

L'arrivée des recommandations en soins intensifs oncologiques: exemple de la neutropénie

AP Meert

Les recommandations en soins intensifs oncologiques

Management of sepsis in neutropenic patients: guidelines from the infectious diseases working party of the German Society of Hematology and Oncology

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REVIEW ARTICLE

Management of sepsis in neutropenic patients: 2014 updated guidelines from the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology (AGIHO)

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Prise en charge de la neutropénie fébrile chez le patient d'onco-hématologie admis en réanimation

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Djamel Mokart²

Transfert des patients allogreffés de cellules-souches hématopoïétiques en réanimation : recommandations de la Société francophone de greffe de moelle et de thérapie cellulaire (SFGM-TC)

Anne-Sophie Moreau¹, Jean-Henri Bourhis², Nathalie Contentin³, Marie-Anne Couturier⁴, Jeremy Delage⁵, Cécile Dumesnil⁶, Virginie Gandemer⁷, Yosr Hichri⁸, Edgar Jost⁹, Laura Platon¹⁰, Mercé Jourdain¹, Frédéric Pène¹¹, Ibrahim Yakoub-Agha¹²

Recomendaciones para el soporte nutricional y metabólico especializado del paciente crítico. Actualización. Consenso SEMICYUC-SENPE: Paciente oncohematológico

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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

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

REVIEW

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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 Schnell¹, Elie Azoulay², Dominique Benoit³, Benjamin Clouzeau⁴, Pierre Demaret⁵, Stéphane Ducassou⁶, Pierre Frange⁷, Matthieu Lafaurie⁸, Matthieu Legrand⁹, Anne-Pascale Meert¹⁰, Djamel Mokart¹¹, Jérôme Naudin¹², Frédéric Pene¹³, Antoine Rabbat¹⁴, Emmanuel Raffoux¹⁵, Patricia Ribaud¹⁶, Jean-Christophe Richard¹⁷, François Vincent¹⁸, Jean-Ralph Zahar¹⁹ and Michael Darmon^{20,21*}

