



DU 21 AU 23  
NOVEMBRE  
2018

18<sup>e</sup>  
CONGRÈS  
DE LA  
SFGM-TC  
Forum de Montpellier



# Réanimation "Standard" du patient d'Hématologie

**K Klouche**

**Département de Médecine Intensive Réanimation CHU Lapeyronie. Montpellier**

2018 © Congrès de la SFGM - TC - Droits réservés - Toute reproduction même partielle est interdite

# Le patient d'hématologie est un patient particulier !

**comorbidités**

**Immunodéprimé: IS, lignes de chimiothérapie, allogreffe, GVH...**

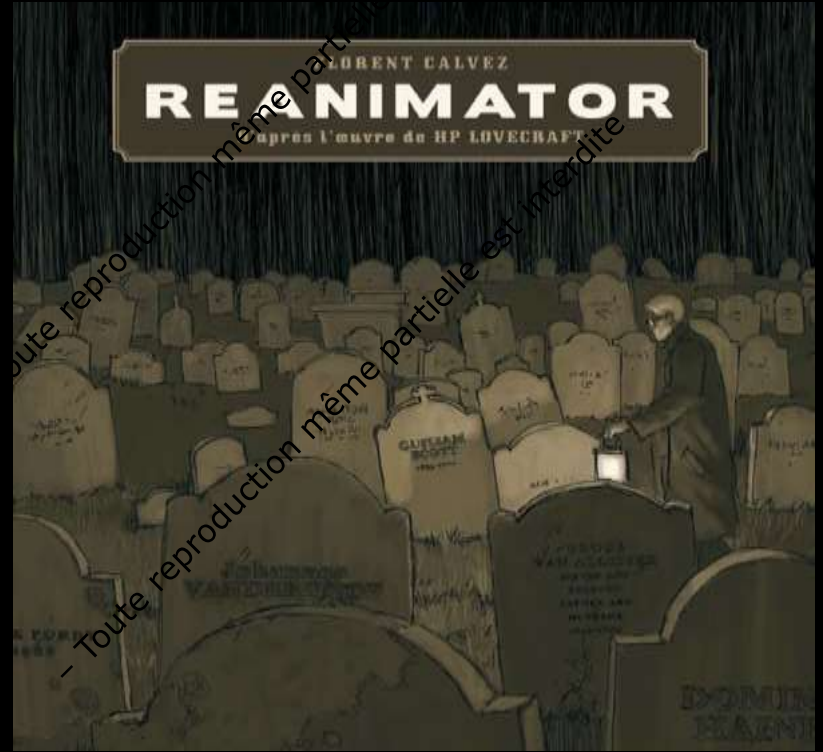
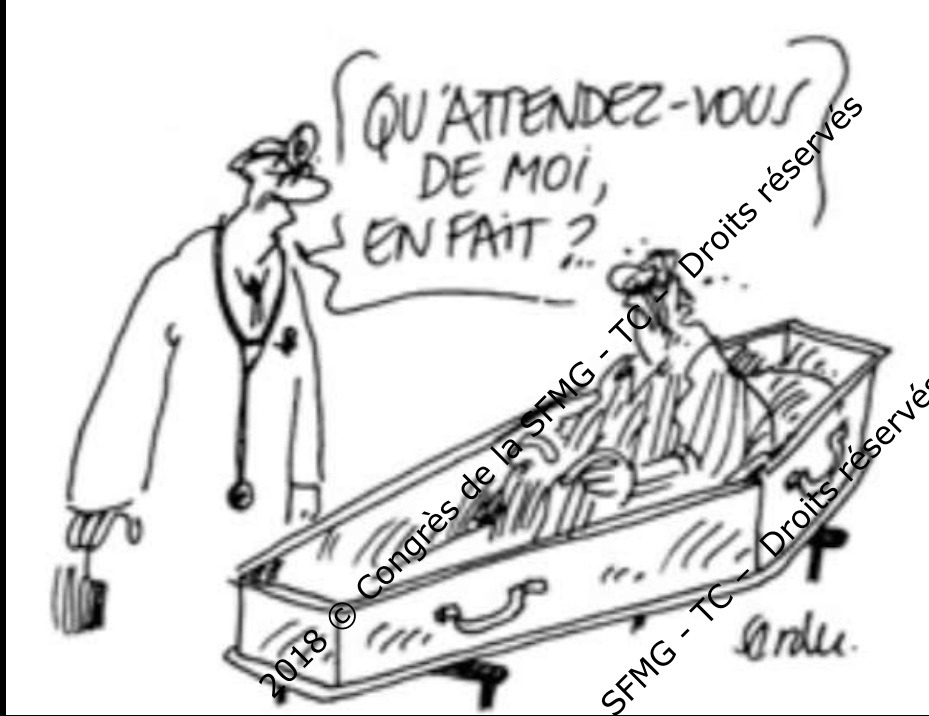
**Longue histoire de la maladie: événement intercurrent**

**Pathologies intriquées**

**Fragile: manœuvres diagnostiques et thérapeutiques invasives**

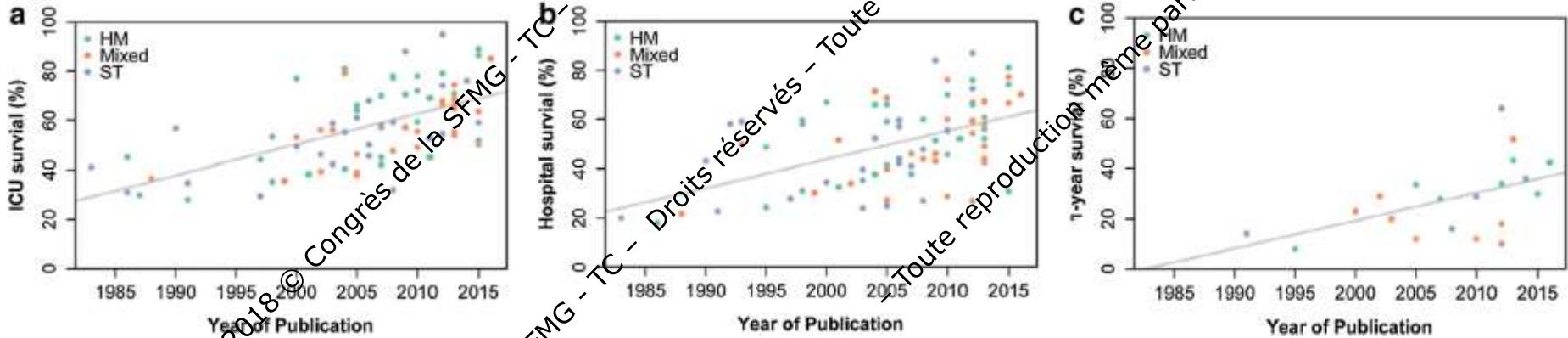
**Pronostic hématologique ?**

**Résultat incertain?**



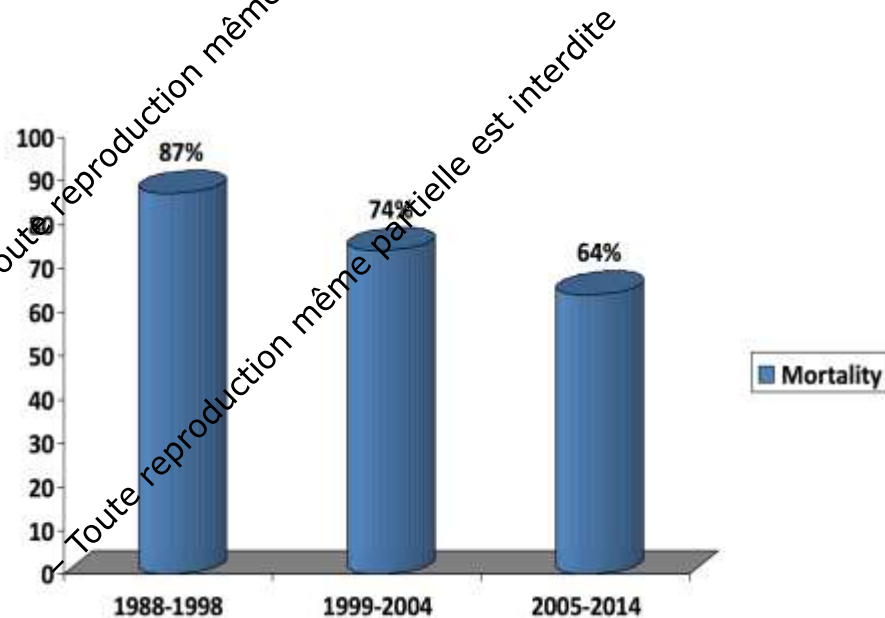
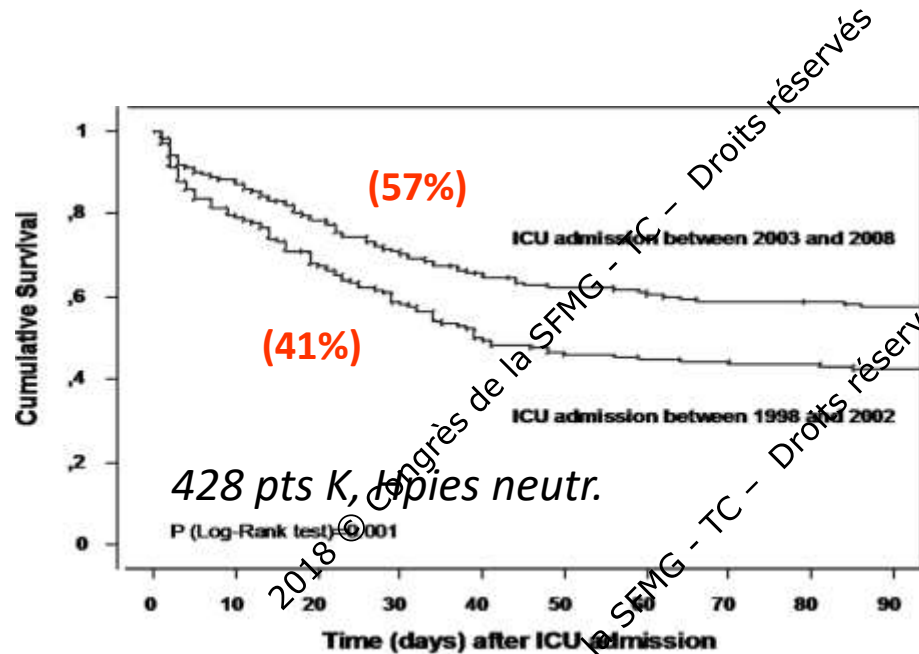
**La mauvaise réputation!**

# Improvement in survival of critically ill patients with cancer.



# HÉMOPATHIES MALIGNES/Greffe MO

## Évolution de la mortalité en Réanimation



Greffés de MO

# Greffe MO: admission en Réanimation 20%

Cohortes 90-03 et 04-11

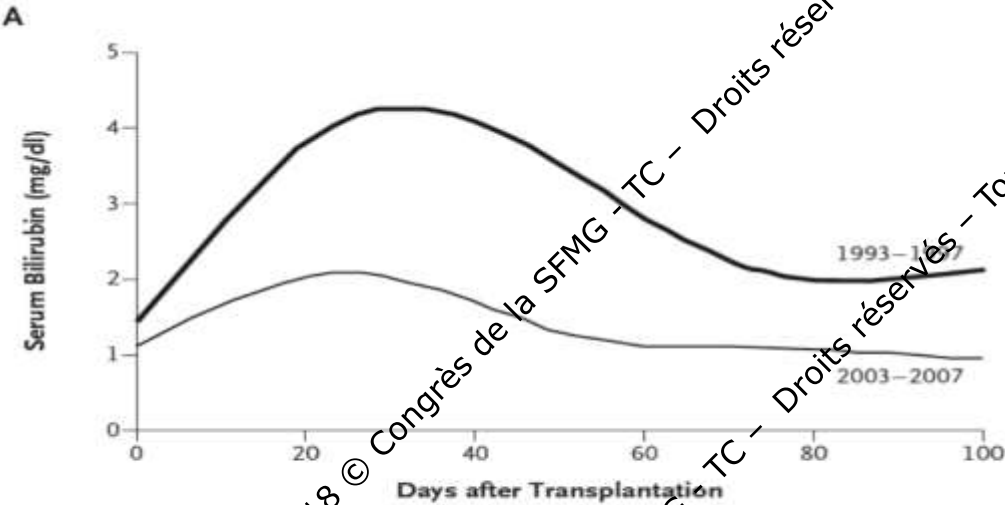
n	Recent cohort 2004-2011	Historical cohort 1997-2003	p
<b>Disease status at ICU admission</b>			
Complete remission	183 (67)	98 (44)	<0,0001
Partial remission / Progressive / chronic phase	91 (33)	107 (56)	
Time from transplant to ICU	72 [14-239]	75 [20-190]	0,68
Time from hospital admission to ICU	14 [1-26]	9,5 [0-23]	
<b>Infection at ICU admission</b>			
CMV reactivation	43 (15)	29 (14)	0,8
Invasive aspergillosis (probable/proven)	7 (10)	30 (14)	0,27
Invasive mycosis other than aspergillosis	10 (3,5)	30 (16)	<0,0001
Gram negative bacteriemia	52 (18)	25 (14)	0,26
<b>HSCT toxicities at ICU admission</b>			
Acute GVHD grade > 2	77 (27)	109 (52)	<0,0001
Steroids > 0,5 mg/kg	106 (36)	104 (50)	0,004
Veno-occlusive disease	14 (5)	12 (6)	0,69
Thrombotic microangiopathy	17 (6)	23 (11)	0,05
White blood cells < 1 G/L	176 (61)		
Creatinine (mmol/L)	106 [71-160]	134 [92-190]	

Maladie contrôlée

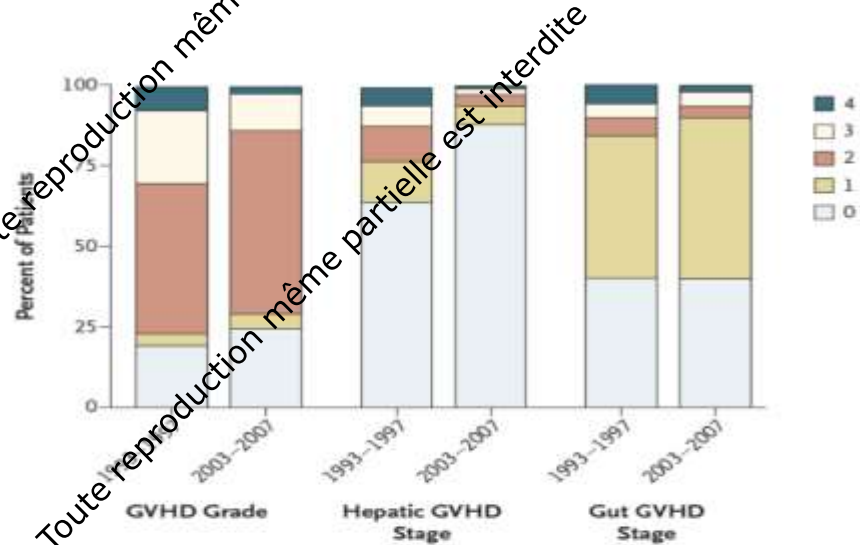
GVH contrôlée

# HÉMOPATHIES MALIGNES/Grefte MO

Amélioration du pronostic 97-2007: quelques explications...



Moins de toxicité



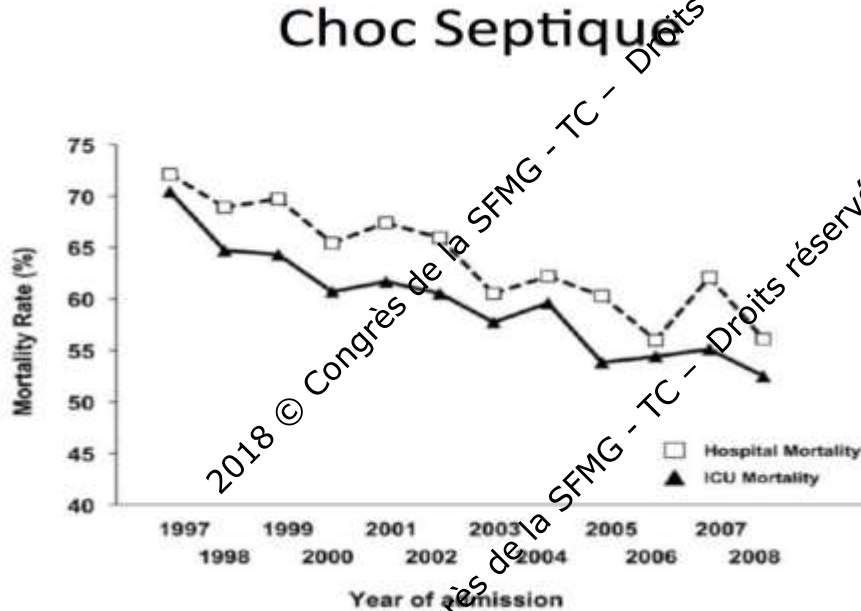
Moins de GvHD ?



