Sepsis & enterocolitis in neutropenic critically ill patient

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Febrile Neutropenia : definitions

- Neutrophils <1500/mm^3
  - Profound neutropenia: neutrophils < 500/mm^3
  - Severe neutropenia: neutrophils < 100/mm^3
- Expected decrease of neutrophil count <500/mm^3 within the next 48 hours
- Functional neutropenia
  - AL at diagnosis or with hyper-leucocytosis
- Prolonged neutropenia(>7 days)
- Fever: oral temperature ≥ 38.3° C or ≥ 38° C ≥ 1 hour

SYSTEMATIC REVIEW

Changes in critically ill cancer patients' short-term outcome over the last decades: results of systematic review with meta-analysis on individual data

Michaël Darmon[1,2,3*], Aurélie Bourmaud[2,4,5], Quentin Georges[6], Marcio Soares[7], Kyeongman Jeon[8], Sandra Oeyen[9], Chin Kook Rhee[10], Pascale Gruber[11], Marlies Ostermann[12], Quentin A. Hill[13], Pieter Depuydt[9], Christelle Ferra[14], Anne-Claire Toffart[15], Peter Schellongowski[16], Alice Müller[17], Virginie Lemiale[1], Djamel Mokart[18] and Elie Azoulay[1,2,3]

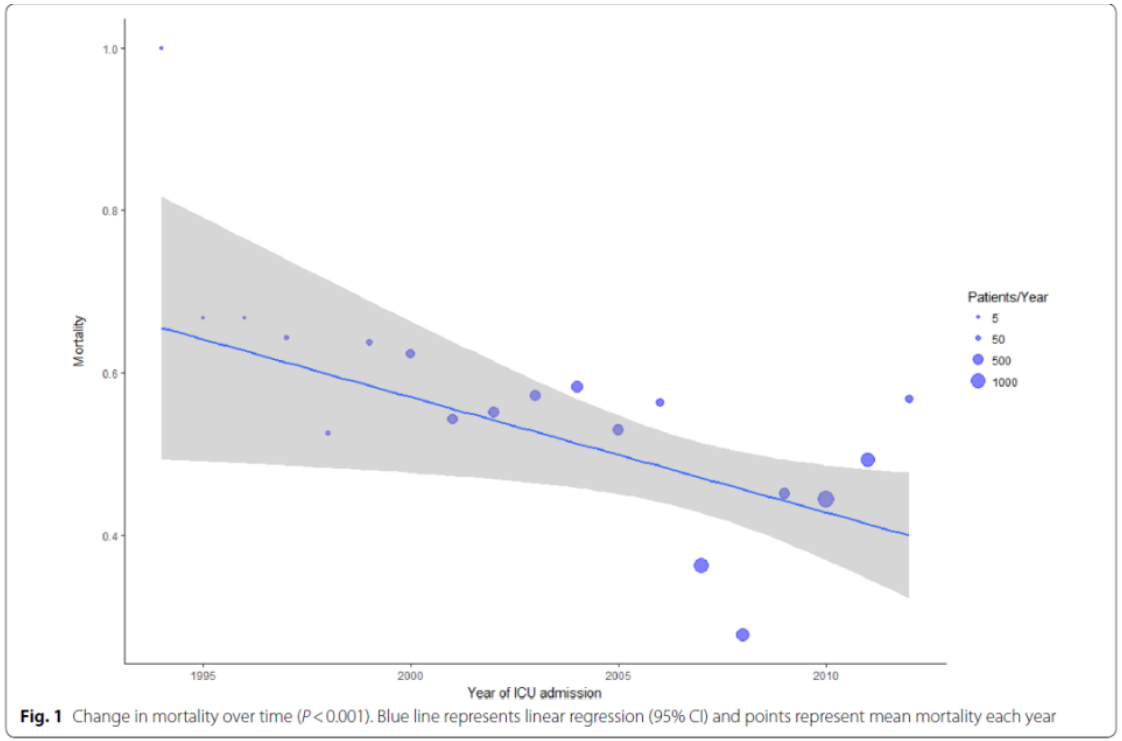


Fig. 1 Change in mortality over time ($P < 0.001$). Blue line represents linear regression (95% CI) and points represent mean mortality each year

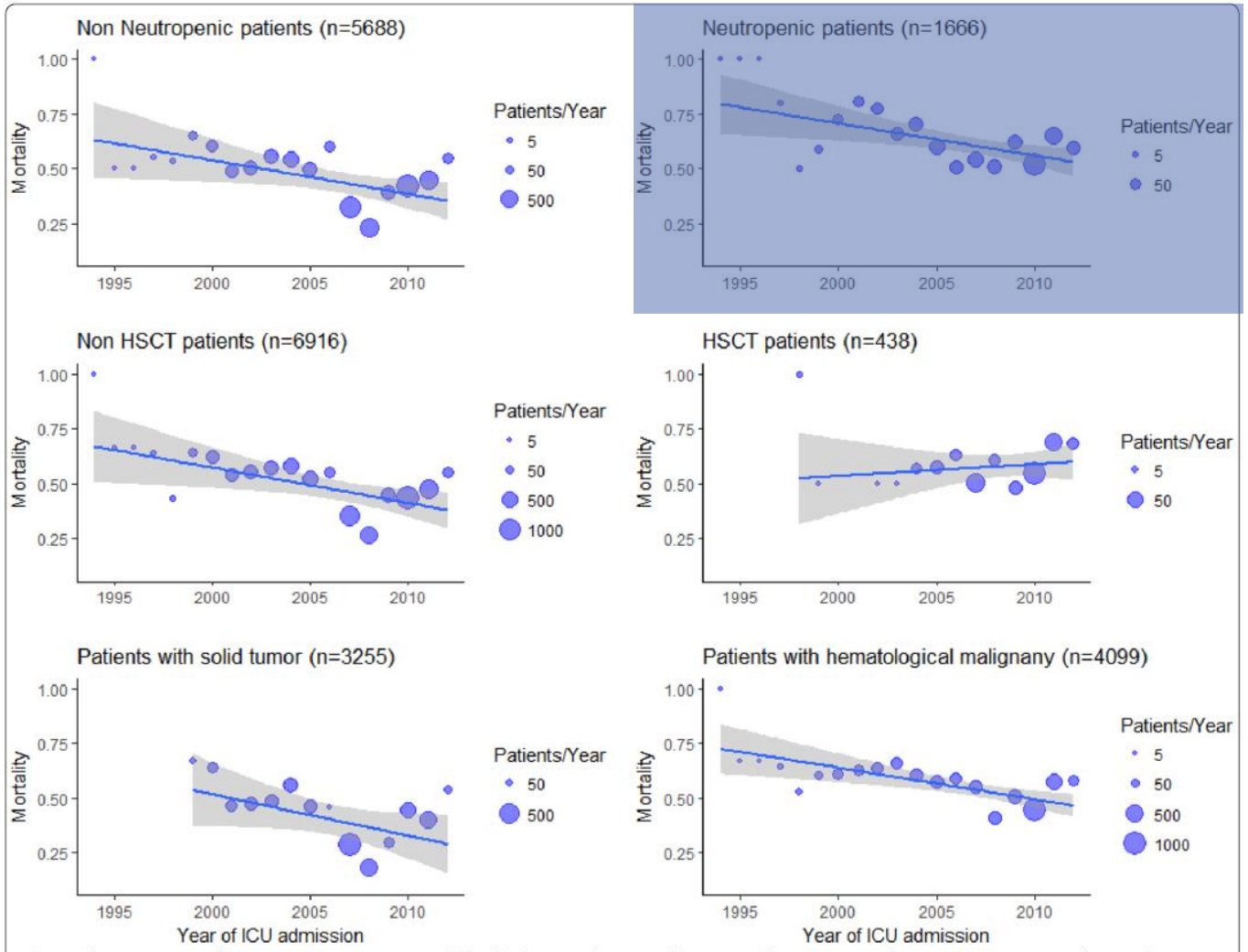


Fig. 3 Change in mortality over time in various predefined subgroup ($P < 0.001$ for every subgroup except hematopoietic stem cell transplant recipients $P = 0.21$). Blue line represents linear regression (95% CI) and points represent mean mortality each year and are weighted for number of observation each year

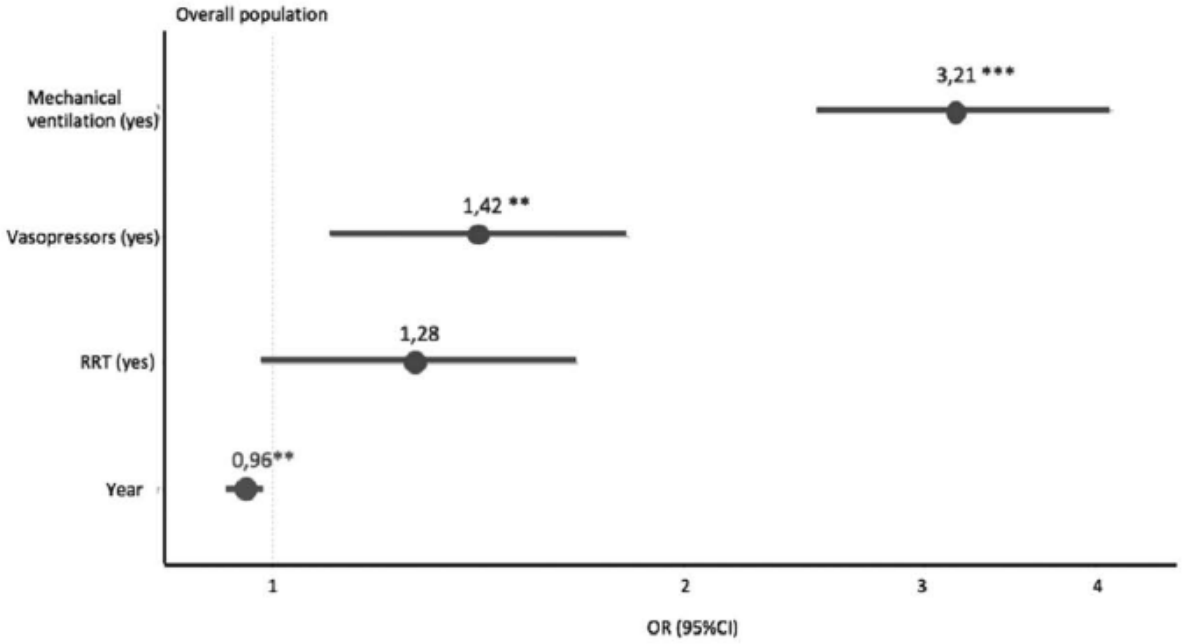
Intensive Care Med
https://doi.org/10.1007/s00134-019-05653-7

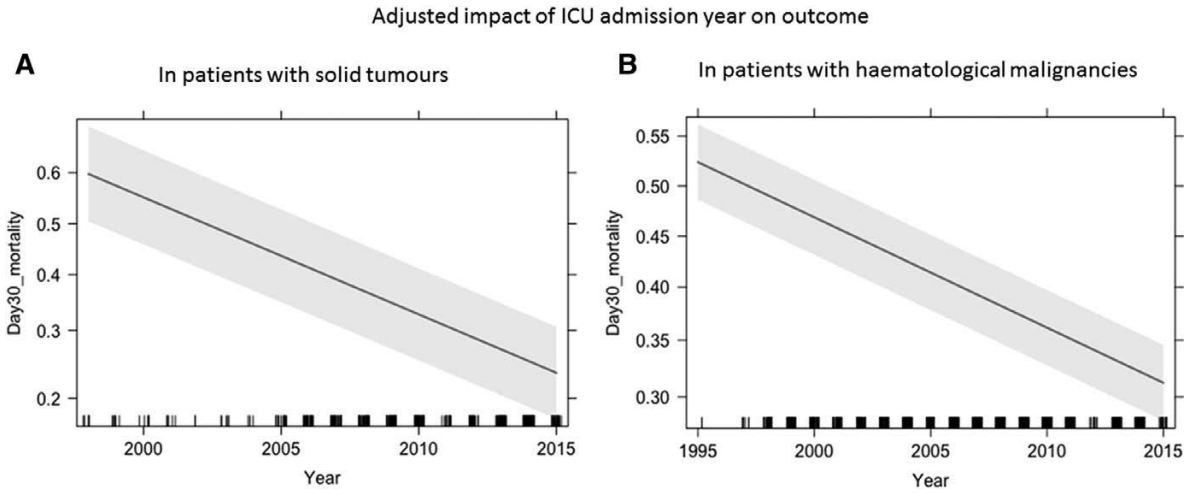
Sepsis and Septic Shock in Patients With Malignancies: A Groupe de Recherche Respiratoire en Réanimation Onco-Hématologique Study*

Virginie Lemiale, MD[1]; Stéphanie Pons, MD[2]; Adrien Mirouse, MD[1]; Jean-Jacques Tudesq, MD[1]; Yannick Hourmant, MD[1]; Djamel Mokart, MD, PhD[3]; Frédéric Pène, MD, PhD[4]; Achille Kouatchet, MD[5]; Julien Mayaux, MD[6]; Martine Nyunga, MD[7]; Fabrice Bruneel, MD[8]; Anne-Pascale Meert, MD, PhD[9]; Edith Borcoman, MD[1]; Magali Bisbal, MD[3]; Matthieu Legrand, MD, PhD[1]; Dominique Benoit, MD, PhD[10]; Elie Azoulay, MD, PhD[1]; Michaël Darmon, MD, PhD[1]; Lara Zafrani, MD, PhD[1,2]

Etude rétrospective multicentrique

- 1994-2015
- 2062 patients
- Mortalité à J30 = 40%





Crit Care Med 2020; 48:822– 829

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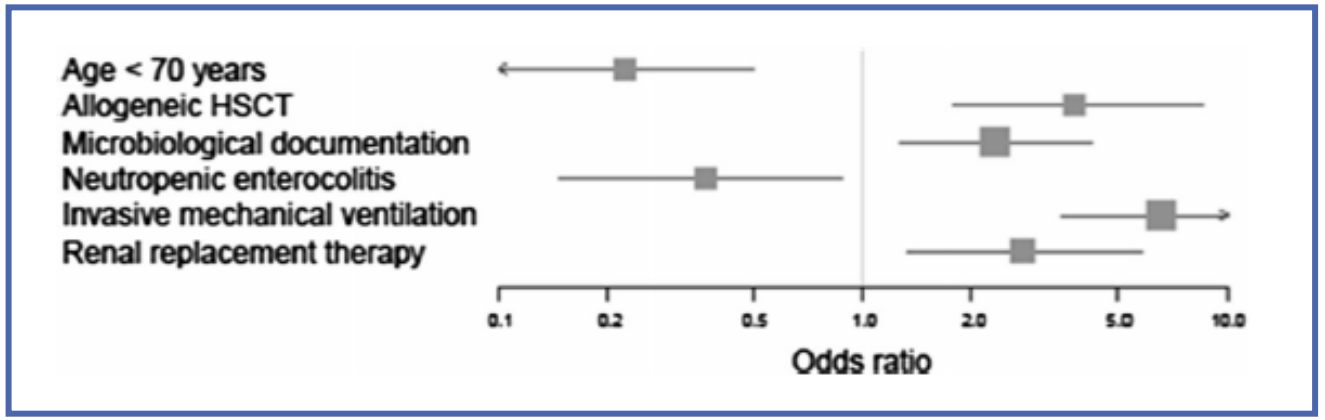
A. Renault
R. Hamidfar
M. Jourdain
A.-P. Meert
D. Benoit
S. Chevret
E. Azoulay

Prognosis of neutropenic patients admitted to the intensive care unit

- 289 neutropenic patients admitted to the ICU
  - 80% with sepsis
  - 80% received antibiotic treatment 10 days prior ICU admission
  - Hospital mortality 30%



Intensive Care Med. 2015 Feb;41(2):296-303

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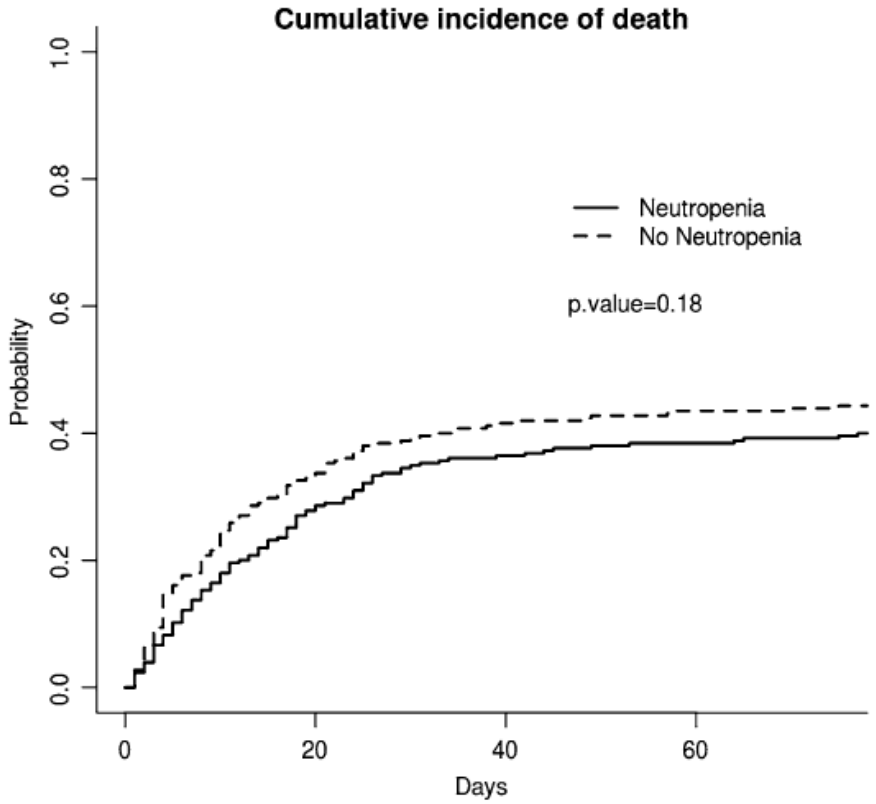


Fig. 2 Cumulative incidence of death in hospital according to the presence of neutropenia in the case–control analysis (251 neutropenic patients vs 251 controls); Gray's test, $p = 0.18$

Intensive Care Med. 2015 Feb;41(2):296-303

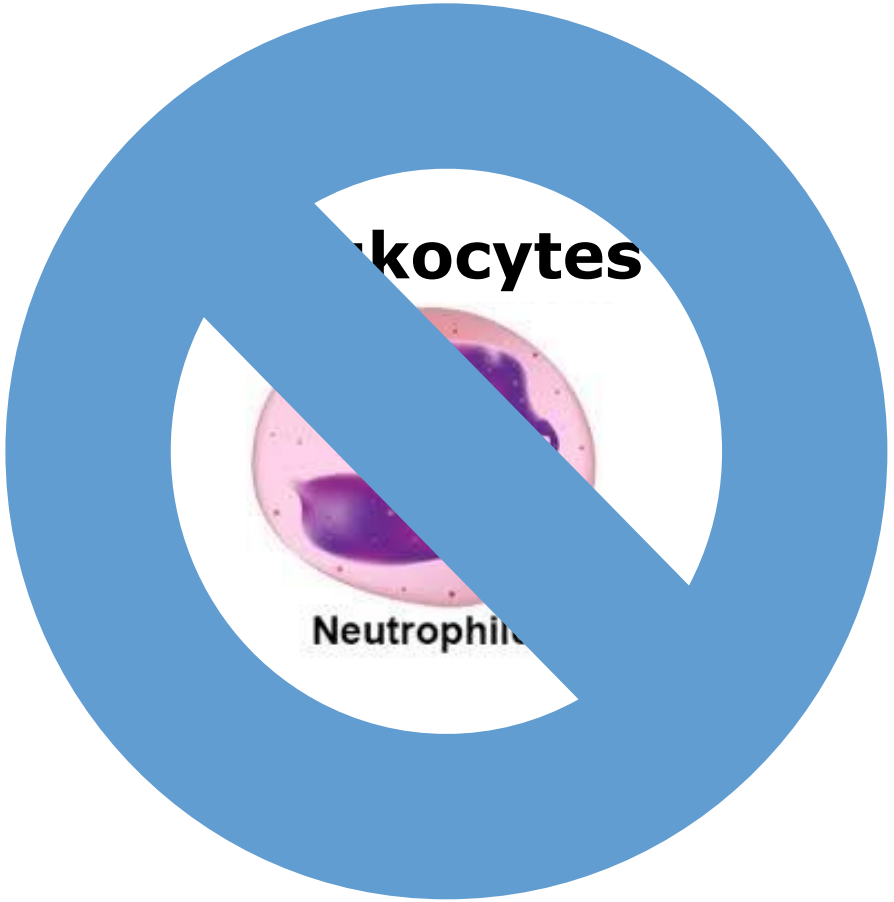
Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America

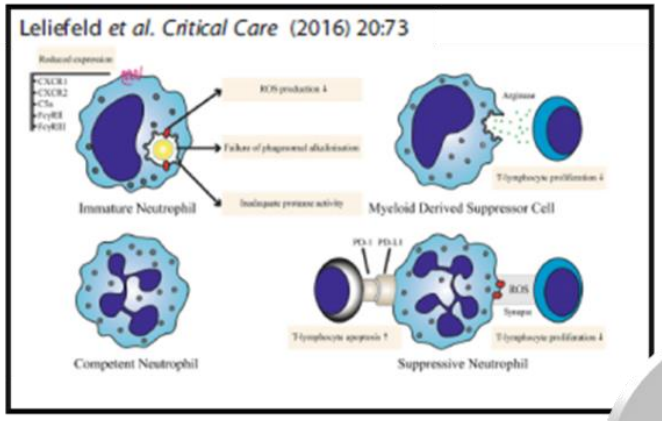
IDSA GUIDELINES

- Classically the risk of infection
  - Duration of neutropenia
  - The magnitude of neutropenia
  - Co-morbidities

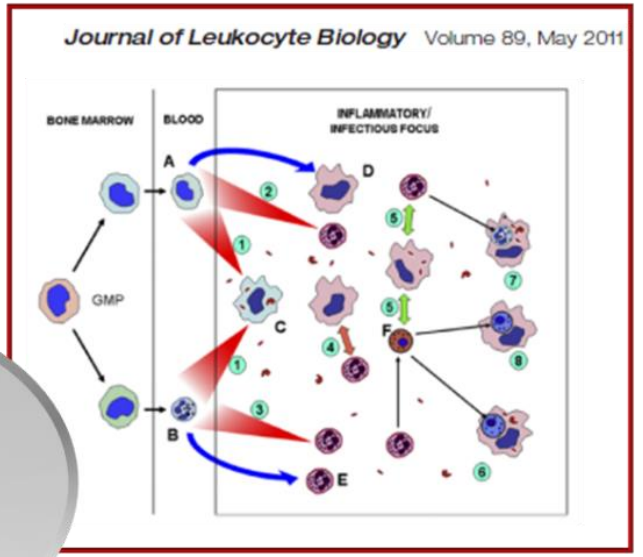
CID 2011:52 (15 February)

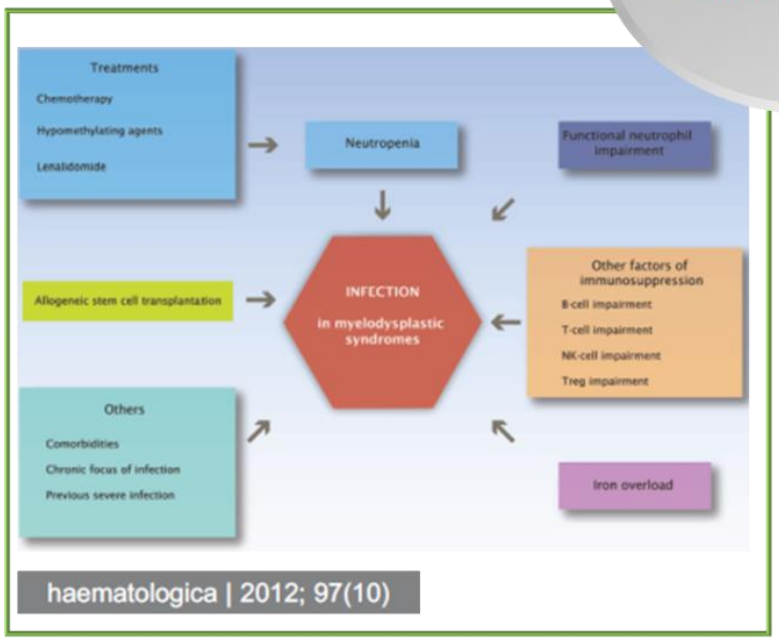
A complex immune dysfunction

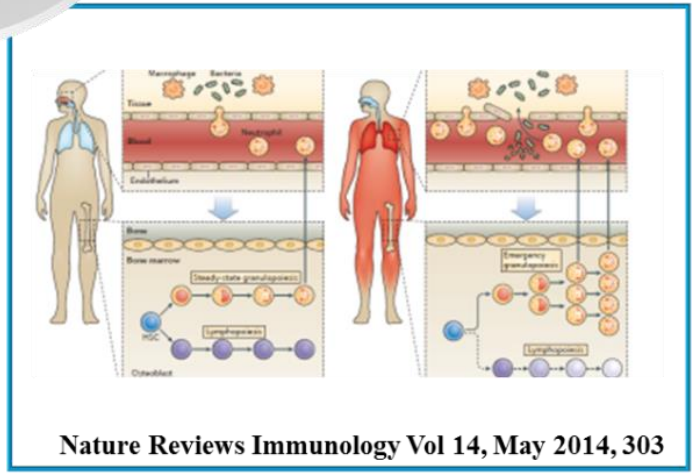




Immunomdulation
Dysfonctions PNN
Granulopoïèse(s)
Interactions PNN-MØ

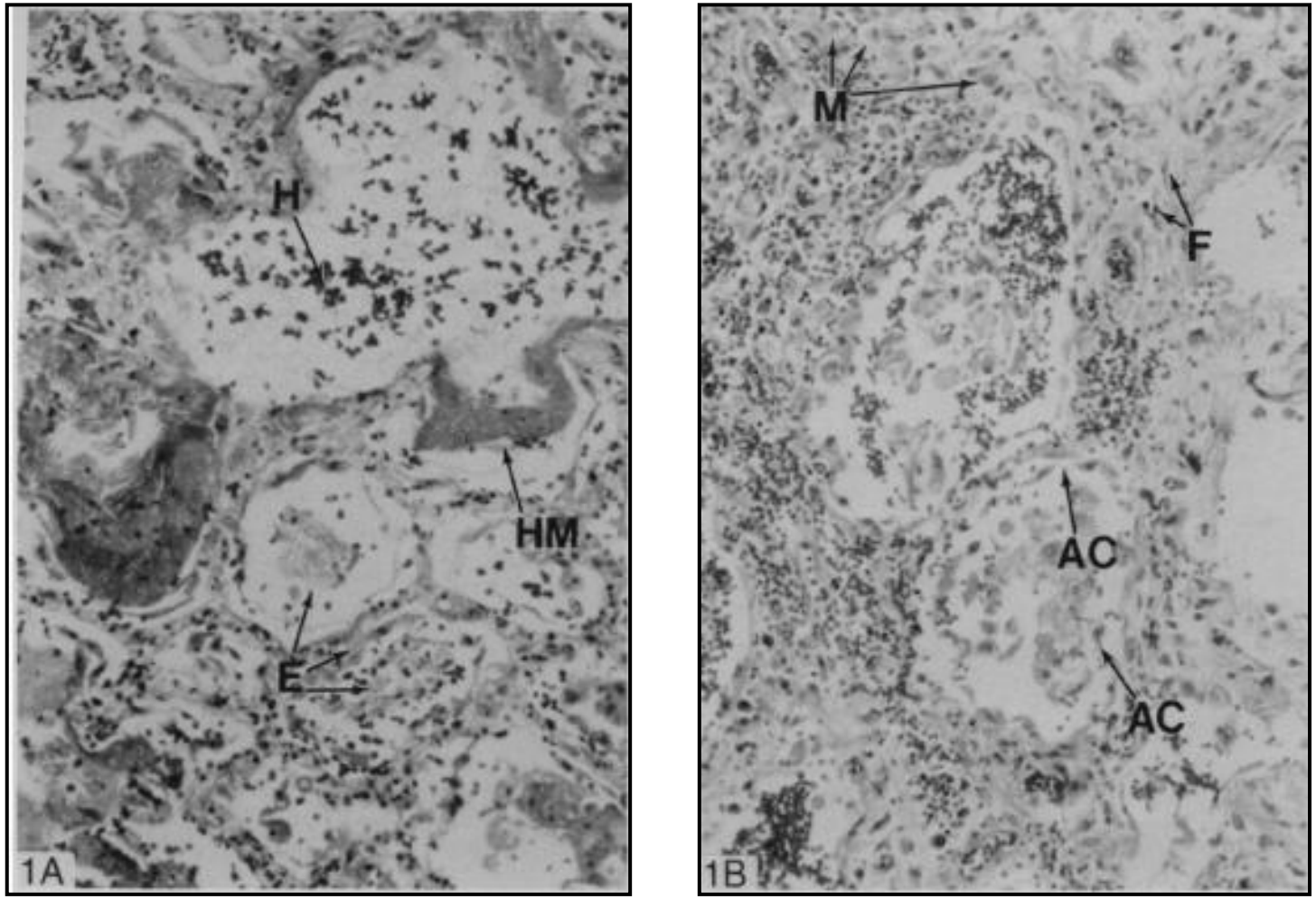






ADULT RESPIRATORY DISTRESS SYNDROME IN PATIENTS WITH SEVERE NEUTROPENIA

Frederick P. Ognibene, M.D., Sue E. Martin, M.D., Ph.D., Margaret M. Parker, M.D., Terri Schlesinger, B.S., Patricia Roach, B.S., Cynthia Burch, B.S., James H. Shelhamer, M.D., and Joseph E. Parrillo, M.D.



