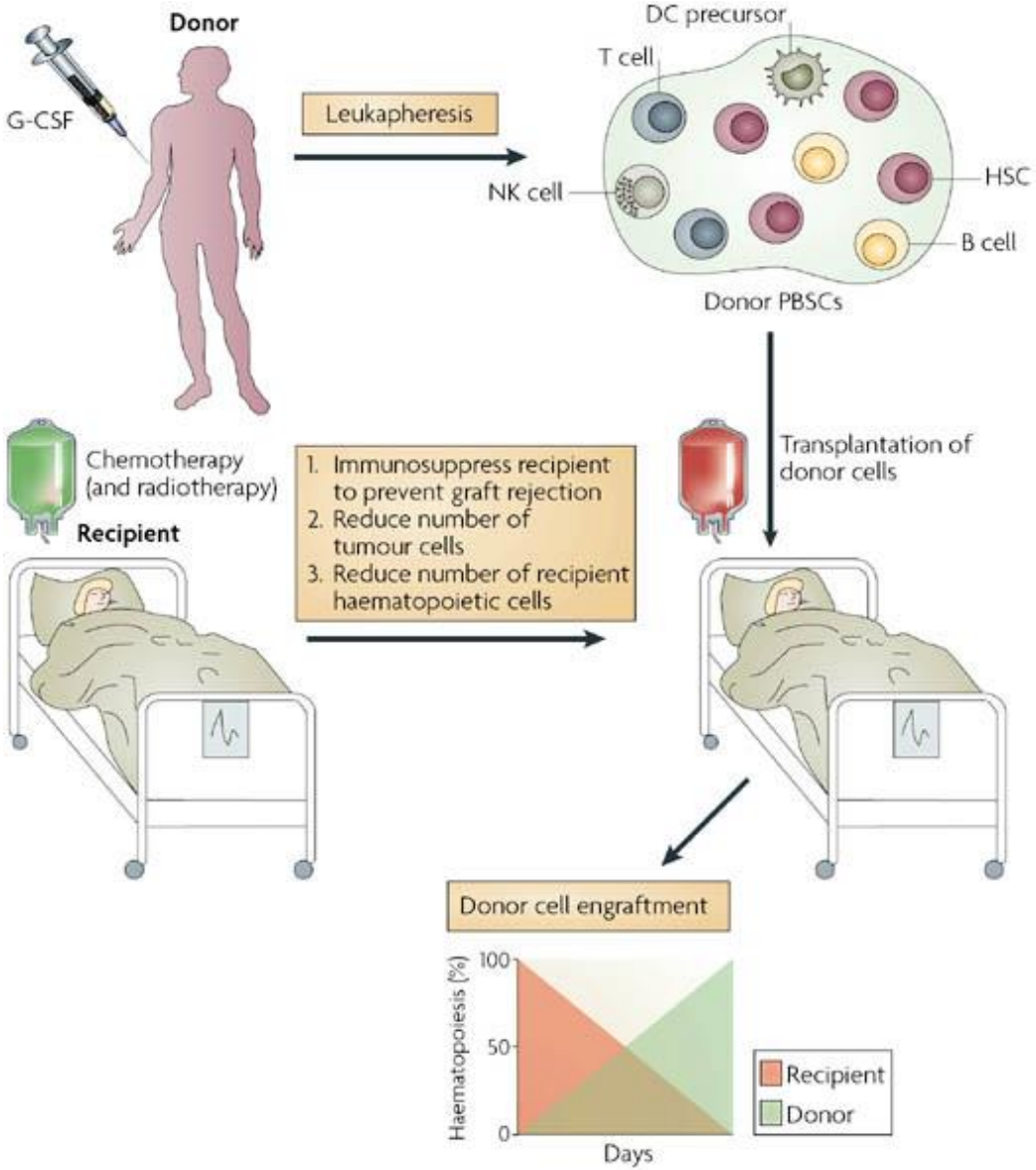
ULB UNIVERSITÉ LIBRE DE BRUXELLES

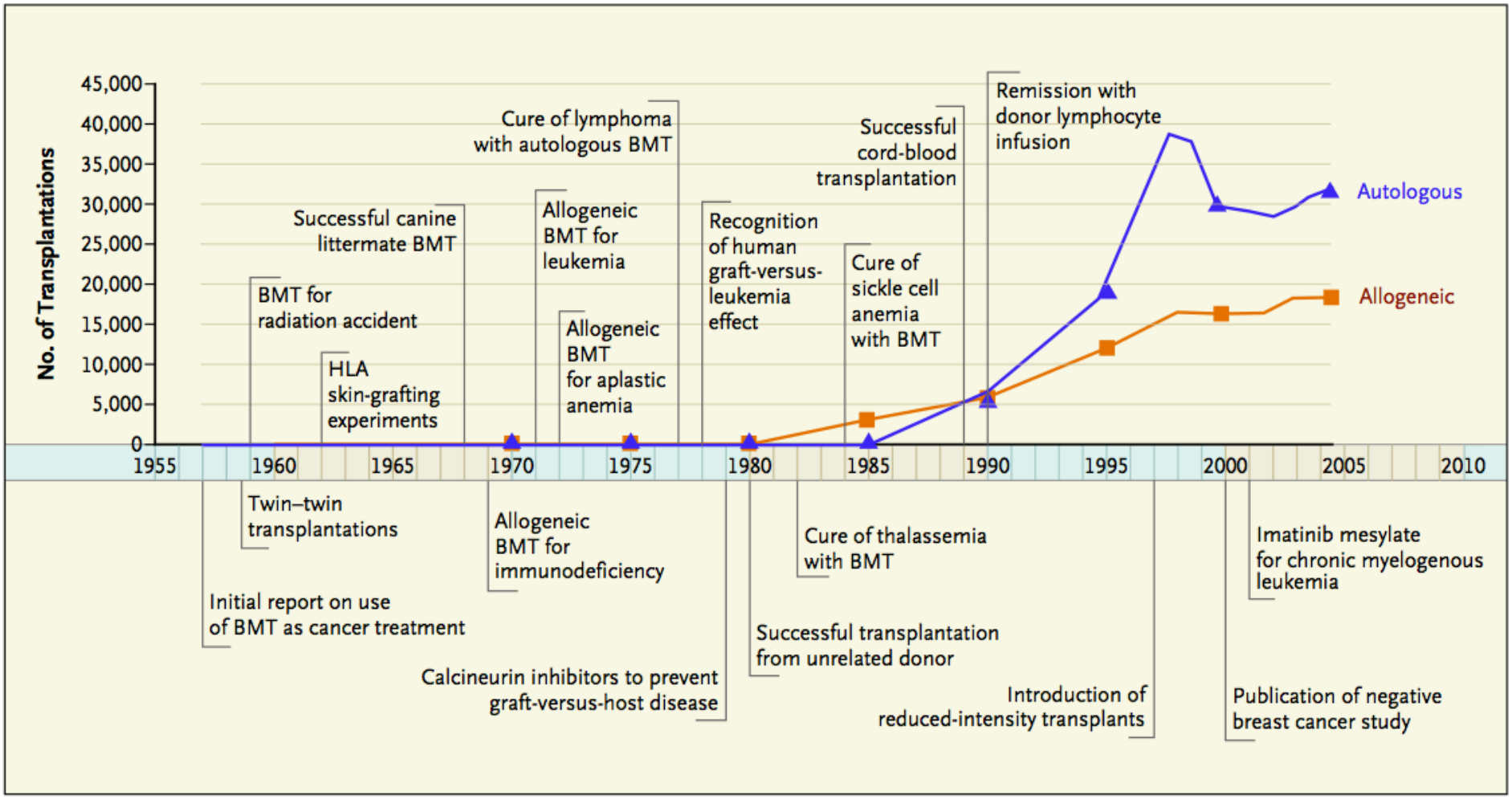
Institut Jules Bordet

Le greffé de moelle/CSH à l'USI

N Meuleman 12/03/2015

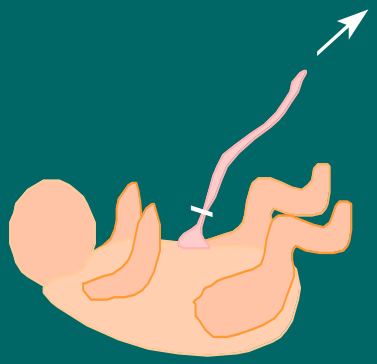
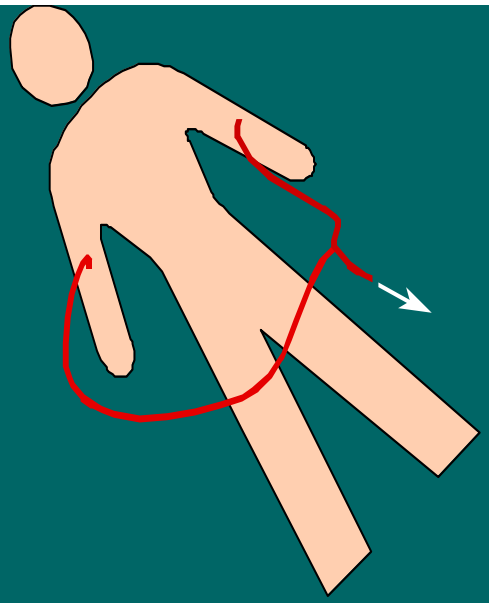
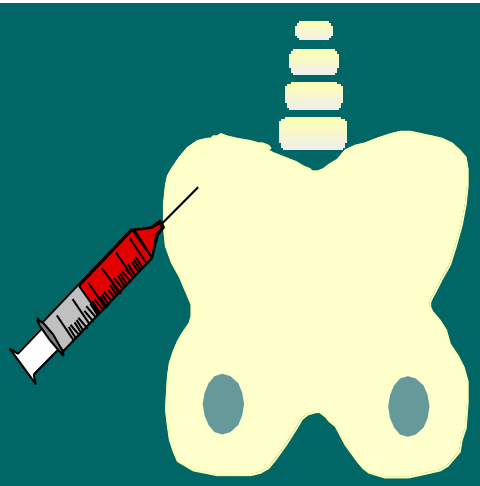