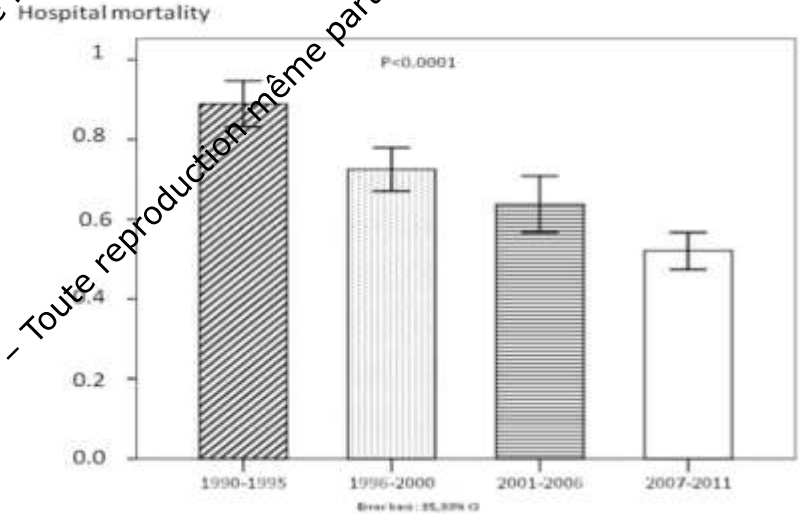
# HÉMOPATHIES MALIGNES/Grefve MO

Amélioration du pronostic 97-2011: quelques explications...

## Les Réanimateurs sont plus compétents!



Zuber et al, CCM 2012



E Azoulay et al, 2014



# Greffe MO: admission en Réanimation 20%

Cohortes 90-03 et 04-11: Le délai d'admission en Réanimation

	04-11	90-03	
<b>Organ dysfunction at ICU admission</b>			
Acute Respiratory failure	180 (62)	134 (64)	0,78
Shock	98 (34)	46 (22)	0,004
Acute kidney injury	123 (45)	56 (27)	0,0003
Coma	58 (21)	18 (9)	0,0004
Liver dysfunction	43 (14)	8 (4)	<0,0001
Monitoring	80 (10)	4 (2)	0,001

<b>ICU severity score at admission</b>			
LOD	5 [3-8]	6 [4-9]	0,005
SAPS-II	42 [33-56]	41 [30-56]	0,49
SOFA	7 [4,25-9]	8 [5-11]	0,012

<b>Life sustaining therapies during ICU</b>			
Non-invasive ventilation	82 (28)	66 (31)	0,49
Number of days with NIV	0 [0-1]	0 [0-1]	0,23
NIV not followed by MV (n of NIV)	42 (51)	22 (33)	0,029
Invasive mechanical ventilation	126 (44)	122 (58)	0,001
Number of days with MV	0 [0-6]	2 [0-6]	0,017
Catecholamines	123 (43)	99 (47)	0,31
Renal replacement therapy	57 (20)	59 (29)	0,018

<b>ICU mortality</b>	86 (30)	108 (52)	
<b>Day 90 mortality</b>	148 (51)	144 (69)	
<b>Hospital mortality</b>	138 (48)	141 (67)	

ICU: Intensive care unit, CMV: Cytomegalovirus, GVHD: Graft versus host disease, LOD: Logistic Organ dysfunction, SOFA: sequential organ failure assessment, SAPS: simplified acute physiology score, NIV: Non-invasive ventilation, MV: Mechanical ventilation

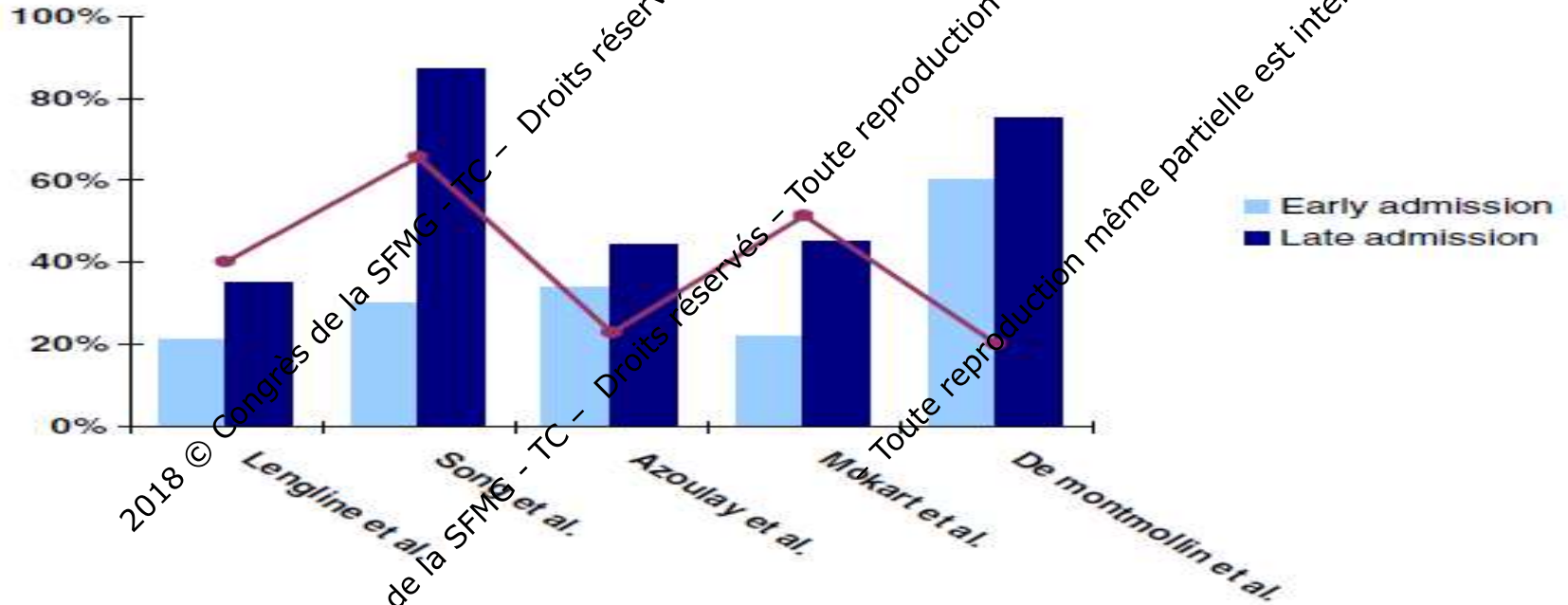
Admission plus précoce

Amélioration de la survie à défaillances similaires

2018 © Congrès de la SFMG - TC Droits réservés - Toute reproduction même partielle est interdite

# Hospital mortality in patients with delayed ICU admission

Hospital mortality (%)



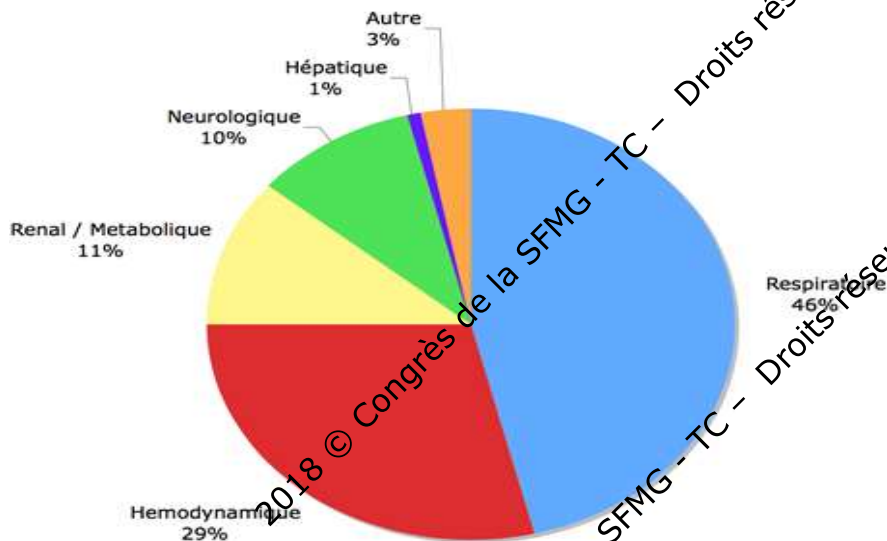
# BUTS de la REANIMATION

- Monitoring
- Diagnostic
- Assistance ventilatoire
- Assistance rénale
- Support hémodynamique et autres défaillances

# HEMOPATHIES MALIGNES, admission en Réa 20%

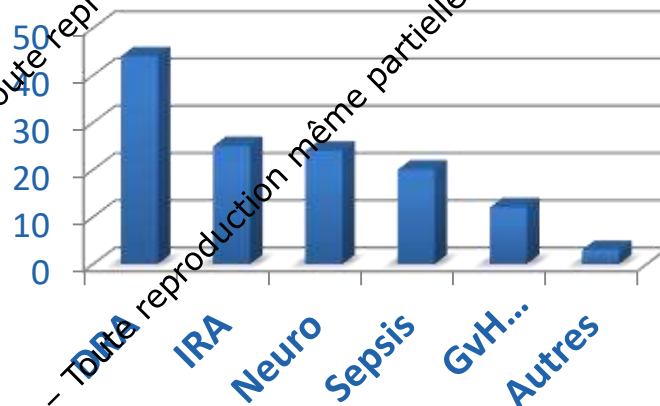
## Motifs d'admission

MOTIF D'ADMISSION EN REANIMATION



## 73 Allo admis en Réanimation

(CHU Lapeyronie, Montpellier)



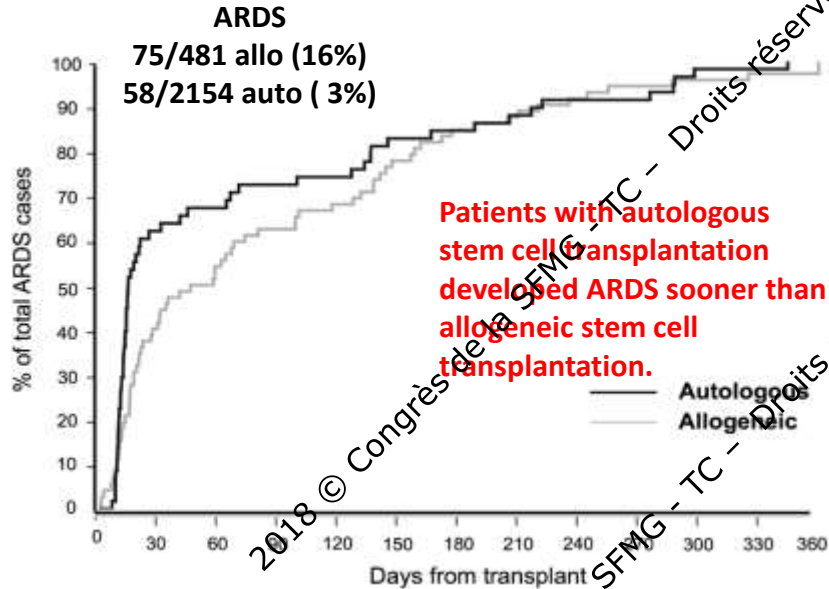
Bone Marrow Transplantation (2015), 1-6

Le problème de l'allogreffe  
=> Intrications des causes!!!

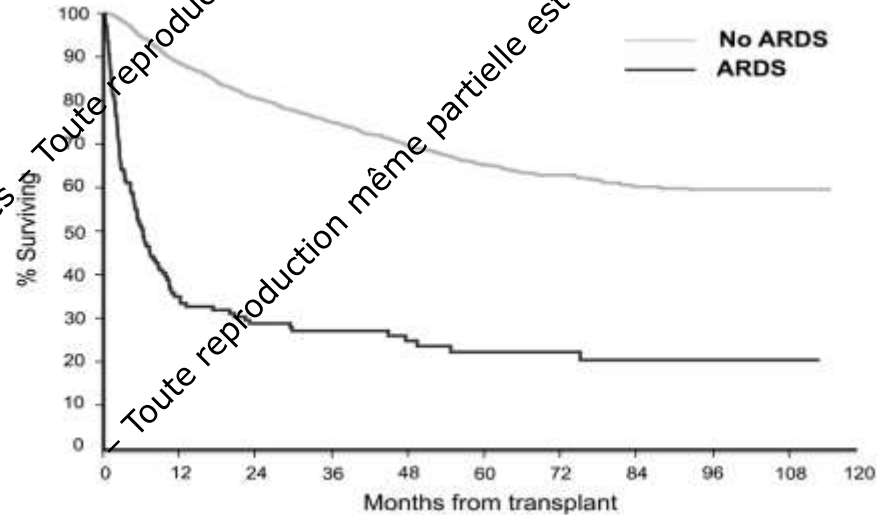


# Epidemiology of Acute Respiratory Distress Syndrome Following Hematopoietic Stem Cell Transplantation

Crit Care Med 2016; 44:1082–1090



Time to ARDS development following hematopoietic stem cell transplantation for allogeneic and autologous transplants.



Overall survival following hematopoietic stem cell transplantation in patients who ARDS vs those who did not.

# Increased mortality in hematological malignancy patients with acute respiratory failure from undetermined etiology: a Groupe de Recherche en Réanimation Respiratoire en Onco-Hématologie (Grrr-OH) study

Contejean et al. Ann. Intensive Care (2016) 6:102

Invasive mechanical ventilation (1st 24hr)  
Undetermined diagnosis  
SOFA score > 7  
Invasive pulmonary aspergillosis



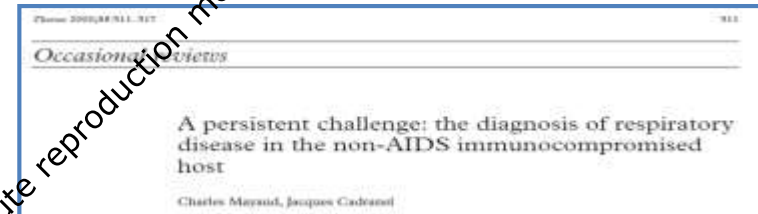
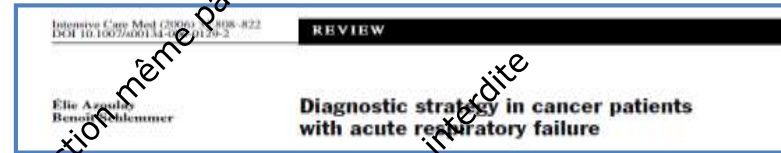
**Multivariable analysis of risk factors for hospital mortality.**

Box size is proportional to the accuracy of the estimate.

# Hémopathie maligne ou cancer

## Stratégie diagnostique d'une IRA

- L'approche **D.I.R.E.C.T** :
  - **D**élai(s) d'apparition des symptômes respiratoires
  - **I**mmunodépression
  - Aspects **R**adiologiques
  - **E**xpérience clinique et littérature
  - Tableau **C**linique
  - **T**omodensitométrie (scanner coupes fines)

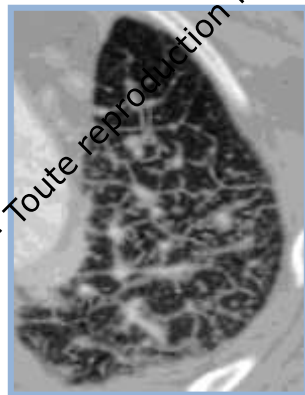




# Hémopathie maligne, IRA

## Orientation diagnostique selon la Radio ou le (CT) scanner

Lésion scannographique	Orientation diagnostique
Alvéolaire	
Localisé (lobaire ou segmentaire)	Infection bactérienne
Diffus	OAP, hémorragie intra-alvéolaire
Interstitiel et/ou verre dépoli	
Verre dépoli diffus ou patchy	OAP, pneumocystose, hémorragie intra-alvéolaire
Verre dépoli péri-nodulaire (signe du halo)	Aspergillose invasive
Verre dépoli centro-nodulaire (halo inversé)	Infections fongiques invasives (dont aspergillose)
Verre dépoli en pavé	Protéinose alvéolaire, pneumocystose
Verre dépoli centro-lobulaire	Hémorragie alvéolaire
Interstitiel diffus d'apparition rapide	Pathologie virale, OAP
Interstitiel diffus d'apparition lente	Cancer bronchique avec obstruction lymphatique, lymphome, tumeur carcinomateuse
Nodules	Métastases, lymphome, aspergillose, embols septiques
Cavitation	
Unique	Abscès bactérien, mycobactériose, tumeur excavée
Multiples	Abscès multiples, mycobactériose, métastases, aspergillome
Atélectasie	Processus tumoral endo- ou extra-bronchique



2018 © Congrès de la SFMG - TC - Droits réservés - Toute reproduction même partielle est interdite