N Engl J Med 1986; 315:547-51.

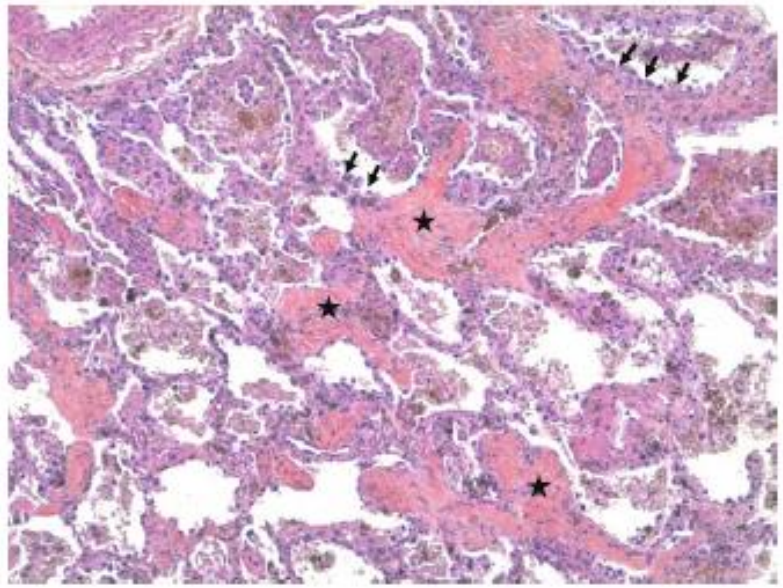
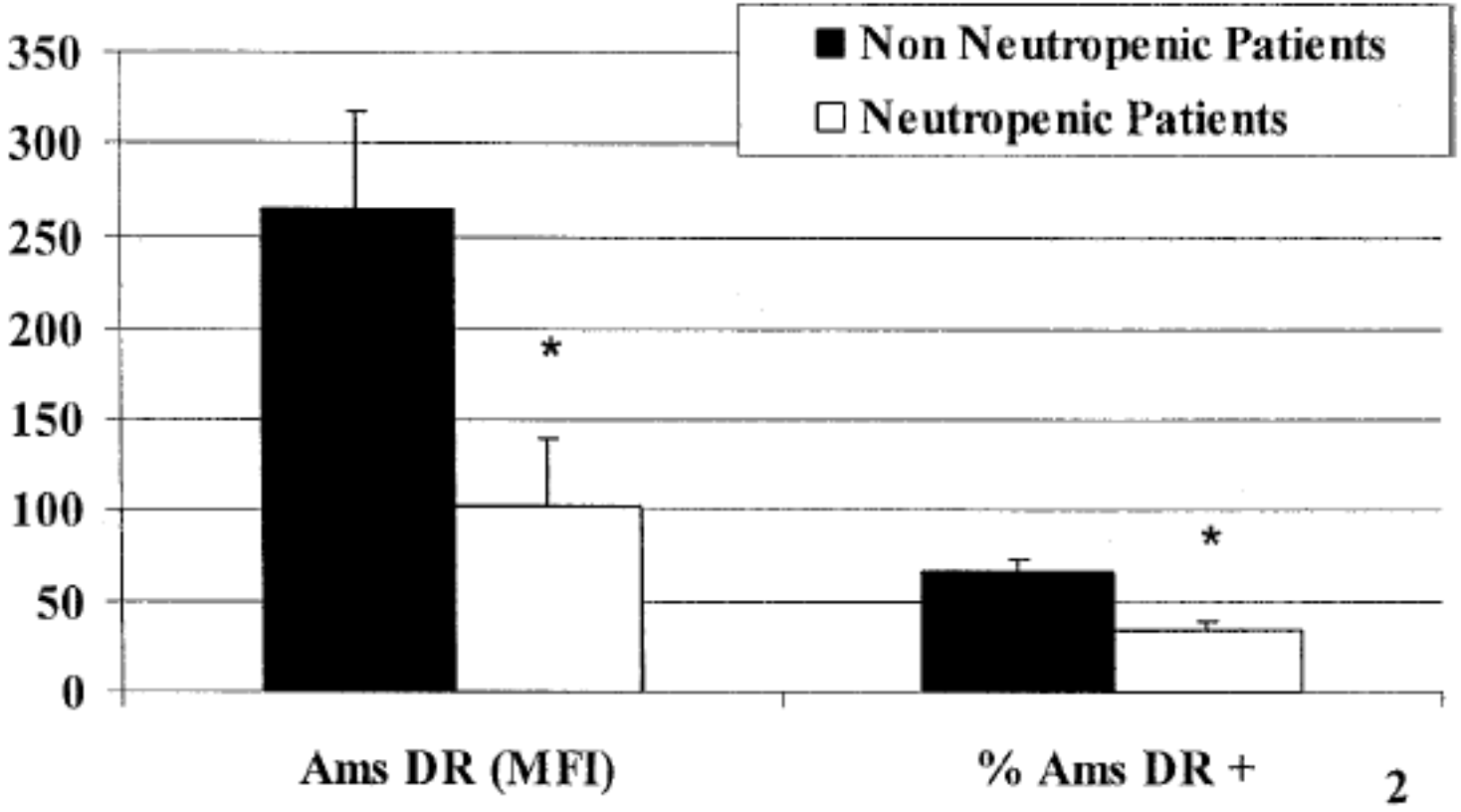


Fig. 36.2 ARDS in a neutropenic patient at the proliferative phase of ARDS, the patient was still neutropenic at this time. Diffuse alveolar damage, organizing phase (H&E, ×100). Alveolar septa are still thickened by congestion, mononuclear infiltrate, and scant interstitial fibrosis. Fibrosis is more prominent in the alveolar lumen (*black stars*). Note the alveolar pneumocyte hyperplasia (*black arrows*)

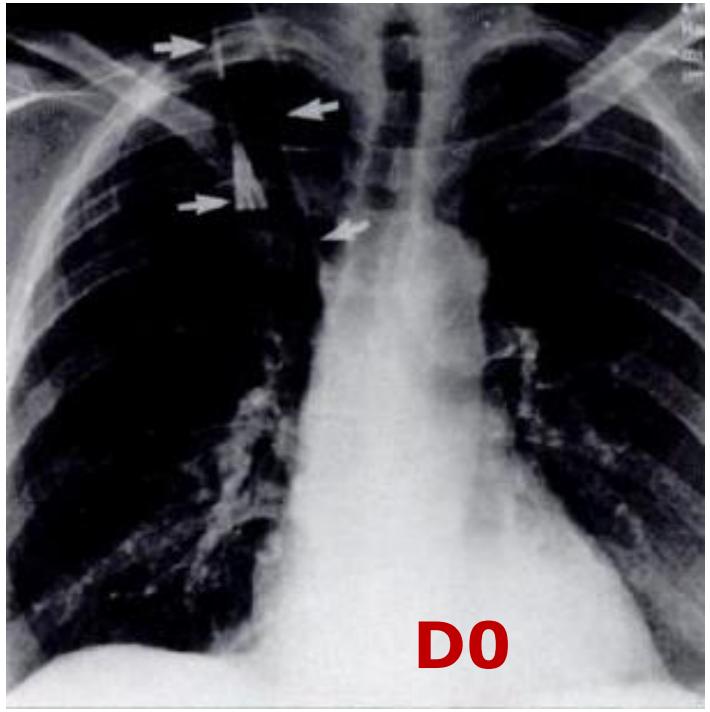
Deactivation of Alveolar Macrophages in Septic Neutropenic ARDS*

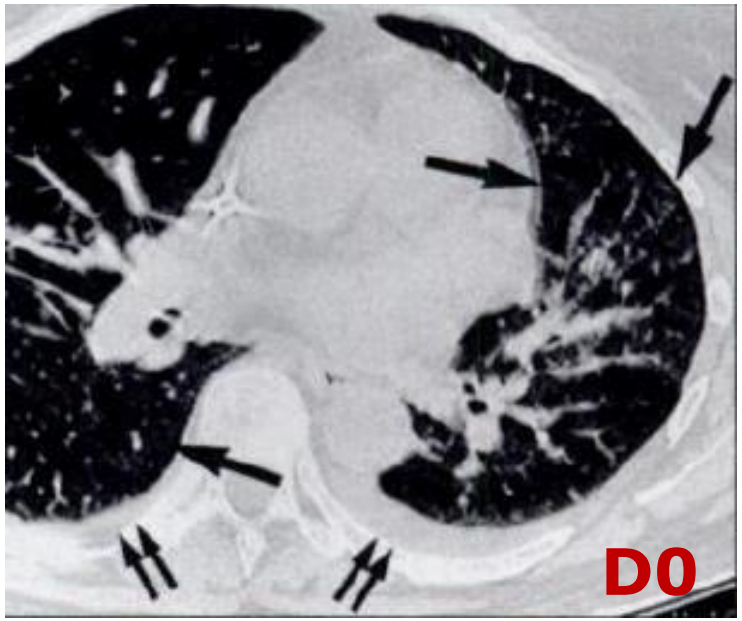
Djamel Mokart, MD; Benoit P. Guery, MD, PhD; Reda Bouabdallah, MD; Claude Martin, MD; Jean-Louis Blache, MD; Christine Arnoulet, MD; and Jean-Louis Mege, MD, PhD

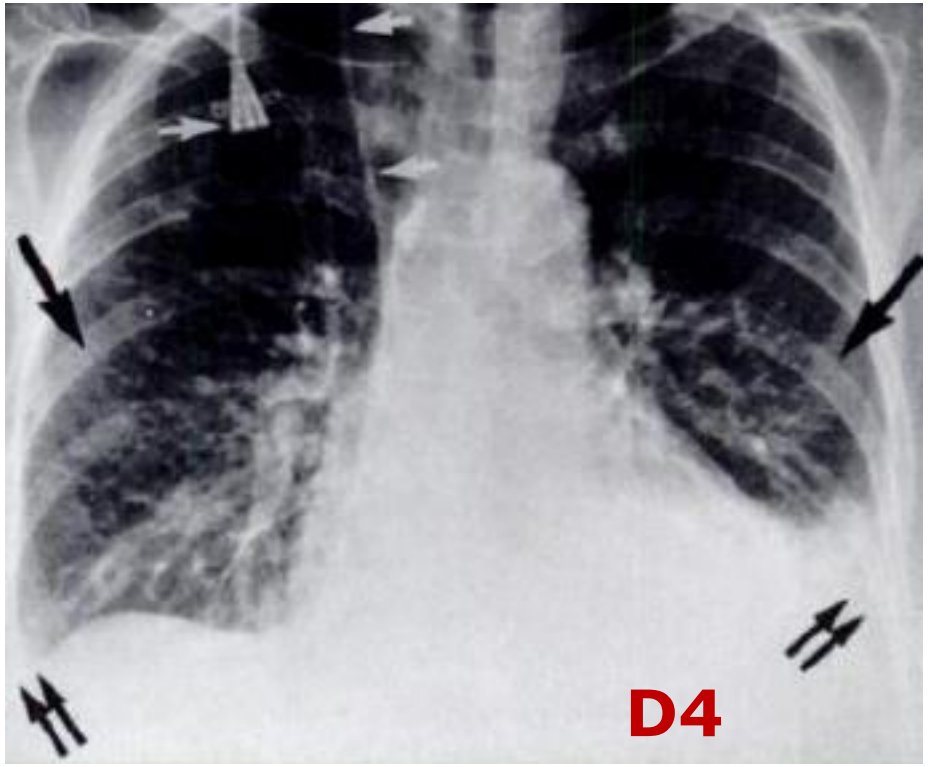


Early Detection of Pneumonia in Febrile Neutropenic Patients: Use of Thin-Section CT

Claus Peter Heussel[1]
Hans-Ulrich Kauczor[1]
Gudula Heussel[2]
Berthold Fischer[3]
Peter Mildenberger[1]
Manfred Thelen[1]







AJR 1997;169:1347–1353

Pulmonary infiltrates in patients with malignancies: why and how neutropenia influences clinical reasoning

É. Azoulay*,#

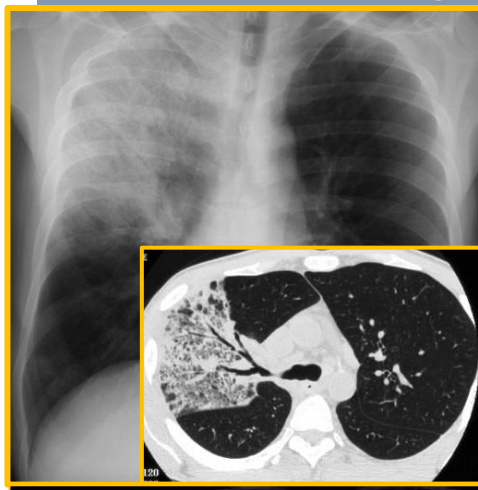
- **Prognostic impact of neutropenia(s) in onco-hematology patients admitted to the ICU**
  - Prognostic impact of first line chemotherapy vs relapse
  - Neutropenia in a context of solid tumour vs haematology disease
  - Neutropenia recovery
    - Associated with good outcome
    - Poor prognosis when associated with prior lung injury

Eur Respir J 2009; 33: 6–8

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

Mokart D, Slehofer G, Lambert J, Sannini A, Chow-Chine L, Brun JP, Berger P, Duran S, Faucher M, Blache JL, Saillard C, Vey N, Leone M.

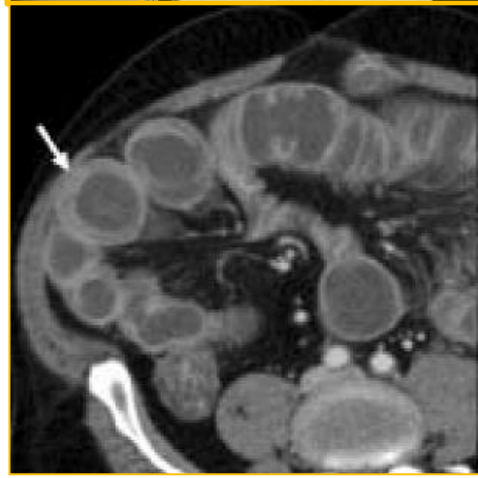
Intensive Care Med. 2014 Jan;40(1):41-9



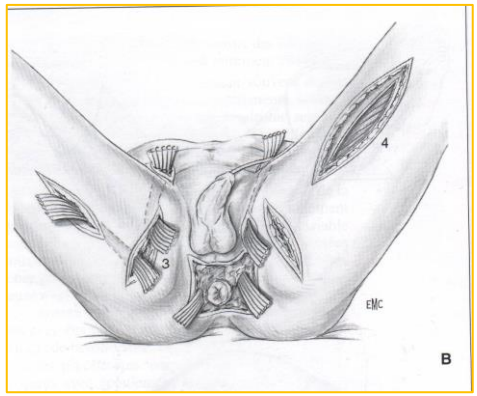
Survival in neutropenic patients with severe sepsis or septic shock

Matthieu Legrand, MD; Adeline Max, MD; Vincent Peigne, MD; Eric Mariotte, MD; Emmanuel Canet, MD; Alexandre Debrumetz, MD; Virginie Lemiale, MD; Amélie Seguin, MD; Michael Darmon, MD; Benoît Schlemmer, MD; Élie Azoulay, MD, PhD

Crit Care Med 2012 Vol. 40, No. 3



- Site of infection in the ICU
  1. Lung
  2. Abdomen
  3. Bacteraemia /catheter
  4. Soft tissue



Acute respiratory failure in immunocompromised adults

Elie Azoulay, Djamel Mokart, Achille Kouatchet, Alexandre Demoule, Virginie Lemiale

Immunological deficiency	Neutrophils	Monocytes/dendritic cells/ macrophages	B lymphocytes	T lymphocytes	Humoral (antibody) immunity
Diseases	Acute leukaemia; myelodysplastic syndrome; aplastic anaemia; chemotherapy and drug-related neutropenia	Hairy cell leukaemia; aplastic anaemia; allogeneic bone marrow transplant; malignant histiocytosis; acute myeloid leukaemia; chronic myeloid leukaemia; solid tumours; haemophagocytic lymphohistocytosis	Multiple myeloma; B-cell lymphoma; chronic lymphocytic leukaemia	T-cell leukaemia; T-cell lymphoma; Hodgkin disease	Multiple myeloma; chronic lymphoid leukaemia
Treatments	Chemotherapy-induced neutropenia	Steroids; basiliximab; antithymocyte globulin; tacrolimus; mycophenolate mofetil; belatacept	Chemotherapy; steroids; asplenia; rituximab	Steroids; fludarabine; cyclophosphamide; methotrexate; azathioprine; alemtuzumab; mycophenolate mofetil; cyclosporine; mTOR inhibitors (sirolimus); tacrolimus; 2-chlorodeoxyadenosine; daratumumab	Ibrutinib; rituximab; daratumumab; cyclophosphamide
Most frequently encountered infections	• Gram-negative bacteria • Gram-positive bacteria • *Candida* • *Aspergillus* • *Nocardia*	• Non-tuberculous mycobacteria • *Salmonella, Listeria, Legionella, Histoplasma, Brucella* • Herpes simplex virus, varicella zoster virus, parainfluenza virus, respiratory syncytial virus • *Candida parapsilosis* • *Staphylococcus aureus, Enterococcus faecalis, Pseudomonas aeruginosa*	• Encapsulated bacteria (*Streptococcus pneumoniae, Streptococcus pyogenes, Haemophilus influenzae*) • *Giardia lamblia, Campylobacter, Salmonella* • *Mycoplasma* • Enterovirus • Recurrent infections	• Herpes simplex virus, cytomegalovirus, Epstein-Barr virus • *Pneumocystis, Aspergillus, Cryptococcus* • Mycobacterial infection • Skin candidiasis • Diarrhoea (rotaviruses, adenoviruses, *Cryptosporidium*, microsporidia, etc) • John Cunningham virus	• Encapsulated bacteria (*S pneumoniae, S pyogenes, H influenzae*) • *Mycoplasma, Ureaplasma urealyticum* • Other infections related to associated T-cell defects

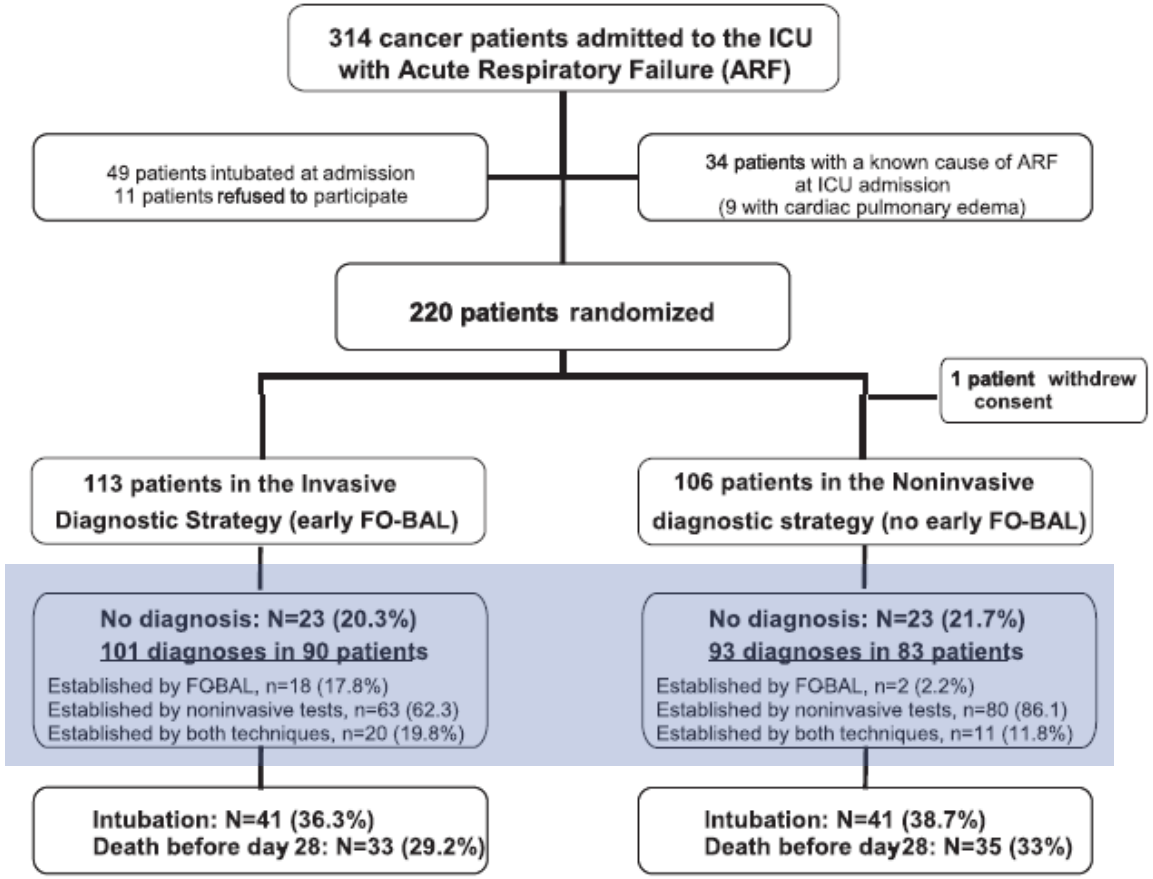
Figure 2: **Risk for specific pathogens according to the type of haematological malignancy or treatment**
This figure illustrates the most frequently encountered types of infection according to the main disease-related or treatment-related immunological deficiency. It focuses mainly on secondary immunosuppression in adults, as data for primary immune deficiencies are scarce.

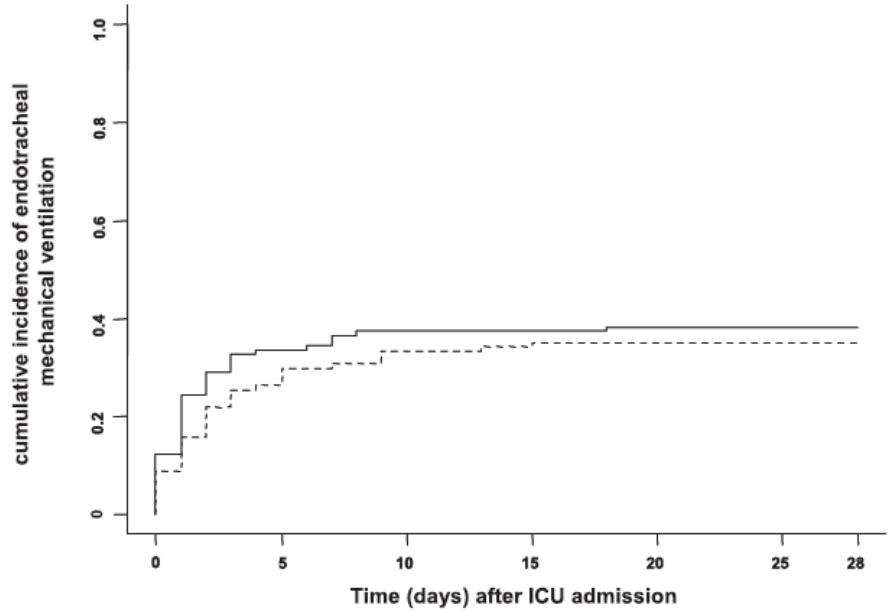
www.thelancet.com/respiratory **Published online December 7, 2018** **http://dx.doi.org/10.1016/PS2213-2600(18)30345-X**

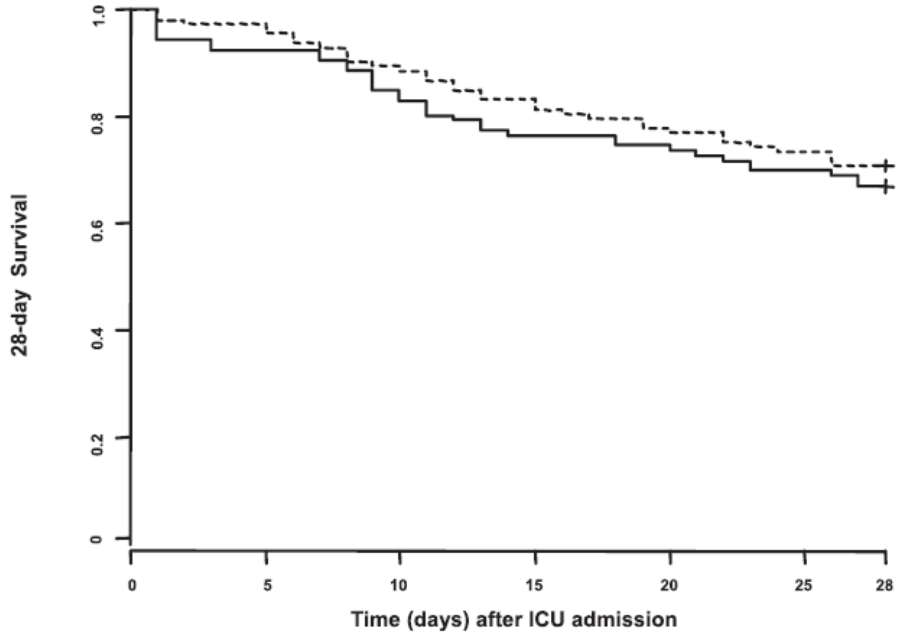
Diagnostic Strategy for Hematology and Oncology Patients with Acute Respiratory Failure

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

Microbiology in the haematology ward

Risk factors for Gram-negative bacterial infections in febrile neutropenia

Haematologica 2005; 90:1102-1109

Epidemiology and Risk Factors for Gram-Positive Coccal Infections in Neutropenia: Toward a More Targeted Antibiotic Strategy

Catherine Cordonnier,[1] Agnès Buzyn,[3] Guy Leverger,[4] Raoul Herbrecht,[5] Mathilde Hunault,[6] Roland Leclercq,[6] and Sylvie Bastuji-Garin,[2] for the Club de Réflexion sur les Infections en Onco-Hématologie

CID 2003:36 (15 January)

- Multicenter study (n=513)
  - Fever of unknown origin: 59%
  - Clinically documented fever: 8%
  - Microbiologically documented fever: 33% (of which 88% bacteremia)
    - G+ cocci: 21%
      - Strepto: 7.8
      - SCN: 10.1%
      - S. aureus: 2.7%
      - Enterococci?
    - GNB: 11%
      - E. coli 5.8%
      - Pseudomonas: 2.5%

Bloodstream infections in neutropenic patients with haematological malignancies

Ana Sofia Carvalho [a,1], Diana Lagana [b,*], Jennifer Catford [a], David Shaw [a], Narin Bak [a,c]

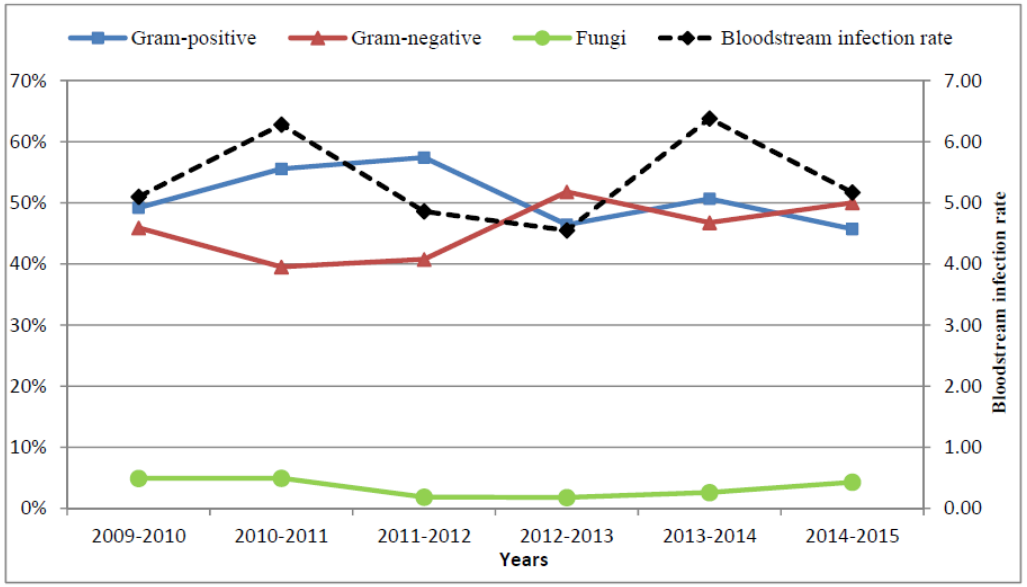


Figure 1 Percentage of Gram-positive, Gram-negative and fungal organisms isolated and bloodstream infection rate per 1000 haematology occupied bed days.

