Le patient neutropénique en réanimation.

AP Meert

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Introduction

La prise en charge des patients neutropéniques en réanimation est souvent basée sur des études de niveau d'évidence faible

- Littérature abondante mais parfois contradictoire
- Petites études observationnelles unicentriques
- Variabilité d'expérience selon les centres (volume de patients…)
- Etudes relativement anciennes

Introduction

- Les spécificités de prise en charge de ces patients aux SI nécessitaient donc l'établissement de recommandations pour les intensivistes

Schnell *et al. Ann. Intensive Care (2016) 6:90*
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Annals of Intensive Care

REVIEW Open Access

Management of neutropenic patients in the intensive care unit (NEWBORNS EXCLUDED) recommendations from an expert panel from the French Intensive Care Society (SRLF) with the French Group for Pediatric Intensive Care Emergencies (GFRUP), the French Society of Anesthesia and Intensive Care (SFAR), the French Society of Hematology (SFH), the French Society for Hospital Hygiene (SF2H), and the French Infectious Diseases Society (SPILF)

David Schnell[1], Elie Azoulay[2], Dominique Benoit[3], Benjamin Clouzeau[4], Pierre Demaret[5], Stéphane Ducassou[6], Pierre Frange[7], Matthieu Lafaurie[8], Matthieu Legrand[9], Anne-Pascale Meert[10], Djamel Mokart[11], Jérôme Naudin[12], Frédéric Pene[13], Antoine Rabbat[14], Emmanuel Raffoux[15], Patricia Ribaud[16], Jean-Christophe Richard[17], François Vincent[18], Jean-Ralph Zahar[19] and Michael Darmon[20,21*]

Panel d' experts

Société de réanimation de langue française (SRLF) +

- Groupe francophone de réanimation et urgences pédiatriques
- Société de pathologie infectieuse de langue française (GFRUP)
- Société française d'anesthésie réanimation (SFAR)
- Socité française d'hématologie (SFH)
- Socité française d'hygiène hospitalière (SF2H)
- French Infectious Diseases Society (SPILF)

- Chaque société scientifique a sélectionné ses experts
- Le coordinateur a défini le champ de questions à couvrir et proposé les experts pour chaque sujet
- Les champs ont ensuite été redéfini plus précisément et validés par les experts.
- L'analyse de la littérature et la formulation des recommandations a été réalisée sur base du système GRADE

Table 1 Evidence grading and recommendations formulation

Risk of bias and grade	Type of recommendation	Formulation
Low: Grade 1	Positive recommendation +	Should be
High level of evidence	Negative recommendation −	Should not be
Intermediate to high: Grade 2	Positive recommendation +	Should probably be
Intermediate to low level of evidence	Negative recommendation −	Should probably not be
High: expert opinion	Positive recommendation +	Should probably be (expert opinion)
No available data	Negative recommendation −	Should probably not be (expert opinion)

1. Admission à l’USI et pronostic

Outcomes of Critically Ill Patients With Hematologic Malignancies: Prospective Multicenter Data From France and Belgium—A Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique Study

Elie Azoulay, Djamel Mokart, Frédéric Pène, Jérôme Lambert, Achille Kouatchet, Julien Mayaux, François Vincent, Martine Nyunga, Fabrice Bruneel, Louise-Marie Laisne, Antoine Rabbat, Christine Lebert, Pierre Perez, Marine Chaize, Anne Renault, Anne-Pascale Meert, Dominique Benoit, Rebecca Hamidfar, Mercé Jourdain, Michael Darmon, Benoit Schlemmer, Sylvie Chevret, and Virginie Lemiale

Table 4. Multivariate Logistic Regression: Variables Independently Associated With Hospital Mortality

Covariate	Model Without Imputation			Model With Imputation		
	Odds Ratio	95% CI	*P*	Odds Ratio	95% CI	*P*
Poor performance status (bedridden/completely disabled)	1.58	1.06 to 2.34	.02	1.13	1.06 to 1.21	.0005
Charlson comorbidity index	1.13/point	1.06 to 1.21	.0004	1.02	1.01 to 1.03	.0006
Recipients of allogeneic BMT/HSCT	2.18	1.33 to 3.57	.002	1.20	1.10 to 1.31	< .001
Complete or partial remission	0.63	0.42 to 0.95	.02	0.890	0.84 to 0.96	.002
Time from hospital to ICU admission < 24 hours	0.7	0.51 to 0.96	.02	0.94	0.89 to 0.99	.02
SOFA score at admission	1.21/point	1.16 to 1.27	< .001	1.04	1.03 to 1.05	< .001
Admission after cardiac arrest	2.63	1.00 to 6.97	.05	1.25	1.06 to 1.47	.008
Admission for acute respiratory failure	1.34	0.94 to 1.90	.09	1.08	1.01 to 1.15	.01
Organ infiltration by the malignancy	1.894	1.23 to 3.07	.004	1.14	1.05 to 1.24	.002
Invasive pulmonary aspergillosis	1.97	1.03 to 3.76	.03	1.14	1.01 to 1.28	.02

J Clin Oncol 31:2810-2818. © 2013

Prognosis of neutropenic patients admitted to the intensive care unit

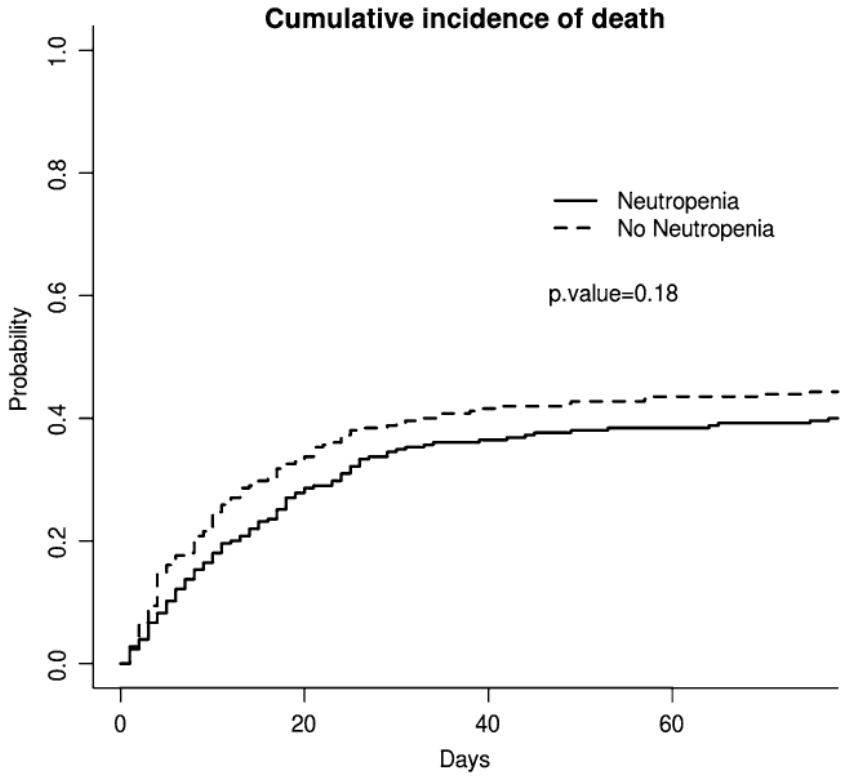

Fig. 2 Cumulative incidence of death in hospital according to the presence of neutropenia in the case–control analysis (251 neutropenic patients vs 251 controls); Gray's test, $p = 0.18$

Intensive Care Med (2015) 41:296–303

Sepsis Severe or Septic Shock : Outcome According to Immune Status and Immunodeficiency Profile

Violaine Tolsma, Carole Schwebel, Elie Azoulay, Michael Darmon, Bertrand Souweine, Aurélien Vesin, Dany Goldgran-Toledano, Maxime Lugosi, Samir Jamali, Christine Cheval, Christophe Adrie, Hatem Kallel, Adrien Descorps-Declere, Maïté Garrouste-Orgeas, Lila Bouadma, Jean-François Timsit

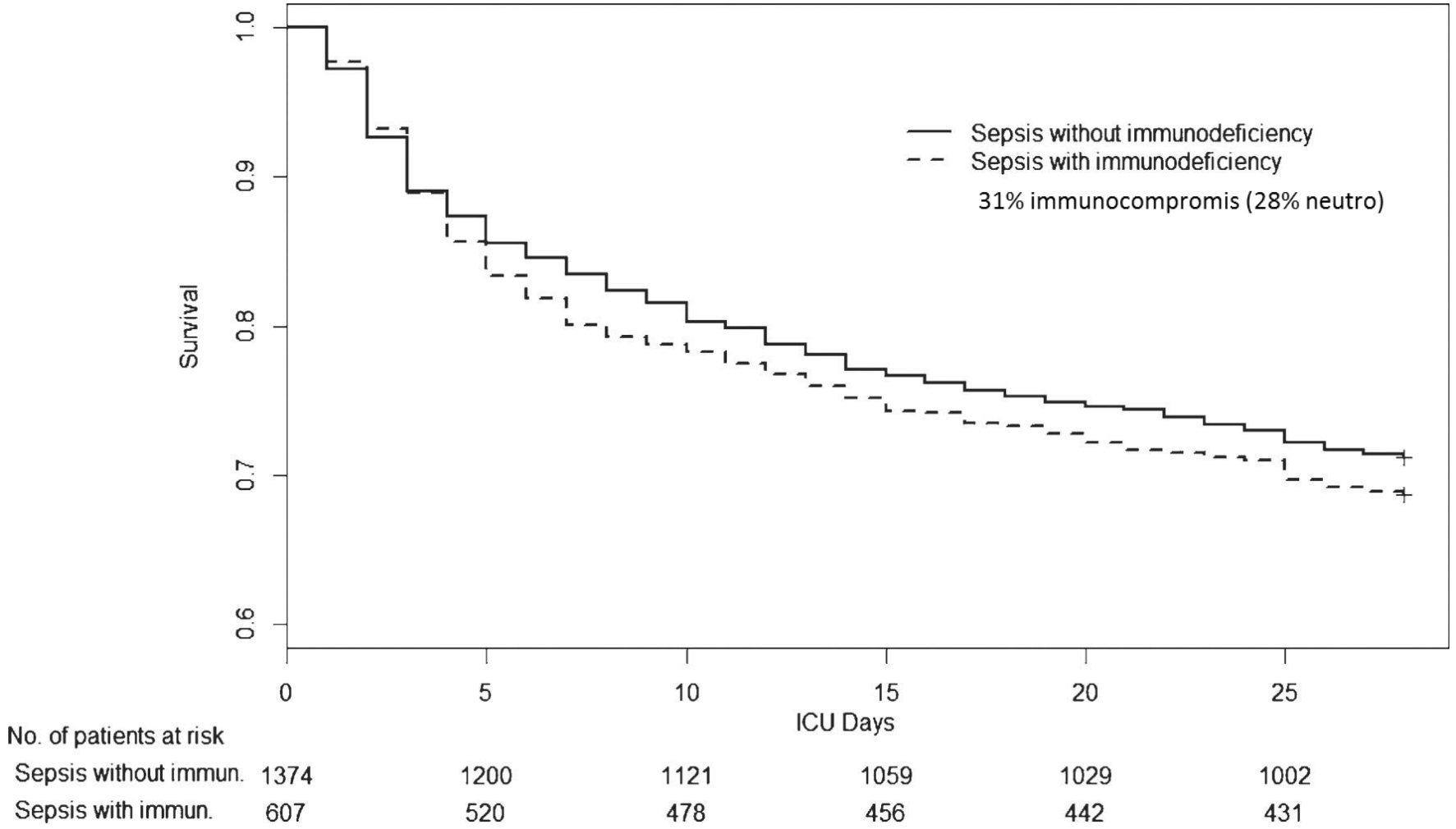

Figure 3. Kaplan-Meier survival curve between d 1 and d 28 according to the immune status. Immun = immunodeficiency.

