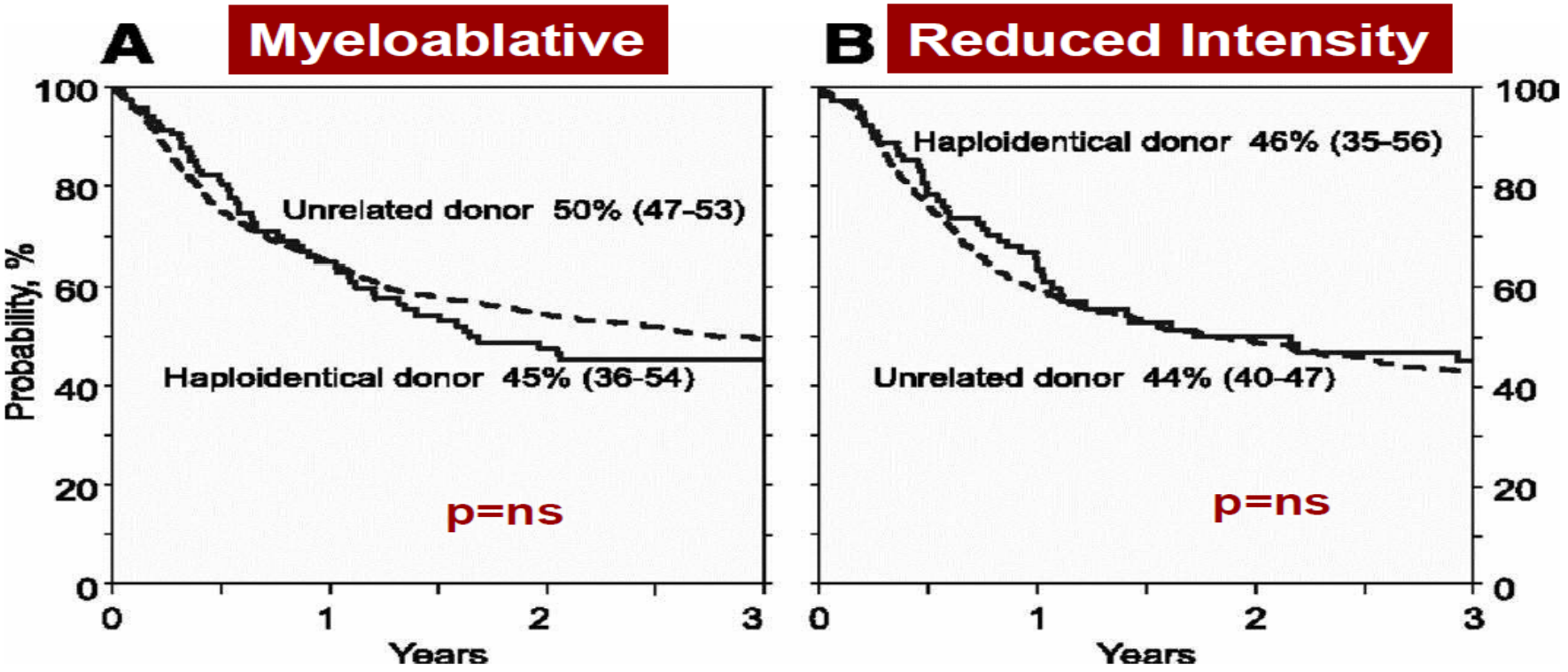
Relapse



Stefan O. Ciurea et al. Blood 2015;126:1033-1040

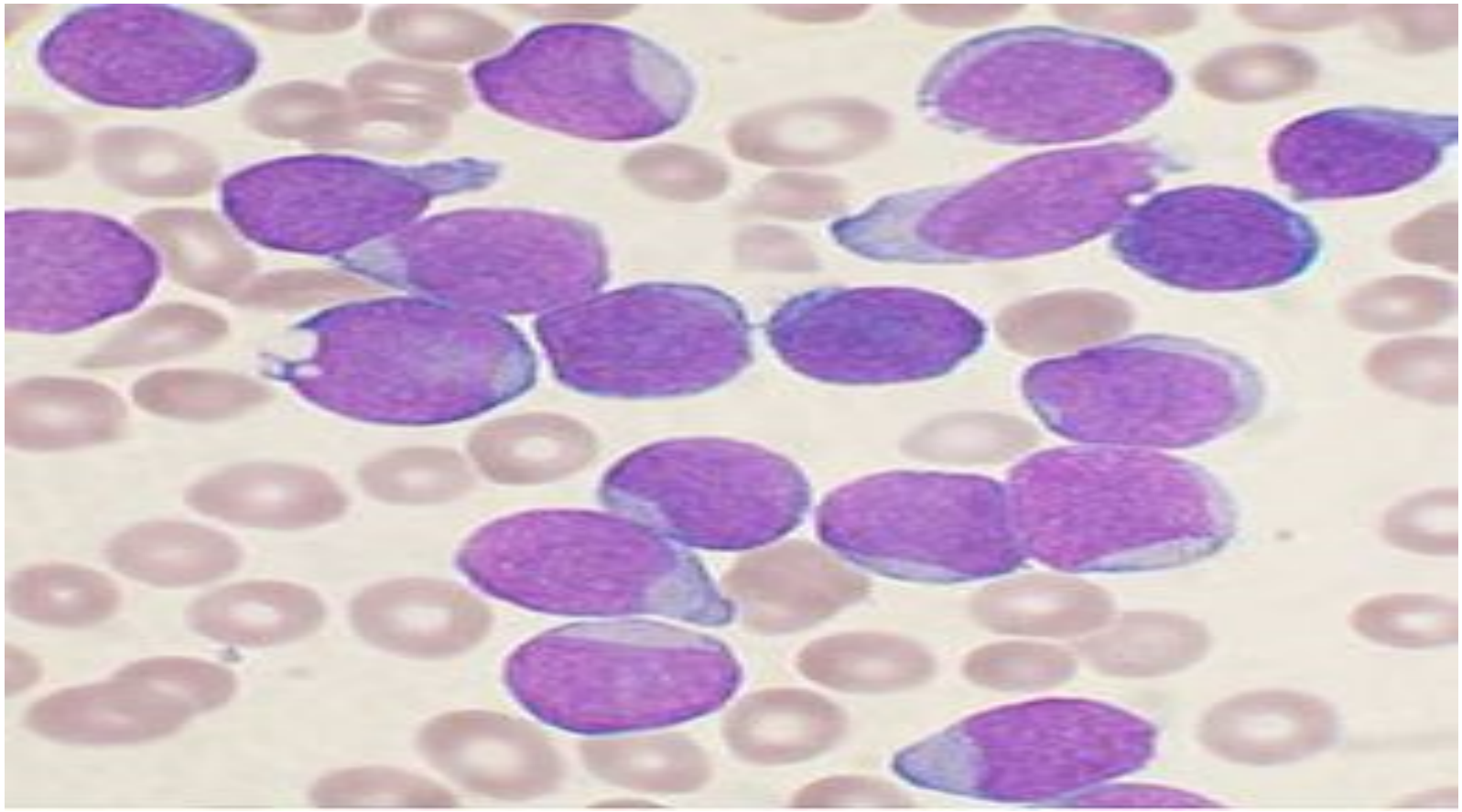
blood

Overall survival



Stefan O. Ciurea et al. Blood 2015;126:1033-1040

blood



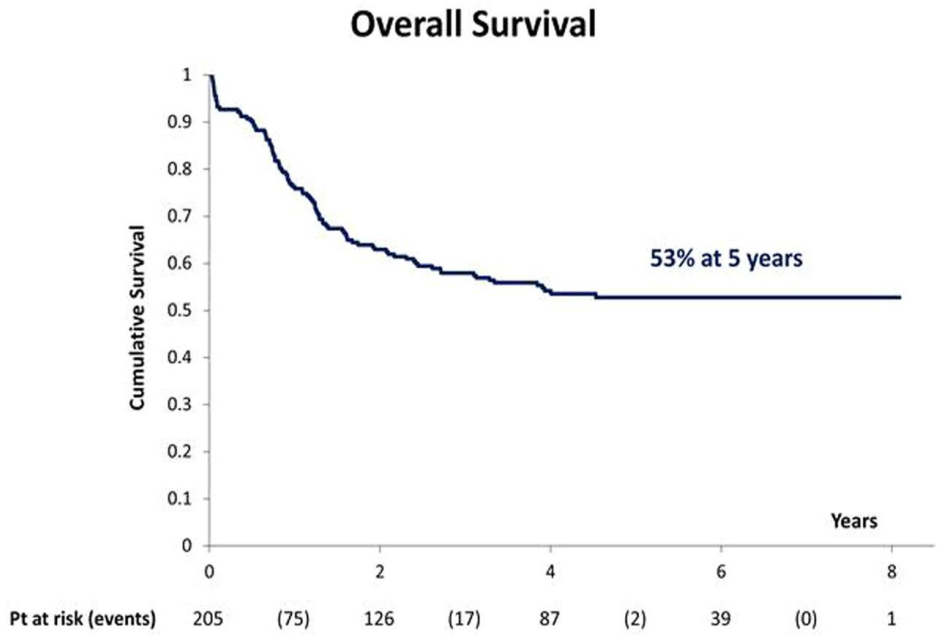
Leucemia acuta linfoblastica (LAL)