WD. Shlomchik
Nature Reviews Immunology 7, 2007

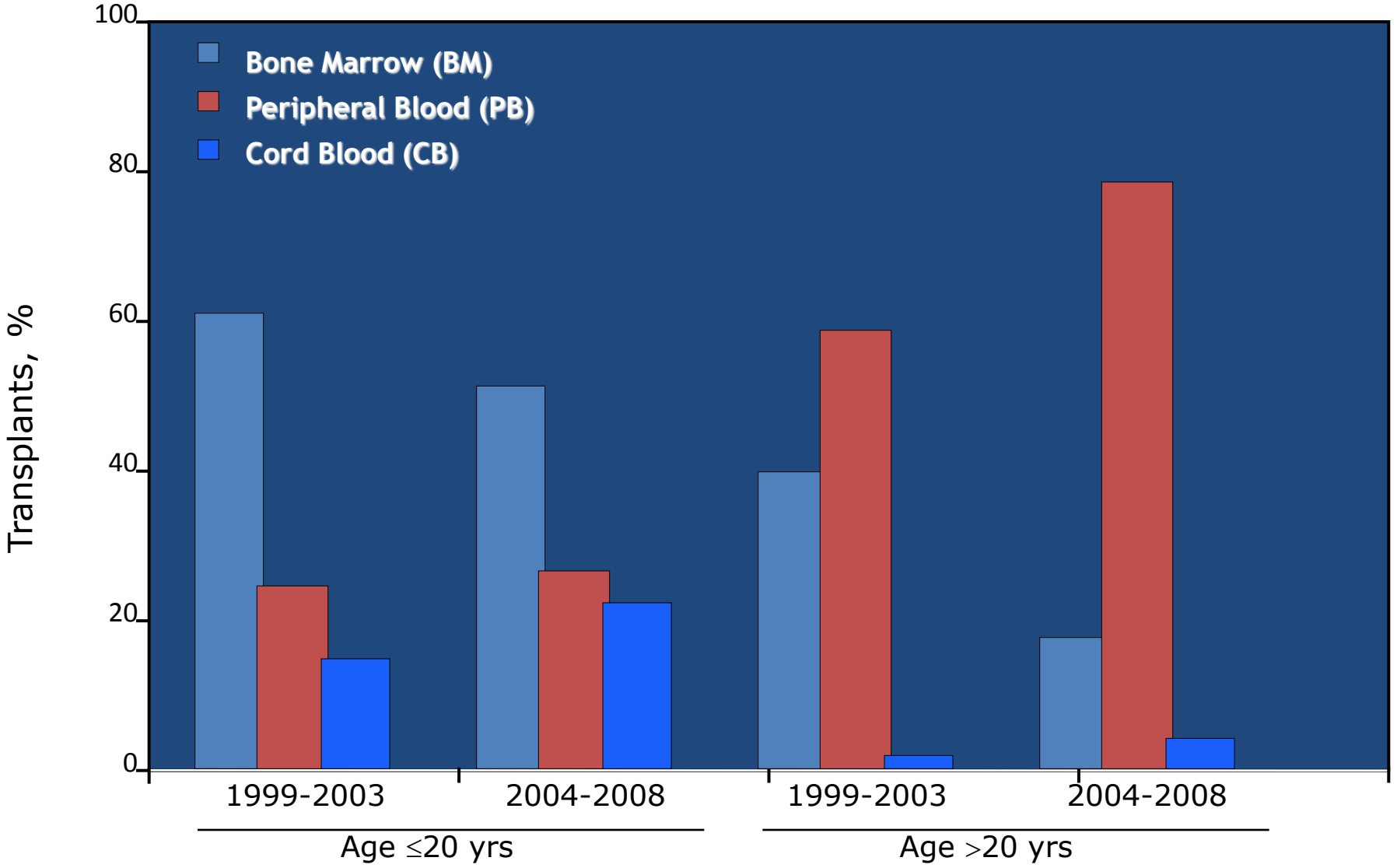


From Copelan, NEJM, 2006

Sources of Hematopoietic Stem Cells

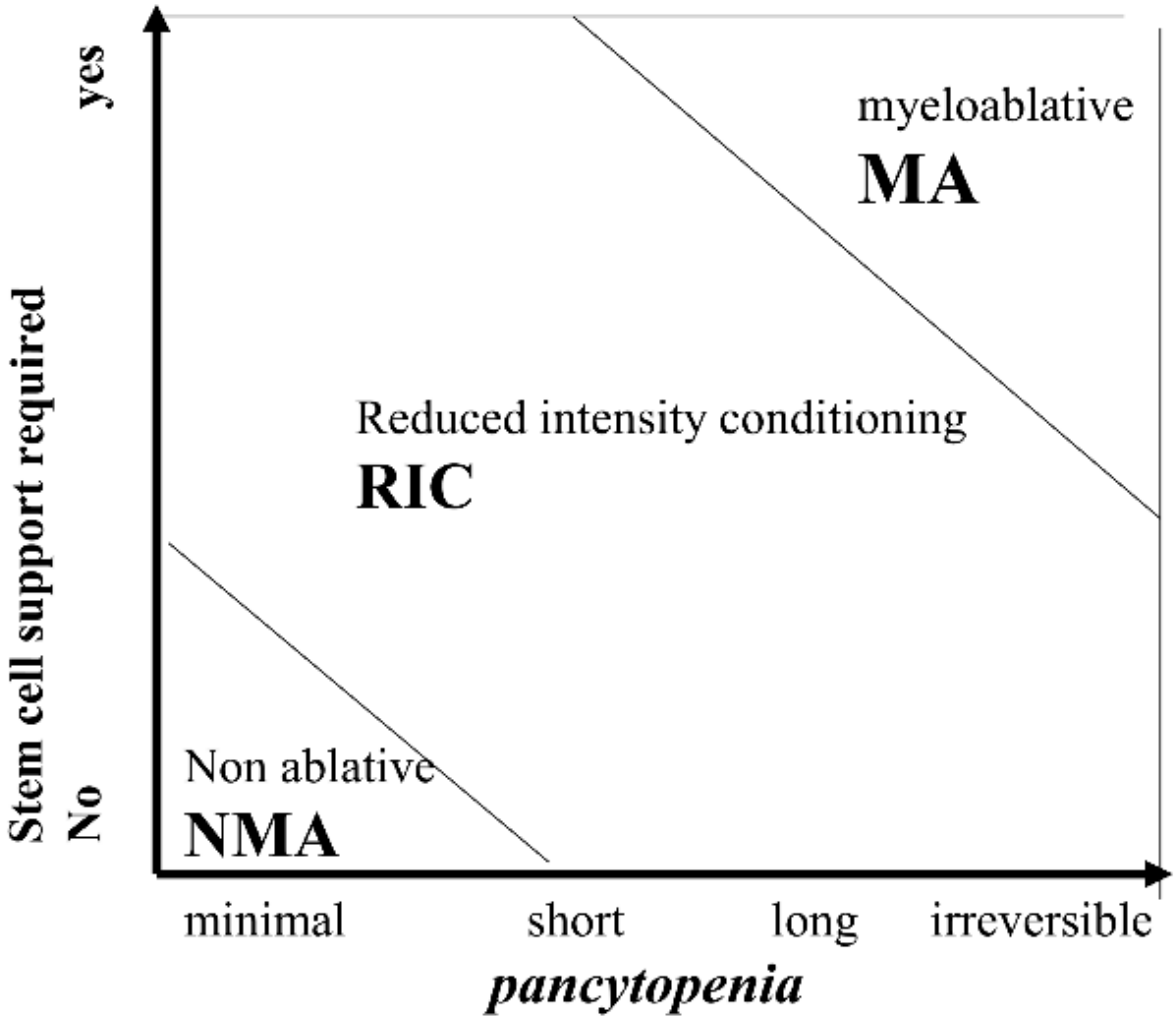
Sources			
Progéniteurs immatures ($CD34^{+}CD38^{-}$)	++++	+++	++
Statut de prolifération	++++	+++	++

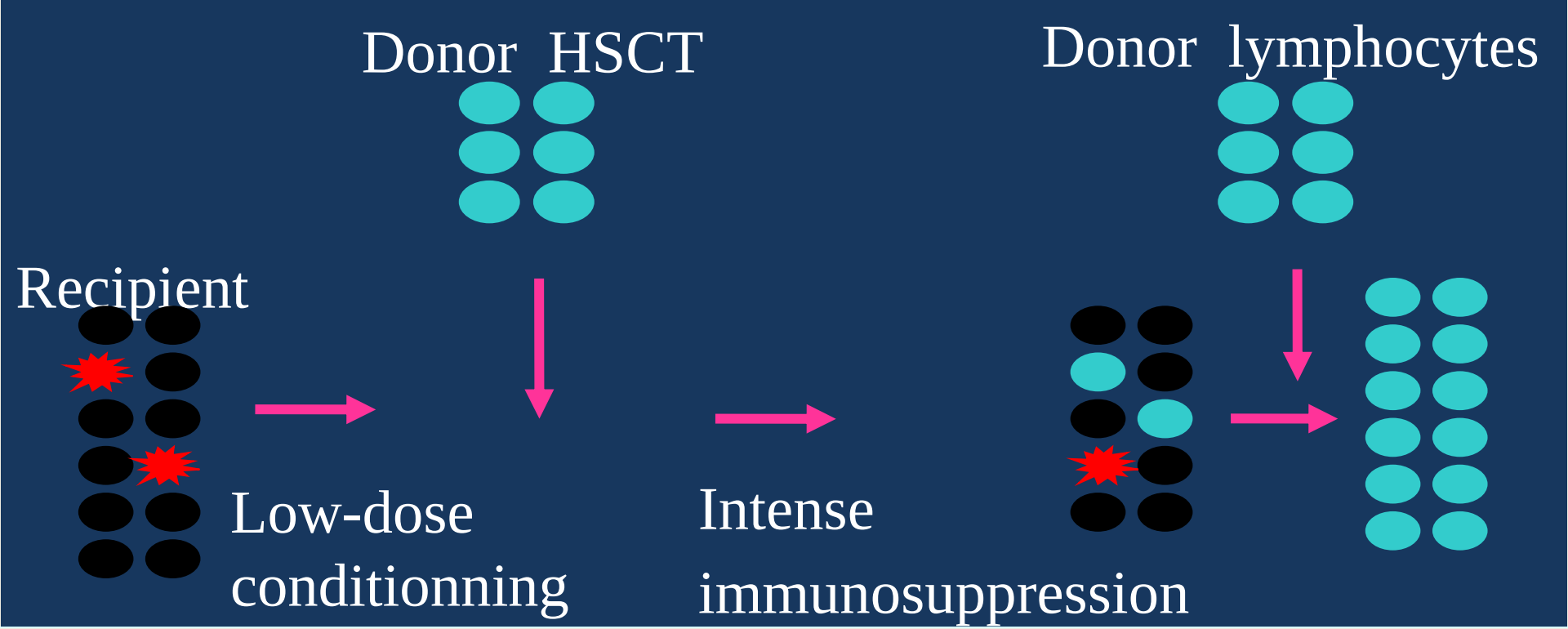
Allogeneic stem cell sources, by recipient age 1999-2008