Chest, Volume 146, Issue 5, 2014, 1205–1213

TABLE 3 | Risk Factors for Death at Day 28: Multivariate Analysis

Variables	sHR	95% CI	*P* Value[a]
Age, y			<.0001
0-54	ref	...	
55-64	1.155	0.884-1.509	
65-74	1.655	1.294-2.117	
≥75+	1.679	1.318-2.139	
Liver comorbidity[17]	1.772	1.360-2.309	<.0001
Cardiovascular comorbidity[17]	1.622	1.308-2.012	<.0001
Therapeutic limitation at day 1	2.806	1.983-3.970	<.0001
Infection site			.04
Other[b]	ref	...	
Lung	1.682	1.171-2.417	
Intraabdominal	1.498	1.017-2.207	
Urinary tract	1.118	0.672-1.859	
Unknown	1.395	0.961-2.027	
Multiple	1.293	0.908-1.840	
Adequate antimicrobials at day 1	0.660	0.557-0.782	<.0001
Septic shock	1.649	1.370-1.983	<.0001
SOFA score (without hemodynamics)			<.0001
<3	ref	...	
3-4	1.549	1.066-2.250	
5-8	2.239	1.584-3.164	
>8	5.455	3.868-7.692	
Immunodeficiency (all causes)	1.368	1.120-1.672	.002
Same model as above, but replacing immunodeficiency by the specific profile of immunodeficiency:			
Immunodeficiency profile[c]			.0003
Not immunocompromised	ref	...	
AIDS[d]	1.921	1.077-3.408	
Solid organ transplant	0.587	0.287-1.200	
Nonneutropenic solid tumor[c]	1.808	1.249-2.616	
Nonneutropenic hematologic malignancy[c]	1.414	1.002-1.994	
Neutropenia[d]	1.653	1.229-2.224	
Immune deficiency or primary immunodeficiency	0.800	0.473-1.352	
Combined profiles (n = 60)	1.289	0.771-2.157	

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So Yeon Lim
Seo Goo Han
Yeh Rim Kang
O Jung Kwon
Sookyoung Woo
Kyeongman Jeon

Early intervention on the outcomes in critically ill cancer patients admitted to intensive care units

Table 4 Multivariable analyses with logistic regression models for probability of in-hospital mortality

Variables	Adjusted odds ratio	95 % confidence interval	*p* value
Age (years)	1.027	0.996–1.058	0.086
Gender (male)	0.926	0.419–2.047	0.849
ECOG performance status (three or more)	1.278	0.562–2.902	0.558
Hematologic malignancy	0.589	0.240–1.450	0.250
Stem cell transplantation	2.537	0.789–8.153	0.118
Number of MET criteria (three or more)	3.089	1.321–7.225	0.009
Time to intervention (hours)	1.445	1.217–1.717	<0.001
Documented infection	2.172	0.901–5.238	0.084
Need for mechanical ventilation	1.307	0.544–3.140	0.550
Need for vasopressor support	0.769	0.312–1.897	0.569
PF ratio	1.002	0.999–1.005	0.207
SOFA score	1.178	1.026–1.352	0.020

Intensive Care Med (2012) 38:1505–1513

Delayed intensive care unit admission is associated with increased mortality in patients with cancer with acute respiratory failure

Djamel Mokart[1], Jérôme Lambert[2], David Schnell[3], Louis Fouché[1], Antoine Rabbat[4], Achille Kouatchet[5], Virginie Lemiale[6], François Vincent[7], Etienne Lengliné[3], Fabrice Bruneel[8], Frederic Pene[6], Sylvie Chevret[2] & Elie Azoulay[3]

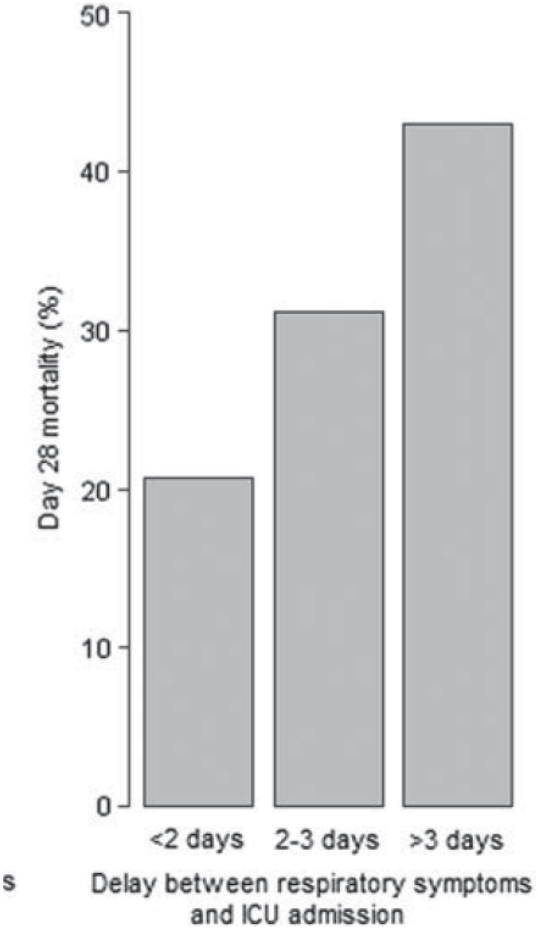

Table III. Predictors of day-28 mortality, model adjusted on LOD score.

Variable	Unadjusted odds ratio*	(95% CI)	Adjusted odds ratio†	(95% CI)	*p*-Value
Age (per 10 years)	1.26	(1.02–1.56)	1.24	(0.96–1.62)	0.09
Chronic renal insufficiency	3.35	(1.02–10.97)	2.62	(0.66–10.35)	0.17
Time between first respiratory symptoms and ICU admission > 2 days	2.43	(1.30–4.51)	2.65	(1.29–5.44)	0.01
More than one line of chemotherapy	2.15	(1.18–3.92)	1.94	(0.96–3.90)	0.06
Extra-thoracic symptoms at ICU admission	2.49	(1.25–4.97)	2.17	(0.96–4.90)	0.06
O_2 delivery (per 1 L/min)	1.09	(1.02–1.15)	1.04	(0.98–1.12)	0.21
At least 3 quadrants with lung infiltrates on chest X-ray	1.82	(1.01–3.28)	1.75	(0.87–3.52)	0.12
Total LOD score (per 1 point)	1.27	(1.14–1.41)	1.20	(1.07–1.35)	0.002

Leukemia & Lymphoma, August 2013; 54(8): 1724–1729

- RI-1–Neutropenia should probably not be used as triage criteria in cancer patients considered for ICU admission. Performance status, comorbidities, and potentially life-prolonging treatment available are more relevant in this regard (Grade 2-, strong agreement).

- RI-2–Neutropenia should probably not be considered as a prognostic factor in critically ill cancer patients (Grade 2-, weak agreement).

- RI-3–Intensive care unit admission should probably not be delayed if ICU admission is deemed necessary in critically ill cancer patients (Grade 2-, strong agreement).

2. Prophylaxie et isolement protecteur

Isolement protecteur

- Isolement « complet »
- En salle
- Etudes anciennes

- Neutropénie < 500 /mm³, > 7 jours

Impact of Air Filtration on Nosocomial Aspergillus Infections

Unique Risk of Bone Marrow Transplant Recipients

TABLE II **Variables Associated with Nosocomial Aspergillus Infection in Bone Marrow Transplant Recipients**

Variable	Aspergillus infection: Yes (14 patients)	Aspergillus infection: No (97 patients)*	p Value
Age (mean ± SD)	26 ± 14	16 ± 10	0.004†
Number of infections (mean ± SD)	2.8 ± 1.6	1.1 ± 1.3	<0.001‡
Duration of fever (days) (mean ± SD)	31 ± 19	18 ± 13	0.004‡
Duration of antibiotic therapy (days) (mean ± SD)	34 ± 16	21 ± 14	0.004‡
Duration of neutropenia (days) (mean ± SD)	24 ± 13	18 ± 10	0.02‡
Graft-versus-host disease	64%	26%	0.006§
Graft-versus-host disease needing therapy	64%	23%	0.002§
Death	93%	62%	0.004§
Underwent transplantation in HEPA room	0%	38%	0.002§

- RII-1–Protective isolation should probably be considered in patients with profound (neutrophil count less than 500/mm3) and prolonged (expected neutropenia duration more than 7 days) neutropenia (Grade 2+, strong agreement).

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Impact of contact isolation for multidrug-resistant organisms on the occurrence of medical errors and adverse events

Table 4 Risk of adverse events and medical errors according to isolation status

	Non-isolated patients 980 (100)	Isolated patients 170 (100)	Unadjusted sHR (95 % CI)	*p*	Adjusted sHR [95 % CI]	*p*[a]
Adverse events						
Accidental removal of endotracheal tube or catheter	41/784 (6.5)	14/148 (9.5)	1.2 (0.6–2.5)	0.6	1.3 (0.6–2.8)	0.5
Phlebitis/pulmonary embolism	26 980 (2.7)	15/170 (8.8)	2.8 (1.4–5.8)	0.004	1.8 (0.8–3.9)	0.15
Haemorrhage	24/980 (2.5)	15/170 (8.8)	2.4 (1.1–5.2)	0.03	1.5 (0.7–3.5)	0.3
Packed red blood cells administration (number of packs)	195/980 (19.9)	76/170 (44.7)	1.9 (1.4–2.7)	0.0001	1.3 (0.9–1.8)	0.2
Hypoglycaemia	168/980 (17.1)	74/170 (43.5)	1.9 (1.4–2.7)	0.0001	1.5 (1.0–2.1)	0.03
Hyperglycaemia	535/980 (54.6)	135/170 (79.4)	1.6 (1.2–2.0)	0.0004	1.5 (1.2–2.0)	0.002
Hypernatremia	23/980 (2.4)	11/170 (6.5)	1.3 (0.5–3.3)	0.6	0.7 (0.2–1.8)	0.4
VAP	64/497 (12.9)	50/125 (40)	1.2 (0.7–2.0)	0.5	1.1 (0.7–1.8)	0.7
VAP (sensitive isolates)	56/497 (11.3)	32/125 (25.6)	1.1 (0.6–1.9)	0.8	1.0 (0.6–1.8)	0.9
VAP (resistant isolates)	16/497 (3.2)	29/125 (23.2)	2.2 (1.4–3.4)	0.0005	2.1 (1.3–3.3)	0.002
Medical errors						
Anticoagulant prescription error	66/980 (6.7)	23/170 (13.5)	2.1 (1.2–3.5)	0.007	1.9 [1.1–3.3]	0.02
Anticoagulant administration error	31/705 (4.4)	12/148 (8.1)	1.3 (0.6–2.9)	0.5	1.0 [0.4–2.2]	0.9
Anticoagulant administration or prescription error	88/705 (12.5)	32/148 (21.6)	1.8 (1.1–2.8)	0.01	1.5 [0.9–2.5]	0.09
Insulin administration error administering insulin	417/711 (58.7)	118/158 (74.7)	1.2 (0.9–1.6)	0.2	1.0 [0.8–1.4]	0.8

Intensive Care Med (2013) 39:2153–2160

- RII-3–Protective isolation should not delay ICU admission or limit patients' clinical monitoring or access to patients' rooms in cases of emergency (Grade 1-, strong agreement).