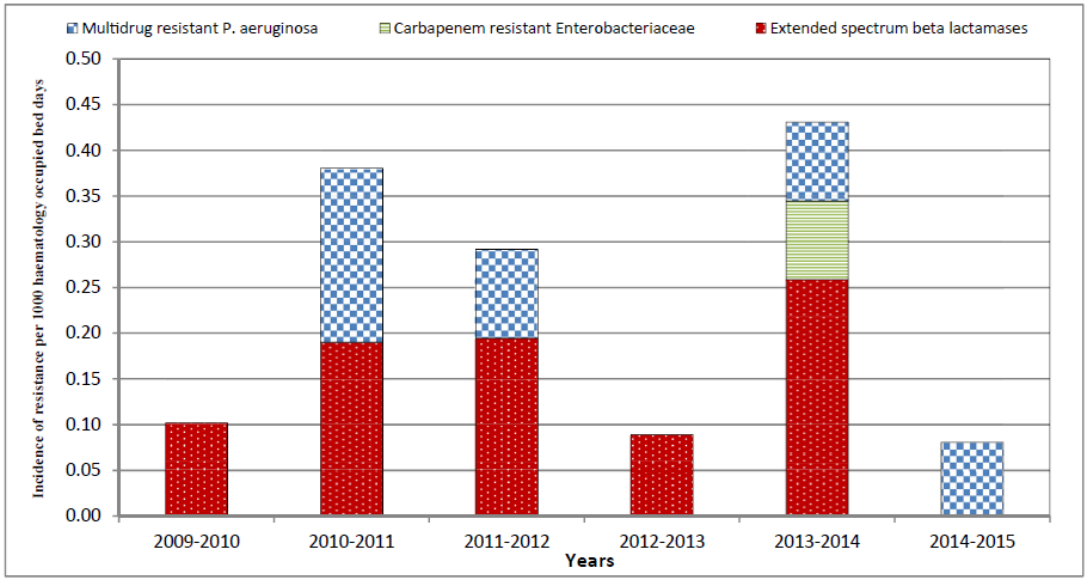


Figure 3 Incidence of multidrug resistant Gram-negative bacilli by year.

Infect Dis Health. 2020 Feb;25(1):22-29.

Microbiological documentation in ICU

Survival in neutropenic patients with severe sepsis or septic shock

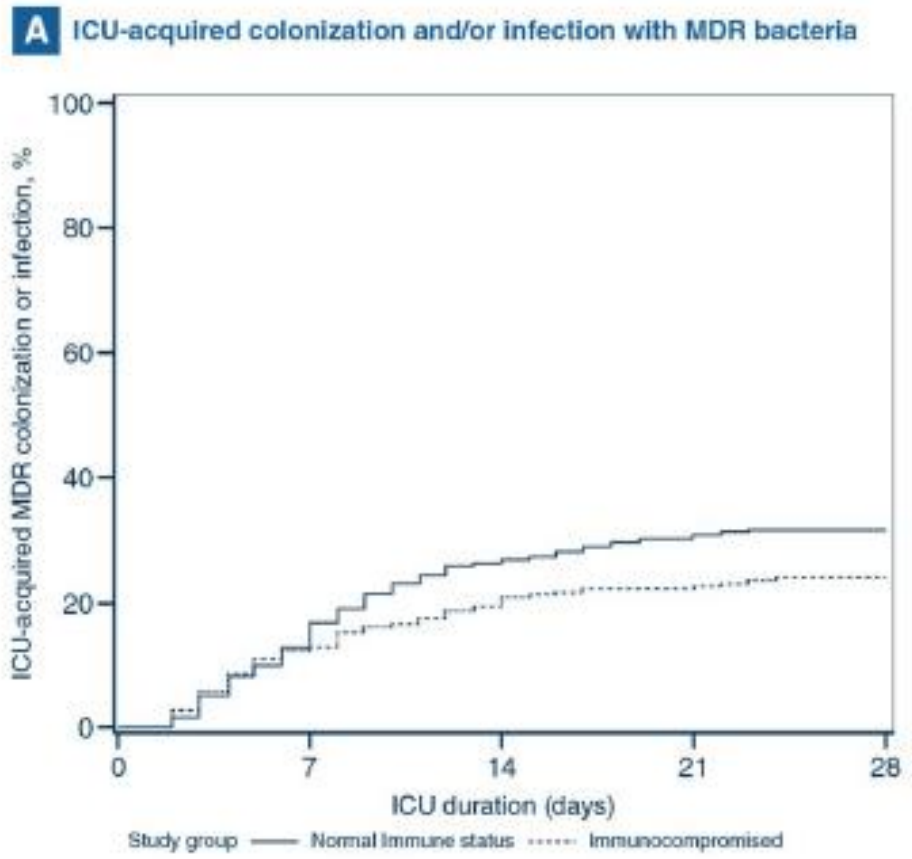
Matthieu Legrand, MD; Adeline Max, MD; Vincent Peigne, MD; Eric Mariotte, MD; Emmanuel Canet, MD; Alexandre Debrumetz, MD; Virginie Lemiale, MD; Amélie Seguin, MD; Michael Darmon, MD; Benoît Schlemmer, MD; Élie Azoulay, MD, PhD

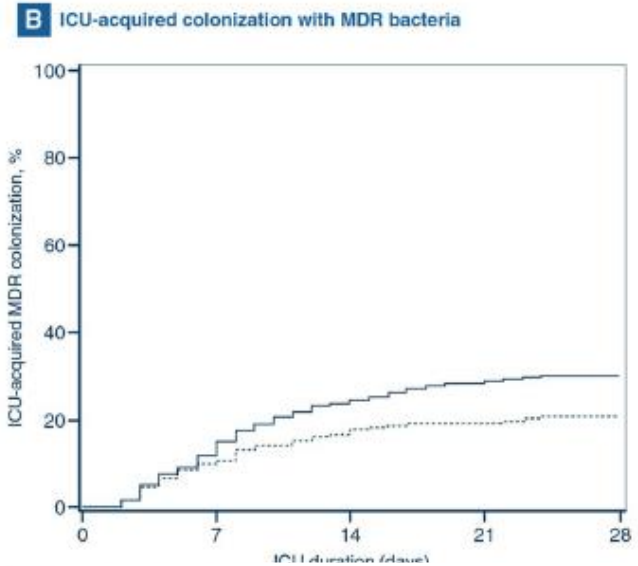
- 488 Severe sepsis or septic shock
  - FUO: 12%
  - Clinically documented: 33%
  - Microbiologically documented: 55% (18% de bacteremia)
    - GP cocci : 23%
      - Strepto :4%
      - SCN: 3%
      - S. aureus :7%
      - Entérococcus?
    - GNB: 67%
      - E.coli : 27%
      - Pseudomonas: 22%

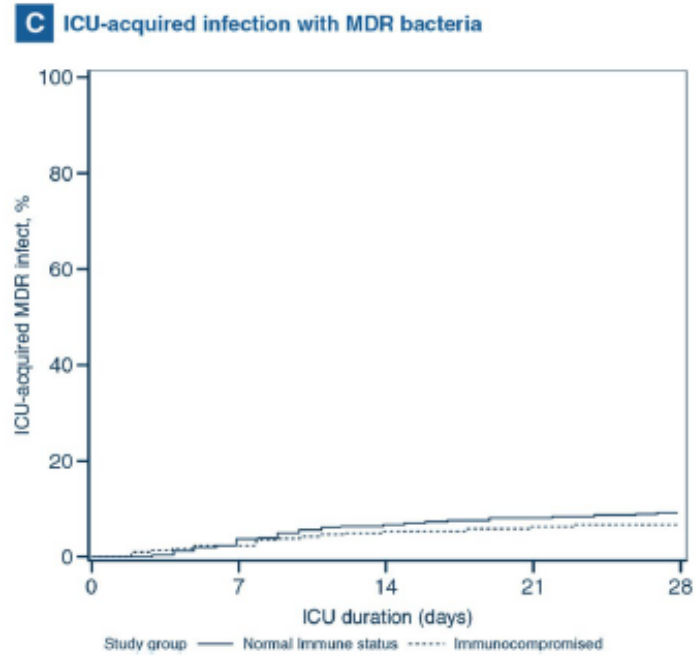
Crit Care Med 2012 Vol. 40, No. 3

Relationship between immunosuppression and intensive care unit-acquired colonization and infection related to multidrug-resistant bacteria: a prospective multicenter cohort study

Louis Kreitmann[1,2], Margot Vasseur[1], Sonia Jermoumi[1], Juliette Perche[3], Jean-Christophe Richard[4], Florent Wallet[5,6], Myriam Chabani[2], Emilie Nourry[2], Pierre Garçon[7], Yoann Zerbib[8], Nicolas Van Grunderbeeck[9], Christophe Vinsonneau[10], Cristian Preda[11,12], Julien Labreuche[13] and Saad Nseir[1,14*]

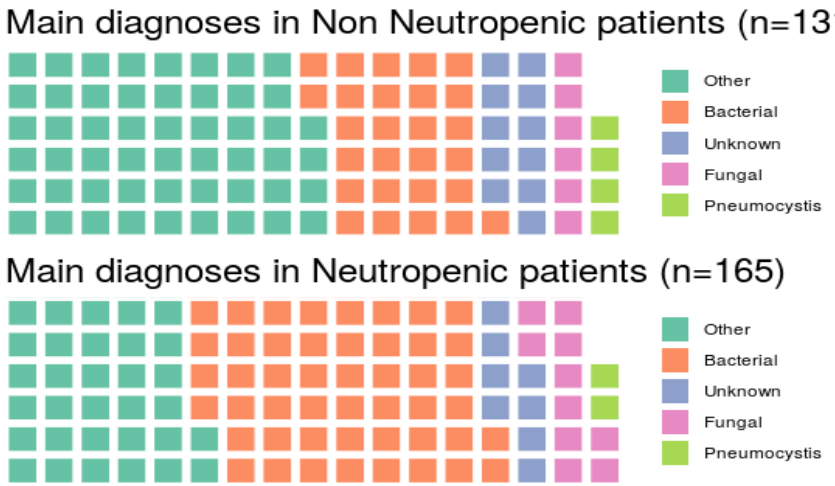






Intensive Care Med (2023) 49:154–165

Acute respiratory failure in immunocompromised patients: outcome and clinical features according to neutropenia status



1

2

Other diagnoses (main etiologies)

	Non-neutropenic (n= 691)	Neutropenic (n= 53)	p-value
Drug toxicity	34 (4.9%)	5(9.4%)	0.27
Cardiogenic pulmonary oedema	75 (10.9%)	13(24.5%)	**0.006**
Tumor infiltration	114 (16.5%)	2 (3.8%)	**0.02**
Aspiration pneumonia	41 (5.9%)	2 (3.8%)	0.73
Viral infection - Influenzae	88 (12.7%)	8 (15.1%)	0.78
Viral infection - Other virus	134 (19.4%)	15 (28.3%)	0.17
Airway obstruction	39 (5.6%)	1 (1.9%)	0.39

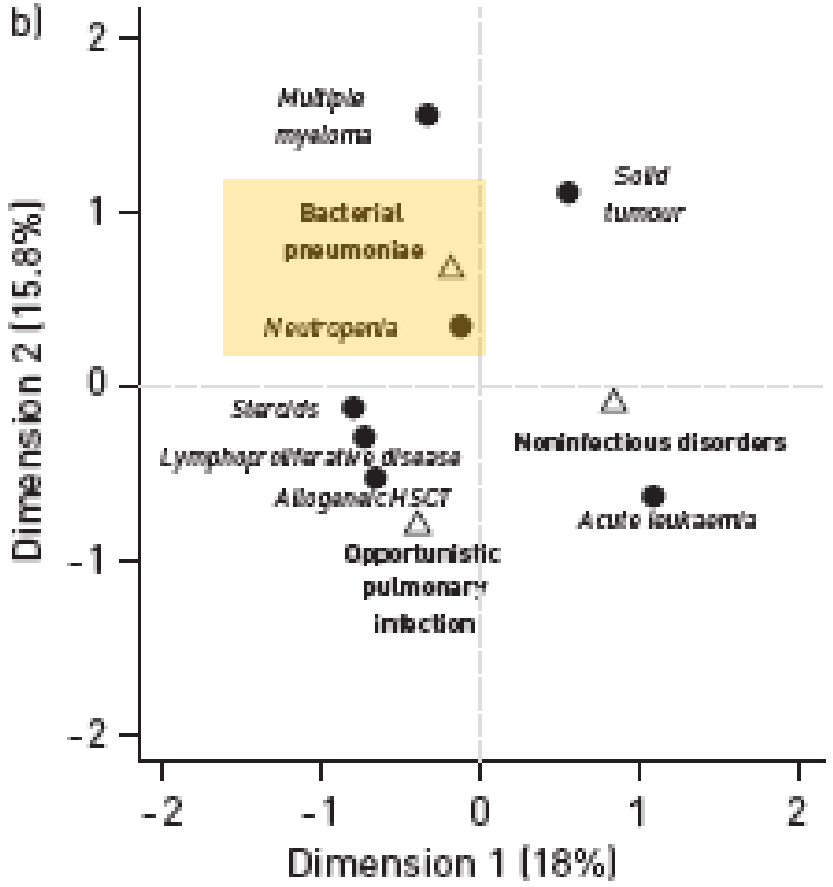
Table 3 Bacterial infectious diagnoses

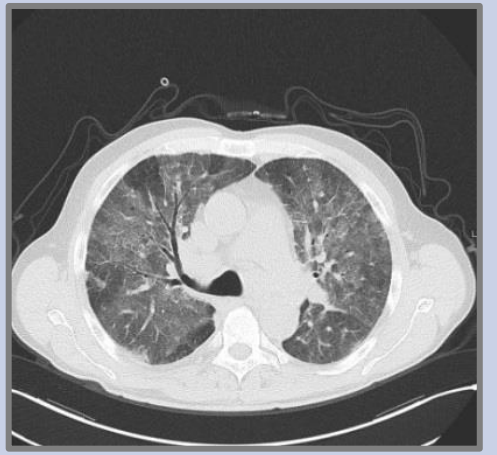
	Non-neutropenic (*n* = 356)	Neutropenic (*n* = 79)	*p* value
			0.044
Gram-negative bacteria			
Pseudomonas	31 (9%)	14 (18%)	
Klebsiella	33 (9%)	14 (18%)	
Escherichia coli	40 (11%)	14 (18%)	
Enterobacter	18 (5%)	3 (4%)	
Stenotrophomonas	3 (1%)	3 (4%)	
Legionella	4 (1%)	2 (3%)	
Branhamella catarrhalis	6 (2%)	2 (3%)	
Acinetobacter	7 (2%)	1 (1%)	
Haemophilus influenzae	13 (4%)	1 (1%)	
Campylobacter jejuni	0 (0%)	1 (1%)	
Citrobacter	1 (0.5%)	1 (1%)	
Proteus	4 (1%)	0	
Hafnia alvei	3 (1%)	0	
Morganella	3 (1%)	0	
Serratia	3 (1%)	0	
Salmonella	2 (0.5%)	0	
Neisseria meningitidis	2 (0.5%)	0	
Bacteroides	1 (0.5%)	0	
Bordetella hinzii	1 (0.5%)	0	
Gram-positive bacteria			
Coagulase-negative staphylococci	49 (14%)	9 (11%)	
Enterococcus	31 (9%)	6 (8%)	
Staphylococcus aureus	49 (14%)	4 (5%)	
Streptococcus	11 (3%)	2 (3%)	
Streptococcus pneumoniae	34 (10%)	1 (1%)	
Actinomyces	3 (1%)	0	
Clostridium	1 (0.5%)	0	
Others			
Mycoplasma	3 (1%)	0	

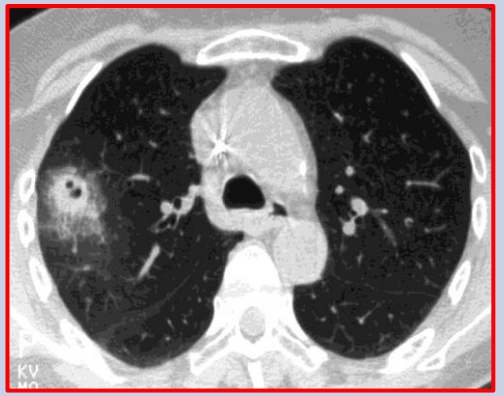
Mokart *et al. Ann. Intensive Care* (2020) 10:146

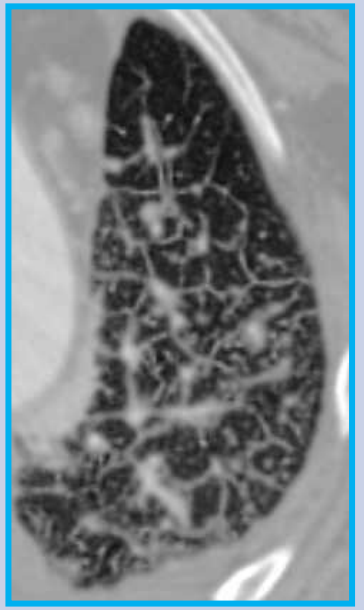
Clinical assessment for identifying causes of acute respiratory failure in cancer patients

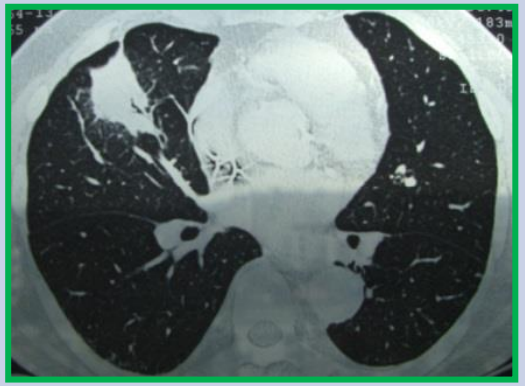
David Schnell[1,2], Julien Mayaux[1,2], Jérôme Lambert[2,3], Antoine Roux[1,2], Anne-Sophie Moreau[1,2], Lara Zafrani[1,2], Emmanuel Canet[1,2], Virginie Lemiale[1,2], Michael Darmon[1,2] and Élie Azoulay[1,2]

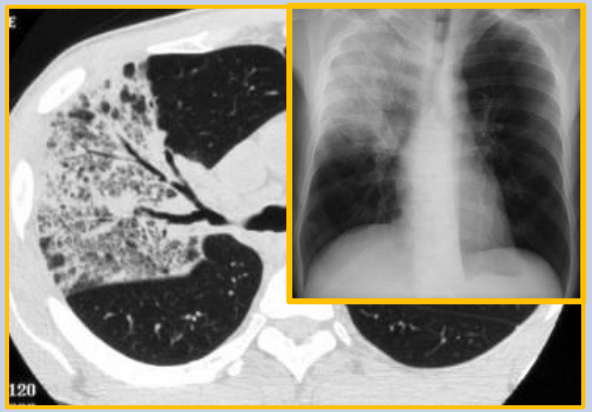












Eur Respir J 2013; 42: 435–443

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

Mokart D, Saillard C, Sannini A, Chow-Chine L, Brun JP, Faucher M, Blache JL, Blaise D, Leone M.

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

ICU intensive care unit, *SOFA* sequential organ failure assessment

Intensive Care Med. 2014 Aug;40(8):1173-4

Initial empirical antibiotic treatment

IDSA GUIDELINES

Table 1 Empiric antibiotic therapy in high risk patients with neutropenic fever (adapted from the IDSA guidelines [4])

Antibiotherapy	Indications	Grade of recommendation
Antipseudomonal β-lactam agent - Carbapenem (meropenem or imipenem-cilastatin) Piperacillin-tazobactam	All high risk patients with neutropenic fever	A-I
Aminoglycosides	Hemodynamic instability	B-III
Vancomycin		A-I
Vancomycin, linezolid or dapto		B-III
Linezolid or daptomycin		B-III
Carbapenem	gram negative bacteria	B-III
Polymyxin-colistin or tigecycline	Risk of Klebsiella pneumonia carbapenemase (KPC)	C-III
- Ciprofloxacin + clindamycin - Aztreonam + vancomycin	Penicillin-allergic patients	A-II

RFE SRLF/SFAR :
β-lactam active on pseudomonal with anti-gram-positive activity

Legrand et al. Annals of Intensive Care 2011, 1:22

Anti-pseudomonal beta-lactams for the initial, empirical, treatment of febrile neutropenia: comparison of beta-lactams (Review)

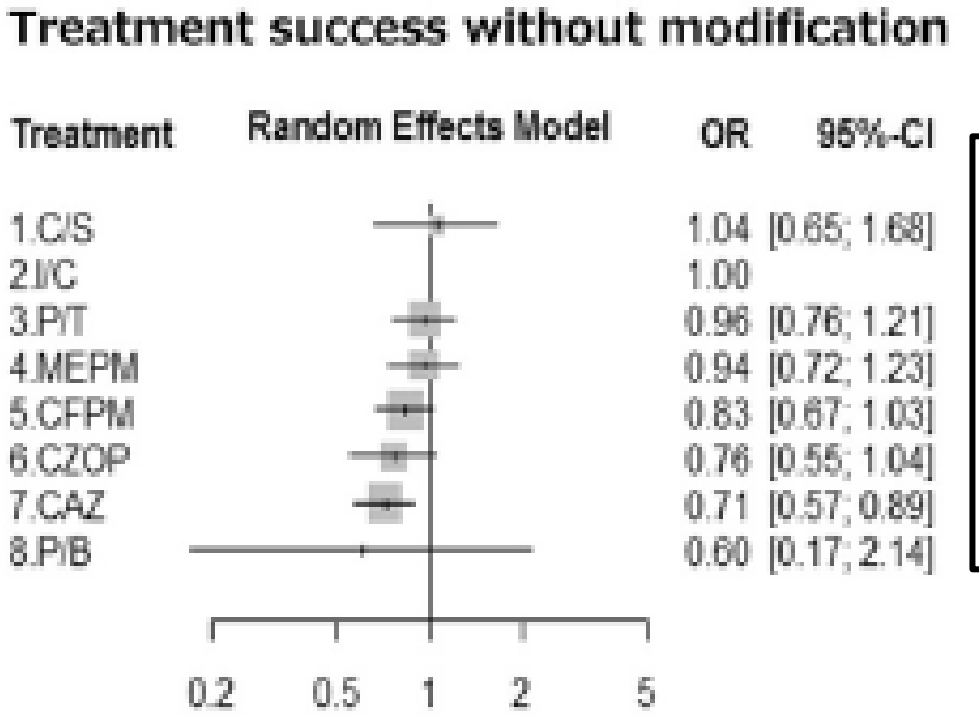
Paul M, Yahav D, Bivas A, Fraser A, Leibovici L

- 44 RCT, patient neutropénique fébrile
  - Comparison of one antipseudomonas beta-lactam vs another (1988-2010)
  - With or without glycopeptide
- All-cause mortality was significantly higher with **cefepime** as compared with other antibiotics, RR 1.39 [1.04, 1.86], 21 trials, 3471 participants
- All-cause mortality was lower with **piperacillin-tazobactam** versus all other antibiotics , RR 0.56 [0.34, 0.92], 8 trials, 1314 participants
- **Ceftazidime** vs others: NS
- **Carbapenem** vs others: NS
  - Fewer therapeutic failures or antibiotic modifications
  - More Clostridium difficile diarrhoea

Cochrane Database Syst Rev. 2010 Nov 10;(11):CD005197

Comparison of antipseudomonal β-lactams for febrile neutropenia empiric therapy: systematic review and network meta-analysis

N. Horita [1,*,3], Y. Shibata [1,3], H. Watanabe [1], H. Namkoong [2], T. Kaneko [1]



Among the recommended anti-pseudomonal β –lactams

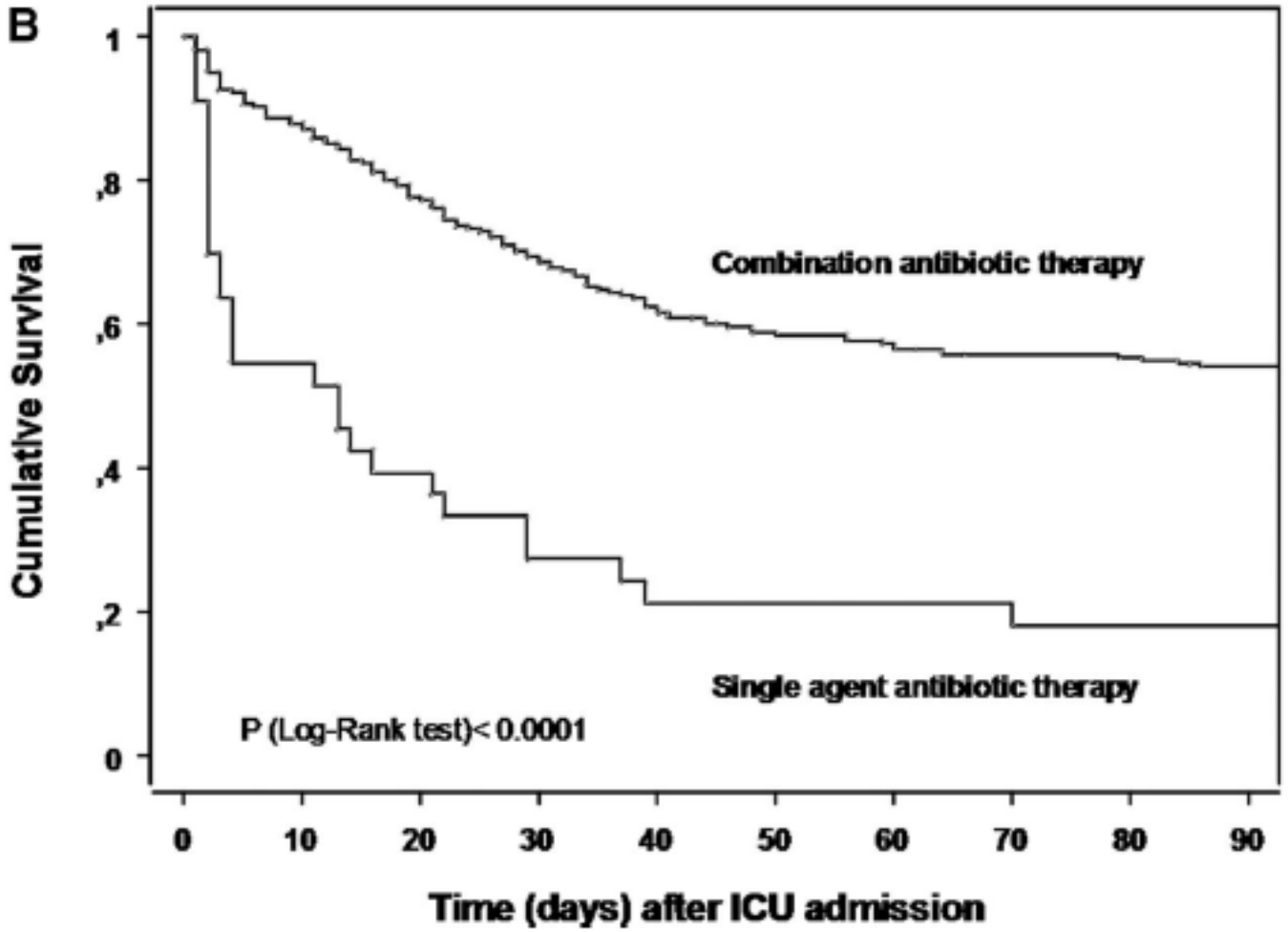
- **Imipenem**
- **Piperacilline/tazobactam**
- **Meropenem**

- **Cefepime**
- **Ceftazidime**

Fig. 2. Forest plots for key findings. Abbreviations: C/S, cefoperazone/sulbactam; CAZ, ceftazidime; CFPM, cefepime; CZOP, cefozopran; I/C, imipenem/cilastatin; MEPM, meropenem P/B, panipenem/betamipron; P/T, piperacillin/tazobactam; OR, odds ratio.

