LEUKEMIA2020-2021

April 26-27, 2021

Coordinator: A.M. Carella
AIL President: S. Amadori

ASSOCIAZIONE ITALIANA CONTRO LE LEUCEMIE-LINFOMI E MIELOMA ONLUS

Transplant options in 2021

fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

GITMO
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

SIES Società Italiana Ematologia Sperimentale

SIE - Società Italiana di Ematologia

ASSOCIAZIONE ITALIANA
CONTRO LE LEUCEMIE-LINFOMI E MIELOMA
ONLUS

LEUKEMIA2020
Rome, Hotel NH Collection - Vittorio Veneto
September 24-25, 2020

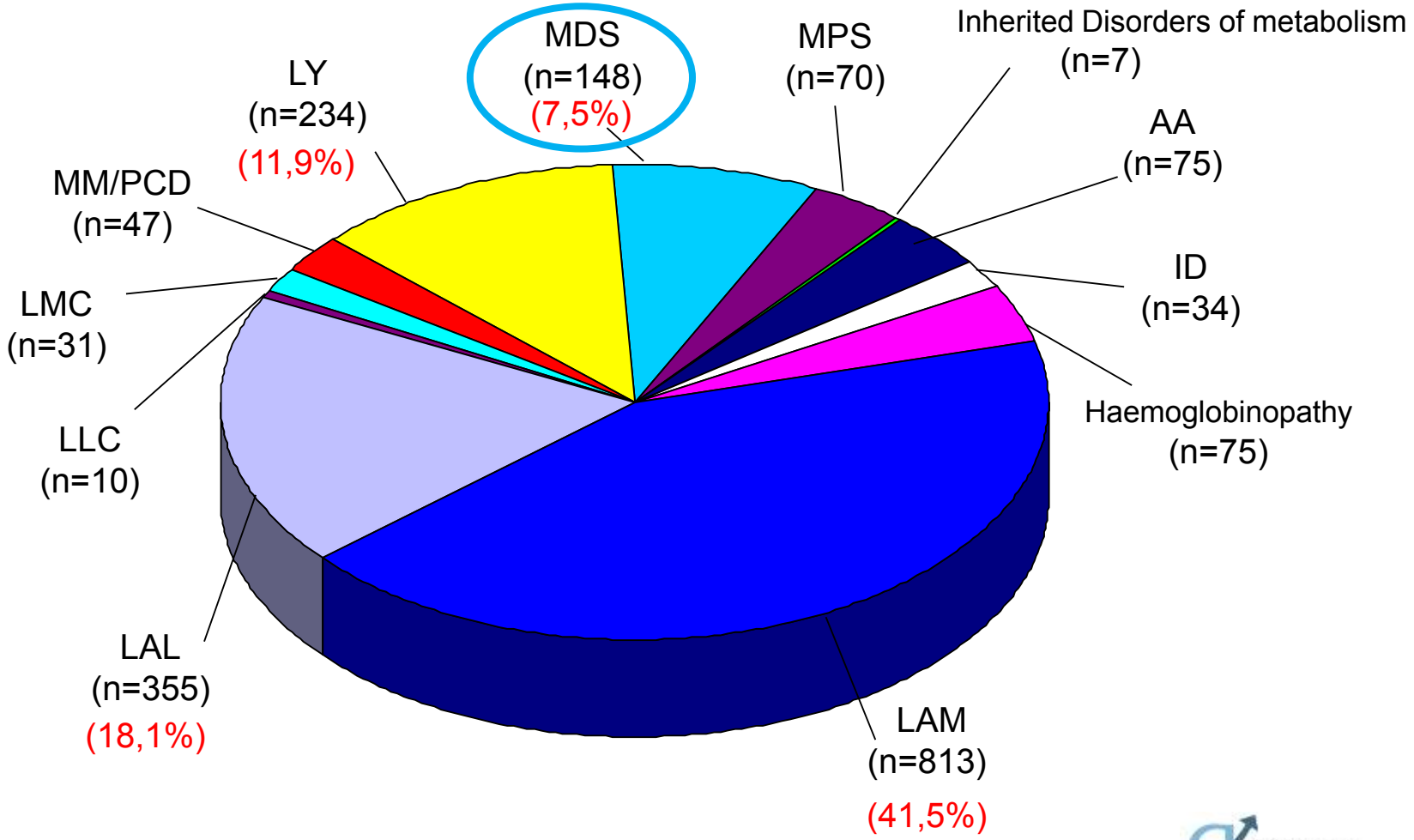
Disclosures of Emanuele Angelucci

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Celgene -(BMS))							**DMC chair**
Crispr CAS9 / Vertex							**DMC chair**
Vifor pharma							**DMC member**
Novartis						**X**	
BlueBird Bio						**X**	
Menarini-Stemline			**X**				
Glaxo						**X**	
GILEAD						**X**	

GITMO Trapianto Allogenico

Numero Trapianti per principali Patologie

Attività 2017



al 28 marzo 2018

ALLOGENEIC HCT IN MDS

WHO AND WHEN…. HOW ?

PATIENT AGE

COMORBIDITIES

DONOR TYPE

CONDITIONIG REGIMEN

TRANSPLANT MORTALITY

HMA PRE TX?

ALLOGENEIC HCT IN MDS

WHO AND WHEN…. HOW ?

PATIENT AGE

COMORBIDITIES

DONOR TYPE

CONDITIONIG REGIMEN

TRANSPLANT MORTALITY

HMA PRE TX?

Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes Risk Assessment Calculator

Variables (units) [usual range]	Value
Hemoglobin (g/dL) [4-20]	
A possible conversion for Hb values:	
10 g/dL= 6.2 mmol/L, 8 g/dL= 5.0 mmol/L	
Absolute Neutrophil Count (x10^9/L) [0-15]	
Platelets (x10^9/L) [0-2000]	
Bone Marrow Blasts (percent) [0-30]	

Cytogenetic Category

○ Very Good ○ Good ○ Intermediate ○ Poor ○ Very Poor

IPSS-R SCORE	IPSS-R CATEGORY
-	-

RISK CATEGORY	RISK SCORE
Very Low	<=1.5
Low	>1.5 - 3
Intermediate	>3 - 4.5
High	>4.5 - 6
Very High	>6

HCT

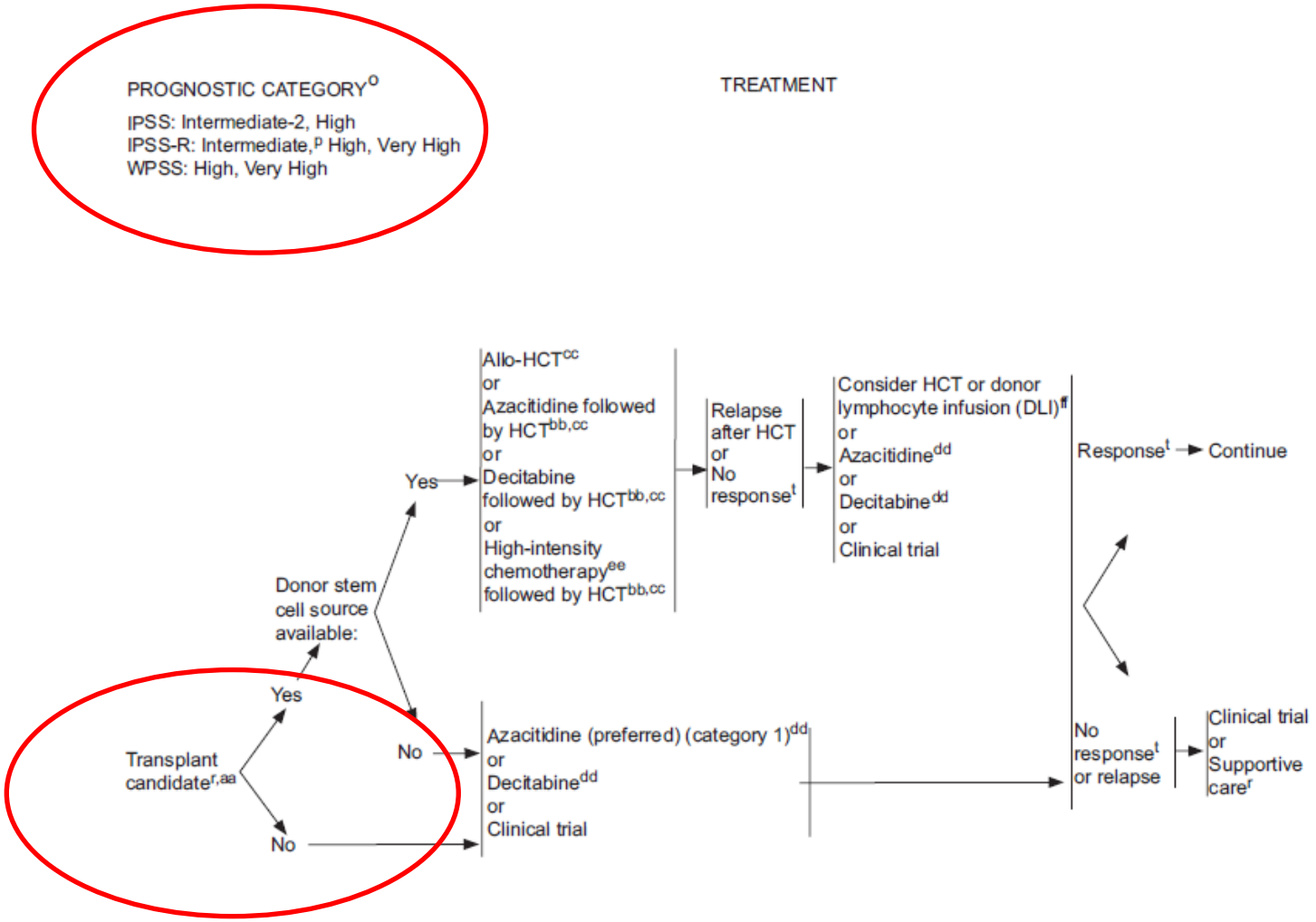
Transplantation policy according to IPSS *vs.* IPSS-R

	*IPSS-based policy**	*IPSS-R*	*%*	*IPSS-R based policy **
IPSS Low	***Delayed***	**Very low**	37	***Delayed***
		Low	50	***Delayed***
		Intermediate	13	***Immediate***
		High	-	
IPSS Intermediate-1	***Delayed***	**Very low / Low**	48	***Delayed***
		Intermediate	40	***Immediate***
		High	11	***Immediate***
		Very high	1	***immediate***