Gruppi di rischio e indicazioni al trapianto in 1ª RC

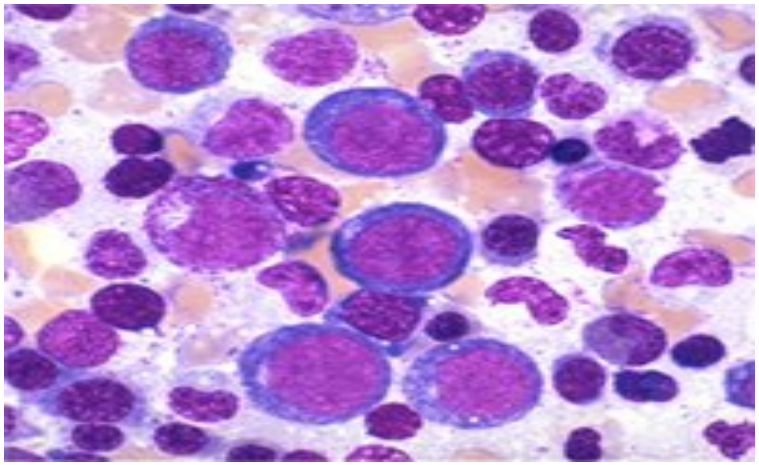
Gruppo	Fattori prognostici		TMO
Sfavorevole alto rischio	clinici	età adulta globuli bianchi d'esordio >30-100.000/mm^2 coinvolgimento SNC immunofenotipo T o pro-B non RC dopo 1° ciclo di chemioterapia malattia residua minima presente	SI
	citogenetici	cromosoma Ph'positivo, t (9;22) t (4;11) t (8;14) t (1;19) del (6q), del (7p), del (17p), -7, -8 cariotipo complesso ipoploidia/triploidia	
	molecolari	BCR/ABL mutazione MLL	

Final results of Northern Italy Leukemia Group (NILG) Trial 10/07 Combining Pediatric-type Therapy with Minimal Residual Disease Study and Risk-Oriented Hematopoietic Cell Transplant in Adult Acute Lymphoblastic Leukemia,

Bassan et al, ASH 2016



The HCT allocation cohort consisted of predefined very high-risk patients (vHR: WBC >100, highly adverse cytogenetics, pre-T/mature T-ALL) regardless of MRD, of HR patients without MRD study (HR: late CR; B-ALL with WBC >30 or pro-B phenotype), and of HR or standard-risk (SR) patients with MRD ≥ 10^{-4} at w10/16 or positive at w22.



Appropriate selection of patients involves **consideration of patient factors,** including use of geriatric assessment tools and comorbidity scales, that predict risks of regimen-related toxicity as well as disease factors, including genetic markers, which predict survival with both non-HCT and HCT therapy.

Optimal timing of HCT for fit patients must consider MDS risk scores and life-years to be gained, with earlier transplantation indicated for patients with intermediate-2 and high-risk disease but judicious delay for lower risk patients.

Selection of suitable conditioning regimens must balance risks of toxicity with opportunity for maximum disease control.

Saber and Horowitz, Blood 2016

Only < 10% of all patients are potential candidates

(age, comorbidities, disease-risk)

TRANSPLANT AT WHICH STAGE OF THE DISEASE ?

IPSS: INT-2/HIGH

IPSS-R: int, high, very high

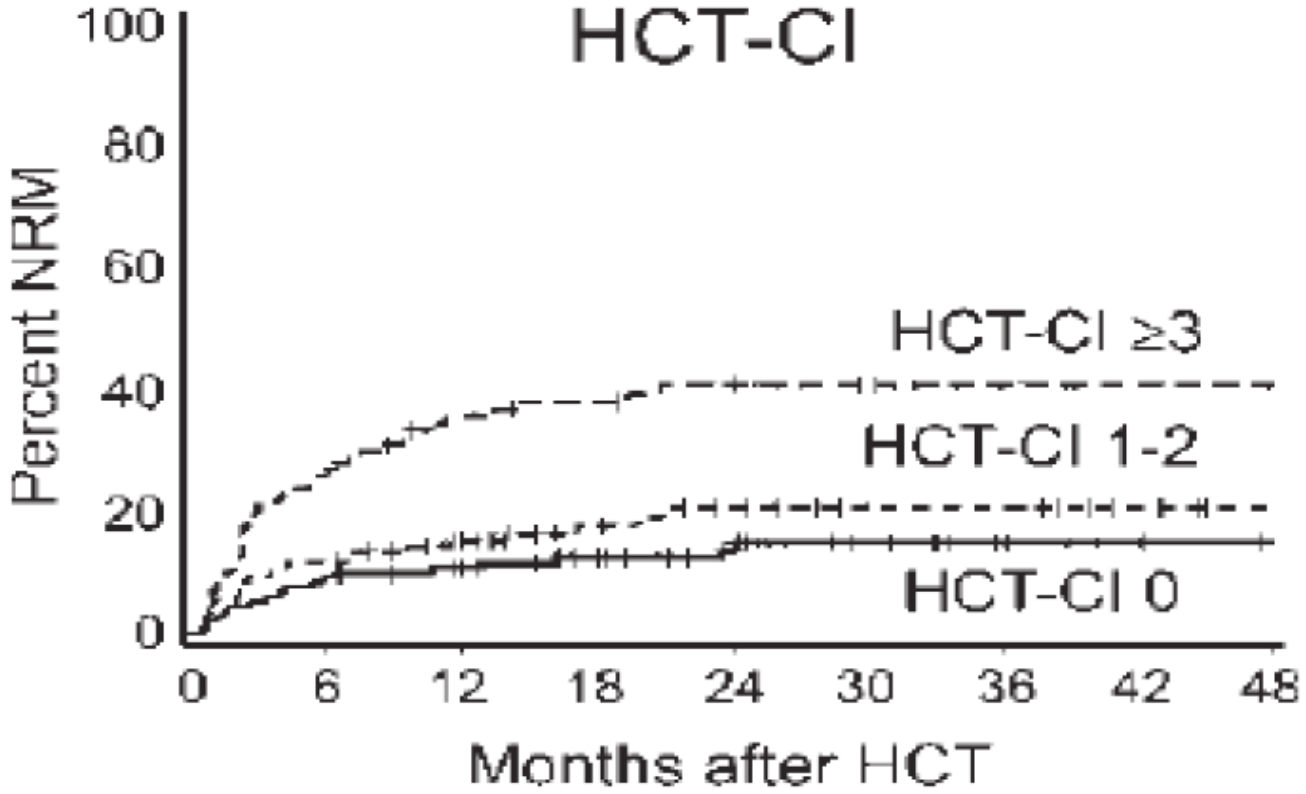
SORROR

Table 1. HCT-CI

Comorbidities	HCT-CI scores
Arrhythmia	1
Cardiovascular comorbidity	1
Inflammatory bowel disease	1
Diabetes or steroid-induced hyperglycemia	1
Cerebrovascular disease	1
Psychiatric disorder	1
Mild hepatic comorbidity	1
Obesity	1
Infection	1
Rheumatologic comorbidity	2
Peptic ulcer	2
Renal comorbidity	2
Moderate pulmonary comorbidity	2
Prior malignancy	3
Heart valve disease	3
Moderate/severe hepatic comorbidity	3
Severe pulmonary comorbidity	3
Total score = _____	