Survival in neutropenic patients with severe sepsis or septic shock

Matthieu Legrand, MD; Adeline Max, MD; Vincent Peigne, MD; Eric Mariotte, MD; Emmanuel Canet, MD;
Alexandre Debrumetz, MD; Virginie Lemiale, MD; Amélie Seguin, MD; Michael Darmon, MD;
Benoît Schlemmer, MD; Élie Azoulay, MD, PhD



Impact of Empirical Antibiotic Regimens on Mortality in Neutropenic Patients with Bloodstream Infection Presenting with Septic Shock

Mariana Chumbita,[a] Pedro Puerta-Alcalde,[a] Carlota Gudiol,[b,c,d] Nicole Garcia-Pouton,[a] Júlia Laporte-Amargós,[b,d] Andrea Ladino,[e] Adaia Albasanz-Puig,[b,d] Cristina Helguera,[f] Alba Bergas,[b] Ignacio Grafia,[e] Enric Sastre,[b] María Suárez-Lledó,[g] Xavier Durà,[b,d] Carlota Jordán,[a] Francesc Marco,[h,i] Maria Condom,[j] Pedro Castro,[k] Jose A. Martínez,[a] Josep Mensa,[a] Alex Soriano,[a] Jordi Carratalà,[b,d] Carolina Garcia-Vidal[a]

TABLE 4 Risk factors for overall mortality, by univariate and multivariate analysis[a]

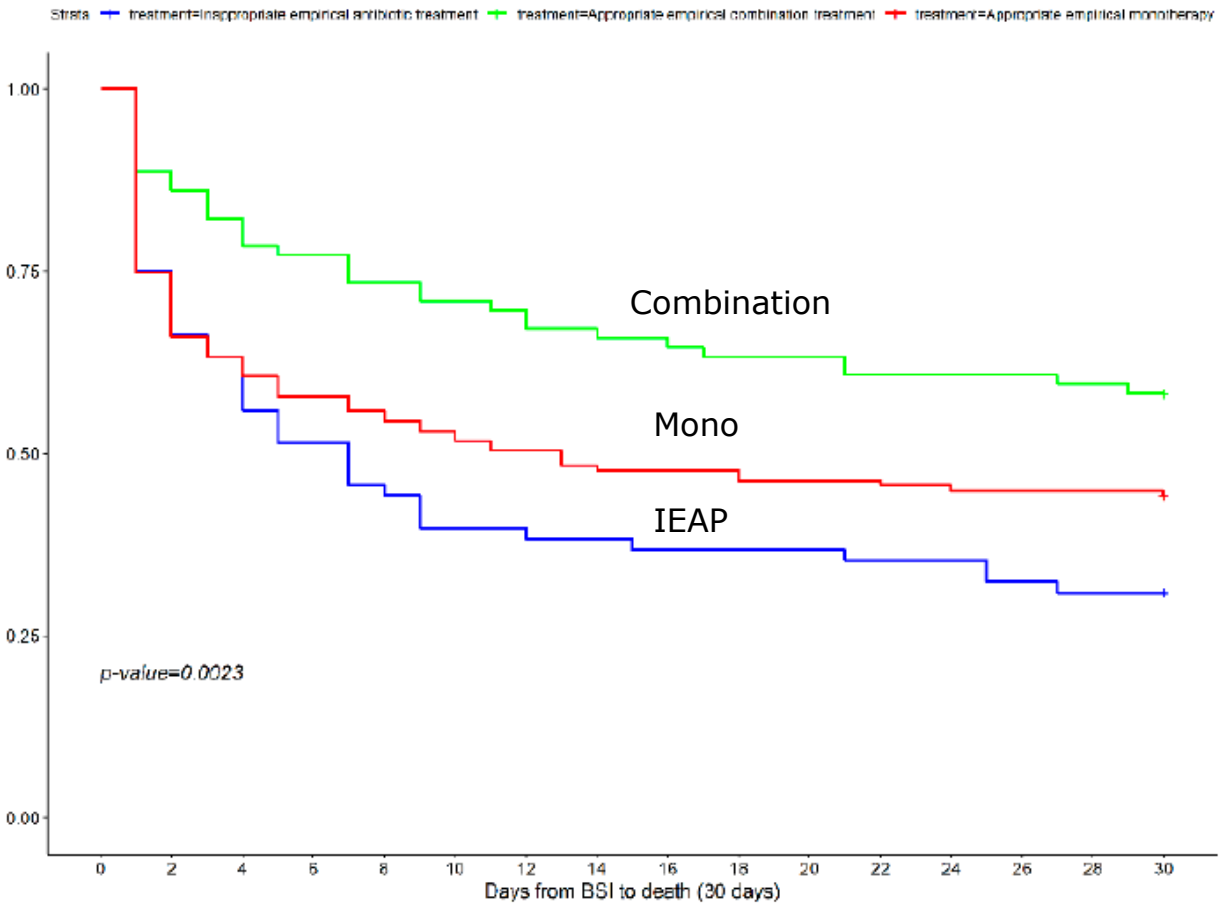
Risk factor	Univariate OR (95% CI)	*P* value	Multivariate OR (95% CI)	*P* value
Male sex	0.78 (0.48–1.30)	0.346		
Age ≥70 yr	2.23 (1.20–4.15)	**0.010**	2.36 (1.19–4.68)	**0.014**
Acute leukemia	0.65 (0.38–1.13)	0.125		
Non-Hodgkin lymphoma	0.94 (0.52–1.72)	0.847		
Multiple myeloma	0.90 (0.37–2.19)	0.811		
Chronic leukemia	8.78 (1.10–69.63)	**0.014**	5.02 (0.60–42.22)	0.138
Solid neoplasia	0.96 (0.57–1.64)	0.906		
Hematopoietic stem cell transplantation	1.29 (0.67–2.48)	0.446		
Any comorbidity	1.04 (0.62–1.75)	0.870		
Corticosteroid therapy	1.16 (0.71–1.89)	0.560		
Nosocomial acquisition	1.41 (0.86–2.31)	0.177		
Pulmonary source	2.06 (1.06–4.01)	**0.032**	1.35 (0.58–3.18)	0.486
Endogenous/unknown source	0.60 (0.37–0.98)	**0.043**	0.69 (0.39–1.23)	0.211
Catheter-related BSI	0.81 (0.35–1.87)	0.615		
Acute kidney injury	2.48 (1.41–4.37)	**0.001**	2.60 (1.39–4.90)	**0.003**
Empirical β-lactam	0.26 (0.73–0.94)	**0.037**	0.41 (0.08–2.16)	0.294
Empirical carbapenem	0.94 (0.58–1.55)	0.819		
Empirical β-lactam plus aminoglycoside	0.30 (0.18–0.50)	**<0.001**	0.32 (0.18–0.57)	**<0.001**
Empirical β-lactam plus specific Gram-positive coverage	0.69 (0.41–1.17)	0.169		
Amikacin as the only active antibiotic	7.84 (0.98–62.83)	**0.025**	15.24 (1.73–134.45)	**0.014**
β-Lactam as the only active antibiotic	1.81 (1.01–3.26)	**0.046**	1.66 (0.72–3.82)	0.236
Coagulase-negative staphylococci	0.34 (0.09–1.34)	0.193		
Staphylococcus aureus	2.10 (0.40–11.01)	0.462		
Enterococcus spp.	1.19 (0.44–3.23)	0.734		
Streptococcus spp.	1.08 (0.45–2.55)	0.867		
E. coli	0.97 (0.58–1.62)	0.901		
Klebsiella spp.	0.80 (0.39–1.64)	0.541		
Pseudomonas aeruginosa	1.32 (0.76–2.29)	0.329		
MDR *P. aeruginosa*	3.19 (0.87–11.71)	0.096		
MDR-GNB	1.57 (0.77–3.18)	0.208		
Candidemia	4.82 (1.05–22.22)	**0.042**	2.18 (0.34–13.94)	0.411
Polymicrobial	1.86 (0.86–3.99)	0.108		
Inappropriate empirical antibiotic therapy for GNB or *Candida* spp.	5.74 (2.14–15.38)	**<0.001**	3.81 (1.31–11.11)	**0.014**

[a]Abbreviations: ESBL, extended-spectrum β-lactamase; MDR, multidrug resistant; GNB, Gram-negative bacilli. Boldface indicates statistically significant values (*P* value < 0.05).

Article

Effect of Combination Antibiotic Empirical Therapy on Mortality in Neutropenic Cancer Patients with *Pseudomonas aeruginosa* Pneumonia

Adaia Albasanz-Puig [1,2,†], Xavier Durà-Miralles [1,†], Júlia Laporte-Amargós [1], Alberto Mussetti [3], Isabel Ruiz-Camps [2,4], Pedro Puerta-Alcalde [5], Edson Abdala [6], Chiara Oltolini [7], Murat Akova [8], José Miguel Montejo [9], Malgorzata Mikulska [10], Pilar Martín-Dávila [2,11], Fabián Herrera [12], Oriol Gasch [13], Lubos Drgona [14], Hugo Manuel Paz Morales [15], Anne-Sophie Brunel [16], Estefanía García [17], Burcu Isler [18], Winfried V. Kern [19], Pilar Retamar-Gentil [2,20], José María Aguado [2,21], Milagros Montero [22], Souha S. Kanj [23], Oguz R. Sipahi [24], Sebnem Calik [25], Ignacio Márquez-Gómez [26], Jorge I. Marin [27], Marisa Z. R. Gomes [28], Philipp Hemmati [29], Rafael Araos [30], Maddalena Peghin [31], José Luis del Pozo [32], Lucrecia Yáñez [33], Robert Tilley [34], Adriana Manzur [35], Andres Novo [36], Natàlia Pallarès [37], Alba Bergas [1], Jordi Carratalà [1,2,*], Carlota Gudiol [1,2,38] and on behalf of the IRONIC Study Group [‡]



Multicentre retrospective study

- Neutropenia + cancer
- PA Bacteriemia (n=1017)
  - PNP+ PA bacteriemia (n=294)
    - Empirical antibiotic => day-30 mortality
      - Mono app vs Combi app vs IEAP

Microorganisms **2022**, *10*, 733. https://doi.org/10.3390/microorganisms10040733

AMINOGLYCOSIDES IN IMMUNOCOMPROMISED CRITICALLY ILL PATIENTS WITH BACTERIAL PNEUMONIA AND SEPTIC SHOCK: A *POST-HOC* ANALYSIS OF A PROSPECTIVE MULTICENTER MULTINATIONAL COHORT

René Lopez,* Jordi Rello,†‡§ Fabio Silvio Taccone,‖ Omar Ben Hadj Salem,¶ Philippe R. Bauer,# Amélie Séguin,** Andry van de Louw,†† Victoria Metaxa,‡‡ Kada Klouche,§§ Ignacio Martin Loeches,‖‖ Luca Montini,¶¶ Sangeeta Mehta,## Fabrice Bruneel,*** T. Lisboa,††† William Viana,‡‡‡ Peter Pickkers,§§§ Lene Russell,‖‖‖ Katerina Rusinova,¶¶¶ Achille Kouatchet,**** François Barbier,†††† Djamel Mokart,‡‡‡‡ Elie Azoulay,* and Michael Darmon*

Intitial cohort

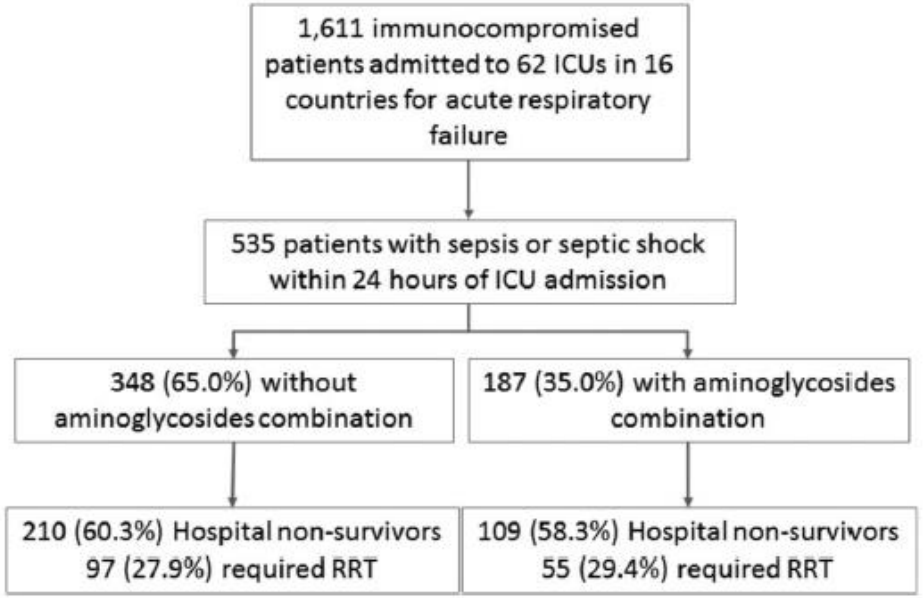


FIG. 1. **Patients' flowchart modified from EFRAIM study (17).**

TABLE 2. **Results of the multivariable mixed regression model with center effect on subsequent mortality risk.**

	Variable of interest: hospital mortality		
	Odds ratio	95% CI	*P* value
Fixed effect			
Performance status			
ECOG 0	*Reference*	–	–
ECOG 1	*1.30*	*0.68–2.47*	*0.43*
ECOG 2	*2.45*	*1.26–4.78*	*0.009*
ECOG 3	*5.55*	*2.61–11.80*	*<0.001*
Solid organ transplant	0.46	0.21–0.99	0.48
Renal replacement therapy	2.84	1.66–4.85	<0.001
Aminoglycosides	**1.14**	**0.69–1.89**	**0.61**
Model discrimination and calibration			
C-stat AUC (95% CI)		0.73 (0.68–0.77)	
Hosmer-Lemeshow-X^2		8.995	0.34

ECOG indicates Eastern Cooperative Oncology Group performance status (19).

Matched cohort 154 vs 154

TABLE 3. **Results of the multivariable mixed regression model with center effect on subsequent mortality risk in propensity score matched cohort.**

	In-hospital mortality		
	Odds ratio	Confidence interval	*P* value
Fixed effect			
D1 Oxygenation modality			
High Flow nasal Oxygen	*Reference*	–	–
Noninvasive ventilation	*1.39*	*0.39–4.91*	*0.61*
Standard oxygen	*0.48*	*0.18–1.28*	*0.14*
Invasive MV	*0.76*	*0.28–2.06*	*0.59*
Aminoglycosides	**0.89**	**0.49–1.61**	**0.69**
Model discrimination and calibration			
C-stat AUC (95% CI)		0.72 (0.68–0.77)	
Hosmer-Lemeshow-X^2		26.248	0.001

MV indicates mechanical ventilation.

Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia (Review)

Paul M, Dickstein Y, Schlesinger A, Grozinsky-Glasberg S, Soares-Weiser K, Leibovici L

THE COCHRANE COLLABORATION®

published in Issue 2, 2014

- 71 RCT (1983-2012)
  - Reduced overall mortality in the monotherapy group(RR 0.87, 95% CI 0.75 to 1.02,ns)
  - Reduced infection-related mortality in the monotherapy group (RR 0.80, 95% CI 0.64 to 0.99).
  - Similar bacterial superinfections in the 2 groups
  - More fungal superinfections in the aminoglycoside group
  - More side-effects in the aminoglycoside group
    - Nephrotoxicity +++

Empirical antibiotics targeting gram-positive bacteria for the treatment of febrile neutropenic patients with cancer (Review)

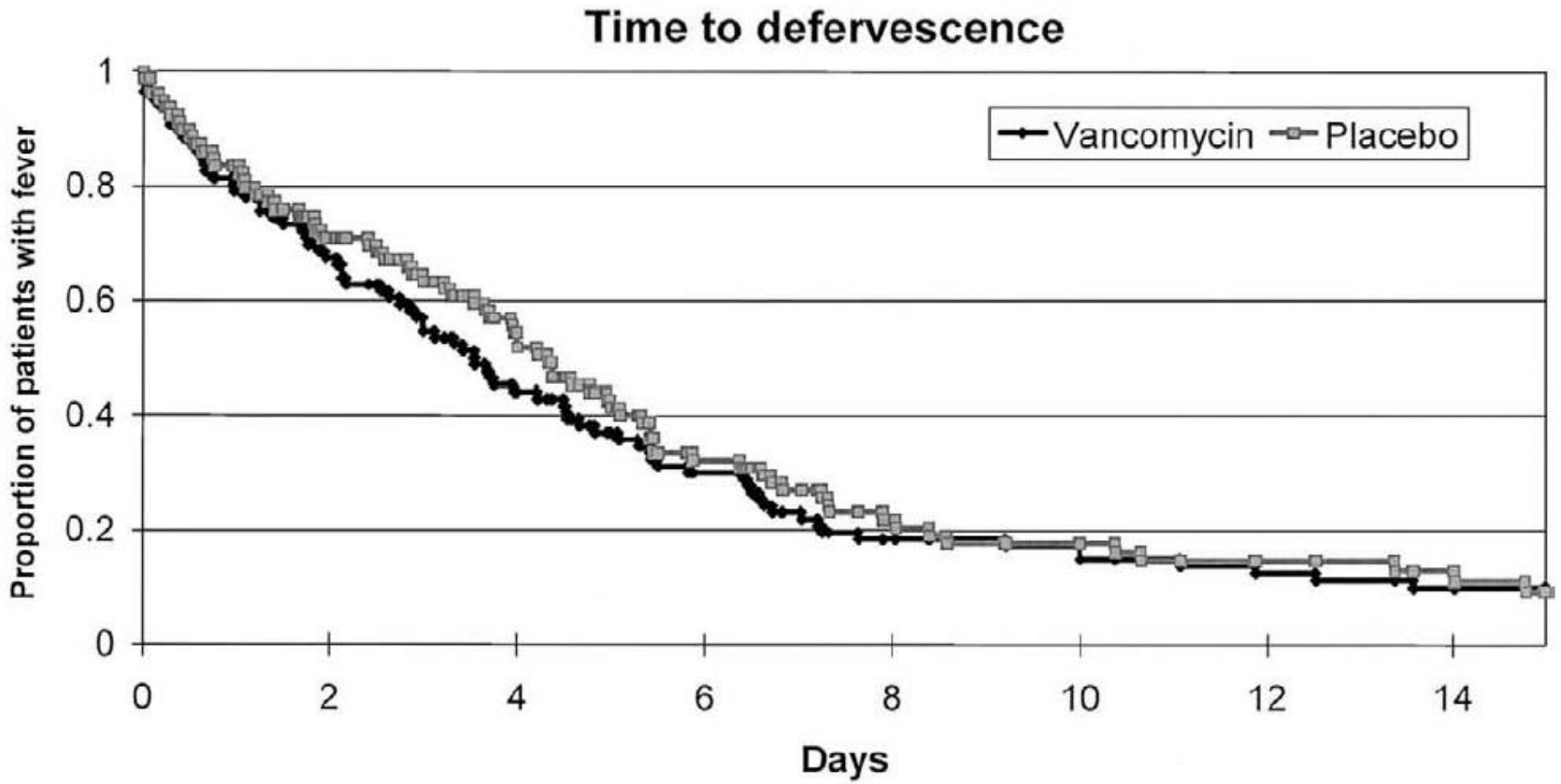
Beyar-Katz O, Dickstein Y, Borok S, Vidal L, Leibovici L, Paul M

- 14 RCTs, 2782 épisodes (2012-2017)
  - BL vs the same BL +anti GPB (or equivalent)
- No difference in terms of mortality (8 RCTs)
- Failure of empirical treatment (11RCTs)
  - More changes in the monotherapy arm (11RCTs)
  - Reduced failures if GPB documentation (5RCTs)
  - Overall same failure rate (7RCTs)
- No increase in fungal superinfections in the anti GPB arm
- No more nephrotoxicity
- Reduced superinfection with GPB in the anti-GPB arm

Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD003914.
DOI: 10.1002/14651858.CD003914.pub4.

Vancomycin versus Placebo for Treating Persistent Fever in Patients with Neutropenic Cancer Receiving Piperacillin-Tazobactam Monotherapy

A. Cometta,[1] W. V. Kern,[2] R. De Bock,[3] M. Paesmans,[4] M. Vandenbergh,[4] F. Crokaert,[4] D. Engelhard,[5] O. Marchetti,[1] H. Akan,[7] A. Skoutelis,[9] V. Korten,[8] M. Vandercam,[5] H. Gaya,[10] A. Padmos,[11] J. Klastersky,[4] S. Zinner,[12] M. P. Glauser,[1] T. Calandra,[1] and C. Viscoli,[13] for the International Antimicrobial Therapy Group of the European Organization for Research Treatment of Cancer[a]



Clinical Infectious Diseases 2003; 37:382–9

Efficacy and Safety of Linezolid Compared with Vancomycin in a Randomized, Double-Blind Study of Febrile Neutropenic Patients with Cancer

Branimir Jaksic,[1] Giovanni Martinelli,[2] Jaime Perez-Oteyza,[3] Charlotte S. Hartman,[4] Linda B. Leonard,[4] and Kenneth J. Tack[4]

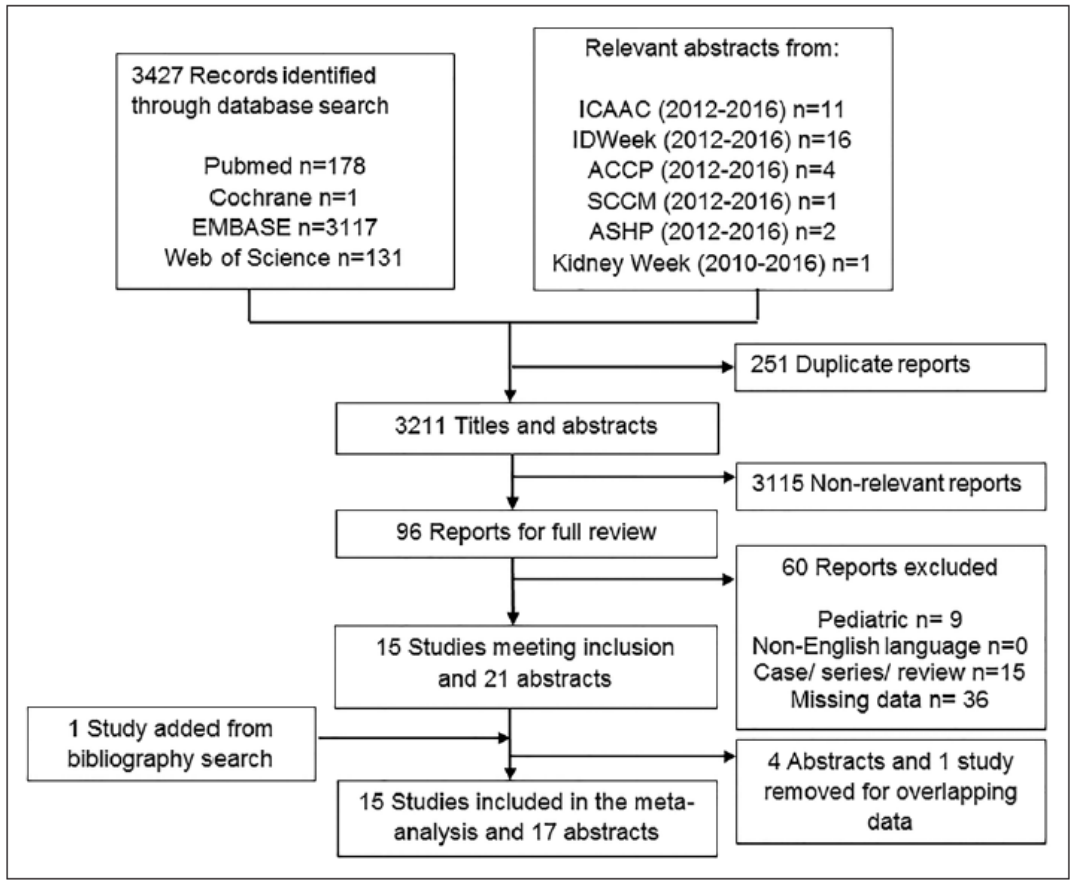
Table 3. Clinical outcome at 7 days after the completion of therapy (i.e., at the test of cure assessment).