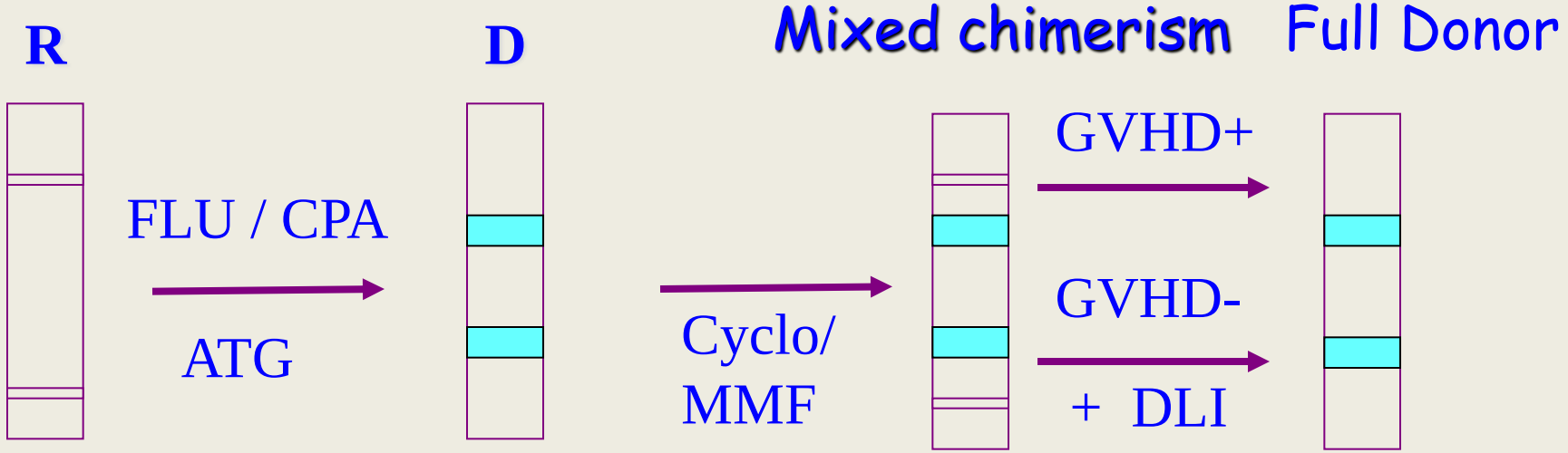


Conditionnement

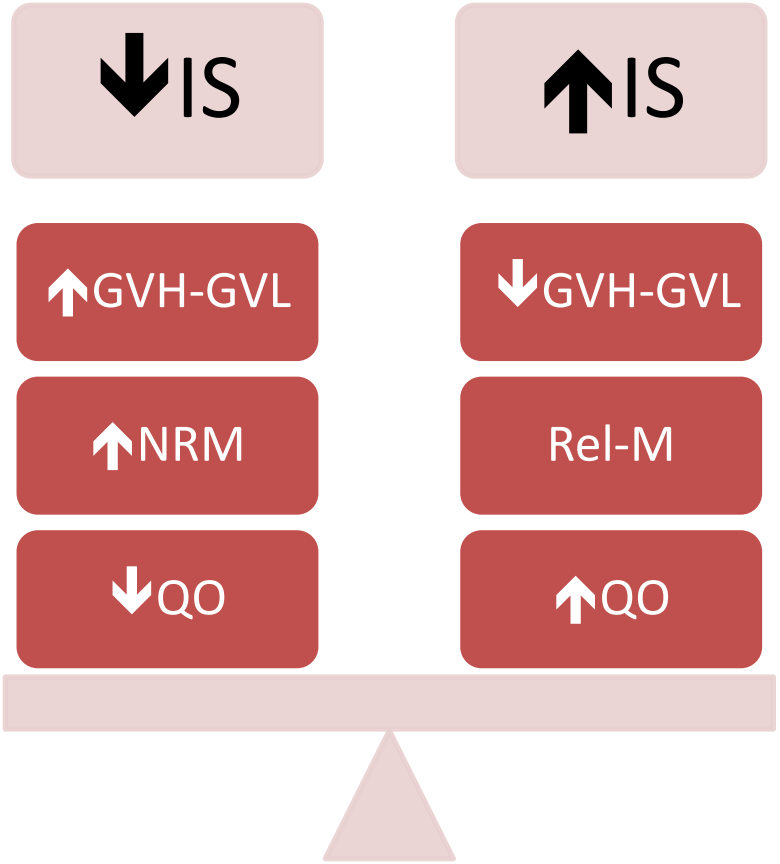
- **Age**
- **Comorbidité**
  - **Cardiaque**
  - **Pulmonaire**
  - **Hépatique**
  - **Infectieuse**



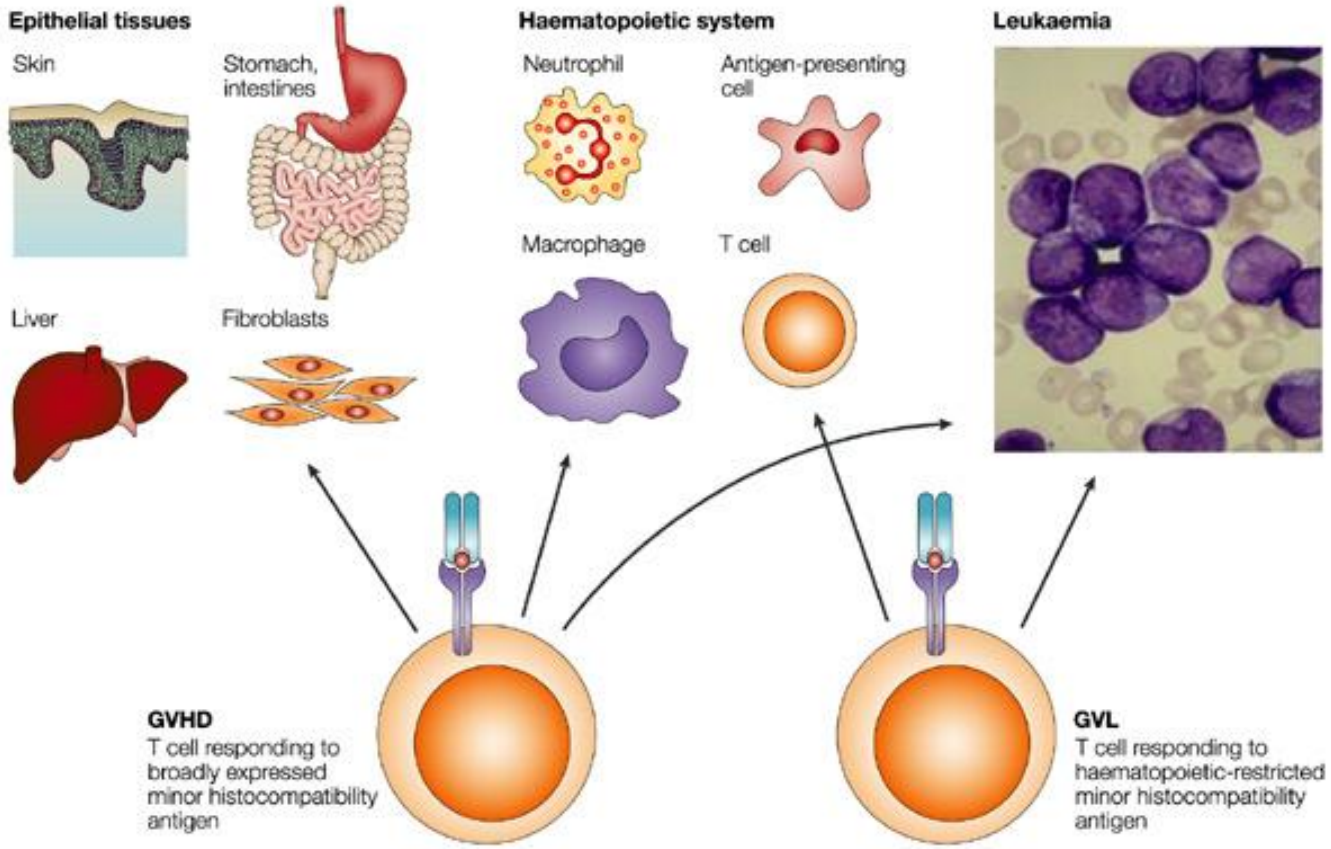

Donor HSCT
Donor lymphocytes
Recipient
Low-dose
conditionning
Intense
immunosuppression


R
D
Mixed chimerism
Full Donor
FLU / CPA
ATG
Cyclo/
MMF
GVHD+
GVHD-
+ DLI

Immunosuppression



Maladie du greffon contre l'hôte et la tumeur



M. Bleakley & SR. Riddell
Nature Reviews Cancer (2004)

Comment définir la greffe?

- Le donneur
  - Familiale
  - Non familiale
- Source de cellules souches
  - CSHP/moelle/cordon
- Histocompatbilité:
  - HLA id (10/10) - Incompatibilité
  - Haplo-identique
- Conditionnement
  - Myéloablatif/ RIC…
  - Déplétion T (greffon/ ATG)

Survie et greffe

TRM dans les années 70 : 48% à J100

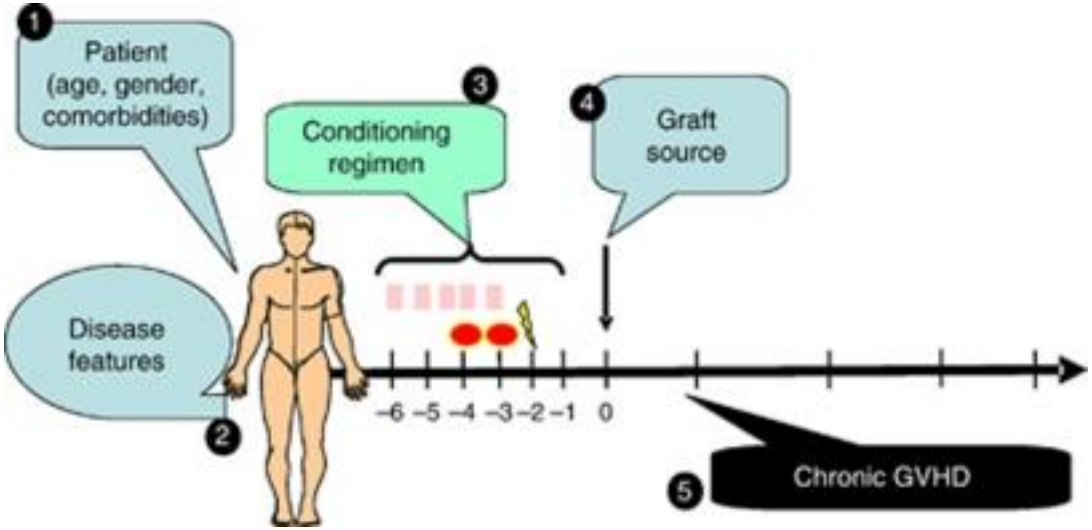
54% à J365

TRM en 2000/2001 : 18% à J100

20 % à J365

(CIBMTR 2004)

Toxicité



B Mohty[1] and M Mohty[2,3,4]

B Mothy et al; 2011

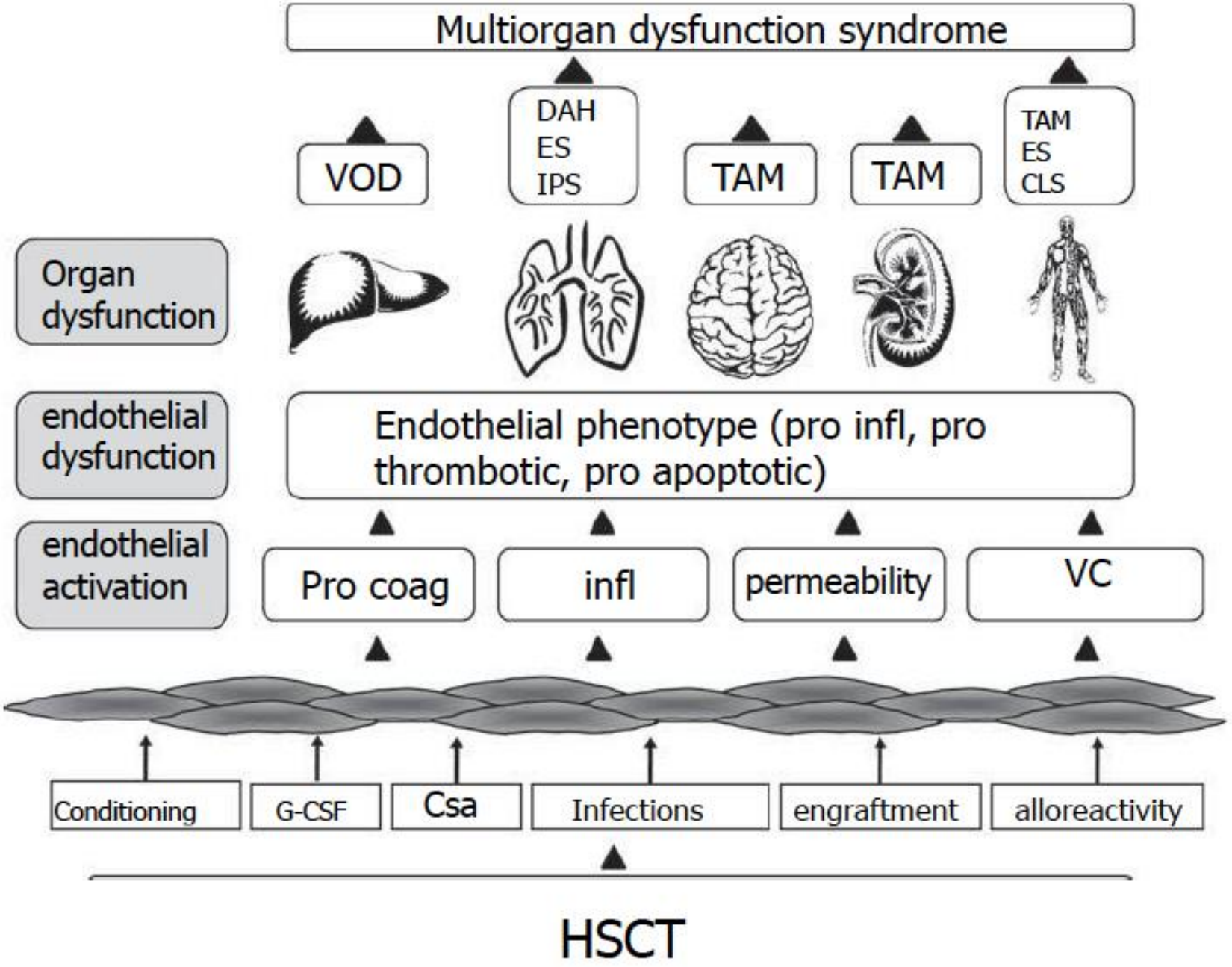
Complications

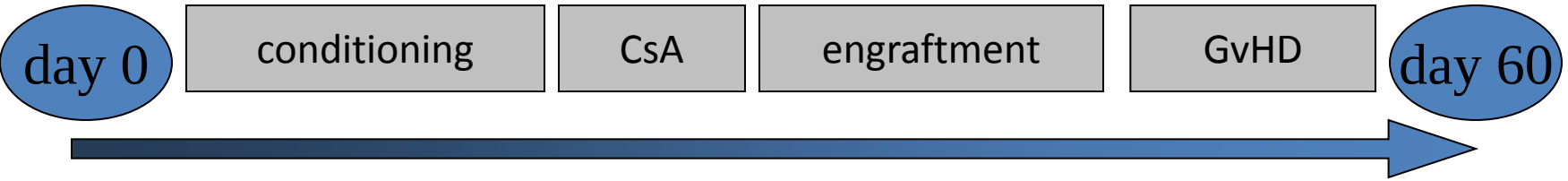
Précoce

- **Radio-chimiothérapie**
  - N-V+, mucosite, diarrhée
  - Alopécie
  - Cystite HH
  - Idiopathic pneumonia syndrome
- **Atteinte de l'endothélium vasculaire**
  - VOD, CLS, MAP, Syndrome de prise de greffe, HHA
- **Traitements associés**
  - IS
- **Infections**
- **GVHD**