1. Admission à l'USI et pronostic

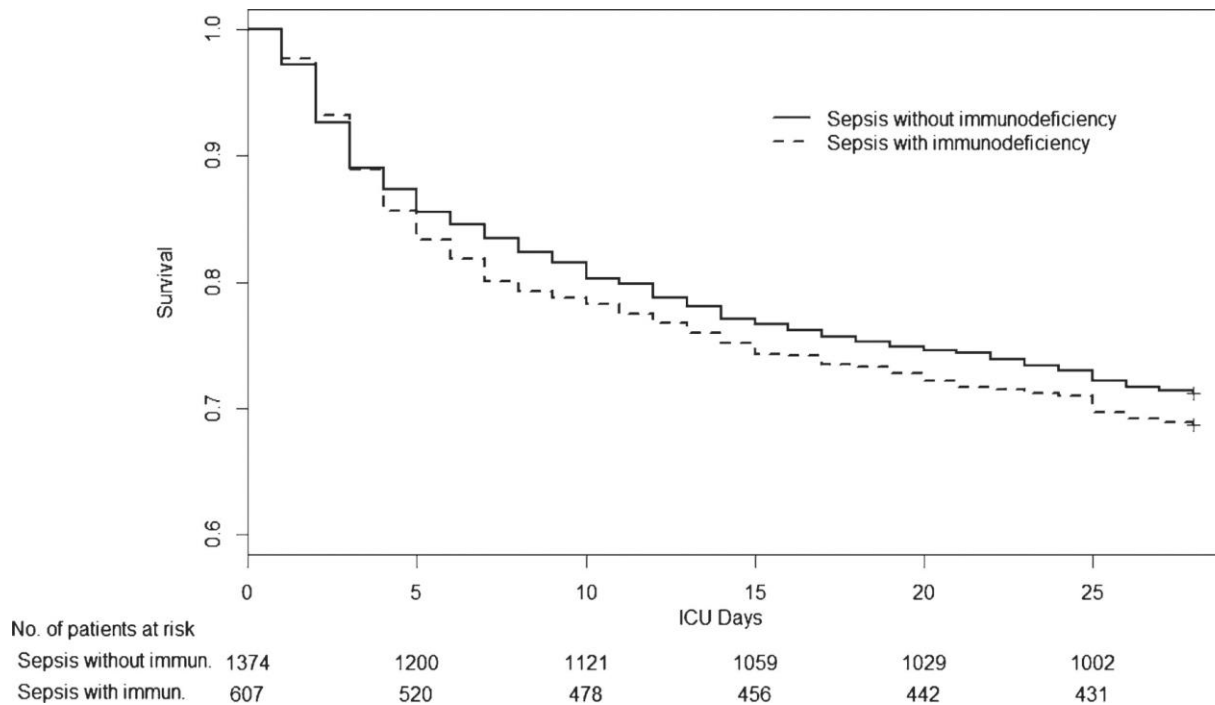


Figure 3. Kaplan-Meier survival curve between d 1 and d 28 according to the immune status. Immun = immunodeficiency.

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

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

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

<http://dx.doi.org/10.1378/chest.13-2618>

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	<i>P</i>	Odds Ratio	95% CI	<i>P</i>
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

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So Yeon Lim
Seo Goo Han
Yeh Rim Kang
O Jung Kwon
Sookyong 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	<i>p</i> 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

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

- Seul le temps entre l'apparition des symptômes respiratoires et l'admission à l'USI (>2 jours) et le score LOD étaient associés indépendamment à la mortalité à 28 jours.

- 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

- 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

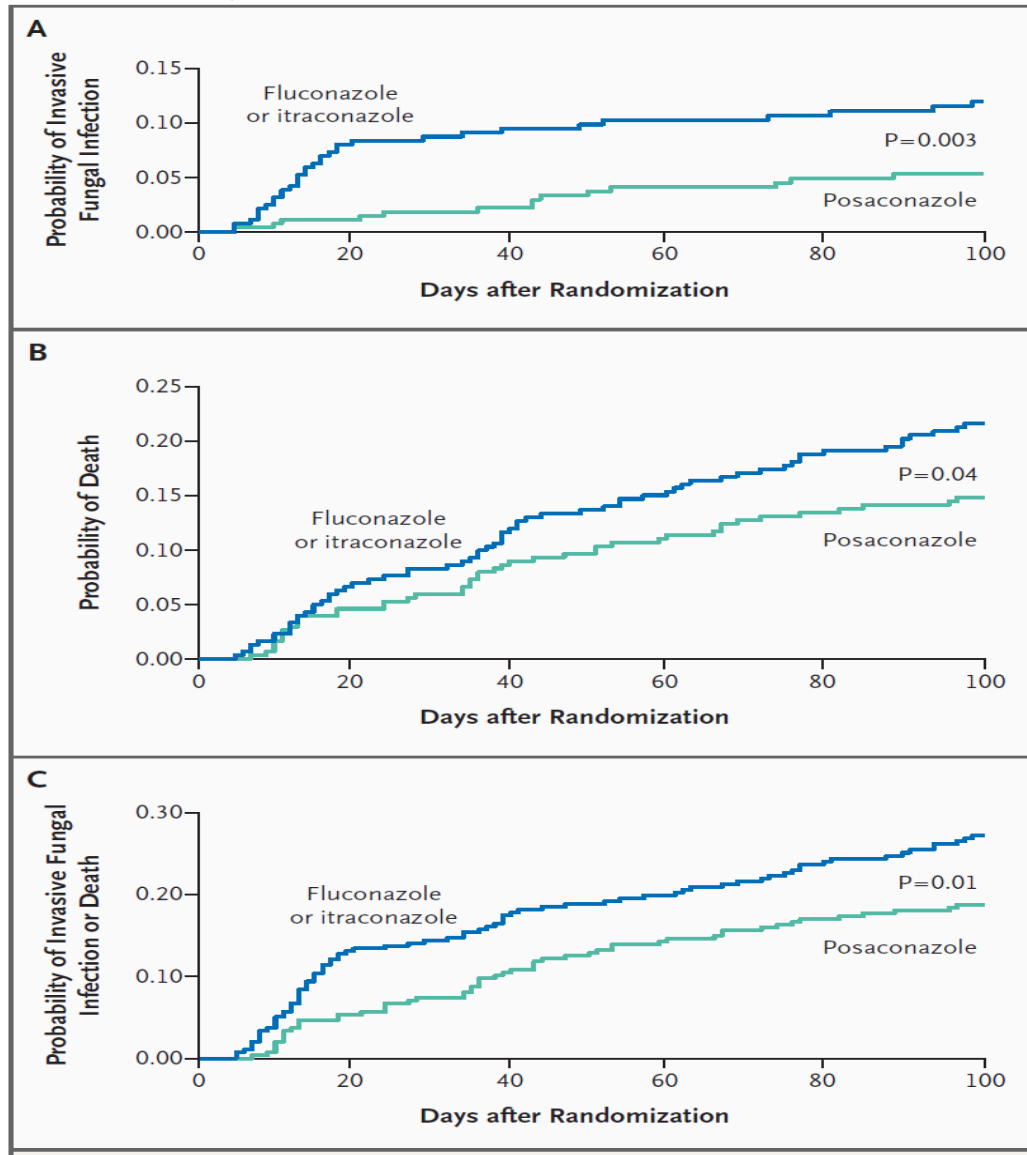
	Non-isolated patients 980 (100)	Isolated patients 170 (100)	Unadjusted sHR (95 % CI)	<i>p</i>	Adjusted sHR [95 % CI]	<i>p</i> ^a
Adverse events						
Accidental removal of endotracheal tube or catheter	41/784 (6.5)	14/148 (9.5)	1.2 (0.6–2.5)	0.6	1.3 (0.6–2.8)	0.5
Phlebitis/pulmonary embolism	26/980 (2.7)	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