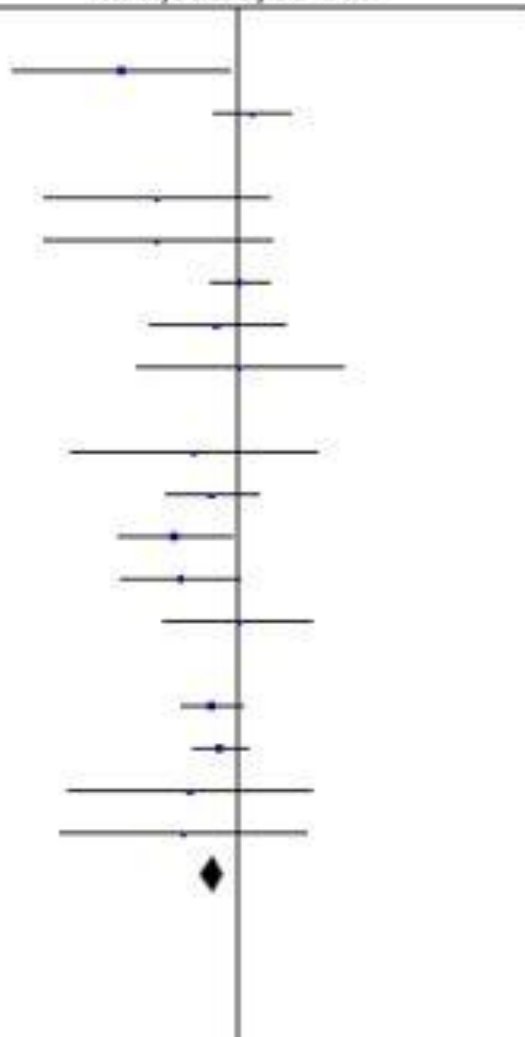
Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy *Cochrane Database Syst Rev.* ;

Anat Gafter-Gvili[1], **Abigail Fraser**[2], **Mical Paul**[3], **Liat Vidal**[1], **Theresa A Lawrie**[4], **Marianne D van de Wetering**[5], **Leontien CM Kremer**[5], and **Leonard Leibovici**[1]

Study or Subgroup	Treatment Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
1.1.1 quinolone vs. placebo/ no intervention							
Sleijfer 1980	0	53	9	52	3.9%	0.05 [0.00, 0.87]	1980
Karp 1987	8	35	5	33	2.1%	1.51 [0.55, 4.15]	1987
Lew 1991	0	7	0	11		Not estimable	1991
Schroeder 1992	0	40	3	36	1.5%	0.13 [0.01, 2.41]	1992
Sampi 1992	0	38	3	35	1.5%	0.13 [0.01, 2.47]	1992
Yamada 1993	11	53	10	53	4.0%	1.10 [0.51, 2.37]	1993
Talbot 1993	2	62	3	57	1.3%	0.61 [0.11, 3.54]	1993
Brodsky 1993	1	12	1	13	0.4%	1.08 [0.08, 15.46]	1993
Moreau 1995	0	44	0	22		Not estimable	1995
Carlson 1997	0	45	1	45	0.6%	0.33 [0.01, 7.97]	1997
Thomas 2000	5	99	5	52	2.7%	0.53 [0.16, 1.73]	2000
Nenova 2001	2	36	9	33	3.8%	0.20 [0.05, 0.87]	2001
Tjan Heijnen 2001	2	82	8	79	3.3%	0.24 [0.05, 1.10]	2001
Lee 2002	2	46	2	49	0.8%	1.07 [0.16, 7.25]	2002
Lalami 2004	0	25	0	23		Not estimable	2004
Bucaneve 2005	10	373	18	363	7.4%	0.54 [0.25, 1.16]	2005
Cullen 2005	12	781	18	784	7.3%	0.67 [0.32, 1.38]	2005
Rahman 2009	0	25	1	23	0.6%	0.31 [0.01, 7.20]	2009
Papaiakovou 2010	0	89	1	68	0.7%	0.26 [0.01, 6.18]	2010
Subtotal (95% CI)		**1945**		**1831**	**41.7%**	**0.54 [0.40, 0.74]**	
Total events	55		97				

Heterogeneity: Chi² = 16.05, df = 15 (P = 0.38); I² = 7%

Test for overall effect: Z = 3.86 (P = 0.0001)



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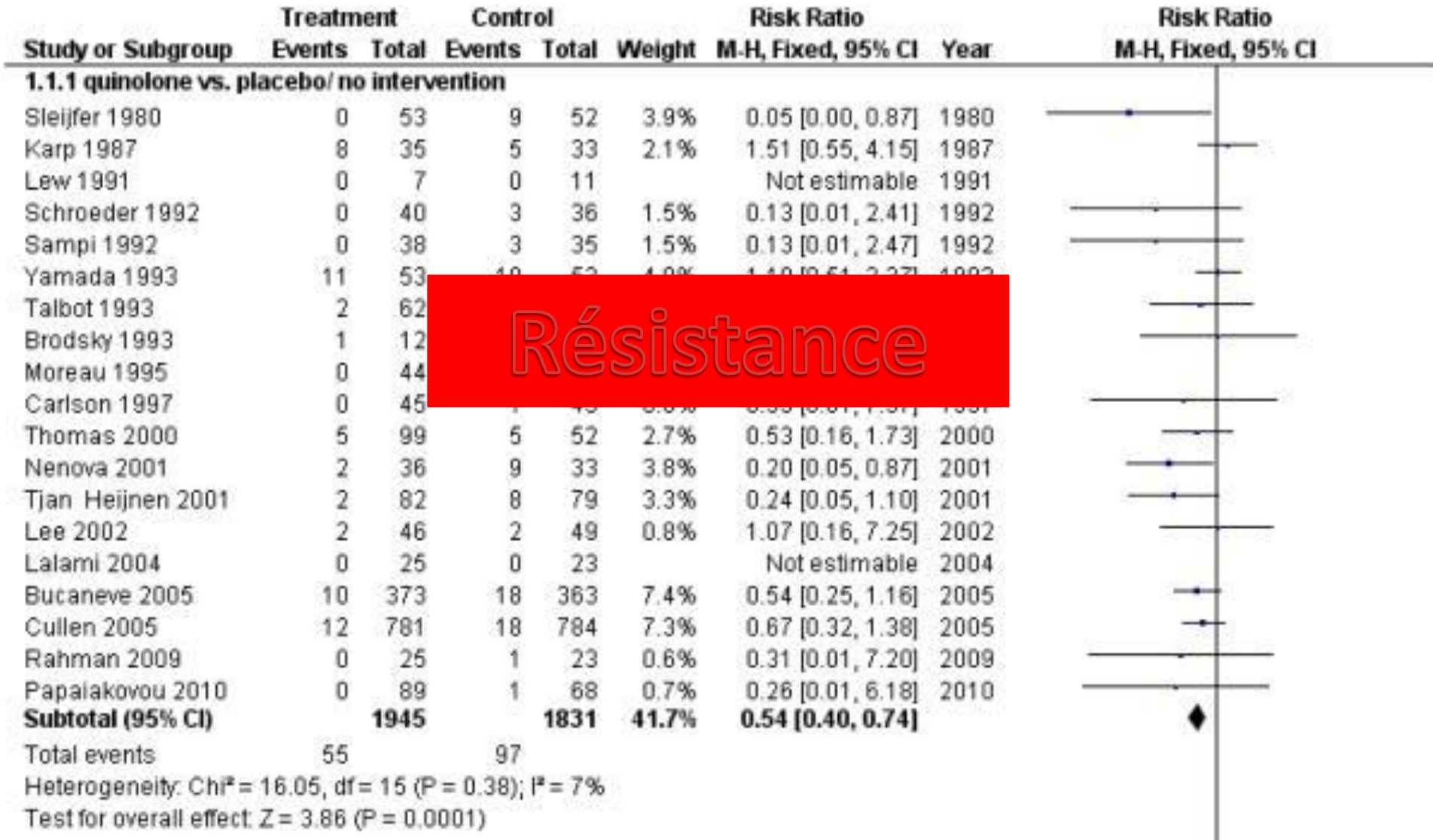
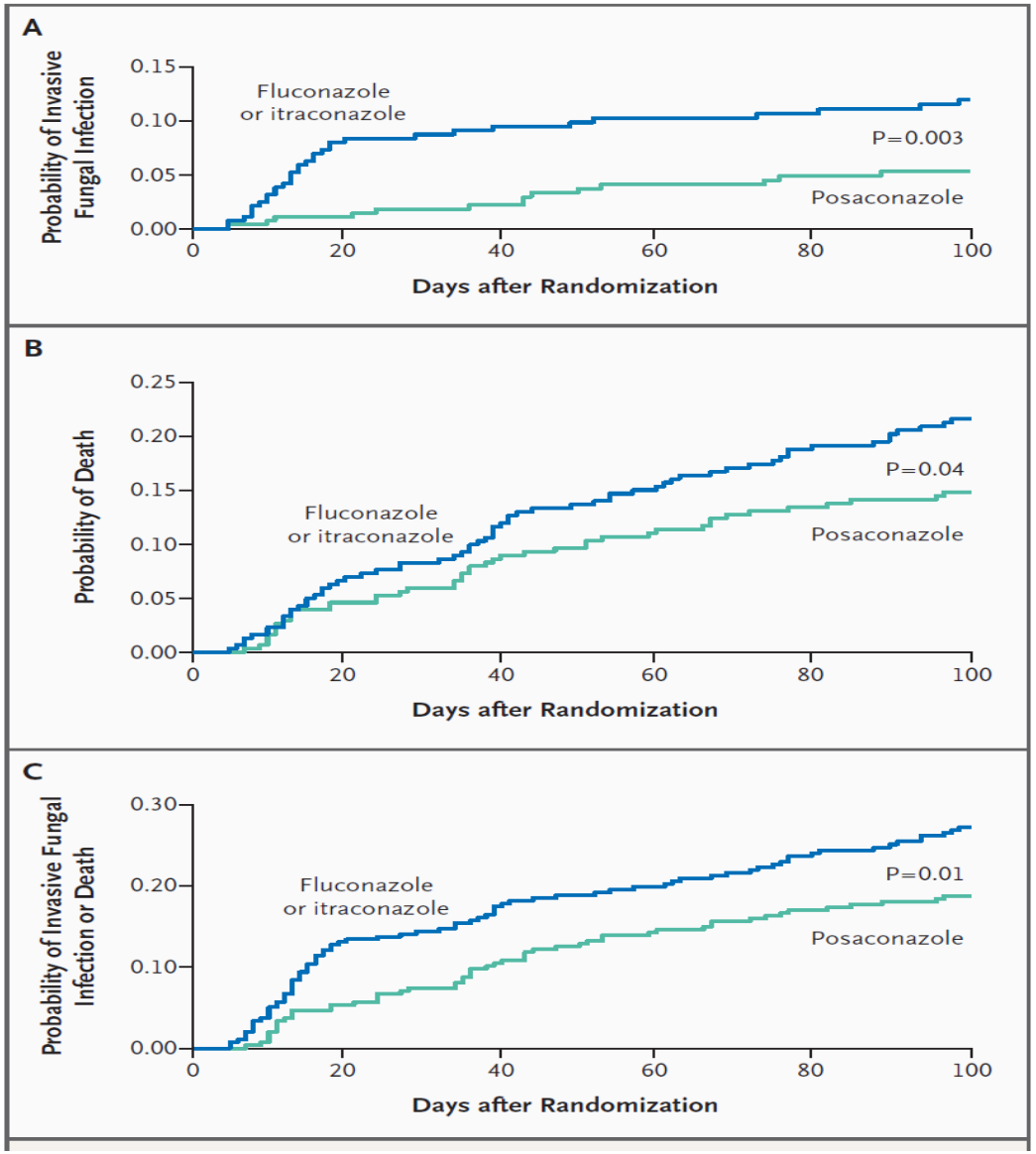


- RII-4 –Antibacterial prophylaxis should probably not be performed in critically patients with neutropenia (Grade 2-, strong agreement).

Posaconazole vs. Fluconazole or Itraconazole Prophylaxis in Patients with Neutropenia

Oliver A. Cornely, M.D., Johan Maertens, M.D., Drew J. Winston, M.D.,



- RII-5–Anti-Aspergillus prophylaxis should probably be used in critically ill neutropenic patients with acute myeloid leukemia or myelodysplastic syndrome with both induction and consolidation therapy used when neutropenia is expected to be profound (neutrophil count less than 500/mm3) and with an expected duration of at least 15 days (Grade 2+, weak agreement).