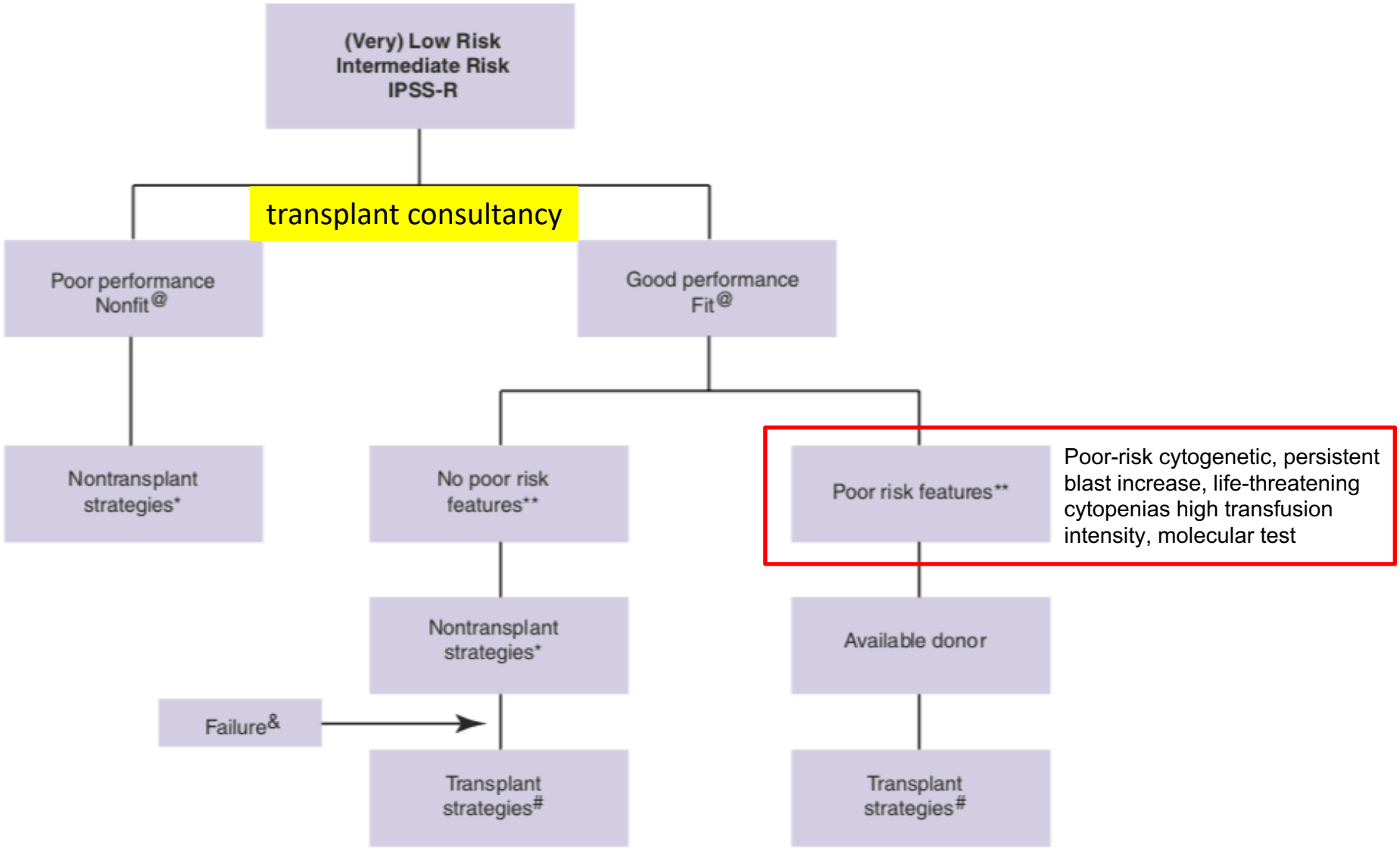
** Cutler CS et al. Blood 2004*

*** Della Porta MG et al. Leukemia. 2017*

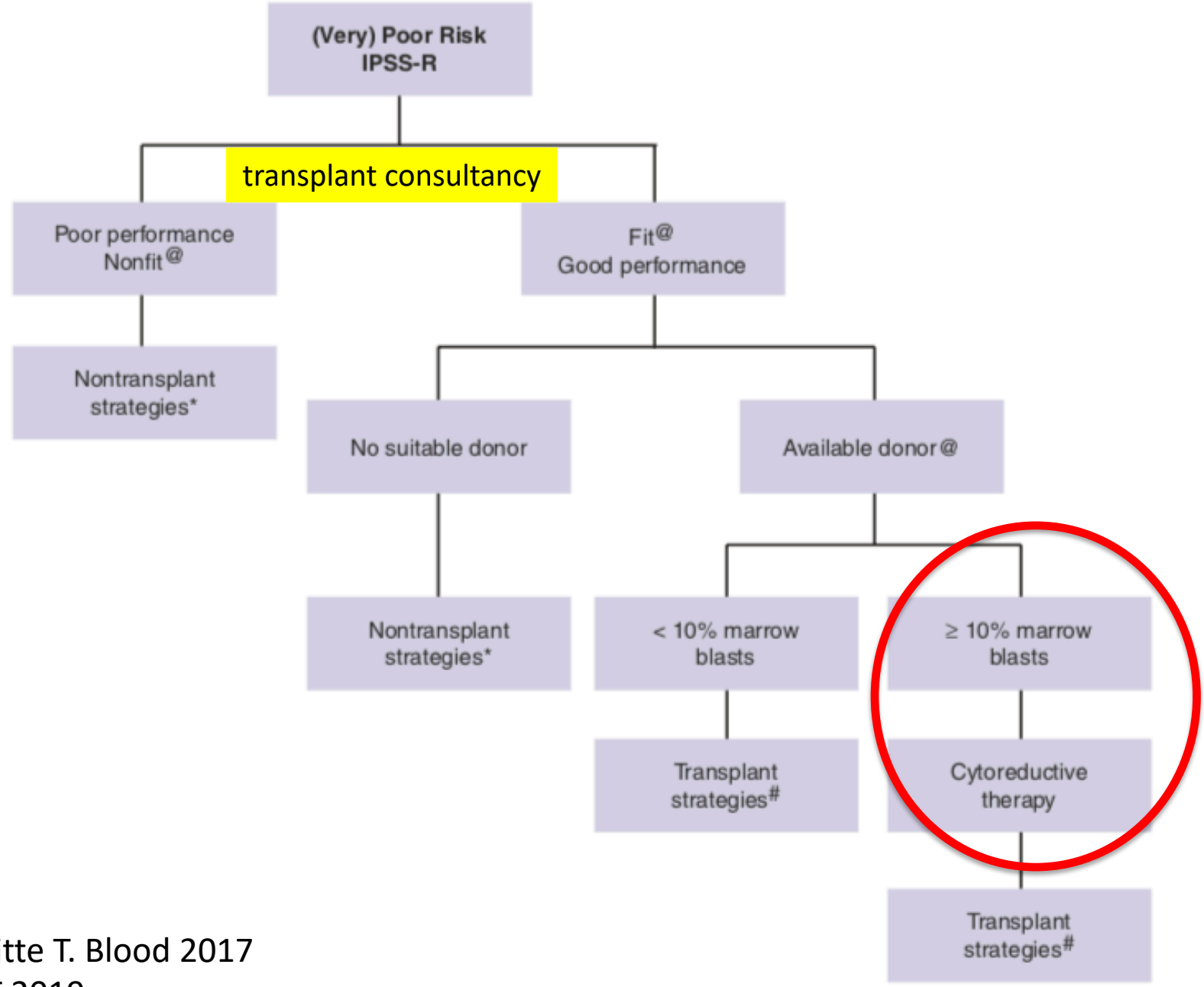
NCCN MDS 2017 guidelines



Greenberg et al. JNCCN 2017



de Witte T. Blood 2017
EBMT 2019



de Witte T. Blood 2017
EBMT 2019

ALLOGENEIC HCT IN MDS PATIENTS

WHO AND WHEN?

 # PATIENT'S AGE

 # COMORBIDITIES

DONOR TYPE

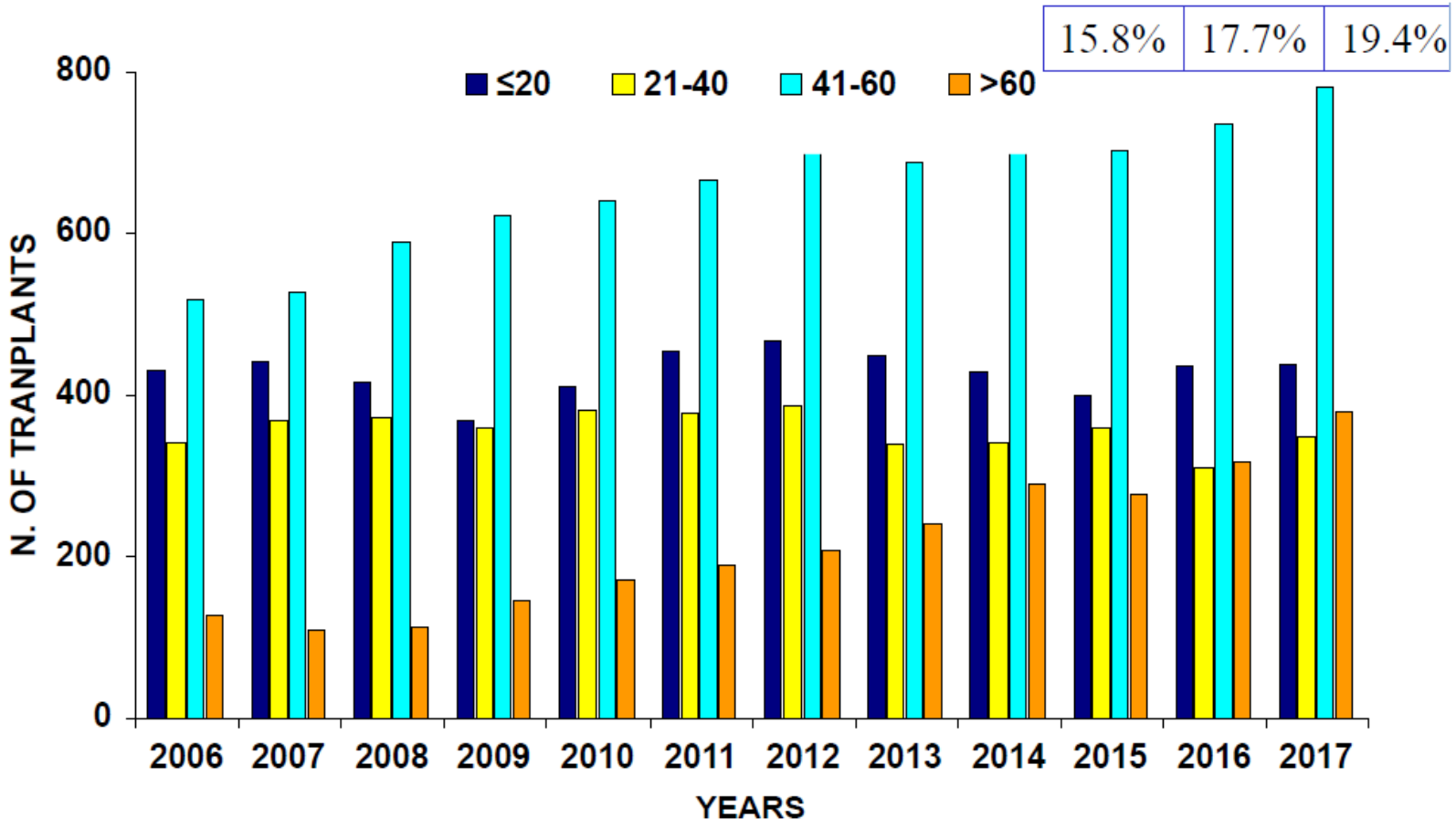
CONDITIONIG REGIMEN

TRANSPLANT MORTALITY

HMA PRE TX?