- 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).

- 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.,

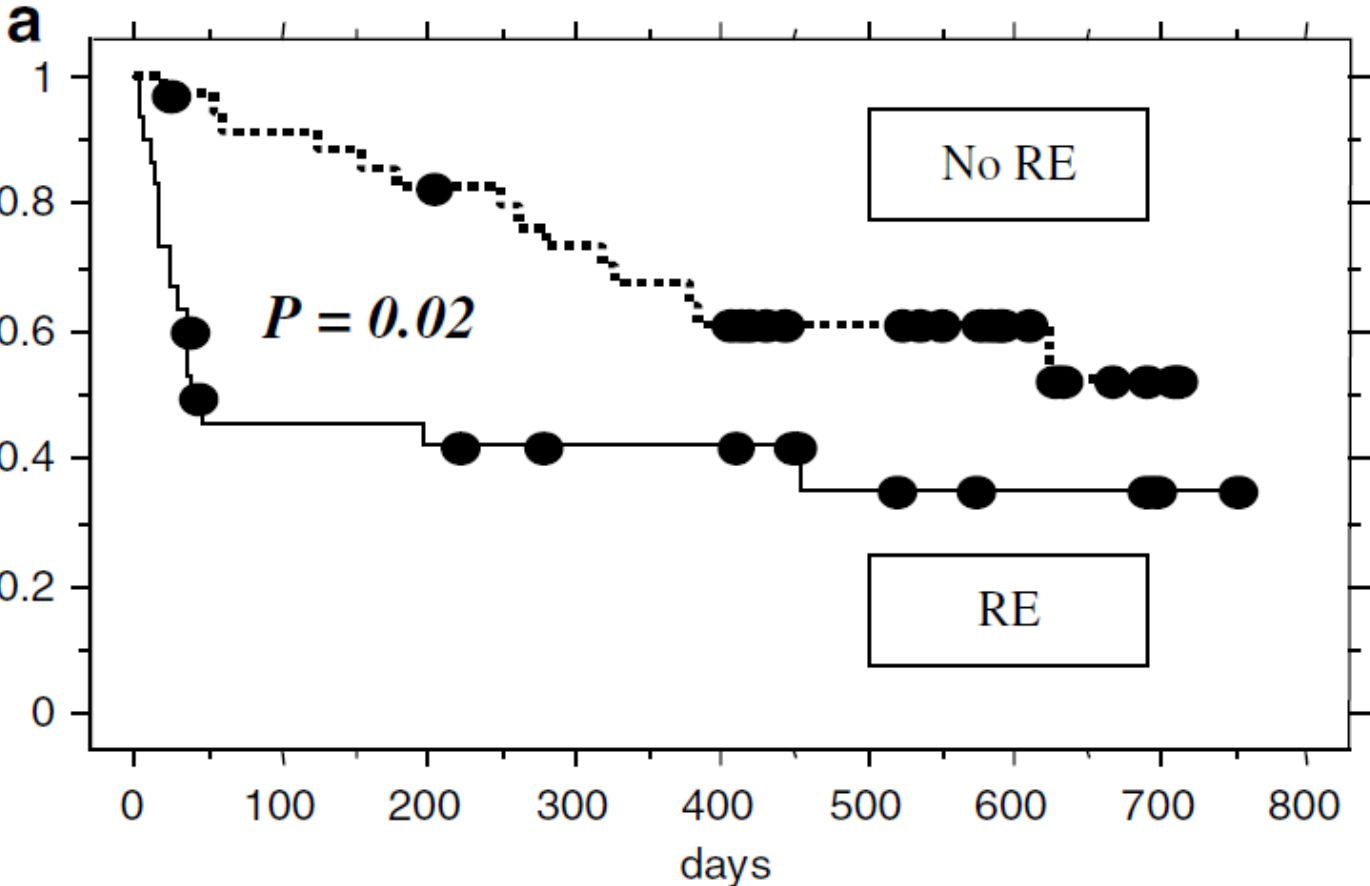


- RII-5—Anti-Aspergillus prophylaxis should probably be used in critically ill neutropenic patients with acute myeloid leukemia or myelodysplastic syndrome with both induction and consolidation therapy used when neutropenia is expected to be profound (neutrophil count less than 500/mm³) and with an expected 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 Chaoui¹, O Legrand¹, N