Tardive

- Infections
- GVHD chronique
- Cancer secondaire
- Fertilité
- Maladie cardio-vasculaire
- Neuro:
  - Leuco-encéphalopathie
  - NP
- Néphropathie
- QOL


Multiorgan dysfunction syndrome
VOD
DAH
ES
IPS
TAM
TAM
TAM
ES
CLS
Organ dysfunction
endothelial dysfunction
Endothelial phenotype (pro infl, pro thrombotic, pro apoptotic)
endothelial activation
Pro coag
infl
permeability
VC
Conditioning
G-CSF
Csa
Infections
engraftment
alloreactivity
HSCT



veno-occlusive disease

capillary leak syndrome

BMT associated thrombotic microangiopathy

diffuse alveolar haemorrhage

idiopathic pneumonia syndrome

engraftment syndrome

Overlapping clinical manifestations

Atteinte endothélium

Syndrome fuite capillaire

- **15 jour de transplantation**
- 10-50 %
- Symptômes
  - Prise de poids , >3%/ 24h00
  - Oedeme généralisé, ascite, EPl, EP
  - Hypo-ta, IR
  - Hypo-albuminémie
- TT:
  - mauvaise réponse au stéroïdes, furosémide
- Facteurs de risques:
  - G-CSF, nbre tt pré greffe, MUD, HLA≠
- **Mortalité:**
  - **8%-40%**

Syndrome de prise de greffe

- **Dans les 96 h00 prise de greffe**
  - **Neutro >500 X2**
- < relargage de cytokines pro-inflammatoires ++++
- 7%-50%
- Symptômes
  - Prise de poids, **OP**, infiltrats po
  - **Fièvre++, Éruption**, diarrhée
  - IR, IH…
- Facteurs de risques:
  - G-CSF, CSP
- TT:
  - M-PDN 2mg/kg 1 semaine et diminution rapide
- **Mortalité:**
  - **10%**
- DD: SFC, GVHA

Idiopathic pneumonia syndrome (IPS)

- Atteinte pulmonaire: toxique, inflammatoire, immunologique, rôle des infections
- Définition
  - Infiltrats multilobaires
  - Symptômes de pneumonie
  - Absence d'infection documentée (LBA x 2 –Biopsie)
  - Pas de surcharge hydrique
  - Pas de réponse rapide aux antibactériens
- **Fievre, toux, tachypnée et hypoxie vers J20** (11-133)
- Incidence :8-10% (2-3% in RIC)
- Facteurs de risque:
  - Conditionnement myéloablatif, âge> 40 , aGVHD, TBI,
- Steroides: NON, antiTNFa?
- Mortalité 50-70% (97% si VM)

Maladie veino-occlusive du foie (VOD)

- Pathophysiologie
  - Atteinte des cellules endothéliales des sinusosides hepatiques et des hépatocytes
  - Hpercoagulation, diminitution du flux sanguin
    - HMG sensible hyperbilirubinémie, ascite
    - Thrombopénie réfractiare
    - Syndrome hépato-rénal
  - Réduction de l'excretion rénale du NA, rétention , prise de poids
- Incidence: 10-50% selon
  - Hépatites avant greffe
  - TBI
  - Conditionnement pré-greffe

Maladie veino-occlusive du foie (VOD)

- Mortalité
  - 4% à > 75% selon grade
- Traitement:
  - Symptomatique
    - Restriction hydrique et salée
    - Maintien perfusion
    - Albumine
    - > 20.000/plt
    - Arrêt hépatotoxique
- Défibrotide (dérivé acide désoxyribonucléique):
  - Augmente PG,PC, tPA
  - Diminue relargage de TF, thrombine, activité endothélium

Microangipoathie et greffe

- Dysfonction de l'endothélium avec activation plaquettaire intravasculaire et micro-thrombi
- Déficit en ADAMTS13 rare < 10%
- Incidence: 7-15%, jour 60 (J4-2 ans)
- Facteurs de risques:
  - TBI, Calcineurin inhibitors, sirolimus, MUD, unrelated or, GVHD, CMV infection.
- Traitement?:
  - La cause sous-jacente
  - Arrêt des inhibiteurs calcineurine
  - Traiter infections, GVHD
  - Plasmaphérèse???, rituximab?, Eculizumab???
  - Pas de traitement de référence

VOLUME 31 · NUMBER 33 · NOVEMBER 20 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Hematopoietic Cell Transplantation–Specific Comorbidity Index Predicts Inpatient Mortality and Survival in Patients Who Received Allogeneic Transplantation Admitted to the Intensive Care Unit

Ulas D. Bayraktar, Elizabeth J. Shpall, Ping Liu, Stefan O. Ciurea, Gabriela Rondon, Marcos de Lima, Marylou Cardenas-Turanzas, Kristen J. Price, Richard E. Champlin, and Joseph L. Nates

Table 2. Demographics and Clinical Characteristics of the Patients Who Receive Allogeneic Transplantation Admitted to the ICU

Characteristic	No. of Patients (N = 377)	%
Age at transplantation, years		
Median	53	
Day of transplantation at ICU admission	25	
Median	25	
Range	−5 to 100	
Transplantation period at ICU admission		
During preparative regimen	13	3
Before engraftment	130	35
After engraftment	234	62
Acute GVHD at the time of ICU admission		
No	269	71
Yes	108	29

Bayraktar U D et al. JCO 2013;31:4207-4214

Raison d'admission

Table 2. Demographics and Clinical Characteristics of the Patients Who Receive Allogeneic Transplantation Admitted to the ICU

Characteristic	No. of Patients (N = 377)	%
Reason for ICU admission		
Respiratory failure	230	61
Septic shock	44	12
Altered mental status	33	9
Arrhythmia	20	5
Non-GI, non-CNS bleeding	15	4
GI bleeding	13	3
Myocardial infarction	6	2
Upper airway compromise	5	1
Chest pain	4	
ARF requiring SLED	4	
Anaphylactic/drug/cell reaction	3	
Hypertension	3	
Thrombotic thrombocytopenic purpura	3	
Unknown	3	
Veno-occlusive disease	2	
Mucositis	2	
Hypotension	1	
Diabetic emergency	1	
Dehydration due to GI fluid loss	1	
For leukapheresis	1	

Bayraktar U D et al. JCO 2013;31:4207-4214

Table 4. Multivariate Analyses of Inpatient Mortality and OS

Factor	Inpatient Mortality No.	Inpatient Mortality %	Multivariate OR for Inpatient Mortality OR	95% CI	P	Median OS (days)	Multivariate HR for OS HR	95% CI	P
Age at transplantation, years									
≤ 55	139	63	Reference			37	Reference		
> 55	101	65	1.17	0.72 to 1.90	.53	28	1.27	0.99 to 1.62	.05
Diagnosis									
Acute leukemia/MDS	127	65	Reference			33	Reference		
Transplantation period at ICU admission									
During preparative regimen	2	15	0.12	0.03 to 0.59	.009				
Before engraftment	84	65	1.08	0.64 to 1.84	.77				
After engraftment	154	66	Reference						
Before engraftment	84	65	1.08	0.64 to 1.84	.77	37	1.09	0.83 to 1.42	.55
After engraftment	154	66	Reference			29	Reference		
Graft source									
Peripheral blood	140	63	Reference			32	Reference		
Umbilical cord	31	74	1.77	0.63 to 4.95	.28	37	1.25	0.78 to 2	.36
Bone marrow	69	62	1.20	0.67 to 2.15	.54	38	1.05	0.79 to 1.40	.72
Reduced intensity	107	60	Reference						
Ablative	133	67	1.64	1.01 to 2.68	.05				
Conditioning dose-intensity									
Reduced intensity	107	60	Reference			37	Reference		
HCT-CI score									
0-1	26	46	Reference						
2	40	67	2.24	1.02 to 4.93	.05				
3	70	63	2.13	1.07 to 4.25	.03				
≥ 4	104	70	2.92	1.49 to 5.72	.002				

MDS, myelodysplastic syndrome; OR, odds ratio; OS, overall survival.

Comorbidities	Definitions	HCT-CI Weighted Scores
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, and ventricular arrhythmias	1
Cardiac	Coronary artery disease,* congestive heart failure, myocardial infarction, or ejection fraction ≤ 50%	1
Inflammatory bowel disease	Crohn's disease or ulcerative colitis	1
Diabetes†	Requiring treatment with insulin or oral hypoglycemic, but not diet alone	1
Cerebro-vascular disease	Transient ischemic attack or cerebro-vascular accident	1
Psychiatric disturbance†	Depression/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 BMI of > 35 for adults or with BMI-for-age ≥ 95th percentile for children	1
Infection†	Documented infection or fever of unknown etiology requiring anti-microbial treatment before, during, and after the start of conditioning regimen	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, 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 > 65%–80% or Dyspnea on slight activity	2
Prior solid tumor	Treated at any time 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