Allogeneic Transplants

Patient Age at transplantation



Export date 28/03/2018

GITMO

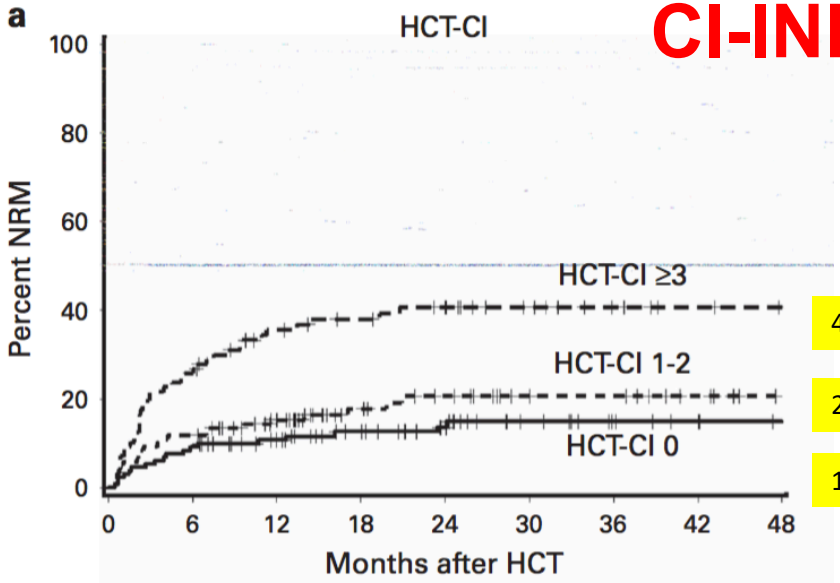
Table 1. HCT-CI

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 = _____

http://www.hctci.org/Home/Calculator

Sorror, Blood 2013

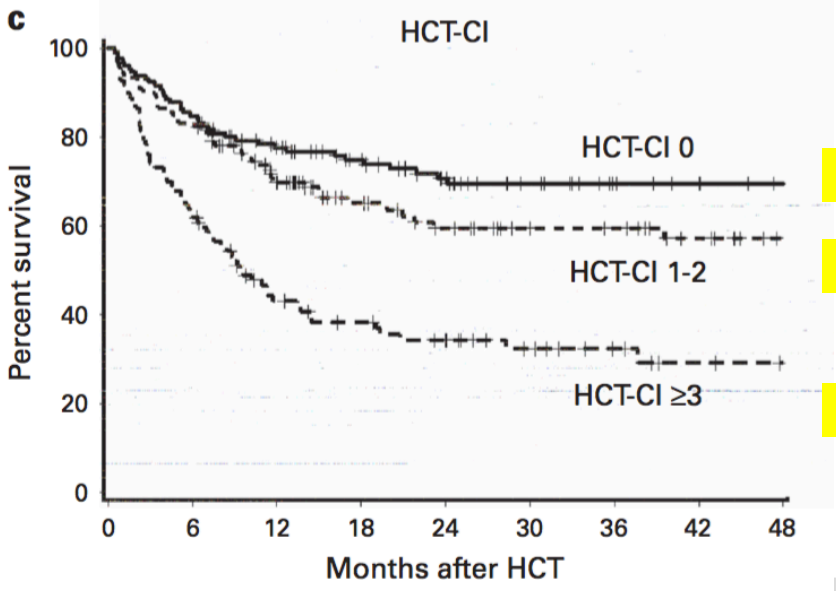
CI-INDEX AND OUTCOME



41%

21%

14%



71%

60%

34%

M Elsawy and ML Sorror , BMT 2016

ALLOGENEIC HCT DONOR

WHO AND WHEN?

PATIENT AGE

COMORBIDITIES

 # DONOR TYPE

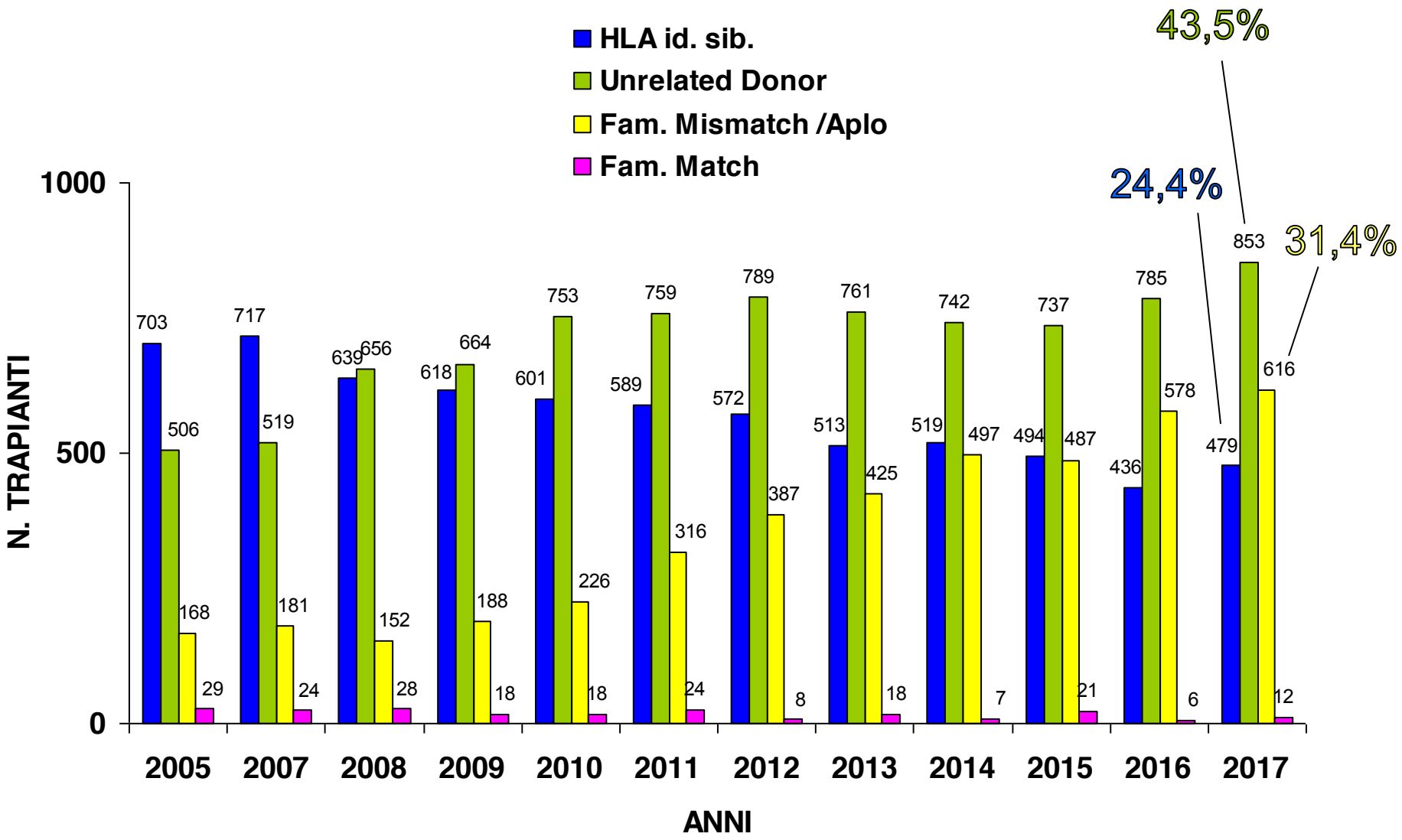
CONDITIONIG REGIMEN

TRANSPLANT MORTALITY

HMA PRE TX?