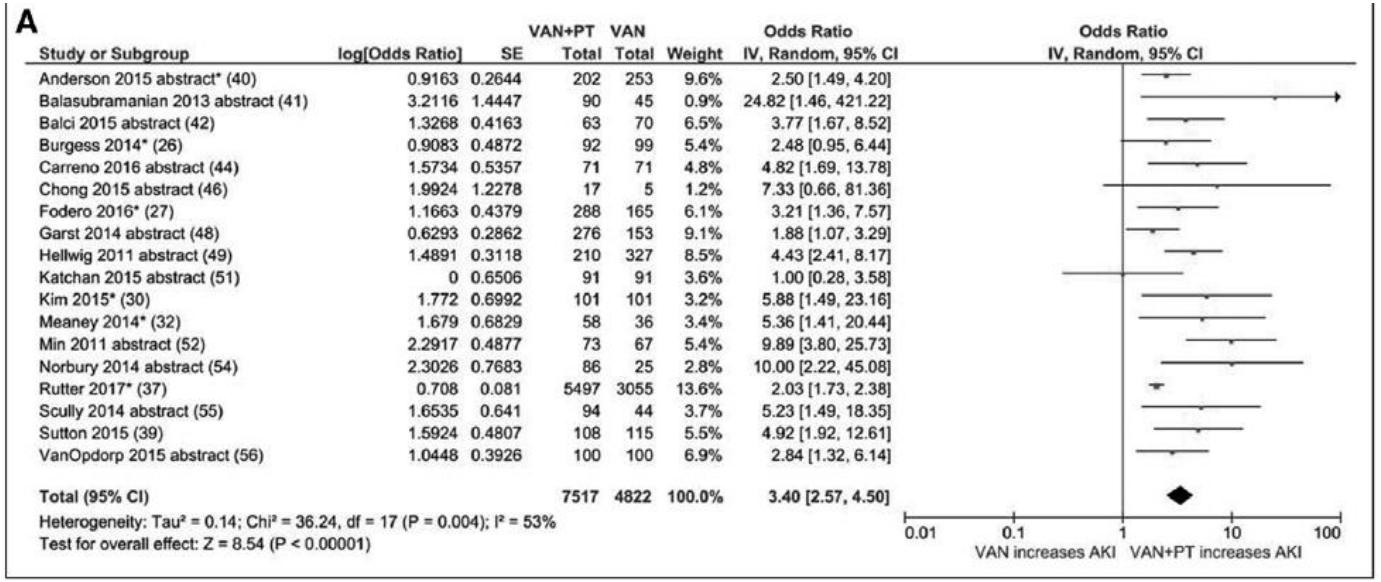
Population, presentation	No. of successes/no. of patients assessed (%)[a]		95% CI, %[b]	P[c]
	Linezolid group	Vancomycin group		
ITT	219/251 (87.3)	202/237 (85.2)	−4.1 to 8.1	.52
Primary malignancy				
Leukemia	119/143 (83.2)	111/138 (80.4)	−6.2 to 11.8	.55
Lymphoma	63/71 (88.7)	56/62 (90.3)	−12.0 to 8.8	.77
Myeloma	24/24 (100)	23/24 (95.8)	−3.8 to 12.2	.31
Tumor	11/11 (100)	11/12 (91.7)	−7.3 to 24.0	.33
Other	2/2 (100)	1/1 (100.0)	Not calculable	
Type of infection				
Fever of uncertain origin	72/78 (92.3)	66/74 (89.2)	−6.1 to 12.3	.51
Bacteremia of unknown source	59/72 (81.9)	53/67 (79.1)	−10.3 to 16.0	.67
Vascular catheter–related infection	23/27 (85.2)	24/28 (85.7)	−19.2 to 18.1	.96
Skin and soft-tissue infection	19/21 (90.5)	14/17 (82.4)	−13.9 to 30.2	.46
Pneumonia	19/23 (82.6)	13/15 (86.7)	−27.2 to 19.1	.74
Urinary tract infection	2/2 (100)	2/3 (66.7)	−20.0 to 86.7	.36
Other	25/28 (89.3)	30/33 (90.9)	−16.7 to 13.5	.83
MITT	55/63 (87.3)	43/50 (86.0)	−11.4 to 14.0	.84
Clinically evaluable	171/185 (92.4)	158/177 (89.3)	−2.8 to 9.1	.30
Microbiologically evaluable	41/47 (87.2)	32/37 (86.5)	−13.8 to 15.3	.92

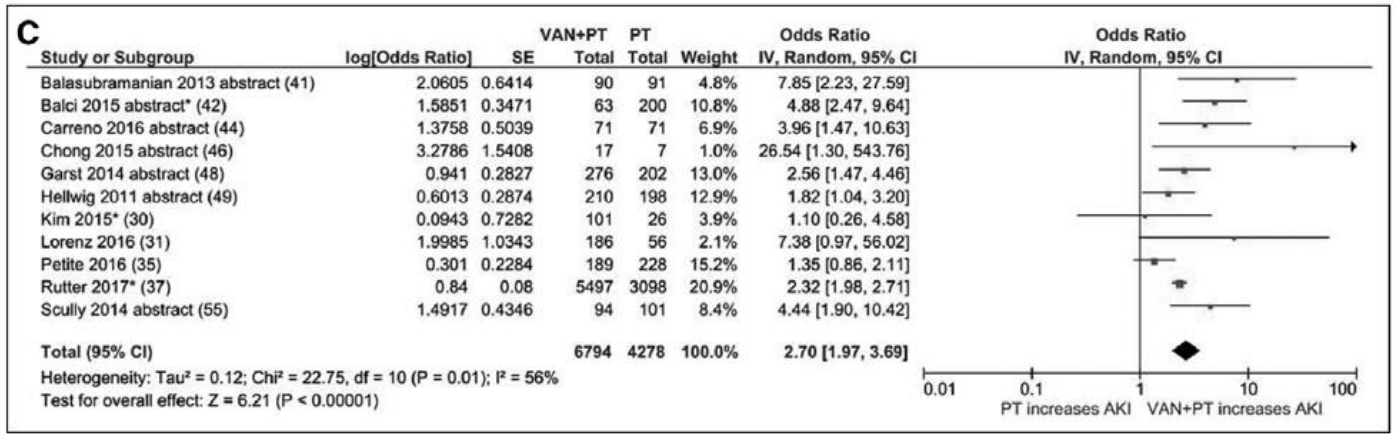
Comparable efficiency
Linezolid
- Longer recovery from neutropenia
- Reduced time to defervescence
- Less renal failure

Vancomycin Plus Piperacillin-Tazobactam and Acute Kidney Injury in Adults: A Systematic Review and Meta-Analysis

Megan K. Luther, PharmD[1–3]; Tristan T. Timbrook, PharmD, MBA, BPCS[1,2]; Aisling R. Caffrey, PhD, MS[1–4]; David Dosa, MD, MPH[3,4]; Thomas P. Lodise, PharmD, PhD[5]; Kerry L. LaPlante, PharmD, FCCP[1–4]







(*Crit Care Med* 2018; 46:12–20)

Antimicrobial stewardship in high-risk febrile neutropenia patients

Adrien Contejean[1,2,3*], Salam Abbara[4,5], Ryme Chentouh[3], Sophie Alviset[3], Eric Grignano[2], Nabil Gastli[6], Anne Casetta[7], Lise Willems[2], Etienne Canouï[3], Caroline Charlier[1,3,8], Frédéric Pène[1,9], Julien Charpentier[9], Jeanne Reboul-Marty[10], Rui Batista[11], Didier Bouscary[1,2] and Solen Kernéis[3,5,12]

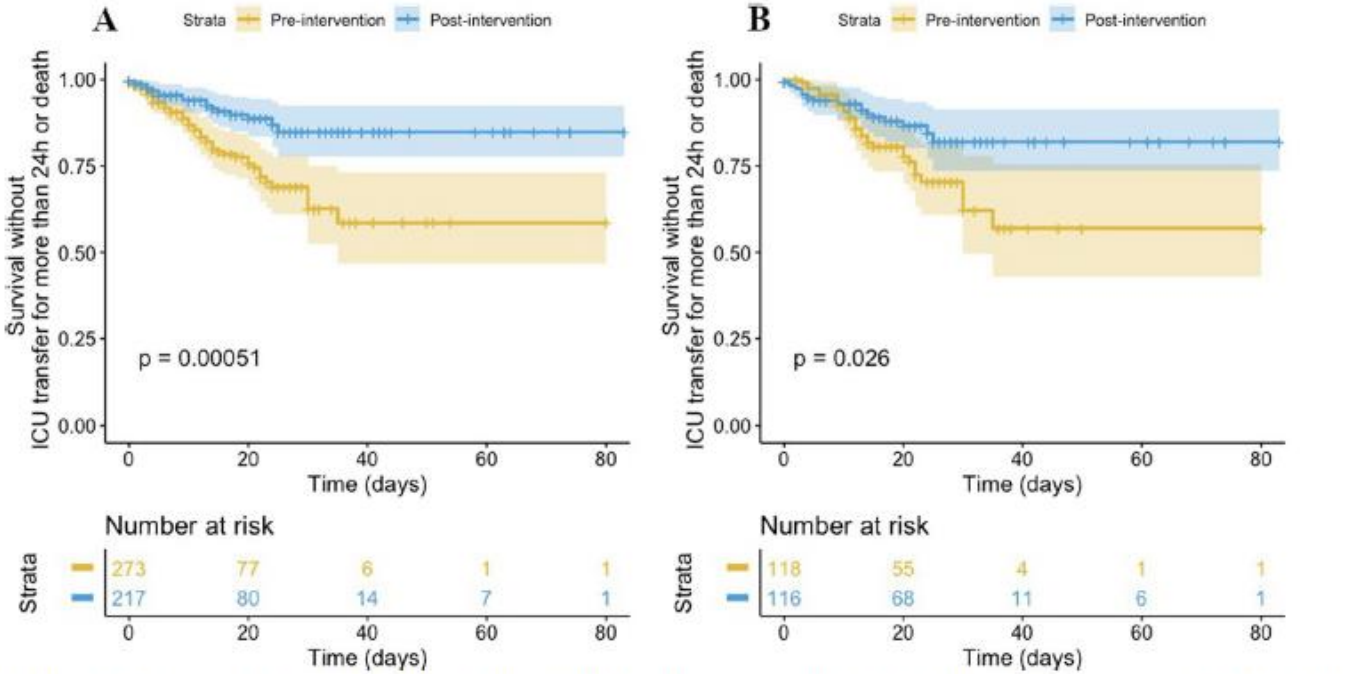


Fig. 2 Kaplan–Meier curves for occurrence of a negative outcome (ICU transfer for more than 24 h or death). A: Overall study population; B: Hospital stays with at least one febrile episode. Log-rank tests were used for statistical comparisons. Faded areas represent the 95% confident interval of each curve

Contejean *et al.*
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Advances in antibacterial treatment of adults with high-risk febrile neutropenia

Adrien Contejean [1,2,3]*, Alexis Maillard [2], Etienne Canouï [2], Solen Kernéis[3,4,5], Bruno Fantin[3,6], Didier Bouscary[3,7], Perrine Parize [8], Carolina Garcia-Vidal[9,10] and Caroline Charlier [2,3,11,12]

Table 4. Main antimicrobial stewardship interventions to consider in patients with febrile neutropenia

Clinical situation	Intervention	References
Fever of unknown origin	Consider stopping antibiotics after at least 3 days of treatment and 48 h of apyrexia	9,10,120–124
CDI or MDI with no severity criteria	Consider the same treatment duration as in non-neutropenic patients if the patient gets at least 4 days of apyrexia and clinical and microbiological resolution Consider de-escalation to targeted therapy against documented bacteria	9,10,25,120,121,123,124
Fever persistence or breakthrough under broad-spectrum antibiotics AND no new clinical sign AND no severity criteria AND no MDR bacteria colonization	Do not consider antibiotic escalation	9,10,120,121
Ongoing combination of anti-Gram-positive and anti-*P. aeruginosa* β-lactam antibiotics and no microbiological documentation at Day 3	Consider stopping anti-Gram-positive antibiotics and pursuing only anti-*P. aeruginosa* β-lactam	9,10,120,121
Ongoing carbapenem AND no microbiological documentation at Day 3 AND patient is stable	Consider de-escalation to a narrower-spectrum β-lactam covering *P. aeruginosa*	10,120,121
Ongoing aminoglycosides	Consider stopping aminoglycosides at Day 2 or 3 when patient is stable	10,120,121
Pneumonia or cutaneous cellulitis	Consider tailored-fit treatment based on bronchoscopy and broncho-alveolar lavage samples	120
Initial severity criteria or corticosteroids	Sometimes excluded from published local guidelines Consider tailored-fit treatment	120,121

CDI, clinically documented infection; MDI, microbiologically documented infection.

Advances in antibacterial treatment of adults with high-risk febrile neutropenia

Adrien Contejean [1,2,3]*, Alexis Maillard [2], Etienne Canouï [2], Solen Kernéis[3,4,5], Bruno Fantin[3,6], Didier Bouscary[3,7], Perrine Parize [8], Carolina Garcia-Vidal[9,10] and Caroline Charlier [2,3,11,12]

Table 1. Main pharmacological modifications of antibiotics in febrile neutropenia

Pharmacological modifications	Involved antibiotics	References
Increase in volume of distribution	β-Lactams[a] Glycopeptides Daptomycin Aminoglycosides	57–65
Increase in drug clearance and decrease in elimination half-life	β-Lactams[a] Glycopeptides Daptomycin Aminoglycosides	57–65
Decrease in peak concentration (C_{max})	Daptomycin Aminoglycosides	63–65
Decrease in AUC	Glycopeptides Daptomycin	61–63
Decrease in post-antibiotics effect	Carbapenems Aminoglycosides	66,67

[a]Ceftolozane/tazobactam and ceftazidime/avibactam have not been specifically studied in patients with febrile neutropenia.

Advances in antibacterial treatment of adults with high-risk febrile neutropenia

Adrien Contejean [1,2,3]*, Alexis Maillard [2], Etienne Canouï [2], Solen Kernéis[3,4,5], Bruno Fantin[3,6], Didier Bouscary[3,7], Perrine Parize [8], Carolina Garcia-Vidal[9,10] and Caroline Charlier [2,3,11,12]

J Antimicrob Chemother 2023; **78**: 2109–2120

Table 2. Proposed dosage and infusion modalities of parenteral antibiotics in patients with high-risk febrile neutropenia and no otherwise specified condition

Antibiotics	Infusion modalities	Administration rules	Stability	Therapeutic drug monitoring	References
Piperacillin/ tazobactam	4 g loading dose over 30 min 12 g/day CI	Dilution in saline serum C_{max} 80 mg/mL + 10 mg/mL	24 h at 25°C	Piperacillin concentration at steady state (≥24 h)	76,78–80
Cefepime	2 g loading dose over 30 min 6 g/day CI	Dilution in saline serum C_{max} 50 mg/mL Administration in three separate infusions over 8 h	8 h at 25°C	Cefepime concentration at steady state (≥24 h)	78–83
Ceftazidime	2 g loading dose over 30 min 6 g/day CI	Dilution in saline serum C_{max} 80 mg/mL Administration in three separate infusions over 8 h	8 h at 25°C	Ceftazidime concentration at steady state (≥24 h)	78–80,84
Meropenem	2 g loading dose over 30 min 6 g/day CI	Dilution in saline serum C_{max} 50 mg/mL Administration in three separate infusions over 8 h	8 h at 25°C	Meropenem concentration at steady state (≥24 h)	80,85,86
Vancomycin	25 mg/kg loading dose over 2 h (max. 2 g) 40 mg/kg/day CI	Dilution in saline serum or G5% C_{max} 40 mg/mL	48 h at 25°C	Vancomycin concentration at steady state (24 h after loading dose)	78,79,87–91
Daptomycin	10 mg/kg/day over 30 min	Dilution in saline serum C_{max} 500 mg/50 mL	12 h at 25°C	Efficacy: 24 h AUC/MIC or daptomycin concentration at peak (30 min after the end of infusion) Toxicity: daptomycin trough concentration, before subsequent infusion	63,79,92–95
Amikacin	30 to 35 mg/kg/day over 30 min	Dilution in saline serum or G5% C_{max} 20 mg/mL	24 h at 25°C	Efficacy: amikacin concentration at peak (30 min after the end of infusion) Toxicity: amikacin trough concentration, before subsequent infusion	64,65
Gentamicin	6 to 7 mg/kg/day over 30 min	Dilution in saline serum or G5% C_{max} 10 mg/mL	24 h at 25°C	Efficacy: gentamicin concentration at peak (30 min after the end of infusion) Toxicity: gentamicin trough concentration, before subsequent infusion	64,65,79

G5%, Glucose 5%.

Advances in antibacterial treatment of adults with high-risk febrile neutropenia

Adrien Contejean [1,2,3]*, Alexis Maillard [2], Etienne Canouï [2], Solen Kernéis[3,4,5], Bruno Fantin[3,6], Didier Bouscary[3,7], Perrine Parize [8], Carolina Garcia-Vidal[9,10] and Caroline Charlier [2,3,11,12]

Table 3. Clinical hypotheses if patient is still febrile at Day 3

Hypotheses	Complementary investigations
Underdosed antibiotics	Therapeutic drug monitoring
Inappropriate antibiotic therapy	Repeat blood cultures
Uncontrolled focal infection	Full body tomography
	Consider [^{18}F]FDG-PET-CT scan
	Therapeutic drug monitoring
	Consider central venous catheter withdrawal and culture
	Search for *Clostridioïdes difficile* infection
Thrombosis (+/− septic) of central venous catheter	Central catheter Doppler ultrasound
	Repeat blood cultures
Undocumented MDR bacteria	Repeat blood cultures
Insufficient antibacterial spectrum	
Viral infection	Nasopharyngeal swab with PCR test
(flu, respiratory syncytial virus, SARS-CoV-2, etc.)	
Invasive fungal infection	Sinus and chest tomography
(aspergillosis, mucormycosis, invasive candidiasis, etc.)	Galactomannan antigen
	Aspergillus sp. blood PCR
	Mucor sp. blood PCR
	β-D-Glucan
	Repeat blood cultures

Antibiotic Resistance in the Patient With Cancer: Escalating Challenges and Paths Forward

Amila K. Nanayakkara, PhD [1]; Helen W. Boucher, MD[2]; Vance G. Fowler, Jr, MD, MHS[3]; Amanda Jezek[4]; Kevin Outterson, JD, LLM[5,6]; David E. Greenberg, MD[1,7]

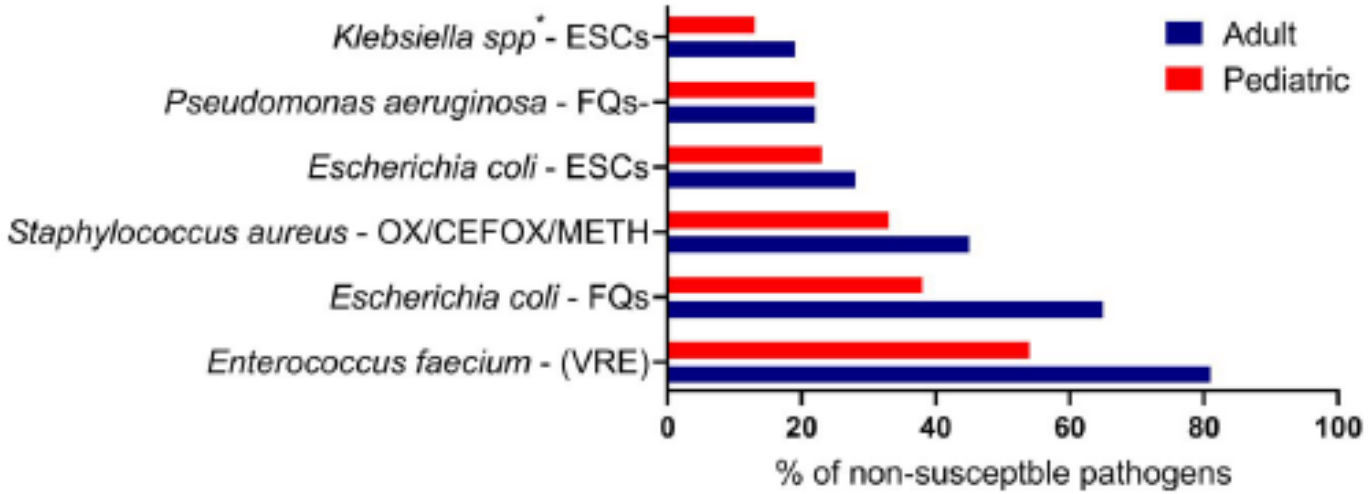

FIGURE 1. Antibiotic Resistance Is Common in Patients With Cancer. This bar graph displays the percentage of pathogens reported from adult and pediatric central line-associated bloodstream infections (CLABSIs) that tested nonsusceptible (NS) to selected antimicrobial agents in hospital oncology units in the United States from 2015 to 2017. Data for the graph were obtained from the National Healthcare Safety Network 2015 to 2017 adult and pediatric antibiotic resistance reports. **Klebsiella* spp. include *K. oxytoca* and *K. pneumoniae*. ESCs indicates extended-spectrum cephalosporins (cefepime, cefotaxime, ceftazidime, or ceftriaxone); FQs, fluoroquinolones (ciprofloxacin or levofloxacin); OX/CEFOX/METH, oxacillin, cefoxitin, or methicillin; VRE, vancomycin-resistant *Enterococcus*.

Carbapenem-resistant Enterobacteriaceae in special populations: Solid organ transplant recipients, stem cell transplant recipients, and patients with hematologic malignancies

Stephanie M. Pouch & Michael J. Satlin

Table 2. Mortality rates after Carbapenem-resistant Enterobacteriaceae (CRE) Infections in patients with hematologic malignancies and haematopoietic stem cell transplant (HSCT) recipients.

Ref.	Geographic Location	Patients (N)	CRE isolate(s)	Types of Infection	HSCT recipients (N)	Neutropenic patients (N)	Overall mortality rate	CRE-related mortality rate
57	Italy 13 centers	161	*K. pneumoniae*	Bacteremia	NR	NR	52% 30-day	NR
64	Italy 52 centers	112	*K. pneumoniae*	Bacteremia (99) Pneumonia only (12) Skin (1)	112	84	52%30-day	54%
54	Italy 5 centers	89	*K. pneumoniae* KPC	NR	NR	70	40% 14-day	NR
56	New York City, USA2 centers	43	Enterobacteriaceae	Bacteremia	15	43	53% 30-day	51%
104	Sao Paolo, Brazil	19	*K. pneumoniae* KPC	Bacteremia (15)UTI (2) Other (2)	1	8	63% 30-day	NR
61	Istanbul, Turkey	16	Enterobacteriaceae OXA-48-type	Bacteremia	NR	15	67% 28-day	NR
105	Cleveland, OH, USA	9	*K. pneumoniae*	Bacteremia	NR	6	33% 14-day	NR
98	Israel	8	*K. pneumoniae*	Bacteremia	5	7	50%	38%
106	Bethesda, MD, USA	6	*K. pneumoniae*	Bacteremia	4	NR	100%	67%

Note. Abbreviations: Ref, reference; N, number; NYC, New York City; KPC, *Klebsiella pneumoniae* carbapenemase; OH, Ohio; MD, Maryland; NR, not reported.

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Risk Factors and Outcomes of Antibiotic-resistant *Pseudomonas aeruginosa* Bloodstream Infection in Adult Patients With Acute Leukemia

Yuanqi Zhao, Qingsong Lin, Li Liu, Runzhi Ma, Juan Chen, Yuyan Shen, Guoqing Zhu, Erlie Jiang, Yingchang Mi, Mingzhe Han, Jianxiang Wang, and Sizhou Feng

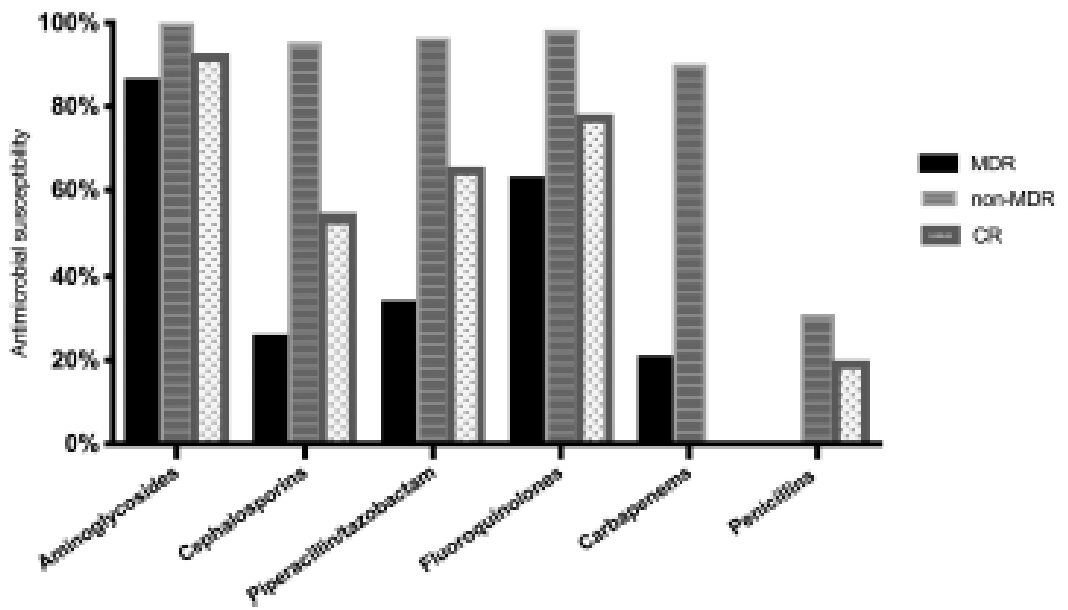


Figure 1. Distribution of antimicrobial susceptibility of *Pseudomonas aeruginosa* isolates according to multidrug-resistant (MDR) and carbapenem-resistant (CR) stratifications.

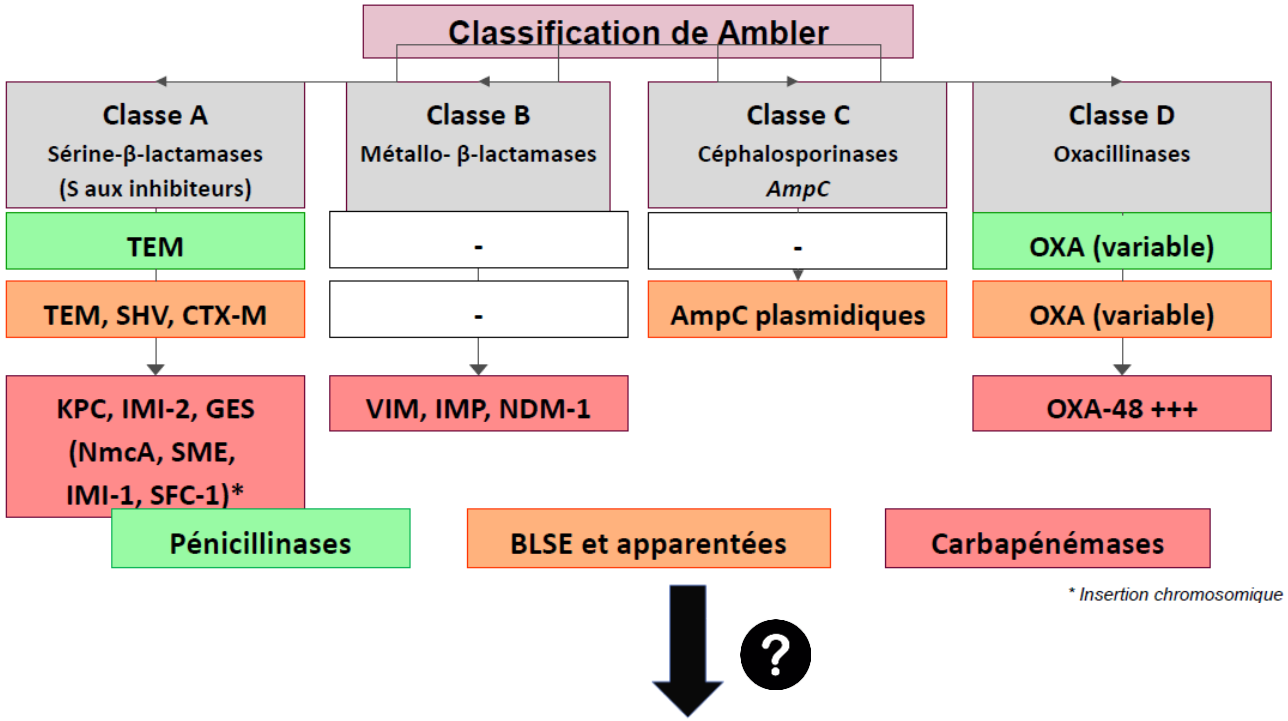
Table 4. Risk Factors for Antibiotic-resistant *Pseudomonas aeruginosa* Bloodstream Infection (BSI) and Death in Patients With *P. aeruginosa* BSI Based on Multivariate Analysis

Variable	OR	(95% CI)	*P* Value
CR-PA BSI			
Previous use of quinolones	2.833	(1.284–6.247)	.010
Previous use of piperacillin/tazobactam	2.466	(1.076–5.654)	.033
Previous use of carbapenems	4.745	(2.019–11.151)	<.001
HSCT	3.145	(1.211–8.197)	.019
MDR-PA BSI			
Previous use of quinolones	5.851	(2.639–12.975)	<.001
Previous use of piperacillin/tazobactam	2.837	(1.151–6.994)	.023
30-day mortality			
Age ≥55 y	2.871	(1.057–7.799)	.039
Perianal infection	4.079	(1.401–11.879)	.010
Pulmonary infection	3.028	(1.231–7.446)	.016
MDR-PA	7.196	(2.773–18.668)	<.001

Abbreviations: BSI, bloodstream infection; CI, confidence interval; CR, carbapenem-resistant; HSCT, hematopoietic stem cell transplantation; MDR, multidrug-resistant; OR, odds ratio; PA, *Pseudomonas aeruginosa*.

Quel traitement des infections à BLSE en réanimation ?

Benoît Pilmis, Thibaud Delerue, Frédéric Mechai, Jean-Ralph Zahar, Françoise Jaureguy



Carbapenems

TABLEAU I

Prérequis pour l'utilisation d'une molécule autres que les carbapénèmes dans le traitement documenté des infections à Entérobactéries productrices de bêtalactamase.