L Sorror et al; Blood 2005

Complications pulmonaires non infectieuses post allogreffe

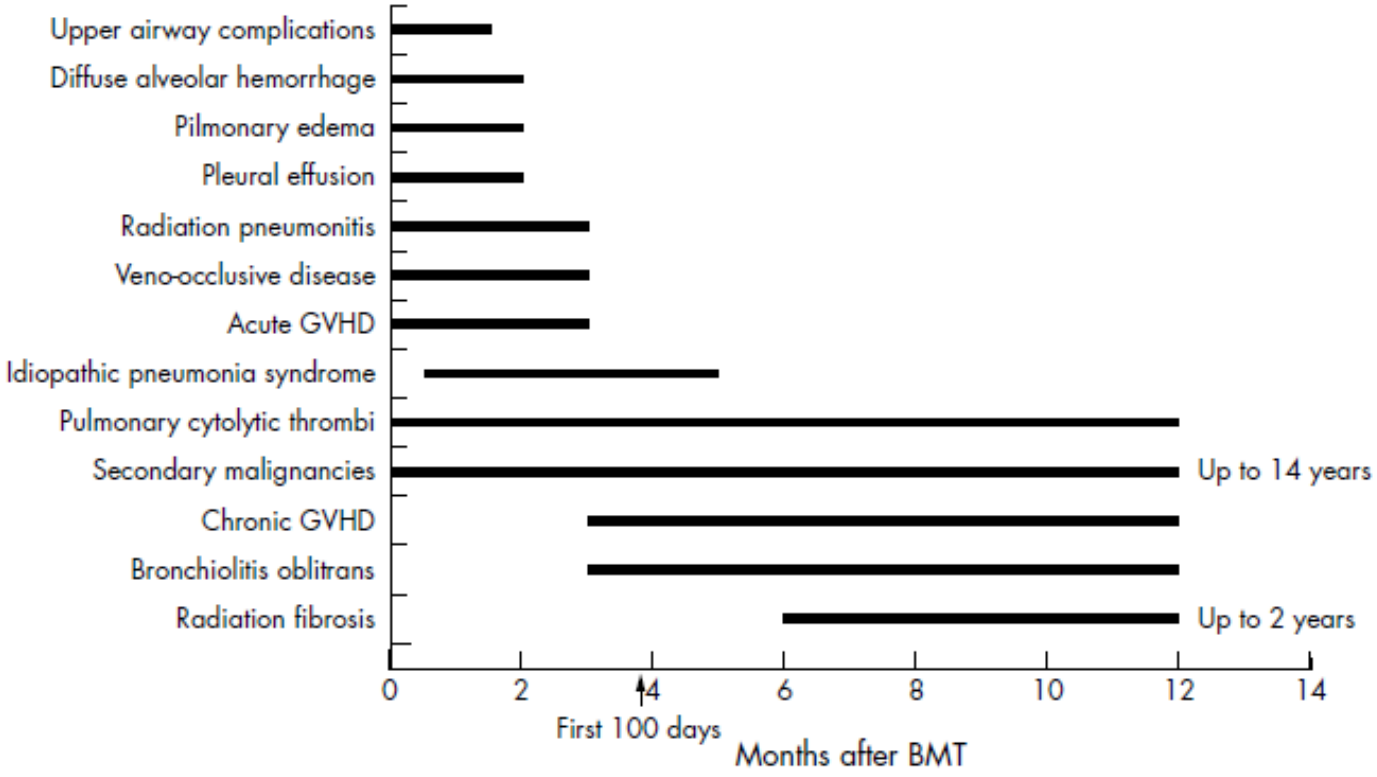


Figure 1 The chronology of non-infectious pulmonary complications after BMT.

Infections

Table 1. Infectious Complications of Allogeneic Hematopoietic Stem Cell Transplantation

	Pre-engraftment: Early (<3 weeks)	Postengraftment: Immediate (<3 weeks–3 months)	Postengraftment: Late
Bacterial	Gram positive cocci Gram negative bacilli Anaerobes	Gram positive cocci Gram negative bacilli Anaerobes	Encapsulated
Fungal	Candida spp. Aspergillus spp.	Aspergillus spp. Pneumocystis carinii	Candida spp. Aspergillus spp. Pneumocystis carinii
Viral	HSV 1,2 RSV Influenza Adenovirus	Cytomegalovirus HHV 6 RSV Influenza Adenovirus	VZV EBV RSV Influenza Adenovirus

Arnout K; Cancer Investigation, 2014

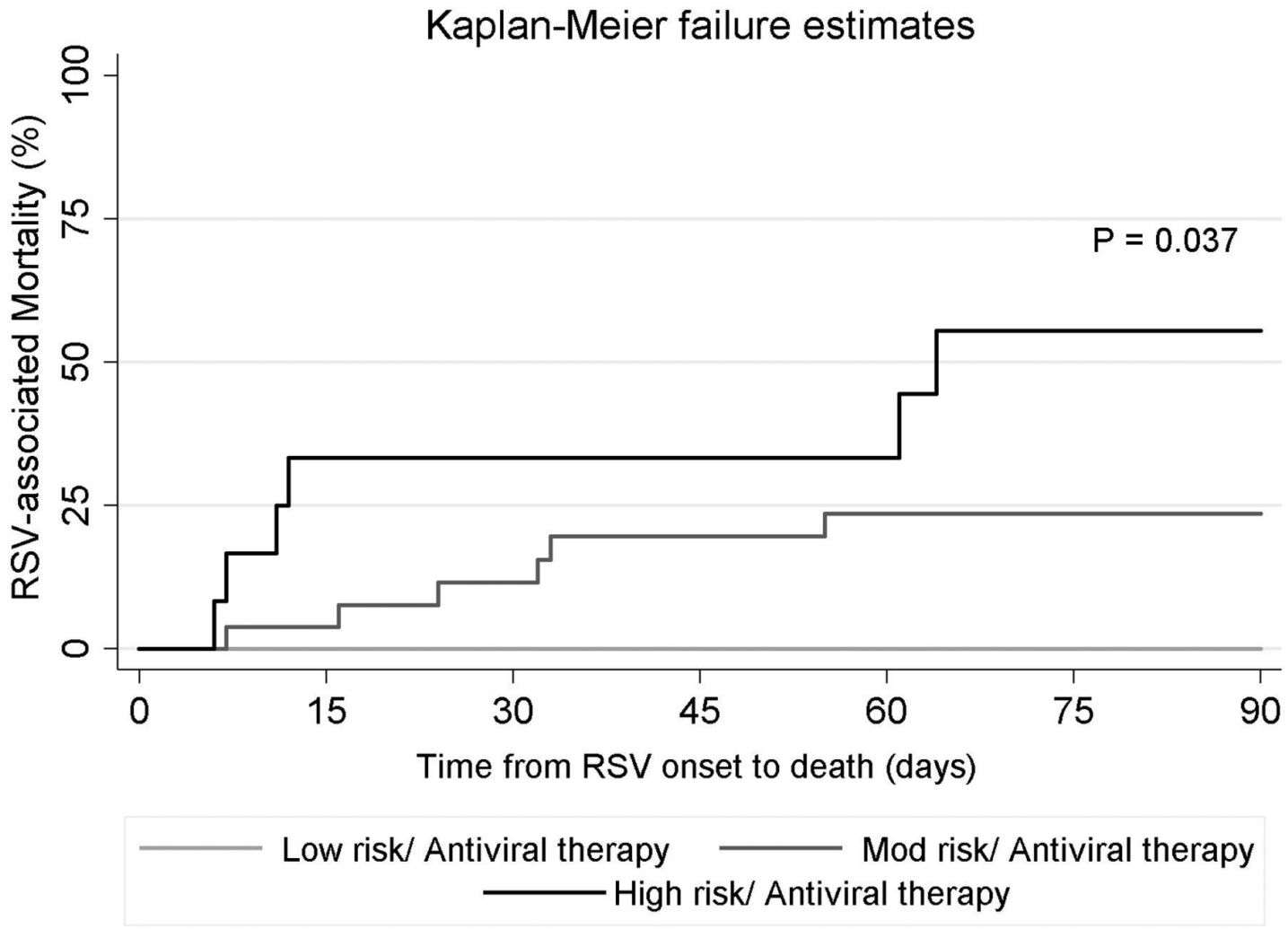
Infection à RSV post allogreffe

Table 1. Development of the ISI-RSV for patients presenting with RSV infections (N = 237)

Criteria		No. (%)		AHR* (95% CI)	Weighing criteria	Assigned weights (score)
		Patients 237, n (%)	Progression to LRTI 37, n (%)			
1	ANC <500/μL	11 (5)	7 (64)	4.1 (1.4-11.6)	>2.5	3
2	ALC <200/μL	35 (15)	11 (31)	2.6 (1.02-6.4)	>2.5	3
3	Age ≥40 y	154 (65)	28 (18)	2.5 (1.1-5.6)	2.0-2.5	2
4	Myeloablative conditioning regimen	98 (41)	17 (17)	1.2 (0.6-2.3)	<2.0	1
5	GVHD (acute or chronic)	149 (63)	19 (13)	1.0 (0.5-2.2)	<2.0	1
6	Corticosteroids†	117 (49)	17 (15)	0.89 (0.4-1.8)	<2.0	1
7	Recent† or pre-engraftment allo-HSCT	21 (9)	5 (24)	0.68 (0.2-2.3)	<2.0	1
	Maximum possible overall score‡					12
	Low risk: 0-2 score, moderate risk 3-6 score, high risk 7-12 score					

Shah D P et al. Blood 2014;123:3263-3268

Kaplan-Meier failure curves for RSV-associated mortality in patients presenting with RSV-LRTI stage stratified according to ISI-RSV risk group.



Shah D P et al. Blood 2014;123:3263-3268

Cas vécu

- Sarah 19 ans
- LAL à 6 mois de greffe haplo-identique
  - Fièvre sus IS non neutropénique
  - Tazo, méro, + vanco..
  - Sepsis, insuffisance respiratoire
  - Asti:
    - + amukin, caspofungine, gancyclovir…
    - RMN cérébrale NL/ PL nl
  - Transfert Erasme: ECMO
- Autopsie: toxoplasmose généralisée

Early central nervous system complications after allogeneic hematopoietic stem cell transplantation in children

Kyung Nam Koh, Meerim Park, Bo Eun Kim, Ho Joon Im, Jong Jin Seo

Type of complication	Type of donor			Total, n=202 (%)
	Matched related, n=60 (%)	Mismatched related, n=9 (%)	Unrelated, n=133 (%)	
CNI neurotoxicity	1 (1.7)	1 (11.1)	14 (10.5)	16 (7.9)
Cerebrovascular	1 (1.7)	0	1 (0.8)	2 (1.0)
Infection	0	0	2 (1.5)	2 (1.0)
TMA-associated	0	0	2 (1.5)	2 (1.0)
Metabolic	0	0	2 (1.5)	2 (1.0)
RT/chemotherapy	0	0	1 (0.8)	1 (0.5)
Unknown	0	0	2 (1.5)	2 (1.0)
Total	2 (3.3)	1 (11.1)	25 (18.8)	27 (13.5)

Korean J Hematol. 2010 Sep; 45(3): 164–170.

GVHA

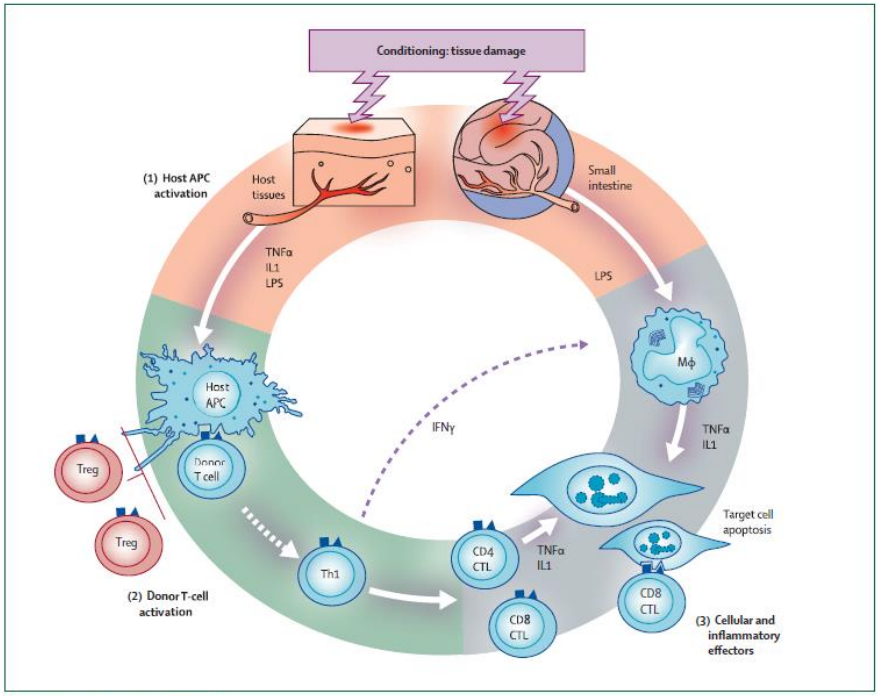


Figure 3: **Pathophysiology of acute GVHD**
IL 1=interleukin 1. IFN γ=interferon γ. LPS=lipopolysaccharide. Treg=regulatory T cell. Th1=T-helper 1 cell. CTL=cytotoxic T lymphocyte.