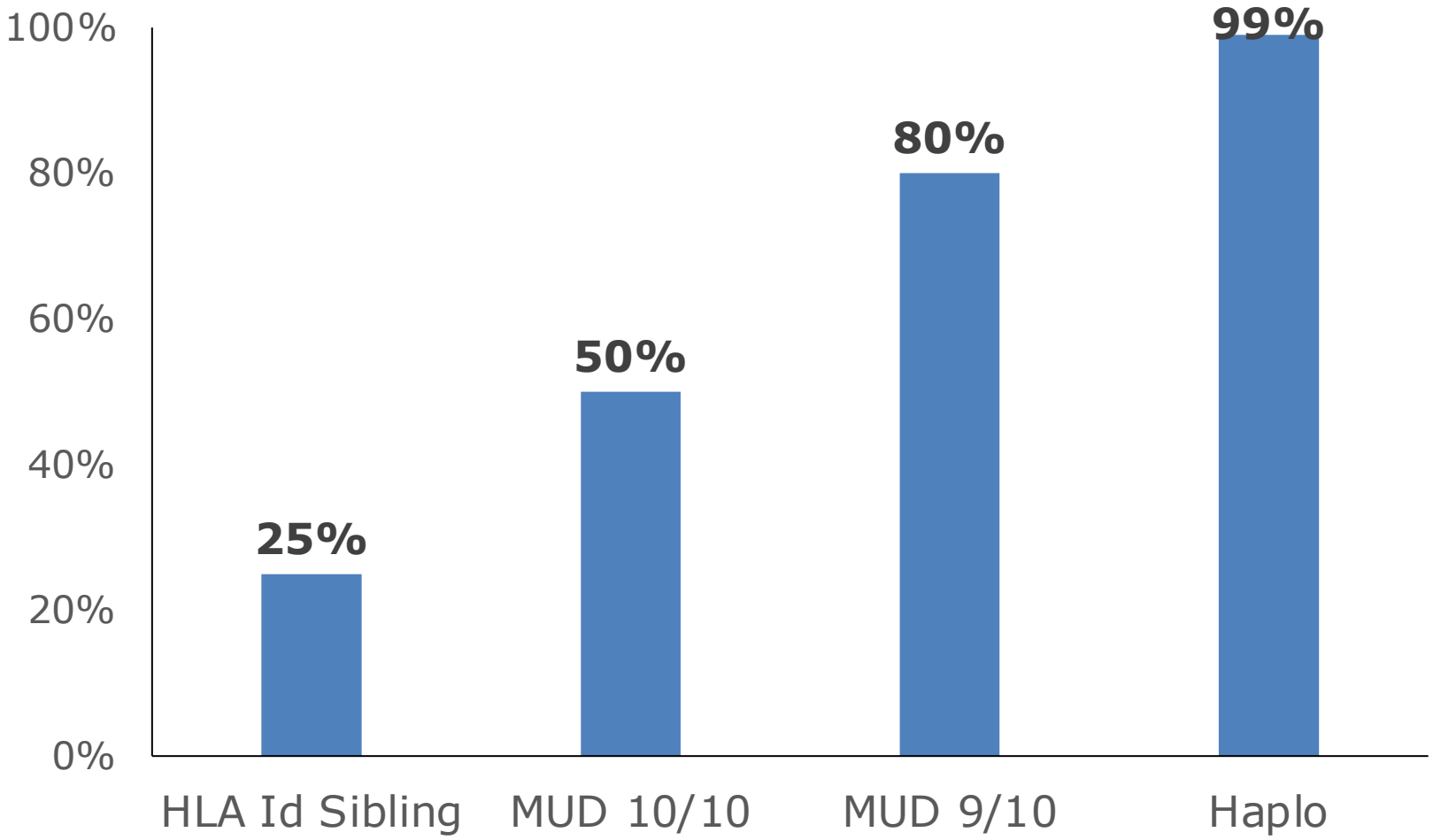
GITMO Trapianto Allogenico

Tipo di trapianto

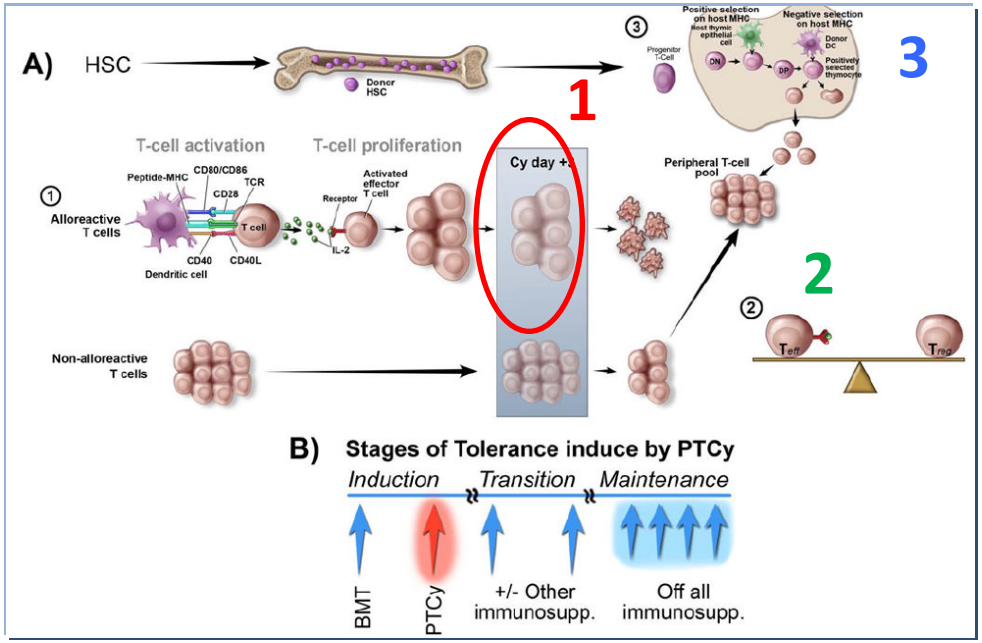


al 28 marzo 2018

Probability to Find a Donor



High dose post-transplant cyclophosphamide + unmanipulated BM haplo transplant.



1 anti-host and anti-donor T cells are destroyed in the periphery

2 development of peripheral tolerance

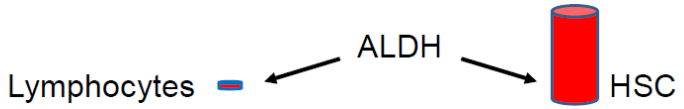
3 Intrathymic clonal deletion of donor-derived anti host T cells

Cy + allo BMT: what do we know ?

1) Cy = drug-induced immunologic tolerance(DIT)
Berenbaum MC. Nature. 1963;200:84.
Santos GW, Owens AH. Nature. 1966;210:139–40.
Mayumi H et al Transplant Proc. 1986;18:363–9.

2) Cy induces selective allodepletion by killing host and donor T cells proliferating in response to donor and host cells,respectively. Mayumi et Immunobiology. 1996;195:129–39.

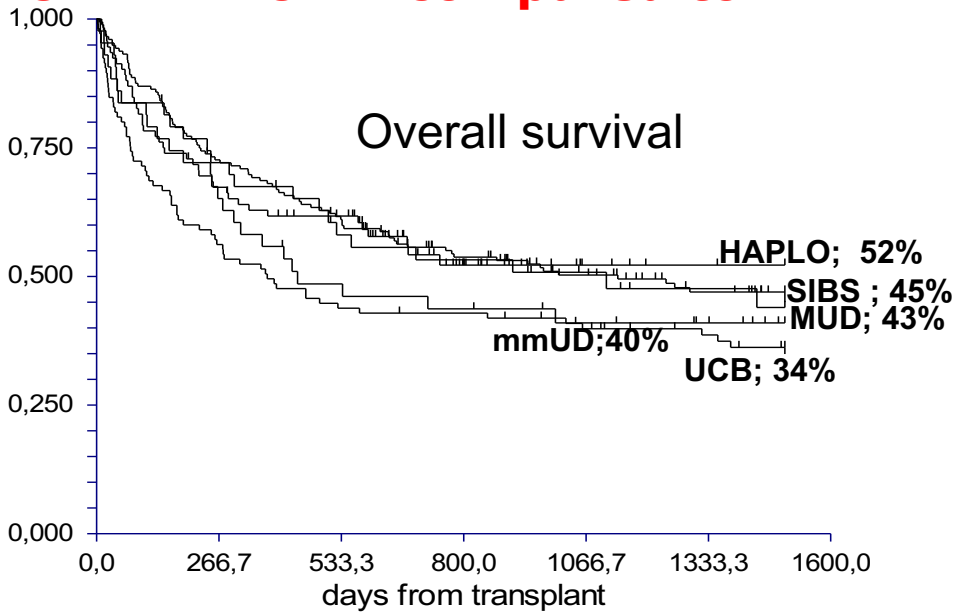
3) The major mechanism of cyclophosphamide detoxification involves aldehyde dehydrogenase (ALDH).

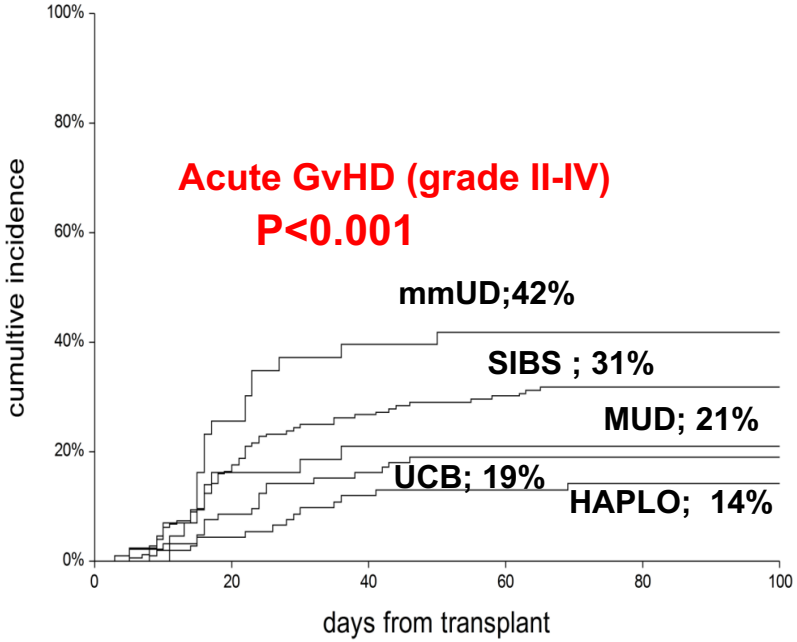


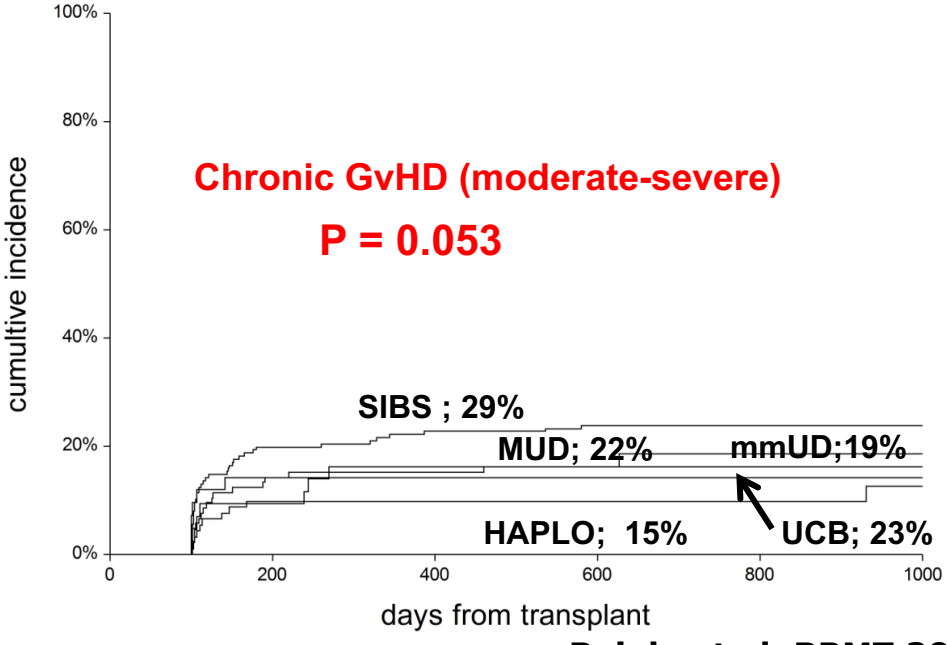
Emadi, A. et al. Nat. Rev. Clin. Oncol. 6, 638–647 (2009)