Roche², M Cornet³, A Lefebvre², R Peffault de Latour¹, L Sanhes¹, G Huchon², J-P Marie¹ and A Rabbat²



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]

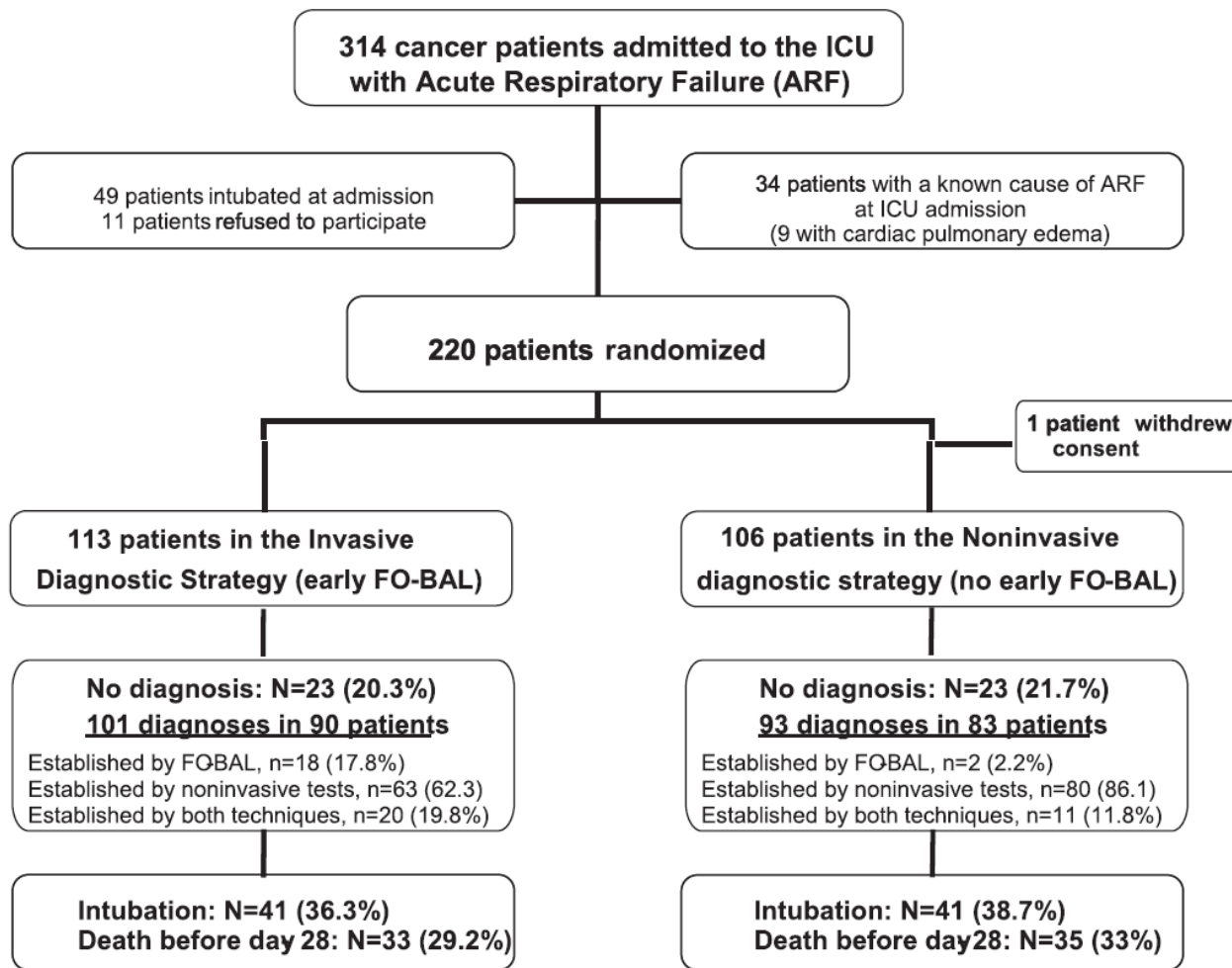
- D**elay since malignancy onset or HSCT, since symptom onset and since implementation of antibiotics/prophylaxis
- P**attern of immune deficiency
- R**adiographic appearance
- E**xperience and knowledge of the literature
- C**linical picture (including ongoing chemoprophylaxis and effective antibiotic therapy)
- F**indings by HRCT