BLOOD, 11 APRIL 2013 • VOLUME 121, NUMBER 15

Sorror Blood 2005



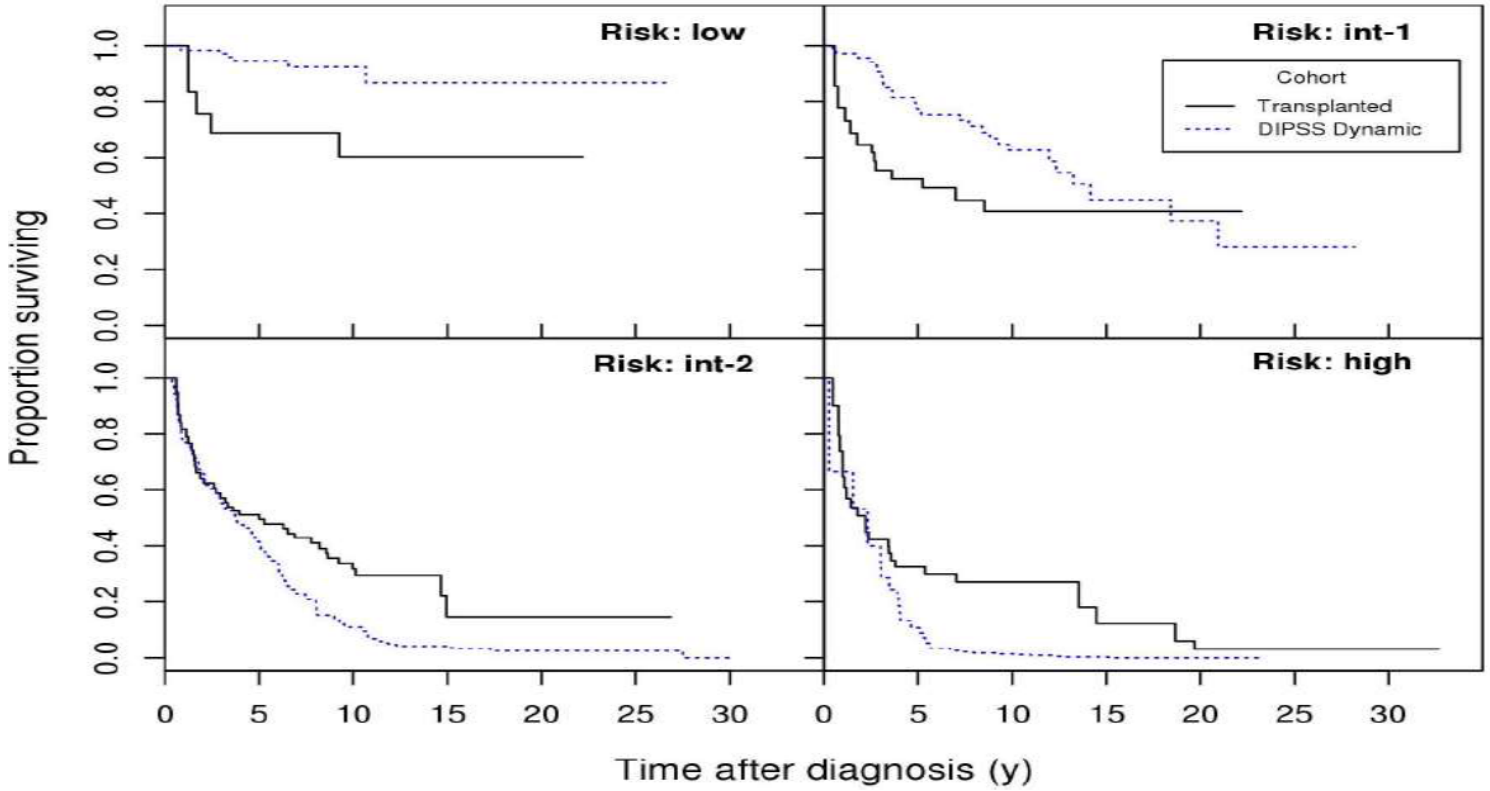
PROGNOSTIC SCORES IN MYELOFIBROSIS

score	Lille score Dupriez et al, 1996	IPSS Cervantes et al, 2008	DIPSS Passamonti 2010	DIPSS-plus Gangat 2011
Adverse factors	• Hb<10g/dL • WCc<4 or >30x10⁶/L	•Age >65y •Hb<10g/dL •Blasts >1% •Constitutional symptoms •WCc >25x10⁶/L	•Age >65y •Hb<10g/dL •Blasts >1% •Constitutional symptoms •WCc >25x10⁶/L	•Age >65y •Hb<10g/dL •Blasts >1% •Constitutional symptoms •WCc >25x10⁶/L • platelets <100x109/L •RBC need •Unfavourable karyotype:+8,-7,-5,17p,11q23,12p-
score	1 point each	1 point each	1 point each Hb: 2 points	The sum of the DIPSS score (int-1: 1 point, int-2: 2 points; high 3 points) plus 1 additional to platelets, karyo, RBC needs
risk	LOW 0 INT 1 HIGH 2	LOW 0 NT-1 1 NT-2 2 HIGH 3	LOW 0 INT-1 1-2 INT-2 3-4 HIGH 5-6	LOW 0 INT-1 1 INT-2 2-3 HIGH 4-6

blood Prepublished online March 17, 2015;
doi:10.1182/blood-2014-10-608315

Impact of allogeneic stem cell transplantation on survival of patients less than 65 years with primary myelofibrosis

Nicolaus Kröger, Toni Giorgino, Bart L. Scott, Markus Ditschkowski, Haefaa Alchalby, Francisco Cervantes, Alessandro Vannucchi, Mario Cazzola, Enrica Morra, Tatjana Zabelina, Margherita Maffioli, Arturo Pereira, Dietrich Beelen, H. Joachim Deeg and Francesco Passamonti



ALLO-TRANSPLANT IN MYELOFIBROSIS

Prognosis of the disease:

Median OS<3 years in

Int-2 and HR pt

Risk of NRM

Non transplant treatments:

Conventional therapy

JAK2 inhibitors

Risk of morbility due cGVHD

Relapse after transplant

CONSENSUS by EBMT/ELN International Working Group

ELEGIBILITY:

• All patients with intermediate-2 or high-risk disease according to IPSS, DIPSS or DIPSS+, and age <70 years, should be considered candidates for allo-SCT.

•Pts with intermediate-1-risk disease and age <65 years should be considered candidates for allo-SCT if they present with transfusion-dependent anemia, or blasts in PB > 2%, or adverse cytogenetic.

Patients with low-risk disease should not be considered candidates for allo-SCT.

PROCEDURE:

•The optimal intensity of the conditioning regimen still needs to be defined.

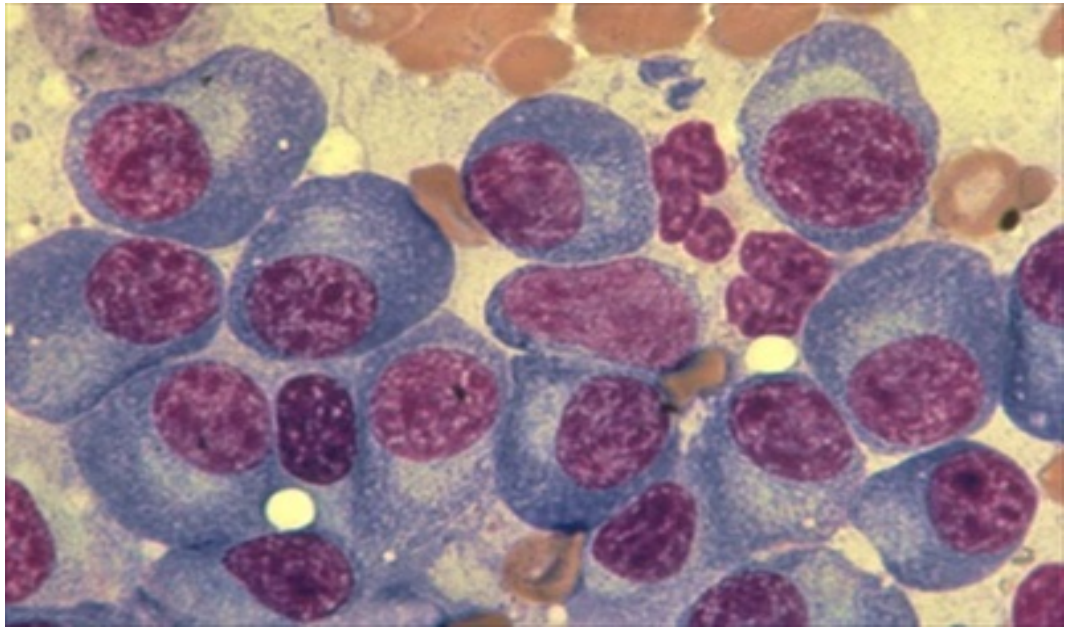
•For patients with higher age and/or comorbidities, a lower Intensity regimen is more appropriate, while for patients with advanced disease and good performance status a more intensified regimen should be selected.

•A spectrum of reduced intensity conditioning regimens and protocols has shown acceptable TRM and OS.

The Panel identified this as an area of a major unmet clinical need

Kroger et al, LEUKEMIA 2015

- In the era of JAK2 inhibitors, allogeneic transplant is still the only curative approach for patients with myelofibrosis.
- Patients with DIPSS intermediate-2 and high-risk myelofibrosis or RBC transfusion dependent or with unfavourable karyotype should be candidated to allogeneic transplant due to median OS < 3 years .
- The choice of the appropriate conditioning regimen is an unmet clinical need.
- Ruxolitinib could be effective to reduce spleen and control symptoms before allo-SCT in about 50% of patients.Ruxolitinib could be stopped the day before conditioning to avoid rebound phenomenon.
- Ruxolitinib is a promising treatment of steroid refractory GVHD.



Ruolo dell'allogenico.....

nell'era nuovi farmaci .....ma soprattutto dell'autologo.....

Reduced-intensity conditioning for myeloma: lower nonrelapse mortality but higher relapse rates compared with myeloablative conditioning

Charles Crawley,[1] Simona Iacobelli,[2] Bo Björkstrand,[3] Jane F. Apperley,[4] Dietger Niederwieser,[5] and Gösta Gahrton,[3] for the Chronic Leukaemia Working Party of the European Group for Blood and Marrow Transplantation (EBMT)

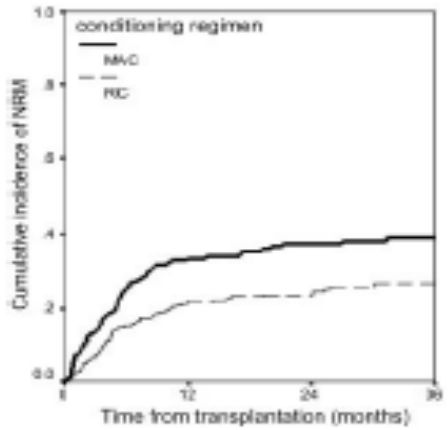


Figure 2. Nonrelapse mortality in 516 patients with myeloma who underwent transplantation with reduced-intensity or myeloablative conditioning.