L Lutznik, BBMT 2008; AM Raiola, BBMT 2013

COMPARABLE OUTCOME but LOWER ACUTE and CHRONIC GvHD FOR HAPLO TX compared to HLAID-SIB/UD/CB



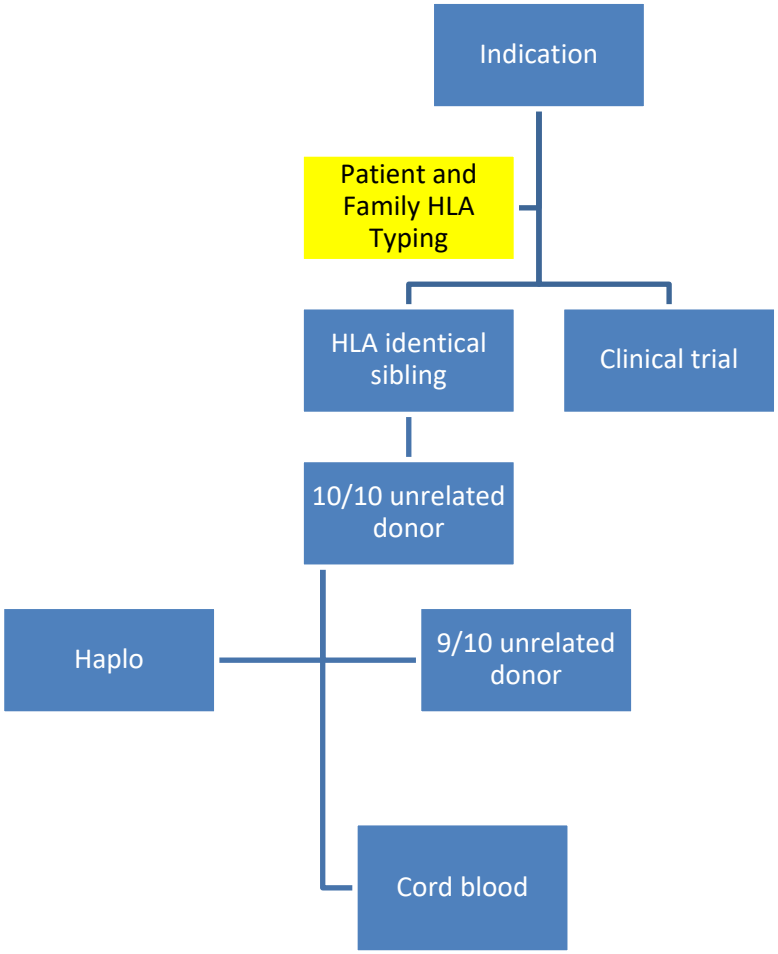




Raiola et al. BBMT 2014

IOH272_0021H3B Policy donor selection.

San Martino Transplant Program



ALLOGENEIC HCT IN MDS PATIENTS

WHO AND WHEN?

PATIENT AGE

COMORBIDITIES

DONOR TYPE

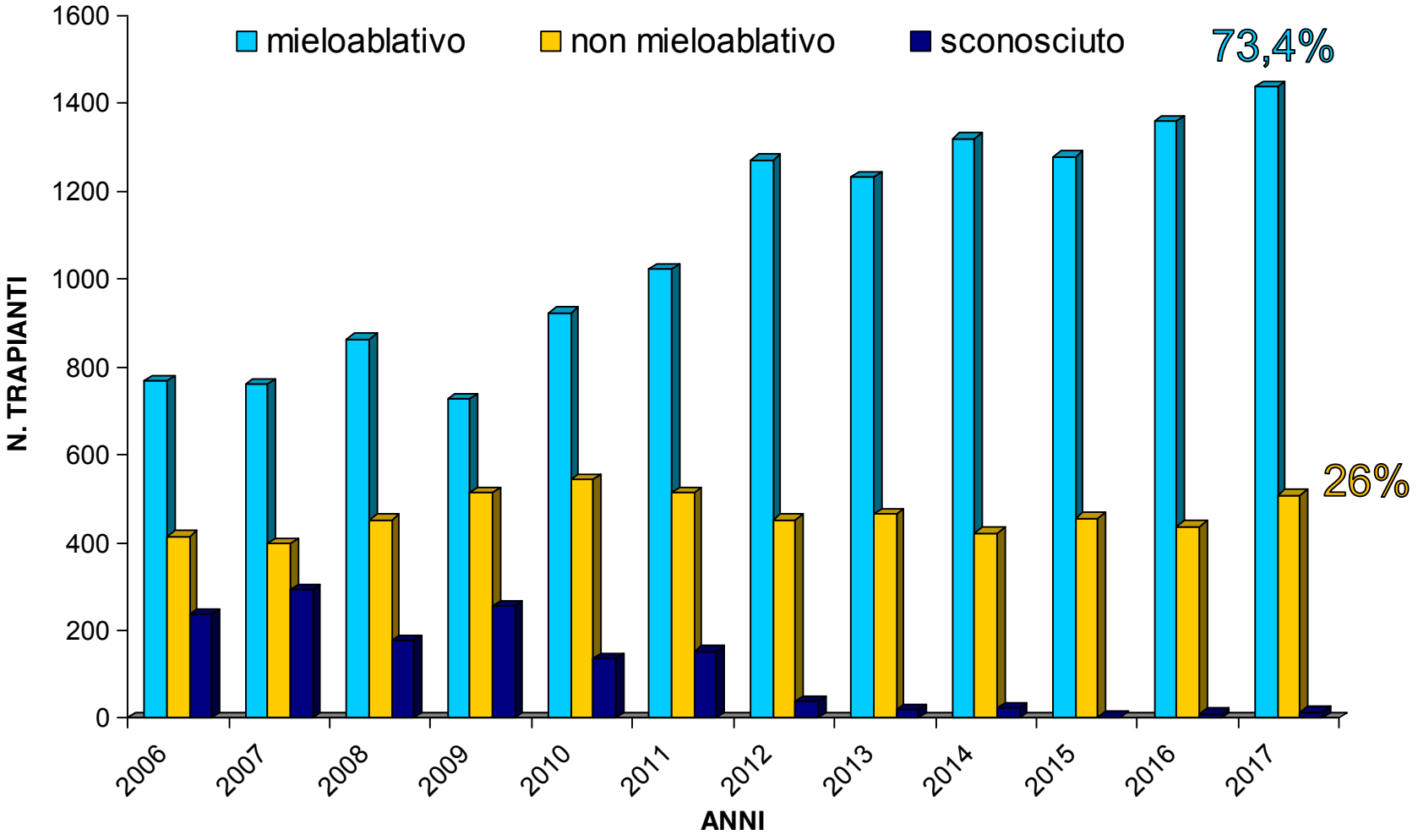
 # CONDITIONIG REGIMEN

 # TRANSPLANT MORTALITY

HMA PRE TX?

GITMO Trapianto Allogenico

Condizionamento nel trapianto Allogenico



al 28 marzo 2018

GITMO

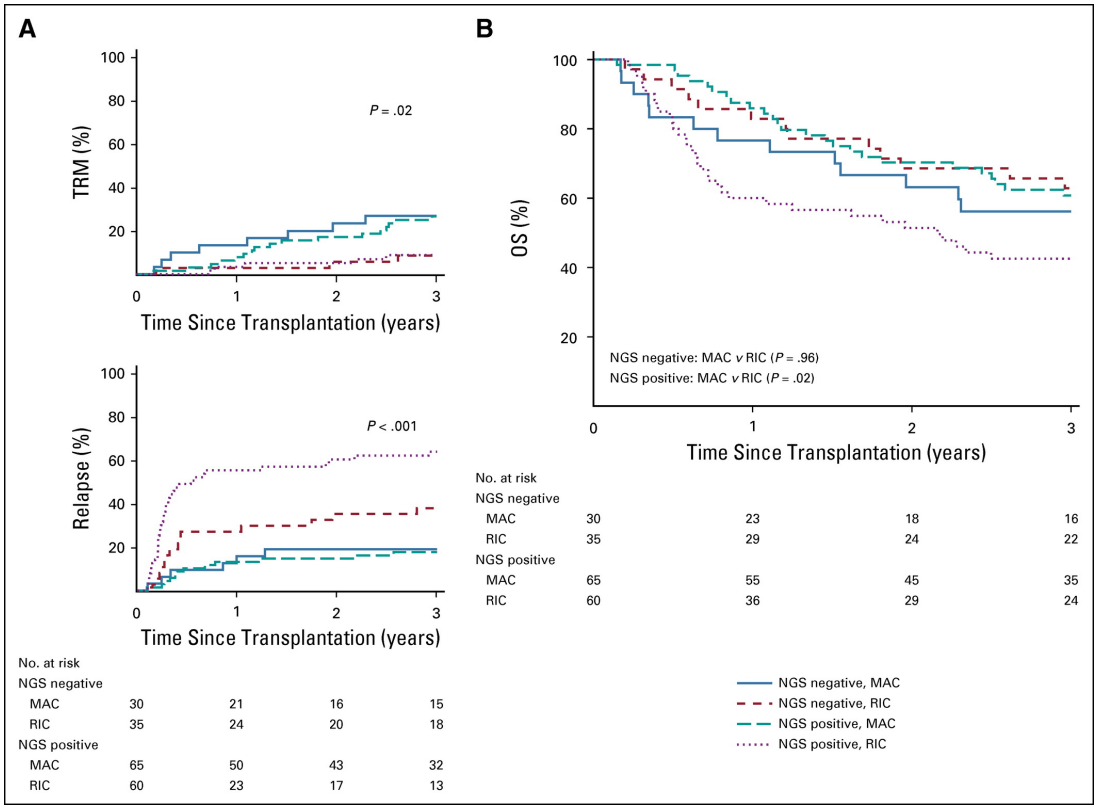


FIG 2. Impact of conditional intensity and mutational status on clinical outcomes. (A) Differences in rates of transplant-related mortality (TRM) were identified between subgroups defined by conditioning intensity and mutational status (P = .02). TRM was significantly higher in patients who underwent treatment with myeloablative conditioning (MAC) v reduced-intensity conditioning (RIC; P = .001), but there was no difference on the basis of mutational status (P = .8). Rates of relapse were different between subgroups (P < .001), with RIC having a higher relapse rate than MAC (P < .001) and the highest rate occurring in next-generation sequencing (NGS) positive patients who received RIC (P < .001). (B) In patients with no mutations detected (NGS negative), overall survival (OS) did not differ on the basis of conditioning intensity (3-year OS, 63% RIC v 56% MAC; P = .96). However, in those with detectable mutations, survival was significantly worse in those who received RIC (3-year OS, 43% RIC v 61% MAC; P = .02).