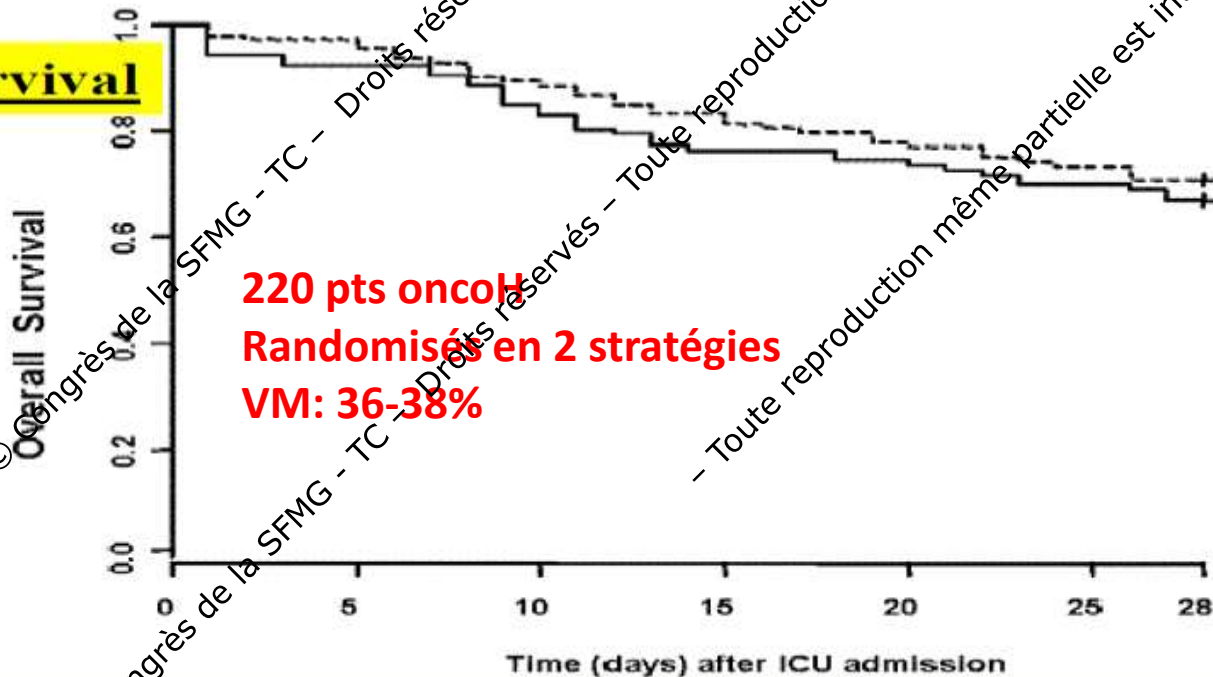
2018 © Congrès de la SFMG - TC - Droits réservés - Toute reproduction même partielle est interdite

# Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

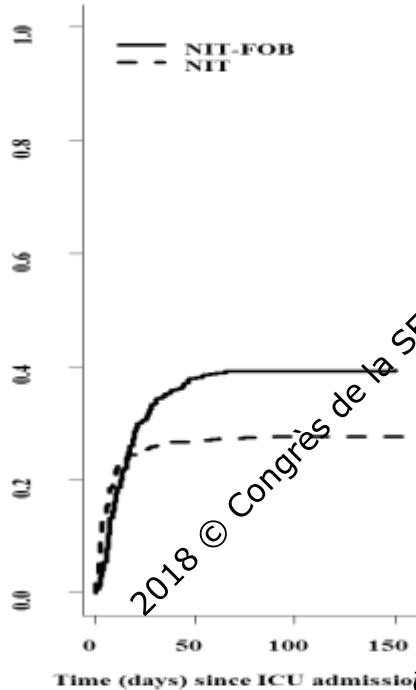
Élie Azoulay<sup>1</sup>, Djamel Mokart<sup>2</sup>, Jérôme Lambert<sup>3</sup>, Virginie Lemiale<sup>4</sup>, Angéline Rabbat<sup>5</sup>, Achille Kouatchet<sup>6</sup>, François Vincent<sup>7</sup>, Didier Gruson<sup>8</sup>, Fabrice Brunel<sup>9</sup>, Géraldine Epinette-Branche<sup>1</sup>, Ariane Labrie<sup>1</sup>, Rebecca Harbarth<sup>10</sup>, Denis Blot<sup>14</sup>, Sylvie Chevret<sup>11</sup>

**D28 Survival**

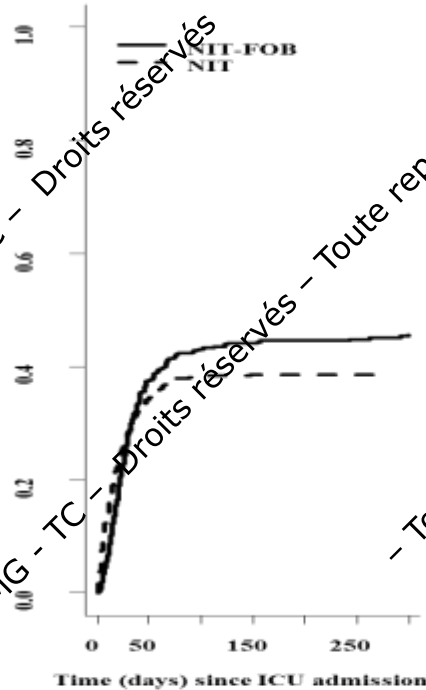


# Diagnosis and Outcome of Acute Respiratory Failure in Immunocompromised after Bronchoscopy (étude ancillaire EFRAIM)

Probability of ICU death



Probability of Hospital death



**1587 immunodépr. dont 339 hpathies**

2015-16, 62 ICU de 16 pays  
969 (61%) NIT, 618 (39%) NIT +FOB

## Fib. Bron

apport diagnostique: 27%

apport thérapeutique: 38%

Mortalité Réa: 40,1 vs 27,6%,  $p < 0,0001$

Mortalité Hôp: 49 vs 41%,  $p = 0,003$

**Risque de mortalité (Score de propension)**

**odd ratio 1,41 (1,08-1,81)**

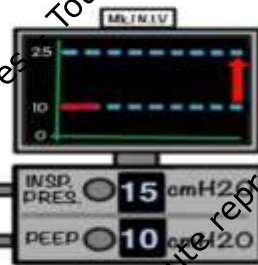
# Hémopathie maligne

## Prise en charge d'une IRA

### Les options...



VS



VS



High-Flow-Nasal-Cannula  
Optiflow™



2018 © Congrès de la SFMG - TC - Droits réservés

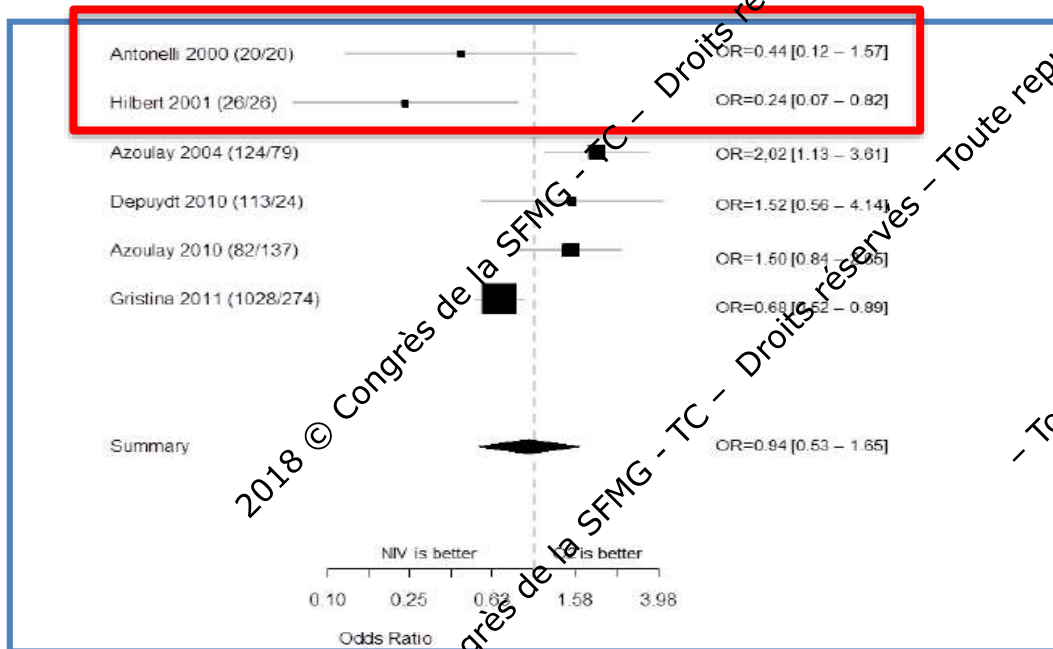
Toute reproduction même partielle est interdite

- Toute reproduction même partielle est interdite

# HÉMOPATHIES MALIGNES

## La ventilation non invasive

Non-invasive mechanical ventilation in hematology patients with hypoxemic acute respiratory failure: a false belief?



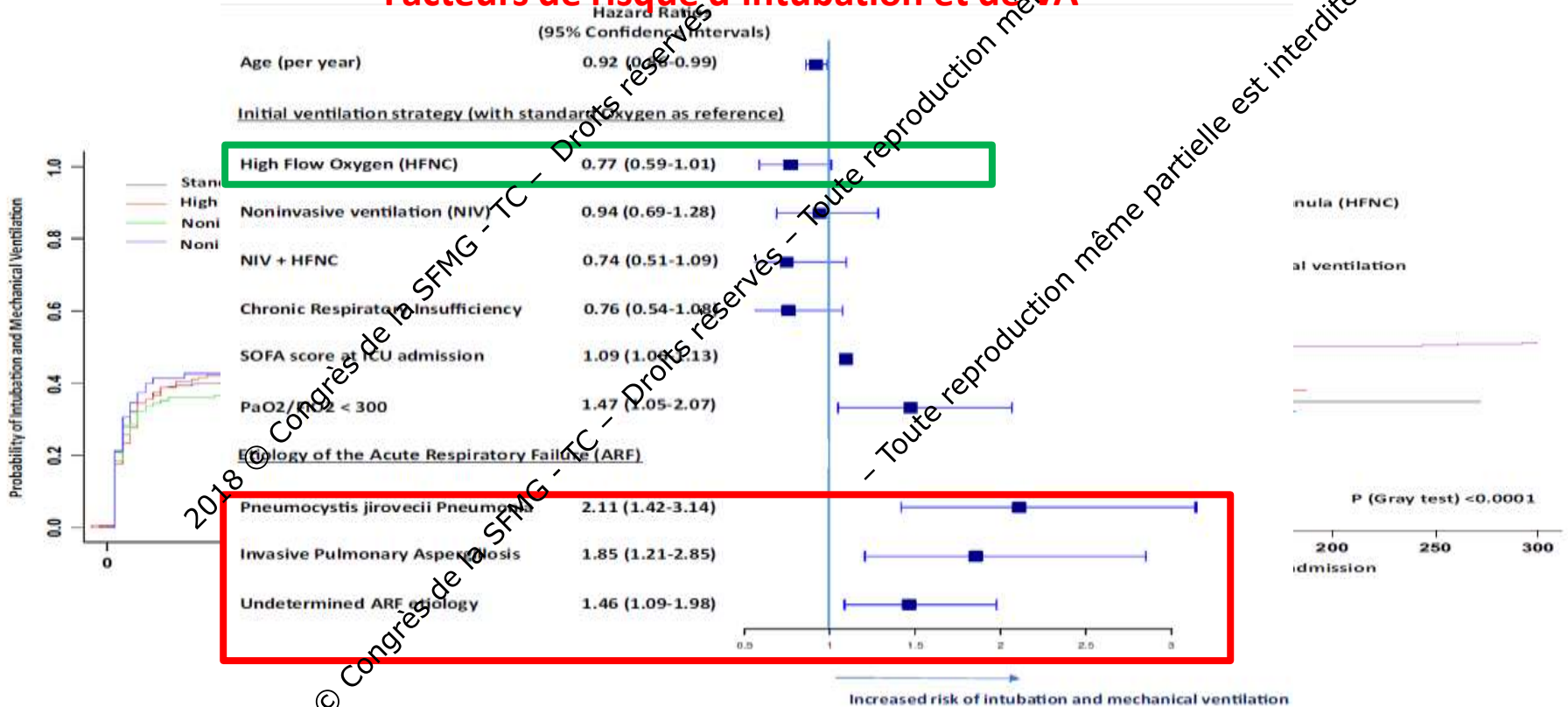
### Predictors of failure of NIV in hypoxemic patients

- Higher illness severity at baseline reflected by SAPSII
- Higher RR under NIV
- Later initiation of NIV after ICU admission
- Need vasopressors
- Need RRT
- Presence de ALI/ARDS

# Acute hypoxemic respiratory failure in immunocompromised patients: the Efrain multinational prospective cohort study

Intensive Care Med (2017) 43:1808–1819

## Facteurs de risque d'intubation et de VA

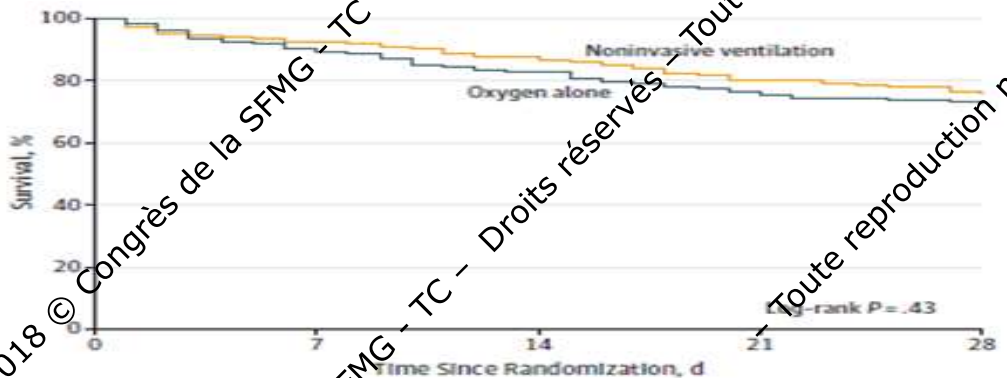




# Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure

## A Randomized Clinical Trial

Virginie Lemiale, MD; Djamel Mokart, MD; Matthieu Resche-Rigon, MD, PhD; Frédéric Pène, MD, PhD; Julien Mayaux, MD; Etienne Fauchet, MD; Martine Nyunga, MD; Christophe Girault, MD, PhD; Pierre Perez, MD; Christophe Guitton, MD, PhD; Kenneth Ekpe, MD; Achille Kouate Met, MD; Igor Théodose, MS; Dominique Benoit, MD, PhD; Emmanuel Cance, MD; François Barbier, MD, PhD; Antoine Rabbat, MD; Fabrice Bruelle, MD; François Vincent, MD; Kada Klouche, MD, PhD; Kontar Loay, MD; Eric Mariotte, MD; Lila Bouadma, MD, PhD; Anne-Sophie Moreau, MD; Amélie Seguin, MD; Anne-Pascale Meert, MD, PhD; Jean Reigner, MD, PhD; Laurent Papazian, MD, PhD; Ilham Mehzari, MD; Yvel Cohen, MD, PhD; Maleka Schenck, MD; Rebecca Hamidfar, MD; Michael Darmon, MD, PhD; Alexandre Demoule, MD, PhD; Sylvie Chevret, MD, PhD; Elie Azoulay, MD, PhD; for the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (ARRR-OH)



No. at risk	0	7	14	21	28
Noninvasive ventilation	191	175	167	153	146
Oxygen alone	183	165	152	140	134

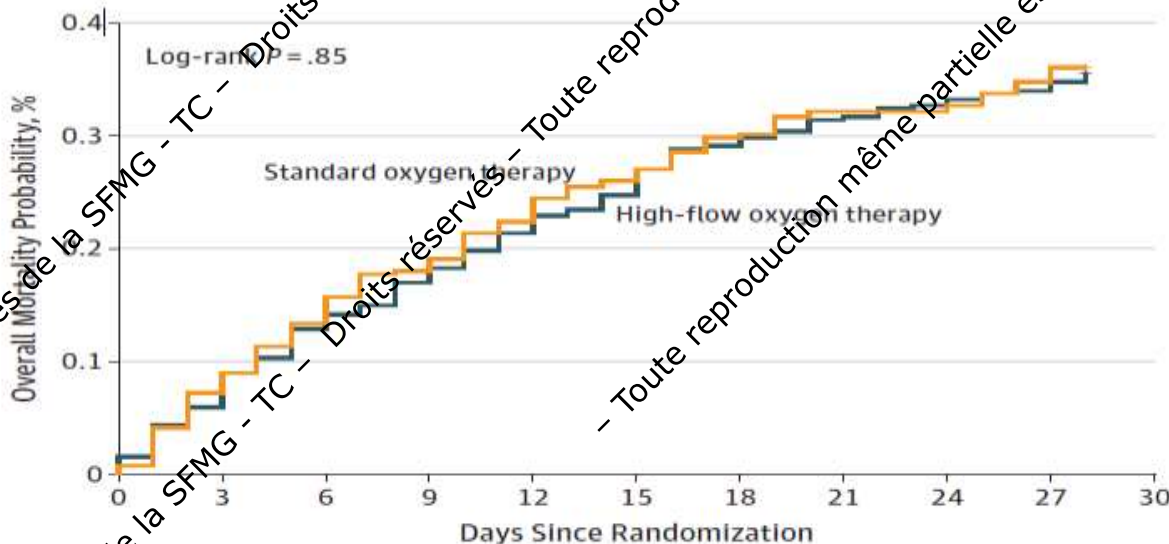
**374 pts**  
immunocompromised patients with acute respiratory failure receiving either early noninvasive ventilation or oxygen only.