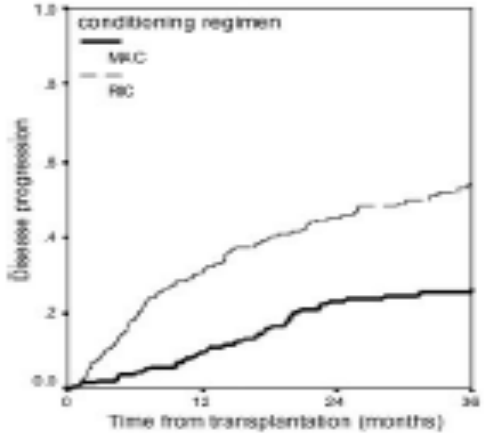


Figure 3. Cumulative incidence of disease relapse or progression in 516 patients with myeloma who underwent transplantation with reduced-intensity or myeloablative conditioning.

Allogeneic Stem Cell Transplantation in Multiple Myeloma Relapsed after Autograft: A Multicenter Retrospective Study Based on Donor Availability

Francesca Patriarca,[1] Hermann Einsele,[2] Francesco Spina,[3] Benedetto Bruno,[4] Miriam Isola,[5] Chiara Nozzoli,[6] Andrea Nozza,[7] Alessandra Sperotto,[1] Fortunato Morabito,[8] Gernot Stuhler,[2] Moreno Festuccia,[4] Alberto Bosi,[6] Renato Fanin,[1] Paolo Corradini[9]

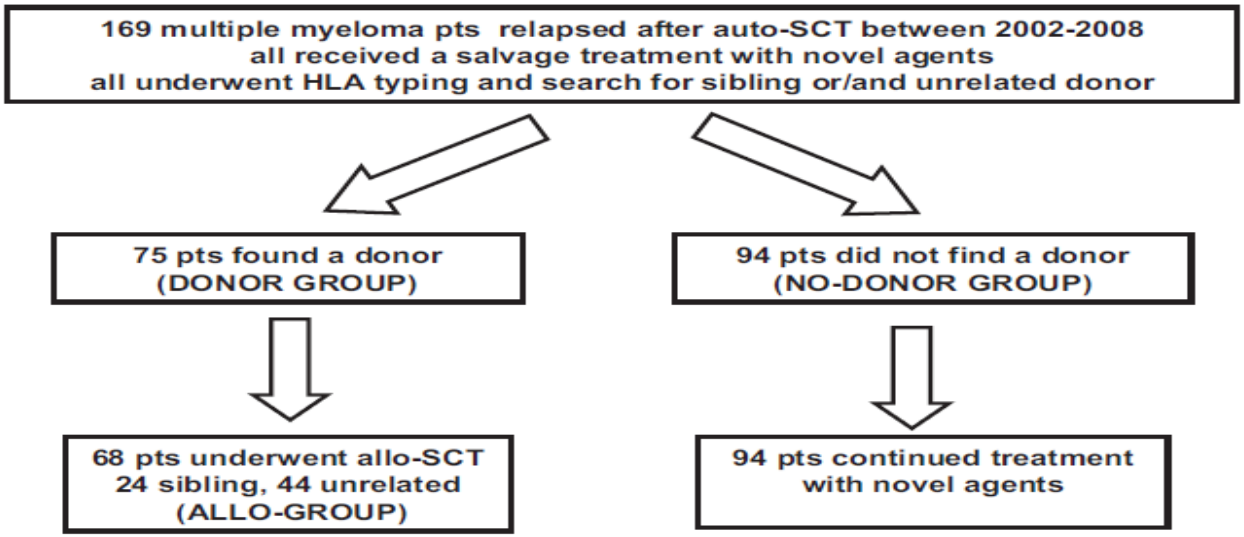


Figure 1. Flow chart of the study.

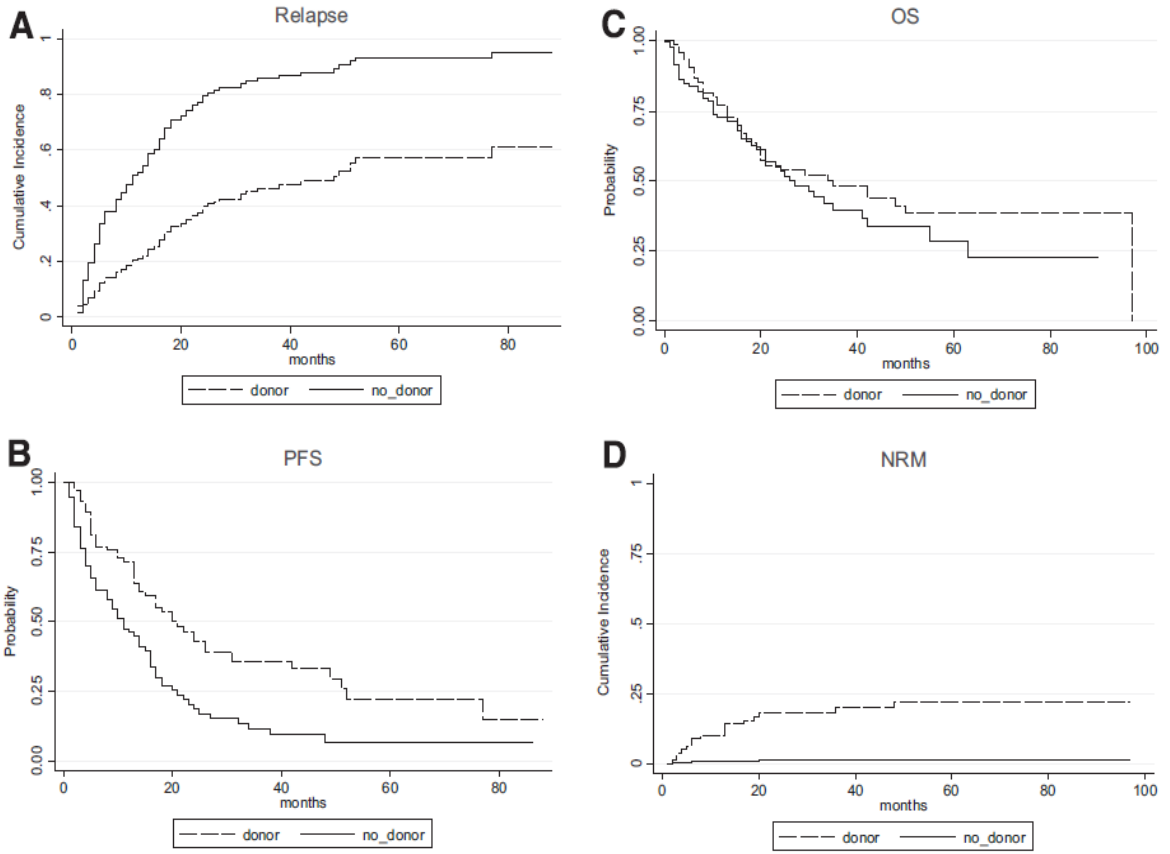


Figure 2. Comparisons between donor and no-donor groups. (A) Incidence of relapse ($P < .0001$). (B) PFS ($P < .0001$). (C) OS ($P = .329$). (D) NRM ($P = .0004$).

International Myeloma Working Group Consensus Statement Regarding the Current Status of Allogeneic Stem-Cell Transplantation for Multiple Myeloma

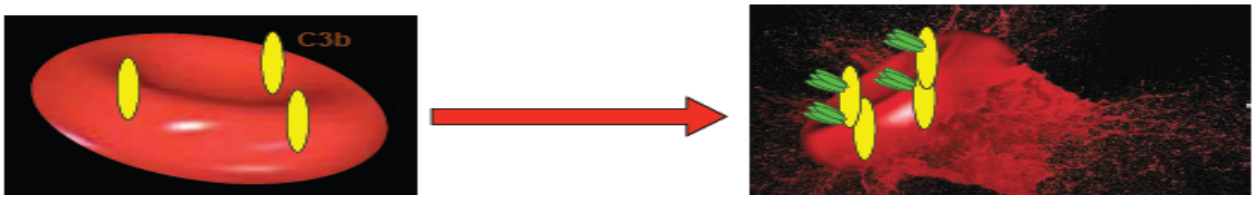
Henk Lokhorst, Hermann Einsele, David Vesole, Benedetto Bruno, Jesus San Miguel, Jose A. Pérez-Simon, Nicolaus Kröger, Philippe Moreau, Gosta Gahrton, Cristina Gasparetto, Sergio Giralt, and William Bensinger

Table 3. Currently Performed and Planned Prospective Trials With Reduced Intensity Allografting in Myeloma