Table 2A. Staging of Acute Graft-versus-Host Disease

Clinical stage	Lower GI	Upper GI	Liver (Bilirubin mg/dL)	Skin
1	Diarrhea <500 mL/d	Nausea/Vomiting	2–3	Rash < 25% of BSA
2	Diarrhea 500–1000 mL/d		3–6	Rash 25–50% of BSA
3	Diarrhea 1000–1500 mL/d		6–15	Generalized erythroderma
4	>1500		> 15	Bullae/Desquamation

Présentation clinique de la GVH

Panel 1: **Acute GVHD symptoms**

Skin
- Maculopapular skin rash

Upper gastrointestinal tract
- Nausea, anorexia, or both, and positive histological findings

Lower gastrointestinal tract
- Watery diarrhoea (≥500 mL)
- Severe abdominal pain
- Bloody diarrhoea or ileus (after exclusion of infectious causes)

Liver
- Cholestatic hyperbilirubinaemia

Panel 2: **Chronic GVHD symptoms**

Skin
Dyspigmentation, new-onset alopecia, poikiloderma, lichen planus-like eruptions, or sclerotic features

Nails
Nail dystrophy or loss

Mouth
Xerostomia, ulcers, lichen-type features, restrictions of mouth opening from sclerosis

Eyes
Dry eyes, sicca syndrome, cicatricial conjunctivitis

Muscles, fascia, joints
Fasciitis, myositis, or joint stiffness from contractures

Female genitalia
Vaginal sclerosis, ulcerations

Gastrointestinal tract
Anorexia, weight loss, oesophageal web or strictures

Liver
Jaundice, transaminitis

Lungs
Restrictive or obstructive defects on pulmonary function tests, bronchiolitis obliterans, pleural effusions

Kidneys
Nephrotic syndrome (rare)

Heart
Pericarditis

Marrow
Thrombocytopenia, anaemia, neutropenia

bjh research paper

Improved intensive care unit survival for critically ill allogeneic haematopoietic stem cell transplant recipients following reduced intensity conditioning

Table I. Characteristics of patients having one or more ICU admission after allogeneic HSCT (n = 164).

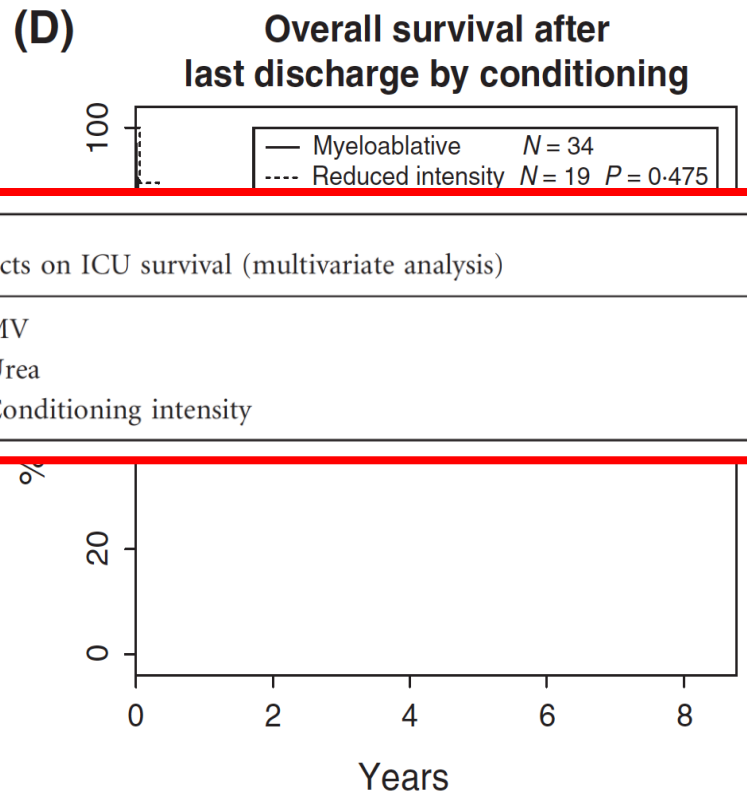
Characteristic	MA N = 127	RI N = 37	P value
Sex			
Male	48 (38%)	17 (46%)	0·446
Female	79 (62%)	20 (54%)	
Age at (last) admission			
Median (range), years	39 (11–60)	50 (23–66)	**0·0001**
Time since transplant			
Median (range), days	32 (1–476)	69 (6–1989)	**0·0007**
Diagnosis			
ALL	34 (27%)	0	**0·0001**
AML	36 (28%)	0	
NHL	20 (16%)	20 (54%)	
HL	5 (4%)	6 (16%)	
CLL	0	4 (11%)	
MF	1 (1%)	3 (8%)	
CML	14 (11%)	3 (8%)	
MDS	6 (5%)	0	
MM	11 (9%)	1 (3%)	
Donor stem cell source			
Sib	66 (40%)	16 (10%)	
UD	61 (37%)*	21 (13%)†	
Number of ICU admissions			
1	99 (78%)	26 (70%)	0·592
2	17 (13%)	8 (22%)	
3	8 (6%)	2 (5%)	
4	3 (2%)	1 (3%)	
Duration of ICU stay			
Median (range) days	4 (0–52)	6 (0–21)	0·4451

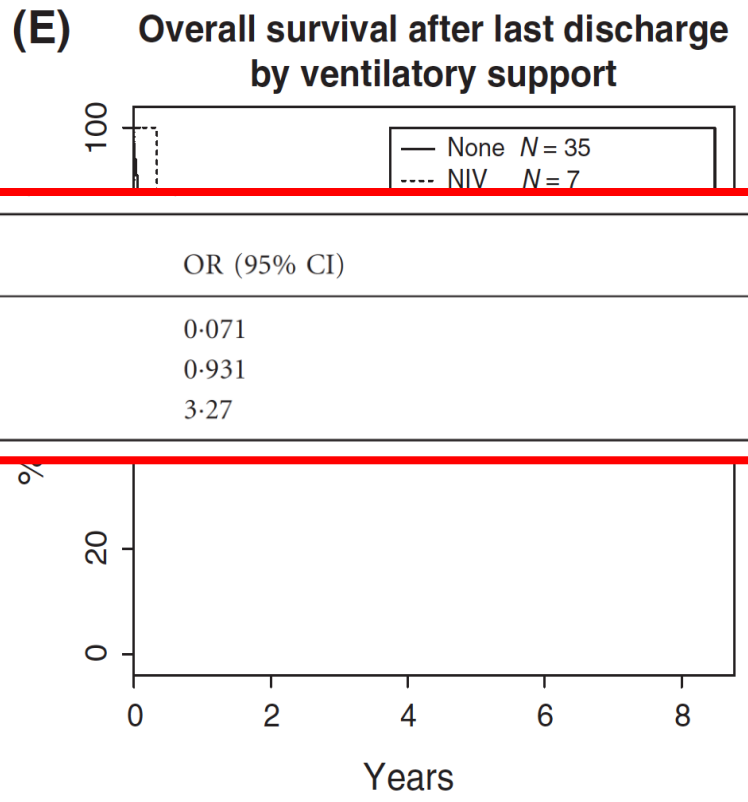
Table II. Characteristics of all Allo-HSCT related ICU admissions (n = 213).

Characteristic		N Median	% Range
Duration of ICU admission	Days	4	1–52
		N	%
Reasons for admission (not mutually exclusive)	Sepsis	142	67
	Respiratory	117	55
	Renal	27	13
	Haemodynamic	26	12
	Neurological	6	3
	Observation	4	2
	Post-operative	3	1
	Liver failure	3	1
	Other*	6	3
	Unknown	3	1
Organ support (not mutually exclusive)	Non-Invasive ventilation	74	35
	Mechanical ventilation	107	50
	Inotropes	96	45
	Renal	56	26
	No support	44	21

WM Townsend, 2013, Br J Hemat

Improved intensive care unit survival for critically ill allogeneic haematopoietic stem cell transplant recipients following reduced intensity conditioning





Effects on ICU survival (multivariate analysis)	OR (95% CI)	*P* value
MV	0·071	<0·001
Urea	0·931	0·007
Conditioning intensity	3·27	0·023

WM Townsend, 2013, Br J Hemat

ORIGINAL ARTICLE

Risk factors for ICU admission and ICU survival after allogeneic hematopoietic SCT

R Benz[1], U Schanz[2], M Maggiorini[3], JD Seebach[4] and G Stussi[5]

A considerable number of patients undergoing allogeneic hematopoietic SCT (HSCT) develop post-transplant complications requiring intensive care unit (ICU) treatment. Whereas the indications and the outcome of ICU admission are well known, the risk factors leading to ICU admission are less well understood. We performed a retrospective single-center study on 250 consecutive HSCT patients analyzing the indications, risk factors and outcome of ICU admission. Of these 250 patients, 33 (13%) were admitted to the ICU. The most common indications for admission to the ICU were pulmonary complications (11, 33%), sepsis (8, 24%), neurological disorders (6, 18%) and cardiovascular problems (2, 6%). Acute GvHD and HLA mismatch were the only significant risk factors for ICU admission in multivariate analysis. Among patients admitted to the ICU, the number of organ failures correlated negatively with survival. Twenty one (64%) patients died during the ICU stay and the 6-month mortality was 85% (27 out of 33). SAPS II score underestimated the mortality rate. In conclusion, acute GvHD and HLA mismatch were identified as risk factors for ICU admission following allogeneic HSCT. Both, short- and long-term survival of patients admitted to the ICU remains dismal and depends on the number of organ failures.

Bone Marrow Transplantation (2014) **49,** 62–65; doi:10.1038/bmt.2013.141; published online 23 September 2013

Keywords: allogeneic hematopoietic SCT; intensive care unit; GvHD; organ failure

Trends in the outcomes of Dutch haematological patients receiving intensive care support

Table 2. *Demographics, ICU characteristics and outcome of patients transferred to an ICU within 100 days post-HSCT in two-year periods (n=49)*

	2004/2005 (n=9)	2006/2007 (n=23)	2008/2009 (n=17)
Age	46.3 (±11.5)	47.6 (±10.3)	47.8 (±13.2)
APACHE II on admission	21.0 (±7.1)	20.1 (±5.6)	21.2 (±6.6)
EBMT estimated risk	4.0 (±1.0)	3.6 (±1.4)	2.8 (±1.1)
Invasive ventilation (days)	0.4 [0-11.3]	1.5 [0-15.5]	1.3 [0-6.3]
Non-invasive ventilation (days)	0.0 [0-0.02]	0.3 [0-1.0]	0.2 [0-0.8]
Vasopressor use (days)	0.2 [0.0-3.9]	0.4 [0.0-3.0]	0.0 [0.0-1.4]
ICU mortality	4 (44%)	8 (35%)	4 (24%)
Hospital mortality	7 (78%)	12 (52%)	7 (41%)
100 day post HSCT mortality	7 (78%)	13 (57%)	6 (35%)

Data are expressed as mean (± standard deviation), median [IQR] or n with (%).