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

Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

Randomized Controlled Trial

Élie Azoulay¹, Djamel Mokart², Jérôme Lambert³, Virginie Lemiale⁴, Antoine Rabbat⁵, Achille Kouatchet⁶, François Vincent⁷, Didier Gruson⁸, Fabrice Bruneel⁹, Géraldine Epinette-Branche¹, Ariane Lafabrie¹, Rebecca Hamidfar-Roy¹⁰, Christophe Cracco¹¹, Benoît Renard¹², Jean-Marie Tonnelier¹³, François Blot¹⁴, Sylvie Chevret³, and Benoît Schlemmer¹



- 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

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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 $>38.0^{\circ}\text{C}$ or rectal temperature $>38.5^{\circ}\text{C}$)

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 Bartlett¹⁰

- AB adaptée à l'écologie microbiologique locale et à la colonisation du patient
- Doit être active sur *Enterococcus*, *Enterobacteriaceae*, anaérobies et *Pseudomonas aeruginosa*
- utilisation systématique de glycopeptide ou de metronidazole est de bénéfice incertain
- Une thérapie antifongique 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 antifongique.

- 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).

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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

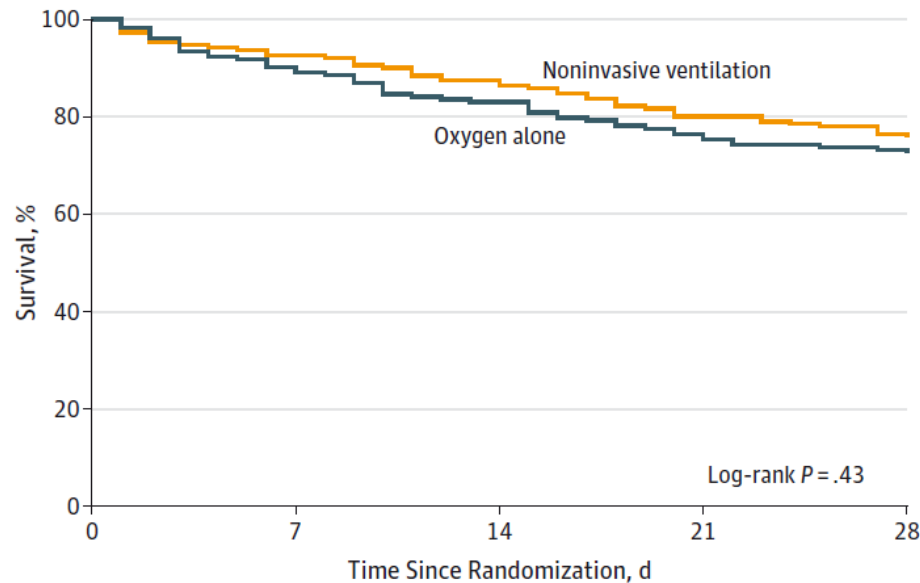
Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure

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	0	7	14	21	28
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.