Study Group	Coordinator(s)	Target No.	Patients	Design	Regimen	Proph GVHD	Post Allo Therapy	Time Period
DSMM XII	Einsele/Berdel/ Bunjes/Finke/ Bornhäuser	160	Newly diagnosed (stratification by prognostic factors)	Phase II	Fludarabin, treosulfan	Mycophenolic acid, cyclopsporin	Lenalidomide	2009-2010
Gimema	Bruno	53	Newly diagnosed (stratification by prognostic factors)	Phase II (match-control analysis included)	Auto/low-dose total-body irradiation	Mycophenolic acid, cyclopsporin	Lenalidomide (start at month 6 after transplantation)	2009-2013
HOVON	Lokhorst	104	Chemotherapy-sensitive first relapse	Randomized phase II	Melphalan/ fludarabin CD3/ CD19 depletion	Short-time cyclopsporin	Lenalidomide *v* lenalidomide/ bortezomib/pre-emptive DLI	2010-2013
Intergroupe Française Myeloma	Yacoub-Agha	30	Newly diagnosed 17 P deletion	Phase II	Tandem Allo/Auto	Cyclopsporin, mycophenolic acid	Lenalidomide/pre-emptive DLI	2010-2012
Pethema/EUMN	Perez-Simon/ SanMiguel	90	Chemotherapy-sensitive first relapse	Phase I/II	Melphalan/ fludarabin /Bortezomib	Rapamycin/ bortezomib *v* tacrolimus/ methotrexate/ bortezomib	Lenalidomid/ bortezomib	2010-2013
Seattle	Mielcarek	40	High-risk first-line or failed autologous	Phase II	Tandem Allo-Auto fludarabin/total-body irradiation	Cyclopsporin, mycophenolic acid	Bortezomib maintenance for 9 months	2009-2011
Hamburg/Münster	Kröger/Kropff	200	Newly diagnosed fewer than 8 cycles induction	Auto-allo with thalidomide/ DLI *v* auto-auto/ thalidomide	Melphalan 140/ fludarabin/ antithymoglobulin	Cyclopsporin/ mycophenolic acid/ antithymoglobulin	Thalidomide 100 for 2 years (in Allo also DLI)	2009-2012
Hamburg/ Heidelberg	Kröger/Hegenbart/ Dreger	180	Relapse after autograft	Allo *v* RD	Busulphan (14 mg/kg/Cy/ antithymoglobulin	Cyclopsporin/ mycophenolic acid/ antithymoglobulin	Lenalidomide 5 mg	2011-2015

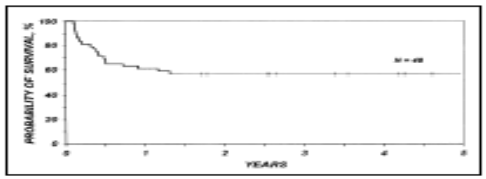
Abbreviations: GHVD, graft versus host disease; Allo, allogeneic stem-cell transplantation; Auto, autologous stem-cell transplantation; DLI, donor lymphocyte infusions; EUMN, European Myeloma Network; RD, lenalidomide and dexamethasone; Cy, cyclophosphamide.

Allo-RIC in myeloma should only be recommended in the context of clinical trials. This recommendation is in agreement with the National Comprehensive Cancer Network guidelines on treatment of myeloma (http://www.nccn.com/multiple-myeloma/).

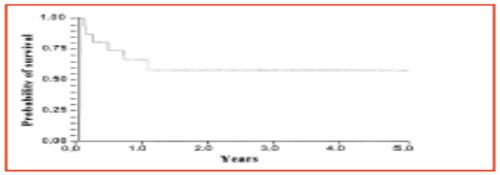


Transplant expericences

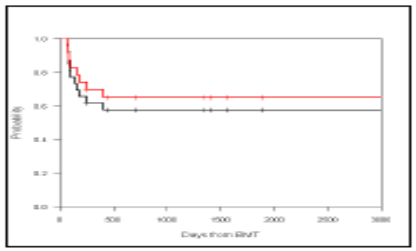
Ref	N°	Conditioning	OS	GVHD
Saso BJH 1999 IBMTR	48 sib 6 MUD 1 aplo 2 Syn	BuCY 53% TBI 21%	5yrs OS 56% (MUD 1/7 alive)	AGVHD II-IV:34% ECGVHD:33%
Bemba BJH 1999 France	16 sib	CyTBI 6 % CyTAI 50% Cybased 43%	5yrs OS 58%	AGVHD II-IV 50% ECGVHD11%
Santarone Haematol 2010 GITMO	22 sib 2 MUD 1 aplo 1 MMR	BuCy 58% RIC 42%	5yrs OS 57%	AGVHD 42% ECGVHD 16%



Saso BJH, 1999



Bemba BJH,1999



Santarone Haematol 2010

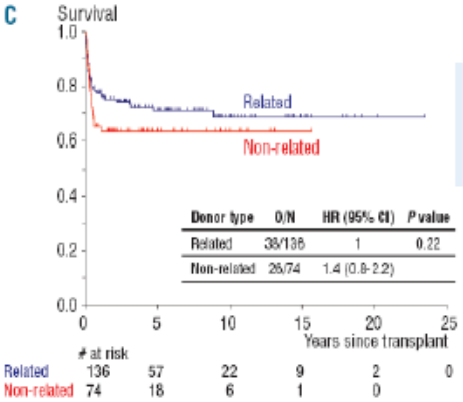
SCT and PNH: an EBMT retrospective study

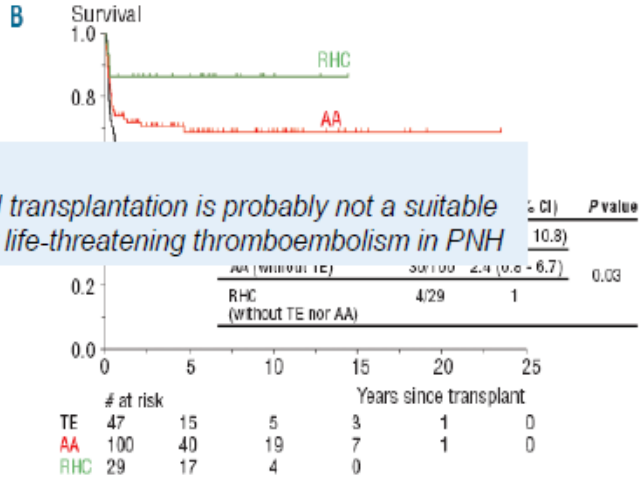
Allogeneic stem cell transplantation in paroxysmal nocturnal hemoglobinuria

haematologica | 2012; 97(11)

by Régis Peffault de Latour, Hubert Schrezenmeier, Andrea Bacigalupo, Didier Blaise, Carmino A. de Souza, Stephane Vigouroux, Roelf Willemze, Louis Terriou, Andre Tichelli, Mohamad Mohty, Sophie de Guibert, Judith Marsh, Jakob Passweg, Jean Yves Mary, and Gerard Socie

211 SCT for PNH from the EBMT database (1978-2007)





Conclusions

Allogeneic stem cell transplantation is probably not a suitable treatment option for life-threatening thromboembolism in PNH

No Difference in AA pts if SCT in upfront or after ISS (16pts)
No Difference in AA pts for stem cell source but BM < CGVHD

Pilot Study – *NEJM* 2004; N = 11


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

TRIUMPH – *NEJM.* 2006; Phase III Trial, N = 87


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Eculizumab was licensed by the Food and Drug Administration in March 2007 and by the European Medicines Agency in June 2007 for the treatment of PNH


blood

2008 111: 1840-1847
Prepublished online Nov 30, 2007;
doi:10.1182/blood-2007-06-094136

Multicenter phase 3 study of the complement inhibitor eculizumab for the treatment of patients with paroxysmal nocturnal hemoglobinuria

Robert A. Brodsky, Neal S. Young, Elisabetta Antonioli, Antonio M. Risitano, Hubert Schrezenmeier, Jörg Schubert, Anna Gaya, Luke Coyle, Carlos de Castro, Chieh-Lin Fu, Jaroslaw P. Maciejewski, Monica Bessler, Henk-André Kroon, Russell P. Rother and Peter Hillmen


blood

2007 110: 4123-4128
Prepublished online Aug 16, 2007;
doi:10.1182/blood-2007-06-095646

Effect of the complement inhibitor eculizumab on thromboembolism in patients with paroxysmal nocturnal hemoglobinuria

Peter Hillmen, Petra Muus, Ulrich Dührsen, Antonio M. Risitano, Jörg Schubert, Lucio Luzzatto, Hubert Schrezenmeier, Jeffrey Szer, Robert A. Brodsky, Anita Hill, Gerard Socié, Monica Bessler, Scott A. Rollins, Leonard Bell, Russell P. Rother and Neal S. Young

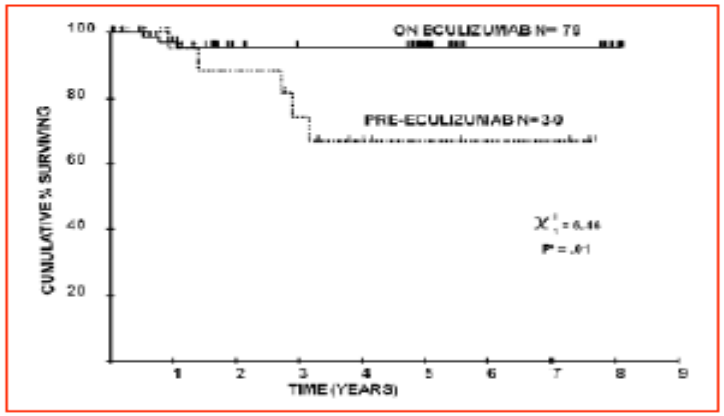
ECULIZUMAB AND PNH: EFFECTS ON SURVIVAL

blood

Long term treatment with eculizumab in paroxysmal nocturnal hemoglobinuria: sustained efficacy and improved survival