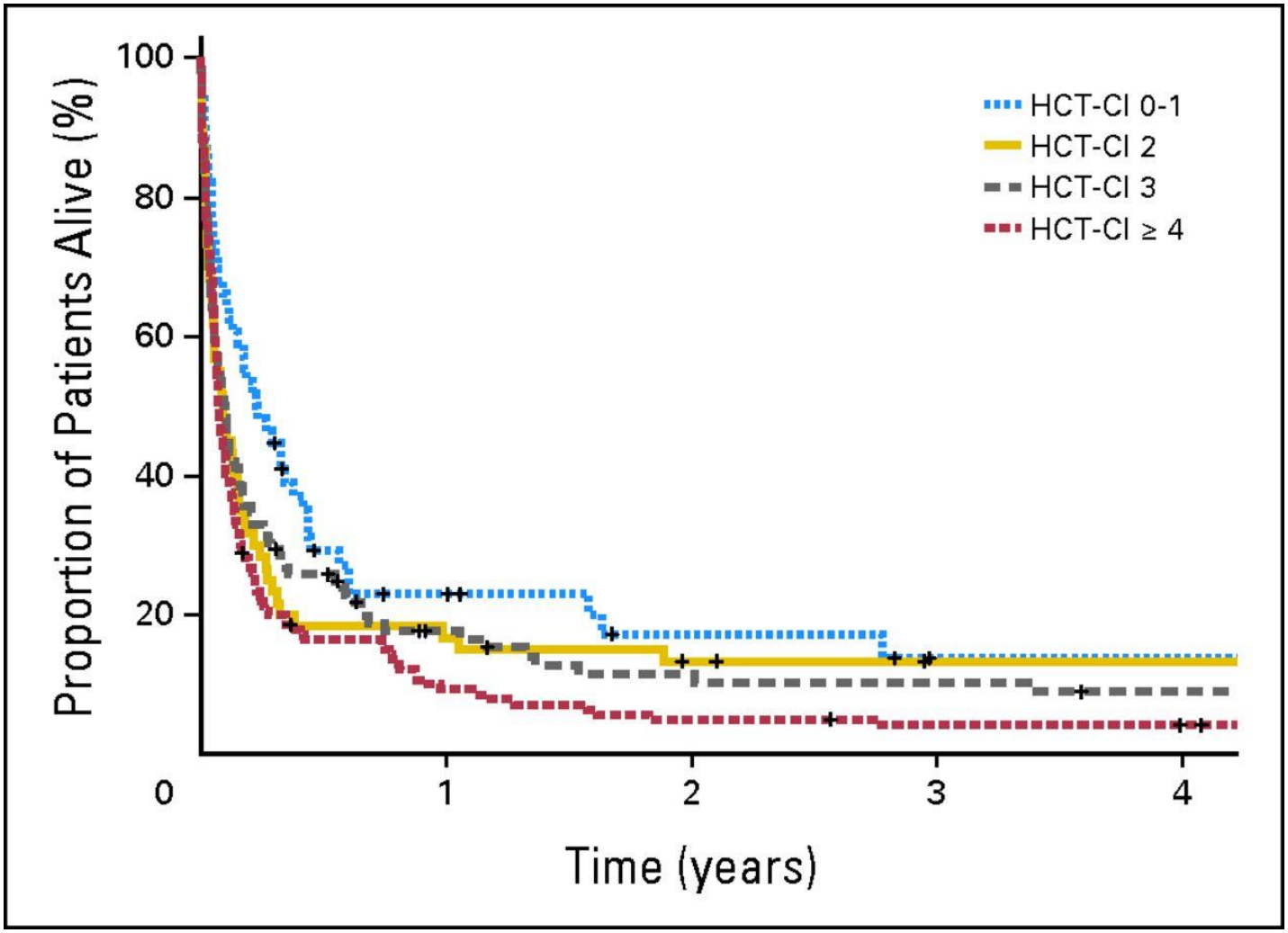
Netherlands The Journal of Medicine

M van Liet et al; 2014

Le patient allogreffé à l'USI

- Patients lourds, pathologies complexes
- Pronostic reste réservé mais…
  - Survie à long terme
  - Amélioration de la survie
- Importance de la prise en charge pluridisciplinaire
  - Intensivistes , hématologues, infectiologues
  - Discussion journalière: USI+ Hémato

Kaplan-Meier plots of overall survival in patients with Hematopoietic Cell Transplantation–Specific Comorbidity Index (HCT-CI) scores of 0 to 1, 2, 3, and ≥ 4.

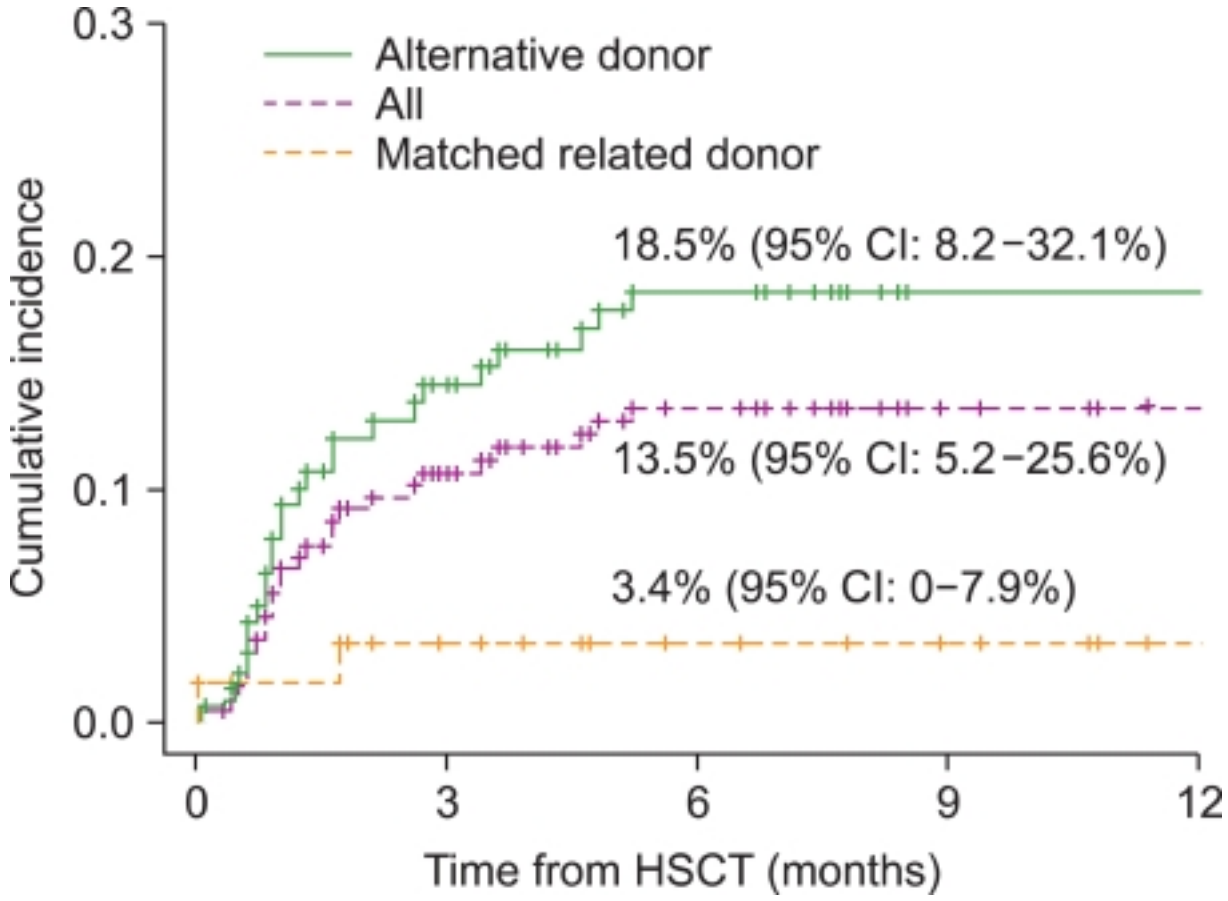


Bayraktar U D et al. JCO 2013;31:4207-4214

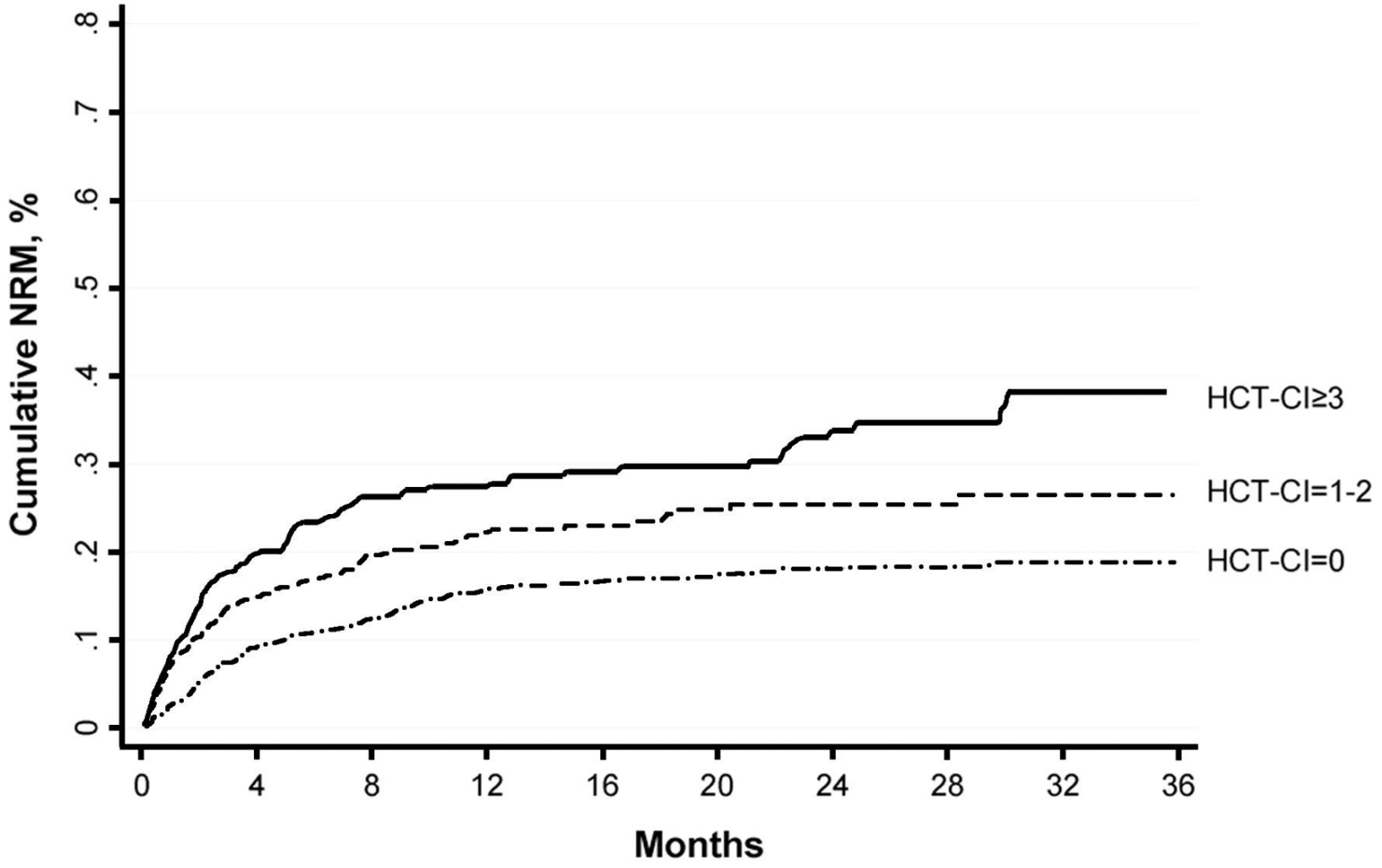
Table 1 Signs and symptoms of chronic GVHD (reproduced from Filipovich *et al.*[24])

Organ or site	*Diagnostic (sufficient to establish the diagnosis of chronic GVHD)*	*Distinctive (seen in chronic GVHD, but insufficient alone to establish a diagnosis of chronic GVHD)*	*Other features*[a]	*Common (seen with both acute and chronic GVHD)*
Skin	Poikiloderma Lichen planus-like features Sclerotic features Morphea-like features Lichen sclerous-like features	Depigmentation	Sweat impairment Ichthyosis Keratosis pilaris Hypopigmentation Hyperpigmentation	Erythema Maculopapular rash Pruritus
Nails		Dystrophy Longitudinal ridging, splitting, or brittle features Onycholysis Pterygium unguis Nail loss (usually symmetric; affects most nails)[b]		
Scalp and body hair		New onset of scarring or nonscarring scalp alopecia (after recovery from chemoradiotherapy) Scaling, papulosquamous lesions	Thinning scalp hair, typically patchy, coarse, or dull (not explained by endocrine or other causes) Premature gray hair	
Mouth	Lichen-type features Hyperkaratotic plaques Restriction of mouth opening from sclerosis	Xerostomia Mucocele Mucosal atrophy Pseudomembranes[b] Ulcers[b]		Gingivitis Mucositis Erythema Pain
Eyes		New-onset dry, gritty, or painful eyes[c] Cicatricial conjunctivitis Keratoconjunctivitis sicca[c] Confluent areas of punctuate keratopathy	Photophobia Periorbital Hyperpigmentation Blepharitis (erythema of the eyelids with edema)	
Genitalia	Lichen planus-like features Vaginal scarring or stenosis	Erosions[b] Fissures[b] Ulcers[b]		
GI tract	Esophageal web Strictures or stenosis in the upper to mid third of the esophagus[b]		Exocrine pancreatic insufficiency	Anorexia Nausea Vomiting Diarrhea Weight loss Failure to thrive (infants and children)
Liver				Total bilirubin, alkaline phosphatases $>2\times$ upper limit of normal[b] ALT or AST $>2\times$ upper limit of normal[b]
Lung	Bronchiolitis obliterans diagnosed with lung biopsy	Bronchiolitis obliterans diagnosed with PFTs and radiology[c]		BOOP
Muscles, fascia, joints	Fascilitis Joint stiffness or contractures secondary to sclerosis	Myositis or polymyositis[c]	Edema Muscle cramps Arthralgia or arthritis	
Hematopoietic and immune			Thrombocytopenia Eosinophilia Lymphopenia Hypo or hypergammaglobulinemia Autoantibodies (AIHA and ITP)	
Other			Pericardial or pleural effusions Ascites Peripheral neuropathy Nephrotic syndrome Myasthenia gravis Cardiac conduction abnormality or cardiomyopathy	

Abbreviations: AIHA, autoimmune hemolytic anemia; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BOOP, bronchiolitis obliterans-organizing pneumonia; GVHD, graft-versus-host disease; ITP, idiopathic thrombocytopenic purpura; PFTs, pulmonary function tests.
[a]Can be acknowledged as part of the chronic GVHD symptomatology if the diagnosis is confirmed.
[b]In all cases, infection, drug effects, malignancy, or other causes must be excluded.
[c]Diagnosis of chronic GVHD requires biopsy or radiology confirmation (or Schirmer test for eyes).