# Effect of High-Flow Nasal Oxygen vs Standard Oxygen on 28-Day Mortality in Immunocompromised Patients With Acute Respiratory Failure

## The HIGH Randomized Clinical Trial

Elie Azoulay, MD, PhD; Virginie Lemiale, MD; Djamel Mokart, MD, PhD; Saad Nseir, MD, PhD; Laurent Argaud, MD, PhD; Frédéric Pène, MD, PhD; Loay Kontar, MD; Fabrice Bruneel, MD; Kada Klouche, MD, PhD; François Barbier, MD, PhD; Jean Reignier, MD, PhD; Lilla Berrahil-Mahen, MD; Guillaume Louis, MD; Jean-Michel Constantin, MD, PhD; Julien Mayaux, MD; Florent Walter, MD; Achille Kouatchet, MD; Vincent Pottier, MD; Igor Théodose, M5; Pierre Perez, MD; Christophe Girault, MD; Samir Jaber, MD, PhD; Jolanta Oziel, MD; Martine Nyunga, MD; Nicolas Terzi, MD, PhD; Lila Bouadma, MD, PhD; Christine Lebert, MD; Alexandre Lautrette, MD, PhD; Naïke B. M. MD, PhD; Jean-Herlé Raphalen, MD; Laurent Papazian, MD, PhD; Michael Darmon, MD, PhD; Sylvie Chevret, MD, PhD; Alexandre Demoule, MD, PhD



No. at risk

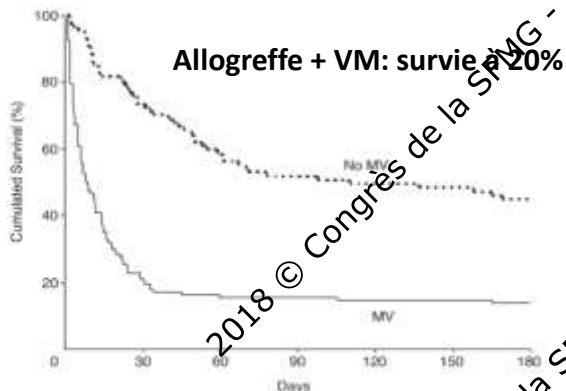
High-flow oxygen therapy	388	365	338	322	305	292	275	266	261	256	0
Standard oxygen therapy	388	360	336	318	301	287	272	263	263	253	0

# HÉMOPATHIES MALIGNES et Greffe MO

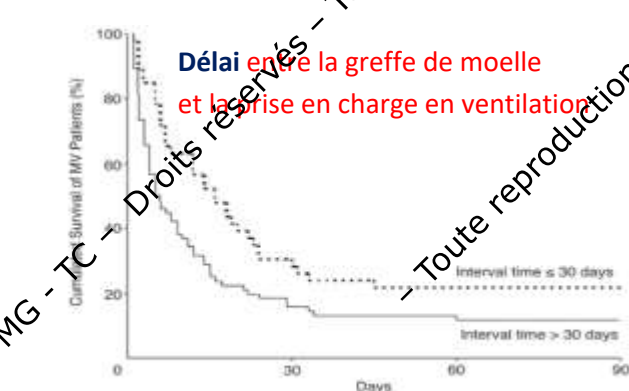
Ventilation Mécanique: délai de VM

## La ventilation Mécanique:

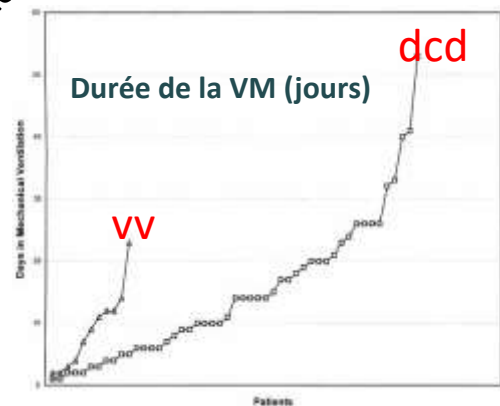
**2 facteurs déterminants:** délai entre la greffe de moelle et la prise en charge en ventilation  
durée de la ventilation



No. at risk:	0	30	60	90	120	150	180
No MV	87	64	51	45	44	43	38
MV	122	25	19	19	18	17	17



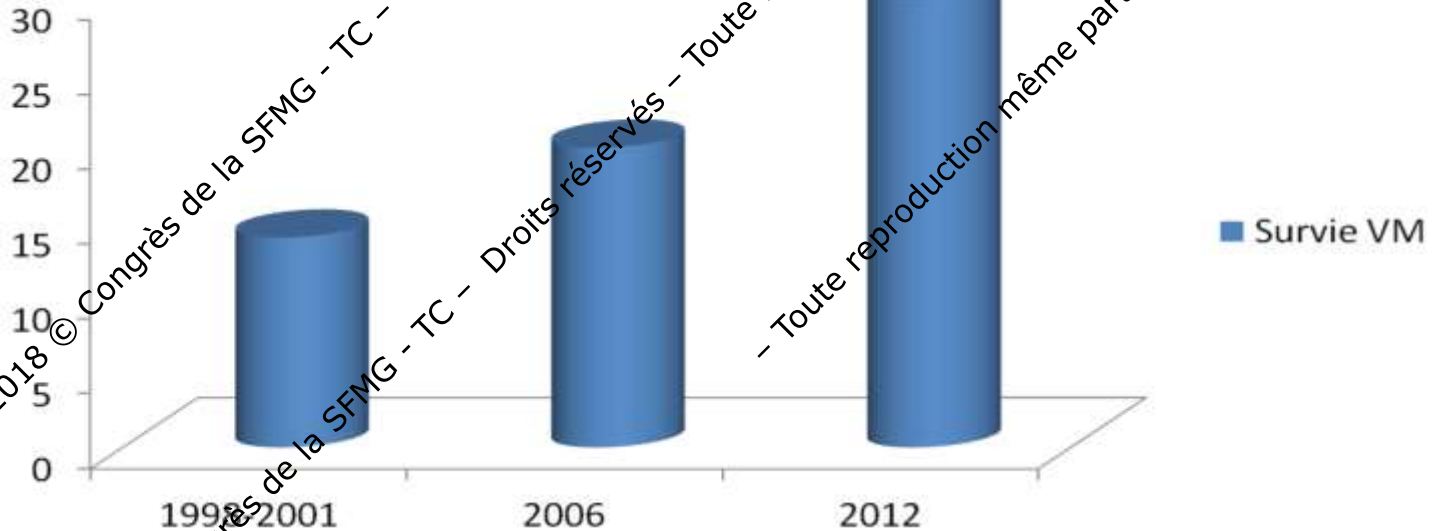
No. at risk:	0	30	60	90
≤ 30 days	46	13	10	10
> 30 days	76	12	10	9



# HÉMOPATHIES MALIGNES et Greffe MO

Evolution de la survie des patients ventilés 1998-2012

Cependant, la ventilation Mécanique ne doit pas être un frein!



# Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome

P Wohlfarth et al. Crit Care Med 2017; 45:e500–e507

Variable	All Patients (n = 37)	Nonsurvivors (n = 30)	Survivors (n = 7)	P
Underlying condition				0.00947
Acute leukemia	22 (59)	21 (70)	1 (14)	
Lymphoma	5 (14)	4 (17)	0	
Myelodysplastic syndrome	3 (8)	0	3 (43)	
Other malignant condition	4 (11)	2 (7)	2 (29)	
Nonmalignant disease	3 (8)	2 (7)	1 (14)	
Conditioning therapy*				0.27
Myeloablative	27 (79)	24 (83)	3 (60)	
Nonmyeloablative	7 (21)	5 (17)	2 (40)	
Stem cell source				1.0
Peripheral blood	27 (79)	21 (70)	6 (86)	
Bone marrow	4 (19)	6 (20)	1 (14)	
Cord blood	3 (8)	3 (10)	0	
Donor type				
Unrelated donor	23 (62)	19 (63)	4 (57)	
Related donor	14 (38)	11 (37)	3 (43)	
Remission status at ICU admission				1.0
Complete remission	27 (79)	22 (79)	5 (83)	
No remission, after engraftment	2 (6)	2 (7)	0	
No remission, prior engraftment	5 (15)	4 (14)	1 (17)	
GvHD at ICU admission				
Acute GvHD	5 (14)	5 (17)	0	0.56
Chronic GvHD	8 (22)	6 (20)	2 (29)	0.63
Immunosuppressive therapy during ICU				0.006823
Any immunosuppressive therapy	31 (84)	28 (93)	3 (43)	
Corticosteroids	22 (59)	20 (67)	2 (29)	
Calcineurin inhibitor	22 (59)	20 (67)	2 (29)	
Mycophenolate mofetil	8 (22)	8 (27)	0	
Others	5 (14)	5 (17)	0	

**37 Allo ARDS ECMO VV**

(12 ICUs Europe),

146 (27-321) jours post-Allo

**survie: 19%**

**100 (dcd) vs 485 (vv) j post-Allo, p=0,01**

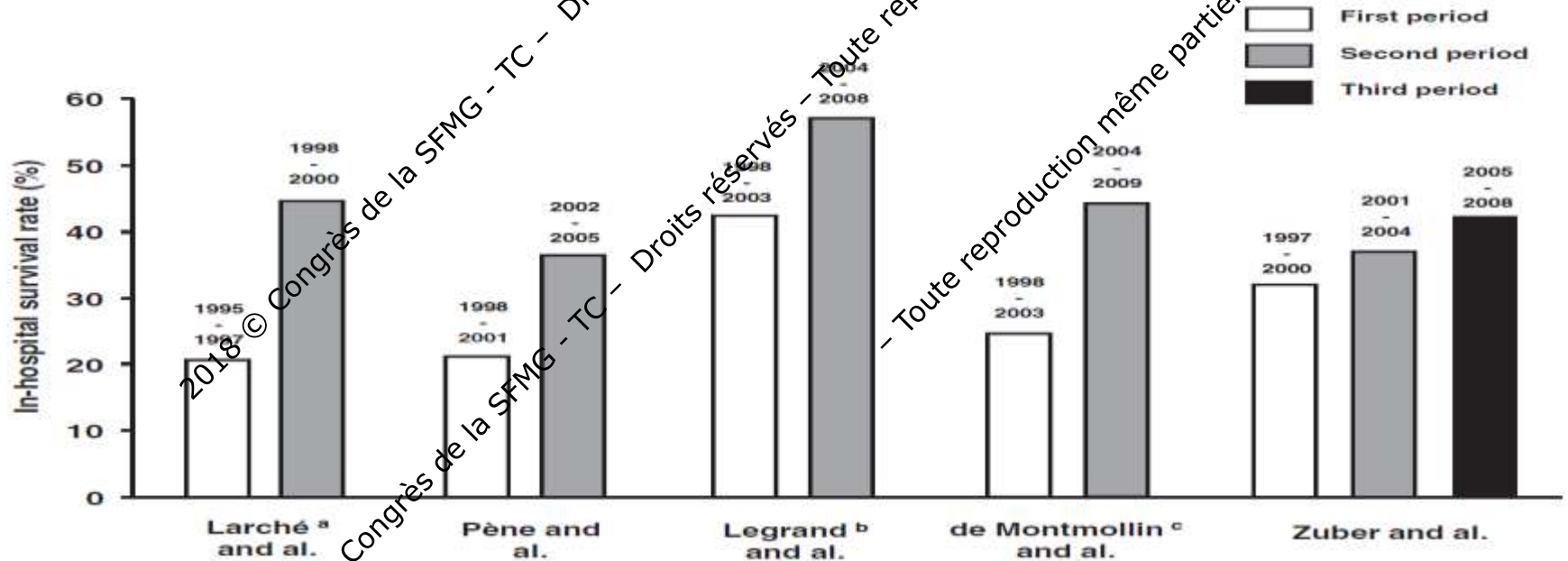
*ECMO should be discouraged for ARDS during the peri- or early posttransplant period. we recommend*

- 1) select patients with no additional organ dysfunctions and of refractory acute GvHD,
- 2) to early inform patients and families about the limited prognosis,
- 3) to discuss and respect their preferences with regards to end-of-life issues as a cornerstone of the decision process.

# Hémopathies malignes, Infection

## Temporal trends in survival of septic shock in patients with cancer

Azoulay E et al. Blood Reviews 29 (2015) 359–367

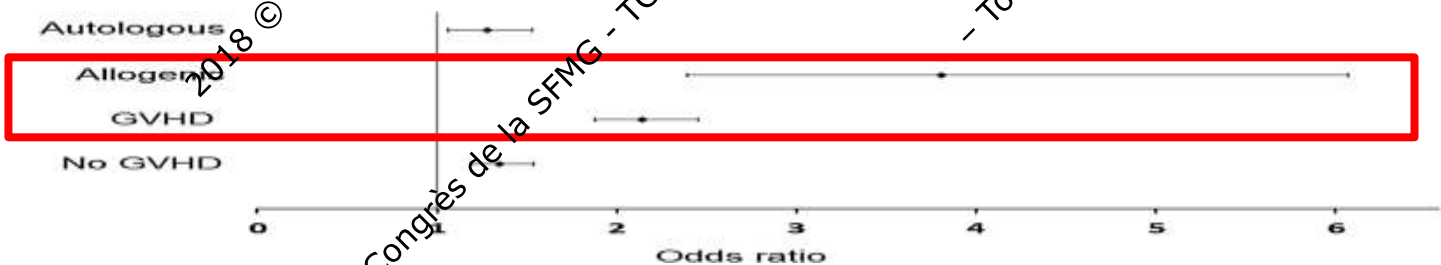
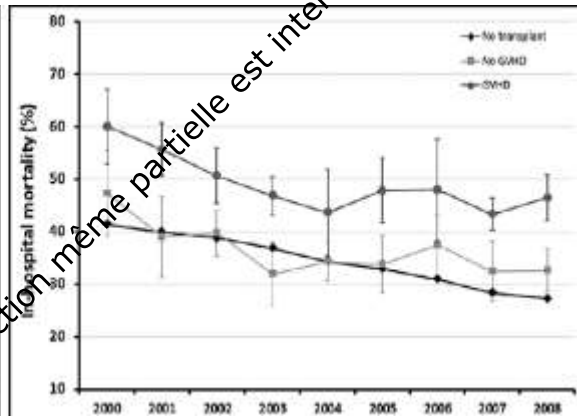
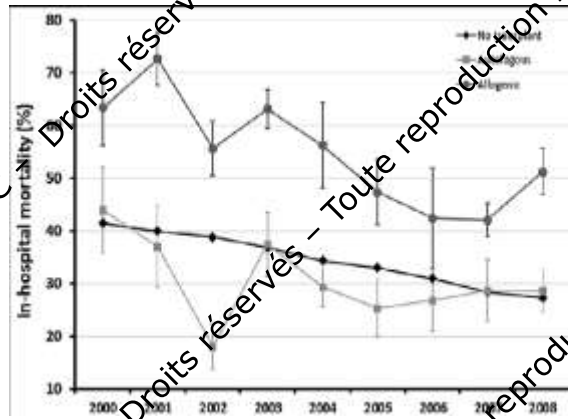
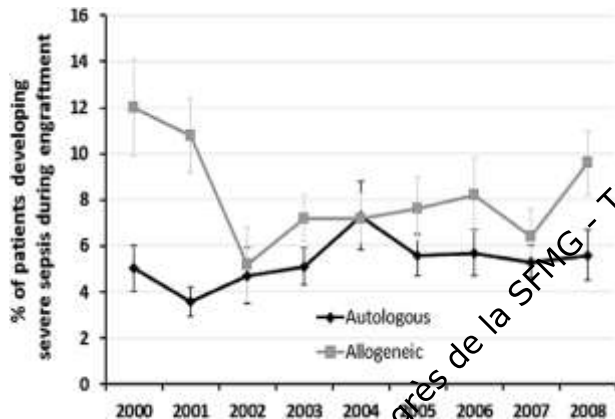


# Severe Sepsis in Hematopoietic Stem Cell Transplant Recipients

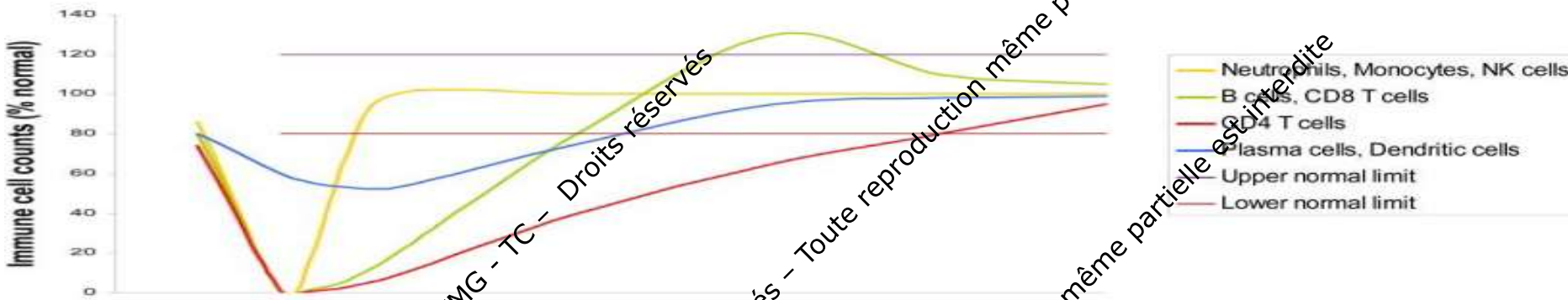
G Kumar et al. Crit Care Med 2015; 43:411-421

**21,898 Greffe MO sepsis sévère (7,5%)**

mortalité: Auto: 30%, Allo: 55%, GVH: 48%



odds ratio of mortality in severe sepsis-HSCT admissions compared with non-HSCT.