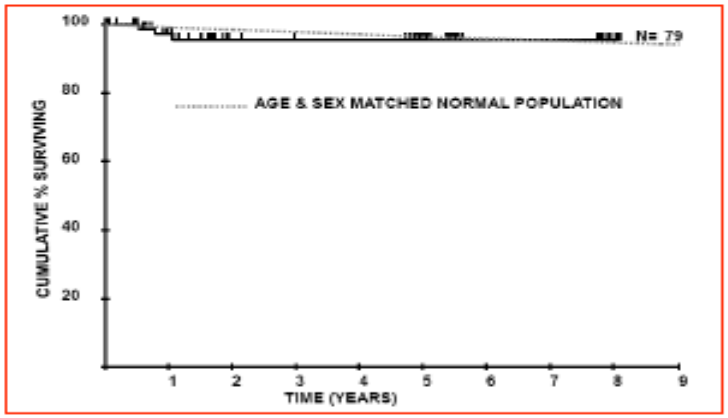
Richard J Kelly, Anita Hill, Louise M Arnold, Gemma L Brooksbank, Stephen J Richards, Matthew Cullen, Lindsay D Mitchell, Dena R Cohen, Walter M Gregory and Peter Hillmen

Untreated vs Ecu-treated PNH



OS of 30 pts with PNH assessed between 1997 and 2004 who fulfilled the criteria for treatment with eculizumab was also compared with the treated patient group

Treated PNH vs normal population



OS on eculizumab was compared with age- and sex-matched control averages obtained using 2001 United Kingdom census data from the United Kingdom Office of National Statistics.

Initial assessment (>3 months)

Severe PNH

Mild PNH

Main problem: pancytopenia

Main problem: severe haemolysis;

Follow-up (living with PNH)

<40-50 yrs

HLA-identical donor?

Worsening

Stable

Main problem: Thrombysis

No

Yes

> 40yrs

ALG+CyA

+/- Eltrombopag

Allo-HSCT

ECULIZUMAB

Supportive management

??Very Young??

If eculizumab is not available:East/Middle est Europe, Africa

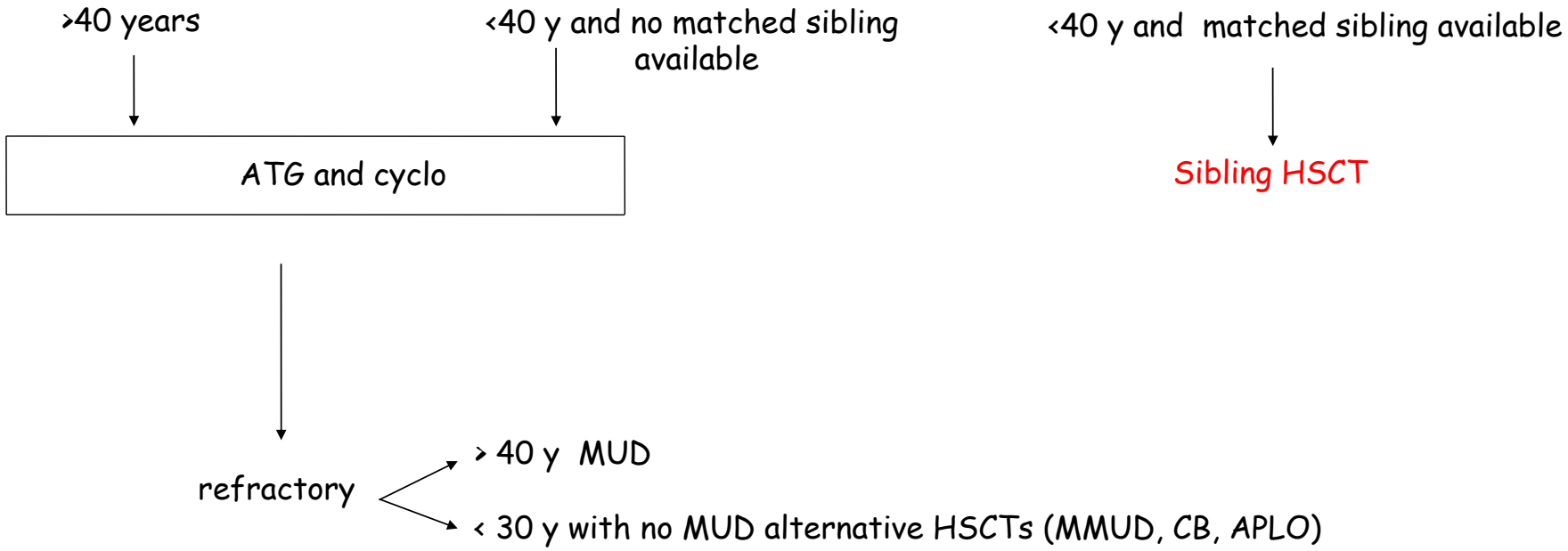
If response to eculizumab is not satisfaying: persistent transfusion-dependency

(even if novel treatment strategies may become available in the near future; shared decision with patient)

Iron support
Vitamin
Renal/Lung monitoring

Adapted by Luzzatto, BJH 2010

Acquired aplastic anemia

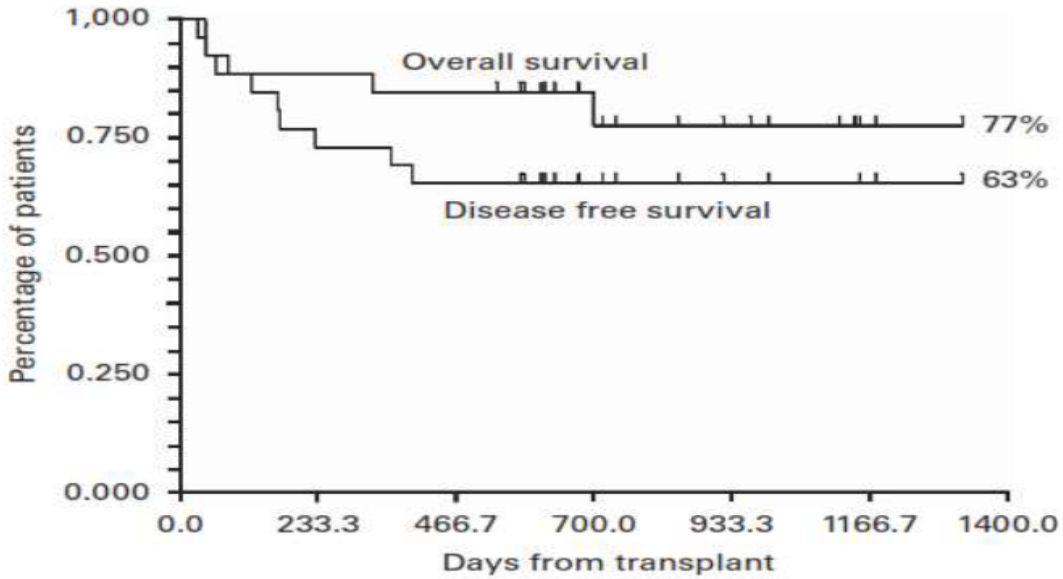


Brentuximab Vedotin (SGN-35) for Relapsed CD30-Positive Lymphomas

Anas Younes, M.D., Nancy L. Bartlett, M.D., John P. Leonard, M.D., Dana A. Kennedy, Pharm.D., Carmel M. Lynch, Ph.D., Eric L. Sievers, M.D., and Andres Forero-Torres, M.D.

N Engl J Med 2010;363:1812-21.

Unmanipulated haploidentical BMT following non-myeloablative conditioning and post-transplantation CY for advanced Hodgkin's lymphoma



Actuarial overall survival (77%) and disease-free durvival (63%) in 26 patients with advanced Hodgkin's disease

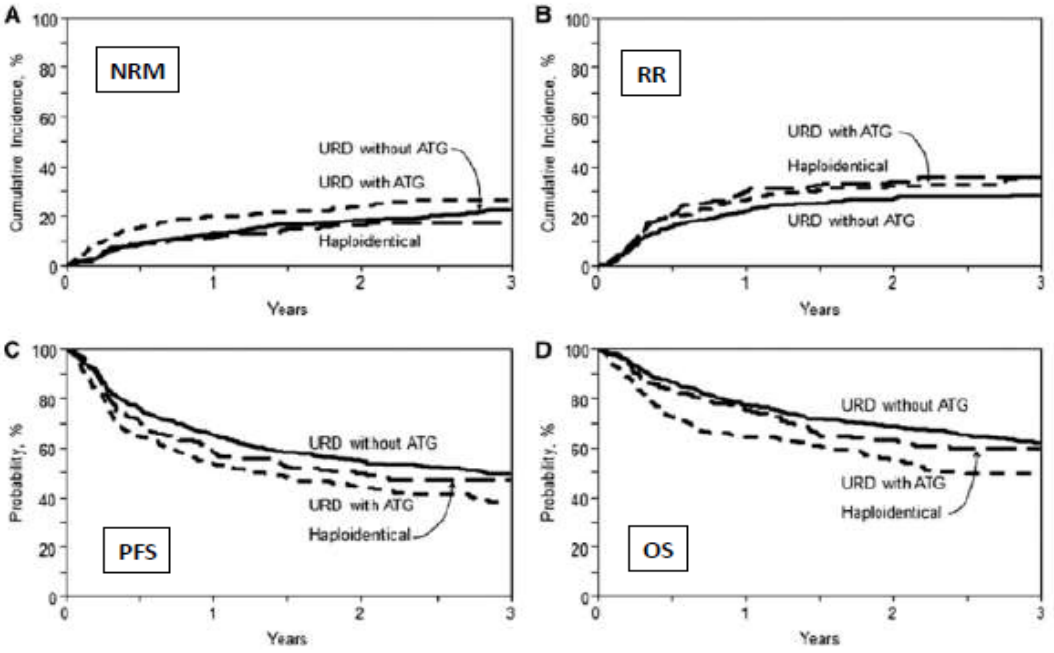
Raiola *et al*. Bone Marrow Transplant. 2014 Feb;49(2):190-4.