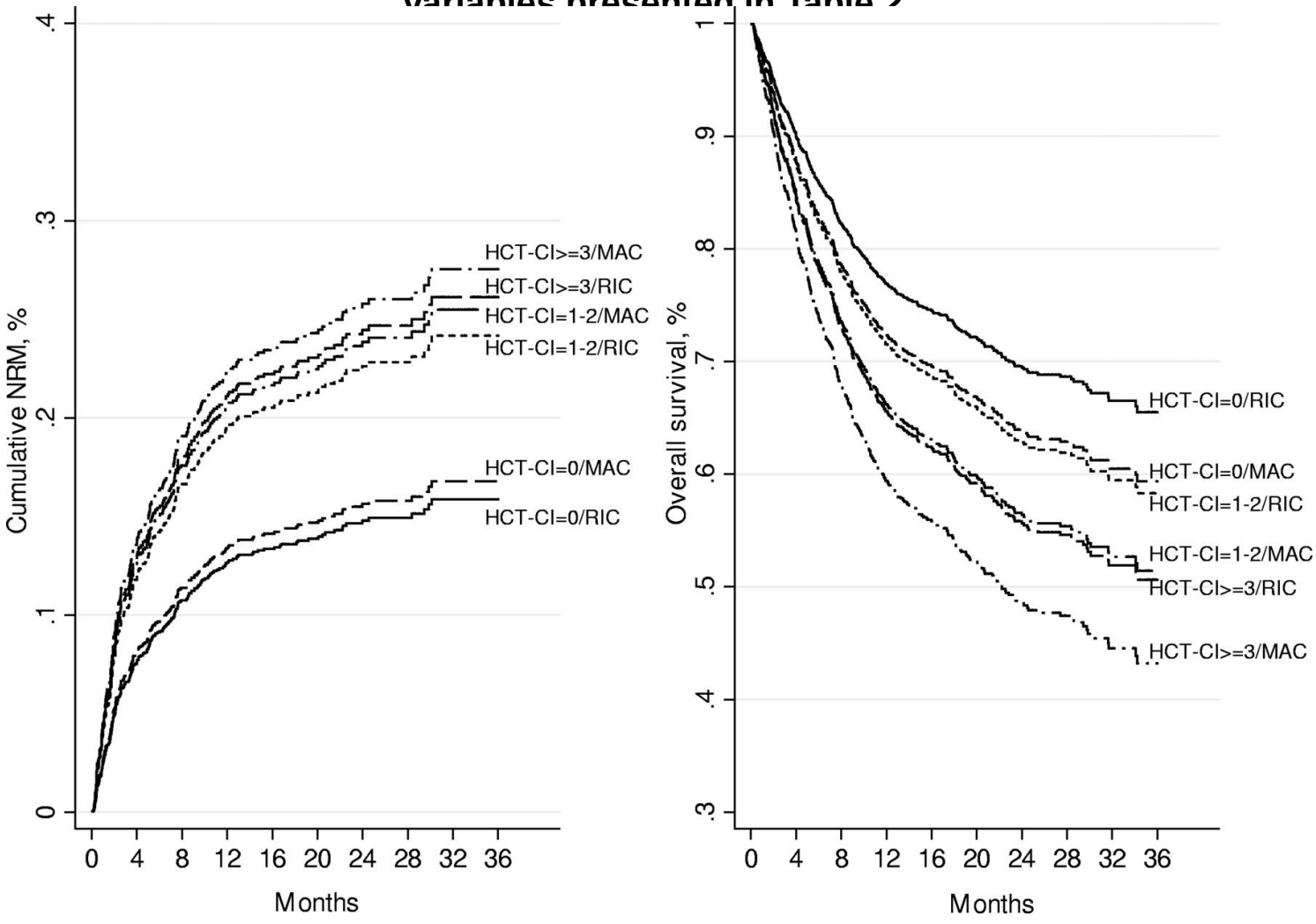

Alternative donor
All
Matched related donor
18.5% (95% CI: 8.2−32.1%)
13.5% (95% CI: 5.2−25.6%)
3.4% (95% CI: 0−7.9%)
Cumulative incidence
0.3
0.2
0.1
0.0
0
3
6
9
12
Time from HSCT (months)

NRM cumulative incidence by HCT-CI score group.



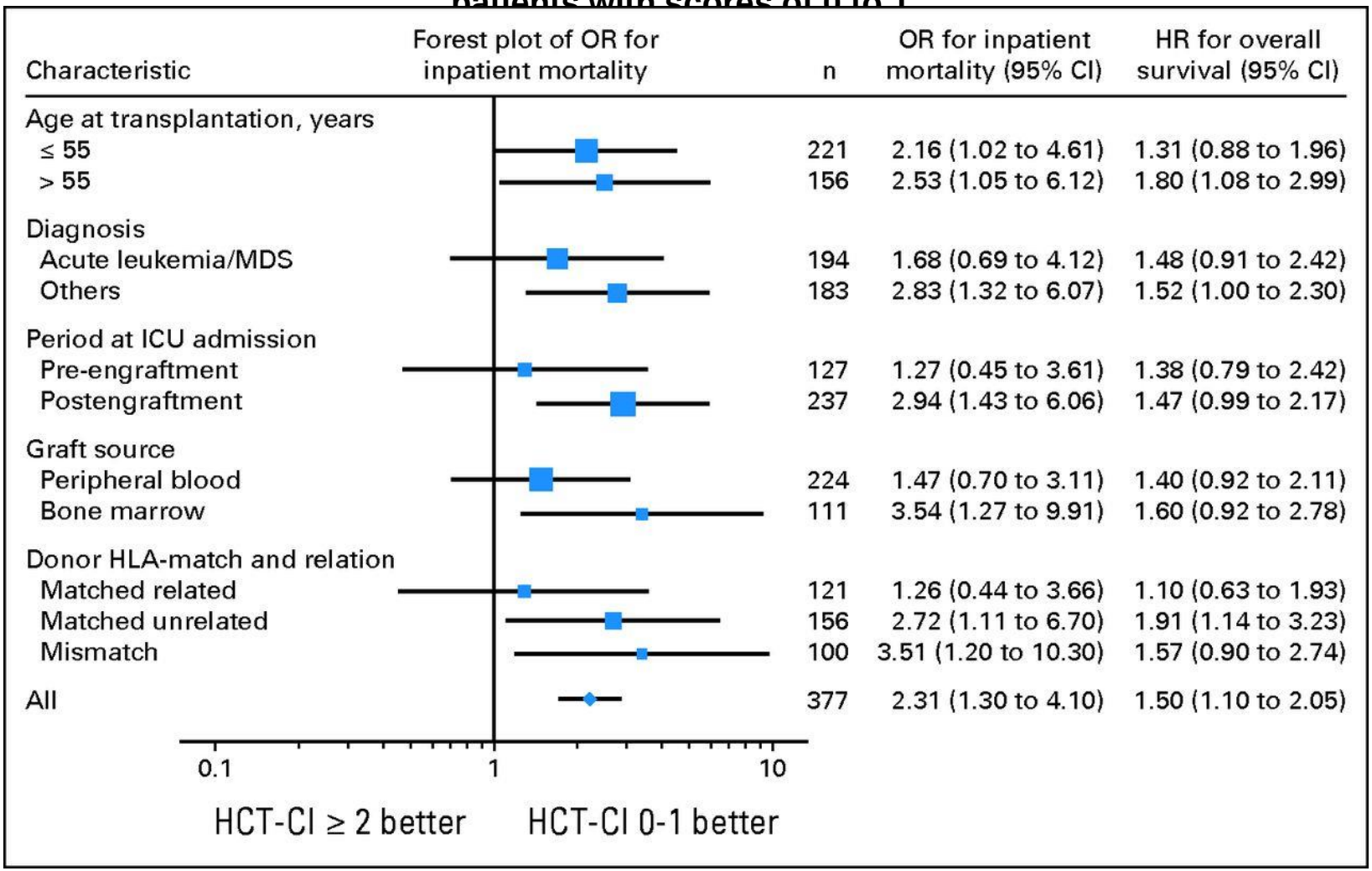
Raimondi R et al. Blood 2012;120:1327-1333

OS and NRM stratified for reduced intensity conditioning (RIC), myeloablative conditioning (MAC), and HCT-CI after Cox (OS) or competing-risk regression (NRM) adjustment for all the variables presented in Table 2



Raimondi R et al. Blood 2012;120:1327-1333

Subgroup analyses of inpatient mortality and overall survival comparing patients with Hematopoietic Cell Transplantation–Specific Comorbidity Index (HCT-CI) scores ≥ 2 versus patients with scores of 0 to 1



Bayraktar U D et al. JCO 2013;31:4207-4214

Table 3. Inpatient Mortality and 1-Year OS Rates According to Patient HCT-CI Scores With Their Respective Univariate ORs and HRs

	Patients (N = 377)		Inpatient Mortality		Univariate OR for Inpatient Mortality			Univariate HR for OS	
HCT-CI Score	No.	%	No.	%	OR	95% CI	1-Year OS	HR	95% CI
0-1	56	15	26	46	1.00		22.2	1.00	
2	60	16	40	67	2.31	1.09 to 4.89	16.7	1.37	0.92 to 2.04
3	112	30	70	63	1.92	1.004 to 3.68	17.7	1.36	0.96 to 1.94
≥ 4	149	39	104	69	2.67	1.42 to 5.01	9.3	1.68	1.20 to 2.35

Abbreviations: HCT-CI, Hematopoietic Cell Transplantation–Specific Comorbidity Index; HR, hazard ratio; OR, odds ratio; OS, overall survival.

	BO	**COP/BOOP**
Incidence	0-49% (8-10%)	2-10% (2-3%)
Début % greffe	Tardif (1an)	En général 100 premiers jours
Clinique	Insidieuse: dyspnée, toux, sibilances	Aigue: dyspnée, toux fièvre
Radiologique	Nl-hyperinflation-bronchectasies	Opacités alvéolaires multiples et en verre dépoli, périphérique, BA
EFR	Obstructive,↓VEMS, DLCO Nl	Restrictif,↓DLCO
LBA	Neutrophiles>	Lymphocytes>
Diagnostic	Clinique+ EFR	Biopsie Po
TT	Corticoïdes et IS	Corticoïdes
Pronostic	Mauvaise réponse au tt , mortalité élevée	Bonne réponse, potentiellement réversible