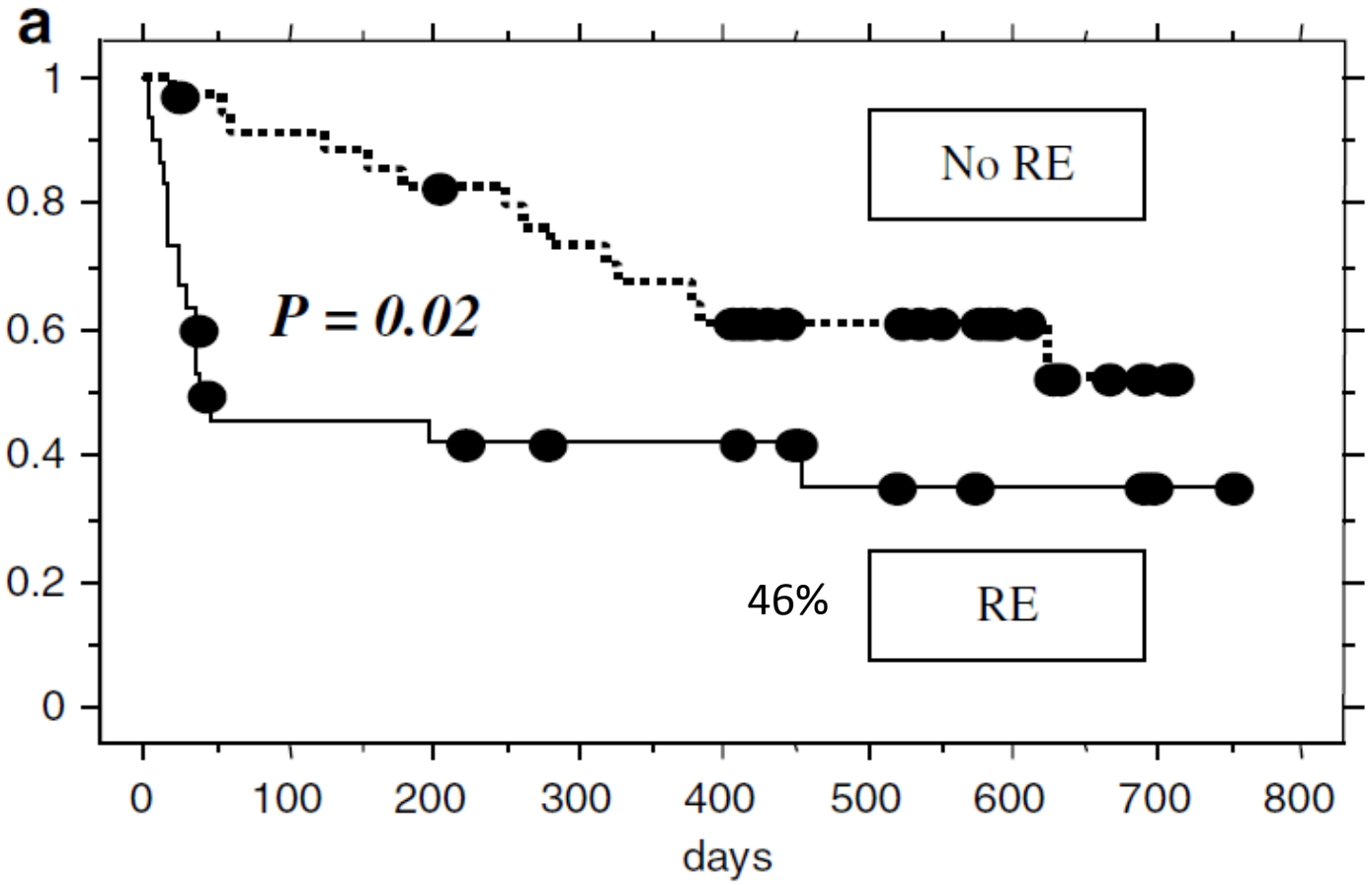
- RII-6–Anti-Aspergillus prophylaxis should probably be used in high-risk critically ill neutropenic patients (myeloablative conditioning regimens, older patients, transplant in patients with active disease, umbilical/placental cord blood transplant) (Grade 2+, weak agreement).

- RII-7–Anti-Aspergillus prophylaxis should probably be used in critically ill neutropenic patients with severe idiopathic medullary aplasia (neutrophil count less than 500/mm3) (Grade 2+, weak agreement).

3. Insuffisance respiratoire aigue

Incidence and prognostic value of respiratory events in acute leukemia

D Chaoui[1], O Legrand[1], N Roche[2], M Cornet[3], A Lefebvre[2], R Peffault de Latour[1], L Sanhes[1], G Huchon[2], J-P Marie[1] and A Rabbat[2]



Leukemia (2004) 18, 670–675

Prognosis of acute respiratory distress syndrome in neutropenic cancer patients

Djamel Mokart*, Thomas van Craenenbroeck*, Jérôme Lambert#, Julien Textoris*, Jean-Paul Brun*, Antoine Sannini*, Laurent Chow-Chine*, Smail Hamouda*, Louis Fouché*, Florence Ettori*, Marion Faucher* and Jean-Louis Blache*

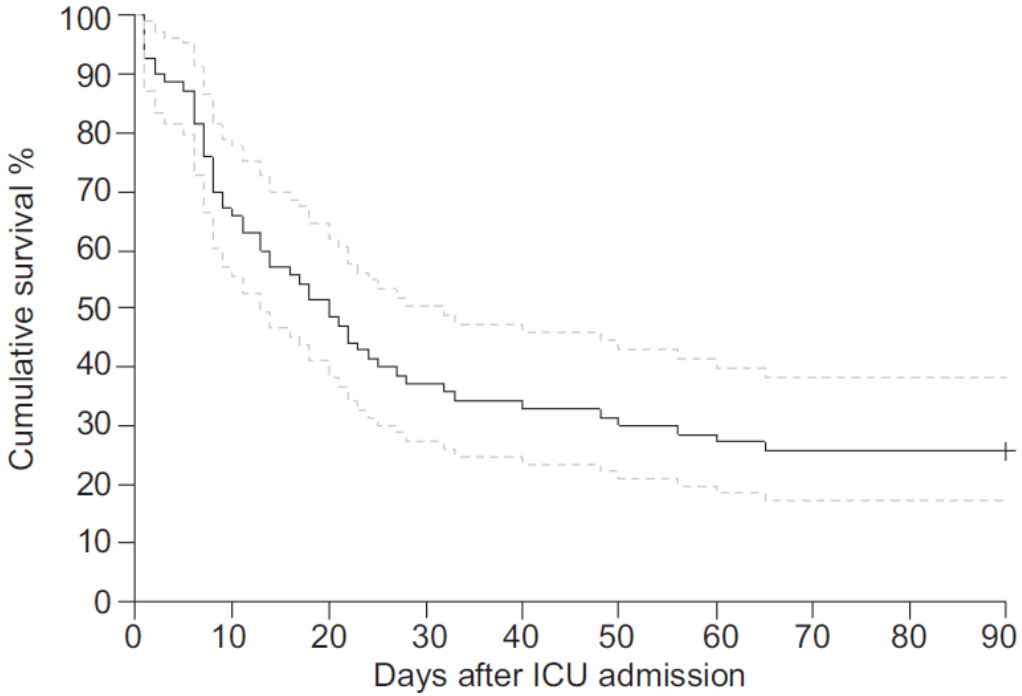


FIGURE 2. Survival in neutropenic patients with aquired respiratory distress sydrome. Overall survival is truncated at 90 days. -----: 95% confidence interval. ICU: intensive care unit.

Eur Respir J 2012; 40: 169–176

TABLE 3 Factors independently related to day-28 survival

	OR (95% CI)	p-value
Lobar ARDS	0.10 (0.02–0.48)	0.0038
Initial antibiotic treatment active on DTT bacteria	0.08 (0.02–0.33)	0.0007
First-line chemotherapy	0.08 (0.02–0.37)	0.0014

Diagnostic strategy in cancer patients with acute respiratory failure.

TABLE 1 DIRECT criteria for identifying the most likely causes of acute respiratory failure in cancer patients [12, 25]

Delay since malignancy onset or HSCT, since symptom onset and since implementation of antibiotics/ prophylaxis
Pattern of **i**mmune deficiency
Radiographic appearance
Experience and knowledge of the literature
Clinical picture (including ongoing chemoprophylaxis and effective antibiotic therapy)
Findings by HRC**T**

HSCT: haematopoietic stem-cell transplantation; HRCT: high-resolution computed tomography.

Azoulay *Intensive Care Med* 2006; 32: 808–822.