Reduced-intensity transplantation for lymphomas using haploidentical related donors vs HLA-matched unrelated donors

Abraham S. Kanate,[1,*] Alberto Mussetti,[2,*] Mohamed A. Kharfan-Dabaja,[3,*] Kwang W. Ahn,[4,5] Alyssa DiGilio,[4] Amer Beitinjaneh,[6] Saurabh Chhabra,[7] Timothy S. Fenske,[8] Cesar Freytes,[9] Robert Peter Gale,[10] Siddhartha Ganguly,[11] Mark Hertzberg,[12] Evgeny Klyuchnikov,[13] Hillard M. Lazarus,[14] Richard Olsson,[15,16] Miguel-Angel Perales,[17] Andrew Rezvani,[18] Marcie Riches,[19] Ayman Saad,[20] Shimon Slavin,[21] Sonali M. Smith,[22] Anna Sureda,[23] Jean Yared,[24] Stefan Ciurea,[25] Philippe Armand,[26] Rachel Salit,[27] Javier Bolaños-Meade,[28] and Mehdi Hamadani[4]

Blood. 2016;127(7):938-947

	Haplo	UD ATG	UD no ATG
n	185	491	241



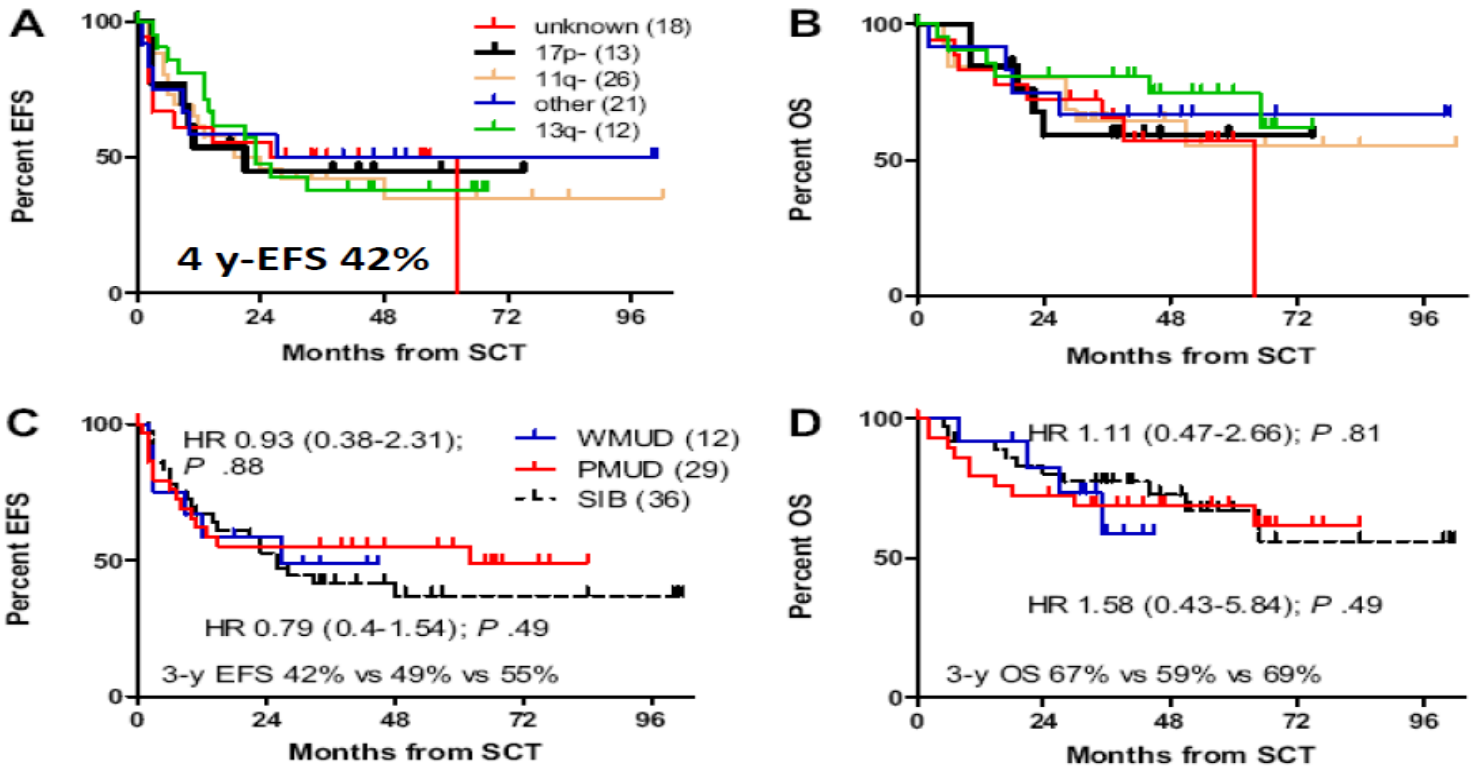
EBMT guidelines for SCT in CLL

Allo-SCT in poor-risk CLL including:

- Fludarabine resistence – non response or early relapse (<12 months) after purine analogue-based tx
- Relapse <24 months after purine analogue combinations or auto-SCT (+ high risk genetics)
- p53 mutation with treatment indication

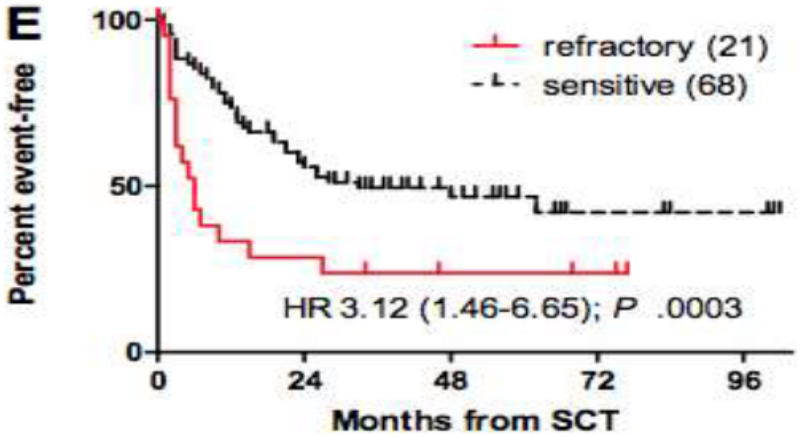
Dreger, Corradini, Kimby et al. Leukemia ' 07 (EBMT consensus panel)