Published in: Christopher S. Hourigan; Laura W. Dillon; Gege Gui; Brent R. Logan; Mingwei Fei; Jack Ghannam; Yuesheng Li; Abel Licon; Edwin P. Alyea; Asad Bashey; H. Joachim Deeg; Steven M. Devine; Hugo F. Fernandez; Sergio Giralt; Mehdi Hamadani; Alan Howard; Richard T. Maziarz; David L. Porter; Bart L. Scott; Erica D. Warlick; Marcelo C. Pasquini; Mitchell E. Horwitz; *Journal of Clinical Oncology* 2020 381273-1283.
DOI: 10.1200/JCO.19.03011

ALLOGENEIC HCT IN MDS PATIENTS

WHO AND WHEN?

PATIENT AGE

COMORBIDITIES

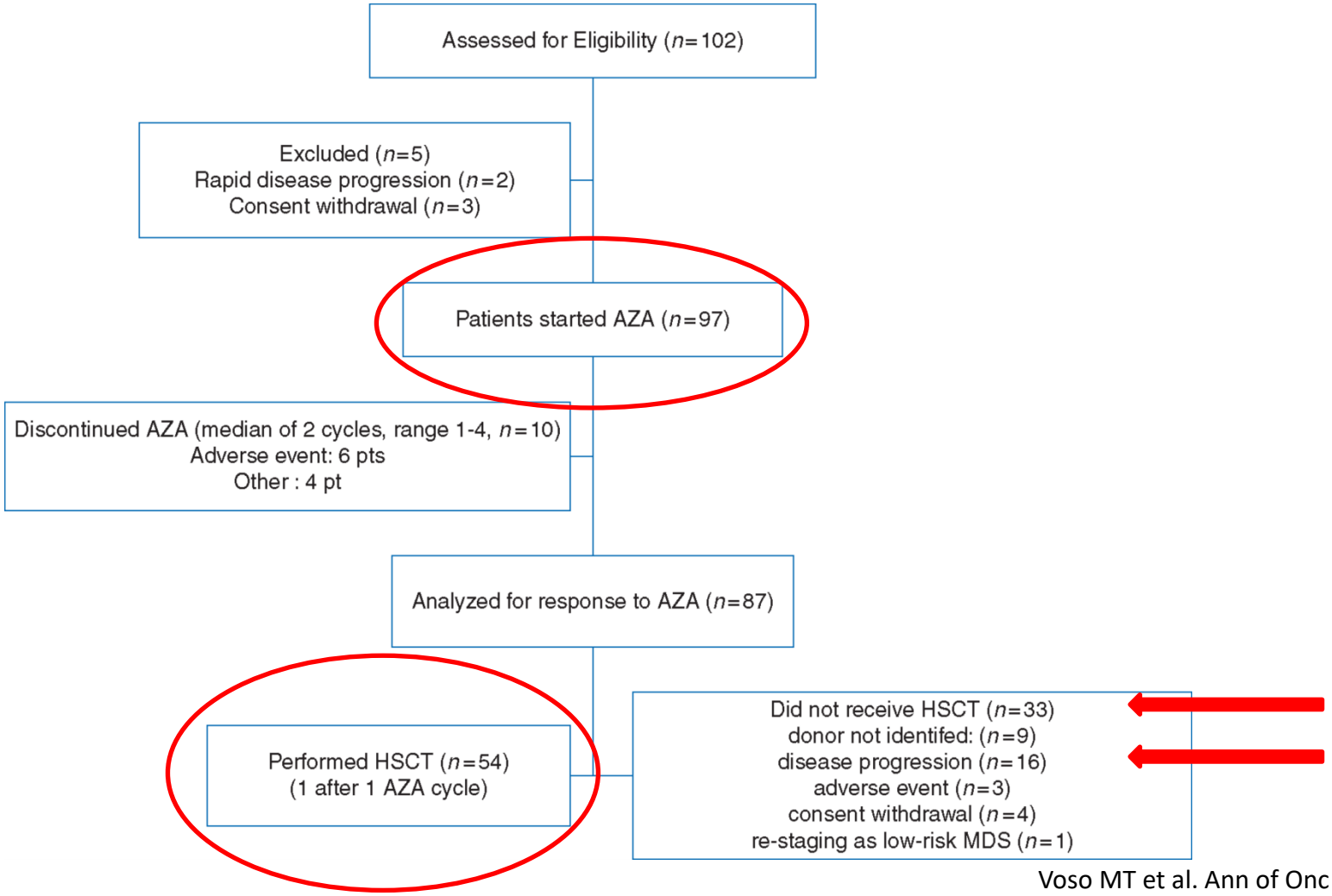
DONOR TYPE

CONDITIONIG REGIMEN

TRANSPLANT MORTALITY

 # HMA PRE TX?

Feasibility of allogeneic stem-cell transplantation after azacitidine bridge in higher-risk myelodysplastic syndromes and low blast count acute myeloid leukemia: results of the BMT-AZA prospective study



Voso MT et al. Ann of Onc 2017

Prospective multicenter phase 3 study comparing 5-azacytidine (5-Aza) induction followed by SCT vs continuous 5-Aza according to donor availability in elderly MDS pts (55-70 years) (VidazaAllo Study)

N. Kröger[1], K. Sockel[2], Chr. Wolschke[1], W. Bethge[3], R. Schlenk[4,5], D. Wolf[6], M. Stadler[7], G. Kobbe[8], G. Wulf[9], G. Bug[10], K. Schäfer-Eckart[11], C. Scheid[12], F. Nolte[13], J. Krönke[4], M. Stelljes[14], D. Beelen[15], M. Heinzelmann[1], D. Haase[9], H. Buchner[16], G. Bleckert[16], U. Platzbecker[2]

on behalf of the German MDS Study Group and the German Cooperative Transplant Study Group

D·MDS
Deutsche MDS-Studiengruppe

Unpublished, with courtesy of Nicolas Kröger

Aim of the study

- To compare Aza treatment alone with Aza followed by allogeneic SCT according to donor availability in elderly pts with newly-diagnosed untreated intermediate II-risk or high-risk or intermediate I with high-risk cytogenetics high risk MDS aged 55-70 years

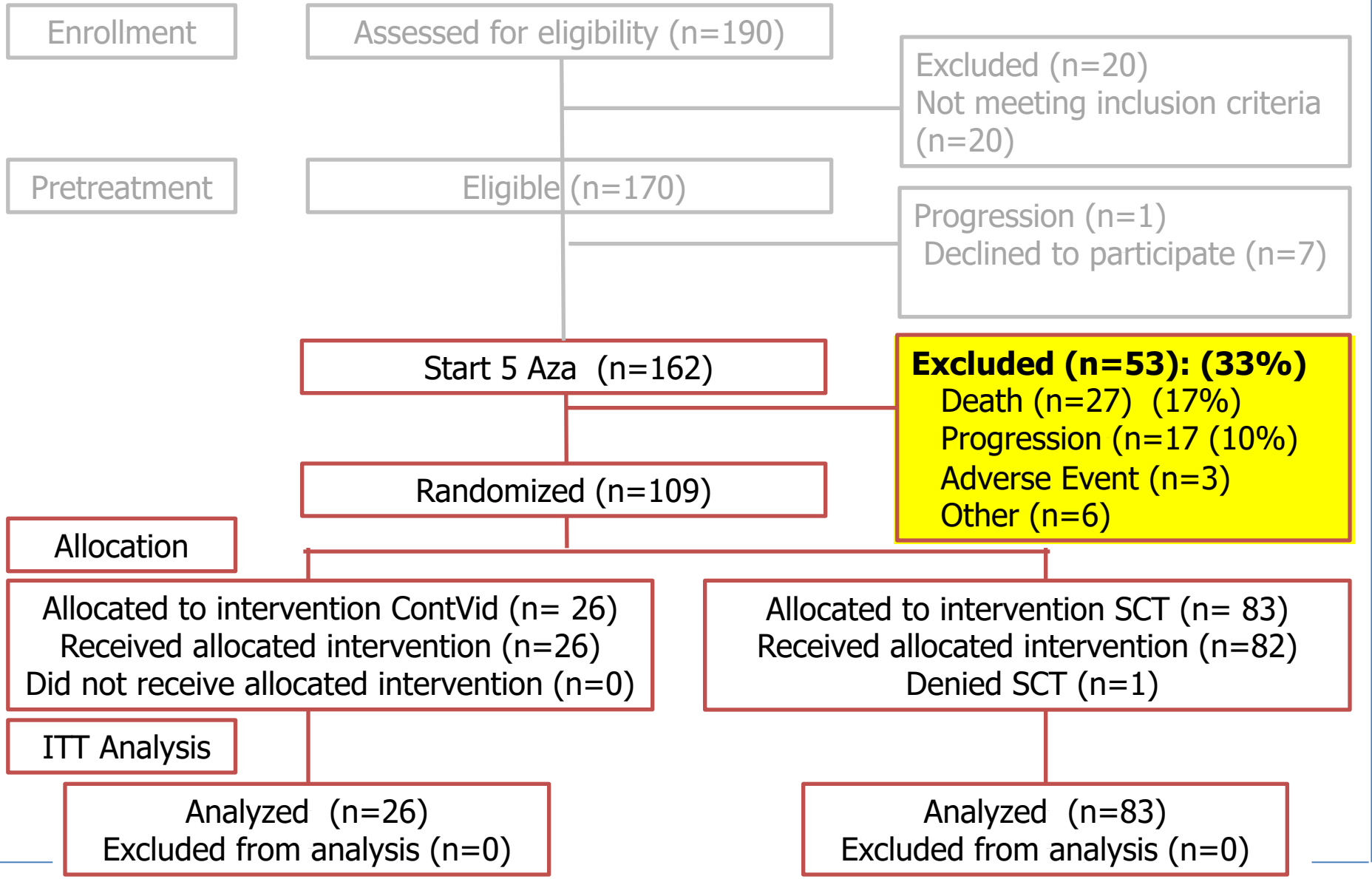
- Primary endpoint: OS at 3 years

- Secondary endpoints: response rate, EFS at 3 years, toxicity, TRM in both treatment arms.