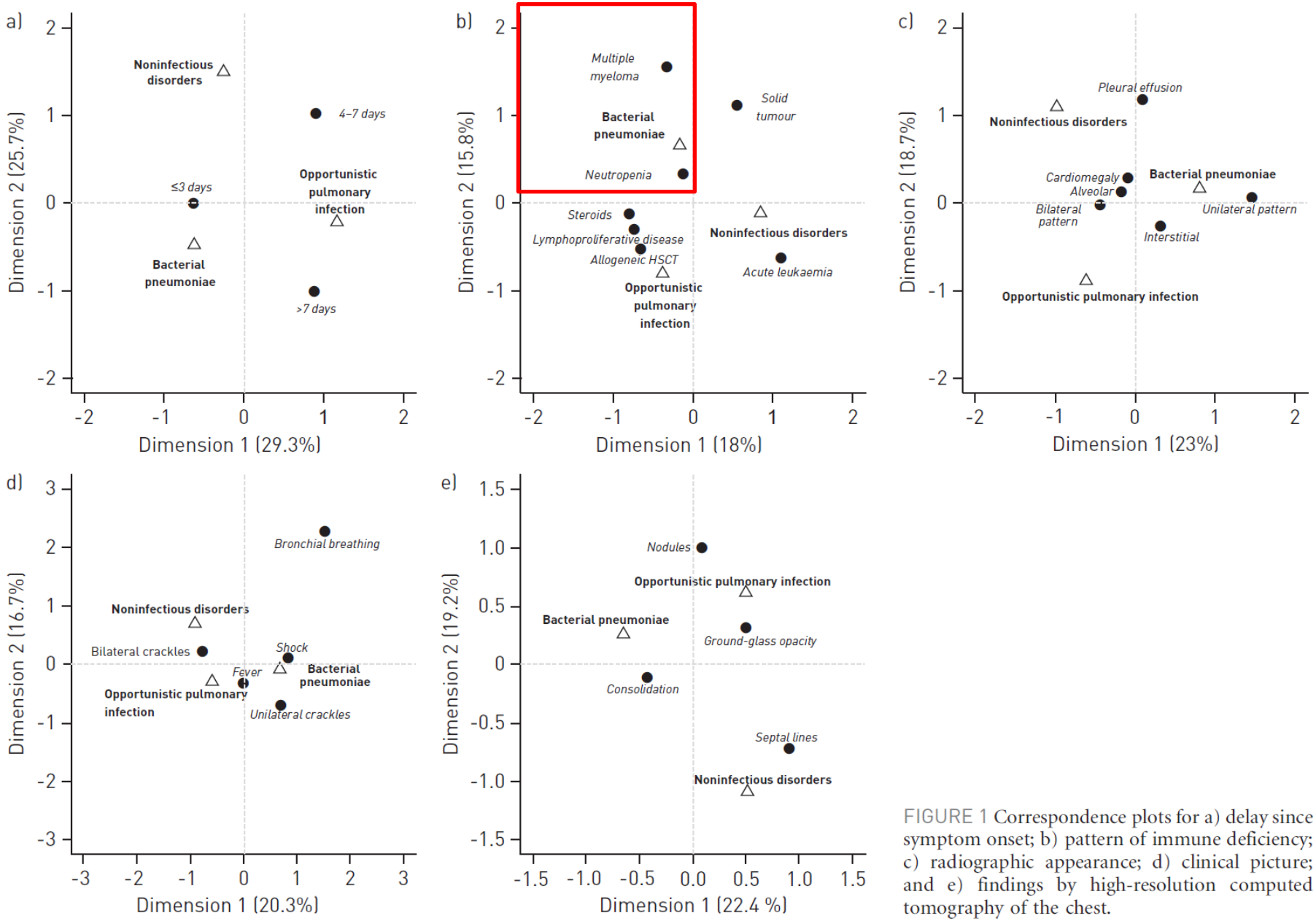
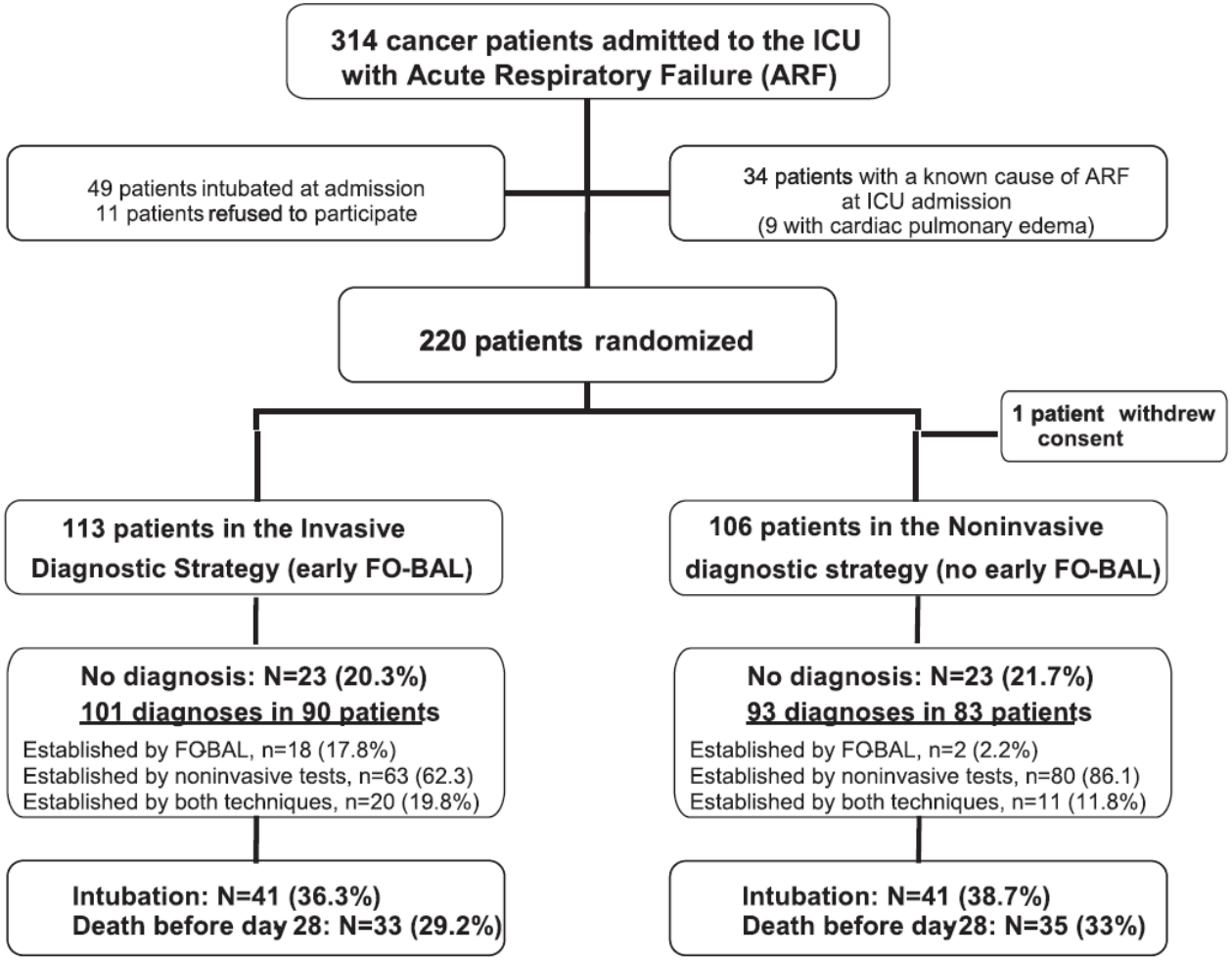


FIGURE 1 Correspondence plots for a) delay since symptom onset; b) pattern of immune deficiency; c) radiographic appearance; d) clinical picture; and e) findings by high-resolution computed tomography of the chest.

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Élie Azoulay[1], Djamel Mokart[2], Jérôme Lambert[3], Virginie Lemiale[4], Antoine Rabbat[5], Achille Kouatchet[6], François Vincent[7], Didier Gruson[8], Fabrice Bruneel[9], Géraldine Epinette-Branche[1], Ariane Lafabrie[1], Rebecca Hamidfar-Roy[10], Christophe Cracco[11], Benoît Renard[12], Jean-Marie Tonnelier[13], François Blot[14], Sylvie Chevret[3], and Benoît Schlemmer[1]



Am J Respir Crit Care Med Vol 182. pp 1038–1046, 2010

Open Lung Biopsy Diagnosis of Diffuse Pulmonary Infiltrates After Marrow Transplantation*

Stephen W. Crawford, M.D., F.C.C.P.;† Robert C. Hackman, M.D.;‡ and Joan G. Clark, M.D.†

Table 2—*Results of Open Lung Biopsies in Marrow Transplantation Recipients with Diffuse Pulmonary Infiltrates**

	Days After Transplantation			
	0-29	30-59	60-180	Total
Noninfectious diagnosis, n (%)				
Idiopathic interstitial	19	6	5	30(27)
Bronchiolitis	1	1	2	4
Edema	1	1		2
Other†		2	3	5
Total noninfectious cases	21(81)	10(25)	10(22)	41(37)
Infectious diagnosis, n (%)				
Cytomegalovirus	4	29	30	63(57)
Pneumocystis carinii		1	5	6
Yeast‡			2	2
Bacteria		1	1	2
Respiratory syncytial virus	1	1		2
Total infections	5	32	38	75
Total cases with infection	5(19)	30(75)	35(78)	70(63)
Total cases	26	40	45	111

Diagnostic contribution from pulmonary biopsies in hematology patients with acute respiratory failure from undetermined etiology

J. GAY [1], V. LEMIALE [1], V. MEIGNIN [2], C. BRON [1], C. DE BAZELAIRE [3]
D. SCHNELL [1], E. CANET [1], A. SEGUIN [1], E. AZOULAY [1]

TABLE II.—*Suspected diagnosis and results of lung biopsy similarity for diagnostic biopsies.*

			DIAGNOSTIC BIOPSIES			
Case	Type of biopsy	Underlying disease	Pre-biopsy diagnosis	Pathologic findings	Final diagnosis	Therapeutic modifications
1	CT scan guided	Idiopathic Aplastic anemia	Invasive aspergillosis	Granulomas with acid fast positive bacilli	Mycobacteria	Antituberculous treatment started
2	CT scan guided	Hodgkin Lymphoma	Invasive aspergillosis	Hodgkin Lymphoma	Relapse	Chemotherapy
3	CT scan guided	Non Hodgkin Lymphoma	Invasive aspergillosis	Inflammation without micro-organism nor lymphoma cells	Bacterial acute pneumonia	Stop antifungal therapy
4	Surgical biopsy	T-cell lymphoma	Lymphoid Interstitial pneumonia	T- cell lymphoma	Relapse	Chemotherapy
5	Surgical biopsy	Chronic lymphocytic leukemia	Solid tumor	Acute bronchiolitis and fibrosis alveolitis	Herpes zoster infection	None
6	Surgical biopsy	Myelodysplastic syndrome	Leukemic infiltrates	Organizing pneumonia	Organizing pneumonia	Steroids
7	Surgical biopsy	MALT lymphoma	Lymphoid Interstitial pneumonia	MALT lymphoma	Relapse	Chemotherapy
8	Surgical biopsy	Hemophagocytic lymphohistiocytosis	Mycobacterial infection	Lung Kaposi sarcoma	Kaposi sarcoma	Comfort care
9	Surgical biopsy	Chronic myeloid leukaemia	Cryptogenic Organizing pneumonia	Bronchiolitis obliterans	Bronchiolitis obliterans	Maintained steroid therapy
10	Surgical biopsy	Hodgkin Lymphoma	Toxicity or pneumocystosis	Inflammation with dystrophic cells	Drug toxicity	None
11	Surgical biopsy	Multiple myeloma	Mycobacteria/ bacteria	Diffuse alveolar damage	No diagnosis	None

- RIII-1–Acute respiratory failure should be considered as a therapeutic emergency in critically ill patients with neutropenia (Grade 1+, strong agreement).

- RIII-2–Etiological diagnosis of ARF should be considered as a primary objective in this setting (Grade 1+, strong agreement).

- RIII-3–The diagnostic workup should include systematic analysis of the underlying condition, severity and duration of neutropenia, underlying immunosuppression, preexisting treatment and prophylaxis, clinical course of ARF, and clinical and radiological features (Grade 1+, strong agreement).

- RIII-4–Invasive and non-invasive diagnostic tests should probably be prescribed according to pretest probability rather than being performed systematically. This should particularly be the case for bronchoscopy with bronchoalveolar lavage (Grade 2+, strong agreement).

- RIII-5–Pulmonary biopsies should probably be performed only on a case-by-case basis by a multidisciplinary team after careful assessment of both clinical suspicion and the risk-to-benefit ratio (Grade 2+, strong agreement).

4. Défaillance et support d’organes

- Typhlite
- Support ventilatoire
- Epuration extra-rénale

4. Défaillance et support d'organes

- Typhlite
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Neutropenic enterocolitis in adults: systematic analysis of evidence quality

Table 4. Suggested diagnostic criteria for neutropenic enterocolitis

Presence of *fever* (axillary temperature >38.0°C or rectal temperature >38.5°C)
Abdominal pain (at least degree 3 determined by the patient using a visual analogous scale pain score ranging from degree 1 to 10)
Demonstration of the *bowel wall thickening* of more than 4 mm (transversal scan) over more than 30 mm (longitudinal scan) in any segment by US or CT

- RIV-1–Neutropenic enterocolitis (Typhlitis) should probably be considered in critically ill neutropenic patients with fever and acute abdomen, particularly in cases of recent cancer chemotherapy known to be associated with a high rate of oral or gastrointestinal toxicity (Grade 2+, strong agreement).

- RIV-2–In adult patients, a complete diagnostic workup, including an abdominal CT scan with contrast media, should probably be performed (Grade 2+, strong agreement). In the pediatric setting, abdominal ultrasonography should probably be performed as first-line imaging (Grade 2+, strong agreement).
- RIV-3–First-line colonoscopy should probably be avoided in patients with high suspicion of typhlitis (Expert opinion, strong agreement).

Guidelines for the Selection of Anti-infective Agents for Complicated Intra-abdominal Infections

Joseph S. Solomkin,[1] John E. Mazuski,[2] Ellen J. Baron,[3] Robert G. Sawyer,[4] Avery B. Nathens,[5] Joseph T. DiPiro,[6,7] Timothy Buchman,[2] E. Patchen Dellinger,[5] John Jernigan,[8] Sherwood Gorbach,[9] Anthony W. Chow,[11] and John Bartlett[10]

- AB adaptée à l'écologie microbiologique locale et à la colonisation du patient
- Doit être active sur *Enterococcus*, *Enterobacteriaceae*, anaerobies et *Pseudomonas aeruginosa*
- Utilisation systématique de glycopeptide ou de metronidazole de bénéfice incertain
- Une thérapie antifungique de première ligne ne peut pas être recommandée au vu de l'incidence faible d'infection fongique invasive (5%) lors des typhlites. Cependant, l'absence d'amélioration clinique à 72 h devrait entraîner l'initiation d'un antifungique.

CID 2003:37 (15 October)

- RIV-4–Management of typhlitis should include broad-spectrum antibiotic therapy along with multidisciplinary management, including consultation of a general or abdominal surgeon (Grade 1+, strong agreement).