No significative impact of karyotype and donor on OS and PFS



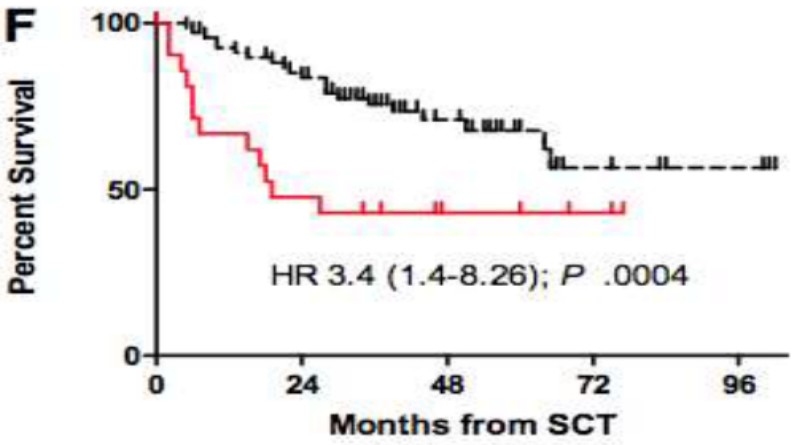
Dreger et al, Blood 2010

Significative impact of pre-transplant response status on OS and PFS



2 y-EFS 60%

4 y-EFS 50%



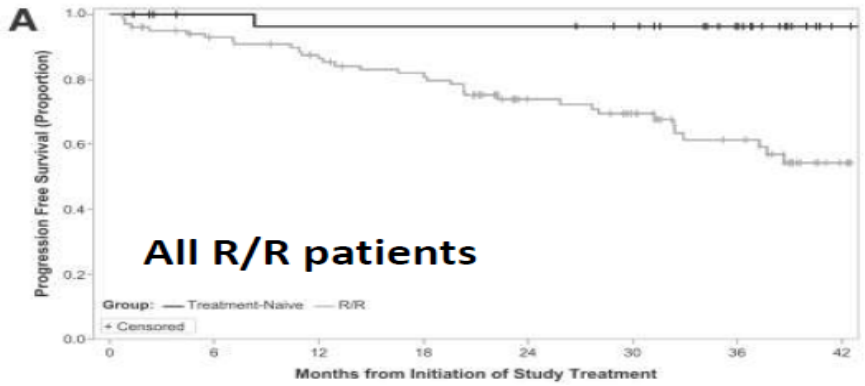
2 y-OS 85%

4 y-OS 70%

Dreger et al, Blood 2010

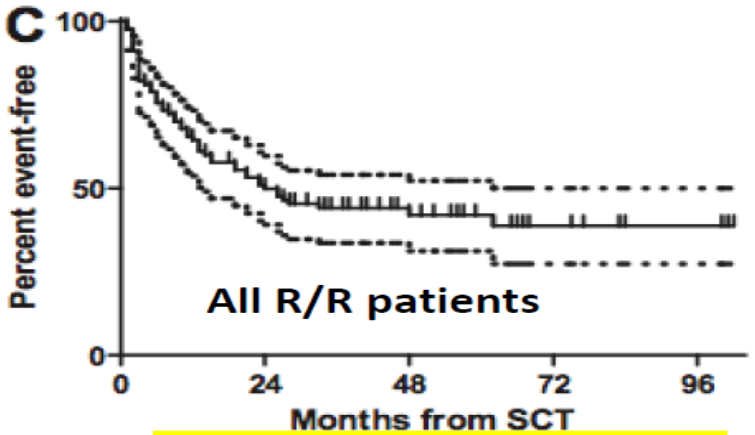
- Consenso su CLL alto rischio
- Allo-SCT RIC è > efficace in pazienti con malattia chemosensibile
- **PFS 40% con plateau**
- **OS 40-60% con plateau**
- Importanza del timing allo-SCT timing
- Non impatto cariotipo sfavorevole
- Risultati simili allo SCT related e unrelated donors
- PFS e OS migliori nei pazienti in cui si raggiunge MRD -

Ibrutinib

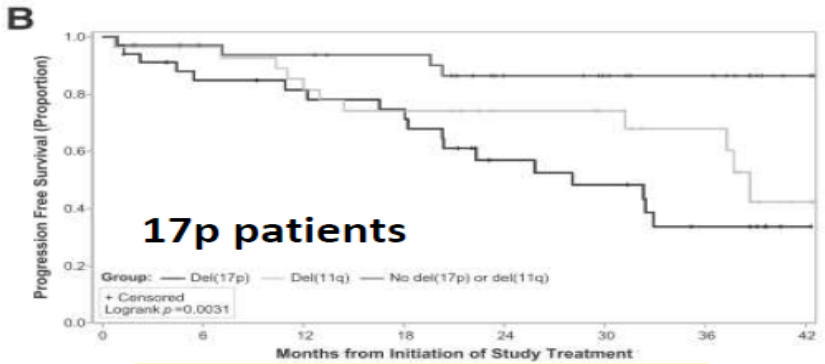


2 and 4 y-PFS: 75% and 55%

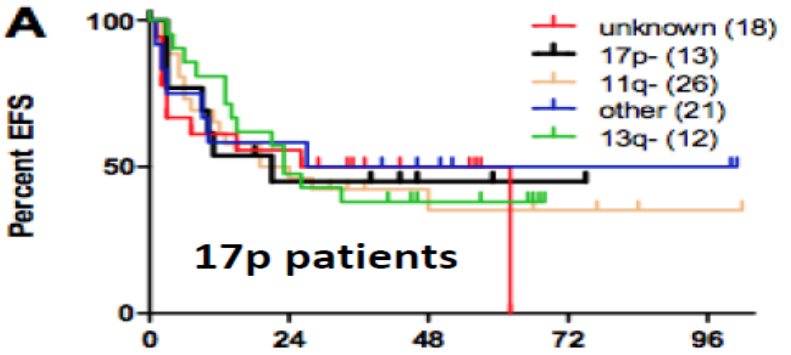
RIC allogeneic SCT



2 and 4 y-PFS: 50% and 42%



2 and 4 y-PFS: 58% and 38%



4 y-PFS: 42%

Byrd 2015, Khouri, 2011, Dreger 2010

Possible future scenario

Therapy	Goal of therapy
1. New agents until progression	QoL, disease stabilization
2. New agents ➔ SCT	MRD
3. New agents ➔ SCT ➔ New agents	MRD

SCT  **New agents**

Need for prospective controlled studies

Review article

The Role of Autologous and Allogeneic Stem Cell Transplantation in Follicular Lymphoma in The New Drugs Era

Francesco Maura[1], Lucia Farina[1] and Paolo Corradini[1,2]

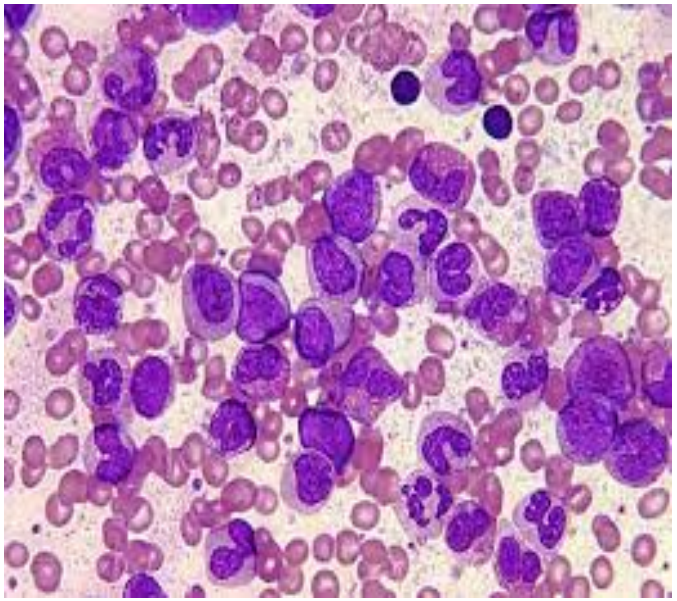
[1] Division of Hematology and Bone Marrow Transplant, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, Milan, Italy.
[2] Department of Oncology and Hemato-oncology, University of Milan, Milan, Italy.

Table 3. A summary of outcomes of allo-SCT for relapsed or refractory FL underwent alloSCT.

Reference	n°pts	Conditioning regimen	TRM	EFS/PFS	OS	REF
Khouri, et al. 2001[#]	20	Flu/Cy - Flu/Cy/Ritux	10% at 2 year	84% at 2 year	84% at 2 year	79
Robinson et al. 2002	52	Fludarabine-based	22%	61% at 1 year	73% at 1 year	90
Morris et al. 2004[%]	41	Flu/Mel/Campath-1H	11% at 3 year	65% at 3 year	55% at 3 year	86
Faulkner et al. 2004[&]	28	BEAM/Campath-1H	13.3%	69% at 2 year	63.1% at 3 year	84
Corradini et al, 2007*	27	Flu/Cy/Thiotepa	14% at 3 year*	86%at 3 year	88% at 3 year	81
Khouri et al, 2008	47	Flu/Cy/Ritux	15% at 5 year	85% at 5 year	83% at 5 year	80
Hari et al, 2008	88	RIC	27% at 3 year	55% at 3 year	62% at 3 year	85
Hari et al, 2008	120	MAC	25% at 3 year	67% at 3 year	71% at 3 year	85
Thomson et al, 2010	82	Flu/Mel/Alemtuzumab	15% at 4 year	74% at 4 year	76% at 4 year	92
Pinana et al. 2010	37	Flu/Mel	41% at 4 year	57% at 4 year	54% at 4 year	87
Delgado et al. 2011	164	RIC	17% at 3 year	58% at 5 year	72% at 5 year	82
Robinson et al. 2013	149	RIC	22% at 3 year	57% at 5 year	67% at 5 year	89
Evens et al. 2013	48	RIC	24% at 3 year	52% at 3 year	61% at 3 year	83
Klyuchnikov et al. 2015	268	RIC	26% at 5 year	58% at 5 year	66% at 5 year	41
Klyuchnikov et al, 2016	61	RIC	27% at 5 year	51% at 5 year	54% at 5 year	42
Robinson 2016[+]	183	RIC	27% at 2 years	48% at 5 year	51% at 5 year	95

[#]Also Small Lymphocytic Lymphoma included, [%]29/41 of indolent lymphoma group were FL, *including also other indolent lymphomas, [&]including also other indolent lymphoma, [+]All patients relapsed after ASCT.

Published: September 1, 2016



alla diagnosi di emopatia acuta
tipizzare subito il paziente....
le acute se hanno indicazione al TMO non possono aspettare

alla recidiva post AUTO nei Linfomi.....

! attenta selezione paziente in MDS e MFI

"abbiamo tempo" con le talassemie:
!! buon donatore e status del ricevente

GRAZIE PER L'ATTENZIONE

ma com'è fatto il "midollo osseo" dell'Ematologia di Pesaro?