Unpublished, with courtesy of Nicolas Kröger

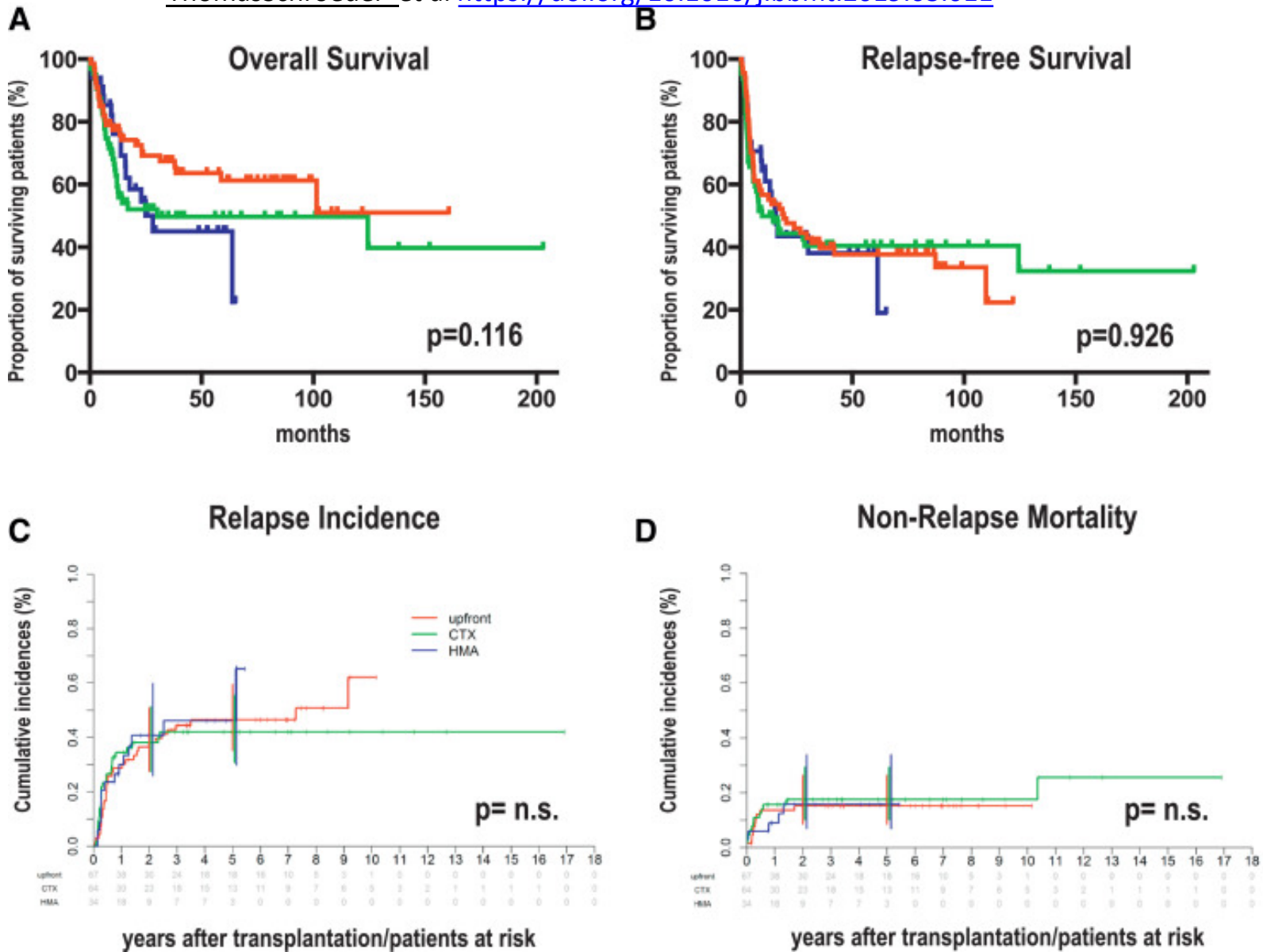
CONSORT Flow Diagramm

Between June 2011 and November 2016 190 patients with a median age of 63 years from 14 German centers were enrolled



Comparison between Upfront Transplantation and different Pretransplant Cytoreductive Treatment Approaches in Patients with High-Risk Myelodysplastic Syndrome and Secondary Acute Myelogenous Leukemia.

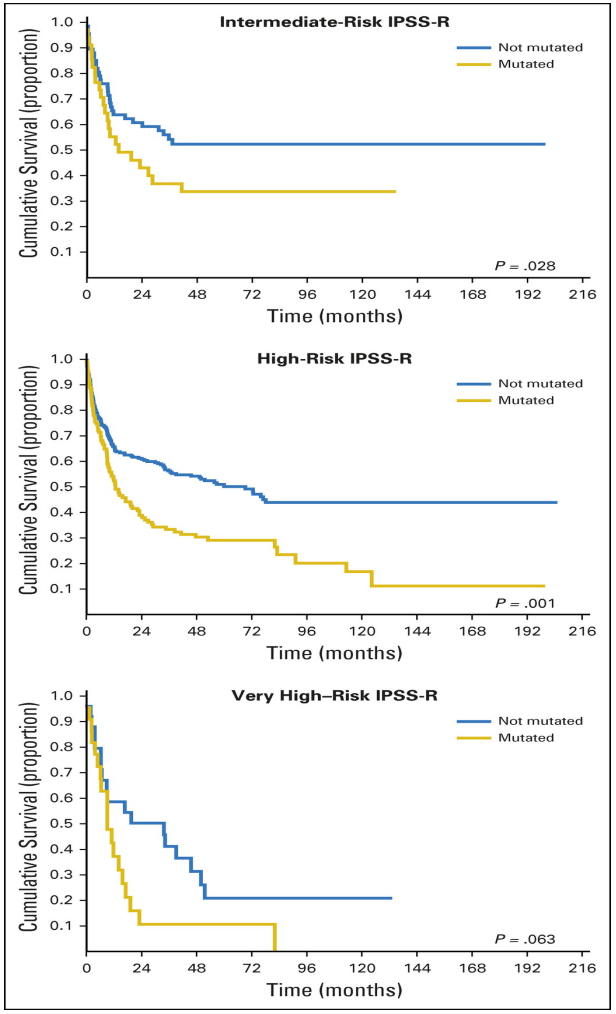
ThomasSchroeder et al https://doi.org/10.1016/j.bbmt.2019.03.011

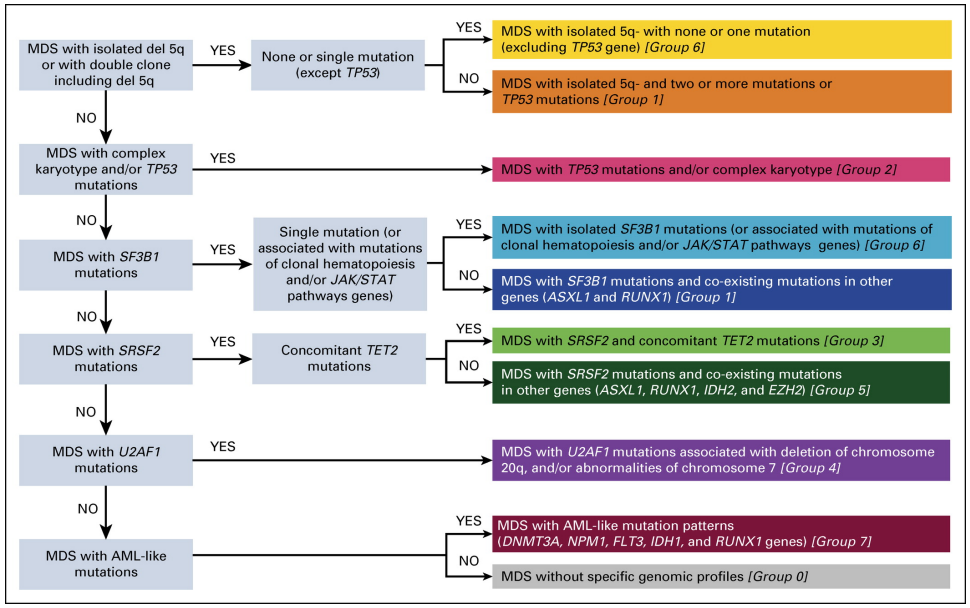


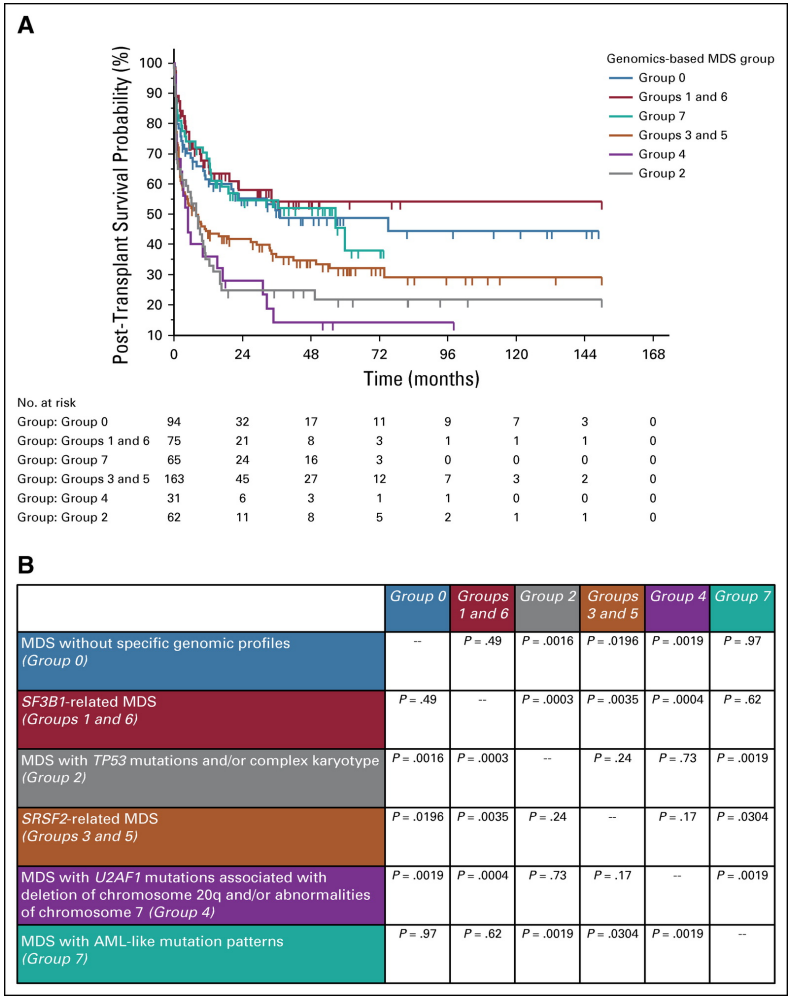
Della Porta et al JCO 2016:

Posttransplantation overall survival of patients with myelodysplastic syndromes classified by the revised International Prognostic Scoring System (IPSS-R) and stratified according to the presence of mutations in the

ASXL1, RUNX1, and TP53 genes.