**BACTERIAL**

- Gram positive organisms
- Gram negative bacilli
- Gastro-intestinal Streptococci species
- Encapsulated bacteria

**VIRAL**

- Respiratory and enteric virus, BK virus
- HSV
- CMV
- VZV
- EBV PTLD

**FUNGAL**

- Candida species
- Aspergillus species
- Pneumocystis Jirovecii

2018 © Congrès de la SFMG - TC - Droits réservés - Toute reproduction même partielle est interdite



# Neutropenic cancer patients with severe sepsis: need for antibiotics in the first hour

Djamel Mokart  
 Colombe Saillard  
 Antoine Sannini  
 Laurent Chow-Chine  
 Jean-Paul Brun  
 Marion Faucher  
 Jean-Louis Blache  
 Didier Blaise  
 Marc Leone

ICU mortality	Odds ratio	95 % confidence interval	<i>p</i>
Efficacy of the first antimicrobial treatment in the ICU			
Appropriate	1	Reference	
Inappropriate	6.4	1.6–26	0.01
Empirical	0.7	0.2–2.5	0.63
SOFA score at admission (per point)	1.4	1.2–1.6	<0.001
Non-fermentative Gram-negative bacilli	4.8	1.3–18	0.02
Interval between the first signs of sepsis in ICU and antimicrobial initiation >1 h	10	2.5–33	0.002

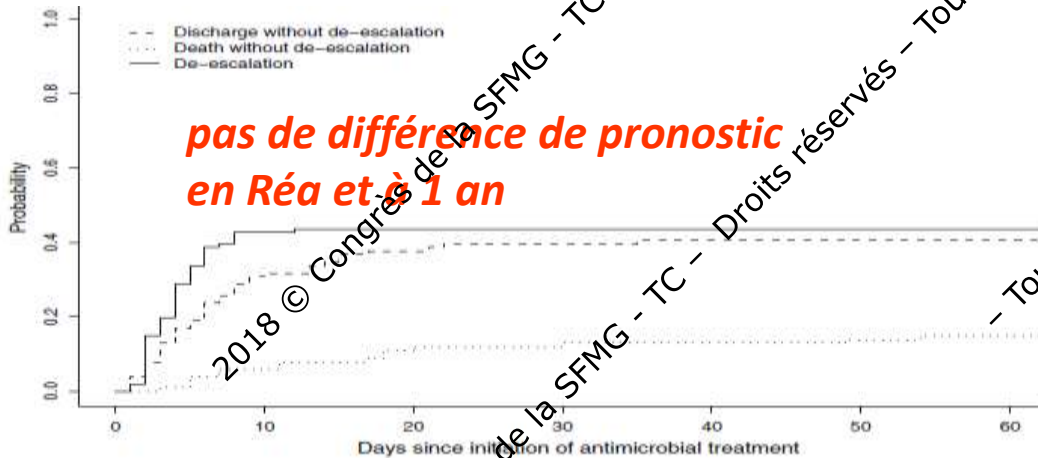
# De-escalation of antimicrobial treatment in neutropenic patients with severe sepsis: results from an observational study

Mokart D et al; *Intensive Care Med* (2014) 40:41–49

Etude prospective observationnelle

101 pts neutropéniques avec sepsis sévère dont 44: désescalade AB (arrêt d'1 AB ou Blact avec un spectre étroit)

Documentation microbio: 63 pts



**pas de différence de pronostic en Réa et à 1 an**

## Facteurs associés désescalade

AB empirique adéquat: OR: 10.8

Choix empirique antipyo: OR:10.8

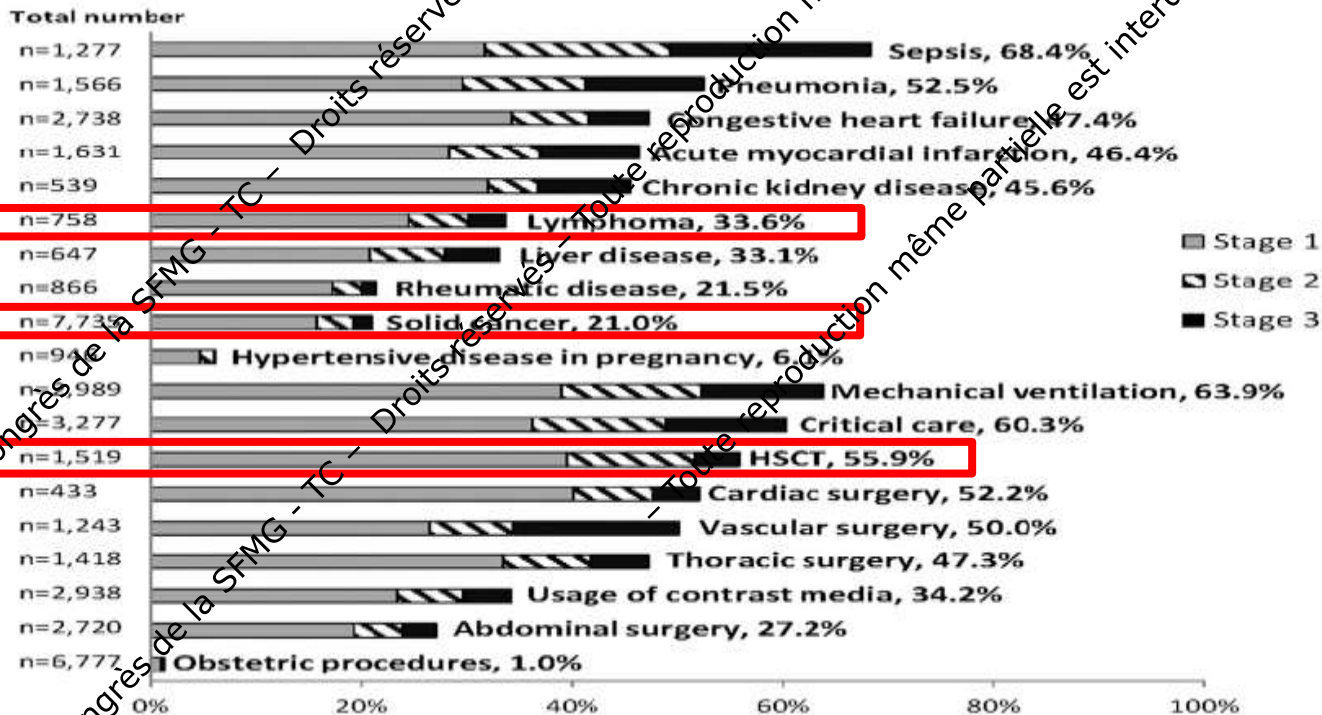
Cumulative incidence of de-escalation, death in ICU without de-escalation, and discharge alive without de-escalation

# Incidence of AKI according to the KDIGO definition across clinical settings.

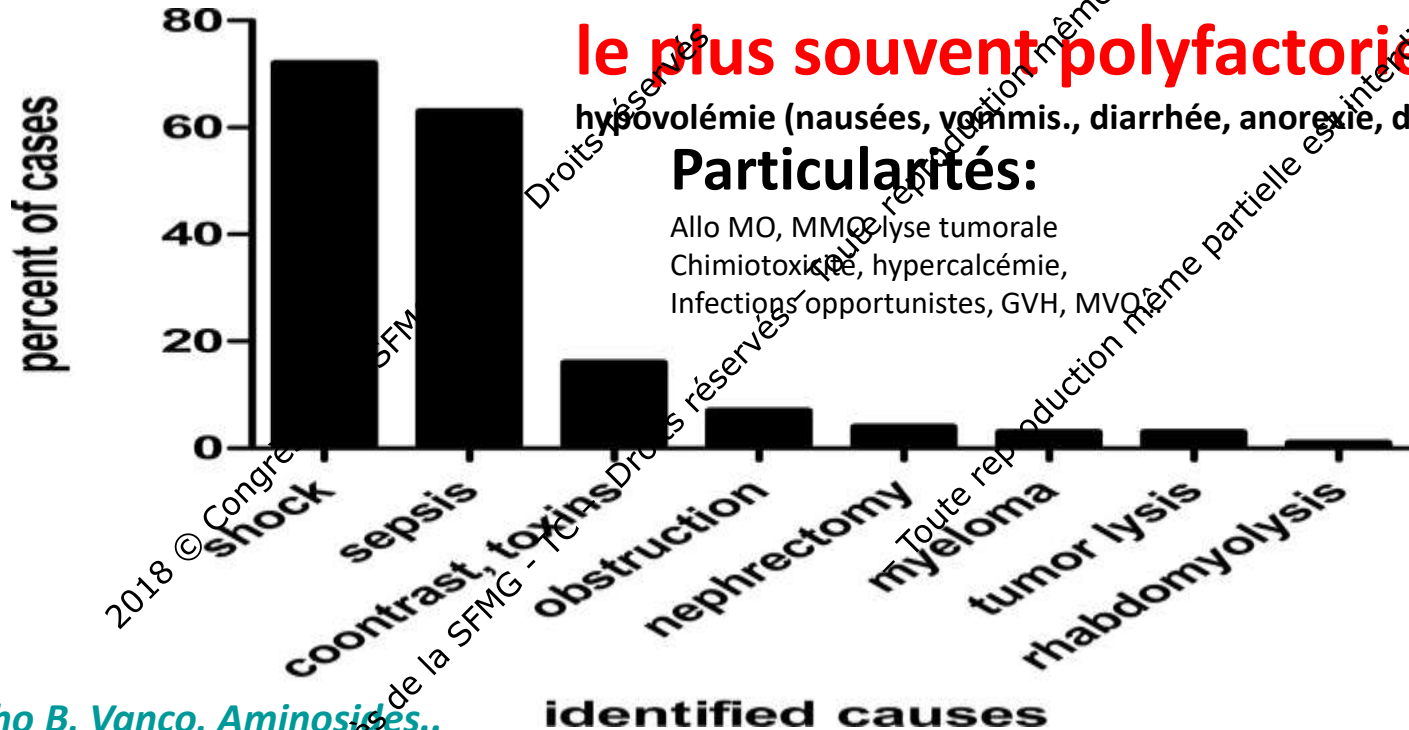
Cohorte rétrospective 2010

31,970 Hosp

IRA :18.3%



# Causes of acute kidney injury in critically ill cancer patients.



**le plus souvent polyfactorielle**

hypovolémie (nausées, vomis., diarrhée, anorexie, desh..)

**Particularités:**

Allo MO, MMO, lyse tumorale  
Chimiotoxique, hypercalcémie,  
Infections opportunistes, GVH, MVO

*Ampho B, Vanco, Aminosides..*

# Acute kidney injury in critically ill patients with haematological malignancies:

results of a multicentre cohort study from the Groupe de Recherche en Reanimation Respiratoire en Onco-Hematologie

M Darmon et al. *Nephrol Dial Transplant* 2015; 2006–2013



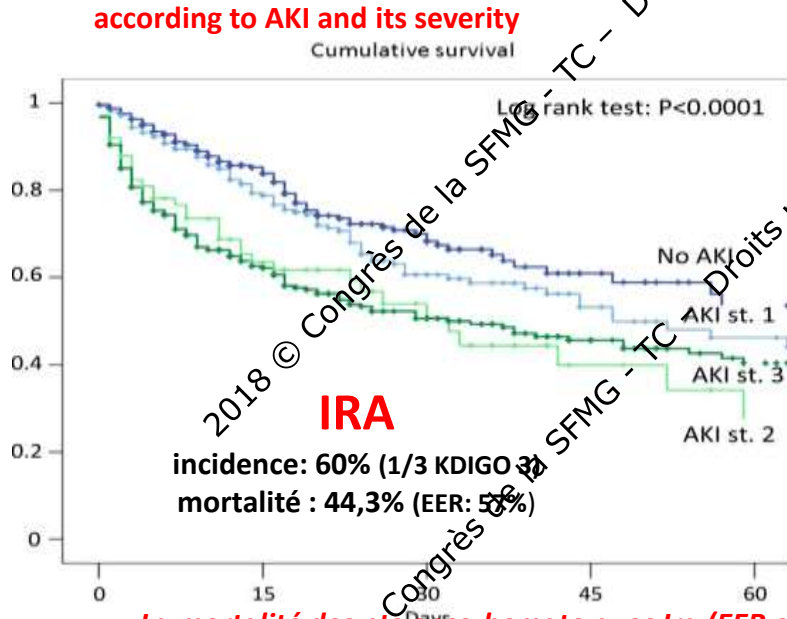
17 Réa France Belgique 2010-2, 1009 Hem.

Mortalité: 38%

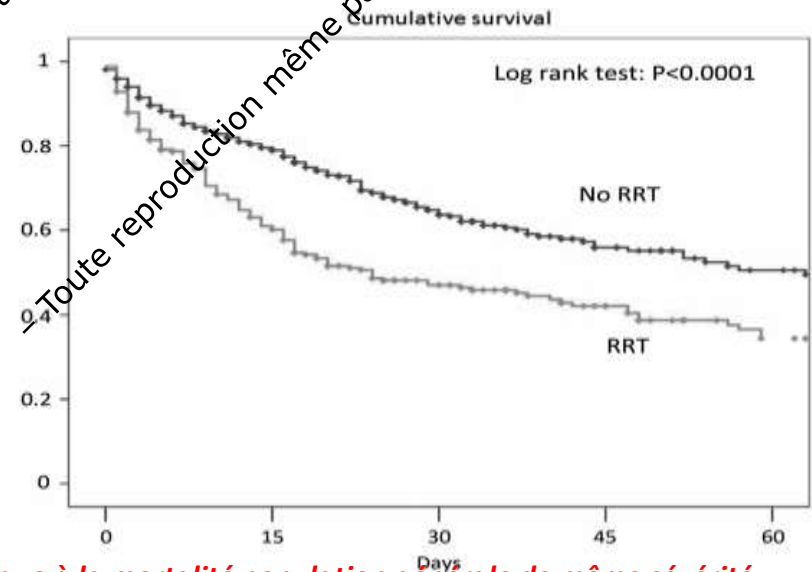
Motif H: IRA 30%

338 ss IRA, 671 (61%) IRA

## Cumulative survival



according to RRT requirement



La mortalité des pts onco-hemato avec Ira (EER ou pas) identique à la mortalité population générale de même sévérité

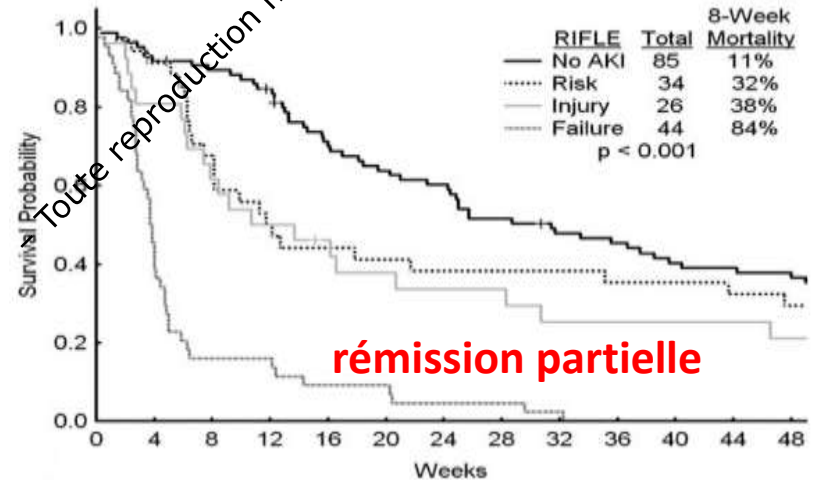
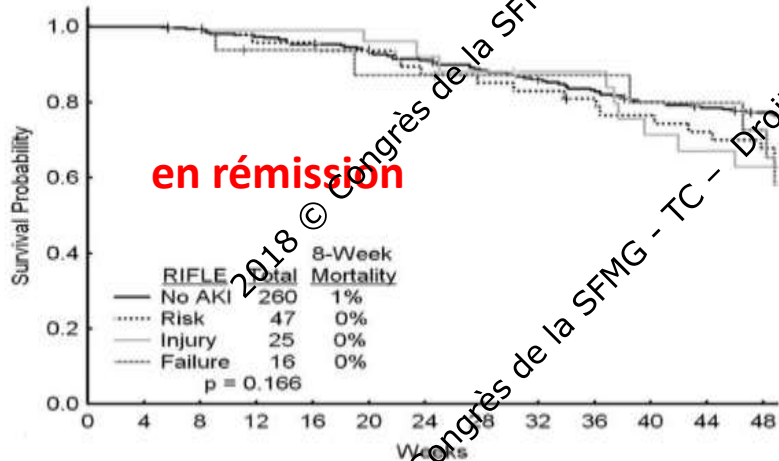
# Predictors and Outcome of Acute Kidney Injury in Patients With Acute Myelogenous Leukemia or High-Risk Myelodysplastic Syndrome

Lahoti A et al. Cancer. 2010; 116(17): 4063–4068.