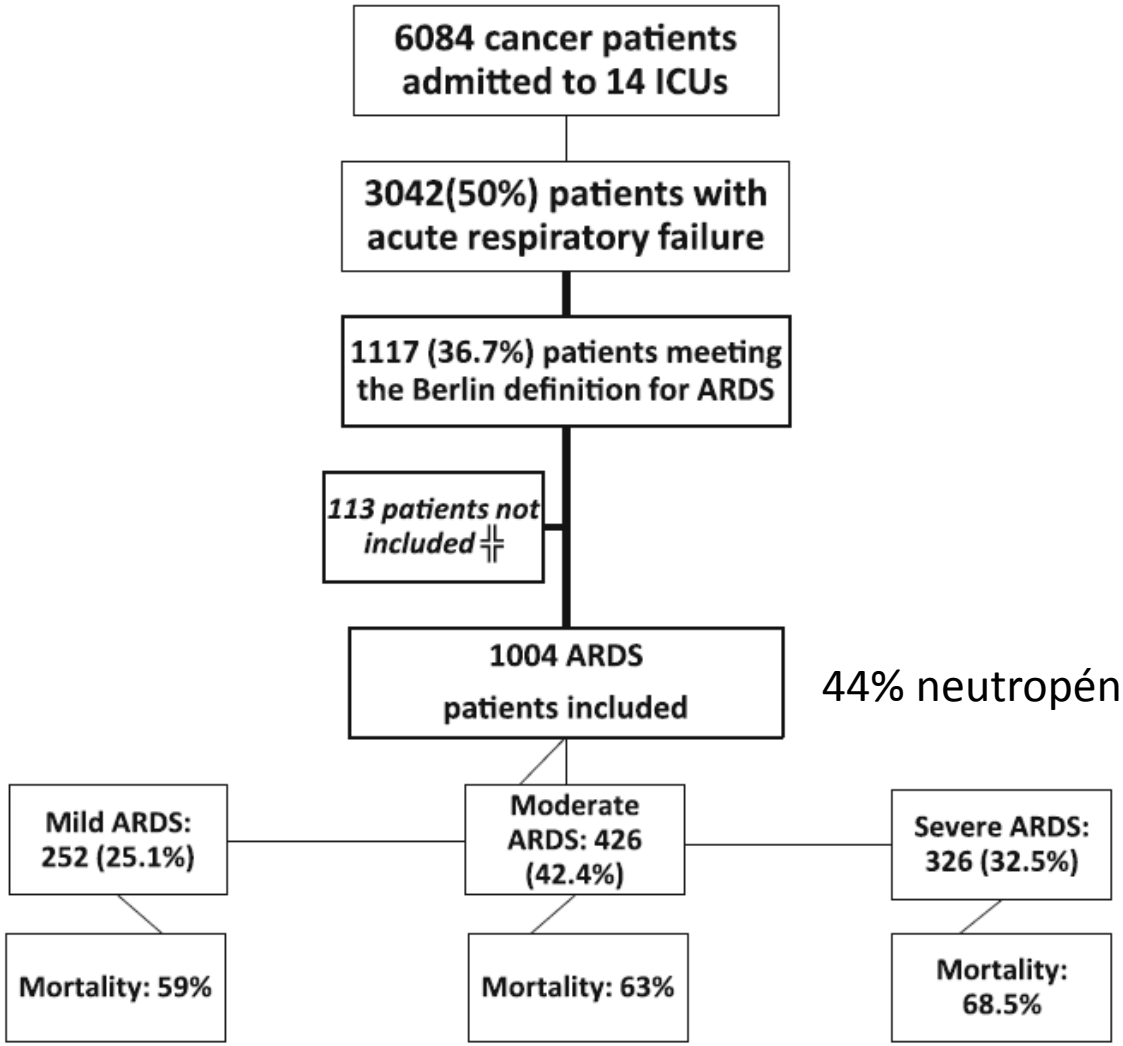
- RIV-5–Neutropenia and thrombocytopenia should not modify the timing of surgery in patients with suspicion of digestive tract perforation (Grade 1+, strong agreement).

4. Défaillance et support d'organes

- Typhlite
- Support ventilatoire
- Epuration extra-rénale

Acute respiratory distress syndrome in patients with malignancies

Elie Azoulay
Virginie Lemiale
Djamel Mokart
Frédéric Pène
Achille Kouatchet
Pierre Perez
François Vincent
Julien Mayaux
Dominique Benoit
Fabrice Bruneel
Anne-Pascale Meert
Martine Nyunga
Antoine Rabbat
Michael Darmon



44% neutropéniques

Intensive Care Med (2014) 40:1106–1114

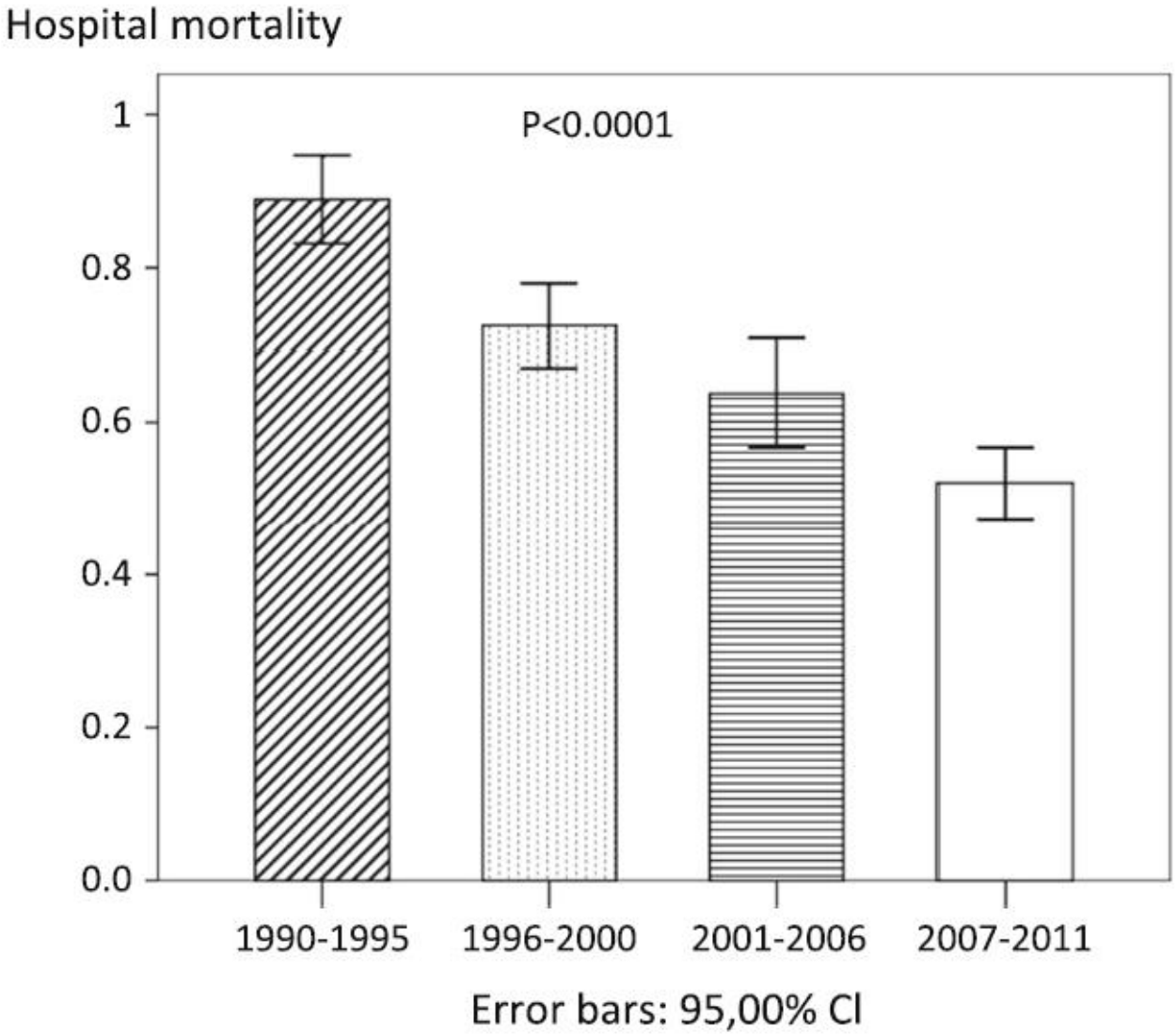


Fig. 2 Hospital mortality according to period of admission to the intensive care unit

Table 3 Factors independently associated with hospital mortality

	OR	95 % CI	*p* value
Solid tumor	0.51	(0.34–0.77)	0.002
Need for emergency surgery	0.61	(0.35–1.05)	0.07
Allogeneic BMT/HSCT	1.71	(1.07–2.71)	0.04
mSOFA (per point)	1.11	(1.06–1.16)	<0.001
Cause of respiratory involvement			
No definite diagnosis	1	(Reference)	–
Primary ARDS	0.41	(0.20–0.88)	0.02
Secondary ARDS	0.90	(0.41–2.01)	0.80
Invasive fungal infection	1.72	(1.25–2.37)	0.001
Ventilation			
NIV	1	(Reference)	–
NIV failure	2.93	(1.80–4.79)	<0.001
Endotracheal MV	3.24	(2.02–5.24)	<0.001
ARDS severity			
Mild	1	(Reference)	–
Moderate	1.25	(0.88–1.78)	0.22
Severe	1.61	(1.10–2.36)	0.01

Improved survival in cancer patients requiring mechanical ventilatory support: Impact of noninvasive mechanical ventilatory support

Elie Azoulay, MD; Corinne Alberti, MD; Caroline Bornstain, MD; Ghislaine Leleu, MD; Delphine Moreau, MD; Christian Recher, MD; Sylvie Chevret, MD, PhD; Jean-Roger Le Gall, MD; Laurent Brochard, MD, PhD; Benoît Schlemmer, MD

- Etude cas-contrôle
- Mortalité USI 43, 7% groupe VNI
  70,8% groupe VMI.

Crit Care Med 29:519-525;2001

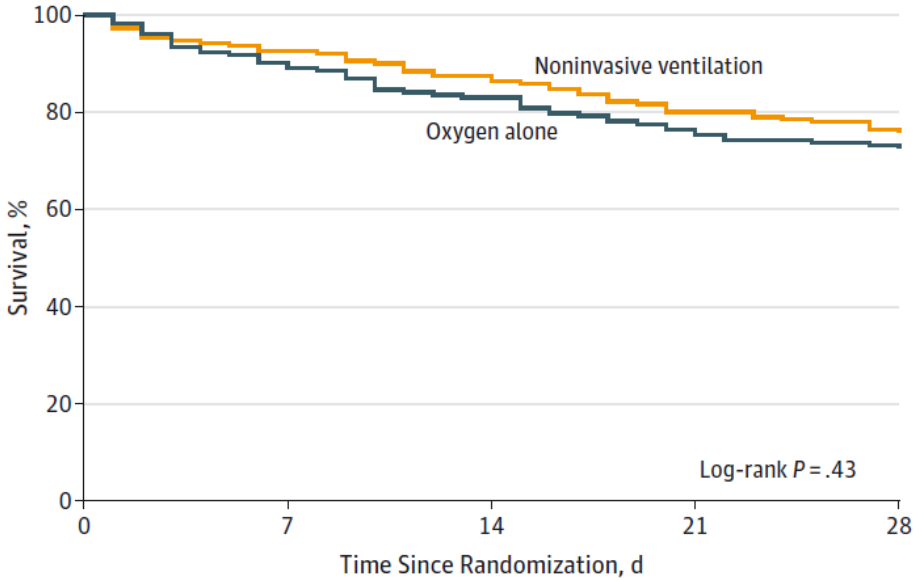
Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure

A Randomized Clinical Trial

JAMA. 2015;314(16):1711-1719.