Site infectieux	Extirpable (drainage, chirurgie, retrait du cathéter)
Contrôle de la source	Effectué
Évolution clinique du patient	Stabilisation clinique, absence de gravité, absence d'immunodépression
Type d'enzymes et niveau phénotypique d'expression	CTX-M
CMI	Strictement inférieure à 8 mg/L pour la tazocilline
Espèce microbienne concernée	*Escherichia coli*

Anesth Reanim. 2019; 5: 310-314

Rationale and evidence for the use of new beta-lactam/beta-lactamase inhibitor combinations and cefiderocol in critically ill patients

François Barbier[1,2*], Sami Hraiech[3], Solen Kernéis[4], Nathanaël Veluppillai[4], Olivier Pajot[5], Julien Poissy[6], Damien Roux[2,7] and Jean-Ralph Zahar[2,8] On behalf of the French Intensive Care Society

Table 1 In vitro activity of novel β-lactam/β-lactamase inhibitor combinations and cefiderocol against carbapenem-resistant Gram-negative bacteria

Main mechanisms of carbapenem resistance	Enterobacterales			*Pseudomonas aeruginosa*	*Acinetobacter baumannii*	*Stenotrophomonas maltophilia*
	Class A carbapenemase (KPC)	Class D carbapenemase (OXA-48-like[a])	Class B carbapenemase (MBL[b])	*OprD2* mutation Efflux[c] MBL[d]	OXA[e]	Chromosomal MBL
Ceftolozane–tazobactam	–	–	–	+++ 75%-90% [f]	–[g]	–[g]
Ceftazidime–avibactam	+++ 96%-99%	+++ 96%-99%	–	++ 60%-70%	–[g]	–[g]
Ceftazidime–avibactam plus aztreonam	+++ 96–99%	+++ 96%-99%	+++ >90%	± (MBL) 0–25%	–[g]	++[h] ~85%
Meropenem–vaborbactam	+++ 95–99%	–	–	–	–	–[g]
Imipenem–relebactam	+++ 88%-95%	±	–	++ 70%-90%	–	–[g]
Cefiderocol	+++ 84–91%	+++ 88–93%	++ VIM: 79%-81% NDM: 41%-51%	+++ >90%	+++[i] MIC ≤ 2 mg/L for > 90% of isolates	+++[i] MIC ≤ 2 mg/L for > 90% of isolates

Is Short-Course Antibiotic Therapy Suitable for *Pseudomonas aeruginosa* Bloodstream Infections in Onco-hematology Patients With Febrile Neutropenia? Results of a Multi-institutional Analysis

Xiaomeng Feng,[1,2] Chenjing Qian,[3] Yuping Fan,[1,2] Jia Li,[1,2] Jieru Wang,[1,2] Qingsong Lin,[1,2] Erlie Jiang,[1,2] Yingchang Mi,[1,2] Lugui Qiu,[1,2] Zhijian Xiao,[1,2] Jianxiang Wang,[1,2] Mei Hong,[3] and Sizhou Feng[1,2]

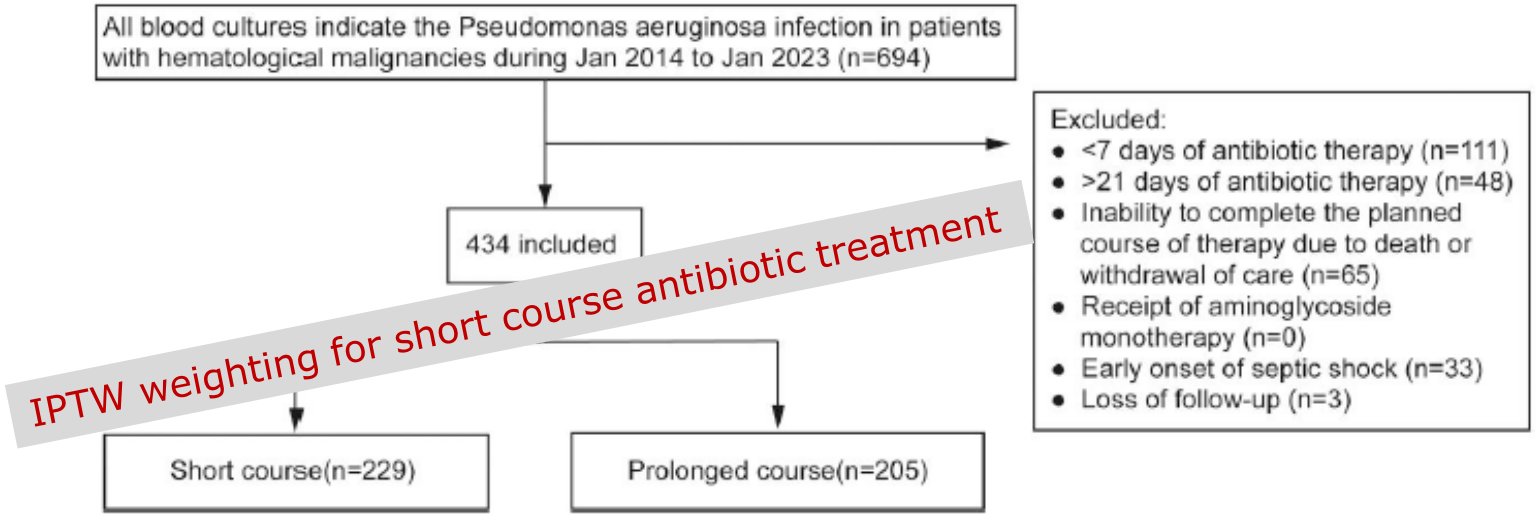


Figure 1. Study population.

Table 2. Univariate Analysis on the Clinical Outcomes of the Weighted Cohort

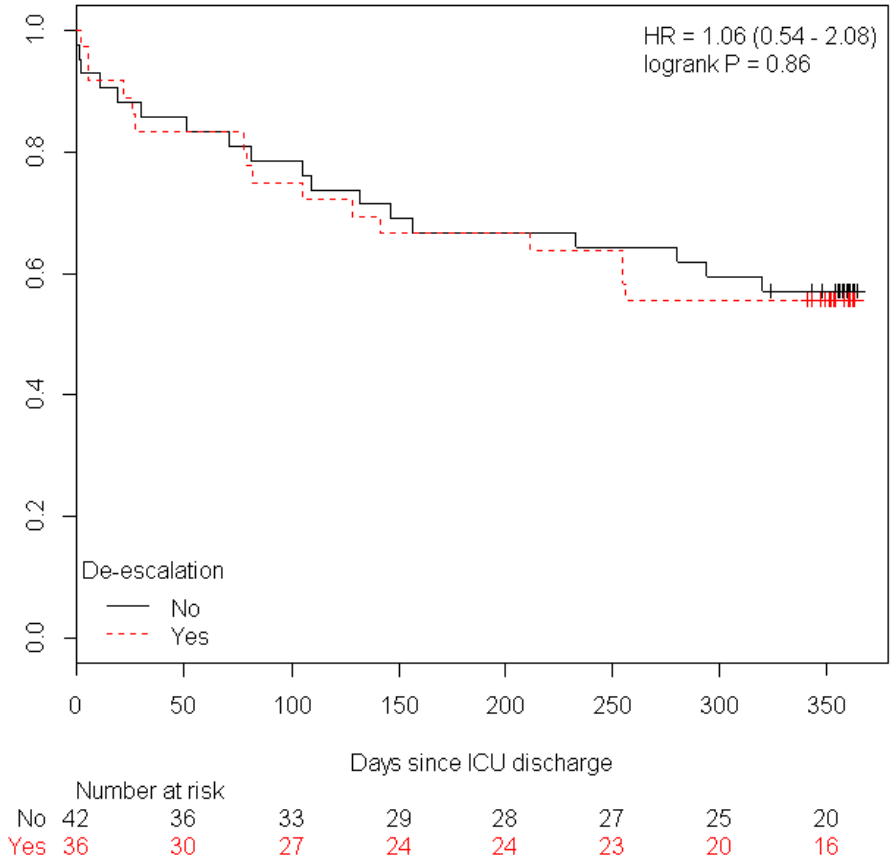
	Mortality or Recurrent Infection Within 30 D			Fever Relapse Within 7 D			Recurrent Infection Within 90 D		
Characteristic	No	Yes	*P* Value	No	Yes	*P* Value	No	Yes	*P* Value
Day 1 ANC 0–100 cells/mL	208 (53.1)	13 (72.2)	.111	202 (53.6)	19 (57.6)	.659	202 (53.3)	19 (61.3)	.391
Duration of neutropenia, median (IQR)	10.0 (4.0–15.0)	10.5 (6.0–22.5)	.391	10.0 (4.0–15.0)	10.0 (5.0–20.0)	.531	10.0 (4.0–15.0)	11.0 (8.0–20.0)	.095
IET48h	34 (8.7)	3 (16.7)	.247	33 (8.7)	4 (12.5)	.694	31 (8.2)	6 (18.2)	.110
ANC 0–500 cells/mL at the day of discontinuation of antibiotics	39 (9.9)	8 (44.4)	**<.001**	36 (9.5)	11 (34.4)	**<.001**	38 (10.1)	9 (27.3)	**.007**
Monotherapy	209 (53.3)	6 (33.3)	.156	199 (52.6)	16 (50.0)	.918	200 (53.1)	15 (45.5)	.512
MDR-PA	42 (10.7)	7 (38.9)	**<.001**	41 (10.8)	8 (25.0)	**.037**	39 (10.3)	10 (30.3)	**.002**
CRPA	76 (19.4)	7 (38.9)	**.044**	74 (19.6)	9 (28.1)	.354	73 (19.4)	10 (30.3)	.203
Short course antibiotic therapy	197 (50.3)	8 (44.4)	.630	190 (50.3)	15 (46.9)	.854	186 (49.3)	19 (57.6)	.468

Abbreviations: ALL, acute lymphoblastic leukemia; allo-HSCT, allogeneic hematologic stem-cell transplantation; AML, acute myeloid leukemia; ANC, absolute neutrophil counts; BSI, bloodstream infection; CRPA, carbapenems-resistant *Pseudomonas aeruginosa*; CZA, Ceftazidime-Avibactam; Day 1 ANC 0–500 cells/mL, day at the onset of BSI; IET48h, inadequate empirical therapy within 48 h of the onset of PA BSI; IQR, interquartile range; MDR-PA, multidrug resistant *Pseudomonas aeruginosa*; Others, containing myelodysplastic syndrome (MDS) and lymphoma; PA, *Pseudomonas aeruginosa*; SMD, standardized mean difference. Values in bold means $P < .05$.

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

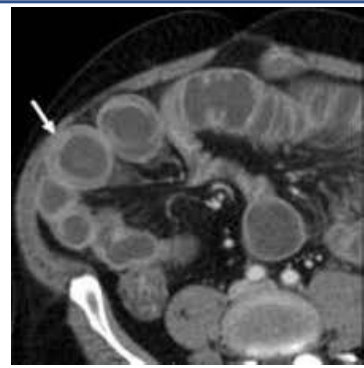
Djamel Mokart
Géraldine Slehofer
Jérôme Lambert
Antoine Sannini
Laurent Chow-Chine
Jean-Paul Brun
Pierre Berger
Ségolène Duran
Marion Faucher
Jean-Louis Blache
Colombe Saillard
Norbert Vey
Marc Leone

- **De-escalation rate = 40%**
- **Associated factors**
  - Adequation of the empirical antimicrobial treatment used in ICU [OR = 10.8 (95 % CI 1.20–96)] for adequate documented treatment versus appropriate empirical treatment
  - Compliance with guidelines regarding the empirical anti-pseudomonal betalactam used in ICU [OR = 10.8 (95 % CI 1.3–89.5)]



Intensive Care Med. 2014 Jan;40(1):41-9.

Neutropenic Enterocolitis, a Growing Concern in the Era of Widespread Use of Aggressive Chemotherapy



Lior Nesher and Kenneth V. I. Rolston

Table 1. Diagnostic Criteria for Neutropenic Enterocolitis[a]

Type of Criteria	Finding	Remarks
Major	Neutropenia	ANC $<500 \times 10^9$ cells/L
	Bowel wall thickening on CT exam or US exam	> 4 mm (transverse scan) thickening in any segment of the bowel for at least 30 mm length (longitudinal scan)
	Fever[b]	> 38.3 (oral or rectal)
Minor/nonspecific	Abdominal pain	> 3 on a visual analog scale (1–10)
	Abdominal distention	
	Abdominal cramping	
	Diarrhea	
	Lower GI bleeding	

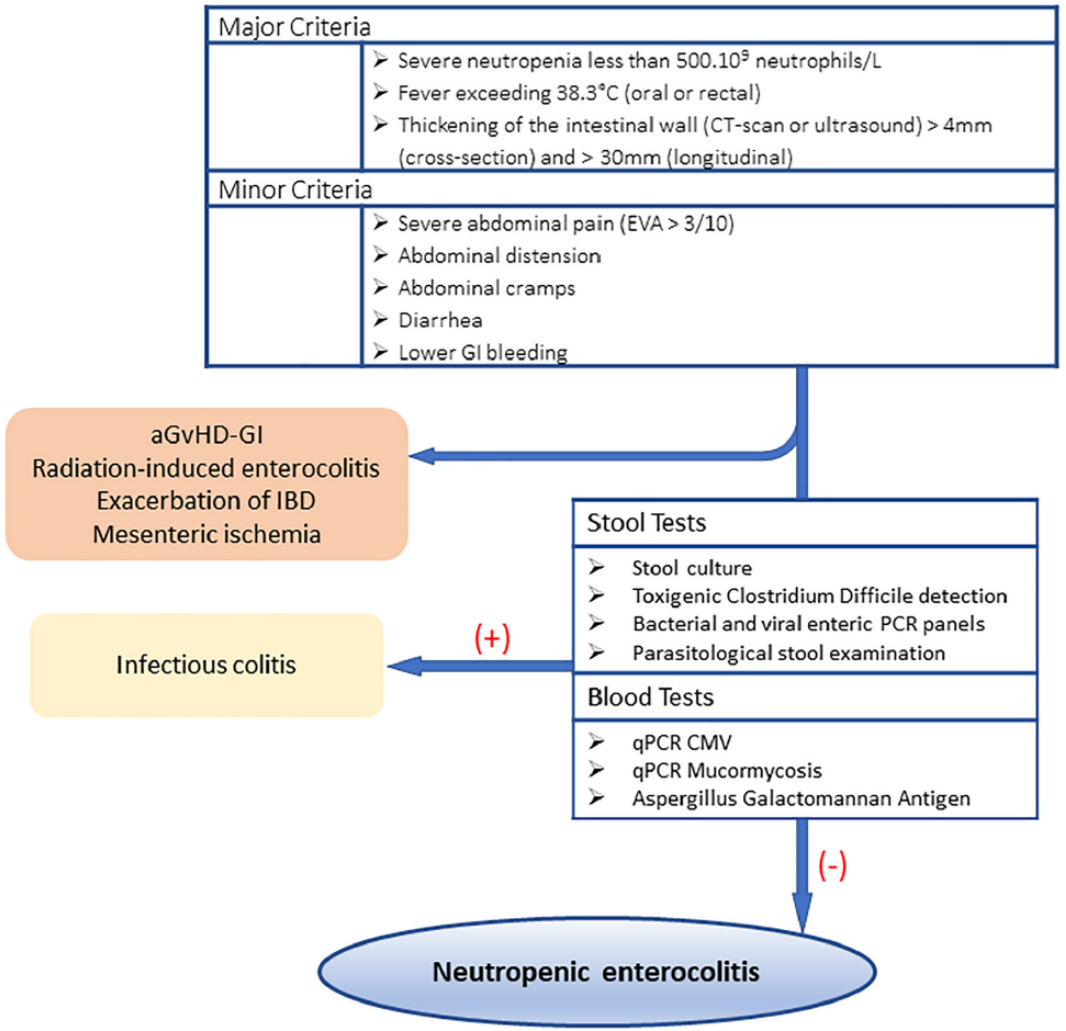
Abbreviations: ANC, absolute neutrophil count; CT, computerized tomography; GI, gastrointestinal; US, ultrasound.

[a] Adapted from Gorschluter et al [11].

[b] Fever may be absent in a minority of patients and some may even be hypothermic.

Recent advances in neutropenic enterocolitis: Insights into the role of gut microbiota

Natacha Kapandji [a,b,*], Elie Azoulay [a], Lara Zafrani [a]



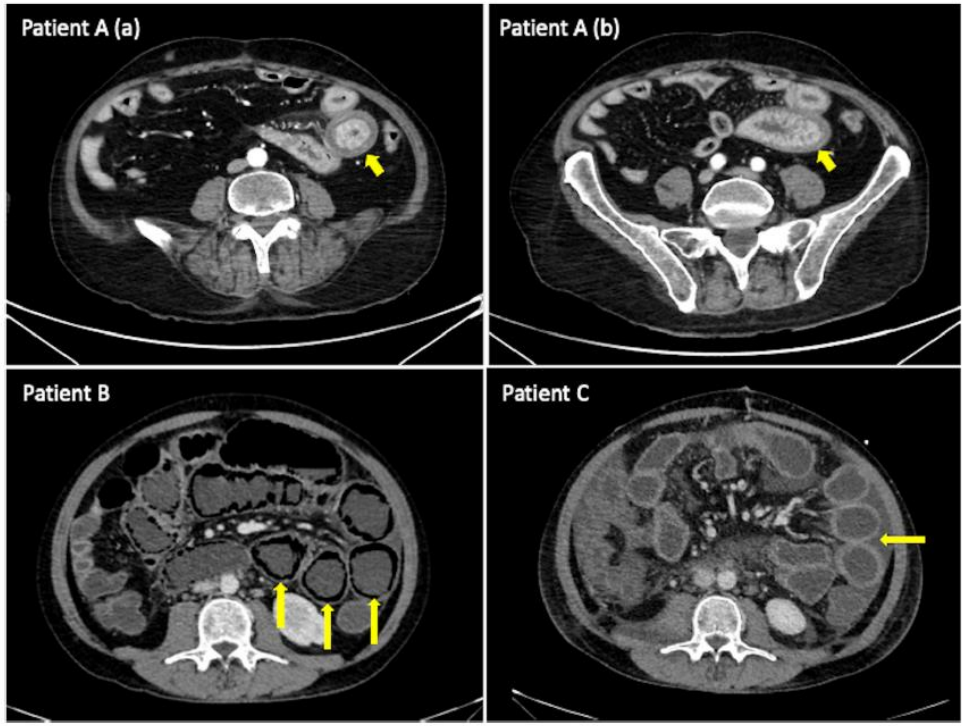
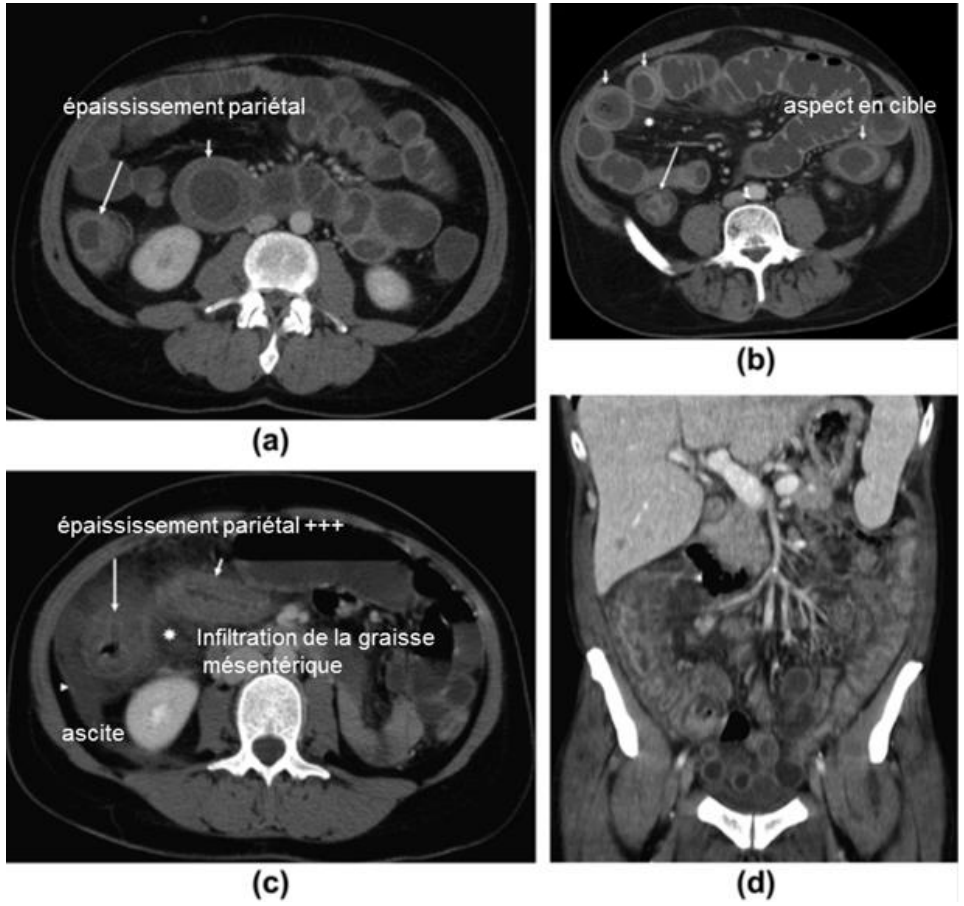


Fig. 2. Contrast enhanced abdominal CT-scans of neutropenic enterocolitis.
A: Segmental bowel wall thickening (→) with mucosal enhancement of the duodenum and the jejunum. a) Cross section (> 4 mm) b) Longitudinal section (>30 mm).
B: Parietal pneumatosis (→) with mucosal enhancement involving the entire digestive tract and no arterial thrombosis.
C: Peritoneal effusion (→) with bowel wall thickening and mucosal enhancement.

Kapandji, Blood Reviews 54 (2022) 100944

Parietal thickening: CT scan and ultrasound



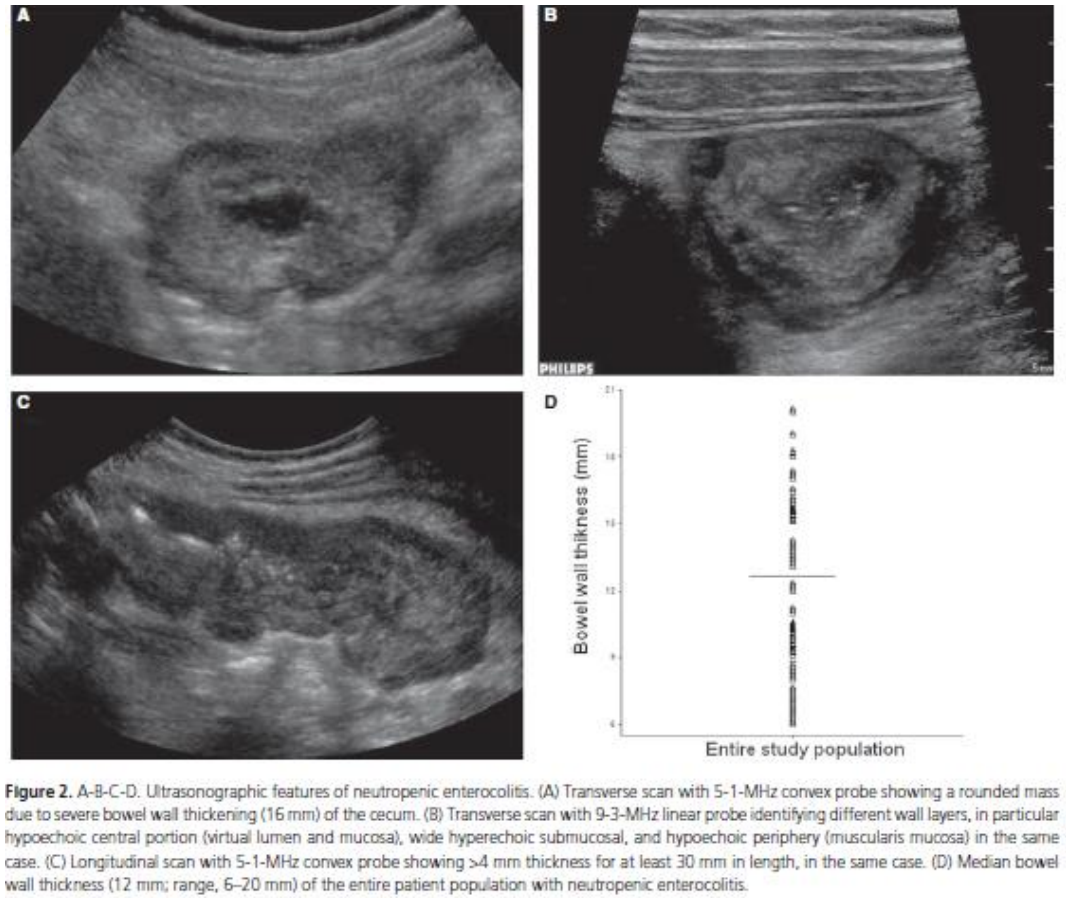
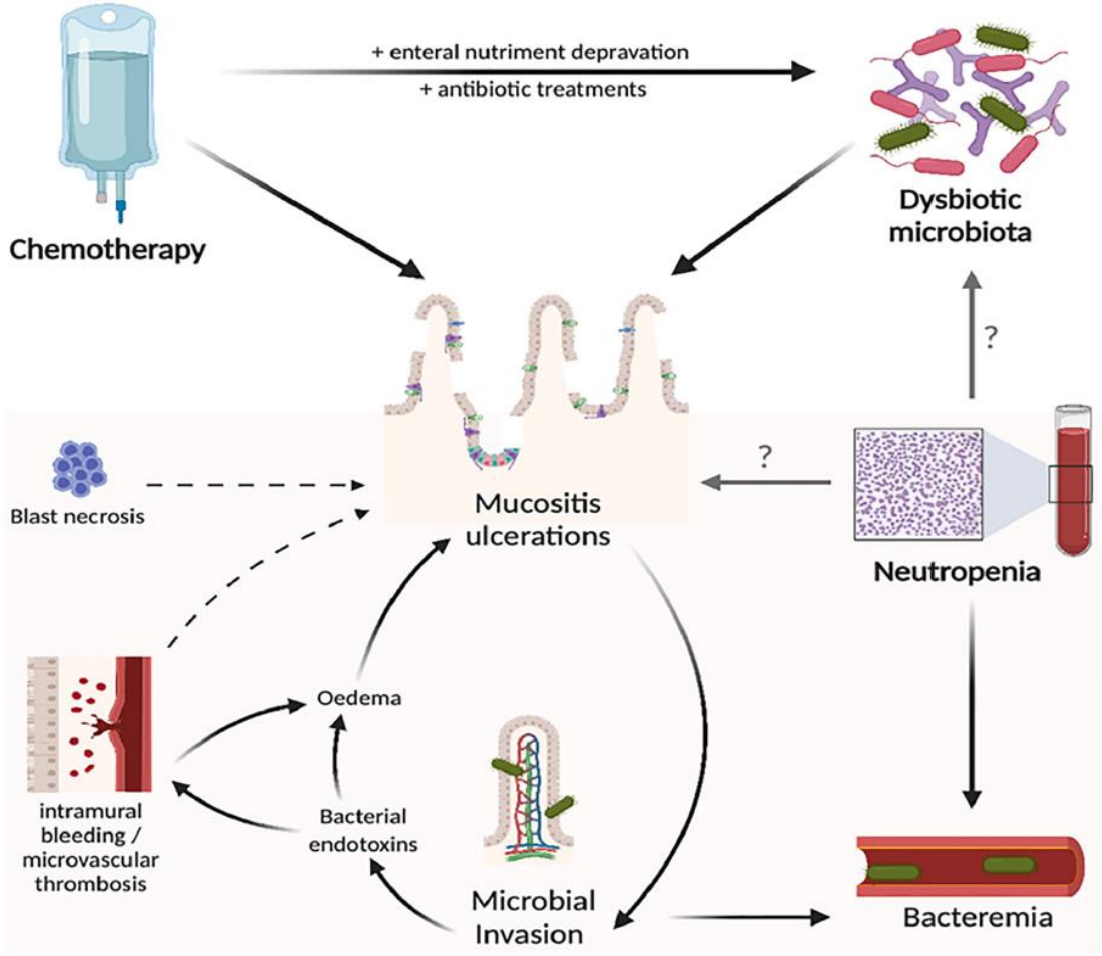


Figure 2. A-B-C-D. Ultrasonographic features of neutropenic enterocolitis. (A) Transverse scan with 5-1-MHz convex probe showing a rounded mass due to severe bowel wall thickening (16 mm) of the cecum. (B) Transverse scan with 9-3-MHz linear probe identifying different wall layers, in particular hypoechoic central portion (virtual lumen and mucosa), wide hyperechoic submucosal, and hypoechoic periphery (muscularis mucosa) in the same case. (C) Longitudinal scan with 5-1-MHz convex probe showing >4 mm thickness for at least 30 mm in length, in the same case. (D) Median bowel wall thickness (12 mm; range, 6–20 mm) of the entire patient population with neutropenic enterocolitis.