B

	Group 0	Groups 1 and 6	Group 2	Groups 3 and 5	Group 4	Group 7
MDS without specific genomic profiles (Group 0)	--	P = .49	P = .0016	P = .0196	P = .0019	P = .97
SF3B1-related MDS (Groups 1 and 6)	P = .49	--	P = .0003	P = .0035	P = .0004	P = .62
MDS with TP53 mutations and/or complex karyotype (Group 2)	P = .0016	P = .0003	--	P = .24	P = .73	P = .0019
SRSF2-related MDS (Groups 3 and 5)	P = .0196	P = .0035	P = .24	--	P = .17	P = .0304
MDS with U2AF1 mutations associated with deletion of chromosome 20q and/or abnormalities of chromosome 7 (Group 4)	P = .0019	P = .0004	P = .73	P = .17	--	P = .0019
MDS with AML-like mutation patterns (Group 7)	P = .97	P = .62	P = .0019	P = .0304	P = .0019	--

Bersanelli M et al. JCO 2021

Classification and Personalized Prognostic Assessment on the Basis of Clinical and Genomic Features in Myelodysplastic Syndromes

- Genomic groups in EuroMDS cohort (N = 2,043) and their relationship with WHO category (defined according to 2016 classification criteria) and overall survival

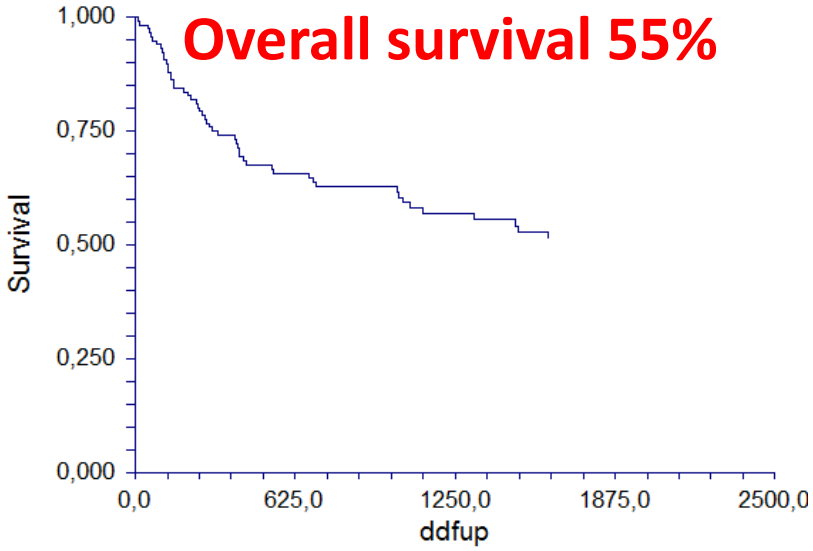
- Probability of overall survival after allogeneic transplantation in the EuroMDS cohort. Patients were stratified according to specific genomic features

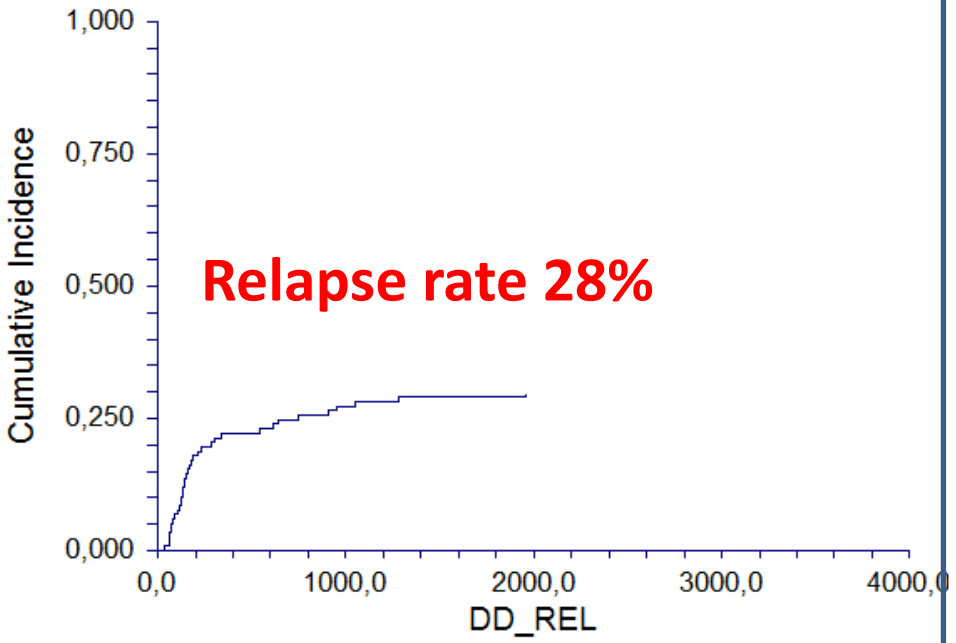
Genova transplant program

MDS patients (2010 -2018)n = **117**

Median Age = 56 (18-70) yy

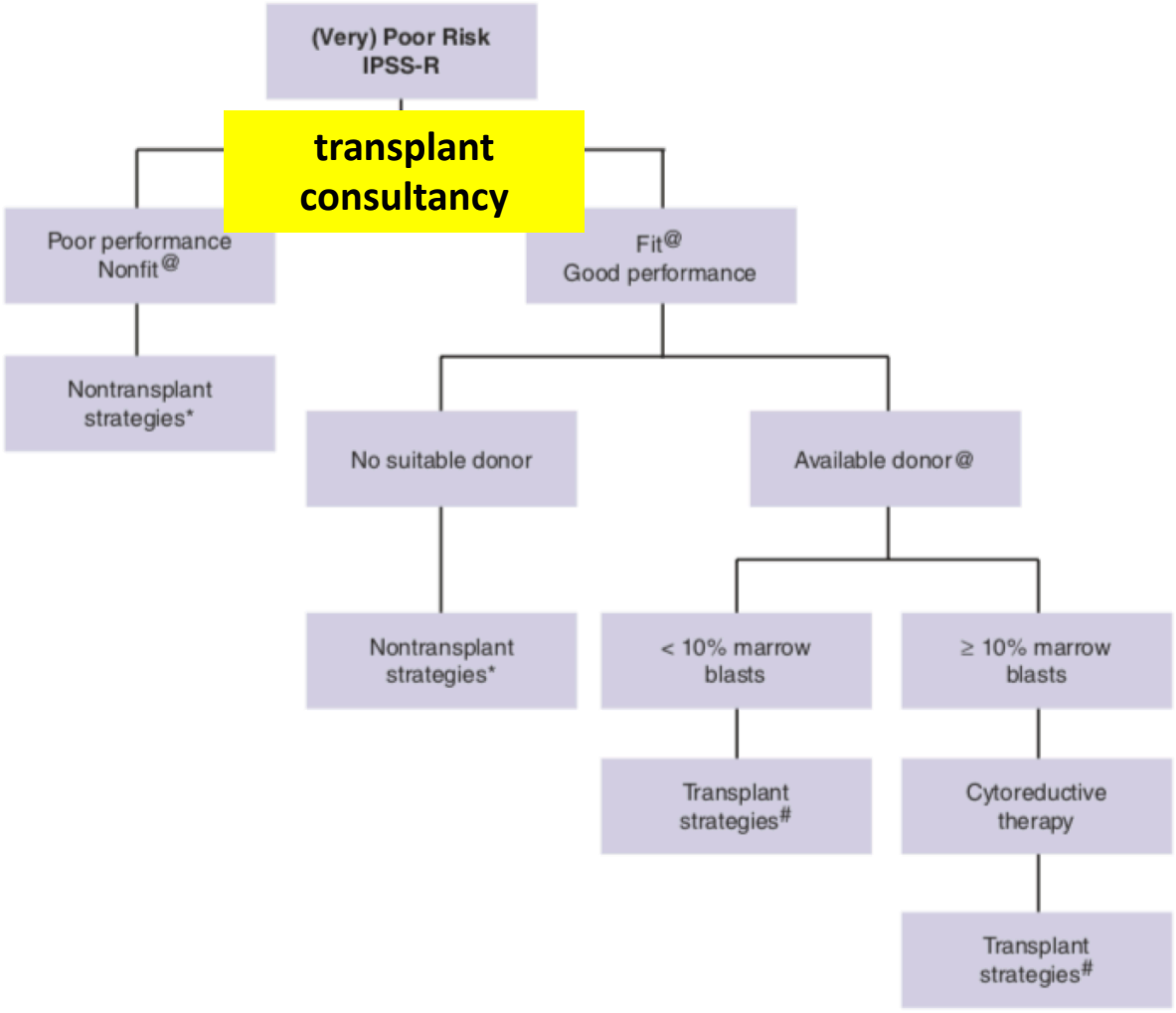
Median Follow up = 1566 (210-3224) day





OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria
Istituto di Ricovero e Cura a Carattere Scientifico

Take home message



LEUKEMIA2020-2021

April 26-27, 2021

Coordinator: A.M. Carella
AIL President: S. Amadori

ASSOCIAZIONE ITALIANA CONTRO LE LEUCEMIE-LINFOMI E MIELOMA ONLUS

fondazione GIMEMA onlus
per la promozione e lo sviluppo della ricerca scientifica sulle malattie ematologiche. FRANCO MANDELLI

GITMO
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

SIES Società Italiana Ematologia Sperimentale

SIE - Società Italiana di Ematologia