Virginie Lemiale, MD; Djamel Mokart, MD; Matthieu Resche-Rigon, MD, PhD; Frédéric Pène, MD, PhD; Julien Mayaux, MD; Etienne Faucher, MD; Martine Nyunga, MD; Christophe Girault, MD, PhD; Pierre Perez, MD; Christophe Guitton, MD, PhD; Kenneth Ekpe, MD; Achille Kouatchet, MD; Igor Théodose, MS; Dominique Benoit, MD, PhD; Emmanuel Canet, MD; François Barbier, MD, PhD; Antoine Rabbat, MD; Fabrice Bruneel, MD; Francois 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 Reignier, MD, PhD; Laurent Papazian, MD, PhD; Ilham Mehzari, MD; Yves 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 (GRRR-OH)

Figure 2. Probability of Survival at Day 28



No. at risk					
Noninvasive ventilation	191	177	167	153	146
Oxygen alone	183	165	152	140	134

Probability of survival and subgroup analyses of the risk of day-28 mortality Kaplan-Meier estimates of the probability of day-28 mortality in immunocompromised patients with acute respiratory failure receiving either early noninvasive ventilation or oxygen only. Statistical test used the log-rank test.

- RIV-6–Neutropenia in itself should probably not modify ventilatory support in critically ill cancer patients (Grade 2-, strong agreement).

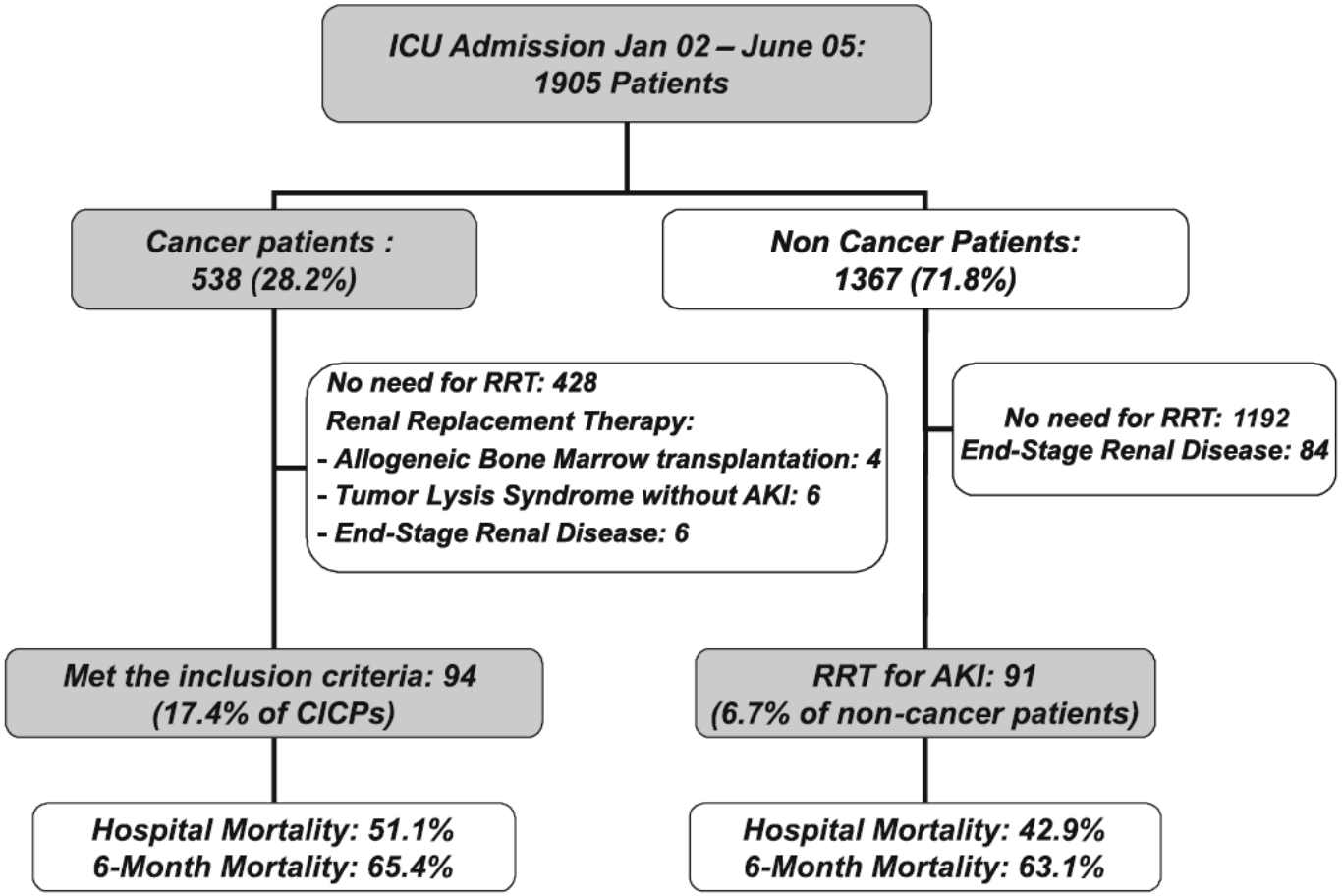
- RIV-7–Invasive mechanical ventilation should probably not be delayed only as a consequence of neutropenia, underlying malignancy, or immunocompromised status (Grade 2-, weak agreement).

4. Défaillance et support d'organes

- Typhlite
- Support ventilatoire
- Epuration extra-rénale

Michael Darmon
Guillaume Thiery
Magali Ciroldi
Raphaël Porcher
Benoît Schlemmer
Élie Azoulay

Should dialysis be offered to cancer patients with acute kidney injury?



Intensive Care Med (2007) 33:765–772

- RIV-8–An indication for renal replacement therapy should probably not be modified by neutropenia in itself (Grade 2-, strong agreement).

5. Antibiothérapie

β lactam monotherapy versus β lactam-aminoglycoside combination therapy for fever with neutropenia: systematic review and meta-analysis

Mical Paul, Karla Soares-Weiser, Leonard Leibovici

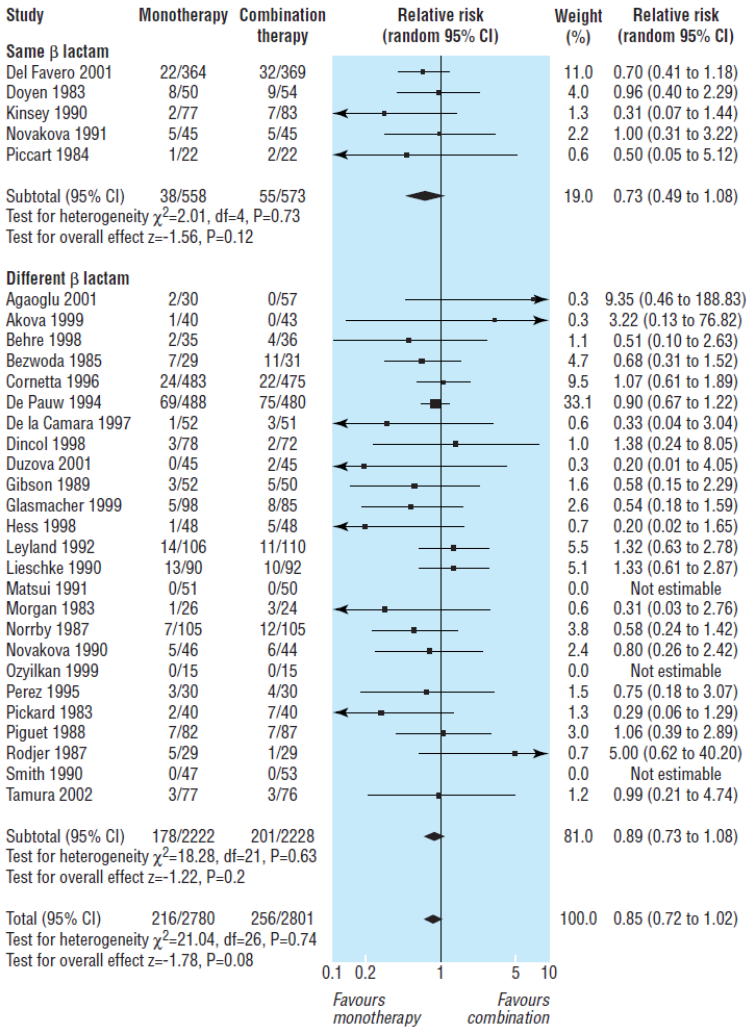


Fig 2 All cause fatality

Monotherapy versus β-Lactam–Aminoglycoside Combination Treatment for Gram-Negative Bacteremia: a Prospective, Observational Study

LEONARD LEIBOVICI,[1]* MICHAL PAUL, ODED POZNANSKI, MOSHE DRUCKER, ZMIRA SAMRA, HANNA KONIGSBERGER, AND SILVIO D. PITLIK

The aim of the present study was to test whether the combination of a β-lactam drug plus an aminoglycoside has advantage over monotherapy for severe gram-negative infections. Of 2,124 patients with gram-negative bacteremia surveyed prospectively, 670 were given inappropriate empirical antibiotic treatment and the mortality rate in this group was 34%, whereas the mortality rate was 18% for 1,454 patients given appropriate empirical antibiotic treatment ($P = 0.0001$). The mortality rates for patients given appropriate empirical antibiotic treatment were 17% for 789 patients given a single β-lactam drug, 19% for 327 patients given combination treatment, 24% for 249 patients given a single aminoglycoside, and 29% for 89 patients given other antibiotics ($P = 0.0001$). When patients were stratified according to risk factors for mortality other than antibiotic treatment, combination therapy showed no advantage over treatment with a single β-lactam drug except for neutropenic patients (odds ratio [OR] for mortality, 0.5; 95% confidence interval [95% CI], 0.2 to 1.3) and patients with *Pseudomonas aeruginosa* bacteremia (OR, 0.7; 95% CI, 0.3 to 1.8). On multivariable logistic regression analysis including all risk factors for mortality, combination therapy had no advantage over therapy with a single β-lactam drug. The mortality rate for patients treated with a single appropriate aminoglycoside was higher than that for patients given a β-lactam drug in all strata except for patients with urinary tract infections. When the results of blood cultures were known, 1,878 patients were available for follow-up. Of these, 816 patients were given a single β-lactam drug, 442 were given combination treatment, and 193 were given a single aminoglycoside. The mortality rates were 13, 15, and 23%, respectively ($P = 0.0001$). Both on stratified and on multivariable logistic regression analyses, combination treatment showed a benefit over treatment with a single β-lactam drug only for neutropenic patients (OR, 0.2; 95% CI, 0.05 to 0.7). In summary, combination treatment showed no advantage over treatment with an appropriate β-lactam drug in nonneutropenic patients with gram-negative bacteremia.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 1997, p. 1127–1133

- RV-1–Combination therapy with aminoglycoside should probably be used as initial antibiotic therapy in neutropenic patients with severe sepsis or septic shock (Expert opinion, Weak agreement).

- RV-2–Glycopeptide antibiotic adjunctive agents (or other agents active against resistant aerobic gram-positive cocci) should probably be considered for the following specific clinical indications:

  V-2-a–Suspected catheter-related infection (Grade 2+, strong agreement).

  V-2-b–Skin or soft tissue infection (Grade 2+, strong agreement).

  V-2-c–Severe sepsis or septic shock (Grade 2+, weak agreement).

  V-2-d–Use of antipseudomonal b-lactam agent with insufficient anti-gram-positive activity (ceftazidime, for example) (Grade 2+, weak agreement).

  V-2-e–Grade III or IV mucositis (Grade 2+, weak agreement).