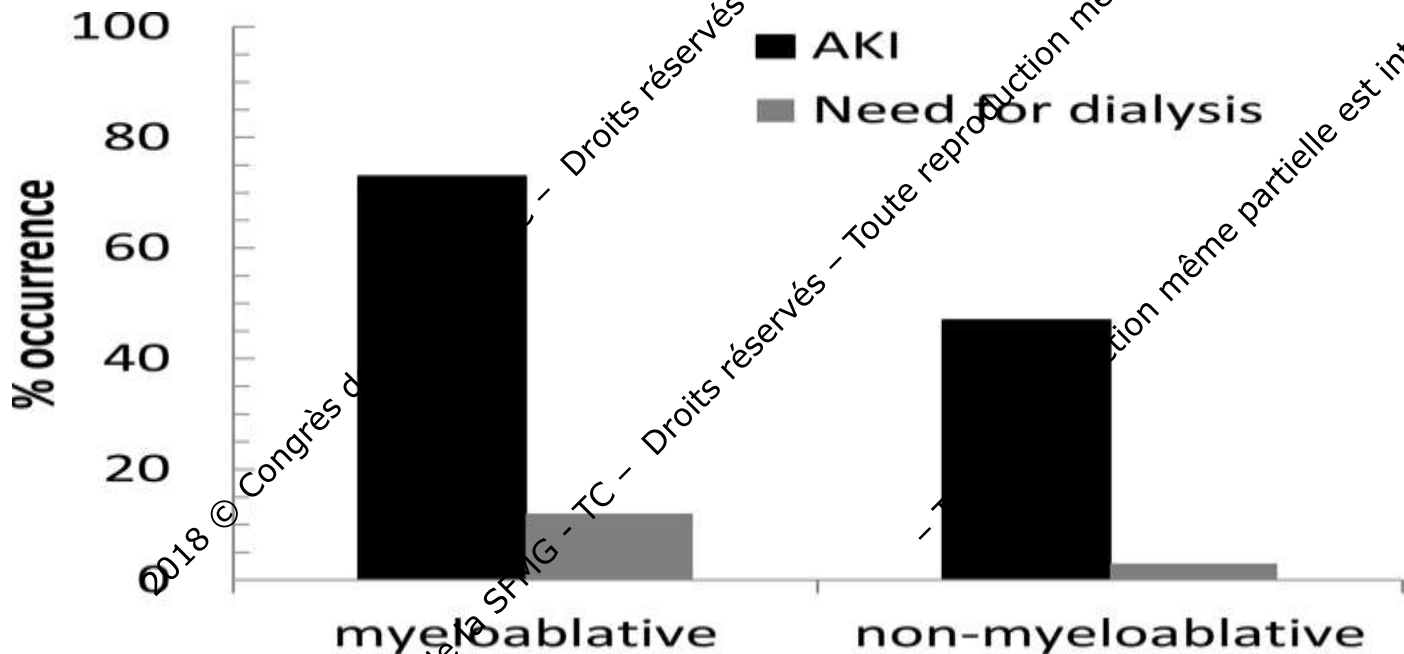
## 537 pts LAM ou SMD traités 99-2007

187 IRA (36%)

Mortalité à 8 semaines: pas d'IRA: 4%; IRA R: 14%, F: 62%



# The occurrence of acute kidney injury after HSC transplantation.



**5% des alloGreffes de Mo avec IRA → EER**



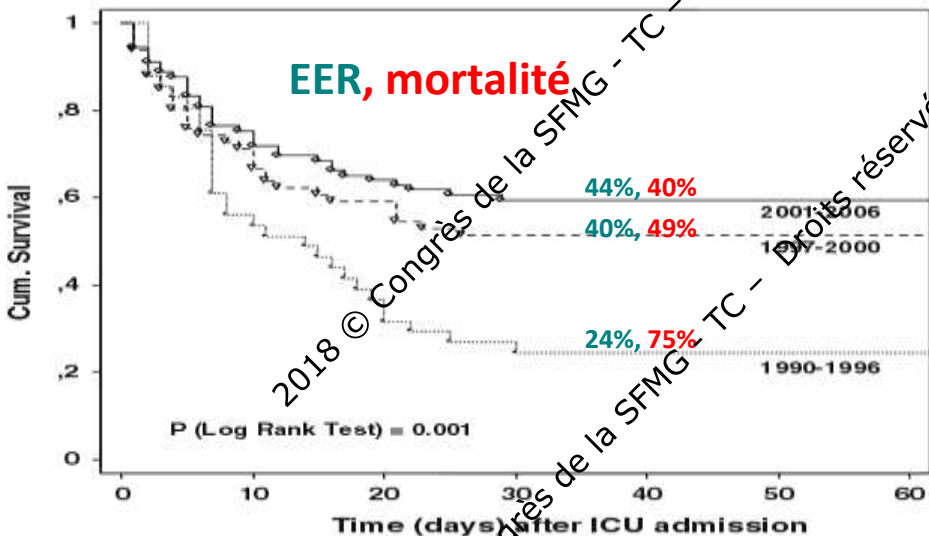
# Continued survival gains in recent years among critically ill myeloma patients

Intensive Care Med (2009) 35:512–518  
 DOI 10.1007/s00134-008-1320-4

ORIGINAL

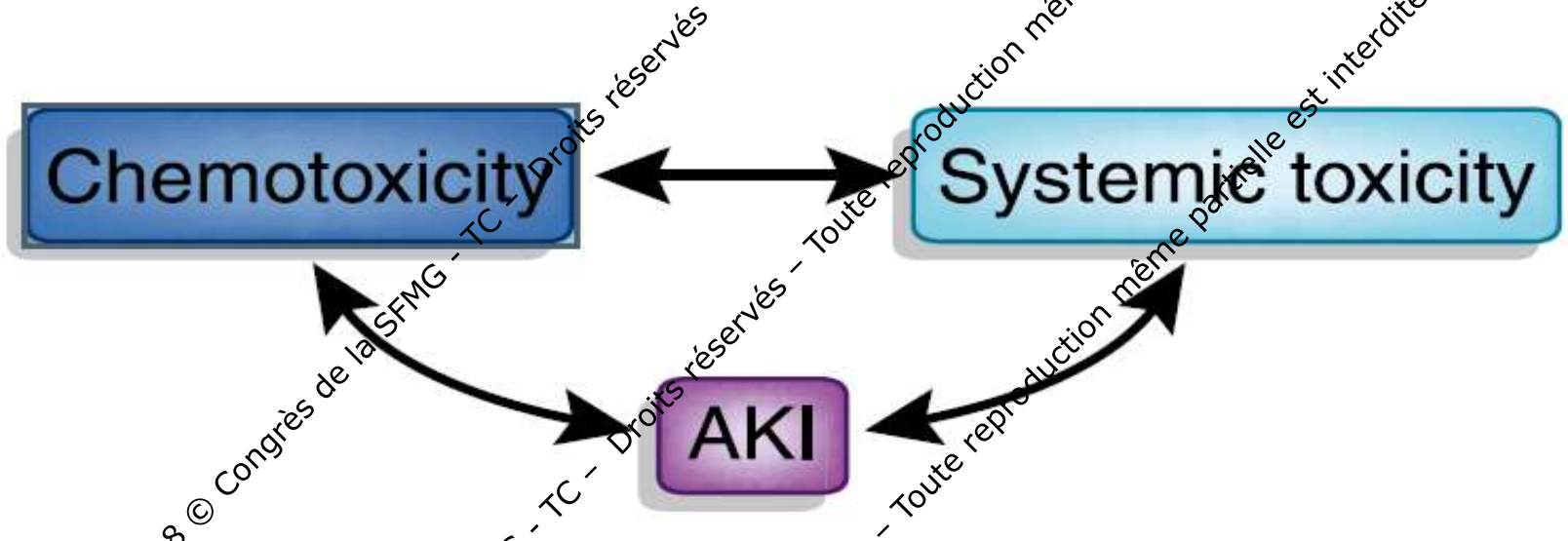
196 pts MMO 90-06

EER, mortalité



Parameters	Odds ratio	95% CI	P value
Poor chronic health status <sup>a</sup>	2.27	1.04-4.99	0.04
Need for vasopressors	2.57	1.12-5.86	0.02
Need for mechanical ventilation	4.33	1.86-10.10	0.0007
Admission to the ICU for complication of myeloma	2.77	1.13-6.79	0.02
Admission to the ICU during the second period (1996-2001)	0.28	0.10-0.84	0.02
Admission to the ICU during the third period (2002-2006)	0.20	0.06-0.64	0.007
Admission to the ICU less than 2 days after hospital admission	0.41	0.19-0.89	0.02

# Chemotoxicity and kidney injury



This vicious cycle leads to enhanced systemic toxicity.



# Critically Ill Patients' Preferences Regarding Aggressive Medical Interventions Can We Hear the Patient's Voice?

Jamie H. Von Roenn, MD

JAMA Oncology January 2016 Volume 2, Number 1

**Il s'agit de soigner et de prendre soin!**  
**Care and take care!**

© Congrès de la SFMG - TC - Droits réservés

- Toute reproduction même partielle est interdite

# En définitive, le patient d'hématologie en Réanimation

## Je sais pourquoi je l'admets en Réa

- full code
- visée diagnostique
- à titre palliatif
- avec un plan de prise en charge
- essai clinique

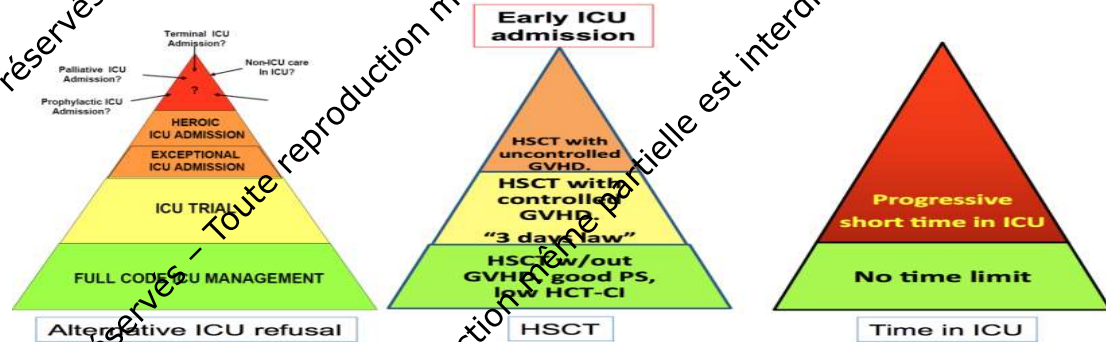
## Je réévalue le patient J3, J5, J10, J15 ?

## Je reste à l'écoute

(patient, famille, staff, hémato)

## Je discute l'admission

- Etat général préexistant très altéré, comorbidités+++
- Espérance de vie courte
- Allogreffe avec GVHD > 2 non contrôlée, corticodépendante (hépatique, pulmonaire)
- MVO ?
- SDRA sévère d'étiologie indéterminée
- Défaillance multiviscérale
- Réadmission après une réanimation « héroïque »
- Défaillance rénale ou hépatique pouvant interdire toute thérapeutique ultérieure



Vi trop tard ni trop tôt  
Early warning score

# New strategies of ICU admission in patients with cancer

## Time-limited Trials

Do everything and reassess, be patient and collaborative)

## Early ICU admission

Patients with sepsis, acute respiratory failure or other organ dysfunction who can be managed using noninvasive diagnostic and therapeutic strategies

## **FULL CODE STATUS**

## High risk patients:

Induction chemotherapy with high risk of tumor lysis syndrome or respiratory deterioration, High tumoral burden with bulky tumors or pericardial effusions

## Palliative ICU-management

(optimal medical care with noninvasive ventilation or vasopressors as the ceiling of therapy, cardiac conversion, pneumothorax, optimization of pain medication)

**Exceptional ICU admission for patients in whom new drugs (approved or not) are available**

# CONCLUSION

Meilleure sélection de patients : comorbidités, sévérité de maladie

Meilleure adhésion aux recommandations : remplissage vasculaire..

**Meilleure collaboration interprofessionnelle: équipe référente**

Détection précoce des patients à risque **systeme d'alerte**

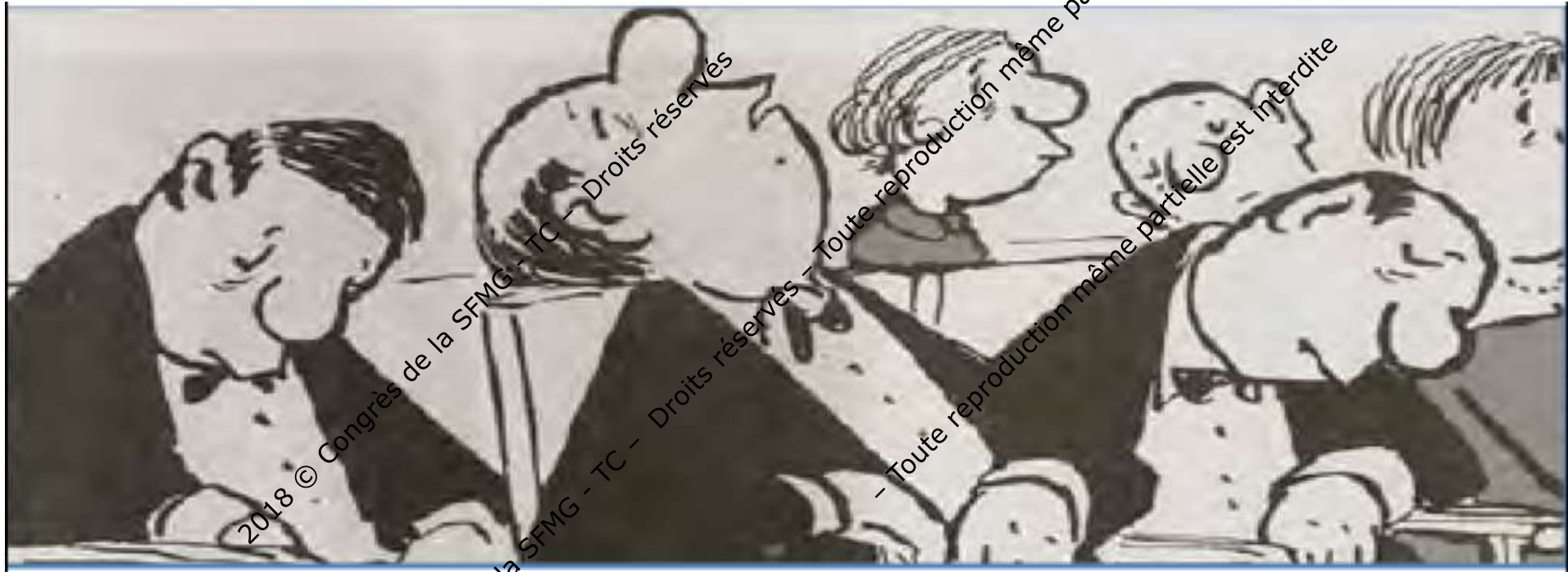
Triage : LATA vs admission précoce en réa de patients avec un bon pronostic

expérience de l'équipe hémato-onco et réa

**Le patient d'hématologie est un patient comme les autres!**



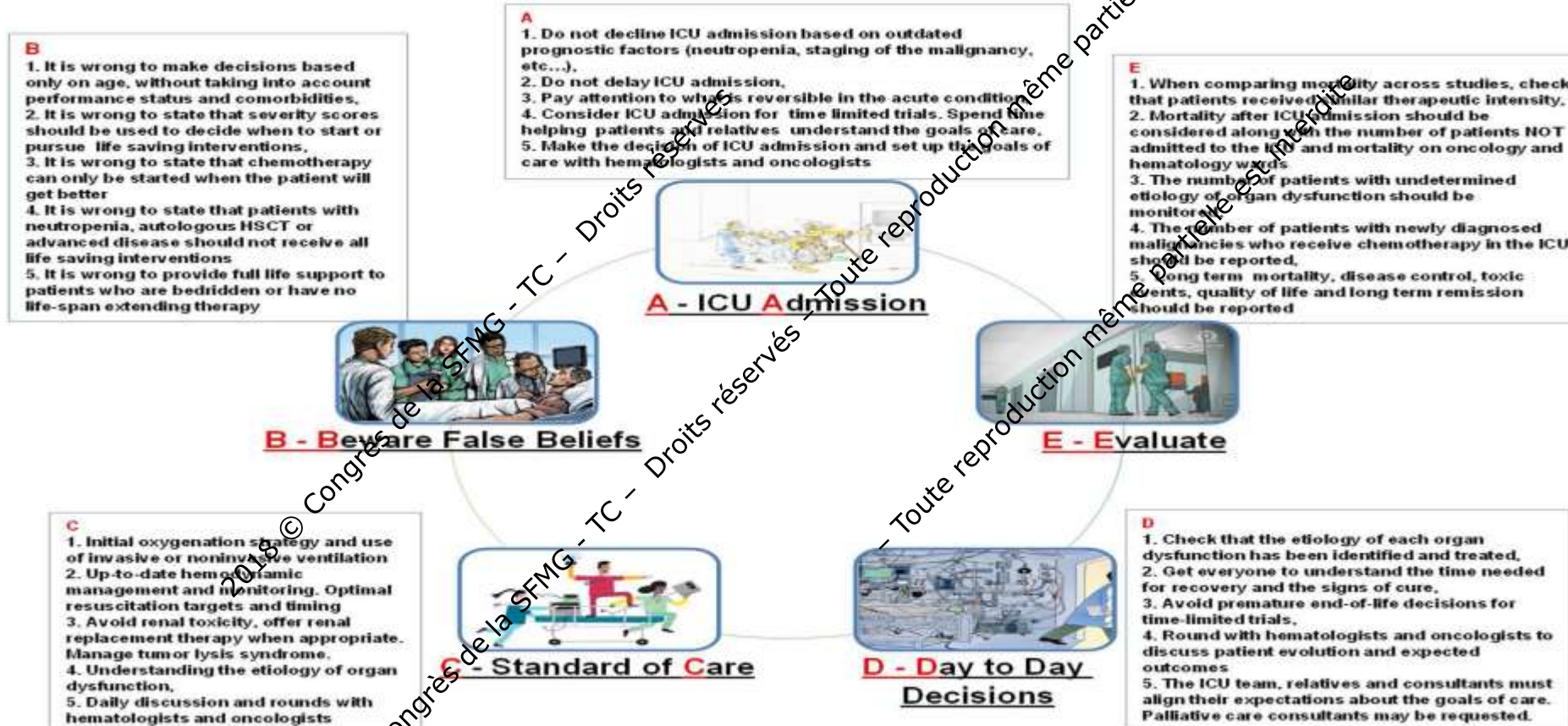
# Merci de votre attention



2018 © Congrès de la SFMG - TC -- Droits réservés

2018 © Congrès de la SFMG - TC -- Droits réservés -- Toute reproduction même partielle est interdite