Pathophysiology

Multifactorial
- Neutropenia
  - Decreased local immunity
  - Microbial invasion
- Mucosal lesions (chemotherapy, radiotherapy)
  - Oedema, necrosis, ulcerations, etc.

Infiltration (leukaemia, lymphoma)
Intramural haemorrhage (thrombocytopenia),
Modification of intestinal flora:
- commensal -> opportunistic



CID 2013:56 (1 March) • 711

Kapandji, Blood Reviews 54 (2022) 100944

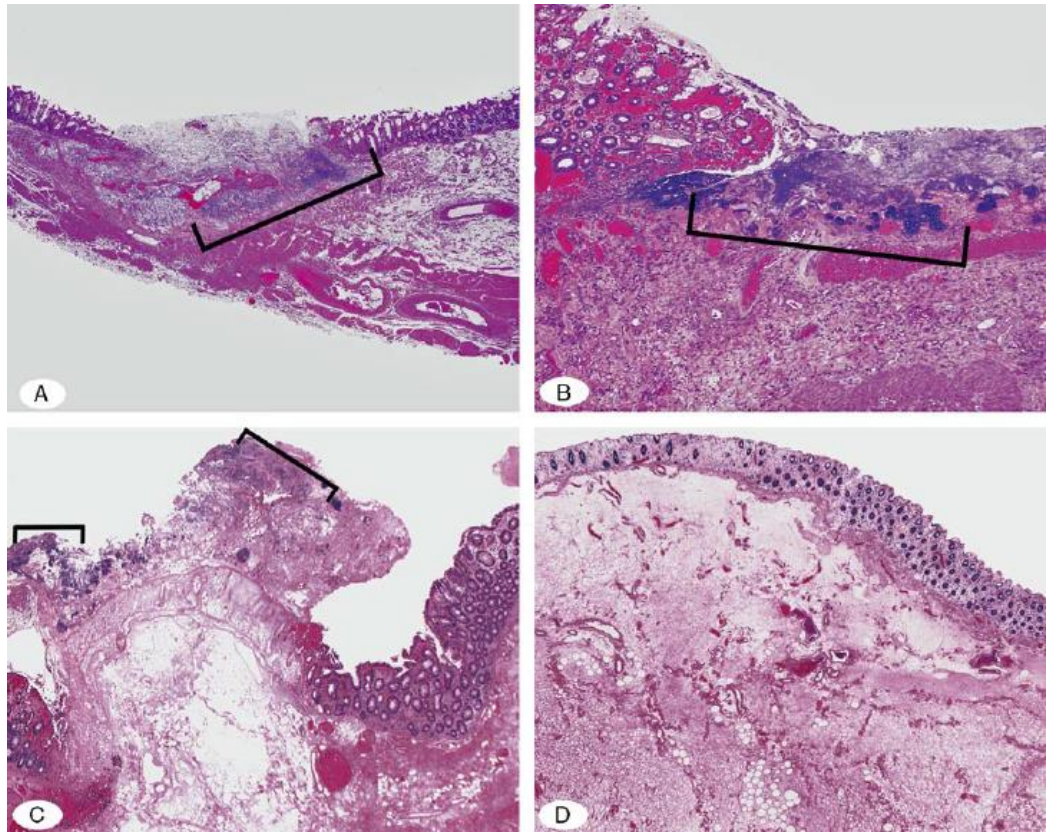
Neutropenic Enterocolitis

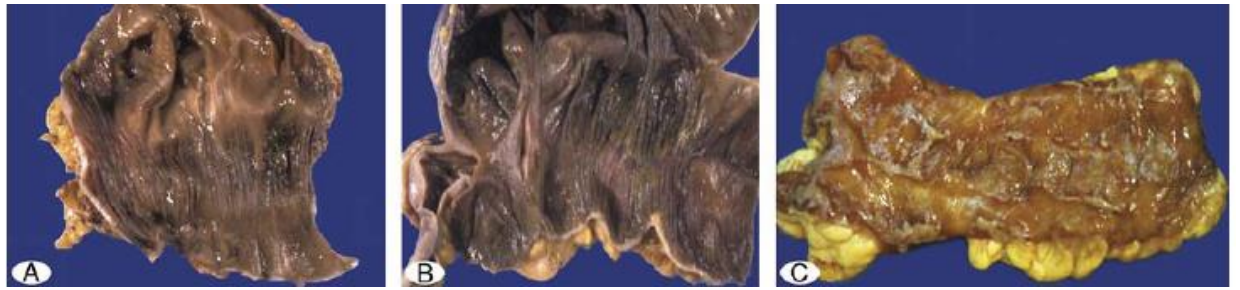
New Insights Into a Deadly Entity

Taha Sachak, MD, Michael A. Arnold, MD, PhD,*† Bita V. Naini, MD,‡*

TABLE 2. Gross and Microscopic Findings in Patients With Histologically Confirmed NE

Gross distribution pattern	
Focal	3/12
Patchy	7/12
Diffuse	1/12
Gross regional involvement	
Small bowel	2/17
Appendix	0/17
Cecum	16/17
Right colon	14/17
Transverse colon	5/17
Left colon	2/17
Rectum	0/17
Necrosis	18/20
Invasive microorganisms	17/20
Ulcer	15/19
Hemorrhage	15/20
Edema	15/20
Depletion of inflammatory cells	15/20
Abnormal terminal ileum	5/16
Pneumatosis	3/20
Perforation	3/20
Pseudomembranes	3/17
Stricture	2/12
Abscess	2/20





Am J Surg Pathol • Volume 39, Number 12, December 2015

Surgical treatment of acute abdominal complications in hematology patients: outcomes and prognostic factors

Djamel Mokart[a], Marion Penalver[a], Laurent Chow-Chine[a], Jacques Ewald[b], Antoine Sannini[a], Jean Paul Brun[a], Magali Bisbal[a], Bernard Lelong[b], Jean Robert Delpero[b], Marion Faucher[a] and Olivier Turrini[b]

Table 2. Etiology of acute abdominal syndrome.

Etiologies	Patients ($n = 58$)	Clinical picture
No cause	1 (1.7)	
Primary peritonitis	2 (3.4)	
Tumoral infiltration	12 (20.7)	10 Digestive lymphomas with gastrointestinal perforations (among them 3 peritonitis), 2 splenic infiltrations (lymphoma, ALL) with haemorraghic shock
Digestive GVHD	2 (3.4)	1 Sigmoid stenosis, 1 gastrointestinal perforation with peritonitis
Neutropenic enterocolitis	3 (5.2)	2 Gastrointestinal perforations, 1 colonic necrosis with peritonitis
Invasive digestive aspergillosis	3 (5.2)	3 Intestinal ischemiae, among them 1 peritonitis
Digestive bleeding	5 (8.6)	2 Intraluminal digestive bleeding related to thrombopenia, 1 intestinal ischemia, 1 spontaneous rupture of a liver subcapsular hematoma, 1 choledocal bleeding after percutaneous drainage, 1 intestinal bleeding in a context of cecum angiodysplasia
Appendicitis	2 (3.4)	1 Appendicular abscess, 1apendicular peritonitis
Cholecystitis	3 (5.2)	2 Gangrenous cholecystis, 1biliary peritonitis
Sigmoïditis	8 (13.8)	8 Peritonitis with digestive perforation
Gastrointestinal obstruction	8 (13.8)	7 Patients with occlusion of small intestine caused by adherences (with 1 digestive perforation with peritonitis), 1 patient with Ogilvie syndrome (colonic pseudo-obstruction)
Mesenteric ischemiae	2 (3.4)	
Others	7 (12)	1 Colonic perforation after biopsy, 1 gastric ulcer perforation, 1 intestinal perforation with peritonitis secondary to a foreign body, 1 pelvic abscess, 2 intestinal perforations of unknown origin with peritonitis, 1 pseudomembranous colitis with peritonitis

GVHD: graft versus host disease. Variables were reported as numbers and percentages, *n* (%).

LEUKEMIA & LYMPHOMA, 2017
http://dx.doi.org/10.1080/10428194.2017.1296145

Prevalence(s)

Between 0.8 and 46%, probably underestimated

- Nesher, CID,2013

5.3% of cancer patients hospitalised and treated with CT

- Gorschlüter, Eur J Haematol, 2005

17% of neutropenic patients admitted to the ICU

- Mokart,ICM, 2015

33% of cancer patients admitted to ICU for digestive emergencies

- Lebon, JCC, 2017

Gastrointestinal emergencies in critically ill cancer patients

Delphine Lebon, MD [a], Lucie Biard, MD, PhD [b], Sophie Buyse, MD [a], David Schnell, MD [a], Etienne Lengliné, MD [c], Camille Roussel, MD [a], Jean-Marc Gornet, MD [d], Nicolas Munoz-Bongrand, MD [e], Laurent Quéro, MD, PhD [f], Matthieu Resche-Rigon, MD, PhD [b,g], Elie Azoulay, MD, PhD [a,g], Emmanuel Canet, MD, PhD [a,*]

Table 2
Characteristics of gastrointestinal diseases.

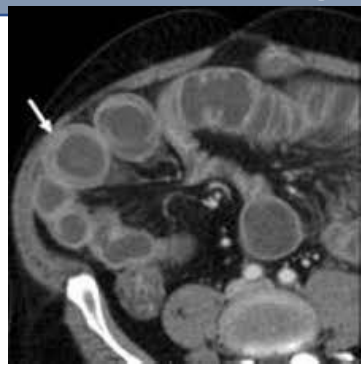
Variables	*n* (%) or median (25th–75th percentiles)
Etiology	
Neutropenic enterocolitis	54 (33)
Others abdominal infections	51 (31)
Clostridium difficile infection	19 (12)
Infectious colitis	16 (10)
Peritonitis	16 (10)
Bowel infiltration by malignancy	14 (9)
Chemotherapy-related severe mucosal toxicity	12 (7)
Bowel graft versus host disease	10 (6)
Mesenteric ischemia	7 (4)
Others†	9 (5)
Unknown	7 (4)
Need for urgent abdominal surgery	27 (16)

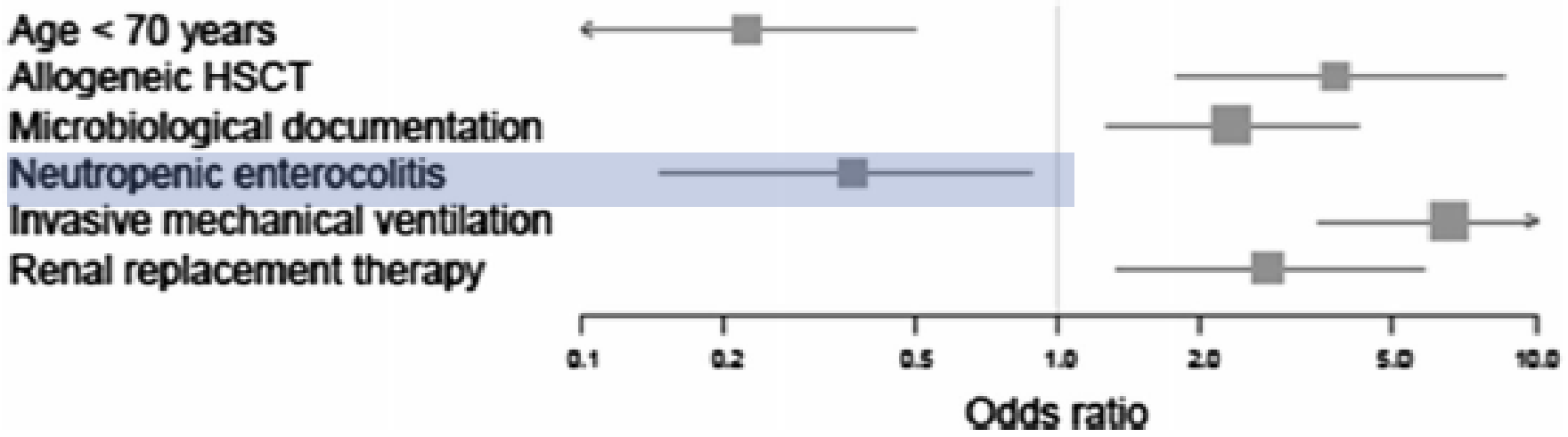
Table 4
Multivariate analysis of variables independently associated with hospital mortality.

	Odds ratio	95% confidence interval	*p* Value
Neutropenia	0.42	0.19–0.95	0.03
Autologous HSCT	0.34	0.07–1.67	0.18[a]
Allogenic HSCT	5.13	1.71–15.4	<0.01[a]
Mechanical ventilation	3.42	1.37–8.51	<0.01
SAPS II score	1.03	1.01–1.05	<0.01
Microbiological documentation	0.27	0.11–0.64	<0.01

D. Mokart
M. Darmon
M. Resche-Rigon
V. Lemiale
F. Pène
J. Mayaux
A. Rabbat
A. Kouatchet
F. Vincent
M. Nyunga
F. Bruneel
C. Lebert
P. Perez
A. Renault
R. Hamidfar
M. Jourdain
A.-P. Meert
D. Benoit
S. Chevret
E. Azoulay

Prognosis of neutropenic patients admitted to the intensive care unit





Intensive Care Med. 2015 Feb;41(2):296-303

The prognostic impact of abdominal surgery in cancer patients with neutropenic enterocolitis: a systematic review and meta-analysis, on behalf the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (GRRR-OH).

Saillard C, Zafrani L, Darmon M, Bisbal M, Chow-Chine L, Sannini A, Brun JP, Ewald J, Turrini O, Faucher M, Azoulay E, Mokart D.

Table 2 Microbial documentation reported in the selected studies

Type of samples	Pathogens identified
Blood cultures	Bacteria
	Klebsiella pneumonia (*n* = 2)
	Pseudomonas aeruginosa (*n* = 1)
	Escherichia coli (*n* = 14)
	Enterococcus faecium (*n* = 6)
	Enterobacter aerogenes (*n* = 1)
	Clostridium septicum (*n* = 1)
	Aeromonas hydrophilia (*n* = 1)
	Clostridium perfringens (*n* = 1)
	Bacteroides fragilis (*n* = 1)
	Gram-negative bacilli (non-specified) (*n* = 39)
	Stenotrophomonas maltophilia (*n* = 1)
	Staphylococcus aureus (*n* = 1)
	Staphylococcus epidermidis (*n* = 2)
	Alpha-hemolytic streptococcus (*n* = 1)
	Viridans streptococcus (*n* = 1)
	Gram-positive Cocci (non-specified) (*n* = 8)
	Bacteria (non-specified) (*n* = 13)
	Fungi
	Candida krusei (*n* = 1)
	Candida glabrata (*n* = 1)
	Fungemia (*n* = 4)
	Candida (non-specified) (*n* = 1)
	Virus
	Cytomegalovirus (*n* = 1)

Type of samples	Pathogens identified
Peroperative digestive samples	Bacteria
	Pseudomonas aeruginosa (*n* = 4)
	Escherichia coli (*n* = 1)
	Klebsiella pneumonia (*n* = 1)
	Diphteroides (*n* = 1)
	Acinetobacter anitratus (*n* = 1)
	Clostridium difficile (*n* = 2)
	Bacteroides fragilis (*n* = 1)
	Enterobacter aerogenes (*n* = 1)
	Gram-negative bacilli (non-specified) (*n* = 21)
	Gram-positive bacilli (non-specified) (*n* = 2)
	Fungi
	Aspergillus fumigatus (*n* = 1)
	Candida glabrata (*n* = 2)
	Candida krusei (*n* = 1)
	Candida (non-specified) (*n* = 7)
	Virus
	Cytomegalovirus (*n* = 1)

Type of samples	Pathogens identified
Autopsy samples	*Candida albicans* (*n* = 3)
	Candida glabrata (*n* = 1)
	Aspergillus fumigatus (*n* = 1)
	Aspergillosis pneumonia (*n* = 5)
	Fungal pneumonia (*n* = 3)
	Kidney and thyroid candida abscess (*n* = 1)
Stool samples	*Clostridium difficile* (*n* = 8)
	Pseudomonas aeruginosa (*n* = 1)
	Escherichia coli (*n* = 1)
	Candida glabrata (*n* = 2)
	Yeasts (non-specified) (*n* = 3)
	Adenovirus (*n* = 1)

Neutropenic Enterocolitis in Critically Ill Patients: Spectrum of the Disease and Risk of Invasive Fungal Disease

Baptiste Duceau, MD[1,2]; Muriel Picard, MD[3]; Romain Pirracchio, PhD[4,5]; Anne Wanquet, MD[6]; Frédéric Pène, PhD[7]; Sybille Merceron, MD[8]; Djamel Mokart, PhD[6]; Anne-Sophie Moreau, MD[9]; Etienne Lengliné, MD[10]; Emmanuel Canet, PhD[1,2]; Virginie Lemiale, MD[1,2]; Eric Mariotte, MD[1,2]; Elie Azoulay, PhD[1,2]; Lara Zafrani, PhD[1,2]

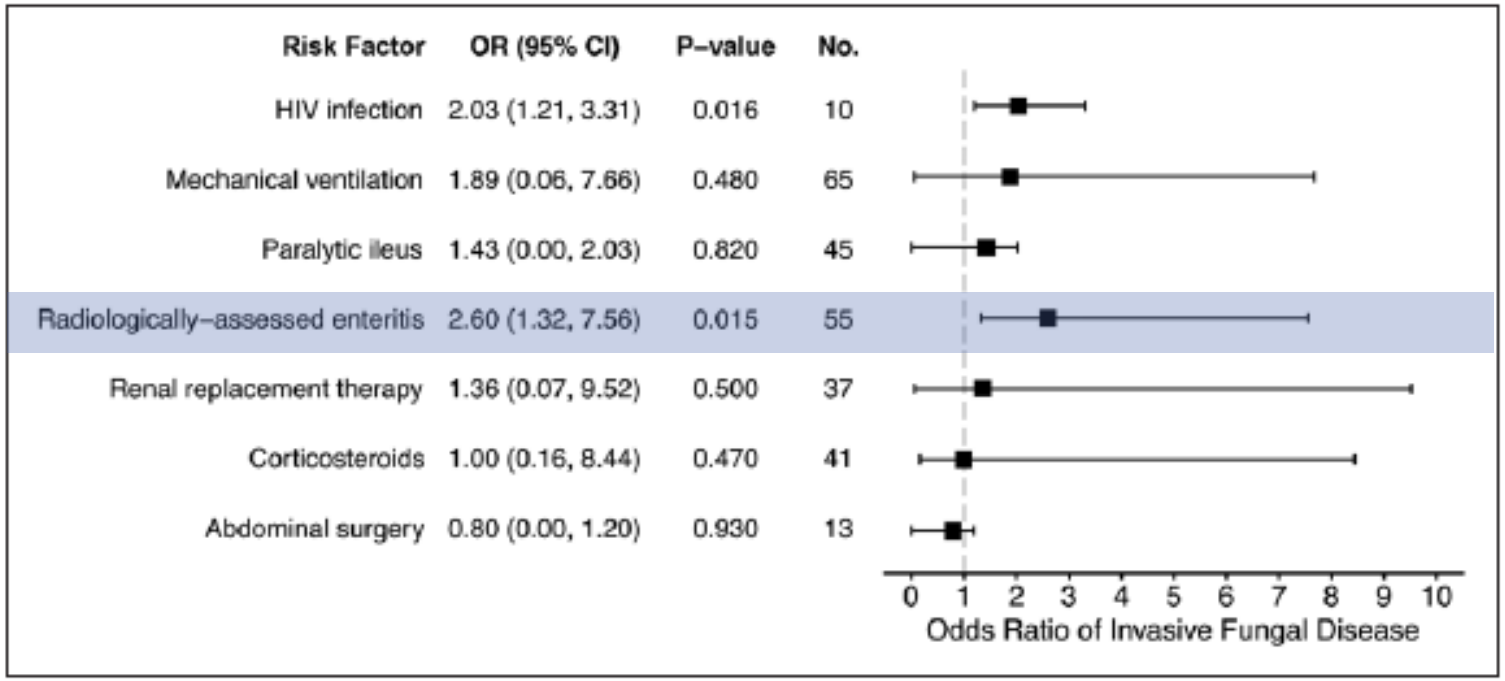
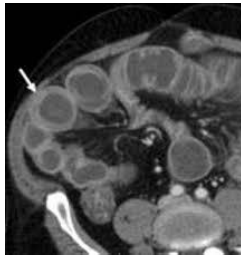


Figure 1. Adjusted odds ratios of invasive fungal infection. Forrest plot of risk-adjusted odd ratios of invasive fungal infection. Least Absolute Shrinkage and Selection Operator regression with selective inference was used to evaluate the risk factors associated with invasive fungal infection. *Black dots* represent the point estimate of the odds ratio, *lines* represent 95% CIs. Number of patients presenting the risk factor is shown (No.).



	n	(%)
Bacteria	**98**	**(100)**
Gram-negative Bacilli	66	(67.3)
Escherichia coli	29	(29.6)
Klebsiella spp.	16	(16.3)
Enterobacter cloacae	10	(10.2)
Pseudomonas aeruginosa	6	(6.1)
Pseudomonas stutzeri	1	(1)
Citrobacter freundii	1	(1)
Campylobacter jejuni	1	(1)
Acinetobacter juni	1	(1)
Aeromonas hydrophila	1	(1)
Anaerobes	5	(5.1)
Bacteroides fragilis	2	(2)
Clostridium septicum	2	(2)
Alistipes finegoldii	1	(1)
Gram-positive Cocci	26	(26.5)
Streptococcus spp.	7	(7.1)
Enterococcus faecium	13	(13.3)
Enterococcus faecalis	3	(3.1)
Staphylococcus aureus	1	(1)
Staphylococcus haemolyticus	1	(1)
Micrococcus	1	(1)
Gram-negative Cocci		
Bacillus cereus	1	(1)
Fungi	**17**	**(100)**
Candida spp.	13	(76.5)
Mucor	3	(17.6)
Trichosporon	1	(5.9)

Neutropenic Enterocolitis in Critically Ill Patients: Spectrum of the Disease and Risk of Invasive Fungal Disease

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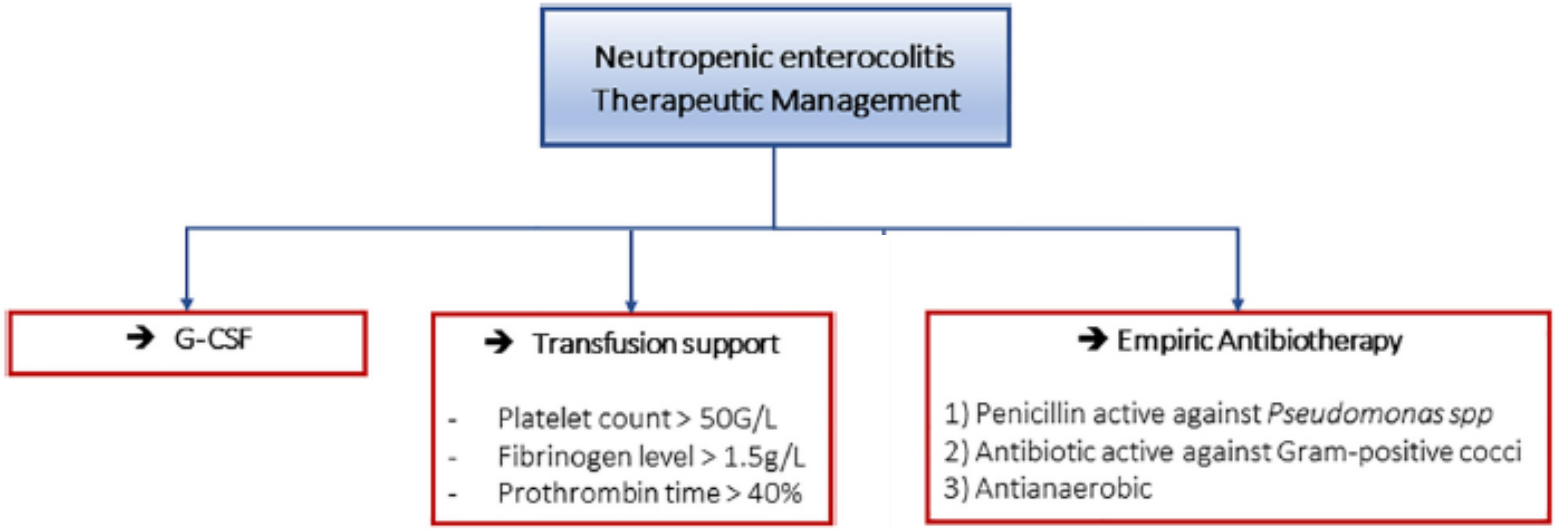
TABLE 3. Cox Proportional Hazards Model for Hospital Mortality ($n = 132$)

Variable, n (%)	Hospital Deaths, $n = 52$	Hospital Survivors, $n = 82$	Hazard Ratio (95% CI)	p
Eastern Cooperative Oncology Group performance status > 2[a]	6 (11.5)	2 (2.4)	1.91 (0.74–4.94)	0.18
Mechanical ventilation	41 (78.8)	27 (32.9)	1.93 (0.83–4.46)	0.13
Vasoactive drugs	45 (86.5)	48 (58.5)	2.61 (1.01–6.70)	0.047
Renal replacement therapy	26 (50.0)	13 (15.9)	1.52 (0.78–2.97)	0.22
Solid tumor	9 (17.3)	5 (6.1)	5.35 (2.39–12.00)	< 0.001
Recipient of allogeneic hematopoietic stem cell transplant	6 (11.5)	2 (2.4)	0.90 (0.31–2.59)	0.84
Microbiological documentation	35 (67.3)	41 (50.0)	0.83 (0.44–1.55)	0.56