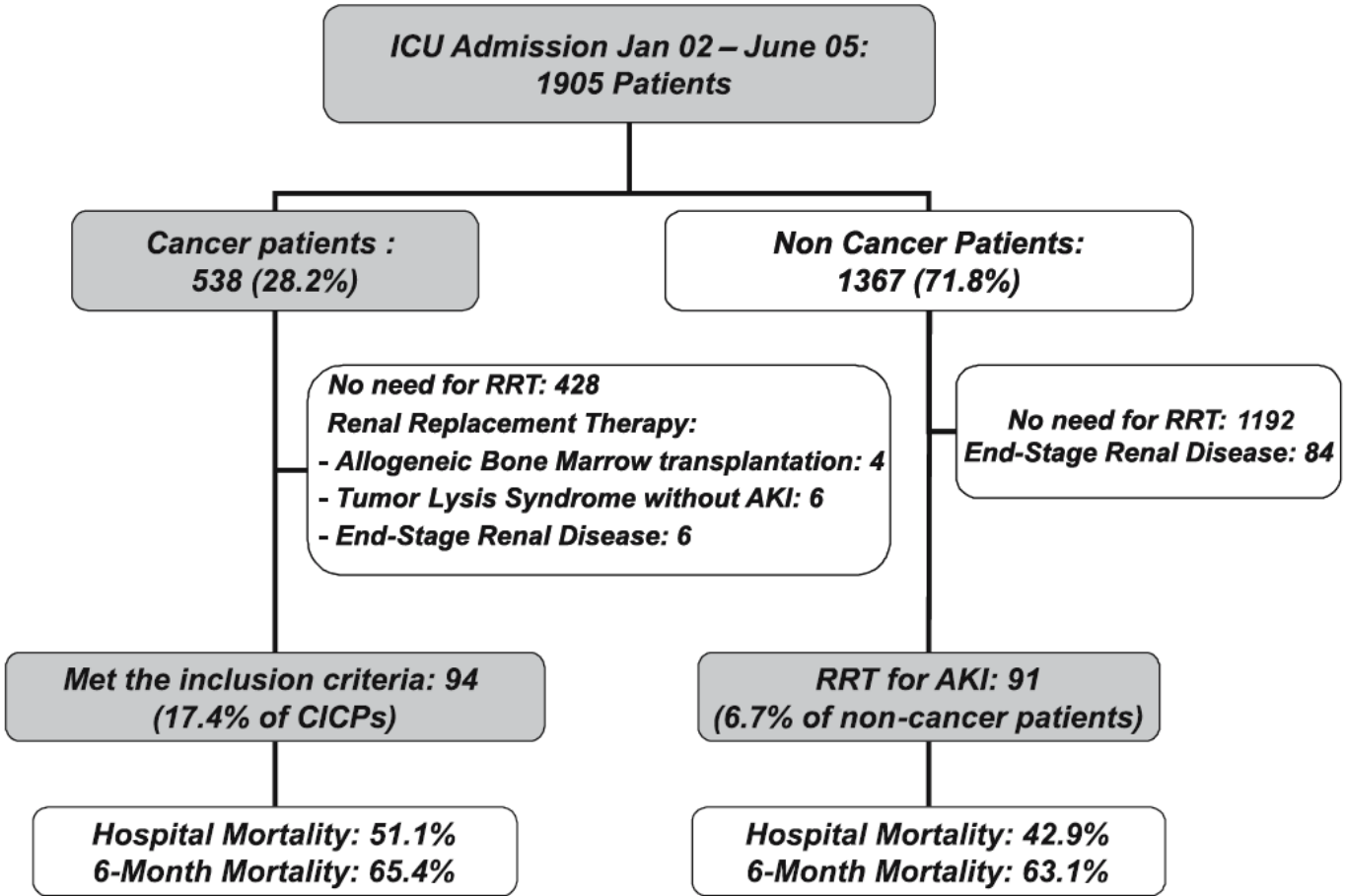
- RIV-6–Neutropenia in itself should probably not modify ventilatory support in critically ill cancer patients (Grade 2-, strong agreement).
- RIV-7–Invasive mechanical ventilation should probably not be delayed only as a consequence of neutropenia, underlying malignancy, or immunocompromised status (Grade 2-, weak agreement)

4. Défaillance et support d'organes

- Typhlite
- Support ventilatoire
- Epuration extra-rénale

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Guillaume Thiery
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Élie Azoulay

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



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

5. Antibiothérapie

- 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).
- 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).

6. Prise en charge hématologique

- 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).

En cours...

Recommandations de pratique clinique pour les
soins intensifs oncologiques,

AP Meert et D Benoit

Table 1 Evidence grading and recommendations formulation

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