# The ABCDE management rules for critically ill cancer patients



# IRA chez le patient d'onco-hématologie

Prise en charge

## Manœuvres préventives

volémie, éviter néphrotoxiques

évaluation de la fonction rénale (AB, antifongiques)

identifier une chimio Toxique: arrêt, antidote (Metho) ou épuration, glucocorticoïdes (PD1)

## EER

on n'en sait pas plus

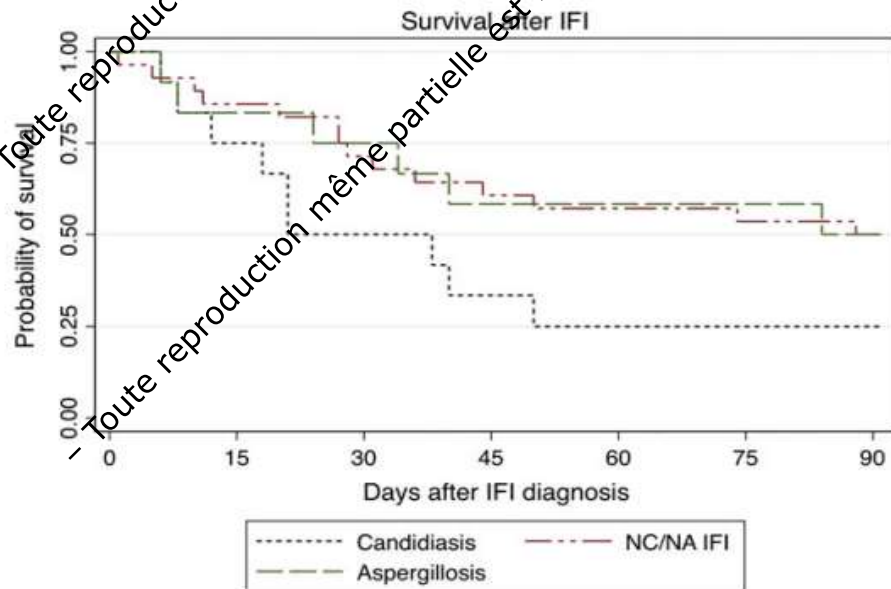
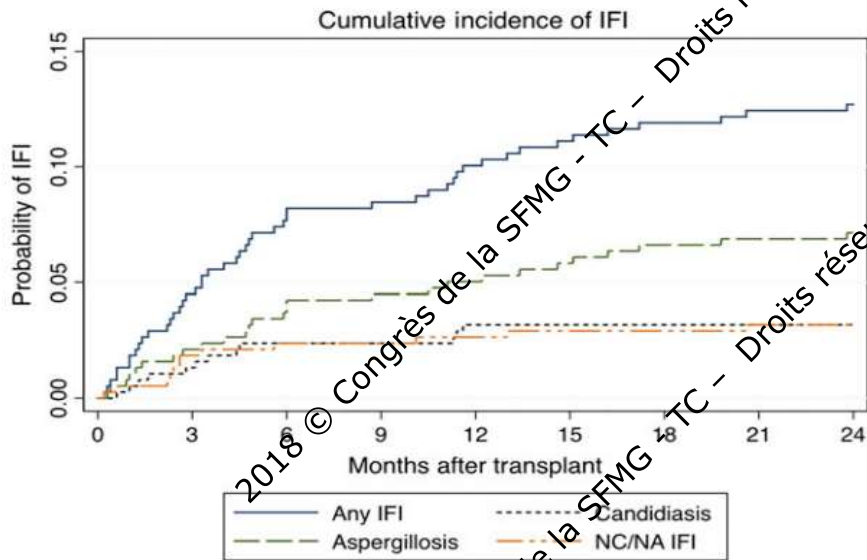
les mêmes questions se posent: timing, modalité, dose, sevrage

plus de complications (citrate?)

**Recouvrement de la fonction rénale et prise en charge ultérieure?**

# Cumulative incidence of invasive fungal infection (IFI), aspergillosis, candidiasis and IFIs other than Candida/Aspergillus, by year of transplant.

D E. Corzo-Leon, et al. Mycoses, 2015, 58, 325–336



# INSUFFISANCE RESPIRATOIRE AIGUE

- Détresse respiratoire aigüe: 70% des causes d'admission

- Eléments d'appréciation:

clinique, SaO<sub>2</sub>, PaO<sub>2</sub>/FiO<sub>2</sub>, lactatémie, tomodynamométrie

- Etiologies:

Infectieuses (60%): Pronostic intermédiaire

Non infectieuses (20%)

OAP très bon pronostic (indépendant du projet thérapeutique)

Spécifiques, Autres...

Aucune étiologie retrouvée (20%)

**Mauvais pronostic**

- Deux types de ventilation:

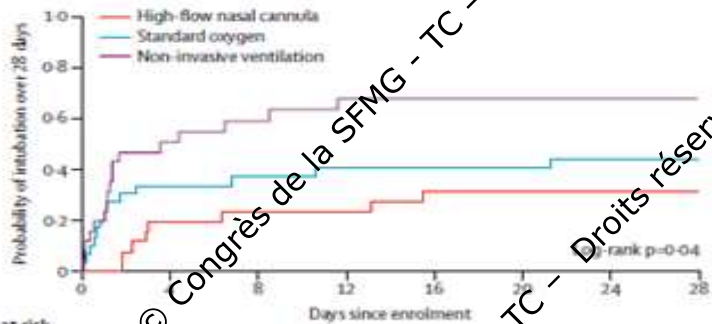
ventilation non invasive

ventilation conventionnelle

# Effect of non-invasive oxygenation strategies in immunocompromised patients with severe acute respiratory failure: a post-hoc analysis of a randomised trial

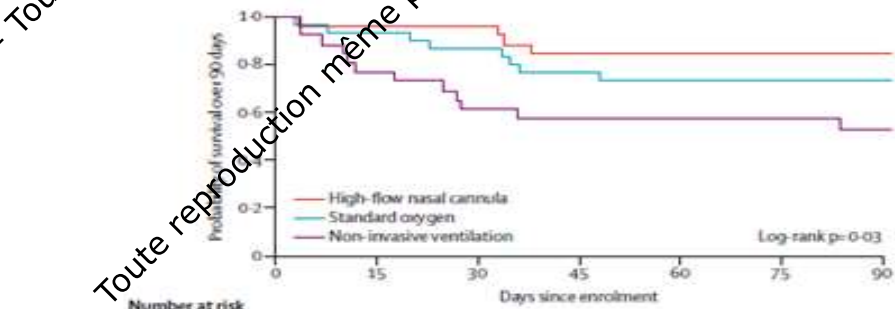
Jean-Pierre Frat, Stéphanie Ragot, Christophe Girault, Sébastien Perbet, Gwénael Prat, Thierry Boulain, Alexandre Demoule, Jean-Emilien Ricard, Rémi Coudroy, René Robert, Alain Mercat, Laurent Brochard, Arnaud W Thille, for the REVA network

thelancet.com/respiratory May 27, 2016



	Days since enrolment							
Number at risk	0	4	8	12	16	20	24	28
High-flow nasal cannula group	26	21	20	20	18	18	18	18
Standard oxygen group	30	20	18	17	17	17	16	16
Non-invasive ventilation group		12	10	8	8	8	8	8

Probability of intubation at day 28 in patients in the non-invasive ventilation group versus standard oxygen and high-flow nasal cannula groups



	Days since enrolment							
Number at risk	0	15	30	45	60	75	90	
High-flow nasal cannula group	26	25	25	22	22	22	22	
Standard oxygen group	30	28	26	23	22	22	22	
Non-invasive ventilation group	26	20	16	15	14	14	13	

Probability of survival at day 90 in patients in the non-invasive ventilation group versus standard oxygen and high-flow nasal cannula groups

2018 © Congrès de la SFMG - TC - Droits réservés - Toute reproduction même partielle est interdite

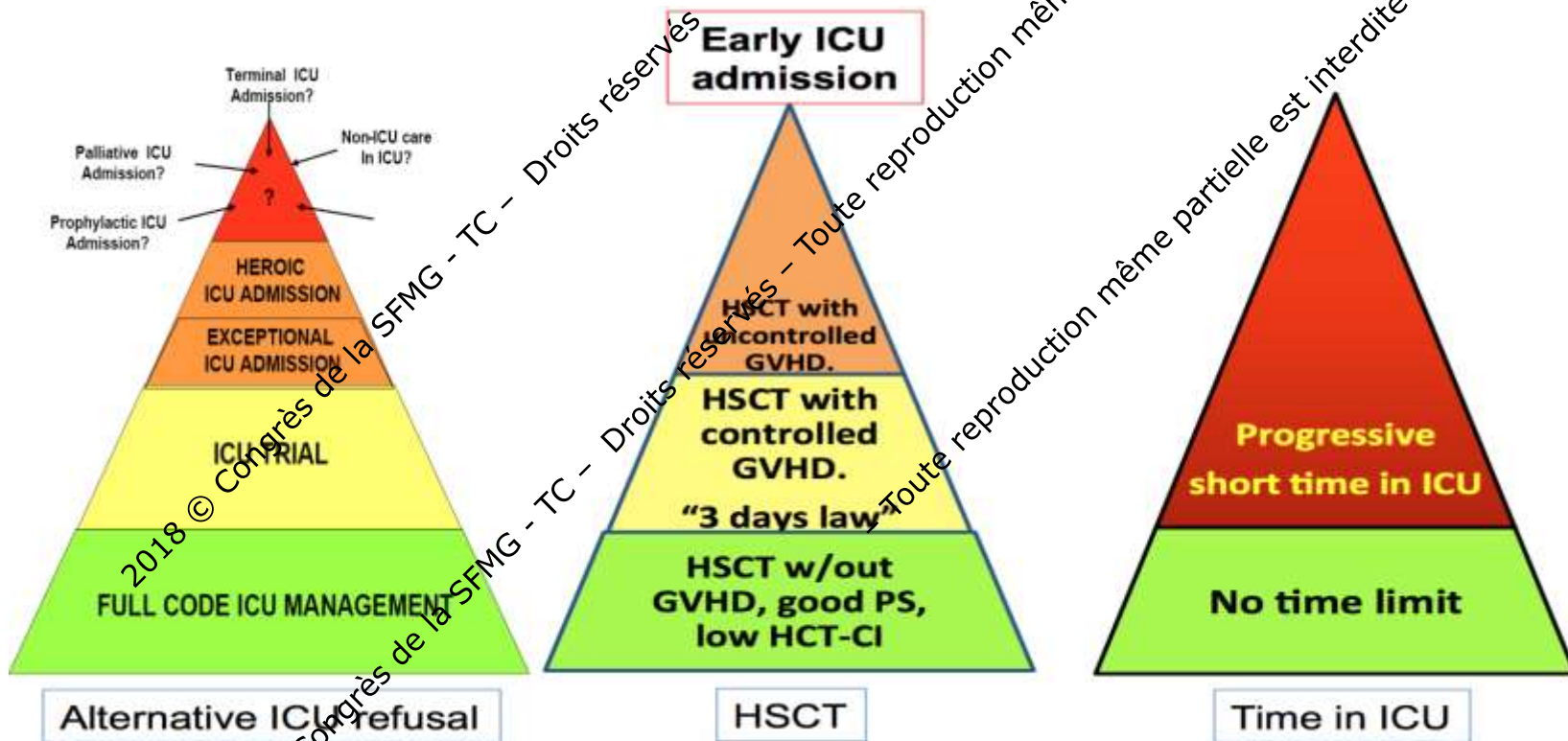


# Components of the standard of care in critically ill patients with hematological malignancies

## Standard of Care

- **What to do**
  - Optimal life support based on most recent data from general ICU patients
  - Noninvasive diagnostic and therapeutic strategies
  - Close collaboration between intensivists and hematologists
- **What to Consider**
  - New ICU admission policies (prophylactic ICU admission, palliative noninvasive ventilation)
  - Start induction chemotherapy in the ICU in high risk patients
  - Medical emergency teams
  - Minimally invasive (CT-driven), diagnostic procedures
- **What to encourage**
  - Early ICU admission
  - Improve our understanding of pathophysiology and of toxicities of newly released drugs
  - Cytoreduction therapy in hyperleukocytic AML
  - Combination therapy (aminoglycosides) in septic shock
  - Catheter withdrawal in septic shock from unknown origin
  - ICU trial
  - Rehabilitation programs
  - Respect patient's preferences and provide early in-ICU palliative care
- **What not to do**
  - Delayed ICU admission
  - Agonization in tumor lysis syndrome
  - Inappropriate use of nephrotoxic agents (contrast agents, antibiotics, etc...)
  - Prolonged noninvasive ventilation in hypoxemic patients meeting criteria for ARDS
  - Bronchoscopy and bronchoalveolar lavage in deeply hypoxemic patients for whom a noninvasive diagnostic test is available
  - Premature end-of-life decisions
- **What to evaluate**
  - Noninvasive ventilation, blood transfusion policies,
  - Effectiveness of new diagnostic tests
  - Impact of cytogenetics and molecular biology on organ dysfunction (e.g., in AML or lymphoma...)
  - Triage criteria by hematologists for ICU referral
  - Current risk factors for adverse events (invasive fungal infections, mortality)
  - Long term outcomes (survival, disease control, quality of life, post-ICU burden)
  - Decision making for patients with prolonged ICU stays

# La prise en charge du patient d'hématologie en Réanimation



# Briser le plafond de verre





**IN LOVE WE TRUST**

***Le réanimateur et l'hématologue !***



2018 © Congrès de la SFMG - TC - Droits réservés

2018 © Congrès de la SFMG - TC - Droits réservés

- Toute reproduction même partielle est interdite



# Insuffisance Rénale Aiguë

## Onco-Hématologie

- ✓ **Liée au K ou à l'hémopathie:**  
lyse tumorale, obstruction urétérale tumorale, allogreffe de MO...  
infiltration rénale (K, lymphome: fréquent mais IRA rare)
- ✓ **Liée au traitement du K ou hémopathie:**  
chimioth; chirurgie
- ✓ **Liée aux conditions: hypovolémie, sepsis, toxiques +++**