Crit Care Med 2019; 47:668–676

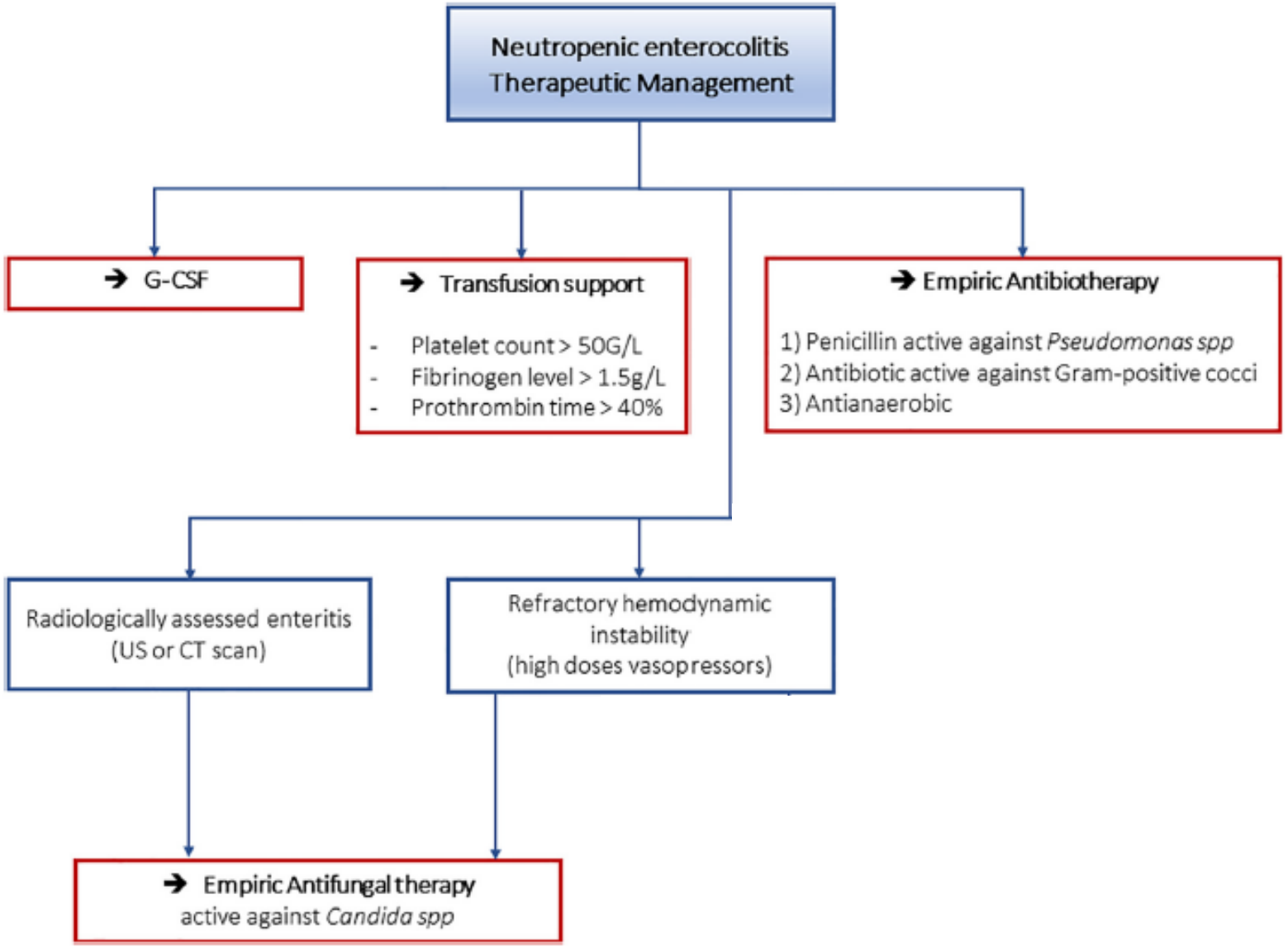
Recent advances in neutropenic enterocolitis: Insights into the role of gut microbiota

Natacha Kapandji [a,b,*], Elie Azoulay [a], Lara Zafrani [a]



Recent advances in neutropenic enterocolitis: Insights into the role of gut microbiota

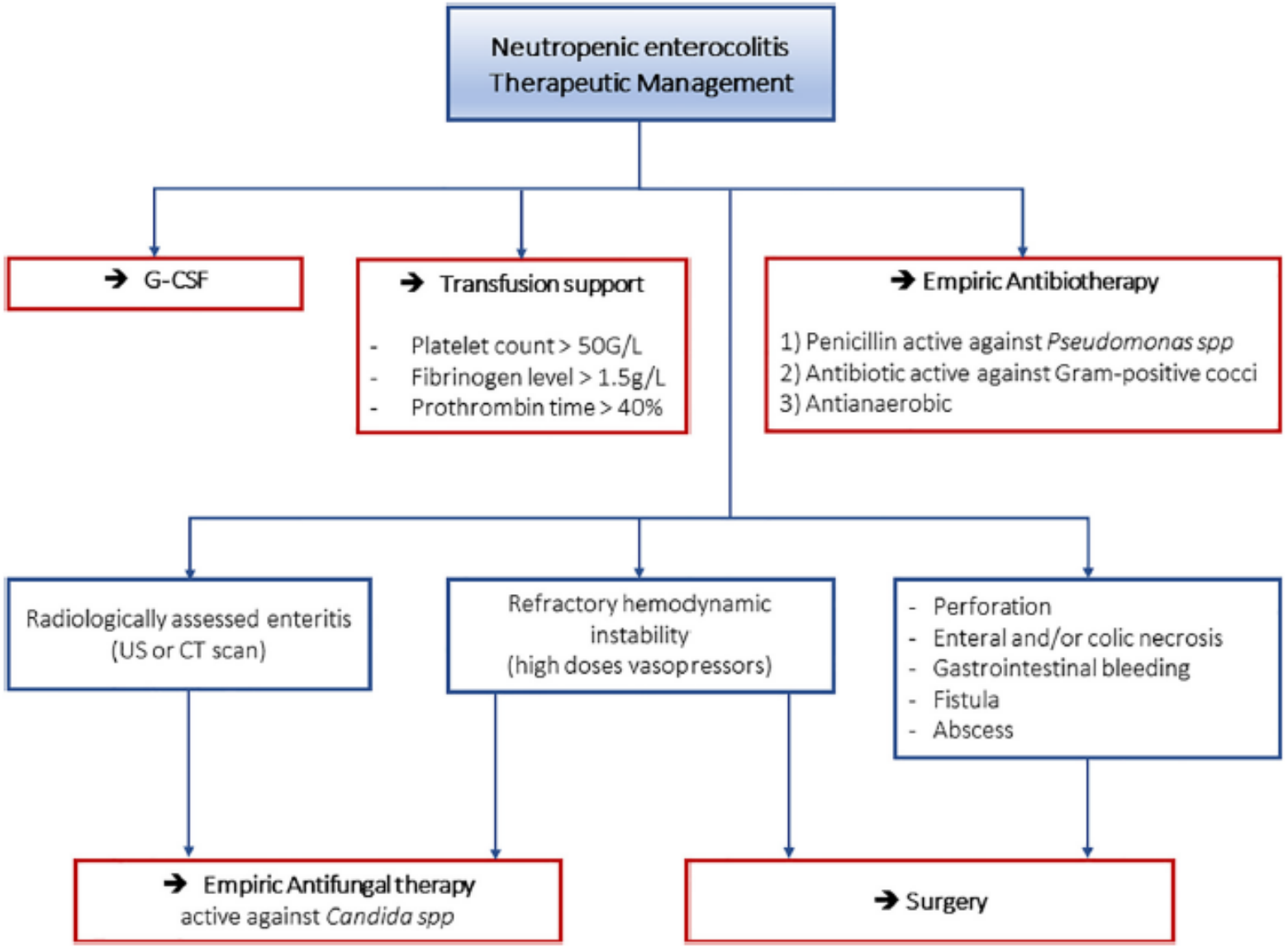
Natacha Kapandji [a,b,*], Elie Azoulay [a], Lara Zafrani [a]



Kapandji, Blood Reviews 54 (2022) 100944

Recent advances in neutropenic enterocolitis: Insights into the role of gut microbiota

Natacha Kapandji [a,b,*], Elie Azoulay [a], Lara Zafrani [a]



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Surgical treatment of acute abdominal complications in hematology patients: outcomes and prognostic factors

Djamel Mokart[a], Marion Penalver[a], Laurent Chow-Chine[a], Jacques Ewald[b], Antoine Sannini[a], Jean Paul Brun[a], Magali Bisbal[a], Bernard Lelong[b], Jean Robert Delpero[b], Marion Faucher[a] and Olivier Turrini[b]

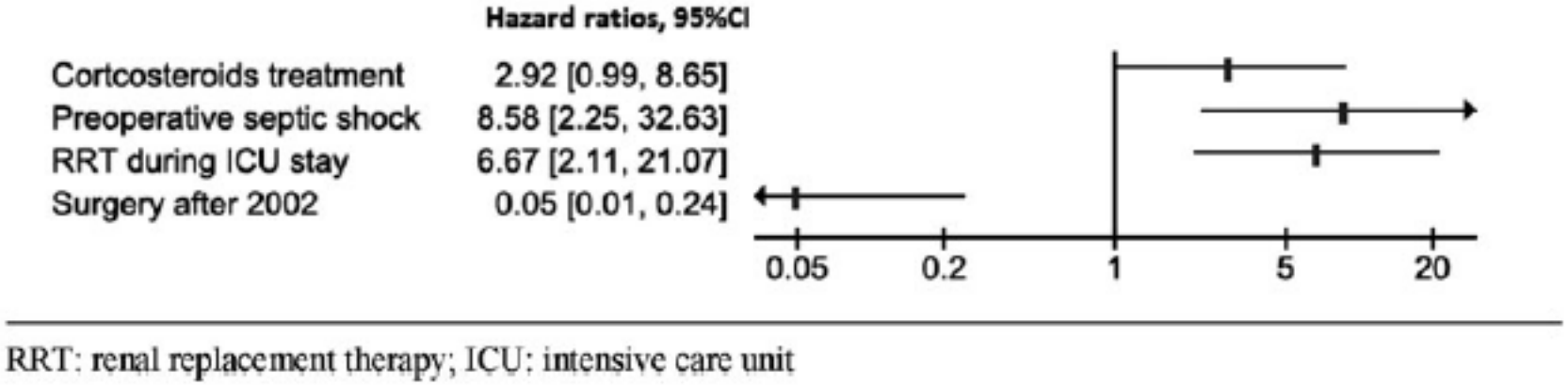
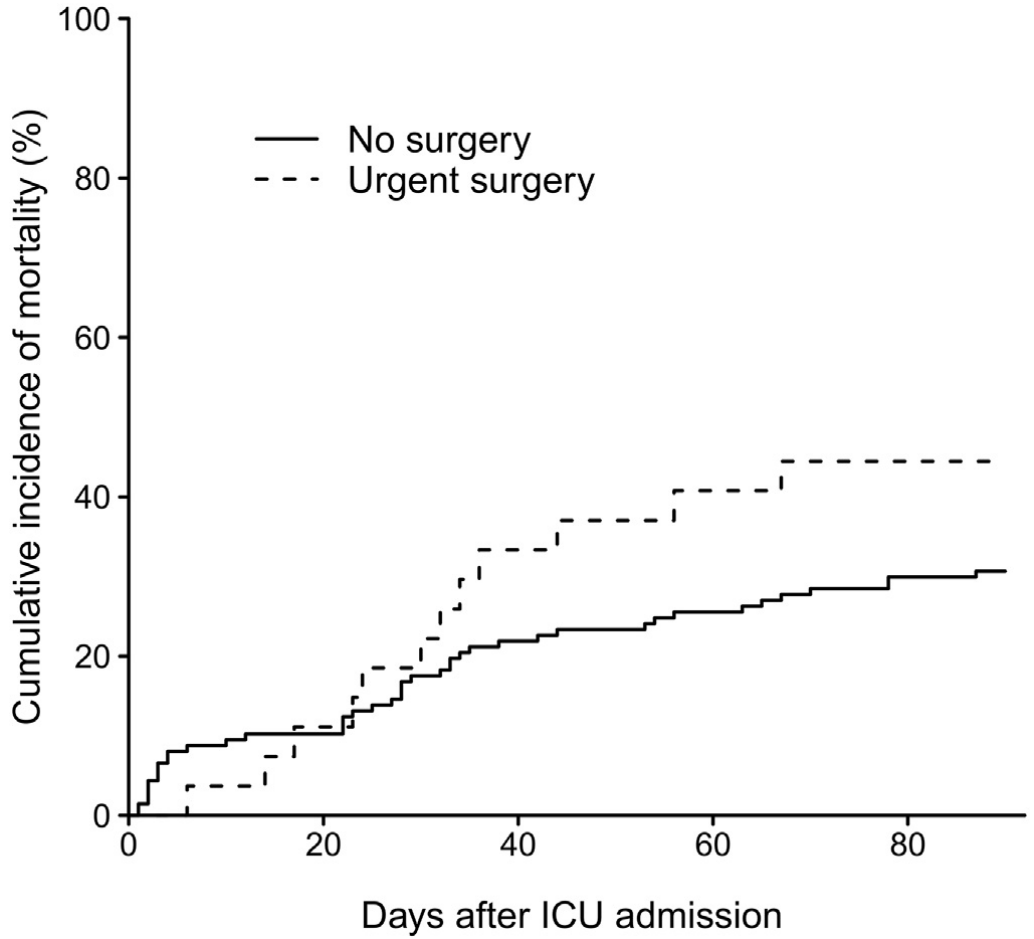


Figure 1. Factors independently associated with hospital mortality (multivariate analysis). RRT: renal replacement therapy; ICU: intensive care unit.

LEUKEMIA & LYMPHOMA, 2017
http://dx.doi.org/10.1080/10428194.2017.1296145

Gastrointestinal emergencies in critically ill cancer patients

Delphine Lebon, MD [a], Lucie Biard, MD, PhD [b], Sophie Buyse, MD [a], David Schnell, MD [a], Etienne Lengliné, MD [c], Camille Roussel, MD [a], Jean-Marc Gornet, MD [d], Nicolas Munoz-Bongrand, MD [e], Laurent Quéro, MD, PhD [f], Matthieu Resche-Rigon, MD, PhD [b,g], Elie Azoulay, MD, PhD [a,g], Emmanuel Canet, MD, PhD [a,*]



Journal of Critical Care 40 (2017) 69–75

The prognostic impact of abdominal surgery in cancer patients with neutropenic enterocolitis: a systematic review and meta-analysis, on behalf the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (GRRR-OH).

Saillard C, Zafrani L, Darmon M, Bisbal M, Chow-Chine L, Sannini A, Brun JP, Ewald J, Turrini O, Faucher M, Azoulay E, Mokart D.

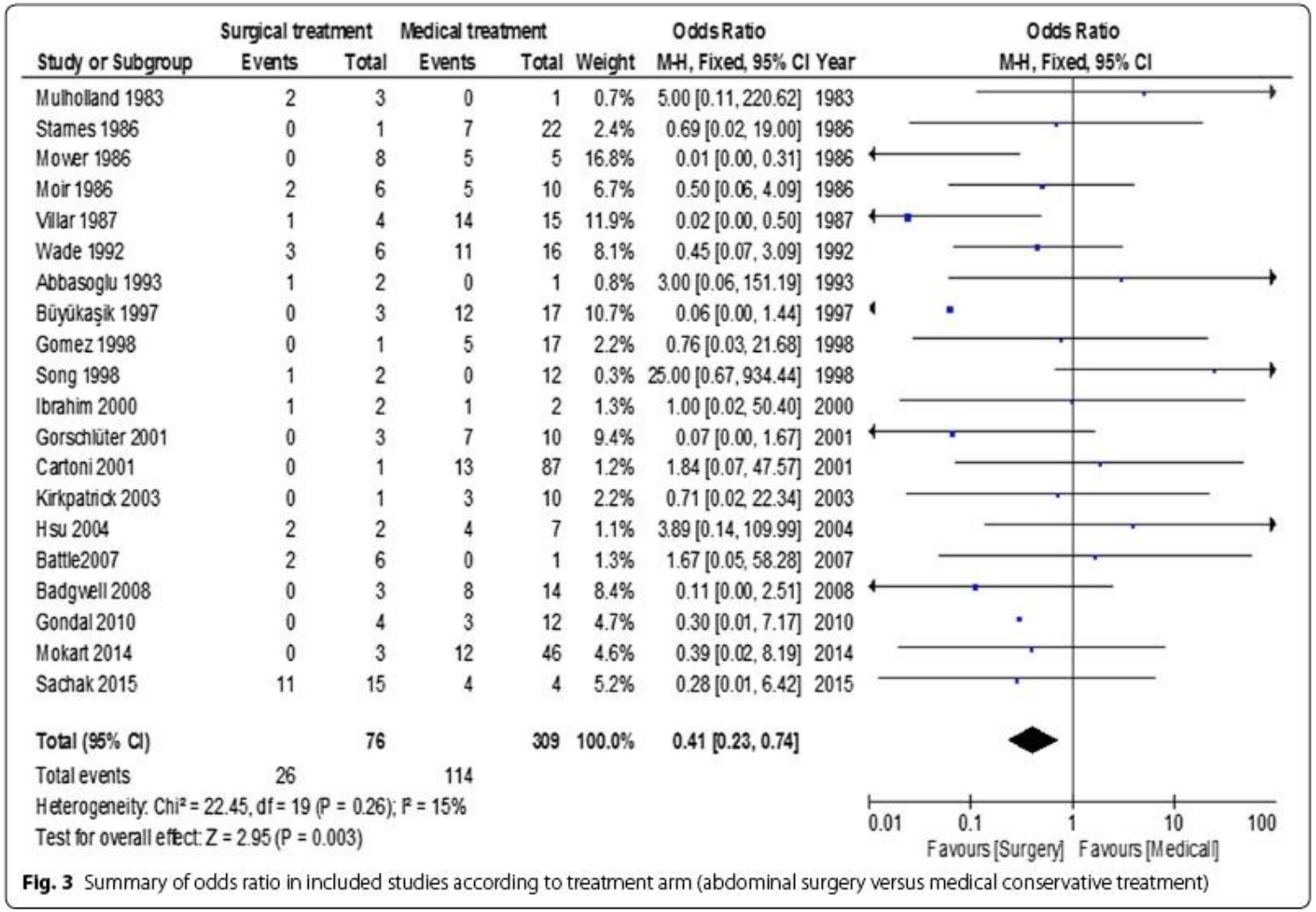


Fig. 3 Summary of odds ratio in included studies according to treatment arm (abdominal surgery versus medical conservative treatment)

The prognostic impact of abdominal surgery in cancer patients with neutropenic enterocolitis: a systematic review and meta-analysis, on behalf the Groupe de Recherche en Réanimation Respiratoire du patient d'Onco-Hématologie (GRRR-OH)

Study or Subgroup	Surgical treatment Events	Total	Medical treatment Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Mulholland 1983	2	3	0	1	4.3%	5.00 [0.11, 220.62]	1983
Wade 1992	3	6	11	16	52.0%	0.45 [0.07, 3.09]	1992
Abbasoglu 1993	1	2	0	1	5.2%	3.00 [0.06, 151.19]	1993
Battle2007	2	6	0	1	8.7%	1.67 [0.05, 58.28]	2007
Mokart 2014	0	3	12	46	29.8%	0.39 [0.02, 8.19]	2014
Total (95% CI)		**20**		**65**	**100.0%**	**0.87 [0.26, 2.89]**	
Total events	8		23				

Heterogeneity: $Chi^2 = 2.03$, $df = 4$ ($P = 0.73$); $I^2 = 0\%$

Test for overall effect: $Z = 0.23$ ($P = 0.82$)

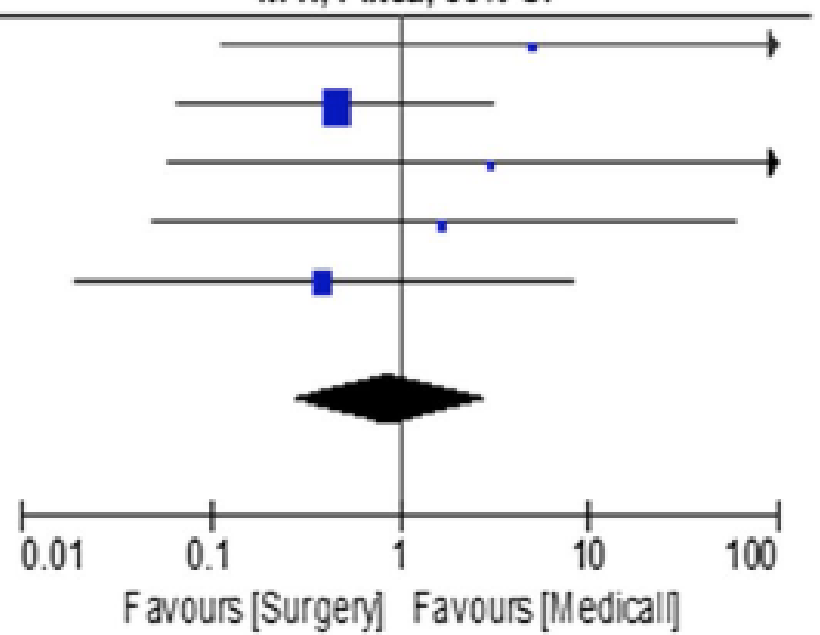


Fig. 6 Summary of odds ratio in included studies according to the presence of neutropenia the day of surgery

Challenges in Surgical Management of Abdominal Pain in the Neutropenic Cancer Patient

Brian D. Badgwell, MD, Janice N. Cormier, MD, MPH,* Curtis J. Wray, MD,* Gautam Borthakur, MBBS,† Wei Qiao, MS,‡ Kenneth V. Rolston, MD,§ and Raphael E. Pollock, MD, PhD**

TABLE 5. Multivariate Cox Proportional Hazards Model for Overall Survival

Variable	HR	95% CI	*P*
Tumor type (solid vs. hematologic)	0.86	0.39–1.87	0.70
Duration of neutropenia (d)	1.02	1.0–1.03	0.05
Treatment with surgery (yes vs. no)	0.30	0.09–1.0	0.05
Pneumonia (yes vs. no)	1.17	0.57–2.43	0.67
Severe sepsis (yes vs. no)	3.35	1.26–8.92	0.02
Any comorbidity (yes vs. no)	1.84	0.78–4.34	0.17

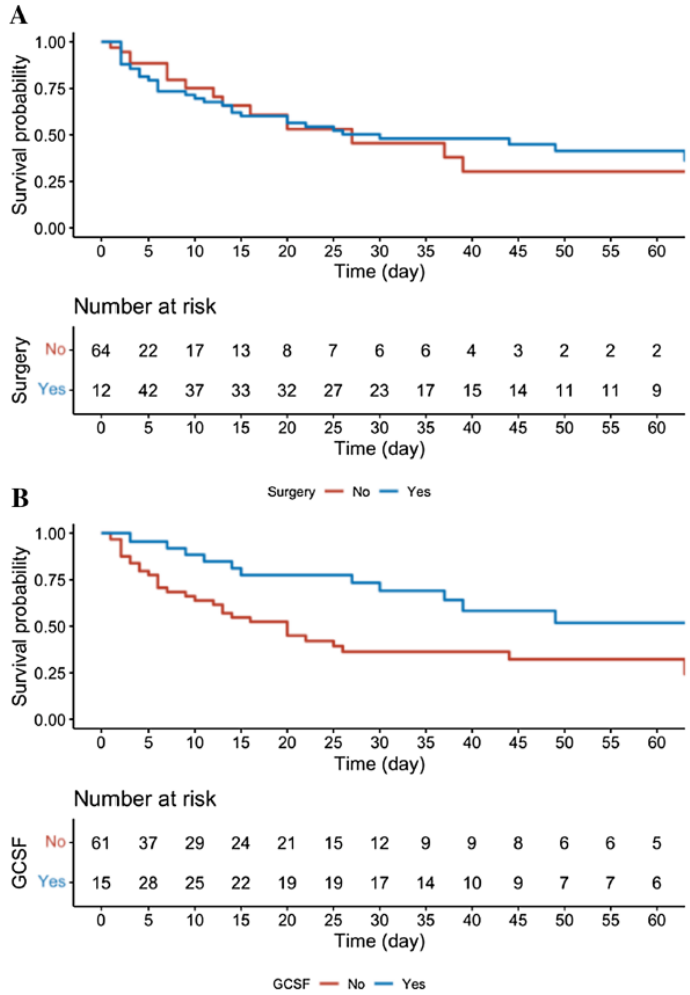
HR indicates hazard ratio; CI, confidence interval.

Necrotizing soft tissue infections in critically ill neutropenic patients: a French multicentre retrospective cohort study

Romain Arrestier[1,2,3*], Anis Chaba[4], Asma Mabrouki[5], Clément Saccheri[6], Emmanuel Canet[7], Marc Pineton de Chambrun[8], Annabelle Stoclin[9], Muriel Picard[10], Florent Wallet[11], François Perier[12], Matthieu Turpin[13], Laurent Argaud[14], Maxens Decavèle[15], Nahéma Issa[16], Cyril Cadoz[17], Kada Klouche[18], Johana Cohen[19], Djamel Mokart[20], Julien Grouille[21], Tomas Urbina[22], Camille Hua[23,24], Olivier Chosidow[23], Armand Mekontso-Dessap[1,2,3], Elie Azoulay[5] and Nicolas de Prost[1,2,3]

	In-hospital mortality			
	Univariable		Multivariable	
	HR [95% CI]	*p*-value	aHR [95% CI]	*p*-value
Model 1				
Surgery	0.81 [0.46–1.4]	0.48	–	
G-CSF	0.43 [0.23–0.82]	**0.010**	0.46 [0.22–0.94]	**0.033**
SAPSII	1 [1–1]	**<0.001**	1.03 [1.01–1.04]	**<0.001**
Age, years	1 [1–1]	**0.03**	1.03 [1.01–1.06]	**0.017**
Abdomino-perineal location	0.63 [0.35–1.1]	0.13	0.52 [0.28–0.98]	**0.042**

HR [95%CI]: hazard ratio [95% confidence interval]; aHR [95%CI]: adjusted hazard ratio [95% confidence interval]; G-CSF: granulocyte colony-stimulating factor; [a]Missing values in 4 patients have been imputed. **Bolded** values are significant at $p < 0.05$

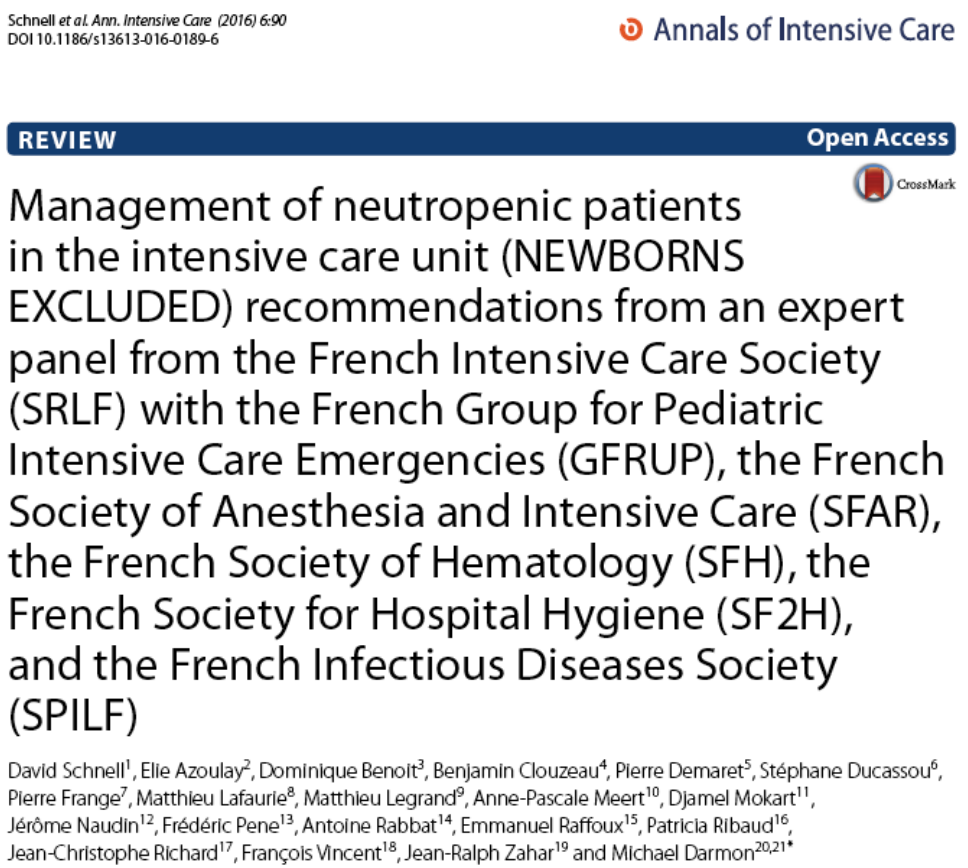


Management of neutropenic enterocolitis: the place of surgery?

- Key points
  - Cure is associated with neutropenia recovery.
    - Role of medical treatment
  - Neutropenia (with or without thrombocytopenia) is not a contraindication to surgery.
- Indications for surgery
  - Perforation
  - Intestinal necrosis
  - Major colonic dilatation
  - Uncontrolled digestive hemorrhage
  - New or worsened organ failures

Conclusion

- Inflammatory response is particular and complex
- Clinical symptoms are time-dependent variables
- Infectious emergency
- ARF is associated with a poor outcome
- NE is associated with favourable outcome in ICU



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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)

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