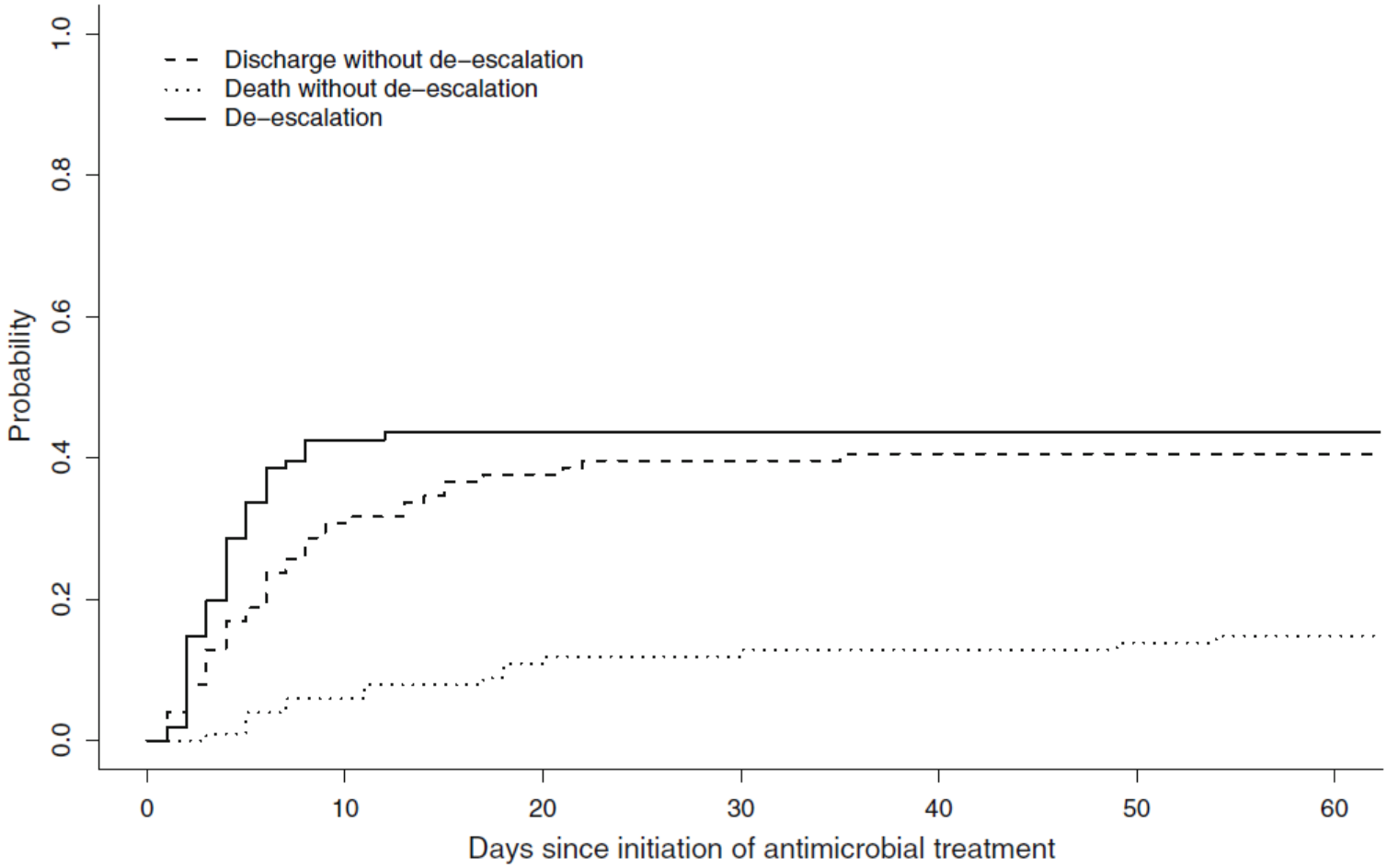
  V-2-f–Known colonization with methicillin-resistant Staphylococcus aureus (Grade 2+, weak agreement).

- RV-3–If used empirically, glycopeptide antibiotics should probably be reconsidered and discontinued in the following situations:

  - After 72 h and if no resistant gram-positive cocci have been identified (Expert opinion, weak agreement).

  - If infection is related to bacteria susceptible to a b-lactam agent (Expert opinion, strong agreement).

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



Intensive Care Med (2014) 40:41–49

- RV-4–Antibiotic de-escalation should probably be considered in the following situations:
  - When infection is related to susceptible organism (Expert opinion, strong agreement).
  - In patients without documented bacterial infection and with stable clinical condition (Expert opinion, weak agreement).

- RV-5–Indwelling catheters should probably be removed immediately in neutropenic patients with septic shock and no identifiable clinical infection (Grade 2+, strong agreement).

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

Table 1 Multivariate analysis of independent factors associated with ICU mortality

ICU mortality	Odds ratio	95 % confidence interval	*p*
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

Intensive Care Med (2014) 40:1173–1174

6. Prise en charge hématologique

A. Bouchama
B. Khan
W. Djazmati
K. Shukri

Hematopoietic colony-stimulating factors for neutropenic patients in the ICU

Table 3 Outcome. Values are mean ± SE or number of patients (%)

	G-/GM-CSF ($n = 30$)	Control ($n = 30$)	p
Neutrophil recovery ($> 1.0 \times 10^9$/l)	11 (36.6)	10 (33.3)	0.168
Recovery time (days)	7.8 ± 1.4	5.7 ± 1.3	0.28
Length of ICU stay (days)	7.8 ± 1.1	8.9 ± 1.5	0.55
ICU survival	7 (23)	3 (10)	0.168

Intensive Care Med (1999) 25: 1003–1005

Impact of colony-stimulating factor therapy on clinical outcome and frequency rate of nosocomial infections in intensive care unit neutropenic patients

Didier Gruson, MD; Gilles Hilbert, MD; Frederic Vargas, MD; Ruddy Valentino, MD; Genevieve Chene, MD; Jean-Michel Boiron, MD; Josy Reiffers, MD; Georges Gbikpi-Benissan, MD; Jean-Pierre Cardinaud, MD

Table 2. Days of leukopenia, leukocyte count at intensive care unit (ICU) admission, and leukocyte count at ICU admission

Variables	Patients With CSF (n = 28)	Patients Without CSF (n = 33)	*p* Value
Time between the onset of neutropenia and ICU admission, days	7 ± 4	6.6 ± 4	.69
Leukocyte count at ICU admission, mm^3/L	240 ± 204	272 ± 191	.52
Leukocyte count at the exit of ICU, mm^3/L (surviving patients)	506 ± 345	615 ± 582	.34
Leukocyte count on day of death, mm^3/L	784 ± 841	797 ± 895	.95
Patients who recovered from neutropenia in ICU, no. (%)	7 (25)	9 (27)	.84
In ICU, no. of days of antibiotherapy	11 ± 6	11 ± 4	.8
Time between ICU admission and the day of recovery from neutropenia, days	14 ± 2	13 ± 3	.22

CSF, colony-stimulating factor.

Table 3. Nosocomial infections occurring during intensive care unit hospitalization, number of patients, sites of infection, and survival

Variable	Patients With CSF (n = 28)	Patients Without CSF (n = 33)	*p* Variable
Microbiologically documented nosocomial infections, (%)	8 (28)	11 (33)	.69
Survival of patients with microbiologically documented nosocomial infections, no.	0	1	—
Recovery from neutropenia before having microbiologically documented nosocomial infection, no. of patients (%)	4 (50)	8 (73)	.59
Nosocomial ventilator-associated pneumonia, no.	5	6	—
Urinary tract infection, no.	2	3	—
Catheter-related infection, no.	1	2	—

Respiratory status deterioration during G-CSF-induced neutropenia recovery

L Karlin, M Darmon, G Thiéry, M Ciroldi, S de Miranda, A Lefebvre, B Schlemmer and É Azoulay

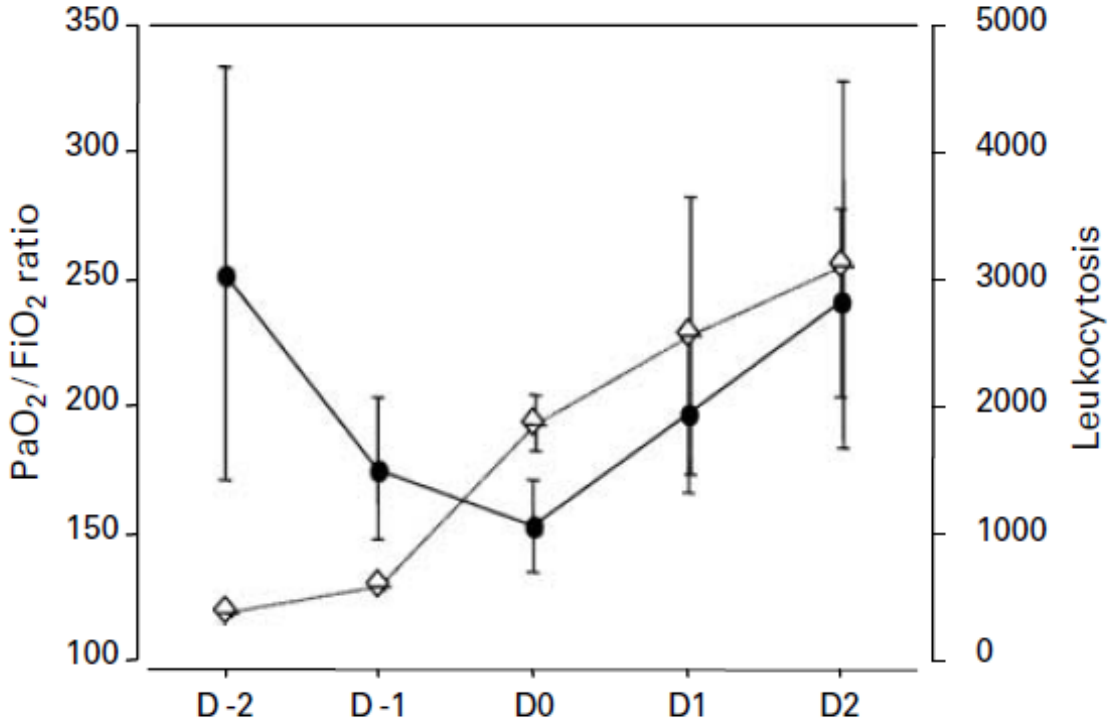


Figure 1 Time course of PaO_2/FiO_2 ratio (closed circles) and total leukocyte count (lozenges) during the 5-day period centered on the day of neutropenia recovery (D0).

Bone Marrow Transplantation (2005) 36, 245–250

- RVI-1–Prophylactic use of G-CSF should probably be initiated or resumed in critically ill patients with neutropenia or requiring cancer chemotherapy with expected medullary toxicity (Grade 2+, weak agreement).

- RVI-2–G-CSF should probably be stopped when worsening of respiratory status during neutropenia recovery is suspected or before neutropenia recovery in patients at high risk of worsening of respiratory status during neutropenia recovery (preexisting respiratory failure or pulmonary infection) (Grade 2+, strong agreement).

Pour en savoir plus…

REAMID

DU de réanimation des patients immunodéprimés (hématologie, oncologie, greffes d'organes, VIH, autres)
Renseignements: florence.delaporte@aphp.fr

Objectifs

1 - Comprendre le bénéfice attendu de la réanimation chez les patients immunodéprimés (VIH, maladies de système, greffés d'organe, oncologie, hématologie, greffes de moelle).

2 - Orienter de façon optimale les patients immunodéprimés atteints de défaillances aiguës d'organe.

3 - Comprendre, pour mieux traiter, la physiopathologie des défaillances aiguës d'organe.

4 - Prendre en charge les principales défaillances aiguës d'organe des patients immunodéprimés.

5 - Renvoi vers des experts de l'immunodépression à même de donner un avis de recours.

Dates 2017-2018

Module 1 :

Comprendre l'immunologie: 19/10/2017

Réanimation des patients infectés par le VIH: 20/10/2017

Module 2 :

Réanimation des patients transplantés d'organe solide: 23/11/2017

Immunodépression médicamenteuse: 24/11/2017

Module 3 :

Réanimation des malades d'oncologie: 14/12/2017

Maladies de système en réanimation: 15/12/2017

Module 4 :