**IRA survient chez 60 % des patients au cours de la maladie**

# IRA chez le patient d'onco-hématologie

## Recouvrement de la fonction rénale

**80 % des patients survivants à une IRA épurées seront sevrés de l'EER**

Darmon M ICM 2007, Canet E Plos One 2013, Park MR J C Care 2011

**Pronostic dépendant de la cause IRA**

**SLT: bon pronostic ≈ 100% de recouvrement de la fonction rénale**

E Canet 2014

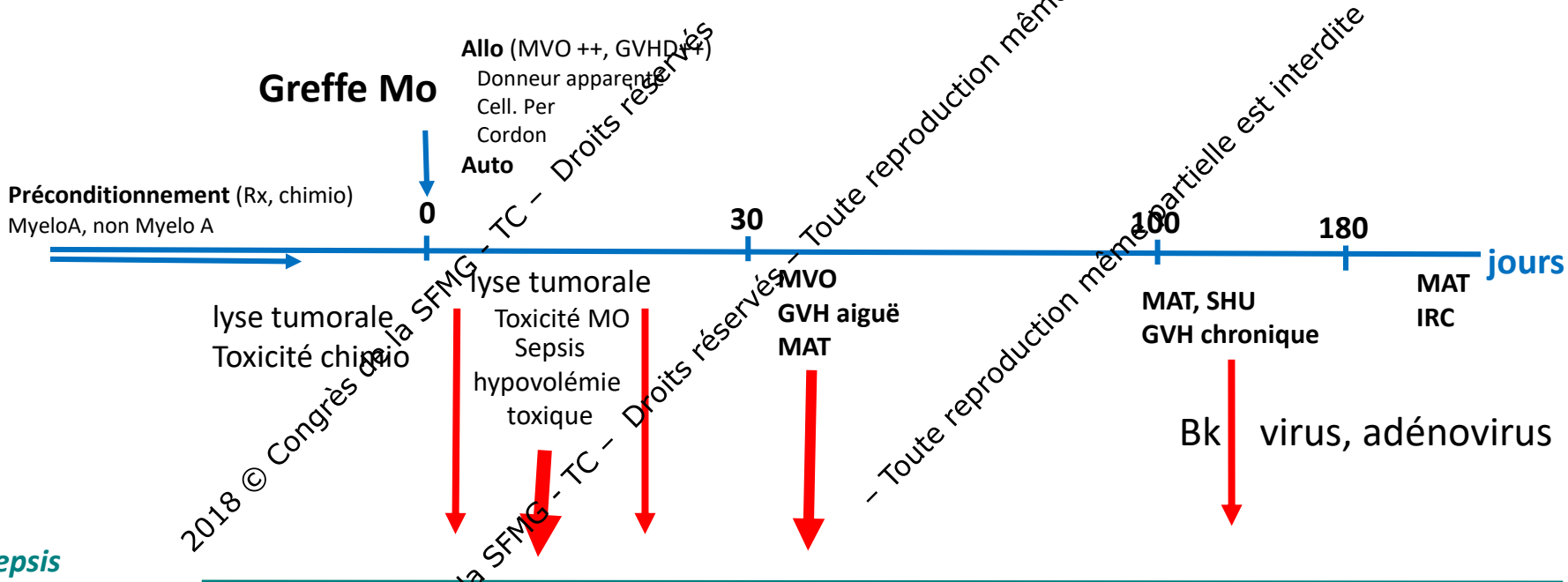
**Allogreffe de MO: peu de récupération**

E Canet BMT 2014

**MMO: 70% de récupération avec bortezomib**

Roussou M Leuk Res 2010

# IRA post allo greffe de moelle osseuse, causes



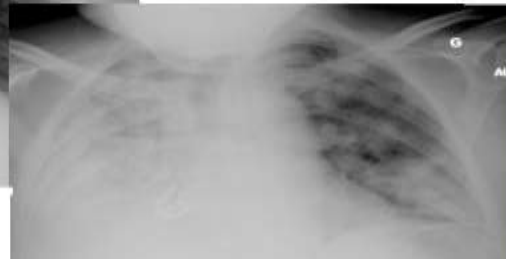
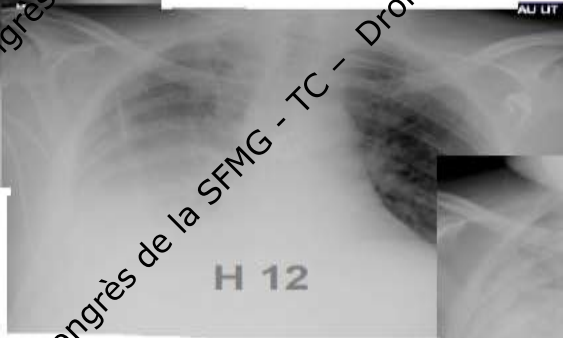
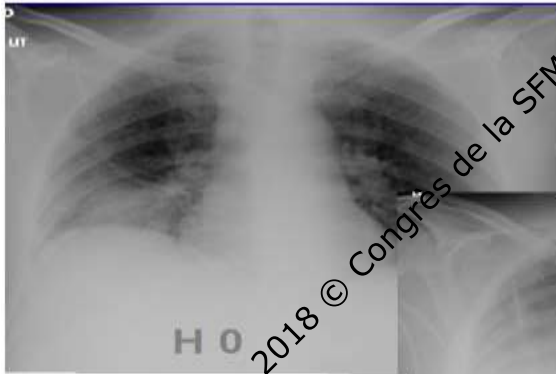
**Sepsis**  
**Hypovolémie**  
**toxique**

## Insuffisance Rénale Aiguë





# Examiner le patient et réaliser les examens complémentaires



**Colite neutropénique**

2018 © Congrès de la SFMG - TC -

2018 © Congrès de la SFMG - TC -

- Toute reproduction

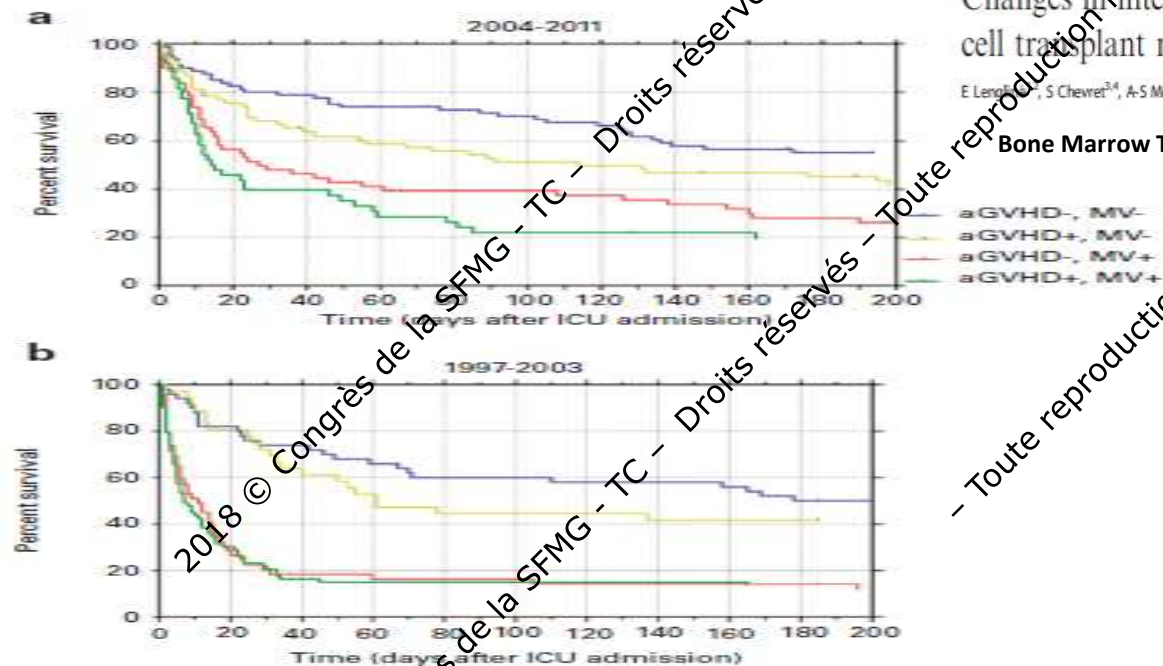
Droits réservés - Toute reproduction

est interdite

partie

# Greffe MO: admission en Réanimation 20%

Cohortes 90-03 et 04-11; Facteurs de pronostic: GVH et VM



**Figure 2.** OS according to the presence of acute GVHD grade > 2 and to the use of mechanical ventilation. aGVHD, acute GVHD; MV, invasive mechanical ventilation; ICU, intensive care unit.

ORIGINAL ARTICLE

Changes in intensive care for allogeneic hematopoietic stem cell transplant recipients

E Lengua<sup>1</sup>, S Chevret<sup>2,4</sup>, A-S Moreau<sup>1</sup>, F Pène<sup>5</sup>, F Blot<sup>6</sup>, J-H Bourhis<sup>7</sup>, A Buzyn<sup>8,9</sup>, B Schlemmer<sup>1</sup>, G Socie<sup>2,10</sup> and E Azoulay<sup>7,8</sup>

Bone Marrow Transplant. 2015 Jun;50(6):840-5.

2018 © Congrès de la SFMG - TC - Droits réservés - Toute reproduction même partielle est interdite

# Greffe MO: admission en Réanimation 20%

Cohortes 97-03 et 04-11

	Recent cohort 2004-2011	Historical cohort 1997-2003	p
n	288	205	
HSCT Procedures	1261	1025	
Age (years)	48 [32-56]	41 [29-49]	<0,0001
Sex (male-%)	191 (67)	118 (56)	
Purpose of HSCT			<0,0001
AML	87 (30)	66 (32)	
ALL	56 (19)	40 (19)	
MDS	25 (9)	11 (5)	
CML	7 (3)	34 (16)	
Mature lymphoid malignancy	1 (0)	43 (20)	
Other	14 (10)	15 (8)	
Time from diagnosis to HSCT (months)	16 [6-49]	12 [6-27]	0,008
Status at transplantation			0,83
Complete remission / chronic phase	210 (73)	150 (73)	
Partial remission / progressive	78 (27)	55 (28)	
Conditioning regimen			< 0,0001
Reduced intensity	131 (46)	21 (10)	
Myeloablative	153 (54)	188 (89)	
TBI overall	161 (80)	136 (65)	0,3
TBI > 10 Gy	82 (28)	132 (63)	<0,0001
ATG	55 (21)	56 (27)	
Source of stem cell			< 0,0001
Peripheral blood stem cell	163 (57)	59 (28)	
Bone marrow	85 (29)	141 (67)	
Cord blood	34 (12)	9 (4)	
Donor type			<0,0001
Sibling	126 (46)	146 (70)	
Matched unrelated	99 (37)	60 (29)	
Mismatched	46 (17)	3 (1)	

Plus vieux

Indications différentes

Procédures différentes

RIC > MAC

CSP > MO

Non apparenté

2018 © Congrès de la SFMG - TC - Droits réservés

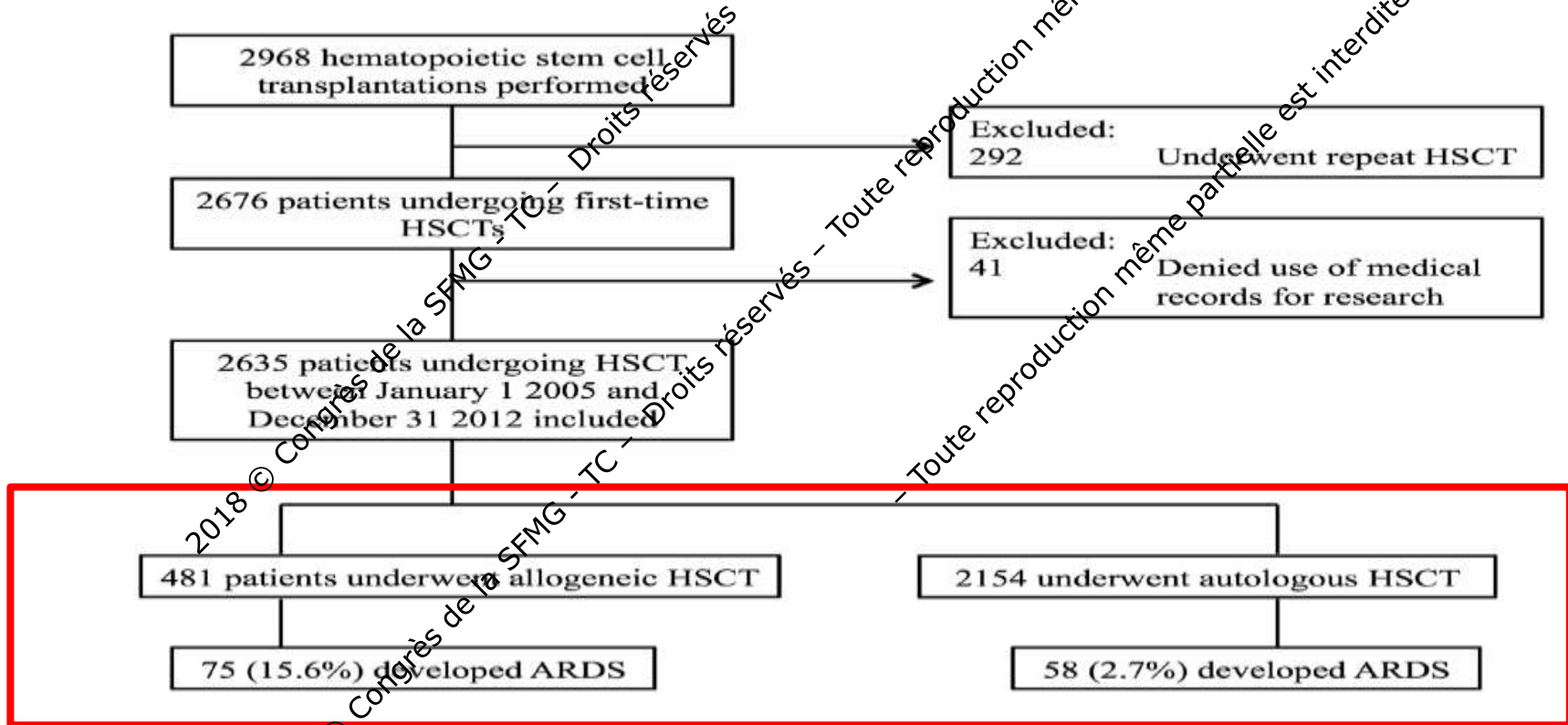
2018 © Congrès de la SFMG - TC - Droits réservés

- Toute reproduction même partielle est interdite

- Toute reproduction même partielle est interdite

# Epidemiology of Acute Respiratory Distress Syndrome Following Hematopoietic Stem Cell Transplantation

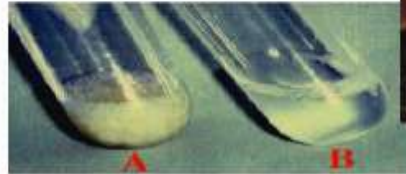
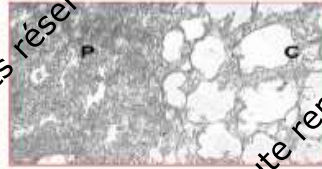
Crit Care Med 2016; 44:1082–1090



# STRATEGIE DIAGNOSTIQUE

## Invasive or noninvasive ?

- **Invasive:**
  - Biopsy
- **Semi-invasive:**
  - FO-BAL
- **Non invasive:**
  - Blood cultures
  - Sputa
  - Induced sputa
  - NPA
  - Antigenes
  - Echography
  - HRCT



© Congrès de la SFMG - TC - Droits réservés - Toute reproduction même partielle est interdite



# Who c(sh)ould benefit from BAL?

- First line
  - Drug-related pulmonary toxicity
  - PCP (first hours)
  - Patient receiving mechanical ventilation ?
- And...
  - Before pulmonary biopsy
  - New nosology
  - Non infectious diagnoses in neutropenic patients



# NONINVASIVE VENTILATION IN IMMUNOSUPPRESSED PATIENTS WITH PULMONARY INFILTRATES, FEVER, AND ACUTE RESPIRATORY FAILURE

GILLES HILBERT, M.D., DIDIER GRUSON, M.D., FRÉDÉRIC VARGAS, M.D., RUDDY VALENTINO, M.D., GEORGES GBIKPI-BENISSAN, M.D., MICHEL DUPON, M.D., JOSY REIFFERS, M.D., AND JEAN P. CARBINAUD, M.D.

TABLE 2. OUTCOMES OF TREATMENT.\*

OUTCOME	NONINVASIVE VENTILATION GROUP (N=26)	STANDARD-TREATMENT GROUP (N=26)	P VALUE	RELATIVE RISK (95% CI)
Intubation — no./total no. (%)	12/26 (46)	20/26 (77)	0.02	0.60 (0.38–0.96)
Immunosuppression from hematologic cancer and neutropenia	8/15 (53)	14/15 (93)	0.02	0.57 (0.35–0.93)
Drug-induced immunosuppression	3/9 (33)	5/9 (56)	0.32	0.60 (0.20–1.79)
Immunosuppression from the acquired immunodeficiency syndrome	1/2 (50)	1/2 (50)	0.83	1.00 (0.14–7.10)
Initial improvement in PaO <sub>2</sub> :FiO <sub>2</sub> — no. (%)	12 (46)	4 (15)	0.02	
Sustained improvement in PaO <sub>2</sub> :FiO <sub>2</sub> without intubation — no. (%)	13 (50)	5 (19)	0.02	
Death in the ICU — no./total no. (%)†	10/26 (38)	18/26 (69)	0.03	0.56 (0.32–0.96)
Immunosuppression from hematologic cancer and neutropenia	7/15 (47)	13/15 (87)	0.02	0.54 (0.30–0.96)
Drug-induced immunosuppression	3/9 (33)	4/9 (44)	0.50	0.75 (0.23–2.44)
Immunosuppression from the acquired immunodeficiency syndrome	0/2	1/2 (50)	0.50	0.50 (0.13–2.00)
Total duration of any ventilatory assistance — days				
Among all patients	6±3	6±5	0.59	
Among survivors	5±2	3±5	0.12	
Length of ICU stay — days				
Among all patients	7±3	9±4	0.11	
Among survivors	7±3	10±4	0.06	
Death in the hospital — no./total no. (%)	13/26 (50)	21/26 (81)	0.02	0.62 (0.40–0.95)
Immunosuppression from hematologic cancer and neutropenia	8/15 (53)	14/15 (93)	0.02	0.57 (0.35–0.93)
Drug-induced immunosuppression	4/9 (44)	6/9 (67)	0.32	0.67 (0.28–1.58)
Immunosuppression from the acquired immunodeficiency syndrome	1/2 (50)	1/2 (50)	0.83	1.00 (0.14–7.10)